



Introduction to Syncona

March 2020

synconaltd.com

Image Freeline labs, Stevenage

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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 cohort¹ treated in Freeline's clinical trial in Haemophilia B FIX activity remains stable and consistent at 40+-5.5%

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

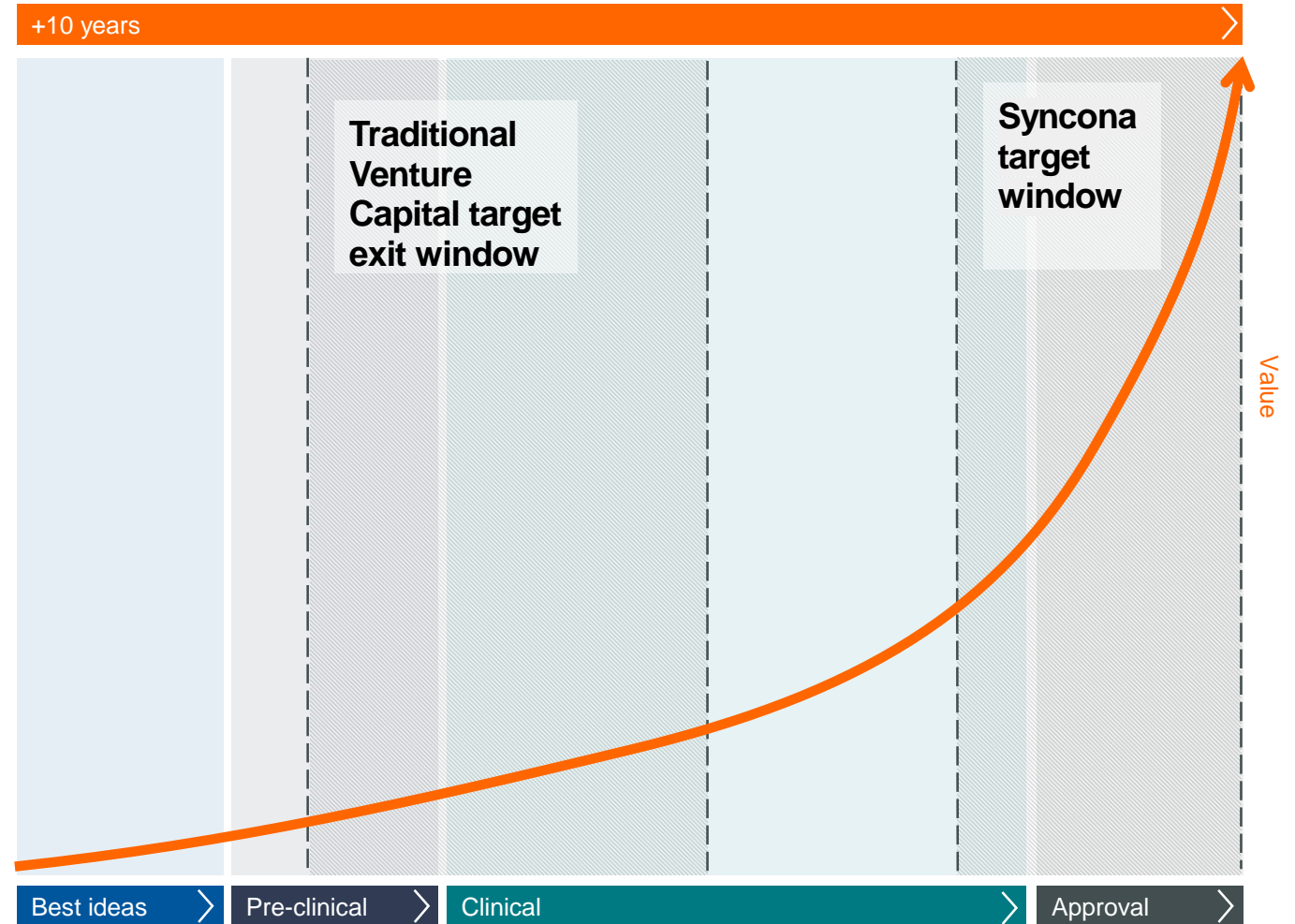
04

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

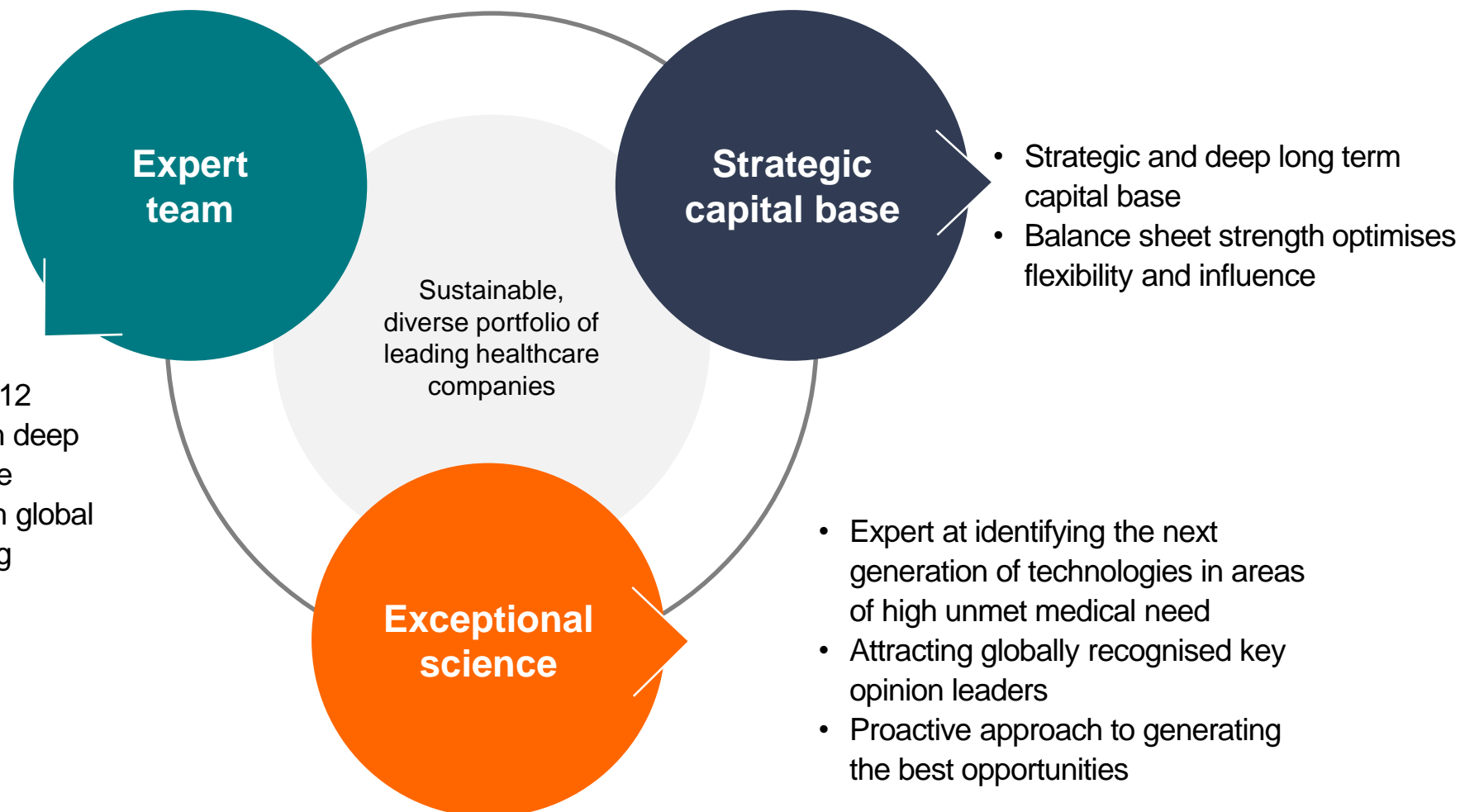


Graph is illustrative and assumes successful clinical development and approval, Syncona team view

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



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 Trialrove.

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

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 %
	CNS gene therapy company 1 clinical programme	Spinal muscular atrophy 23,500	\$8.7bn	88%
	Liver gene therapy company 3 clinical programmes	Haemophilia A 174,000	\$4.3bn	122%
	Neuromuscular gene therapy company 1 clinical programme	X-linked Myotubular Myopathy 1 in 40,000	\$3.0bn	110%

Syncona portfolio

A differentiated and focused portfolio

Diversified across a range of modalities where Syncona has deep domain expertise

- Clinical stage
- Preclinical stage



Autolus Cell therapy

- Published encouraging data in AUTO1 adult ALL showing favourable safety profile, high level of clinical activity, potential for durable responses
- Four clinical programmes across range of indications
- Proprietary manufacturing; commercial scale

