



Scaling for growth

Interim Results 2022

synconaltd.com



Image Freeline labs, Stevenage

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Agenda



01 Where we are today

02 The opportunity in the next 10 years

03 Scaling for growth

04 New companies and the pipeline

05 Interim results and portfolio update

06 Summary

Building the next generation of healthcare leaders

A clear purpose, vision and strategy



Purpose

To invest to extend and enhance human life

Vision

To unlock the potential of truly innovative science to transform patients' lives

Strategy

To create, build and scale a portfolio of globally leading life science companies that have the potential to transform the lives of patients and deliver strong risk-adjusted returns

Where we are
today

A long-term vision: 10 years of Syncona

Co-founded in 2012 with the Wellcome Trust, our purpose is to invest to extend and enhance human life

Building global leaders

19

Syncona portfolio companies since 2012 foundation

12

Number of companies in the portfolio today

1,200+

Number of employees across Syncona portfolio

Our growing track record

26%

IRR since 2012; 1.6x multiple on cost across whole portfolio¹

£965m

Syncona capital deployed since 2012

£933m

Generated from three successful exits; 4.6x multiple of cost²

Patient impact

165k

Patients benefitting from Blue Earth's Axumin™

3

Products to pivotal trial, with 15 programmes progressed into the clinic

383k

Total Addressable Market (TAM) for the clinical-stage portfolio³

1- Includes sales of Nightstar, Blue Earth, Gyroscopic and closure of 14MG and Azeria, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis

2 - Includes sales of Nightstar, Blue Earth, upfront proceeds from sale of Gyroscopic, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis

3 - Total addressable market calculated from estimated new patients diagnosed per annum in lead indications of clinical stage portfolio companies, as defined by the company or the Syncona investment team estimate

