SYNCONA

Synconaltd.com

Syncona: cell and gene therapy overview

January 2024

What is cell and gene therapy?

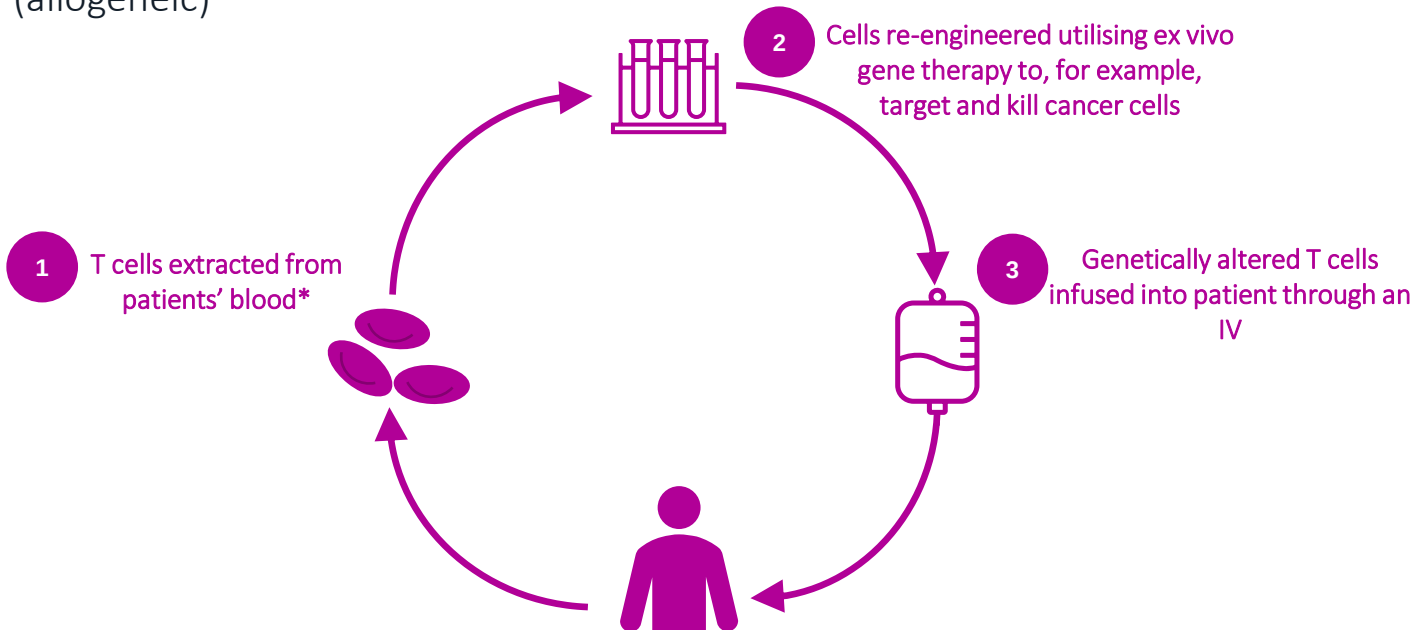
Offering the potential for cures for a range of intractable diseases

Cell therapy

- Cells are removed, restored or altered, and given back to that same person to treat disease (autologous) or a donor (allogeneic)