FREELINE Gene therapy

- Dose optimisation continuing in Haemophilia B; six patients have completed follow-up for six months, and amongst those, three have FIX activity levels over 50%
- Two patients at the low dose
- First patient dosed in Fabry's disease

GYROSCOPE Gene therapy

- Dose escalation ongoing in lead programme for dry AMD
- Completed £50.4 million Series B financing; £48.0 million Syncona commitment

SwanBio Gene therapy

- Leadership team build out, developing pipeline indications, progressing towards candidate nomination for lead programme

YOMass Small molecule

- Leveraging unique technology platform which is deployed as a discovery engine for small molecule therapeutics
- Appointment of Ros Deegan, highly experienced in drug discovery, as Chief Executive

ANAVEON Biologics

- Leadership team build out; progression of lead programme to candidate nomination, expanding operations.

QuellTX Cell therapy

- Iain McGill, appointed CEO (ex SVP Europe, Jazz Pharmaceuticals)
- Team and manufacturing build out; Syncona Partner, Freddie Dear, working in company

ACHILLES Cell therapy

- £100.0 million Series B financing; £35.1m cornerstone Syncona commitment
- Phase 1/2 clinic sites open in NSCLC**, melanoma; enrolling patients in NSCLC

AZERIA Small molecule

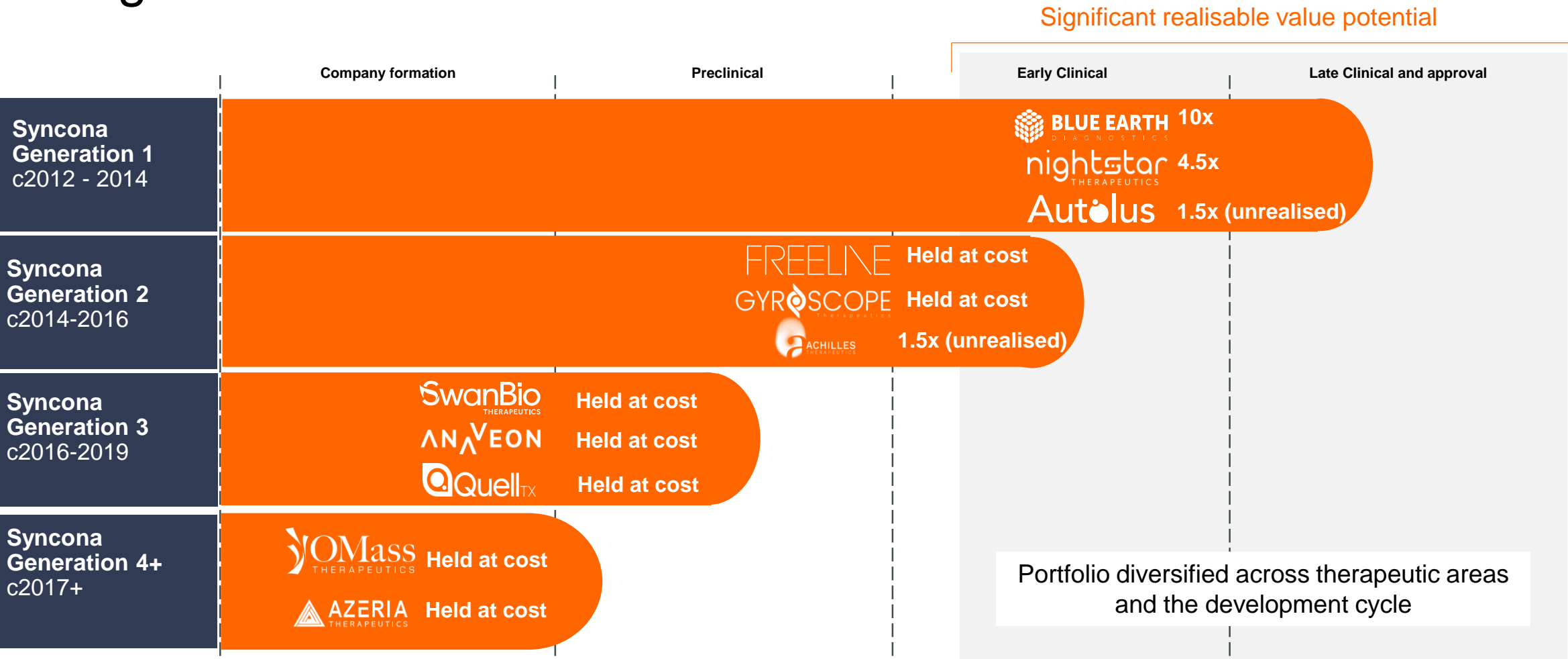
- New investment, £29.5m Syncona commitment in £32.0m Series B financing; 75% percent ownership holding*
- Opportunity to build world-class pioneer factor oncology company