All financial data at 30 September 2022, employee figures as at 31 March 2022

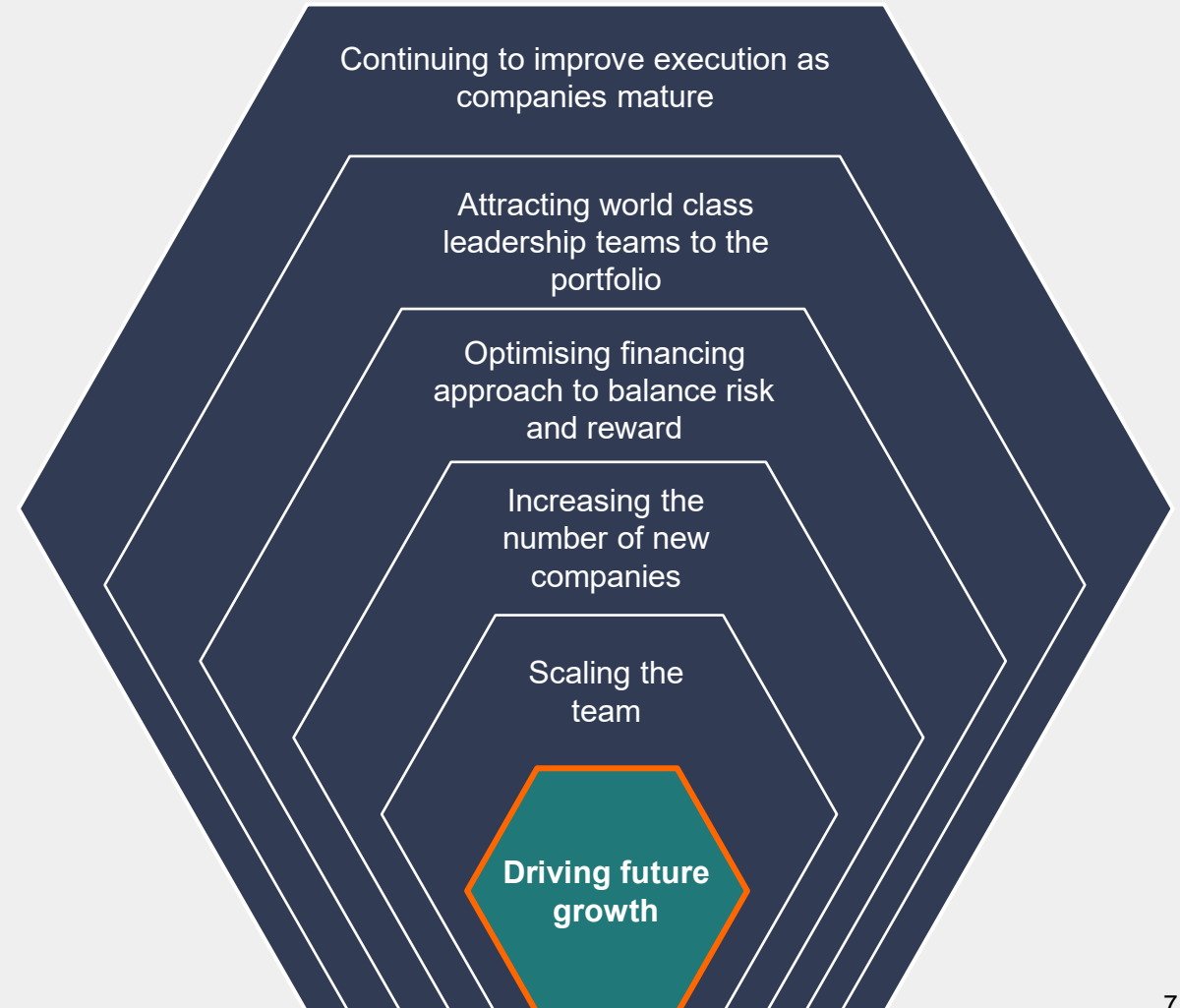
Building on our success

Leveraging our successes and applying the lessons learnt from last 10 years to drive the business forward over the next decade

The Syncona model

- Core team skill is to identify science and create companies with the potential to deliver transformational treatments
- We scale these businesses and their teams to be globally competitive
- Strength of balance sheet provides a differentiated market position through the cycle

Lessons
learnt



The opportunity in the
next 10 years

Well positioned to capture strong market opportunity



Syncona believes the out return in life science is weighted towards late development and product approval

Leveraging a world-class scientific research base

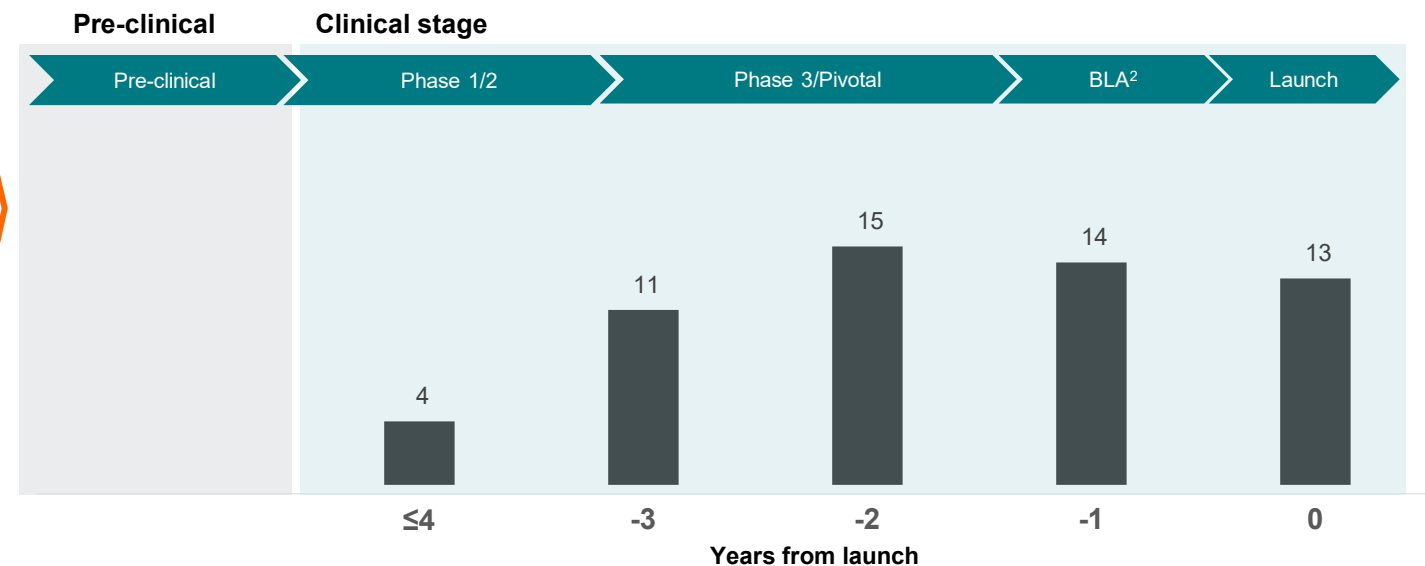
- Syncona is located within the richest concentration of life science research universities and also has a global network