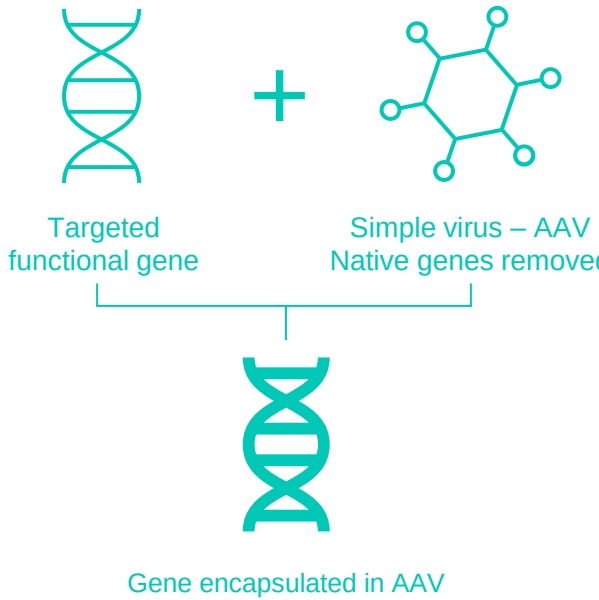
Ex vivo gene therapy

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



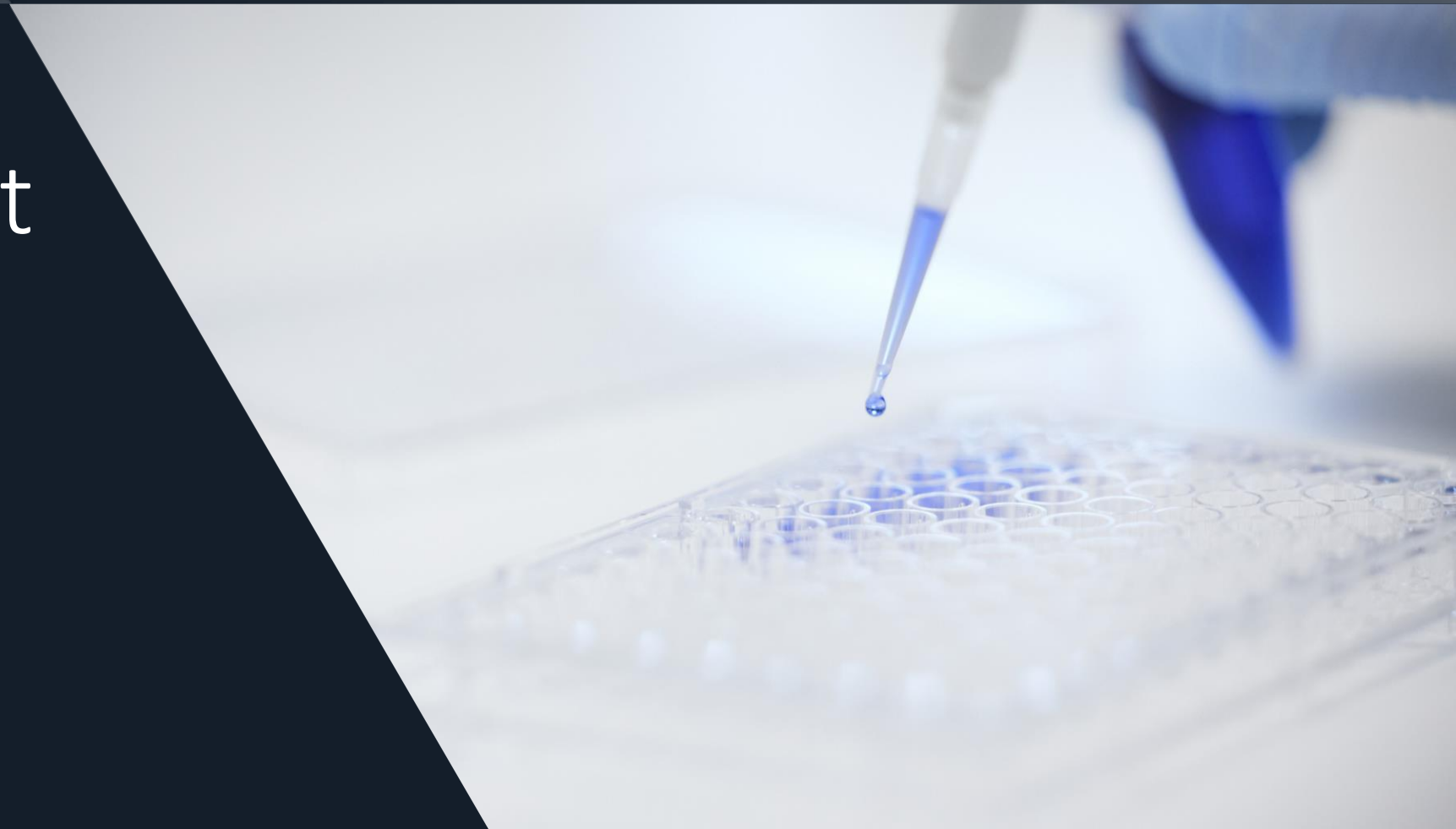
In vivo gene therapy

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



*Autologous Cell therapy process

Current market landscape



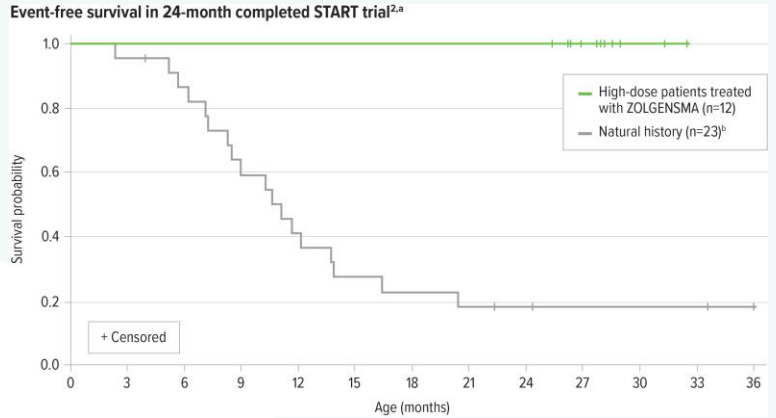
Potential to transform patient lives

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]

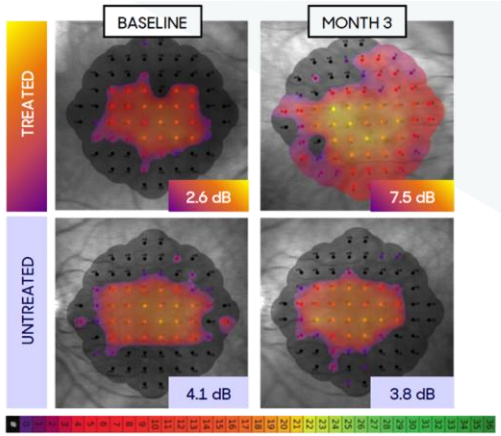
Novartis – Zolgensma

- One-time therapy for spinal muscular atrophy (SMA)
- SMA is a genetic disease resulting in the rapid and irreversible loss of motor neurons
- Most often impacts babies and children
- Demonstrated durable efficacy



Beacon – AGTC-501

- X-linked retinitis pigmentosa, a progressive photoreceptor degeneration with no approved treatment options
- Effects can impact patients' work, school and social interactions
- Encouraging efficacy profile seen in Phase II trial



