Syncona

Syncona Capital Markets Day

February 2020

synconaltd.com

Image Freeline labs, Stevenage

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Agenda

01 **Syncona's strategy and vision for the future**
Martin Murphy, Chief Executive Officer

02 **Portfolio company review**
Chris Hollowood, Chief Investment Officer

03 **Q&A**

04 **Panel discussions**
- Translating exceptional science and building companies
- The future of cell therapy
- Building a commercial gene therapy platform

05 **Wrap-up**

Syncona

Strategy and vision for the future

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Image Freeline labs, Stevenage

Strategy and vision

Building the next generation of healthcare leaders

Capturing the out-return from commercialising exceptional science

Globally significant scientific research base

Leverage the quality of the European life science research base

01

Focus on products and patients

Select technology that can:

- deliver dramatic efficacy for patients
- credibly be taken to approval by an innovative biotech

02

Founding companies with strategic ownership

Invest through company life cycle to maintain significant ownership positions, enabling:

- strategic influence; leveraging expertise in Syncona team
- participation in the out return available from taking products to approval

03

Long-term, ambitious capital

Fund ambitiously over time frames necessary to develop innovative medicines

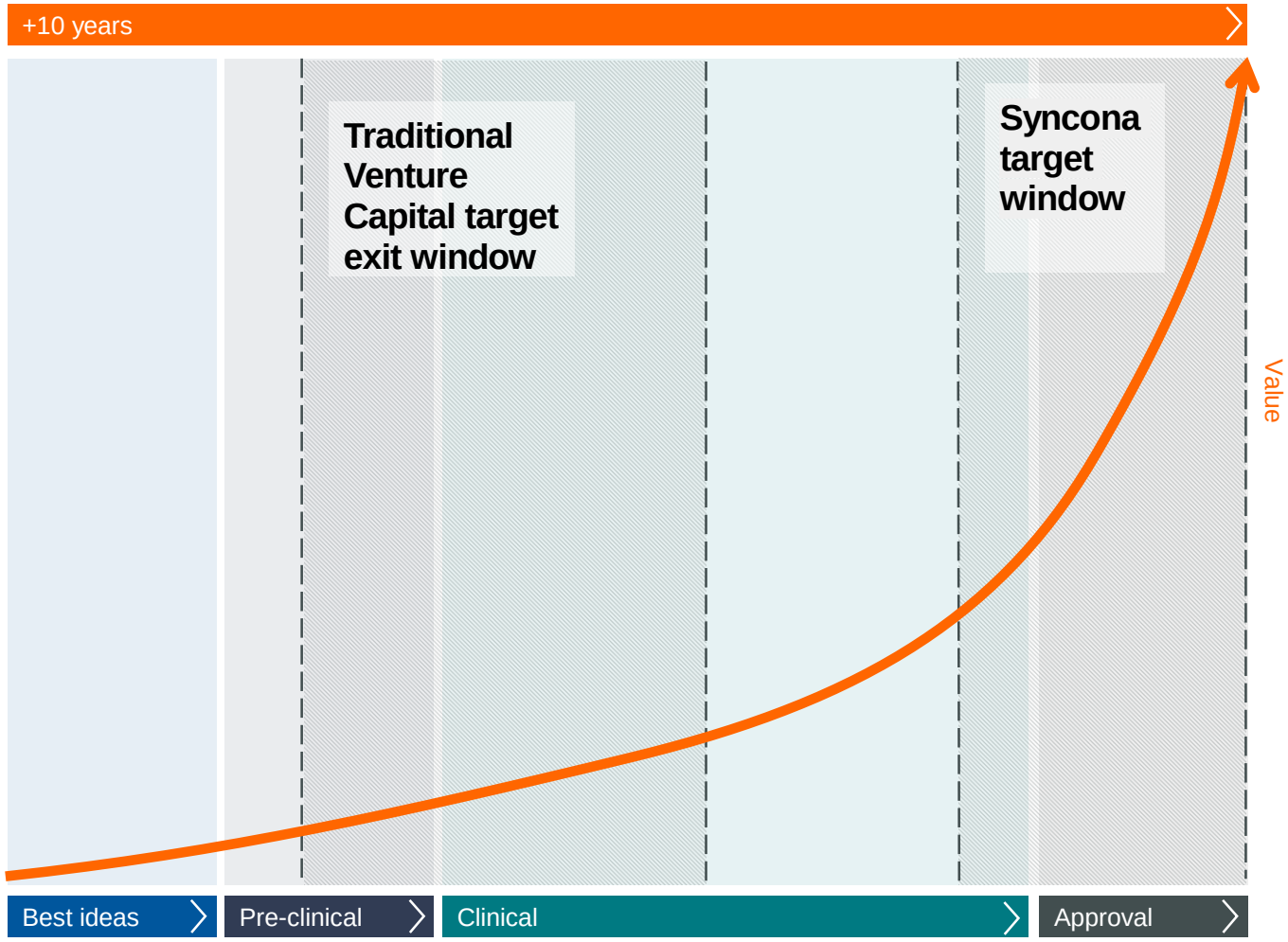
04

Capturing the out return in life science

Strategy designed to deliver strong risk adjusted returns for shareholders

Out return in life science weighted towards late development and product approval:

- Set companies up with the ambition of taking products to market
- Target the steepest part of the value curve



Graph is illustrative and assumes successful clinical development and approval, Syncona team view

Our differentiated platform

Founding, Building and Funding global leaders from exceptional science

- Track record of 44% IRR since 2012
- Investment team of 14 people with deep scientific and commercial expertise
- Extensive experience working with global key opinion leaders and appointing leading management teams

- Strategic and deep long term capital base
- Balance sheet strength optimises flexibility and influence

- Expert at identifying the next generation of technologies in areas of high unmet medical need
- Attracting globally recognised key opinion leaders
- Proactive approach to generating the best opportunities

Syncona today

Strong track record delivering for patients and shareholders

Returns and capital deployment

44% IRR since 2012

£553m Syncona capital deployed since 2012

>£1bn Value – 2.1x cost

Building global leaders

13 Syncona portfolio companies since 2012 foundation, 9 in the portfolio today

2 Companies sold since Syncona established generating significant returns

700+ Number of employees across Syncona portfolio

Patient impact

>50k Patients benefitted by the first Syncona marketed product (Blue Earth's Axumin)

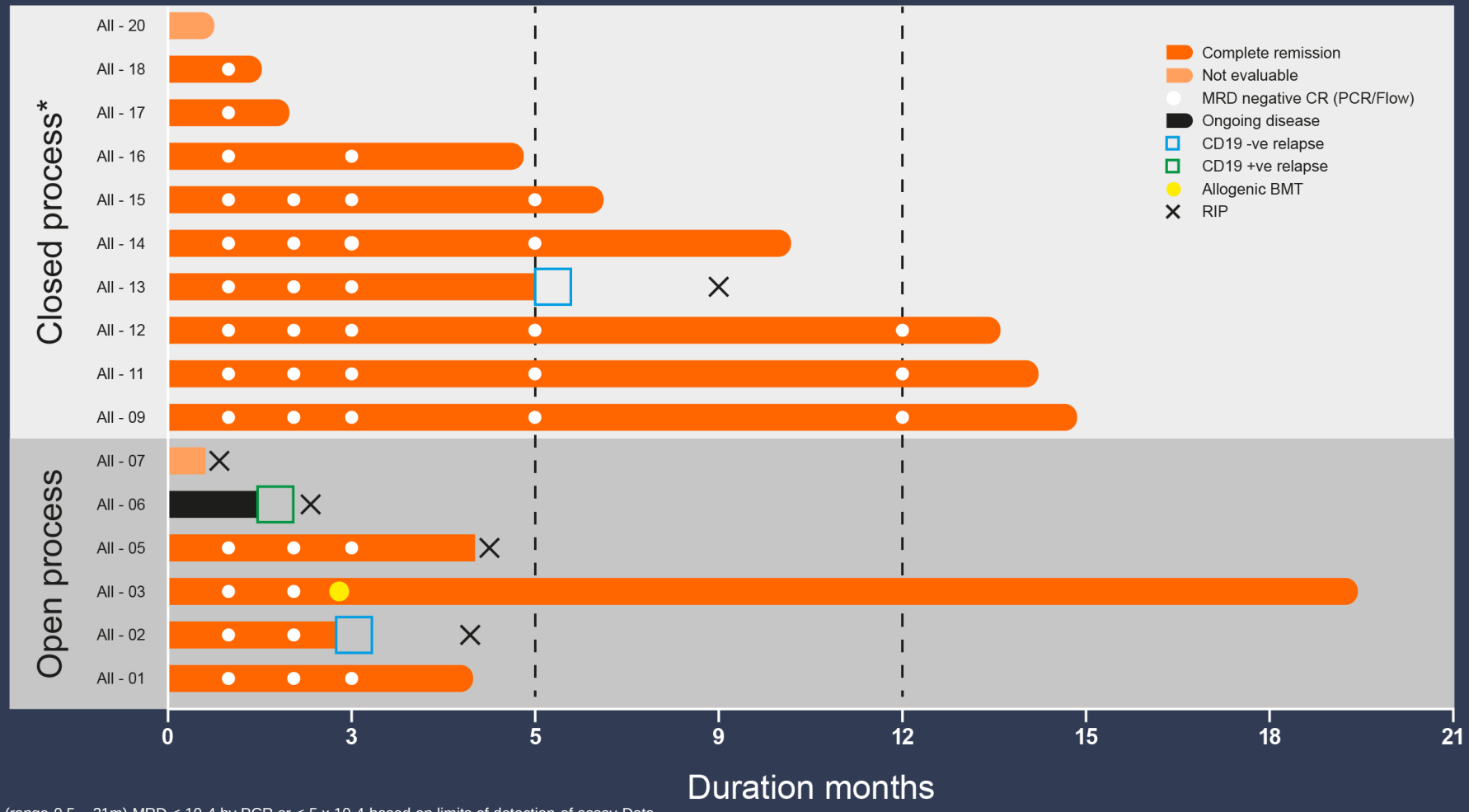
5/9 Patients in cohorts 3, 4 and 5 treated in Nightstar's clinical trial in XLRP saw preliminary efficacy signals with durable improvements in macula sensitivity

2 Patients in the first cohort[1] treated in Freeline's clinical trial in Haemophilia B FIX activity remains stable and consistent at 40+-5.5%