*American Society of Hematology conference, December 7-10 2019

**Non small cell lung cancer

* 61% direct holding, 75% total ownership including CRT holding, both percentages reflect full current commitments

Significant value creation opportunity in the next generation



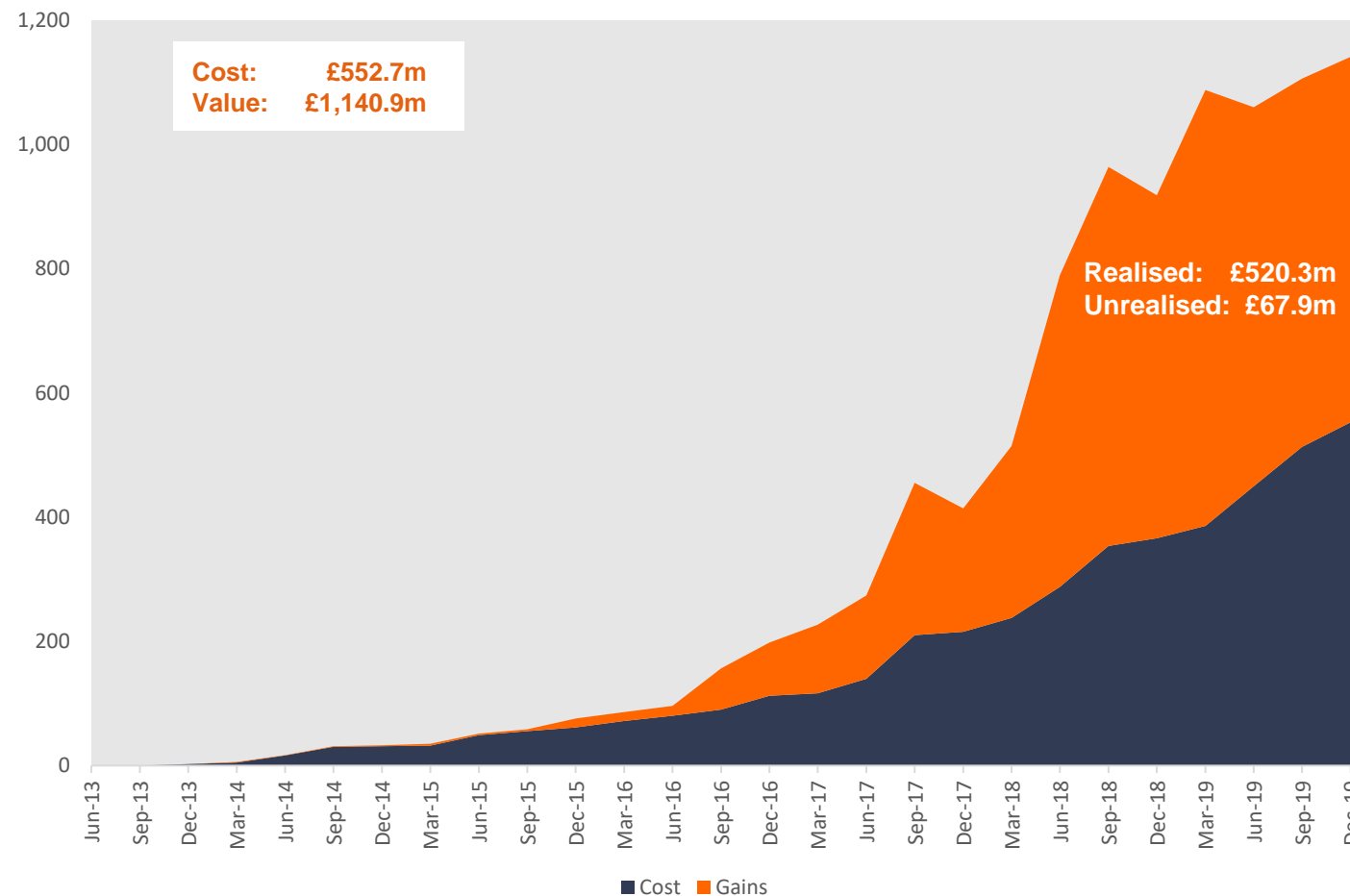
Financial performance

Delivering 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



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
GYRSCOPE	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
YOMass THERAPEUTICS	46	9.8	-	-	9.8	Cost	0.7
ANVEON	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

The background is a solid teal color with several large, overlapping geometric shapes in varying shades of teal. These shapes include circles and triangles, creating a layered, abstract effect. The text "Found and Build" is centered horizontally and partially overlaid by one of the larger teal shapes.