1. World Health Organisation

Commercial success of cell and gene therapy

High rewards for successful execution

Pharma landscape

- Cell and gene therapies (C&GT) are core focus areas of pharma
- Numerous therapies have had commercial success with increasing sales YoY
- Pharma are expanding inhouse C&GT manufacturing facilities and expertise to help meet increases in demand
- C&GT are still emerging modalities with more therapies to come to market
  - Currently 34 approved C&GT therapies[7]
  - 17 potential new C&GT approvals in 2024[7]

Company/drug	Approved indication(s)	Type of therapy	YTD sales[6]	Patient population (US)
Yescarta GILEAD	Adult relapsed/refractory (r/r) B-cell lymphoma	CAR-T cell therapy	$1.1bn	24k patients per year[1]
Zolgensma NOVARTIS	Spinal muscular atrophy	Gene therapy	$928mn	300-450 patients per year[1]
Kymriah NOVARTIS	Adult r/r B-cell lymphoma and r/r B-cell acute lymphoblastic leukaemia (ALL)	CAR-T cell therapy	$388mn	6.5k ALL patients per year[4]
Abecma Bristol Myers Squibb	Multiple myeloma	CAR-T Cell therapy	$372mn	25k patients per year[1]
Carvykti Johnson & Johnson / LEGEND BIOTECH	Multiple myeloma	CAR-T cell therapy	$341mn	35k patients per year[2]
Tecartus GILEAD	r/r mantle cell lymphoma and ALL	CAR-T Cell therapy	$272mn	35k patients per year[2]
Breyanzi Bristol Myers Squibb	r/r B-cell lymphoma	CAR-T Cell therapy	$263mn	6.5k ALL patients per year[4]
Luxturna Roche	Leber's congenital amaurosis, retinitis pigmentosa	Gene therapy	$51mn	14k total patients[3]

1. PwC. 2. Chimeric antigen receptor T-cell therapy in multiple myeloma: A comprehensive review of current data and implications for clinical practice 3. Bristol Myers Squibb 4. American Cancer Society 5. https://my.clevelandclinic.org/health/diseases/24167-lebers-congenital-amaurosis. 6. Q1 2023 – Q3 2023 7. Alliance for Regenerative Medicine

Cell and gene therapy deal environment

Strong M&A and collaboration activity in cell and gene therapy

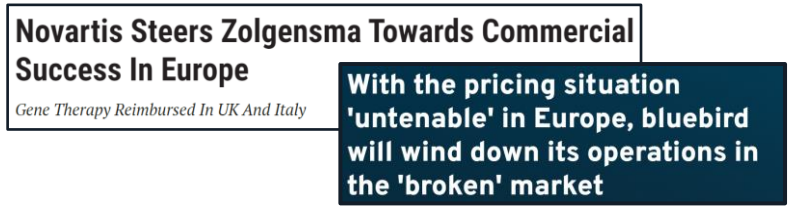
Pharma landscape

- Strong M&A activity to acquire C&GT companies
  - Particularly at early-clinical stages (Phase I/II)
  - M&A activity predominantly targeting larger indications
  - Decrease in deal flow around smaller indications solely to gain technology/capability
- Steady flow of collaboration agreements with biotechs for research and development of C&GT
- Inflation Reduction Act in the US incentivises development of innovative medicines in areas of high unmet need at expense of 'me-too' drugs

Company	Date	Therapeutic area(s)/deal	Type of therapy	Stage	Deal size	Market size
Gracell Biotechnologies (acquisition) AstraZeneca	Dec 2023	Oncology and autoimmune diseases	Cell therapy	Phase I/II	$1.2bn	› $20 billion total multiple myeloma market › $2.3 billion total ALL market
Cellectis AstraZeneca **(collaboration)**	Nov 2023	Design and develop cell and gene therapy products	C&G therapy	-	$2bn+	-
Orchard Therapeutics (acquisition) Kyowa Kirin	Oct 2023	Immunologic, neurometabolic and neurodegenerative disorders	Gene therapy	Approved in EU	$478mn	› $1 billion+ in lead indication
Decibel Therapeutics (acquisition) REGENERON	Aug 2023	Hearing loss and hair cell regeneration	Gene therapy	Phase I/II	$213mn	› $13.6 billion total hearing loss market
Sigilon Therapeutics (acquisition) Lilly	Jun 2023	Type 1 diabetes, lysosomal diseases and liver disease	Cell therapy	Pre-clinical	$920mn	› $7.6 billion total type 1 diabetes market size
Life Edit Therapeutics (collaboration) novo nordisk	Jun 2023	Discover and develop gene editing therapies	Gene therapy	-	$2bn+	-

US and European payer environment

Factors influencing the commercial success of cell and gene therapies



Key challenges and requirements for commercialisation

- Suitable indication that addresses prevalent or high-burden diseases with unmet need
- Promising clinical evidence and potential for marked enhancement in standard of care over long period of time, with strong safety profile
- Importance of trial design and package of data
- Evaluation of the long-term economic benefits over standard of care, supported by existing pricing benchmarks
- Tailoring innovative pricing strategies to align with diverse reimbursement frameworks across regions, e.g. different EU member states
- Regional manufacturing strategy and the capability to manufacture products at scale

Novartis – Zolgensma (spinal muscular atrophy)

- Now available in more than 45 countries including EU and US
- Price benchmark already set by Spinraza ($600-800k for first year's treatment and $400k per year for the rest of life)
- Lack of other treatment options with most patients having a life expectancy of two years

Bluebird Bio – Zynteglo (beta-thalassemia)

- Existing treatment options exist in stem cell transplant and regular blood transfusions
- Lack of long-term durability or comparative data
- In spite of offering five-year results driven payment plan, difficulty in agreeing pricing in EU (first in Germany) led to market withdrawal