1 Treated with the lowest study dose $4.5x10^{11}$vg/kg
All financial data at 31 December 2019

Progress to date: Patient impact

High level of clinical activity in end-stage patients



>87%

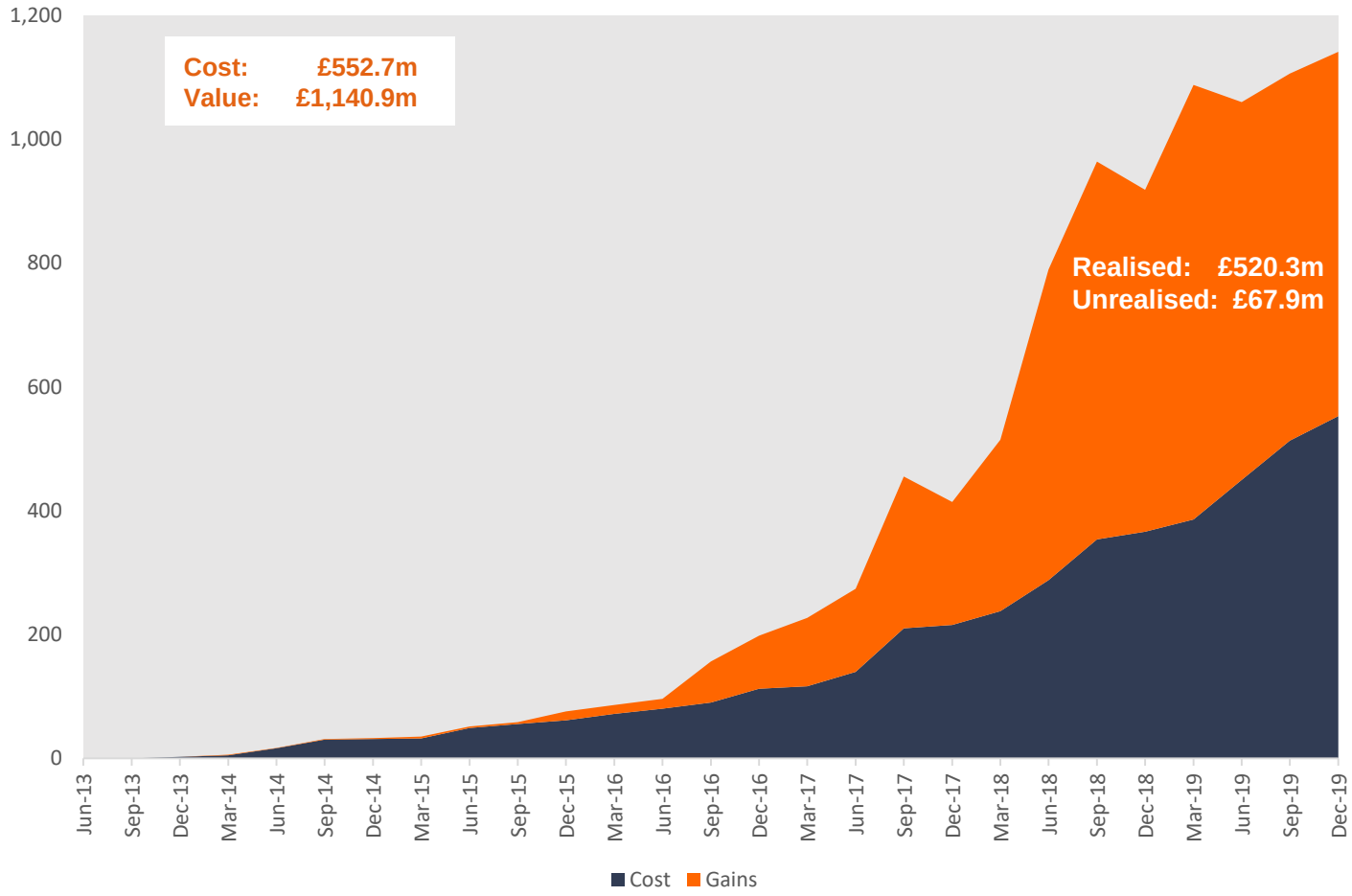
of patients achieved a complete response at 1 month

Roddie et al., (2019) ASH presentation 1 Median 11 months follow up (range 0.5 – 21m) MRD < 10-4 by PCR or < 5 x 10-4 based on limits of detection of assay Data cutoff 25-Nov-2019, Evaluable = All patients with at least M1 follow-up or RIP prior to Month 1. *Commercial manufacturing process

Progress to date: Strong risk-adjusted returns

Strong Track Record

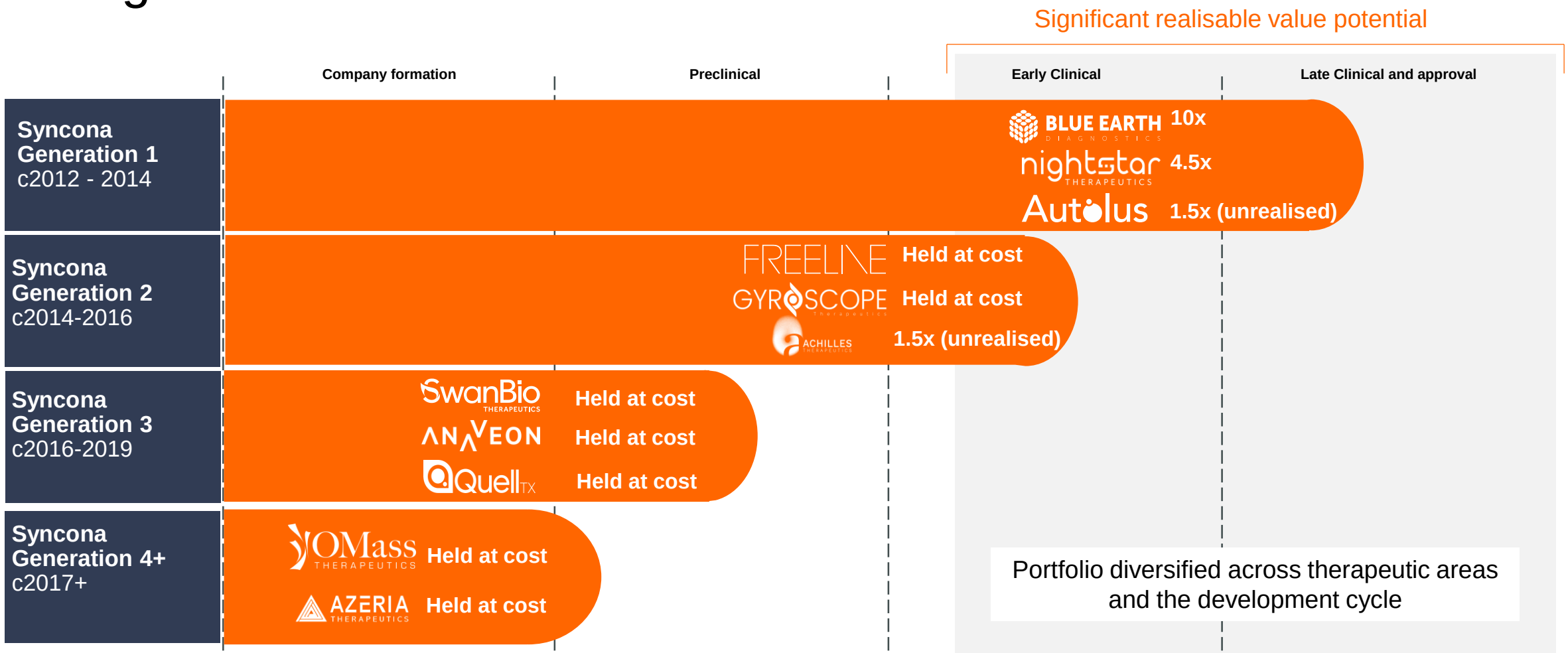
- Founded Nightstar (NITE.US) in 2013 - sold to Biogen for $877m in 2019; 4.5x return (IRR 72%) – **3rd largest UK biotech transaction in the last 20 years**
- Founded Blue Earth Diagnostics (private) in 2013 sold to Bracco Imaging for $476m in 2019; 10x return (IRR 87%)
- £553m capital deployed into life sciences since 2012
  - 44% IRR and 2.1x cost generated on portfolio since 2012
- Since listing in December 2016, Total Shareholder Return of 68%*



Unless stated data at 31 December 2019
*As at 31 Jan 2020

Significant value creation opportunity in the next generation

Syncona



All data as at 31 December 2019

Found and Build

What do we look for in a scientific asset?

Syncona

Technology

Globally leading academics

Intellectual Property

Transformational efficacy for patients in areas of high unmet need

Defined, commercial lead programme with pipeline potential

Opportunity to develop differentiated platform or no incumbent

Therapeutic areas where Syncona has deep domain expertise

Defined patient segments / targeted markets

Accelerated development and regulatory pathways

Our approach to company creation and development

Translating technology to products to reach full value potential

Our partnership approach provides a strategic premium

Identify area of compelling new science / technology

Approach key opinion leaders in the space
Work with key opinion leaders to leverage their differentiated scientific insight into commercial vision

9-12 months of diligence: define commercial opportunity and write plan
Found company and provide capital over the long term to maintain strategic ownership position

Build out team with globally leading executives
Actively drive business strategy – take operational roles and Board seats across portfolio

Hands-on build out: scaling our companies for success

Focus on founding companies

Optimises strategy, control, ownership and returns

Strategy: ensure company targets products that can credibly be taken to approval / market

Influence: sole or majority investor position maximises ability to influence company, especially in crucial early years when strategy and management are set

Ownership and returns: aim for best cost basis of any investor, supporting opportunity to deliver best returns for shareholders

Syncona

Company	Founded by Syncona	Syncona majority ownership position
Autolus	✓	Largest investor (30%)
FREELINE	✓	✓
GYROSCOPE Therapeutics	✓	✓
ACHILLES THERAPEUTICS	✓	✓
SwanBio THERAPEUTICS	✓	✓
OMass THERAPEUTICS	OSI (seed)	Largest investor (47%)
ANAVEON	UZH Fund (seed)	✓
QuellTX	✓	✓
AZERIA THERAPEUTICS	CRT Pioneer Fund[1]	✓

1 Syncona holds 64% of the CRT Pioneer Fund

Founding Quell Therapeutics

Proactive and creative company creation: proprietary sourcing

Syncona insight

- Deep Syncona domain expertise in cell therapy; identified T-Regs cells as an area of high interest in 2017
- Sought opportunity to found a company with the potential to be a global leader in an emerging area
- Identified leading academics in T-regs with deep clinical expertise
- Led by Elisa Petris and Freddie Dear

Company foundation

- Syncona brought together six leading academics from three institutions (KCL, UCL and Hannover) with complementary expertise and technology
- 11 months diligence, developing strategy and licensing key IP
- Focused effort on securing key team members pre Series A closing
- £35 million Series A financing

Commercial vision

- Syncona team wrote business plan; first candidate in liver transplant setting identified
- Work ongoing on pipeline of further indications to target
- Recruited: Chief Executive Iain McGill. CBO Luke Henry, CMO Berndt Schmidt
- Board: Martin Murphy Chair, Elisa Petris, Director
- Syncona Partner, Freddie Dear, in business as Director of Operations

Fund

Balance sheet strength is strategic and a key differentiator

Peers demonstrate scale of capital deployed into development stage biotechs

Spark Gene therapy

$1.05bn

Capital raised

Phase 3

Clinical stage of lead programme

UniQure Gene therapy

$746m

Total capital raised

Phase 3

Clinical stage of lead programme

Figures as at 28 January 2020
Source: Dealogic

Syncona

Strategic capital is central to delivery of strategy

- Founding investors have the best ability to set strategy
- Life science companies require significant capital as they scale; ability to maintain influence through financing rounds essential
- Balance sheet strength provides best negotiating position for external financing rounds or M&A
- Capital to execute ambitious vision optimises ability to attract the best academics, founders, managers and partners

Disciplined approach

- Each financing dependent on company specifics (scale of opportunity, risk, capital requirement) and size of Syncona's balance sheet
- Funding commitments tranched and based on milestone delivery

Funding model for our companies

Capital pool provides control and flexibility over the long-term

Series A

Investing in
- Pre-clinical trials
- Laboratory and office space
- Attracting global talent

Typical key risks
- Pre-clinical data outcomes to validate academic discovery in industrial setting

Typical Syncona financing approach
- Sole institutional investor
- c£20-40m

Series B

Investing in
- Clinical trials
- Expanding platform – manufacturing, delivery and further programmes

Typical key risks
- Safety and efficacy in clinical trials
- Execution risk

Typical Syncona financing approach
- Typically sole institutional investor
- c£50-100m

Series C and beyond

Investing in
- Late stage clinical trials (i.e. approval studies)
- Developing infrastructure to deliver commercial scale and launch

Typical key risks
- Safety and efficacy in clinical trials
- Execution and regulatory approval

Typical Syncona financing approach
- Option to fund on sole basis
- c£50-250m, more likely to bring in partners to share risk

Summary

Building a sustainable, scalable model

Delivering strong risk-adjusted returns for shareholders

Syncona

Current portfolio: 2012-19

Autolus
QuellTx
Achilles Therapeutics
Anaveon
SwanBio Therapeutics
Gyroscope Therapeutics
JOMass Therapeutics
Azeria Therapeutics
Freeline

Previous portfolio companies

Blue Earth Diagnostics
Nightstar Therapeutics

£592.6m proceeds from exits

Aggregate 6.2x multiple[1]

9
High quality portfolio of leading life science companies

13
Portfolio companies to date

1
Product delivered to patients

Rolling 10 year targets

15-20
High quality portfolio of leading life science companies

2-3
New companies p.a.

