



# Syncona Corporate presentation

January 2021

[synconaltd.com](http://synconaltd.com)

*Image Freeline labs, Stevenage*

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# Strategy and vision

# Building the next generation of healthcare leaders

Our purpose is to invest to extend and enhance human life

## 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

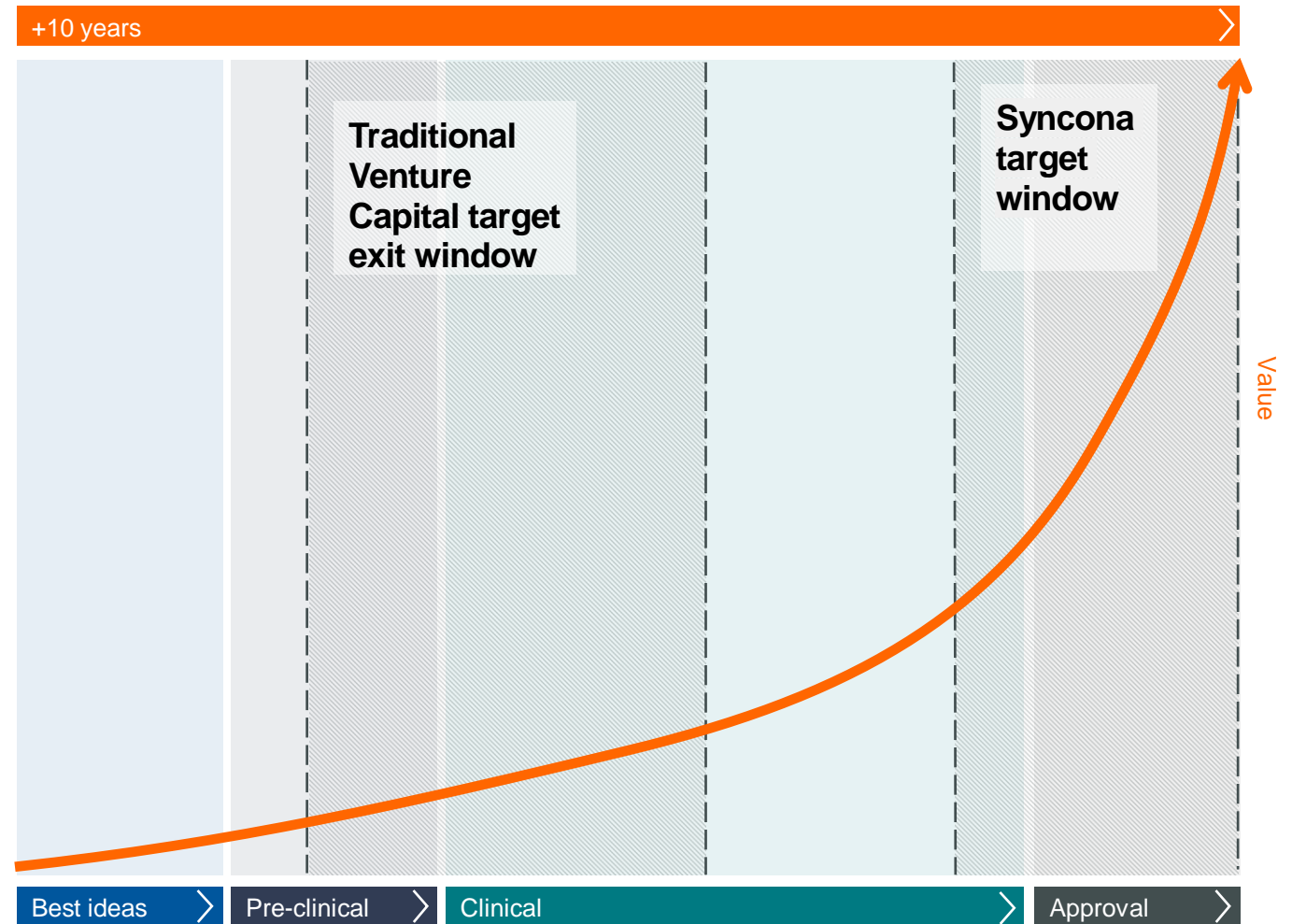


# Capturing the out return in life science

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

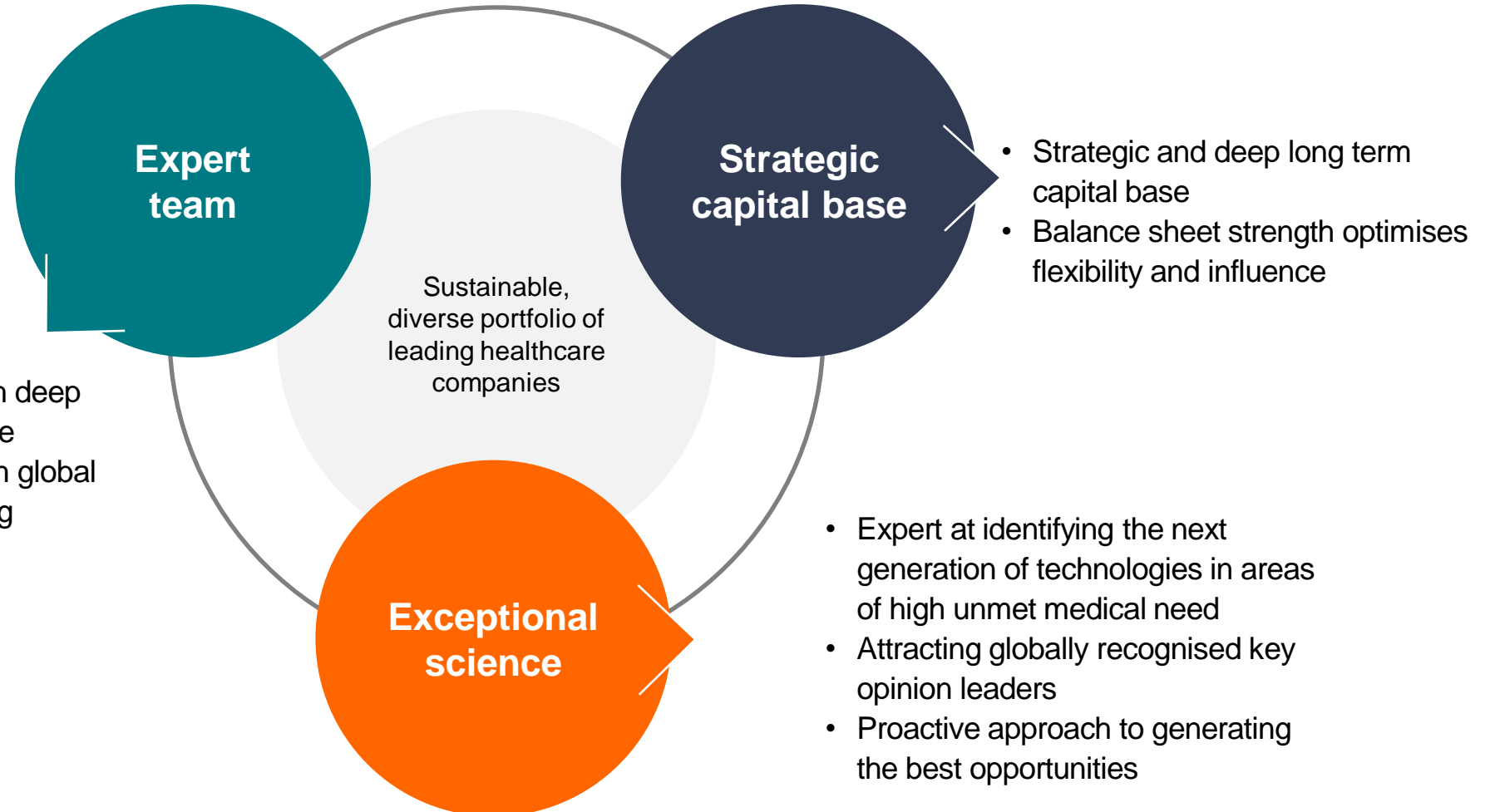


Graph is illustrative and assumes successful clinical development and approval, Syncona team view

# Our differentiated platform

Founding, Building and  
Funding global leaders  
from exceptional science

- Investment team of 14 people with deep scientific and commercial expertise
- Extensive experience working with global key opinion leaders and appointing leading management teams



# Delivering value through biotech company creation



Building sustainable companies and delivering transformational outcomes for patients

## Strong track record

42%

Gross IRR since inception (2012)

2.1x

Gross multiple on invested capital

£607m

Value of exits from the portfolio<sup>1</sup>; £510m realised gain

6.2x

Gross multiple on realised companies; aggregate IRR 72%

## Building sustainable leaders

£661m

Capital deployed since 2012

15

Syncona companies founded and invested in since 2012<sup>2</sup>

3

Companies progressed products through to pivotal study, including 1 delivered marketed product to patients

13

Programmes progressed to clinical stage

## Patient impact

>50k

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

nightstar  
THERAPEUTICS

Patient testimonial: "For over 30 years I have been living with the awful inevitability that I was going blind but now, thanks to the operation, there is a real prospect that I will continue to be able to see...."

84%

Of 19 Adult acute lymphoblastic leukaemia patients in Autolus Phase 1/2 trial achieved complete response; encouraging durability of remissions across all treated patients<sup>3</sup>

FREELINE

Patient testimonial: "I have got new hopes for the future. Before the gene therapy treatment, travel wasn't an option but now I can chuck on a backpack and go, as long as the gene therapy continues to work."

Unless stated all data at 30 September 2020

<sup>1</sup> Including dividends from Blue Earth

<sup>2</sup> Including Purespring (announced November 2020)

<sup>3</sup> <https://autolus.gcs-web.com/static-files/f38a593a-a058-4c77-a9ea-ce24e7c70a85>