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What is next for cell and gene therapy

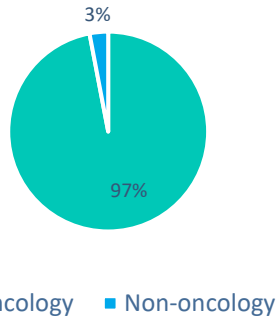
Evolution of the competitive landscape

Acquisitions targeting large markets as pharma look to fill the patent gap

What we expect to see

- We expect to see a continuation of reliance on biotech for early-stage C&GT research and development
  - Patents for almost 200 drugs will expire over the next six years[1]
  - Accounting for $200bn in large pharma revenue at risk of patent expiry[2]
- Further expansion of manufacturing capability, to overcome bottleneck challenges, particularly for cell therapies
  - Includes developing manufacturing facilities, building the necessary expertise and utilising innovative solutions (e.g. automation)
- Higher number of C&GT approvals by regulators as companies refine regulatory strategies
- Pharma M&A in C&GT to continue focus on large disease areas (including oncology indications), with polygenic disorders a future area of growth (including through the application of emerging CRISPR-based therapies)

CAR-T cell therapy pipeline[3]



exa-cel

First ever approved CRISPR-based gene therapy (for severe sickle cell disease), preparing for commercial launch

1. The Economist 2. Lazard 3. ASGCT

Monogenic vs polygenic gene therapies

Harnessing diverse gene therapy applications allows for bespoke approaches in managing a wide spectrum of disorders

Monogenic Gene Therapy

- Targets diseases caused by mutations in a single gene
- Field has progressed from clinical trial successes to regulatory approvals
- Expansion of approved therapies and increased investment has enhanced scalability and broadened access to these therapies
- Success in monogenic diseases helps to pave the way for breakthroughs in polygenic disorders

Polygenic Gene Therapy

- Focuses on conditions influenced by multiple genes, genetic, and environmental factors
- Field has evolved from early-stage research; integrating new advancements to improve precision in targeting multiple genes
- New frontier in gene therapy with unique hurdles to overcome in order to advance into polygenic indications

Blockbuster potential in the portfolio

A potential path to prevalent chronic diseases across multiple tissues

Expanding to prevalent indications

- We believe the next generation of gene therapy programmes will transform the treatment of prevalent diseases
- Success in prevalent diseases relies on a clear understanding of the modality, and established platforms
- High quality manufacturing and optimised delivery is critical for accessing larger indications

FREELINE → Gaucher disease → Blockbuster potential

beacon therapeutics → XLRP → Blockbuster potential → Dry AMD (IVT)

FREELINE — Parkinson's

- Targeting subset of Parkinson's disease, targeted at GBA1 mutations to restore GCase enzyme function[1]
- Leverages existing technology from Gaucher programme
- 190k patients across US and EU5
- No current approved therapy

FREELINE forcefield — CHF

- Licensing agreement, broadening gene therapy application to polygenic cardiac conditions
- Forcefield's technology will enable Freeline to identify genes associated with causing heart failure
- Cardiovascular disease is the #1 cause of death worldwide

GCase: Glucocerebrosidase; Source: 1. Freeline corporate presentation

Autologous vs allogeneic cell therapy

Harnessing therapeutic benefits of autologous therapies and unlocking potential of allogeneic therapies

Autologous

- Cells are removed, modified and given back to the same patient
- Offers enhanced safety profile and long-term compatibility due to reduced rejection risk
- Active R&D to address scalability
  - E.g. automation and decentralised manufacturing to decrease turnarounds and increase accessibility
- Growing number of approved products on the market with impressive efficacy

Allogeneic

- Uses modified donor cells
- Simplified production with potential for 'off-the-shelf' availability
- Challenges around safety and immune rejection
- Limited clinical data and approvals

Syncona Portfolio

- Portfolio currently focused on autologous cell therapy applications
- Four companies with lead autologous cell therapy programme
- Allogeneic programmes and partnerships in portfolio across Resolution, Quell and Clade

Spotlight: Autolus

- Lead product, obe-cel, potentially best-in-class therapy for r/r adult ALL
- Expected commercial launch in CY2024
- Proprietary manufacturing facility with launch ready capacity
- Blincyto®, current market leader, in adult ALL $620mn YTD sales (Q1-Q3)

Cell therapy – beyond T effector cells

Macrophage cell therapies - leveraging the impact of cell therapy into chronic liver disease

Macrophages and liver disease

- Immune system cells, commonly known for engulfing pathogens
- In liver disease, macrophages remain pro-inflammatory, exacerbating disease and preventing organ repair
- Only therapeutic option for chronic liver failure currently is transplantation
  - Involves morbidity and mortality issues as well as lifetime immunosuppression
  - Significant costs associated with transplantation, and recurring costs for immunosuppression

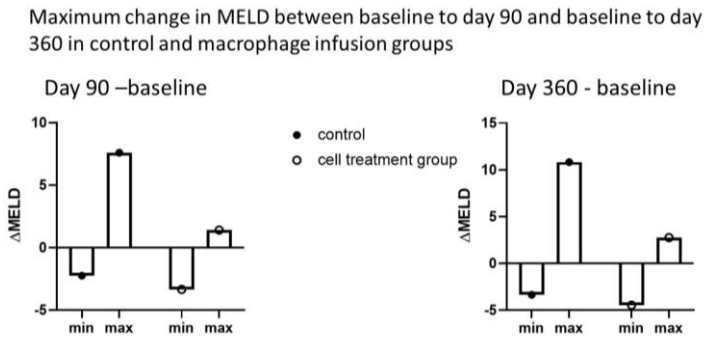
Syncona portfolio

Resolution Therapeutics

- Focused on treatment of chronic liver disease
- Resolution's autologous lead programme engineers macrophages to exhibit pro-restorative functions
  - Switches off inflammatory response and promotes organ repair
- Encouraging clinical data obtained in cirrhotic patients in previous generation academic study, MATCH-II