3-5
Companies to approval, accessing the steepest part of the life science value curve

[1]14MG, Nightstar, Blue Earth

Syncona

Portfolio company review

Capital Markets Day 2020

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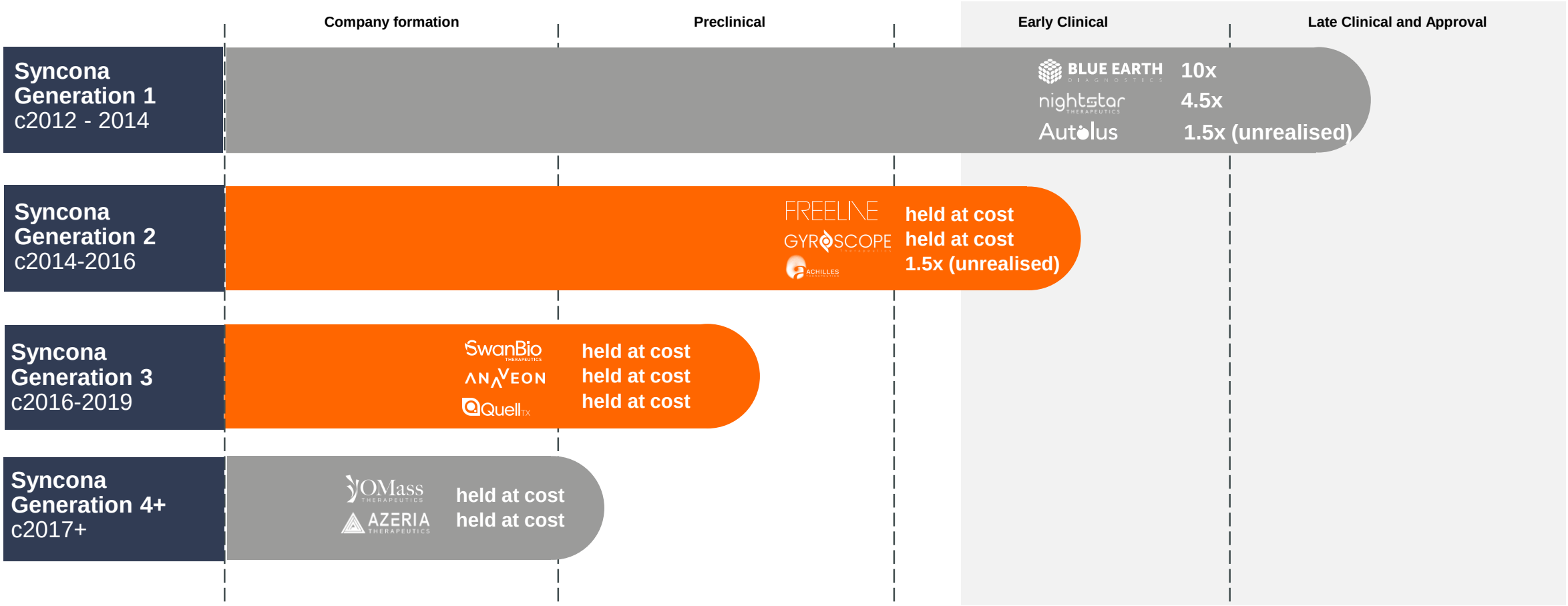
Significant value creation opportunity in the next generation



Figures as at 31 December 2019

The Third Wave: Market Context

The promise of precision medicine

Enables faster development, 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 low 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*

3x

Medicines targeted at defined patient groups 3x more likely to succeed than conventional drugs**

+50%

Trials initiated in 2018 using some form of genetic based selection***

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

Third Wave therapies have strong momentum

Syncona has established a leadership position in gene and cell therapy

"First Wave"

1950's
Small Molecule drugs, dominated by large pharmaceutical companies.

01

"Second Wave"

1990's
Large Molecule (antibody therapies, 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, less than 50 with treatments

9
'Third Wave' therapies approved in the US

10
'Third Wave' programmes taken into the clinic by Syncona founded companies

6/9
Of Syncona's portfolio companies in Third Wave

+75%
Of Syncona total capital invested in 6 Third Wave companies

2014
Syncona's first Third Wave company founded

Figures as at 31 December 2019

What are Third Wave therapies?

Offering the potential for cures for a range of intractable diseases

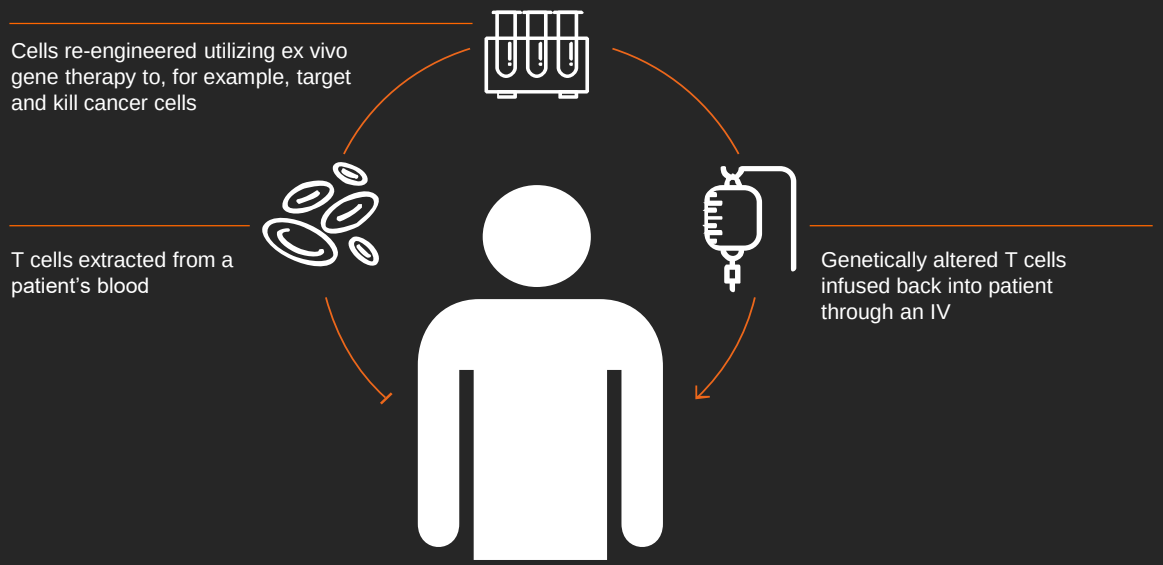
Syncona

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.



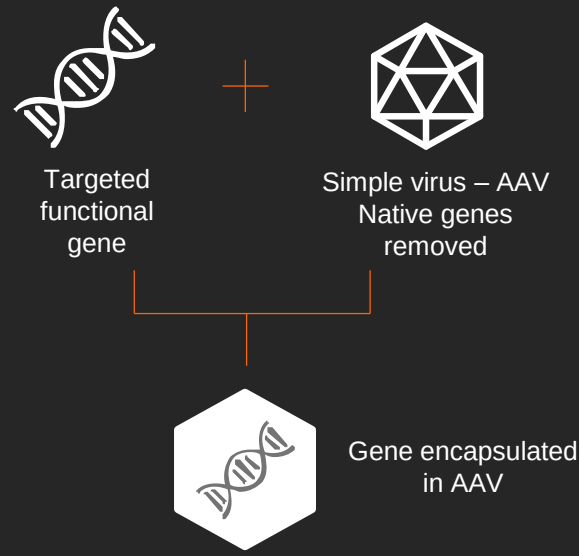
ACHILLES THERAPEUTICS

Autolus

QuellTX

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.



GYROSCOPE Therapeutics

FREELINE

SwanBio THERAPEUTICS

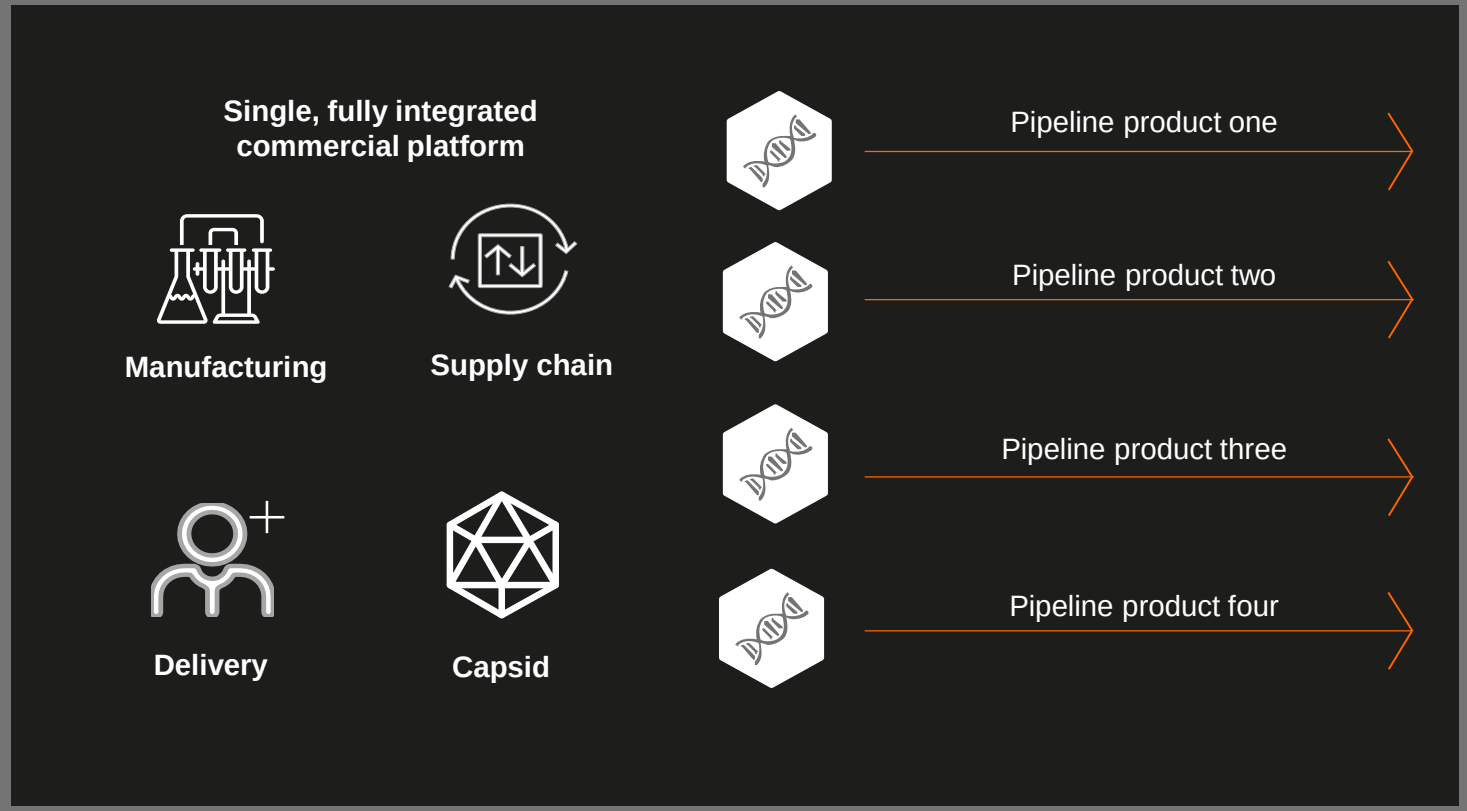
nightstar THERAPEUTICS

Platforms have strategic value in the Third Wave

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
First and Second wave products required individual platforms; Third Wave pipelines can be delivered by a single platform once established