# 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

10

‘Third Wave’ therapies approved in the US

10

‘Third Wave’ programmes taken into the clinic by Syncona founded companies

8/10

Of Syncona's companies in Third Wave<sup>1</sup>

+85%




Of Syncona total capital invested in 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 <b>1 clinical programme</b>	Spinal muscular atrophy <b>23,500</b>	<b>\$8.7bn</b>	<b>88%</b>
	Liver gene therapy company <b>3 clinical programmes</b>	Haemophilia A <b>174,000</b>	<b>\$4.3bn</b>	<b>122%</b>
	Neuromuscular gene therapy company <b>1 clinical programme</b>	X-linked Myotubular Myopathy <b>1 in 40,000</b>	<b>\$3.0bn</b>	<b>110%</b>

# Syncona portfolio

# Strong clinical and financial progress

Clinical trials across the portfolio are continuing where possible



## Gene therapy

**FREELINE**

NASDAQ listed  
Value: £227.2m  
48% ownership

Seeking to deliver constant high protein expression levels with curative potential across a broad pipeline of systemic diseases

- Successfully undertook a Series C financing
- Listed on NASDAQ
- Raised \$299m in total bring in specialist, long-term capital

### Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical

Haem. B  
Fabry  
Gaucher  
Haem. A  
Undisclosed disorders



uniQure

**GYROSCOPE**  
VISION FOR LIFE

Private  
Value: £82.0m  
80% ownership

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

- Dose escalation ongoing in phase I/II trial and first patient dosed in phase II trials
- Granted FDA fast-track designation
- Appointed Sean Bohen to the Board

### Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical

Dry AMD –G.A (sub-set)  
Dry AMD –G.A (broad)  
Other inflammatory



Apellis



## Cell therapy

**Autolus**

NASDAQ listed  
27% ownership  
Valuation: £144m  
Cost: £106m

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

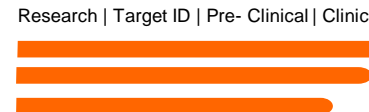
### Financing

- Cash balances of \$178m
- Cash burn \$110m p.a. (30 Sept 20)

### Clinical pipeline\*

Research | Target ID | Pre- Clinical | Clinical

Auto 1 - aALL  
Auto 1/22 - pALL  
Auto 4 TCL



### Competitive landscape



**ACHILLES**  
THERAPEUTICS

Private  
Value: £72.4m  
44% ownership

Differentiated cell therapy approach targeting solid tumours utilising Tumour Infiltrating Lymphocytes and clonal neoantigens to develop personalised treatments

- Dosed first patients in phase I/II trials in melanoma and NSCLC
- Appointed Karl Peggs as CMO
- Raised £52.7m in Series C in November 2029

### Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical












Melanoma  
Non-cell lung cancer  
Other indications





# Momentum building in preclinical companies

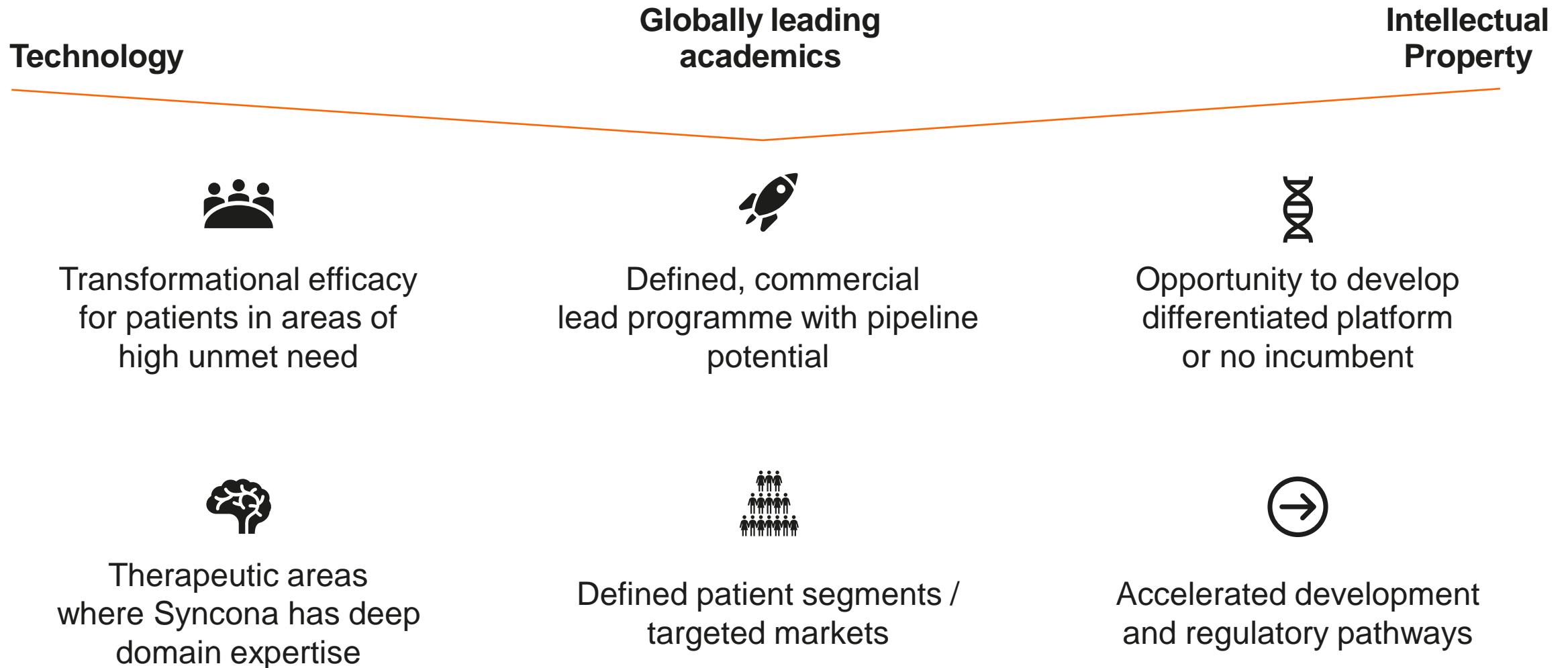
Building out management teams and manufacturing capabilities; making strides towards the clinic

Company	Focus	Value	Operational progress	Clinical progress	Competitors
 QuellTX	Cell therapy	£19.9m	<ul style="list-style-type: none"> <li>Team build out</li> <li>Manufacturing build out</li> </ul>	<ul style="list-style-type: none"> <li>Clinical candidate nomination</li> <li>Pipeline development (neuroinflammation)</li> </ul>	 SONOMA
 neogene THERAPEUTICS	Cell therapy	£11.8m	<ul style="list-style-type: none"> <li>Series A financing of \$110 million</li> <li>Appointment of Franz Humer as Chair</li> </ul>	<ul style="list-style-type: none"> <li>Pre-clinical development</li> </ul>	
 ORTx	Cell therapy	£1.8m	<ul style="list-style-type: none"> <li>Series A financing of £26.8m</li> </ul>	<ul style="list-style-type: none"> <li>Pre-clinical development</li> </ul>	Resolution with first mover advantage
 SwanBio THERAPEUTICS	Gene therapy	£33.0m	<ul style="list-style-type: none"> <li>Team build out</li> <li>Continuing to develop a scalable manufacturing process for commercial supply</li> <li>Completed engineering run of its product</li> </ul>	<ul style="list-style-type: none"> <li>Pre-clinical development continues with lead programme</li> <li>Made strong progress in its clinical trial design</li> <li>Developing pipeline indications</li> </ul>	 
 ANVEON	Biologics	£12.4m	<ul style="list-style-type: none"> <li>Continued team build out</li> <li>Expanding operations</li> </ul>	<ul style="list-style-type: none"> <li>Clinical candidate nomination</li> </ul>	
Purespring	Gene therapy	£3.9m	<ul style="list-style-type: none"> <li>Series A financing of £45.0m</li> <li>Richard Francis appointed CEO</li> </ul>	<ul style="list-style-type: none"> <li>Pre-clinical development</li> </ul>	Purespring with first mover advantage
 OMass THERAPEUTICS	Small molecule	£14.6m	<ul style="list-style-type: none"> <li>Continue to recruit senior leadership team</li> </ul>	<ul style="list-style-type: none"> <li>Progressing a pipeline of small molecule targets</li> </ul>	N/A

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Found and Build

# What do we look for in a scientific asset?



# 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

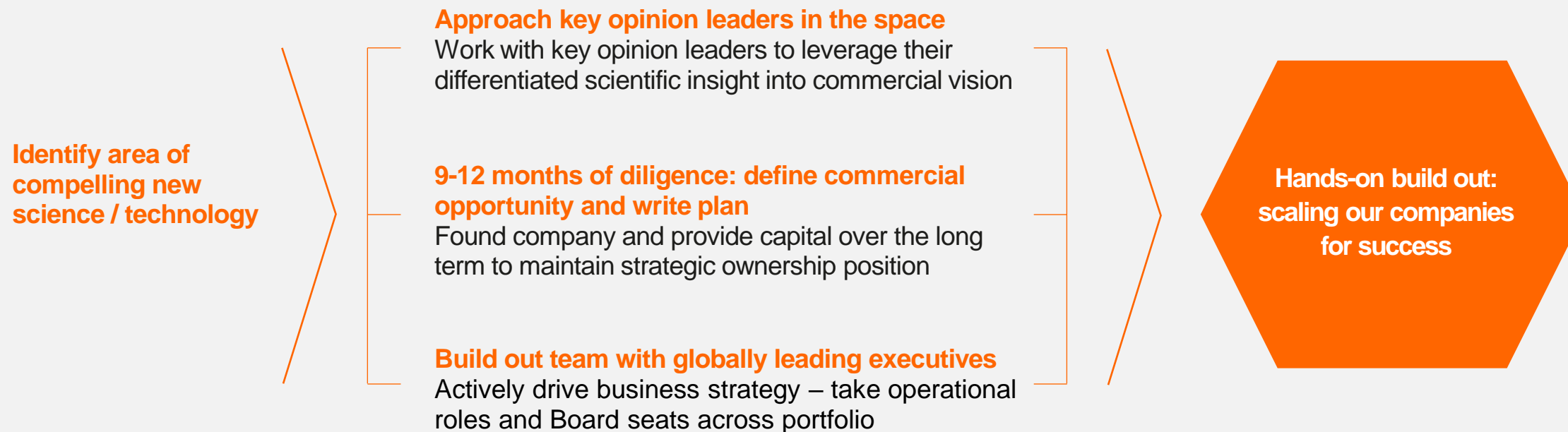


Company	Founded by Syncona	Syncona majority ownership position
	✓	Largest investor (27%)
	✓	Largest investor (48%)
	✓	✓
	✓	Largest investor (34%)
	✓	✓
	OSI (seed)	Largest investor (49%)
	UZH Fund (seed)	✓
	✓	✓
	✓	✓
Purespring	✓	✓