Data from MATCH-II

- Phase II study provided PoC for macrophage cell therapy in end-stage liver disease
- Demonstrated significant improvement and less variability in Model for End-stage Liver Disease (MELD) score
- No adverse events in treated group



1. https://www.ema.europa.eu/en/clinical-investigation-immunosuppressants-solid-organ-transplantation.

Cell therapy – beyond T effector cells

T-regs - advancing cell therapy into autoimmunity

Regulatory T-cells

- Regulatory T-cells (Tregs) are a specialised subpopulation of T-cells that can inhibit T-cell proliferation and cytokine production, suppressing the immune response
- By playing a role in suppressing the immune response, Tregs are key to maintaining homeostasis and self-tolerance
- Tregs therefore have a critical role in preventing autoimmunity, organ rejection and inflammatory diseases

Syncona portfolio

QuellTx

- Developing engineered Treg cell therapies, lead indication in liver transplant setting
- Potential to durably reset immune dysregulation with a single treatment, in transplantation, auto-immunity and inflammation
- First trial in liver transplantation – a de-risked setting with significant unmet need for patients
- Current standard of care for prevention of solid organ transplant rejection is life-long immunosuppression which leaves the patient open to serious infections and cancer[1]

Pharma interest in Tregs

REGENERON® SONOMA BIOTHERAPEUTICS

- Signed $120 million collaboration agreement (November 2023)

AstraZeneca QuellTx

- Signed $2 billion collaboration agreement (June 2023)

Lilly TRexBio

- Expanded original agreement for $1.1 billion+ (January 2023)

1. https://www.ema.europa.eu/en/clinical-investigation-immunosuppressants-solid-organ-transplantation. Deal values include potential milestones.

Summary

Huge progress in cell and gene therapies with further commercial traction to come

- Cell and gene therapies are gaining more traction in R&D and commercial settings
- Pharma have shown a growing interest in cell and gene therapies, particularly in large indications
  - Interest is expected to grow as pharma will need to recover lost revenue from patent cliff and as the cell and gene therapy landscape develops
- These therapies still have potential for huge growth, expanding into different indications, including polygenic disorders, with growing evidence of the strong efficacy and commercial potential of CAR-T cell therapies
- Commercial hurdles remain but are being improved, e.g. expansion of manufacturing facilities and improved regulatory strategies
- Macrophage and CAR-Treg cell therapies have potential within the next wave of cell therapies to address large indications
- Exciting opportunities across the Syncona portfolio

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Appendix

Big pharma cell and gene therapy strategy and activity

Large pharma focused on large indications

GILEAD

- Team at Kite are singularly focused on cell therapies
- Expanding cell therapy offering in oncology

Activity in 2023

- Expanded Arcellx/Kite collaboration ($285mn+) to in-license multiple myeloma cell therapy

AstraZeneca

- Strong C&GT capability, exploring a number of therapeutic areas

Activity in 2023

- Gracell Biotechnologies acquisition ($1.2bn), expanding AZ's cell therapy offering
- Subsidiary Alexion acquired Pfizer's early-stage rare disease gene therapy portfolio ($1bn+)

Bristol Myers Squibb

- C&GT are core areas of focus
- Proprietary CAR-T manufacturing process and expanding its cell therapy manufacturing network

Activity in 2023

- Abecma received approval for multiple myeloma in Japan in earlier lines of therapy

sanofi

- Dedicated to developing gene therapies
- Cell-based therapies a key pillar for oncology

Activity in 2024

- Expanded collaboration with Scribe Therapeutics ($1bn), to advance gene therapies

Pfizer

- Deprioritised new viral-base gene therapies, focusing on non-viral based gene therapies

Activity in 2023

- Collaboration with Beam Therapeutics ($1.4bn), advancing gene therapies for rare diseases

Johnson&Johnson LEGEND BIOTECH

- J&J and Legend have a worldwide collaboration agreement for gene therapy, Carvykti

Activity in 2023

- Signed 3-year manufacturing contract with Novartis for Carvykti to help meet demand

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Gene therapy companies

Beacon Therapeutics

Progressing to pivotal study in X-linked retinitis pigmentosa programme

Late-clinical stage

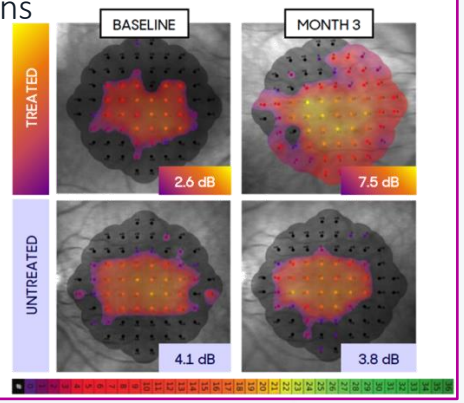
Initial investment	2022
Financing stage	Series A
Stage of lead programme	Phase II