Found and Build

What do we look for in a scientific asset?

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

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



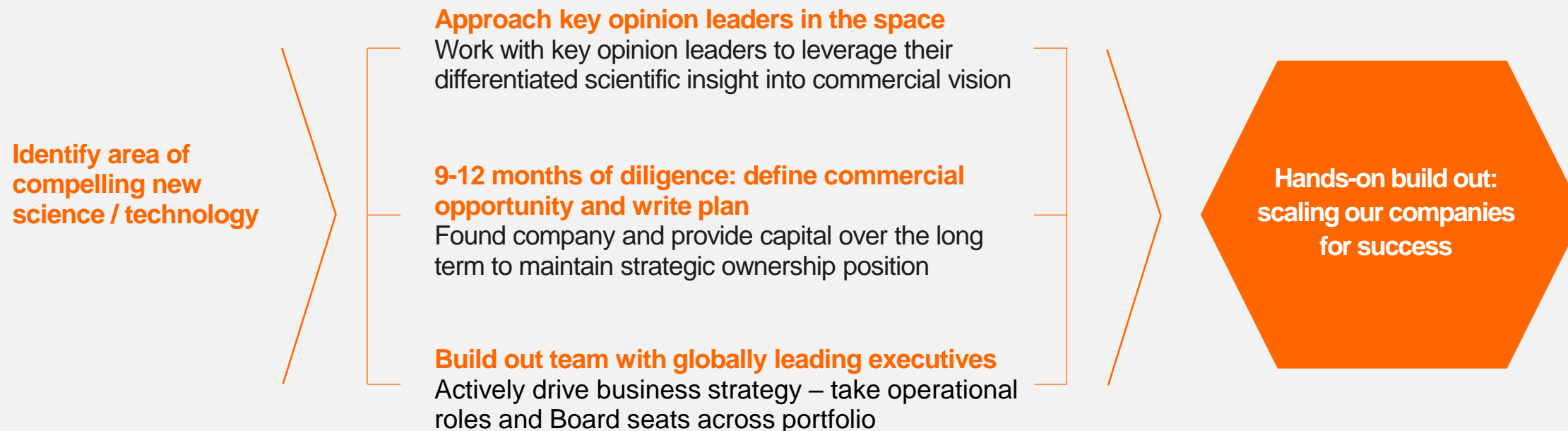
Company	Founded by Syncona	Syncona majority ownership position
Autolus	✓	Largest investor (30%)
FREELINE	✓	✓
GYROSCOPE THERAPEUTICS	✓	✓
ACHILLES THERAPEUTICS	✓	✓
SwanBio THERAPEUTICS	✓	✓
JOMass THERAPEUTICS	OSI (seed)	Largest investor (47%)
ANAVEON	UZH Fund (seed)	✓
QuellTX	✓	✓
AZERIA THERAPEUTICS	CRT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

¹ Syncona holds 64% of the CRT Pioneer Fund

Our approach to company creation and development

Translating technology to products to reach full value potential

Our partnership approach provides a strategic premium



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

The background is a solid orange color with several large, overlapping geometric shapes in a darker shade of orange. These shapes include triangles and a large, rounded rectangle, creating a modern, abstract design.

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

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 tranching and based on milestone delivery

Funding model for our companies



Capital pool provides control and flexibility over the long-term; deployment in FY2020 expected to be £200-250m

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

Outlook and summary

Outlook for Syncona Generation 1 and 2



Strong momentum with near term catalysts

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 with further data to be reported in H2 CY2020
- Expect to enter Phase 3 in Haem B in 2021
- 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

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



- 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

Building a sustainable, scalable model



Delivering strong risk-adjusted returns for shareholders

Current portfolio: 2012-19

Previous portfolio companies

£592.6m proceeds from exits

Aggregate 6.2x multiple¹

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

¹14MG, Nightstar, Blue Earth

Appendix

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

£27m

Donations since 2012

25

Charities
donated to in 2019

0.3%

of NAV donated on an
annual basis



- 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.