Syncona is a leader in building fully integrated Third Wave platform companies

Third Wave commercial context

Platforms attract premiums

	Company description and number of clinical programmes	Market size of lead programme on a global basis	Take-out price $bn	Premium %
avexis	CNS gene therapy company **1 clinical programme**	Spinal muscular atrophy **23,500**	**$8.7bn**	**88%**
Spark THERAPEUTICS	Liver gene therapy company **3 clinical programmes**	Haemophilia A **174,000**	**$4.3bn**	**122%**
AUDENTES	Neuromuscular gene therapy company **1 clinical programme**	X-linked Myotubular Myopathy **1 in 40,000**	**$3.0bn**	**110%**

Syncona Generation 2

FREELINE

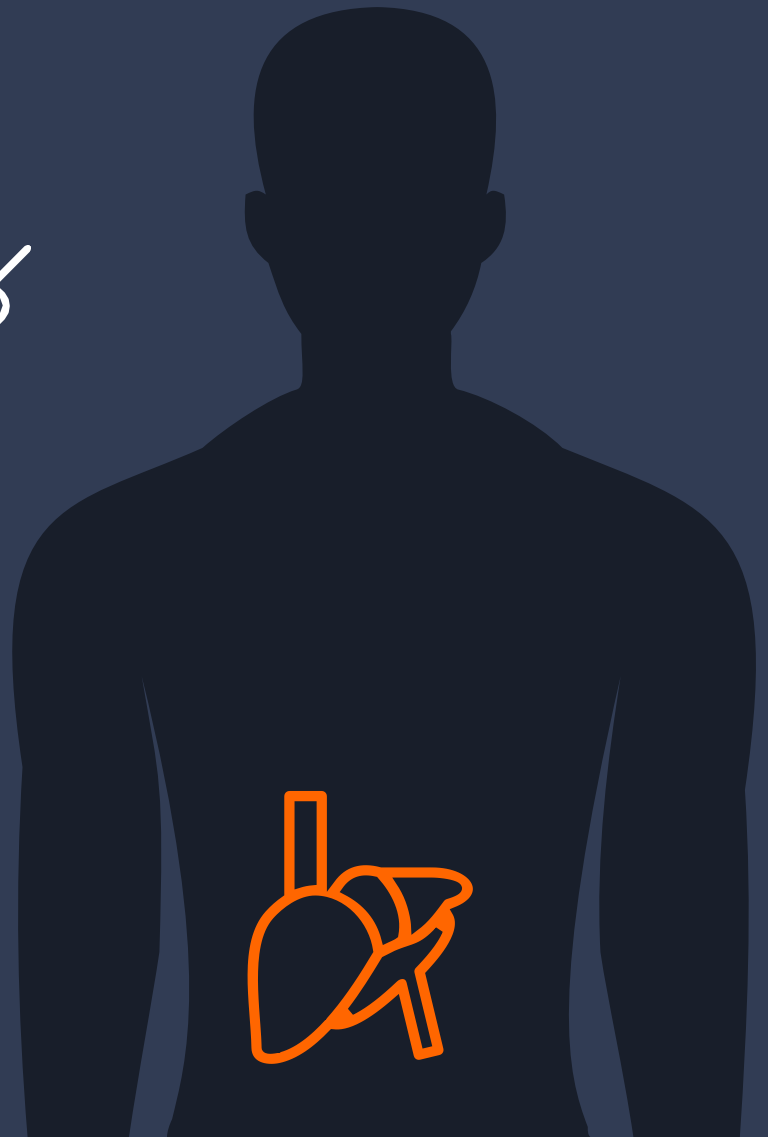
A next generation leader in systemic gene therapy

What is systemic gene therapy?

Targeted functional gene

Gene Encapsulated in AAV

Injected into patients



- Gene therapy delivers a functioning gene to the liver
- From there, protein will be sent into circulation where it can reach targeted cells throughout the body
- The delivery of constant high protein expression has curative potential across a broad pipeline of systemic diseases
- Curative potential by replacing a mutated gene with a functioning gene

At a glance

Leading clinical-stage gene therapy company focused on chronic systemic diseases

Capital invested	**£149.0m**
Stage	**Clinical**
Uncalled commitment	**$40.0m**
% Ownership	**79%**
Employees	**183**
Founder	**Professor Amit Nathwani**
Syncona team	**Chris Hollowood** **Dominic Schmidt**

FREELINE

Focus: Systemic AAV Gene Therapy, targeting chronic degenerative systemic conditions such as Haemophilia B, Fabry Disease and Gaucher's

Current standard of care:

- Significant number of systemic diseases with genetic drivers where patients have poor or no treatment options
- Current standard of care in Haemophilia B is Enzyme Replacement Therapy where infusions of a missing enzyme, Factor IX (FIX activity) in Haemophilia are delivered into the blood
- Treatment is expensive and burdensome for the patient; requires regular administration via IV
- Treatment does not cure the diseases: FIX activity does not remain stable, patients still experience breakthrough bleeds and pain in the joints

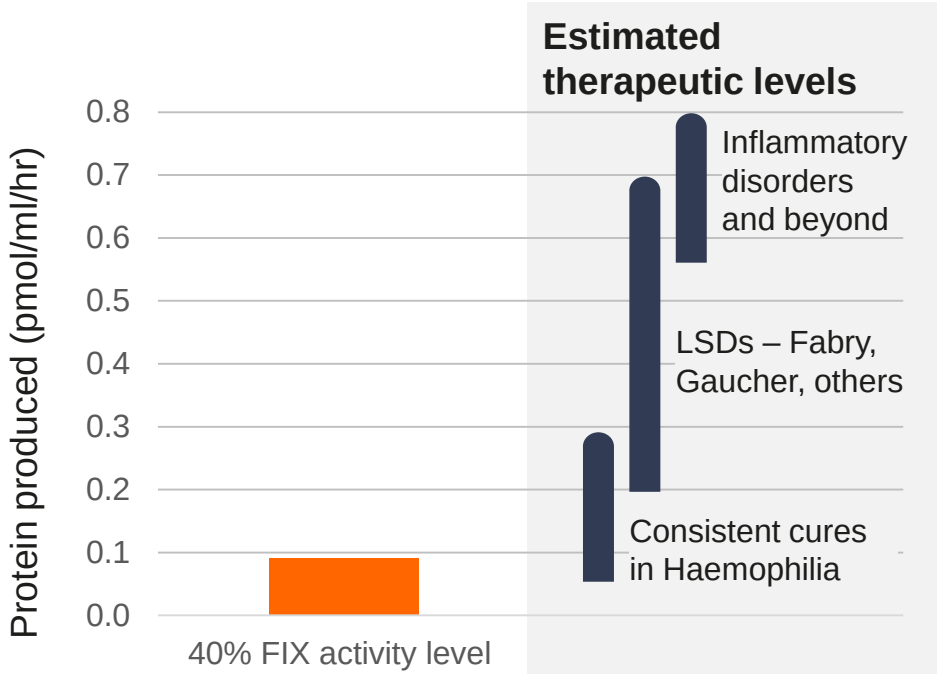
Competitive Context: peers in systemic gene therapy include[9,10]:

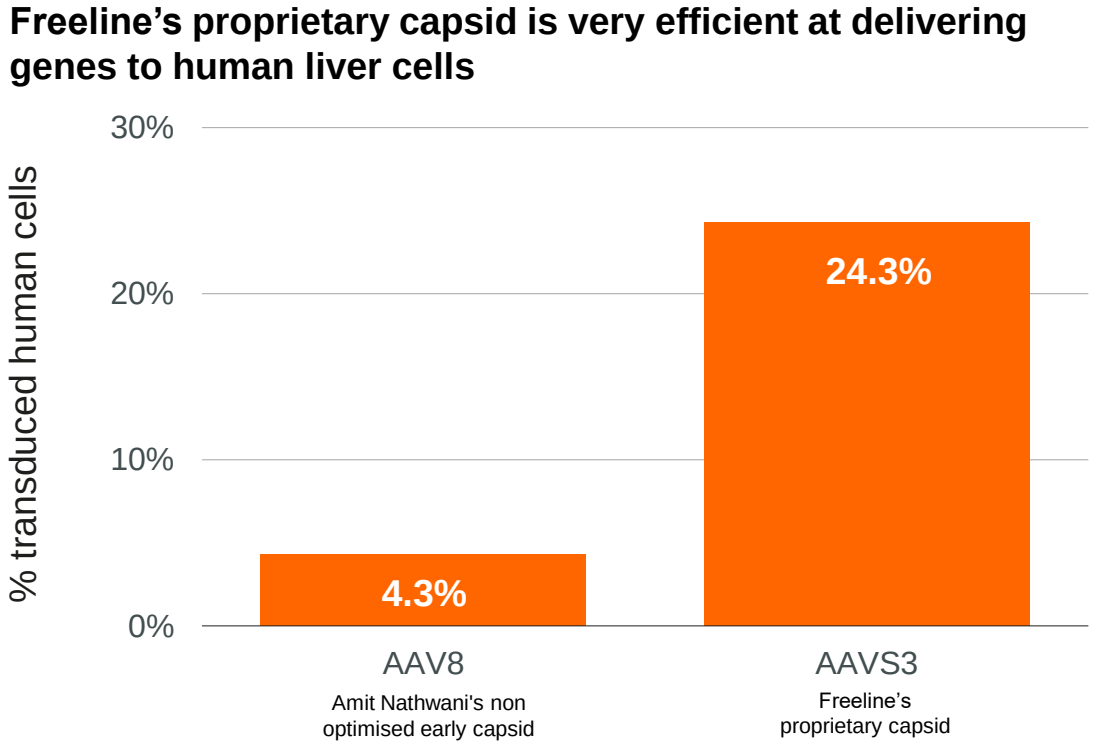
uniQure Spark THERAPEUTICS

Figures as at 31 December 2019
Footnote, please refer to page 73 in the Appendix

A fully integrated next generation systemic gene therapy company

Freeline's proprietary capsid has the potential to deliver next generation performance





40% activity assumes padua; average FIX activity reported in first dose cohort
Estimates of therapeutic levels for different endogenous proteins are shown
Dane A et al; abstract 2197, ASH 2018

A focus on manufacturing from the outset

Manufacturing platform delivers highest quality and potency at competitive cost.