Investment thesis

- Beacon has a highly attractive gene therapy programme targeting X-linked retinitis pigmentosa (XLRP), a blinding disease
- Clinical data generated by the company so far has been encouraging demonstrating improvements in visual sensitivity sustained for 24+ months
- Retinal gene therapy is an area where Syncona has significant expertise and XLRP is a disease setting the team knows well from Nightstar experience
- Business has an integrated gene therapy manufacturing platform and leading management team

Targeting an area of high unmet need

- XLRP is a severe, aggressive, inherited retinal disease
- Disease progression – moves from night blindness to central vision loss and legally blind by median age 45
- No treatment options



Market opportunity

- 17,000 patients in US/EU5
- Although XLRP accounts for 15% of all cases of retinitis pigmentosa (RP), it is characterised to have the most severe vision loss - with XLRP patients four times more likely to have visual acuity ≤20/200 (legally blind), than those with autosomal dominant RP

Freeline Therapeutics

Potential to deliver a company to late-stage development

Clinical stage

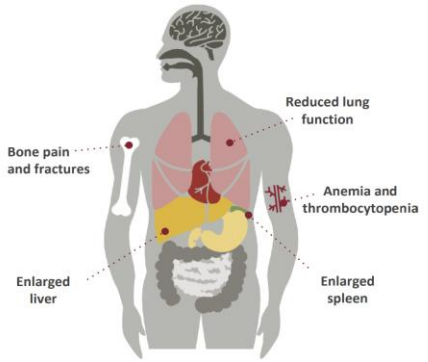
Initial investment	2015
Financing stage	NASDAQ
Stage of lead programme	Phase I/II

Investment thesis

- Freeline has a potential first- and best-in-class lead programme
- Highly differentiated gene therapy candidate FLT201 for Gaucher disease type 1
- Published compelling initial data demonstrating robust enzyme activity and favourable safety and tolerability in first two patients treated with FLT201
- Experienced management team executing well
- Potential to extend innovation into Parkinson's disease

Targeting an area of high unmet need

- Gaucher disease type 1 is a debilitating, chronic and progressive disorder
- Affects multiple organs, leading to wide range of symptoms and shortening life span



Market opportunity

- Freeline estimates that Gaucher Disease Type 1 has approximately 18,000 patients
- Wholly owned $1bn plus peak sales potential

1. Freeline Corporate Presentation. Note: The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy

Clinical stage

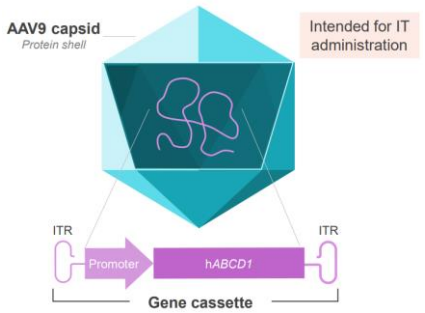
Initial investment	2018
Financing stage	Series B
Stage of lead programme	Phase I/II

SwanBio Therapeutics

Developing AAV-based therapies for the treatment of devastating, inherited neurological conditions

Investment thesis

- Gene therapy has the potential to be transformational in neurology
- Focus on the spine – an uncrowded space and only tissue with proven transduction and clinical efficacy
- In lead adrenomyeloneuropathy (AMN) programme, have completed dosing of low-dose cohort, and initiated dosing of high-dose cohort
- Efficacy proof of concept established pre-clinically



Targeting an area of high unmet need

- AMN is an inherited neurodegenerative disease in which the causative gene is definitively known and well characterised
- AMN is a devastating disease characterised by progressive muscle weakness, leading to loss of mobility, incontinence and debilitating pain
- As the disease progresses and becomes more debilitating, most people with AMN require a wheelchair
- There are no current treatments and few in development

Market opportunity

- AMN impacts 8,000-10,000 male patients in the US and EU5[1]
- Zolgensma, a gene therapy which treats spinal muscular atrophy, has a reported list price of £1.79m per dose[2]

1. SwanBio analysis. 2. https://www.england.nhs.uk/2021/03/nhs-england-strikes-deal-on-life-saving-gene-therapy-drug-that-can-help-babies-with-rare-genetic-disease-move-and-walk/

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Pre-clinical stage

Initial investment	2020
Financing stage	Series A

Purespring Therapeutics

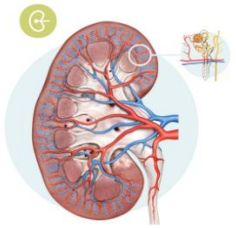
First company to treat kidney diseases by directly targeting the podocyte with AAV gene therapy

Investment thesis

- Developing a proprietary platform to enable kidney gene therapy
- Targeting the podocyte allows it to directly treat a significant portion of kidney diseases
- We only have a finite number of podocytes in our kidneys: unlike other human cells such as liver cells or skin cells, podocytes do not regenerate over our lifetime.
- Injuries to the podocytes lead to issues in the filtration barrier, reducing the kidney's filtration capacity, causing kidney diseases.