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

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



John Bradshaw
CFO



Lorenz Mayr
Entrepreneur
in Residence



Elisa Petris
Partner



Edward Hodgkin
Partner



Dominic Schmidt
Partner



Magda Jonikas
Partner



Alex Hamilton
Partner



Freddie Dear
Partner



Michael Kyriakides
Partner



Alice Renard
Partner



Gonzalo Garcia
Partner



Hitesh Thakrar
Partner



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*}	<ul style="list-style-type: none"> Unmet medical need: only 30-40% of patients with Adult ALL achieve long term remission with combination chemotherapy, the current standard of care⁴ No CAR-T therapy approved for adult ALL for patients AUTO1 targets a differentiated safety profile (reduce high grade CRS⁵) and improved persistence to address limitations of current T cell therapies 	<ul style="list-style-type: none"> CAR-T active programmes in clinical development for ALL include Gilead⁷ 	<ul style="list-style-type: none"> 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**}	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Active clinical programmes in gene therapy for Haem B include: Spark/Pfizer⁹, UniQure¹⁰ 	<ul style="list-style-type: none"> 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**}	<ul style="list-style-type: none"> 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 treatments¹². 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. 	<ul style="list-style-type: none"> No directly competitive gene therapy approach targeting complement system Apellis¹³ (clinical); Gemini (pre-clinical)¹⁴, Hemera¹⁵ (non-gene therapy) 	<ul style="list-style-type: none"> 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*}	<ul style="list-style-type: none"> Unmet medical need: lung cancer, of which NSCLC accounts for approximately 85%¹⁷, with limited treatment options and is the leading cause of cancer deaths¹⁸. TILs have shown convincing efficacy in solid tumours¹⁹ 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 	<ul style="list-style-type: none"> Key competitors in the neoantigen/ personalised immunotherapy space include: Iovance²⁰, Neon Therapeutics²¹, Gritstone Oncology²² 	<ul style="list-style-type: none"> Highly innovative concept in an emerging space Significant manufacturing challenge Increasing competition

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	<ul style="list-style-type: none"> 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 neurology²³ 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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 survival²⁹ 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 population³⁰ Pre-clinical stage: first programme to address solid organ transplant 	T Reg field is nascent; TX Cell/Sangamo ³¹	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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 toxicity³² 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 markets³³ 	Companies developing products in the IL-2 field include: Nektar ³⁴ , Roche ³⁵ , Alkermes ³⁶ , Synthorx ³⁷ .	<ul style="list-style-type: none"> Highly competitive Technical risk around product
OMASS Drug Discovery platform with differentiated technology	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Pre clinical and clinical attrition of potential drugs

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



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 care⁴

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 CRS⁵) 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 Leukaemia³ (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

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



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

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

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 tumours¹⁹
- 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 annum¹⁶

Competitive context

- Key competitors in the neoantigen/ personalised immunotherapy space include: lovance²⁰, Gritstone Oncology²²

Key risks

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

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



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 neurology²³
- 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 Voyager²⁴, Uniqure²⁵, Amicus²⁶, Prevail Therapeutics²⁷ and PTC Therapeutics²⁸

Key risks

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

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

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 toxicity³²

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 markets³³

Competitive context

- Companies developing products in the IL-2 field include: Nektar³⁴, Roche³⁵, Alkermes³⁶, Synthorx³⁷.

Key risks

- Highly competitive
- Technical risk around product

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

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



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 include 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-1a3b0bfb56a>. 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-1a3b0bfb56a>
5. Cytokine Release Syndrome
6. Source: Autolus – see Autolus corporate presentation November 2019 <https://autolus.gcs-web.com/static-files/cd8dc1d9-6a7b-496d-933f-1a3b0bfb56a>
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>.
17. Source: American Cancer Society <https://www.cancer.org/cancer/small-cell-lung-cancer/about/key-statistics.html>
18. Source: American Cancer Society <https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html>
19. Source: Rosenberg et al 2011 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131487/pdf/nihms286994.pdf>
20. <https://www.iovance.com/clinical/pipeline/>
21. <https://neontherapeutics.com/product-pipeline/>
22. <https://gritstoneoncology.com/our-pipeline/>
23. See for example existing approved product Zolgensma for spinal muscular atrophy – <https://www.zolgensma.com/>
24. <https://www.voyagertherapeutics.com/our-approach-programs/gene-therapy/>
25. <http://uniqure.com/gene-therapy/huntingtons-disease.php>
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32. Source: <https://www.cancernetwork.com/renal-cell-carcinoma/managing-toxicities-high-dose-interleukin-2>
33. Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4938354/>
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37. <https://synthorx.com/therapeutics/>