Strategic control of supply chain
Single manufacturing platform meets demand from tox to commercial

Highest quality for safety and potency
Quality built-in to product using propriety technology and supported by world class analytics leading to highest 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

FREELINE

First employee – Markus Hörer – Founder and Chief Technology Officer (2014)

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

86/183 employees in CMC

Commercial scale
Attractive COGS
Leading the industry in quality

In-house manufacturing

A strong clinical pipeline

Proprietary platform with two clinical stage programmes and pipeline of 4 programmes expected in the clinic in 24 months

Significant unmet medical need in Haemophilia B:

Patient aspiration
Parity with general population

- Confidence in a cure
- Eliminate bleeds and the need for life-long, frequent IV infusions of enzyme replacement therapy top up in any circumstances

Payer aspiration
Improved treatment at lower cost

- Eliminate need for expensive and burdensome Enzyme Replacement Therapy in healthcare system

Clinical pipeline leveraging the same proprietary platform

Programme	Research	IND enabling studies	Phase 1/2	Next Milestone	Patient No (US & EU5)
Haemophilia B FLT180a				Dose Selection	9,000
Fabry FLT190 and FLT191				Results from dose escalation	9,000
Gaucher FLT200 and FLT201				CTA/IND	6,000
Haemophilia A FLT210				CTA/IND	38,000
Undisclosed inflammatory disorders				Candidate Selection	50,000 – 200,000

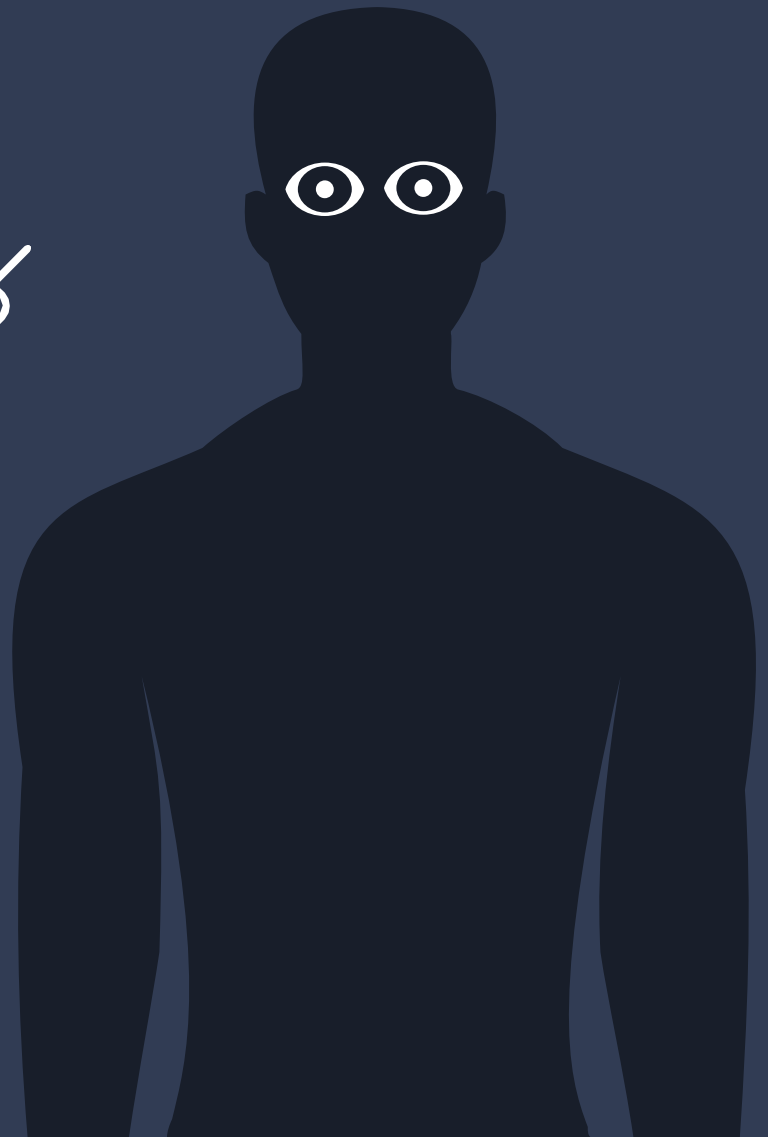

GYROSCOPE
Therapeutics
Developing Gene Therapy Beyond Rare Disease

What is retinal gene therapy?

Targeted functional gene

Gene Encapsulated in AAV

Injected into patients



- Gene therapy delivers a functioning gene to the eye, which may stimulate a patient's cells to produce the proteins needed to restore the mutated gene in the eye, with curative potential
- Research suggests that when the complement system (part of the immune system) is overactive it leads to inflammation that can damage healthy eye tissues
- Gene therapy may stimulate a patient's cells to produce the proteins needed to restore balance to the complement system

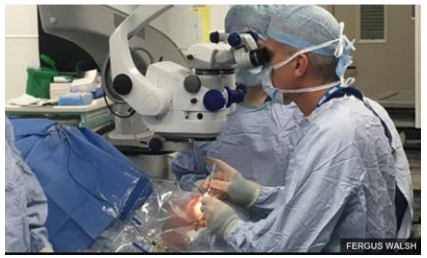
At a glance

Leading clinical-stage retinal gene therapy company

Capital invested	**£56.0m**
Stage	**Clinical**
Uncalled commitment	**£26.0m**
% Ownership	**80%**
Employees	**100**
Founders	**Peter Lachmann** **David Kavanagh** **Andrew Lotery**
Syncona team	**Chris Hollowood** **Dominic Schmidt** **Michael Kyriakides**

Focus: Retinal AAV Gene Therapy

- Developing gene therapy beyond rare diseases to target one of the leading cause of blindness among the elderly in the developed world[12]
- Targeting dry age related macular degeneration (dry AMD), where there are currently no treatments[12]
- Exploring the complement system and the role genetics play in the risk of developing this disease
- Research suggests that when the complement system is overactive it leads to inflammation that can damage healthy eye tissues
- Opportunity for gene therapy to stimulate cells in the eye to produce therapeutic proteins to restore balance in the complement system.



Competitive Context: peers in retinal AAV gene therapy include[13,14]:

gemini

Apellis

Figures as at 31 December 2019
Footnote, please refer to page 73 in the Appendix

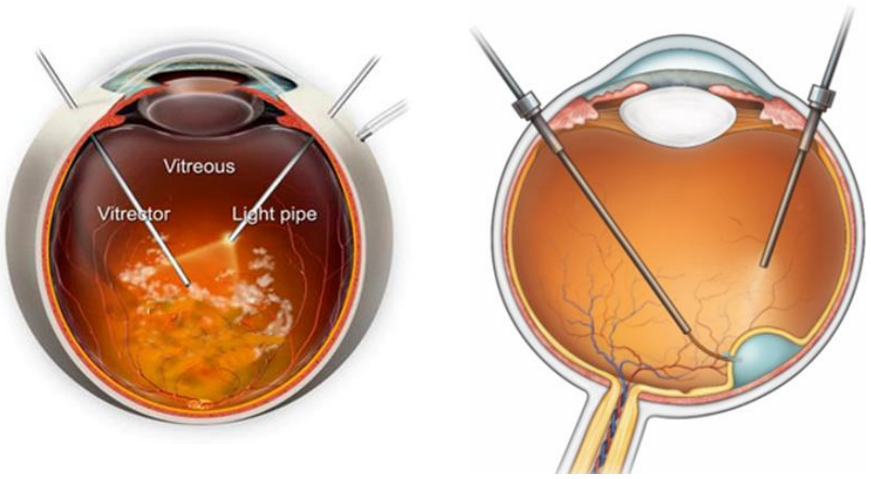
Scaling delivery to large patient populations

Orbit device innovation will enable retinal gene therapy to scale

Current subretinal delivery requires a vitrectomy

Potential drawbacks include:

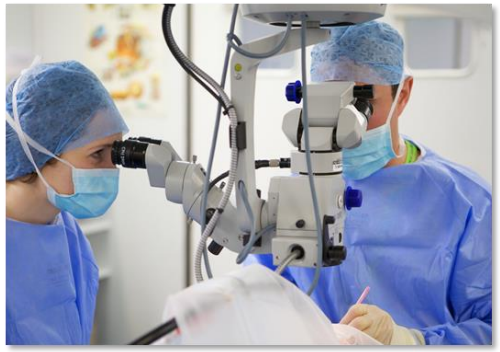
- Potential for retinal tears, retinal detachment, cataracts
- Uncertainty of dose delivered, loss of valuable product, lack of scalability.



Orbit SDS device is designed to protect the structure of the eye

- Optimised surgical procedure could lead to consistent clinical outcome
- World-class inhouse surgeon training capability
- Partnering 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



Developing a portfolio of medicines

Targeting one of the world's leading causes of blindness

Significant unmet need in dry AMD

- Presents as a progressive and debilitating loss of vision in the centre of the visual field
- 2 million people in the US and EU5 alone are affected by the advanced stage of the disease[11]
- Frequency of the disease increases significantly with age, with more than 10% of the population over 70 years old showing signs of AMD
- There are no treatment options available – an area of extreme interest for patients and the healthcare system.

The Stages of AMD

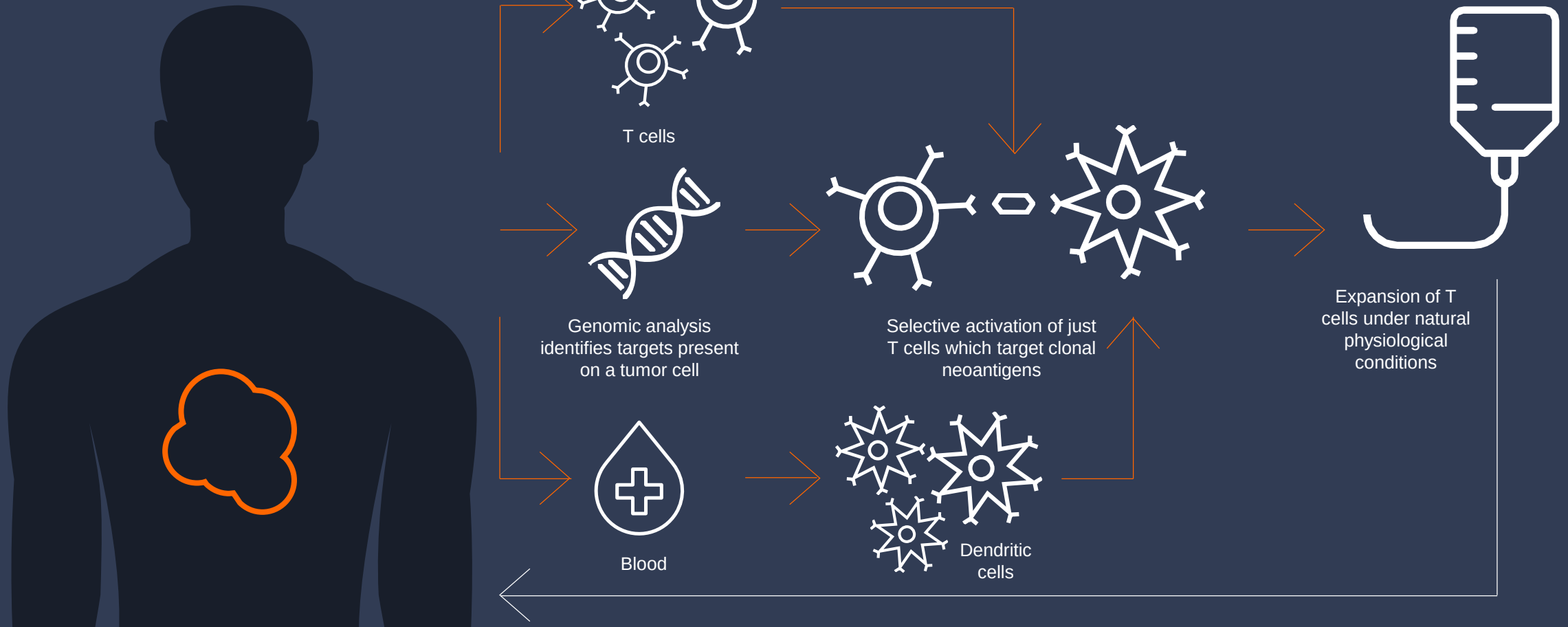
186m people worldwide affected; pipeline initially targeting late stage disease

Candidate	Indication	Status
		Research / Target ID / Pre-clinical / Clinical
GT005	Geographic Atrophy (defined sub-set)	
GT005/7	Geographic Atrophy (broad population)	
GT005/7	Other inflammatory retinal disease	

For references please see to page 73 in the Appendix

Achilles Therapeutics

Using cutting edge genomics to target all tumour cells in the body



At a glance

Developing potentially transformative T cell therapies targeting multiple solid tumours

Capital invested	**£49.0m**
Stage	**Pre-clinical**
Uncalled commitment	**£11.7m**
% Ownership	**44%**
Employees	**70**
Founders	**Karl Peggs** **Mark Lowdell** **Charles Swanton** **Sergio Quezada**
Syncona team	**Martin Murphy** **Elisa Petris**

Focus: Cell Therapy – Tumour Infiltrating Lymphocytes

- Developing personalised T cell therapies guided by the DNA sequence of each patient's tumour
- Differentiated approach targeting solid tumours utilising Tumour Infiltrating Lymphocytes (TILs) and clonal neoantigens
- Able to target multiple clonal neoantigens which helps minimise the possibility of evolved resistance and disease relapse
- Combining cutting edge genomics with a clinically validated cell therapy approach.