Building companies capable of seizing the commercial opportunity of translating science to products

- Syncona has demonstrated a differentiated company building capability
- Underpinned by a strong capital base, Syncona is able to bridge the gap between scientific research and commercial opportunity

Global transaction volume by expected years to market; Number of global biopharma deals greater than \$1bn¹ from 2005 to 2021



¹ Source Centerview, BCIQ, Syncona analysis

² Biologic license application

Scaling the business to continue to deliver strong returns

Growing NAV by increasing the size of the life science portfolio reduces cash impact for shareholders

Key metrics

Expanding the portfolio is central to growing NAV to £5bn

- To date, we have added 1-2 new companies p.a to the portfolio
- To grow NAV, we believe we need to add 3 new companies p.a to deliver an expanded life science portfolio of 20-25 companies
- We will be targeting top quartile returns for the life science portfolio
- Financing strategy will support our expanded portfolio

Companies founded per year

Capital base underpins the delivery of strategy

- Runway of 2-3 years of capital provides the investing confidence to build and scale companies strategically to deliver long-term value
- As a result a minimum amount of balance sheet capital is required
- Growing the NAV by increasing the size of the life science portfolio reduces impact of cash for shareholders

No. of years funding

Progressing to self-sustainable financing

- Ambition to fund companies on sole basis to proof-of-concept on a selective basis
- Optimised financing strategy with syndicated options has the potential to deliver more frequent NAV uplifts and improve risk profile of portfolio
- Recycling of exit proceeds into the portfolio will support us in maintaining a runway of 2-3 years of capital and deliver further growth

Risk-adjusted returns

Syncona 2032



Unlocking truly innovative science to transform patients' lives

**Leveraging our
successful
platform and
model built
over the last 10
years**

What will we have changed in 2032?

- Business of scale with expanded portfolio
- Increase in rate of company creation to three per year
- Institutionalised operational model for scale and efficiency
- Expanded team with additional capabilities
- Demonstrated differentiated capability to build companies to pivotal entry
- Demonstrated model repeatability
- Progressive balance sheet efficiency and more established self sustained financing

Strategic optionality beyond 2032

- Continue to build more companies where Syncona has significant ownership positions that have taken products to market
- Business of scale and improved capital access allows opportunities to hold companies for longer on sole basis

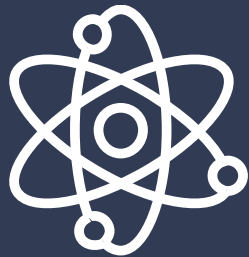
Scaling Syncona to £5bn

We are updating our 10 year targets with increased ambition



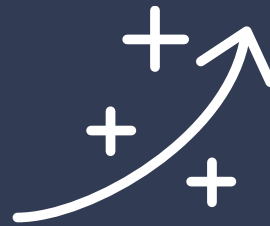
3

New companies
created p.a



20-25

Portfolio of leading
life science companies



3-5

Companies to product
approval where Syncona
has a majority
shareholding



£5bn

Net Assets

Scaling for growth

Embedding a differentiated model

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

Create

Proactively source **world-class** science – bringing commercial vision

Focus on dramatic impact for patients in areas of high unmet need

Select products a biotech company can credibly take to approval

Build

Leverage expertise and track record to drive success

Take **long-term decisions** consistent with a company taking product to approval independently