# Our approach to company creation and development

Translating technology to products to reach full value potential

## Our partnership approach provides a strategic premium





# Sourcing technology in growing areas has led to multiple Syncona companies and investments



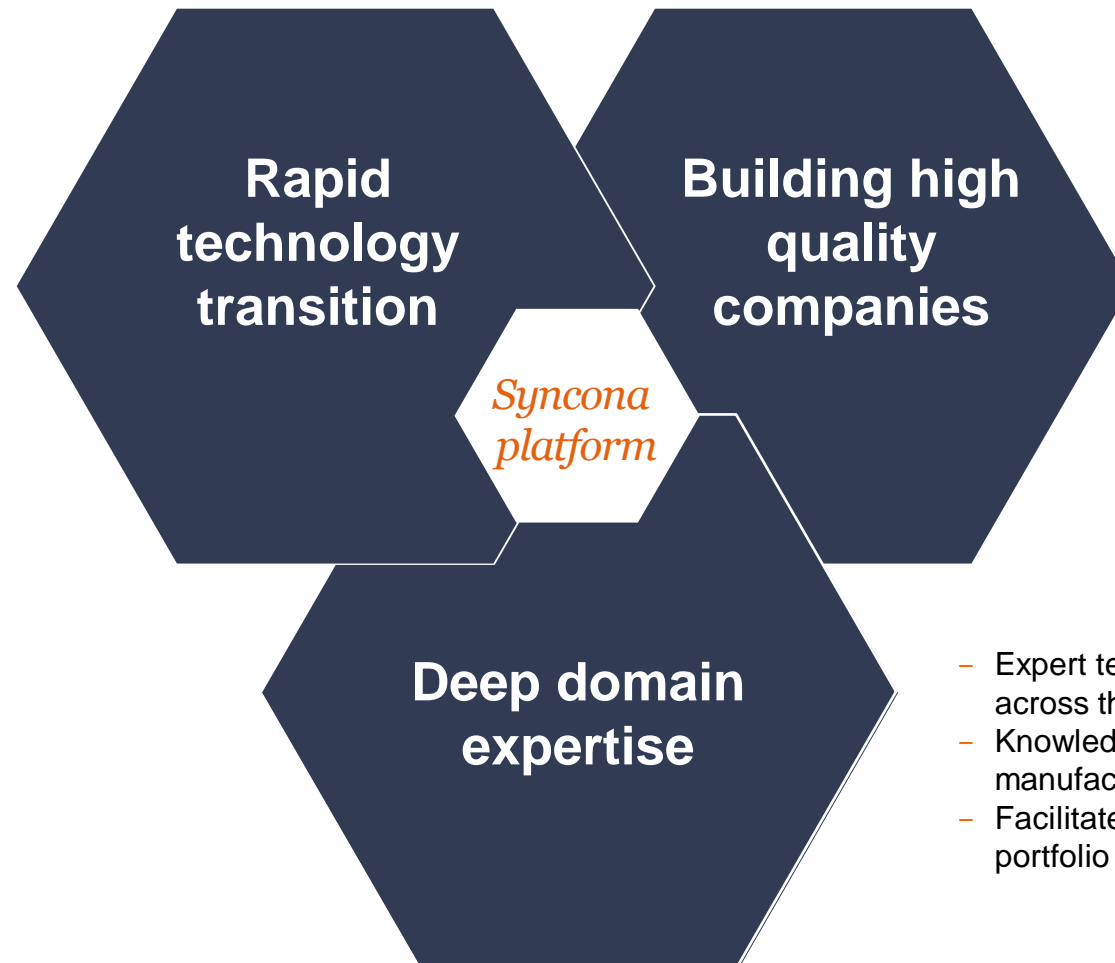
The strength of our platform and the depth of our diligence allows us to identify new areas where there is the potential to found multiple companies

# Syncona platform: a growing competitive advantage



Platform enables rapid translation of basic scientific research into companies with the potential to be global leaders

- Ability to identify a compelling new area of science where a differentiated business can be built
- Expertise to define the commercial opportunity for the science/innovation, develop company strategy and write the best business plan



- Increased capability, expertise and network to support company build out
- Growing reputation and track record enables us to attract the best managers at company launch

- Expert team with significant knowledge base to leverage across the portfolio
- Knowledge sharing across commercial, research and manufacturing aspects specific to cell and gene therapy
- Facilitate introductions of management teams across the portfolio

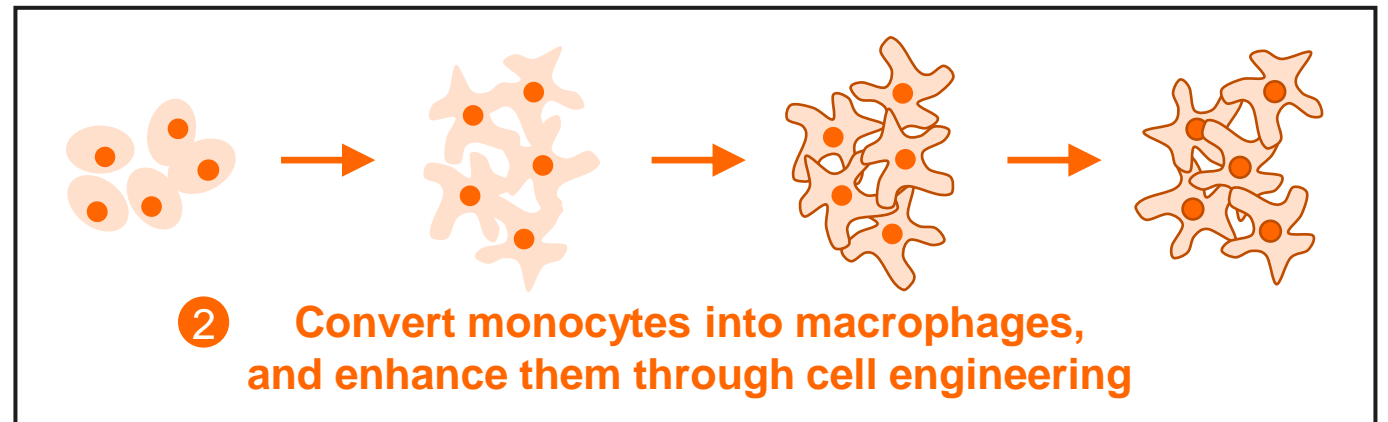
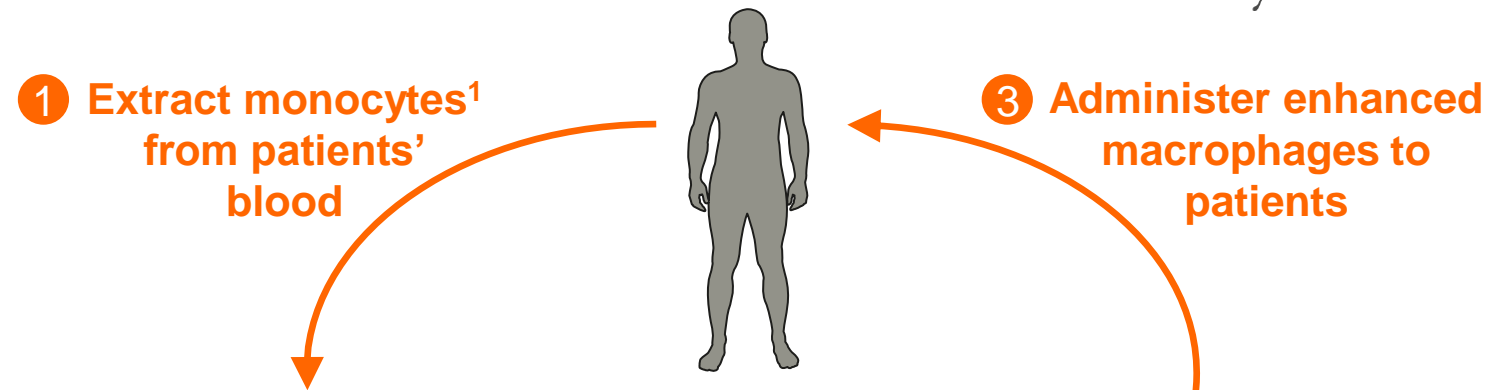
# Resolution: harnessing the healing properties of macrophages