Targeting an area of high unmet need

- There are currently no curative or disease-modifying therapies
- Current standard of care for end-stage renal disease relies on either dialysis or kidney transplant
- Haemodialysis can cause low blood pressure and leave patients at risk of infection, whilst kidney transplant patients will still need to take lifelong immunosuppression



Market opportunity

- 4m patients are on renal replacement therapy[1]
- Kidney diseases are common. Around 10% of the population suffers from chronic kidney diseases.[2]
- More than 840m people globally suffer from chronic kidney disease, including 3m in the UK and more than 37m in the US
- The podocyte is implicated in 60% of renal disease[3]

1. https://www.nature.com/articles/s41581-022-00542-7 2. Health Survey for England, 2016; CDC, Chronic Kidney Disease in the US, 2021; GBD Chronic Kidney Disease Collaboration. Nephrol Dial Transplant (2019) 34: 1803–1805 3. Purespring analysis

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Cell therapy companies

Late-clinical stage

Autolus Therapeutics

Leading cell therapy company preparing for commercial launch of its lead programme in adult ALL

Initial investment	2014
Financing stage	NASDAQ
Stage of lead programme	Phase II

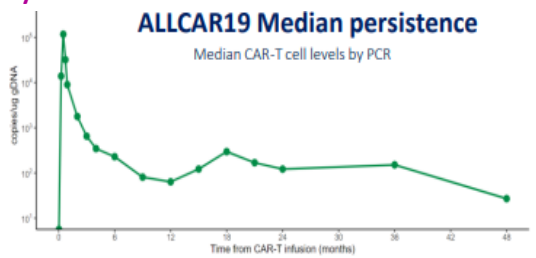
Investment thesis and company update

- Chimeric Antigen Receptor (CAR) T cell therapies have been shown to be effective in some haematological malignancies and may have wide applications as a cancer treatment, with the potential for cure in some patients
- Lead product candidate, obe-cel, potentially best-in-class therapy for relapsed refractory for adult acute lymphoblastic leukaemia (ALL), has a competitive profile in B-cell non-Hodgkin's lymphoma (B-NHL) and has potential in autoimmune diseases
- BLA filing for obe-cel in adult ALL filed in November 2023
- Advanced in-house manufacturing facility ready for commercial launch

Targeting an area of high unmet need

- Only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care[1]
- If approved, obe-cel has the potential to be a best-in-class curative therapy in adult ALL and expanding use beyond academic transplant centres

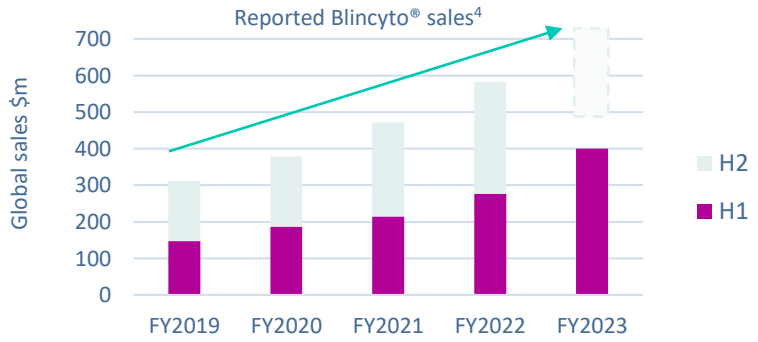
Key data[2]



- Launching a Phase I trial in systemic lupus erythematosus (SLE) in H1 2024, a multi-organ systemic autoimmune disease that affects approximately 160K - 320K patients in the US[3]

Market opportunity for lead programme

- Over 8,000 new cases of adult ALL annually worldwide
- Obe-cel could launch into an expanding ALL market if approved with commercial rollout planned for 2024
- Tecartus® (approved in 2022) is expected to establish CAR-T in adult ALL
- Blincyto®, current market leader, sales increased 48% year-over-year to $206 million for the second quarter 2023[4]



1. Autolus corporate presentation 2. ALLCAR19 academic study 3. Mackensen et al., Nat Med. 2022, Mougiakakos et al. N Engl J Med. 2021, Müller et al. Lancet. 2023, Bergmann et al. Ann Rheum Dis. 2023, Taubman et al. Rheumatology (Oxford). 2023 4. As per Amgen quarterly SEC filings

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Clinical stage

Initial investment	2016
Financing stage	NASDAQ
Stage of lead programme	Phase I/II

Achilles Therapeutics

Developing AI-powered precision T cell therapies targeting clonal neoantigens to treat solid tumours

Investment thesis

- Lead product is a precision tumour-derived T cell therapy targeting clonal cancer neoantigens
- Uses DNA sequencing data from each patient, together with a proprietary bioinformatics platform, to identify clonal neoantigens specific to that patient and to potentially enable the development of personalised cell therapies
- Focusing on treating solid tumours with precision T cell therapy by targeting multiple clonal neoantigens present on all cancer cells
- NSCLC patient with a 56% reduction in total target lesion size vs. baseline at week 36

Targeting an area of high unmet need

- High unmet need in lead indications, advanced NSCLC and recurrent metastatic melanoma
- Of all NSCLC patients, 65% are diagnosed with advanced disease (stage III/IV)[1], of which less than 10% survive for 5 years or more[2]
- Metastatic melanoma suffers from a similarly poor prognosis, with the 5-year survival rate estimated at 10%[3]

Market opportunity

- Lung cancer is the leading cause of global cancer incidence and mortality, accounting for an estimated 2 million diagnoses and 1.8 million deaths[4]
- NSCLC accounts for around 80% of lung cancers, which has limited treatment options and is the leading cause of cancer deaths[4]
- In 2022, 97,610 patients in the US are expected to be diagnosed with melanoma, 13% have disease which can't be managed by removal of the tumour alone[5]

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7867742. 2. https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.24871 3. https://www.ncbi.nlm.nih.gov/books/NBK470358/ 4. GLOBOCAN 2020 5. https://seer.cancer.gov/statfacts/html/melan.html

Quell Therapeutics

On track to be the first company to deliver engineered Tregs in the liver transplant setting