Targeting

- Lead indications in advanced non-small cell lung cancer and recurrent metastatic melanoma
- Selected for their high mutational burden, high level of T cell infiltration and high unmet medical need.

Competitive Context: peers in TIL therapy include[20,22]

IOVANCE BIOTHERAPEUTICS

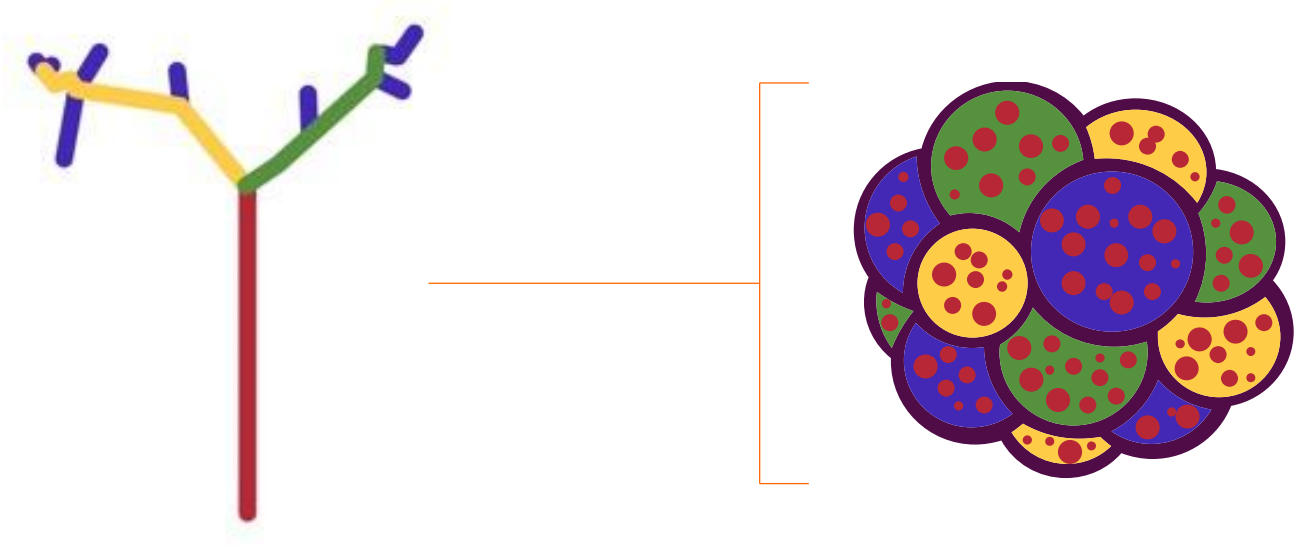
gritstone ONCOLOGY

Figures as at 31 December 2019
Footnote, please refer to page 73 in the Appendix

Platform underpinned by proprietary technology

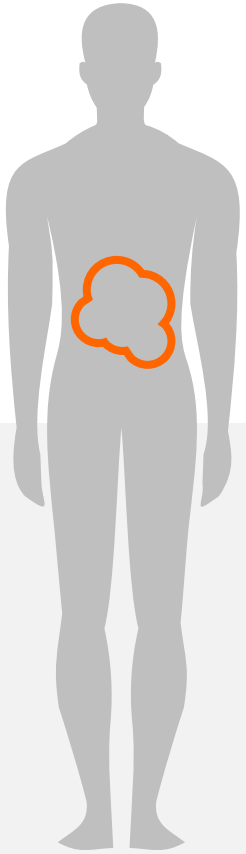
PELEUS™ bioinformatics platform is a unique a proprietary tool to identify clonal neoantigens

- TIL has demonstrated profound efficacy in multiple solid tumour settings
- Clonal neoantigen offer the potential to improve first generation TIL therapy
- Achilles can specifically identify clonal neoantigens using its world leading bioinformatics tool, PELEUS™
- PELEUS™ is built on exclusive access to largest global study of tumour evolution in lung cancer, the TRACERx study



- Sub-clonal neoantigens (branches) present on only some cancer cells
- Clonal neoantigens (trunk) are formed early in evolution and are present on all cancer cells

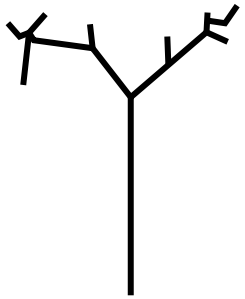
Opportunities exist for improvement of first generation TIL therapy



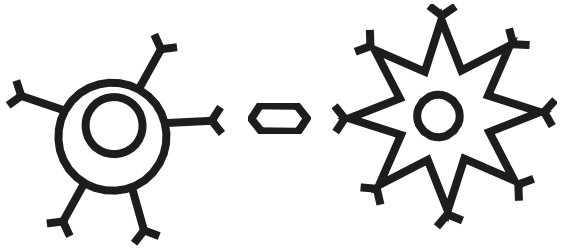
cNet*

TIL

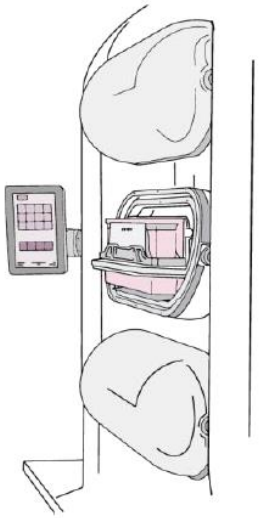
cNet process selectively targets clonal neoantigens



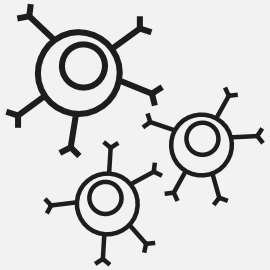
Natural dendritic cell driven T Cell expansion



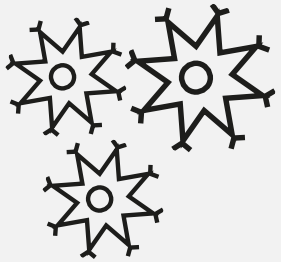
Modern proprietary process



Non-specific expansion of all T cells



Very high levels of IL-2



Manufacturing process developed in the 1980's

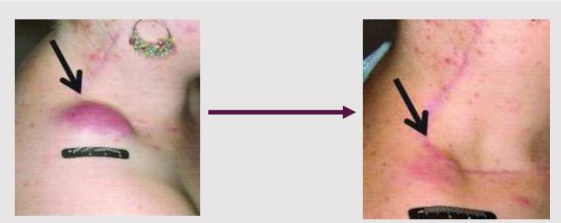
cNet: clonal neoantigen t cell

Driving a revolution in cancer treatment for patients

Targeting a pipeline of diseases where there is a high unmet need

Significant unmet need in solid tumour setting

- Deaths from non-small cell lung cancer outnumber those from breast cancer, colon cancer and prostate cancer combined
- Limited approved treatment options for lung cancer and melanoma patients whose disease has not responded well to other therapies
- 234,000 estimated prevalence of NSCLC in US and UK per annum[16]



Pipeline selected for high unmet need

Disease	Preclinical	Phase 1/2	Pivotal
Advanced non-small cell lung cancer			
Metastatic/recurrent melanoma			
Other indications			

Focused on generating rapid proof-of-concept in two lead indications and developing a pipeline targeting at least four indications

Generation 3 and Summary

Syncona Generation 3

Leveraging deep domain expertise into the next generation

Syncona

SwanBio THERAPEUTICS

Gene therapy focused on neurological disorders

- Fourth Syncona gene therapy company – third therapeutic domain: CNS
- Transformative potential in CNS – hard to access with 1st & 2nd wave therapies
- Targeting Adrenoleukodystrophy - one of the most common monogenic neurological disorders with no available therapies
- Severely debilitating progressive movement disorder
- Developing pipeline of indications –ultimately with opportunity to break out of rare disease
- Establishing manufacturing capabilities at the outset – high dose levels required for CNS.

QuellTX

Novel cell therapy approach using T-regulatory cells

- Third Syncona cell therapy company
- Developing T-reg cell therapies with a suppressive action to downregulate the immune system
- Targeting solid organ transplant rejection, autoimmune and inflammatory diseases
- Standard of care for prevention of solid organ transplant rejection is life-long immunosuppression – long-term serious side effects
- First indication in liver transplant; potential pipeline to treat serious, chronic conditions mediated by the immune system.

ANAVEON

Immuno-oncology company developing a selective IL-2 Receptor Agonist

- Human Interleukin 2 “IL-2” approved as a medicine for the treatment of certain cancers, but with frequent administration schedule and significant toxicity
- Developing a selective IL2 Receptor Agonist with improved administration and tox burden
- Wide potential utility across multiple oncology indications in large markets
- Potential utility in combination with cell therapies, an area of deep domain expertise.

Q&A

Panel 1
Translating Exceptional Science

Panel 2
The future of cell therapy

Panel 3

Building a commercial gene therapy platform

Wrap up

The Syncona Foundation

"With Syncona's support, we're moving further and faster. Syncona's funding has helped to drive some of our key projects."

THE BRAIN TUMOUR CHARITY

- 50% of the donation is provided to the Institute of Cancer Research (ICR), one of the world's most influential cancer research organisations
- The other 50% of the donation is provided to The Syncona Foundation
- The Syncona Foundation focuses on the prevention, treatment, cure and ultimately eradication of cancer and other diseases.

£27m
Donations since 2012

25
Charities donated to in 2019

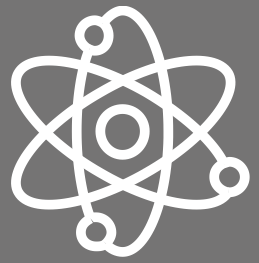
0.3%
of NAV donated on an annual basis

Long-term value creation potential – our ambition

Rolling 10 year targets

2-3

new companies created each year



15-20

sustainable portfolio of leading life science companies

3-5

companies to approval; accessing the steepest part of the life science value creation curve

Appendix

Outlook for Syncona Generation 1 and 2

Strong momentum with near term catalysts

Syncona

Autolus

- Plans to initiate a pivotal programme in AUTO1 adult ALL in first half of CY2020
- Expects to report further data in AUTO3 in H2 2020 which will enable decision for triggering Phase 2 initiation
- Pipeline progressing including Phase 1/2 trial in AUTO4; expect to present initial Phase 1 data H2 CY2020

FREELINE

- Dose optimisation continuing in Haemophilia B; disclosing further data on Friday 7 February 2020 at 13th Annual Congress of the European Association for Haemophilia and Allied Disorders
- Early data in Fabry programme expected to be reported in FY2021
- Plans for four clinical stage programmes within 24 months (Haemophilia A and Gaucher currently preclinical)

GYROSCOPE Therapeutics

- Dose escalation ongoing in lead programme for treatment of dry AMD; anticipate completing first dose escalation this financial year
- Initial data reported by FY2022

ACHILLES THERAPEUTICS

- Phase 1/2 clinic sites in Non small cell lung cancer and melanoma are open and enrolling patients
- Initial data in first two programmes in non-small cell lung cancer and melanoma expected by FY2022

Executing a differentiated strategy

An expert team with the skill set, track record and strategic capital base to build a sustainable, diverse high quality portfolio

Found

Proactively source globally competitive science, leveraging UK opportunity

Focus on products that move the needle for patients; dramatic efficacy in areas of high unmet need

Select products an SME can credibly take to market

Build

Leverage expertise and track record using Syncona resource to drive success

Take long term decisions consistent with a company taking product to market independently

Attract the best global talent

Fund

Scale ambitiously, maintain significant ownership positions to product approval; option to fund to market

Ownership position provides strategic influence; flexibility and control

Balance sheet protects against risk of being a forced seller

10 year targets

2-3 new portfolio companies p.a.