Macrophage cells are a key immune cell type

Based on the research of Prof. Stuart Forbes and Prof. John Campbell from the University of Edinburgh

Built over a 3-year partnership between Syncona and the University:

- Research Collaboration launched in Jan 2018 to develop the technology further
- Series A commitment of £26.8m from Syncona
- Vision to develop an autologous macrophage cell therapy for treatment of liver cirrhosis
- Syncona partners Ed Hodgkin and Gonzalo Garcia to become CEO and Chief of Staff respectively



Resolution of inflammatory organ damage  
e.g., in a cirrhotic liver

1. Monocytes are precursor cells of macrophages

# Purespring: one of the first kidney AAV gene therapy companies



New Syncona company in area of deep domain expertise

Source	2019	Syncona identified opportunity to apply gene therapy to kidney diseases	 Engaged with world leading KOL, Prof. Moin Saleem, University of Bristol	 Worked with Prof Saleem to identify potential programmes where gene therapy could be applied
Investment and strategic fit	£45m	Series A financing; carefully tranchised with initial investment of £3.9m <sup>1</sup>	 Key components of a 'Syncona company': world-class founder, differentiated technology and attractive clinical setting	 Deep domain expertise in gene therapy and successful approach to building platform companies in the space

Foundation of one of the first AAV gene therapy company's globally to target the kidney

1 Investment in Purespring made post period end

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

Life science companies requires significant capital as they scale

## Syncona capital base

£700m

to fund growing life science portfolio and found new companies

£150m-250m

FY 2021 capital deployment

based on further investment in our existing portfolio and the opportunities we see in our investment pipeline



## Strong capital base is central to delivery of strategy and provides competitive advantage

- 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

# Financial performance

# Financial review

NAV of £1,366.7m, 203.4p; capital pool of £700.1m

## NAV increase of 9.6% in the six months to 30 September 2020

- Life science portfolio valued at £666.6m, a return of 24.8% in six months:
  - Performance driven by the increase in the Autolus share price and the write-up of Freeline in its recent Series C financing and IPO
  - Azeria closed resulting in a write off of £4.5m
- Capital base of £700.1m ; £68.9m of capital deployed in the six months
- Post period end:
  - £42.9m capital deployed
  - £10.7m write up of Achilles following its £52.7m Series C financing; Syncona retains a 34% holding

- Clinical stage
- Pre-clinical stage
- Drug discovery



Portfolio company	Ownership* %	31 March 2020 value £m (Fair value)	Net invested/returned the period £m	Valuation change in period £m	FX move ment £m	30 Sept 2020 value £m (Fair value)	Valuation basis (Fair value)**	% of NAV
Autolus	27	77.0	-	72.6	(5.9)	143.7	Quoted	10.5
FREELINE	48	150.7	18.6	65.1	(7.2)	227.2	Quoted	16.6
GYRSCOPE	80	73.0	9.0	-	-	82.0	Cost	6.0
Achilles	44	72.4	-	-	-	72.4	PRI	5.3
SwanBio	79	18.5	15.8	-	(1.3)	33.0	Cost	2.4
ANAVEON	51	12.3	-	-	0.1	12.4	Cost	0.9
QuellTX	69	8.3	11.6	-	-	19.9	Cost	1.5
RTX	79	1.4	0.4	-	-	1.8	Cost	0.1
AZERIA	60	6.5	-	(4.5)	-	2.0	Cost	0.1
YOMass	49	14.6	-	-	-	14.6	Cost	1.1
<b>Syncona Investments</b>								
neogene	11	-	11.4	-	0.4	11.8	Cost	0.9
Other investments		44.8	1.2	0.1	(0.3)	45.8		3.3
<b>Total</b>		<b>479.5</b>	<b>68.0</b>	<b>133.3</b>	<b>(14.2)</b>	<b>666.6</b>		<b>49.0</b>

\*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

# Outlook and summary

# Portfolio company outlook

Strong momentum in the portfolio with near term catalysts



Company	Status of pipelines	Next steps
	Four programmes in clinical trials	<ul style="list-style-type: none"> <li>– Progress on AUTO1 pivotal trial</li> <li>– Initial data in Phase I/2 AUTO4 and AUTO1/22 programmes CY2021</li> </ul>
	Two lead programmes in Phase I/II clinical trials, pipeline of preclinical programmes	<ul style="list-style-type: none"> <li>– Initiate pivotal study in haemophilia B in CY2021</li> <li>– Dose its next patient in its second programme in Fabry's when its safe to do so</li> </ul>
	Lead programme completed dose escalation in Phase I/II trial and initiation of Phase II trial	<ul style="list-style-type: none"> <li>– Initial data from its lead phase I/II trial targeting dry AMD FY2021</li> </ul>
	Two lead programmes in Phase I/II trials	<ul style="list-style-type: none"> <li>– Report initial data in H1 CY2021 from its melanoma and NSCLC studies</li> </ul>
	Lead programme in pre clinical development	<ul style="list-style-type: none"> <li>– Complete first clinical manufacturing batch in this financial year. Expand leadership team</li> </ul>
	Seeking to build pipeline of therapeutics	<ul style="list-style-type: none"> <li>– Initiation of pre-clinical development of lead programme</li> </ul>
	Nominated clinical candidate in lead programme	<ul style="list-style-type: none"> <li>– Initiation of phase I/II clinical trial FY2022</li> </ul>
	Pre-clinical development of lead programme	<ul style="list-style-type: none"> <li>– Company and leadership team build out</li> </ul>
Purespring	Pre-clinical development of lead programme	<ul style="list-style-type: none"> <li>– Company and leadership team build out</li> </ul>



# Building a sustainable, scalable model



Delivering strong risk-adjusted returns for shareholders

## Current portfolio: 2012-21

**Previous portfolio companies**

£592.6m proceeds from exits

Aggregate 6.2x multiple<sup>1</sup>

10  
High quality portfolio of leading life science companies

15  
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

<sup>1</sup>14MG, Nightstar, Blue Earth

# Appendix

# An expert multi-disciplinary team

## Our unique skill set



Scientific



Commercial



Company creation



Investment



### Investment committee

#### Nigel Keen

Co-founder and Chairman  
FIET, FCA



- Commercial and company creation
- Chairman of Oxford University Innovation, Oxford Academic Health Network, MedAccess