Clinical stage

Initial investment	2019
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Potential to durably reset immune dysregulation with a single treatment, in transplantation, auto-immunity and inflammation
- On track to be the first trial in liver transplantation – a de-risked setting with significant unmet need for patients
- Collaboration with AstraZeneca with $85m upfront (cash and equity) and potential payments of over $2bn
- Funded through key datasets with strong investor syndicate

Targeting an area of high unmet need

- Current standard of care for prevention of solid organ transplant rejection is life-long immunosuppression which results in an array of serious long-term side effects significantly impacting patient quality of life[1]
- Immunosuppression leaves the patient open to attack by pathogens which cause serious infections
- Immunosuppression can also leave a patient susceptible to develop cancer due to it not being recognised and cleared by the body

Market opportunity

- 15,000 liver transplants per year across US and Europe[2]
- GMP manufacturing capacity on-line in Quell facilities

1. https://www.ema.europa.eu/en/clinical-investigation-immunosuppressants-solid-organ-transplantation 2. OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015

SYNCONA

Pre-clinical stage

Initial investment	2021
Financing stage	Series A

Clade Therapeutics

Seeking to dramatically broaden the impact of cell therapy by establishing a more robust cellular platform

Investment thesis

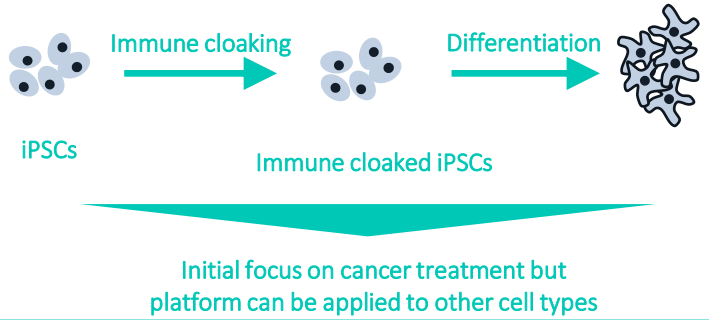
- Building the foundation for engineerable, off-the-shelf, scalable, and consistent cell medicines:
- Delivery of scalable next generation induced pluripotent stem cell (iPSC) derived medicines that address the supply and cost challenges of autologous cell therapy, and the efficacy challenge of allogeneic cell therapy
- Combining three leading proprietary platforms:
  - Advanced immune cloaking technology to increase persistence
  - Differentiation to key target cell types in a reproducible and scalable manner
  - Universal targeting discovery platform

Targeting an area of high unmet need

- Replicating the benefits of the autologous CAR-T products, while addressing their profound limitations – inconsistent quality, challenging patient logistics, cost, and lack of scalability
- Broadening the applicability of cell therapies, e.g., for solid tumour indications, where cell therapies have had underwhelming impact due to the limited engineerability of autologous cells
- Significant potential for best-in-class iPSC-derived therapies for applications outside of oncology

Market opportunity

- Technology has the potential to deliver greater efficacy than the first generation of allogeneic cell therapies
- "Off the shelf" stem cell-based therapies have potential to deliver practical and commercial benefits in cell therapeutics



SYNCONA

Pre-clinical stage

Initial investment	2018
Financing stage	Series A

Resolution Therapeutics

Seeking to extend the impact of cell therapy into chronic inflammatory liver disease

Investment thesis

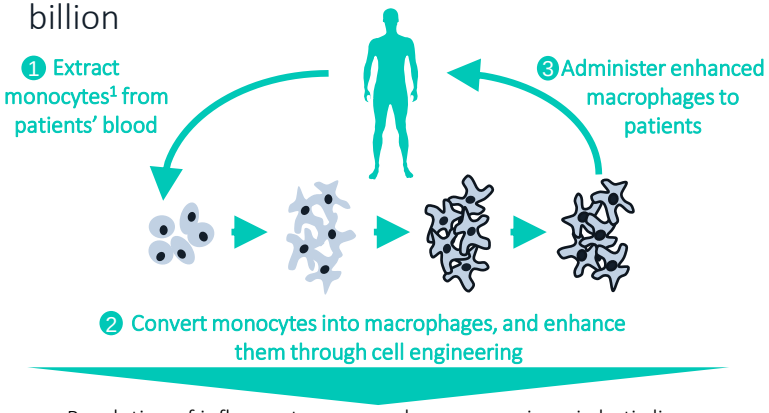
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries
- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest scar tissue, switch off the inflammatory response and promote organ repair
- Encouraging clinical data already obtained in cirrhotic patients with earlier generation (academic) programme
- Company's lead program is an engineered, autologous macrophage product

Targeting an area of high unmet need

- Cirrhotic patients experience severe "decompensation" episodes as a result of failing liver function
- Decompensation episodes include life-threatening GI bleeding, ascites and coma, all of which contribute to a high cost of treatment and the need for liver transplantation
- Liver transplant, the only therapeutic treatment for chronic liver failure, is associated morbidity, mortality and cost, and requires lifetime immunosuppression

Market opportunity

- 1-2 million people estimated to be affected by liver cirrhosis across major Western markets[1]
- The all-in cost of a liver transplant today is several $100k, yielding a total annual market size across the US and EU5 in the region of c.$10 billion



1. Scaglione et al., Journal of Clinical Gastroenterology, 2015

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Synconaltd.com

SYNCONA INVESTMENT MANAGEMENT LIMITED

2nd Floor
8 Bloomsbury Street
London
WC1B 3SR

020 3981 7909
investorrelations@synconaltd.com