Build a sustainable portfolio of 15-20 companies

3-5 companies to approval

Portfolio Overview

- Approval stage
- Clinical stage
- Pre-clinical stage

31 December 2019 NAV of £1,340.0m (199.4p per share); capital pool of £823.4m

Portfolio company	Ownership* %	30 Sep 2019 value £m	Net invested/ returned the period £m	Valuation change in period £m	31 December 2019 value £m (Fair value)	Valuation basis (Fair value)**	% of NAV
Autolus	29	147.4	-	(2.2)	145.2	Quoted	10.8
FREELINE	79	118.5	30.5	(0.4)	148.6	Cost	11.1
GYROSCOPE Therapeutics	80	56.0	-	-	56.0	Cost	4.2
ACHILLES THERAPEUTICS	44	72.4	-	-	72.4	Recent financing (within 0-6 months)	5.4
SwanBio THERAPEUTICS	70	18.7	-	(1.4)	17.3	Cost	1.3
OMass THERAPEUTICS	46	9.8	-	-	9.8	Cost	0.7
ANAVEON	51	3.9	2.2	(0.1)	6.0	Cost	0.5
QuellTX	69	8.3	-	-	8.3	Cost	0.6
AZERIA THERAPEUTICS	61	-	6.5	-	6.5	Cost	0.5
Syncona Investments		46.3	0.7	(0.5)	46.5		3.5
Total		**481.3**	**39.9**	**(4.6)**	**516.6**		**38.6**

*Percentage holdings reflect Syncona's ownership stake at the point full current commitments are invested
**Cost indicates that the fair value has been determined to be equal to the total funding invested by Syncona

Significant opportunity across lead programmes

Potential to deliver multiple approved products which will cornerstone the creation of leading life science companies

Company & investment thesis	Lead programme / disease population p.a	Opportunity in and differentiation of lead programme	Key comparators[2]	Key risks[1]
Autolus Applying a broad range of technologies to build a pipeline of precisely targeted T cell therapies designed to better recognise and attack cancer cells	AUTO1 ALLCAR19 Phase 1/2 in Adult Acute Lymphoblastic Leukaemia 3k[3*]	• Unmet medical need: only 30-40% of patients with Adult ALL achieve long term remission with combination chemotherapy, the current standard of care[4] • No CAR-T therapy approved for adult ALL for patients • AUTO1 targets a differentiated safety profile (reduce high grade CRS[5]) and improved persistence to address limitations of current T cell therapies	• CAR-T active programmes in clinical development for ALL include Gilead[7]	• Differentiated product required • Complex manufacturing
Freeline Seeking to deliver constant high protein expression levels with curative potential across a broad pipeline of systemic diseases; opportunity to deliver curative gene therapies	B-AMAZE Phase 1/2 in Haemophilia B 9.5k[8**]	• Unmet medical need: current standard of care, Enzyme Replacement Therapy (infusions of FIX into the blood), requires regular administration and FIX activity does not remain stable • Opportunity to deliver a single dose cure for patients by achieving FIX levels in the 'normal' range in the blood of 50-150% • Utilising a novel, proprietary capsid and industrialised proprietary manufacturing platform	• Active clinical programmes in gene therapy for Haem B include: Spark/Pfizer[9], UniQure[10]	• Highly competitive environment • Differentiated product required • Manufacturing
Gyroscope A novel company developing gene therapy beyond rare disease by understanding the immune system and the role genetics play in a patient's risk of developing late stage AMD.	FOCUS Phase 1/2 in Dry Age-Related Macular Degeneration 2m[11**]	• Unmet medical need: age related macular degeneration is one of the leading causes of permanent vision impairment for people aged 65 and older with no approved treatments[12]. • Research suggests that when a part of the immune system, the complement system, is overactive it leads to inflammation that can damage healthy eye tissues • Gene therapy may stimulate a patient's cells to produce the proteins needed to restore balance to the complement system • Developing a subretinal delivery system to safely, precisely and consistently deliver therapies into the eye and help scale the surgical procedure for larger patient populations.	• No directly competitive gene therapy approach targeting complement system • Apellis[13] (clinical); Gemini (pre-clinical)[14], Hemera[15] (non-gene therapy)	• Highly innovative concept which is currently unsupported by a significant existing data set
Achilles Differentiated cell therapy approach targeting solid tumours utilising Tumour Infiltrating Lymphocytes & clonal neoantigens to develop personalised treatments	Phase 1/2 Non small cell lung cancer 234k[16*]	• Unmet medical need: lung cancer, of which NSCLC accounts for approximately 85%[17], with limited treatment options and is the leading cause of cancer deaths[18]. • TILs have shown convincing efficacy in solid tumours[19] • Achilles' world leading bioinformatics platform, PELEUS™ is built on exclusive access to world largest study of tumour evolution in lung cancer (TRACERx) • Achilles process uses the patient's own genomic information to create a truly personalised medicine targeting the clonal neoantigens	• Key competitors in the neoantigen/ personalised immunotherapy space include: Iovance[20], Neon Therapeutics[21], Gritstone Oncology[22]	• Highly innovative concept in an emerging space • Significant manufacturing challenge • Increasing competition

See slide 73 for references *Estimated new patients diagnosed per annum, **Estimated prevalent patient populations

Significant opportunity in earlier stage portfolio

Potential to deliver multiple approved products delivering transformational treatment for patients.

Company	Investment thesis	Key comparators[2]	Key risks[1]
SwanBio Gene therapy focused on neurological disorders where there is existing proof of concept	• Unmet medical need: one of the most common monogenic neurological disorders, with no available therapies for severely debilitating progressive movement disorder • Gene therapy has the potential to be transformational in neurology[23] • one-off delivery mechanism and hundreds of single gene disorders • First programme in preclinical development for an inherited neurodegenerative disease in which the causative gene is definitively known and well characterized	Several clinical trials for gene therapy within CNS field, including programmes within Voyager[24], Uniqure[25], Amicus[26], Prevail Therapeutics[27] and PTC Therapeutics[28]	• Manufacturing and delivery challenges in the CNS (substantial dose required) • Clinical endpoints can be challenging to define
Quell Engineered cell therapy company addressing immune dysregulation	• Unmet medical 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 (e.g. renal function, malignancy, infection, cardiovascular disease) materially impacting patient quality of life and long-term survival[29] • Novel cell therapy approach using T-regulatory cells with a suppressive action to downregulate the immune system to treat conditions including solid organ transplant rejection, autoimmune and inflammatory diseases • Potential pipeline to treat serious, chronic conditions mediated by the immune system; in the autoimmune setting alone, there are >70 chronic disorders estimated to affect over 4% of the population[30] • Pre-clinical stage: first programme to address solid organ transplant	T Reg field is nascent; TX Cell/Sangamo[31]	• Highly innovative concept, limited clinical data supporting application of CAR-T technology in Treg cells
Anaveon Immuno-oncology company developing a selective IL-2 Receptor Agonist	• Unmet medical need: Human Interleukin 2 “IL-2” approved as a medicine for the treatment of metastatic melanoma and renal cancer, but with a frequent administration schedule and significant toxicity[32] • Preclinical stage, developing a selective Interleukin 2 (“IL-2) Receptor Agonist with improved administration and tox burden • Wide potential utility across multiple oncology indications in large markets[33]	Companies developing products in the IL-2 field include: Nektar[34], Roche[35], Alkermes[36], Synthorx[37].	• Highly competitive • Technical risk around product
OMASS Drug Discovery platform with differentiated technology	• Opportunity to build a drug discovery platform employing a differentiated Modified Mass Spectrometry technology with the potential to yield high quality chemical hits to discover novel small molecule drug therapeutics for a variety of complex targets, including membrane receptors	N/A	• Pre clinical and clinical attrition of potential drugs

See slide 73 for references

An expert multi-disciplinary team

A life sciences team with a track record of creating value in the life science sector

Our unique skill set

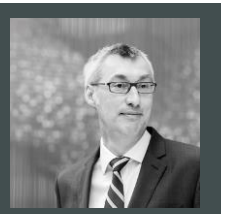
- Scientific
- Commercial
- Company creation
- Investment

Syncona

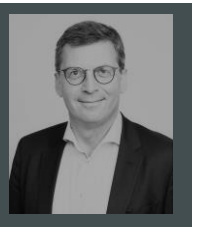
Martin Murphy
CEO
QuellTx · Autolus · Achilles · Azeria Therapeutics

Chris Hollowood
CIO
Freeline · SwanBio Therapeutics · Nightstar Therapeutics · Gyroscope

John Bradshaw
CFO

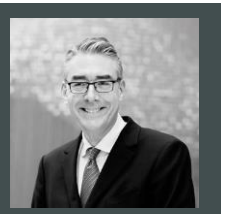


Lorenz Mayr
Entrepreneur in Residence



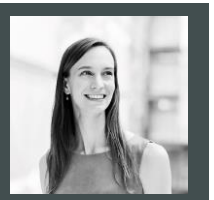
Elisa Petris
Partner
Achilles · QuellTx

Edward Hodgkin
Partner
UMass Therapeutics · Autolus



Dominic Schmidt
Partner
Gyroscope · Anveon · Freeline

Magda Jonikas
Partner
Azeria Therapeutics · UMass Therapeutics



Alex Hamilton
Partner
Autolus · SwanBio Therapeutics

Freddie Dear
Partner
QuellTx

Michael Kyriakides
Partner
Azeria Therapeutics · Gyroscope · Freeline

Alice Renard
Partner
Anveon

Gonzalo Garcia
Partner

Hitesh Thakrar
Partner

Autolus Therapeutics

Precisely targeted, controlled and highly active T cell therapies for cancer

Value	**£145.2m**
Uncalled commitment	**N/A**
Stage	**Clinical**
% Ownership	**29%**
Valuation basis	**Quoted**
Syncona team	**Martin Murphy** **Edward Hodgkin**

Syncona

Company overview

- Applying a broad range of technologies to build a pipeline of precisely targeted T cell therapies designed to better recognise and attack cancer cells

Unmet medical need

- In lead programme of AUTO1 only 30-40% of patients with Adult ALL achieve long term remission with combination chemotherapy, the current standard of care[4]

Investment thesis overview in lead programme

- No CAR-T therapy approved for adult ALL for patients
- AUTO1 targets a differentiated safety profile (reduce high grade CRS[5]) and improved persistence to address limitations of current T cell therapies

Market opportunity

- 3,000 patients p.a. in lead programme of Adult Acute Lymphoblastic Leukaemia[3] (estimated new patients diagnosed per annum)

Competitive context

- CAR-T active programmes in clinical development for ALL include Gilead, and in the wider CAR-T space include Novartis, Celgene, BlueBird

Key risks

- Differentiated product required
- Complex manufacturing

Figures as at 31 December 2019
See slide 73 for references

Freeline Therapeutics

Leveraging the convergence of gene therapy, complement system biology and complement system genomics

Value	**£148.6m**
Uncalled commitment	**$40.0m**
Stage	**Clinical**
% Ownership	**79%**
Valuation basis	**Cost**
Syncona team	**Chris Hollowood Dominic Schmidt**

Syncona

Company overview

- Seeking to deliver constant high protein expression levels with curative potential across a broad pipeline of systemic diseases; opportunity to leverage proprietary platform to deliver curative gene therapies

Unmet medical need

- Significant number of systemic diseases with genetic drivers which have poor or no treatment options
- Current standard of care in lead programme of Haemophilia B is Enzyme Replacement Therapy (ERT) (infusions of Factor IX (FIX) into the blood); requires regular administration, FIX activity does not remain stable

Investment thesis

- Opportunity to deliver single dose cure by achieving FIX levels in ‘normal’ range of 50-150%
- Leveraging Freeline’s proprietary platform; novel capsid, industrialised manufacturing

Market opportunity

- Haemophilia B addressable market: 9.5k patients8 (estimated prevalent population)
- Global ERT market expected to be +$13bn revenues p.a.by 2024

Competitive context

- Peers in systemic gene therapy include Spark/Pfizer, UniQure

Key Risks

- Highly innovative concept in an emerging space
- Significant manufacturing challenge
- Increasing competition

Figures as at 31 December 2019
See slide 73 for references

Gyroscope Therapeutics

Leveraging the convergence of gene therapy, complement system biology and complement system genomics

Value	**£56.0m**
Uncalled commitment	**£26.0m**
Stage	**Clinical**
% Ownership	**80%**
Valuation basis	**Cost**
Syncona team	**Chris Hollowood** **Dominic Schmidt** **Michael Kyriakides**

Company overview:

- A novel company developing gene therapy beyond rare disease by understanding the immune system and the role genetics play in a patient's risk of developing late stage Age related macular degeneration (AMD).