#### Martin Murphy <sup>1,2</sup>

Co-founder and CEO  
PhD



- Scientific, commercial, company creation and investment
- PhD in Biochemistry
- 20 years in venture capital and management consultancy

#### Chris Hollowood <sup>1</sup>

CIO

PhD



- Scientific, commercial, company creation and investment
- PhD in Organic Chemistry
- 19 years in venture capital

**Lorenz Mayr**  
Entrepreneur  
in Residence  
PhD



25 years experience

**Elisa Petris <sup>2</sup>**  
Partner  
PhD



13 years experience



**Edward Hodgkin <sup>1,2</sup>**  
Partner  
PhD



30 years experience



**Dominic Schmidt <sup>2</sup>**  
Partner  
PhD



9 years experience



**Magda Jonikas <sup>2</sup>**  
Partner  
PhD



10 years experience



**Alex Hamilton <sup>2</sup>**  
Partner  
PhD

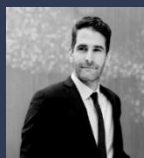


7 years experience



**Michael Kyriakides**  
Partner  
PhD

GYROSCOPE FREELINE  
5 years experience



**Freddie Dear <sup>2</sup>**  
Partner  
BSc



4 years experience



**Alice Renard <sup>2</sup>**  
Partner  
PhD



5 years experience



**Gonzalo Garcia <sup>2</sup>**  
Partner  
PhD



2 years experience



**Hitesh Thakrar**  
Partner  
BChem

27 years experience



<sup>1</sup> Portfolio company chairman

<sup>2</sup> Portfolio company board member/observer

# 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

# The Syncona Foundation

Supporting excellent charities that are meeting pressing needs within society, particularly those that are related to healthcare systems

Focused on cancer, neuro-degenerative diseases, gene therapy. Alongside other health and society related areas including mental health, bereavement and diversity

“The Syncona Foundation has been critical in equipping us with the ability to respond to emergencies. By allowing us to use donations flexibly, our frontline services have been able to respond quickly and effectively to the pandemic.”

Marie Curie

£31m

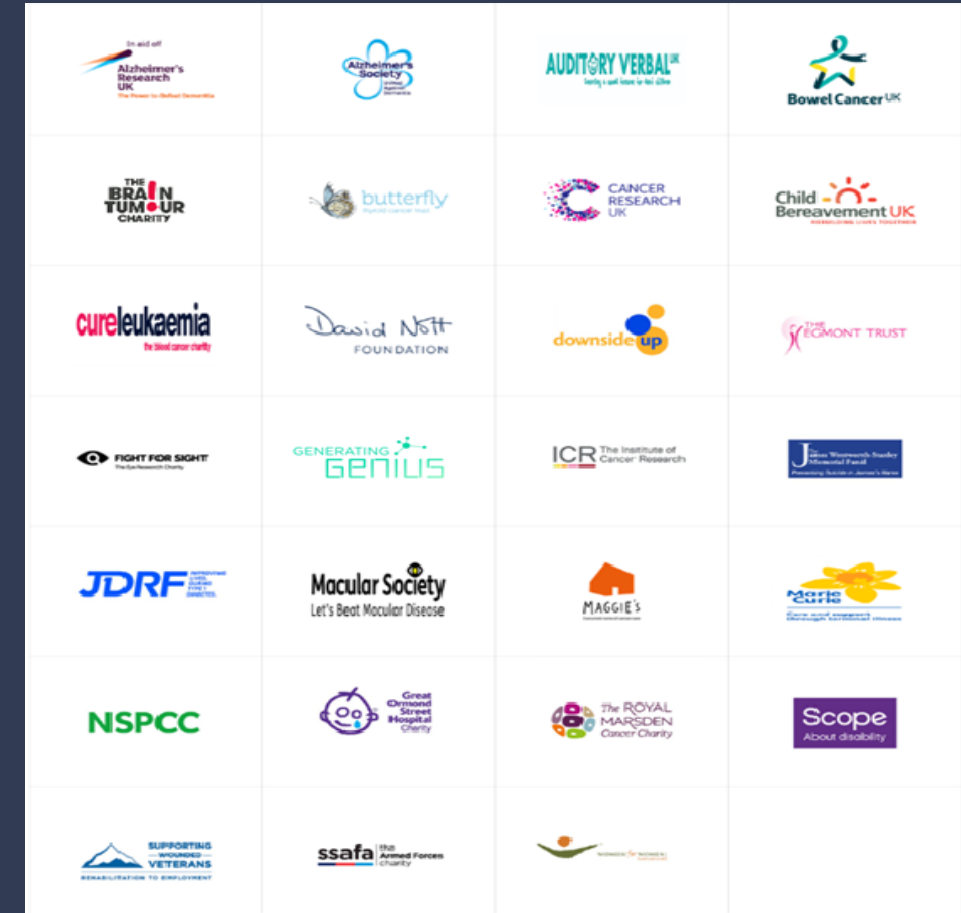
Donations since 2012

27

Charities donated to in 2020

0.35%

of Syncona's NAV donated on an annual basis



# Autolus Therapeutics

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

Board Seat	1
Date of Founding	2014
Date of Syncona investment	2014
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£106.0m
No. of employees	300+

Competitor Landscape



Key risks<sub>A</sub>

- Highly competitive environment
- Differentiated product requirement
- Complex manufacturing

Clinical pipeline\*\*

Research | Target ID | Pre- Clinical | Clinical

Auto 1 - aALL  
Auto 1/22 - pALL  
Auto 4 TCL



## Key management team

**Christian Itin**, Chief Executive (formerly CEO of Micromet)

**Martin Pule**, Founder and Chief Scientific Officer

**David Brochu**, Chief Technical Officer (formerly VP of Technical Operations at Kedrion SpA)

## Founders

**Martin Pule**, Clinical Senior Lecturer in the Dept. of Haematology at UCL Cancer Institute and Honorary Consultant in Haematology at University College London Hospital

For more information see <https://www.autolus.com/about-us/executive-team>

Unless stated all data at 30 September 2020

\* Source; Autolus Corporate Presentation January 2019

\*\* Clinical pipeline updated to reflect the announcement by Autolus on 6 Jan 2021 that it intends to partner its AUTO 3 programme in DLBCL. Autolus is also running two extension clinical trials in AUTO1, one in Non-Hodgkin Lymphoma and one in Primary CNS Lymphoma



## Investment thesis

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

## 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\*

## Market opportunity

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

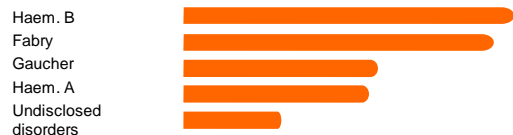
# Freeline Therapeutics

Clinical-stage, fully integrated, next generation, systemic AAV gene therapy company