Attract and retain the best global talent

Early decision taken on financing approach for these companies to **ensure level of capital necessary** with appropriate risk profile for Syncona

Scale

Scale ambitiously, maintain significant ownership positions through the clinic; option to fund to market

Ownership position provides **strategic influence**; flexibility and control

Selective approach to funding companies to market on a sole basis (1-2 over a cycle)

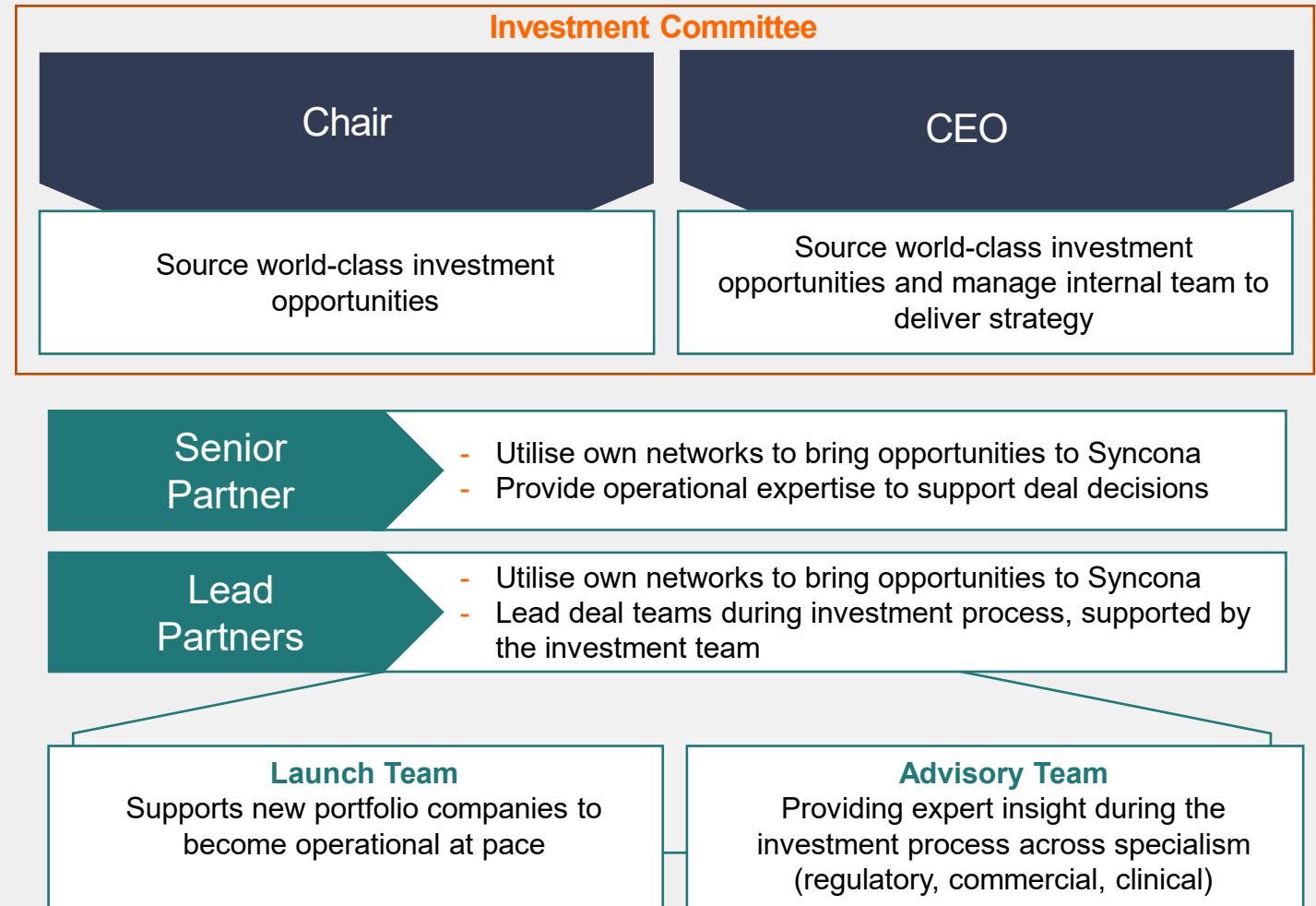
Strength of our balance sheet protects against risk of being a forced seller