Unmet medical need:

- AMD is one of the leading causes of permanent vision impairment for people aged 65 and older with no approved treatments.

Investment thesis overview:

- Research suggests that when the complement system (part of the immune system) is overactive it leads to inflammation that can damage healthy eye tissues
- Gene therapy may stimulate a patient's cells to produce the proteins needed to restore balance to the complement system
- Gyroscope developing a subretinal delivery system to safely, precisely and consistently deliver therapies to the eye; ability to scale surgical procedure for large patient populations.

Market opportunity

- Initial population of an estimated 2 million people in the US & EU5 with geographic atrophy11 – late stage dry AMD. No current treatment.

Competitive context

- No directly competitive gene therapy approach targeting complement system
- Apellis13 (clinical); Gemini14 (pre-clinical), Hemera15 (non-gene therapy) operating in the field

Key Risks

- Highly innovative concept which is currently unsupported by a significant existing data set

Figures as at 31 December 2019
See slide 73 for references

Achilles Therapeutics

Developing personalised T cell therapies targeting neoantigens

Value	**£72.4m**
Uncalled commitment	**£11.7m**
Stage	**Pre-clinical**
% Ownership	**44%**
Valuation basis	**Recent financing**
Syncona team	**Martin Murphy** **Elisa Petris**

Company overview

- Differentiated T cell therapy approach targeting solid tumours utilising Tumour Infiltrating Lymphocytes (TILs) & clonal neoantigens

Unmet medical need:

- Lung cancer has limited treatment options and is the leading cause of cancer deaths.[18]

Investment thesis overview:

- TILs have shown convincing efficacy in solid tumours[19]
- Achilles' world leading bioinformatics platform, PELEUS™ built on exclusive access to largest global study of tumour evolution in lung cancer (TRACERx)
- Achilles' process uses patient's genomic information to create truly personalised medicine targeting clonal neoantigens

Market opportunity

- 234,000 estimated prevalence of Non Small Cell Lung Cancer in US and UK per annum[16]

Competitive context

- Key competitors in the neoantigen/ personalised immunotherapy space include: Iovance[20], Gritstone Oncology[22]

Key risks

- Highly innovative concept in an emerging space
- Significant manufacturing challenge
- Increasing competition

Figures as at 31 December 2019
See slide 73 for references

SwanBio Therapeutics

Developing leading-edge gene therapies to deliver dramatic clinical efficacy for the treatment of neurological diseases

Value	**£17.3m**
Uncalled commitment	**N/A**
Stage	**Pre-clinical**
% Ownership	**70%**
Valuation basis	**Cost**
Syncona team	**Chris Hollowood** **Alex Hamilton**

Syncona

Company overview

- Gene therapy focused on neurological disorders where there is existing proof of concept

Unmet medical need

- Hundreds of single gene disorders with poor or no treatment options
- Lead programme targeting one of the most common monogenic neurological disorders for a severely debilitating progressive movement disorder, with no available therapies

Investment thesis overview

- Gene therapy has the potential to be transformational in neurology[23]
- One-off delivery mechanism
- First programme in preclinical development for an inherited neurodegenerative disease in which the causative gene is definitively known and well characterized

Competitive context

- Several clinical trials for gene therapy within CNS field, including programmes within Voyager[24], Uniqure[25], Amicus[26], Prevail Therapeutics[27] and PTC Therapeutics[28]

Key risks

- Manufacturing and delivery challenges in the CNS (substantial dose required)
- Clinical endpoints can be challenging to define

Figures as at 31 December 2019
See slide 73 for references

Omass Therapeutics

Drug Discovery platform with differentiated technology

Value	**£9.8m**
Uncalled commitment	**N/A**
Stage	**Pre-clinical**
% Ownership	**46%**
Valuation basis	**Cost**
Syncona team	**Martin Murphy** **Magda Jonikas** **Edward Hodgkin**

Company overview

- Opportunity to build a drug discovery platform employing differentiated Modified Mass Spectrometry technology

Investment thesis overview

- Proprietary technology enables the discovery of products with unique pharmacological profile
- Potential to yield high quality chemical hits to discover novel small molecule drug therapeutics for a variety of complex targets, including membrane receptors
- Opportunity to implement commercial partnerships in other commercial settings

Competitive context

- No direct technology competitors. Similar business models include Sosei Heptares and Galapagos

Key risks

- Pre clinical and clinical attrition of potential drugs

Figures as at 31 December 2019
See slide 73 or references

Anaveon

Immuno-oncology company developing a selective IL-2 Receptor Agonist

Value	**£6.0m**
Uncalled commitment	**£15.9m**
Stage	**Pre-clinical**
% Ownership	**51%**
Valuation basis	**Cost**
Syncona team	**Martin Murphy** **Dominic Schmidt** **Alice Renard**

Company overview

- Developing a selective Interleukin 2 ("IL-2) Receptor Agonist seeking to achieve improved administration and tox burden versus existing products

Unmet medical need

- Human Interleukin 2 "IL-2" approved as a medicine for the treatment of metastatic melanoma and renal cancer, but with a frequent administration schedule and significant toxicity3[2]

Investment thesis overview

- Company seeking to develop biased IL-2 agonists to selectively promote T cell functions
- Wide potential utility across multiple oncology indications in large markets[33]

Competitive context

- Companies developing products in the IL-2 field include: Nektar[34], Roche[35], Alkermes[36], Synthorx[37].

Key risks

- Highly competitive
- Technical risk around product

Figures as at 31 December 2019
See slide 73 for references

Quell Therapeutics

Engineered cell therapy company addressing immune dysregulation

Value	**£8.3m**
Uncalled commitment	**£25.7m**
Stage	**Pre-clinical**
% Ownership	**69%**
Valuation basis	**Cost**
Syncona team	**Martin Murphy Elisa Petris Freddie Dear**

Company overview

- Novel cell therapy approach using T-regulatory cells with a suppressive action to downregulate the immune system

Unmet medical need

- First programme addressing solid organ transplant: current standard of care to prevent transplant rejection is life-long immunosuppression, resulting in long-term side effects which materially impact quality of life and long-term survival

Investment thesis overview

- Seeking to treat conditions including solid organ transplant rejection, autoimmune and inflammatory diseases to novel cell therapy approach
- Employing proprietary and innovative technologies to genetically enhance Tregs, to enable their suppressive potential to be focused precisely where it is needed
- Potential pipeline to treat serious, chronic conditions mediated by the immune system; >70 chronic disorders in autoimmune setting estimated to affect >4% of the population

Competitive context

- Field is nascent in T Reg field; potential competitors include TX Cell/Sangamo

Key risks

- Highly innovative concept, limited clinical data supporting application of CAR-T technology in Treg cells

Figures as at 31 December 2019
See slide 73 for references

Azeria Therapeutics

Building a world class pioneer factor oncology company

Value	**£6.5m**
Uncalled commitment	**£23.1m**
Stage	**Pre-clinical**
% Ownership	**61%**
Valuation basis	**Cost**
Syncona team	**Martin Murphy Magda Jonikas**

Figures as at 31 December 2019

Company overview

- Seeking to develop breakthrough treatments based on targeting pioneer factors, a specialised type of transcription factor, able to 'open' compacted DNA to initiate the expression of genes to make sure they are expressed in the right cell at the right time.

Unmet medical need

- Significant unmet patient need in oestrogen receptor positive breast cancer where c.30% of patients progress to late stage endocrine resistant disease

Investment thesis overview

- Scientific insights by academic founder have led to a new approach to target FOXA1 driven cancer, an essential pioneer factor pivotal in tumour growth, progression and maintenance of oestrogen receptor positive luminal breast cancer.

Market opportunity

- Current therapies [in endocrine resistant breast cancer] forecast to reach sales of >$20bn; potential to have significant impact for patients

Competitive context

- Companies developing therapies for oestrogen receptor (ER) positive luminal breast cancer includ Eisai, AstraZeneca, Genentech

Key risks

- Highly innovative concept, limited clinical data set

1. Syncona investment team analysis of key risks facing the companies; the companies are subject to other known and unknown risks, uncertainties and other factors
2. Syncona investment team analysis of lead programmes in this area, indicative only
3. Source: Autolus – see Autolus corporate presentation November 2019 https://autolus.gcs-web.com/static-files/cd8dc1d9-6a7b-496d-933f-1a3b0bfbd56a. Autolus project the addressable population at 3,000 patients US & EU5
4. Source: Autolus – see Autolus corporate presentation November 2019 https://autolus.gcs-web.com/static-files/cd8dc1d9-6a7b-496d-933f-1a3b0bfbd56a
5. Cytokine Release Syndrome
6. Source: Autolus – see Autolus corporate presentation November 2019 https://autolus.gcs-web.com/static-files/cd8dc1d9-6a7b-496d-933f-1a3b0bfbd56a
7. https://www.gilead.com/science-and-medicine/pipeline
8. Source: Freeline analysis of prevalence in US and EU5. Analysis is based on World Federation of Haemophilia Global Annual Survey 2017 http://www1.wfh.org/publications/files/pdf-1714.pdf and National Haemophilia Foundation; CDC.
9. https://sparktx.com/scientific-platform-programs/
10. http://www.uniqure.com/gene-therapy/hemophilia.php
11. Source: Gyroscope estimate. Age related macular degeneration, of which one type is dry AMD, is estimated to affect 195.6 million people globally (https://www.who.int/publications-detail/world-report-on-vision). Gyroscope's estimate is that there is a population of 2 million people in the US & EU5 with geographic atrophy, which is late stage dry AMD.
12. Source: WHO https://www.who.int/blindness/causes/priority/en/index7.html
13. https://www.apellis.com/focus-pipeline.html
14. https://www.geminitherapeutics.com/approach-progress/
15. https://www.hemerabiosciences.com/clinical-trials/
16. Source: Achilles calculation of US and UK prevalence. There are 275,000 new cases of lung cancer in US and UK each year, of which 85% are estimated to be NSCLC. US: 228,150 https://seer.cancer.gov/statfacts/html/lungb.html; UK: 47,235 https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer/incidence.
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23. See for example existing approved product Zolgensma for spinal muscular atrophy – https://www.zolgensma.com/
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32. Source: https://www.cancernetwork.com/renal-cell-carcinoma/managing-toxicities-high-dose-interleukin-2
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