Board Seat	1 (Chair)
Date of Founding	2015
Date of Syncona investment	2015
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£167.7m
No. of employees	200+
Competitor Landscape	The competitor landscape shows two main competitors: uniQure, marked with a '2', and Roche, marked with a '3'. Both are represented by their respective logos.
Key risks <sub>A</sub>	<ul style="list-style-type: none"><li>- Highly innovative concept in emerging space</li></ul>

## Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical



## Key management team

**Theresa Heggie**, Chief Executive (formerly Head of CEMEA at Alnylam Pharmaceuticals)

**Julie Krop**, Chief Medical Officer (formerly CMO at AMAG Pharmaceuticals)

**Jan Thirkettle**, Chief Development Officer (formerly led the establishment of GSK's cell and gene therapy platform)

**Professor Amit Nathwani**, Founder and Clinical and Scientific Adviser. Prof. Nathwani is renowned for his pioneering work on gene therapy for hemophilia B, and was first to show successful correction of bleeding diathesis in patients with severe hemophilia B

**Markus Hörer**, Founder and Chief Technology Officer (over 30 years' experience working in AAV biology, as well as over 23 years' experience in industrial vaccine and biologics development)

**Romuald Corbau**, Chief Scientific Officer (formerly Translational Lead at Spark Therapeutics)

## Founders

**Professor Amit Nathwani**, as above

**Markus Horer**, as above, brought the Rentschler manufacturing platform to Freeline

For more information see: <https://www.freeline.life/about-us/our-team/>

Unless stated all data at 30 September 2020

\*Source: Freeline Corporate Presentation January 2021

## Investment thesis

- To deliver curative gene therapies that will transform patients' lives.
- Deliver therapies for a broad pipeline of systemic diseases which require the delivery of high protein expression levels

## 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



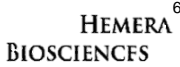



## Market opportunity\*

- 9,000 patient opportunity in lead programme in Haemophilia B
- 9,000 patient opportunity in Fabry's disease
- 6,000 patient opportunity in Gaucher's
- 38,000 patient opportunity in Haemophilia A



# Gyroscope Therapeutics

Developing gene therapy beyond rare disease by understanding the immune system & the role genetics play in a patient's risk of developing late stage AMD

Board Seat	2 (inc. Chair)
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	Series B
Stage	Clinical
Syncona capital invested	£82.0m
No. of employees	100+
Competitor Landscape	 <sup>5</sup>  <sup>4</sup>  <sup>6</sup>
Key risks <sub>A</sub>	<ul style="list-style-type: none"> <li>- Highly innovative concept in emerging space</li> </ul>
Clinical pipeline	<p>Research   Target ID   Pre- Clinical   Clinical</p> <p>Dry AMD –G.A (sub-set) </p> <p>Dry AMD –G.A (broad) </p> <p>Other inflammatory </p>



## Key management team

**Khurem Farooq**, Chief Executive (formerly SVP of Immunology and Ophthalmology at Genentech)

**Nadia Waheed**, Chief Medical Officer (formerly Director of the Boston Image Reading Center and Consultant at the New England Eye Center, Tufts University School of Medicine)

**Jane Hughes**, Chief Scientific Officer (formerly Senior Director of Integrated Drug Discovery at Charles River)

**Ian Pitfield**, SVP, Technical Operations (formerly project leadership in GSK's cell and gene therapy CMC platform)

## Founders

**Peter Lachmann**, Emeritus Sheila Joan Smith Professor of Immunology, University of Cambridge

**David Kavanagh**, Professor Of Complement Therapeutics at National Renal Complement Therapeutics Centre

**Andrew Lotery**, Professor of Ophthalmology within Medicine at the University of Southampton

## Scientific Advisory Board

**Keith Peters, Peter Lachmann, David Kavanagh, Alberto Auricchio, Pete Coffey, Clare Harris, Robert Maclaren, Matthew Pickering, David Steel and Timothy Stout**

For more information see: <https://www.gyroscoptx.com/scientific-advisory-board/>

## Investment thesis

- Seeking to take application of gene therapy beyond rare diseases

## Unmet medical need

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

## Market opportunity\*

- Initial population of an estimated 3.5 million people in the US & EU5 with geographic atrophy, late stage dry AMD



# Achilles Therapeutics

Differentiated cell therapy approach targeting solid tumours utilising Tumour Infiltrating Lymphocytes and clonal neoantigens to develop personalised treatments

Board Seat	1
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	Series B*
Stage	Clinical
Syncona capital invested	£49.0m
No. of employees	100+

## Competitor Landscape



## Key risks<sup>A</sup>

- Highly innovative concept in emerging space
- Complex manufacturing
- Increasing competition

## Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical



## Key management team

**Iraj Ali**, Chief Executive (former Syncona Partner)

**Karl Peggs**, Founder and Chief Medical Officer

**Sergio Quezada**, Founder and Chief Scientific Officer

**Edwin Moses**, Chair (formerly CEO at Ablynx)

## Founders

**Karl Peggs**, Professor of Transplant Science and Cancer Immunotherapy at UCL Cancer Institute, Scientific Director of the NIHR Blood and Transplant Research Unit for Stem Cells and Immunotherapies, and Clinical and Scientific Director of the Sir Naim Dangoor Centre for Cellular Immunotherapy at UCLH

**Mark Lowdell**, Director of the Centre for Cell, Gene & Tissue Therapeutics at the Royal Free and Professor of Cell & Tissue Therapy at UCL

**Charles Swanton**, Royal Society Napier Professor of Cancer and consultant thoracic oncologist at UCL Hospitals, Chief Clinician at Cancer Research UK (CRUK) and group Leader of the Cancer Evolution and Genome Instability laboratory at CRUK and the Francis Crick Institute

**Sergio Quezada**, Professor of Cancer Immunology and Immunotherapy at University College London Cancer Institute and CRUK senior research fellow

## Scientific Advisory Board

**Dr Elizabeth M. Jaffee**, **Dr Scott Antonia** and **Dr Christopher A. Klebanoff**

For more information, please see <https://achillestx.com/about-us>

Unless stated all data at 30 September 2020

\*In November 2020 Achilles completed a £52.7m Series C financing

\*\* Achilles analysis



## Investment thesis

- TIL's have shown convincing efficacy in solid tumours<sup>9</sup>
- Leveraging clonal neoantigens to develop patient specific immunotherapies and reduce risk of relapse

## Unmet medical need

- Lung cancer has limited treatment options and is the leading cause of cancer deaths<sup>10</sup>

## Market opportunity\*\*

- 234,000 patient opportunity in non-small cell lung cancer
- In 2020, over 196,000 patients expected to be diagnosed with melanoma in the US

# SwanBio Therapeutics

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

Board Seat	2 (inc. Chair)
Date of Founding	2018
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-Clinical
Syncona capital invested	£33.6m
No. of employees	25+