Evolving and leveraging the investment team

Reviewed the company's organisational structure to enable the business to scale

- Chris Hollowood is stepping up into the role of CEO, leading delivery of growth plans for next 10 years and managing team, alongside creating new companies and managing portfolio companies
- Martin Murphy will be Chair of SIML, continuing to source and drive the creation of new companies, alongside managing portfolio companies
- Ed Hodgkin has been promoted to the role of Senior Partner, with Magdalena Jonikas and Elisa Petris promoted to Lead Partners
- Will be further expanding the team to support growth
- Company launch team and advisory team now formed

Team behind the investment process
delivering 3 new deals p.a.



Institutionalising the operating model



Leadership Team and Senior Partners leverage their functional expertise to support the Lead Partners and portfolio throughout the development cycle

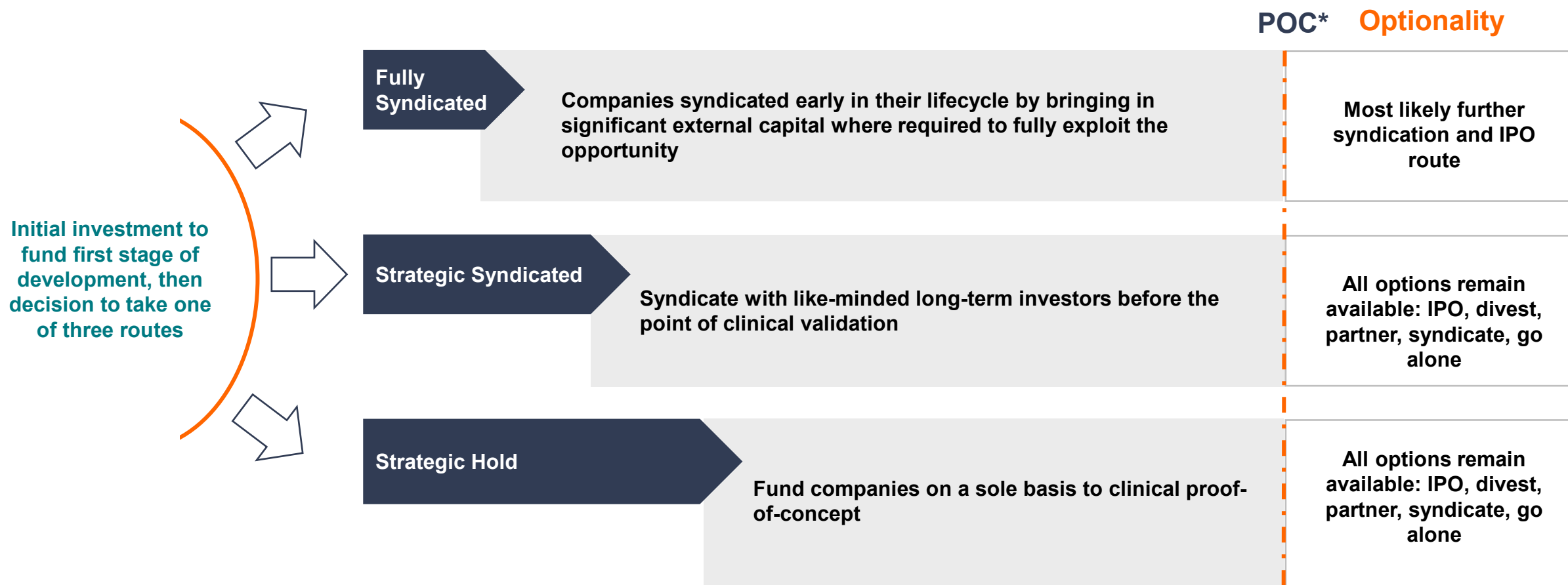
More pace and bandwidth across the team



Our financing strategy



Providing our shareholders with exposure to a set of high-growth companies, both private and public



* Proof of concept. Syncona view is that this is the point when a company has generated a maturing clinical data set that validates its investment thesis

New companies and the pipeline

An exciting investment landscape

Creating commercial concepts around ground-breaking science has always been a point of differentiation for Syncona

- Over the last 10 years, we have been an early mover in a significant technology disruption (cell and gene therapy)
- The technology disruption meant that there were often no incumbents where we were operating – now institutionalising best practice for pace is critical
- We are focused on targets that have been de-risked by genetics or data - lots of opportunities to apply this position across biologics and small molecules
- Significant opportunity in cell and gene therapy remains

Syncona identifies science that will make a difference for patients in areas of high unmet need



The diagram consists of three teal hexagons arranged horizontally. To the left of the first hexagon is an orange bracket-like shape pointing towards it. The text 'Syncona identifies science that will make a difference for patients in areas of high unmet need' is positioned to the left of this bracket. Each hexagon contains white text representing a focus area.

Biologics

**Cell and Gene
therapy**

Small molecules

AGTC

Opportunity to apply Syncona's differentiated strategy to a late-stage asset and drive value for shareholders

A clinical-stage gene therapy business in an area where Syncona has unique expertise

- Recommended all-cash tender offer to acquire all outstanding shares of Applied Genetic Technologies Corporation (AGTC) for \$0.34 per share, valuing AGTC at \$23.5m
- Potential for up to an additional \$50.0m in contingent value rights payable on the achievement of specified milestones
- We believe AGTC's X-Linked Retinitis Pigmentosa (XLRP) programme has the potential to be a best-in-class product
- XLRP programme has orphan drug designations from the FDA and European Commission
- Syncona able to leverage its previous experience with Nightstar and Gyroscope



Syncona's ideal characteristics for a scientific asset

Defined patient segments / target market	✓
Defined, commercial lead programme with commercial potential	✓
Therapeutic areas where Syncona has deep domain expertise	✓
Transformational efficacy in area of high unmet need	✓
Accelerated development and regulatory pathways	✓
No current incumbent	✓