## Competitor Landscape



## Key risks<sup>A</sup>

- Challenging clinical endpoint
- Complex manufacturing

## Key management team

**Tom Anderson**, Chief Executive (formerly Chief Commercial Strategy Officer at Sage Therapeutics)

**Karen Kozarsky** – Chief Scientific Officer (former President of Vector BioPartners)

**Steven Zelenkofske** – Chief Medical Officer (former Chief Medical Officer of Achillion Pharmaceuticals)

**Scott McMillan**, Chief Technical Officer, (formerly Chief Executive Officer of Saliogen Inc.)

## Founders

**Florian Eichler**, Director of the Leukodystrophy Service and of the Center for Rare Neurological Diseases at Massachusetts General Hospital and Associate Professor of Neurology, Harvard Medical School

**Rachel Salzman**, Former Chief Science Officer of The Stop ALD Foundation

**Karen Kozarsky**, (as above)

For more information see: <https://www.swanbiotx.com/>

Unless stated all data at 30 September 2020

<sup>A</sup> Adrenomyeloneuropathy

<sup>\*\*</sup> SwanBio analysis



## Investment thesis

- Gene therapy has the potential be transformational in neurology<sup>14</sup>
- Lead programme targeting, AMN<sup>\*</sup>, an inherited neurodegenerative disease in which the causative gene is definitively known and well characterised
- One-off delivery mechanism and multiple tractable pipeline programmes

## Unmet medical need

- Hundreds of single gene disorders with poor or not treatment options
- Lead programme targeting one of the most common monogenic neurological disorders for a severely debilitating progressive movement disorder, with no available therapies

## Market opportunity<sup>\*\*</sup>

- AMN impacts 10,000-20,000 patients in the US and EU5

# Quell Therapeutics

Engineered cell therapy company addressing immune dysregulation

Board Seat	2 (inc. Chair)
Date of Founding	2018
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-Clinical
Syncona capital invested	£19.9m
No. of employees	25+

## Competitor Landscape



## Key risks<sub>A</sub>

- Highly innovative concept in emerging space

## Key management team

**Iain McGill**, CEO (formerly on the Executive Committee and as Head of Europe and Rest of World for Jazz Pharmaceuticals)

**Nathalie Belmonte**, SVP Research & Translation (formerly Chief Operating Officer at Promethera Biosciences)

**Luke Henry**, VP Operations & Corporate Development (formerly Senior Director of Business Development & Strategy at Neon Therapeutics)

**Bernd Schmidt**, VP Product Delivery (formerly MPD Leader at GSK Stevenage with overall accountability for the CMC development, governance and end to end supply chain)

## Founders

**Giovanna Lombardi**, Professor of Human Transplant Immunology at King's College London

**Marc Martinez-Llodella**, Senior Lecturer at King's College London

**Alberto Sanchez-Fueyo**, Head of the Liver Sciences Department at King's College London

**Hans Stauss**, Director of the Institute of Immunity & Transplantation at UCL

**Emma Morris**, Professor of Clinical Cell and Gene Therapy at UCL

**Elmar Jaeckel**, Co-Leader Liver Transplant program MHH and Group Leader Immune tolerance" in the Department of Gastroenterology, Hepatology and Endocrinology at Hannover Medical School.

For more information see: <https://quell-tx.com/about/>



## Investment thesis

- Current standard of care for prevention of solid organ transplant rejection is life-long immunosuppression which results in an array of serious long-term side effects significantly impacting patient quality of life<sup>17</sup>
- Potential pipeline to treat serious, chronic conditions mediated by the immune system
- Potential to be first-in-class in CAR-T-egs; an early mover in the space

## 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

# Anaveon Therapeutics

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

Board Seat	2 (inc. Chair)
Date of Founding	2017
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£11.7m
No. of employees	5+

## Competitor Landscape



## Key risks<sub>A</sub>

- Highly competitive environment

## Key management team

**Andreas Katapodis**, Chief Executive and Founder (former Director in the Autoimmunity, Transplantation & Inflammation group at the Novartis Institutes for BioMedical Research)

**Christoph Bucher**, Chief Medical Officers (Previously at Roche pRED Immunology, where he led the transition to the late-stage development of Crovalimab)

**Christoph Huber**, Chief Scientific Officer (previously held leadership positions at Roche, Pfizer and COI Pharmaceuticals)

## Founder

**Andreas Katapodis** (as above)

## Scientific Advisory Board

Jane K. Osbourn, Wolf H. Fridman and Robert Hawkins

For more information see: <https://anaveon.com/board/>



## Investment thesis

- Developing a selective IL-2 agonist with improved administration and tox burden
- Wide potential utility across multiple oncology indications in wider Markets<sup>23</sup>

## 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<sup>22</sup>

# OMass Therapeutics

Focused on structural mass spectrometry to discover novel medicines for immunological and genetic disorders

Board Seat	2 (inc. Chair)
Date of Founding	2017
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Drug discovery
Syncona capital invested	£14.6m
No. of employees	25+
Key risks	
- Pre-clinical and clinical attrition of potential drugs	

## Key management team

**Rosamund Deegan**, Chief Executive (former Chief Business Officer at Bicycle Therapeutics, where she established the company's Boston-based subsidiary)

**Ali Jazayeri**, Chief Scientific Officer (Previously Chief Technology Officer at Heptares)

**Jonathan Hopper**, VP of Platforms and Founder; worked with Carol Robinson on developing mass spectrometry

## Founder

**Professor Dame Carol Robinson**, Founder and Scientific Adviser; recognised for using mass spectrometry to further research into the 3D structure of proteins and their complexes and is the first female Professor in Chemistry at the University of Cambridge

For more information see: <https://omass.com/our-team/>



## Investment thesis

- 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

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.qcs-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.qcs-web.com/static-files/cd8dc1d9-6a7b-496d-933f-1a3b0bfb56a>
5. Cytokine Release Syndrome
6. Source: Autolus – see Autolus corporate presentation November 2019 <https://autolus.qcs-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://unique.com/gene-therapy/huntingtons-disease.php>
26. <http://r.amicusrx.com/news-releases/news-release-details/amicus-therapeutics-acquires-gene-therapy-portfolio-ten-clinical>
27. <https://www.prevailtherapeutics.com/>
28. <http://r.ptcbio.com/news-releases/news-release-details/ptc-therapeutics-announces-strategic-gene-therapy-licensing>
29. Source: [https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-immunosuppressants-solid-organ-transplantation\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-immunosuppressants-solid-organ-transplantation_en.pdf)
30. Source: <http://www.autoimmuneregistry.org/autoimmune-statistics>
31. <https://investor.sangamo.com/news-releases/news-release-details/sangamo-and-bcell-announce-completion-acquisition-sangamo>
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/>
34. <https://www.nektar.com/pipeline/rd-pipeline/nkr-214>
35. [https://www.roche.com/research\\_and\\_development/who\\_we\\_are\\_how\\_we\\_work/pipeline.htm](https://www.roche.com/research_and_development/who_we_are_how_we_work/pipeline.htm): RG7835
36. <https://investor.alkermes.com/news-releases/news-release-details/alkermes-announces-clinical-collaboration-fred-hutchinson-cancer>
37. <https://synthorx.com/therapeutics/>
38. <https://www.sonoma.bio.com/#home>