Discovery

IND enabling

Phase I/II

Phase II/III

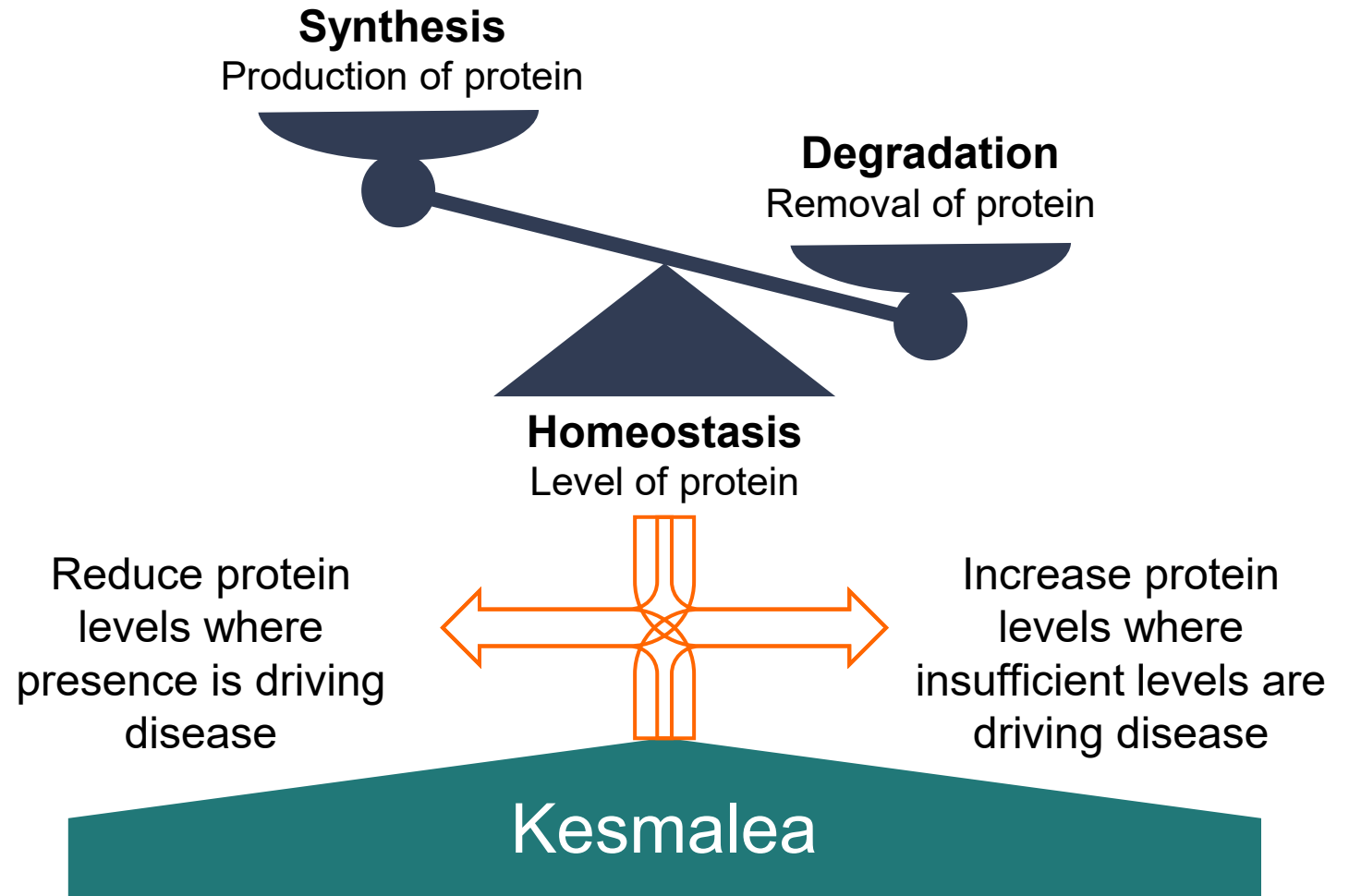
XLRP programme

Kesmalea Therapeutics

Small molecule drug discovery platform
focused on protein homeostasis

An opportunity to create a new generation of oral drugs addressing diseases through modulating protein homeostasis

- £16.0m commitment in a £20.0m Series A financing alongside Oxford Science Enterprises
- Founded by Dr Harry Finch, a world-class chemist and co-inventor of GSK's Serevent™
- Protein homeostasis company which utilises its small molecule drug discovery platform to address some of the challenges in developing oral therapeutics against targets in areas of high unmet medical need
- Syncona Lead Partner Magdalena Jonikas led the launch of the company and will join the Board of Directors



Interim results and portfolio update

Positive clinical and operational progress across portfolio

Meaningful clinical milestones approaching in the next 6-12 months

7

Clinical read outs

- Encouraging safety and early signs of potential efficacy data from Anaveon's IL-2 selective agonist

12

Clinical milestones expected by end of CY 2023

- Initial results from Phase II pivotal trial of Autolus' lead programme obe-cel in Q4 2022 with data in H1 2023

3

Companies expected to enter the clinic in next six months

- SwanBio, Quell and Neogene

Cell therapy

- Focused on key cell types and T-cell biology backed by leading academics
- In areas of high unmet medical need

CAR-T

Autolus

T-Reg

QuellTx

TCR

neogene

TILs

ACHILLES

Macrophage

RTx

iPSC cells

Clade Therapeutics

Gene therapy

- Operating in key tissue compartments backed by leading academics
- In areas of high unmet medical need

Systemic

FREELINE

CNS

SwanBio

Renal

purespring

Biologics

- T-cell immunotherapy - selective IL-2 agonist, wide potential utility across multiple oncology indications

Selective IL-2 agonist

ANAVEON

Small molecule

- Small molecule and drug discovery platforms focused on targets in immunological and orphan diseases and addressing some of the challenges in developing oral therapeutics

Small molecule therapeutics

OMass

Kesmalea

Anaveon

Harnessing the power of IL-2 for patients with solid tumours

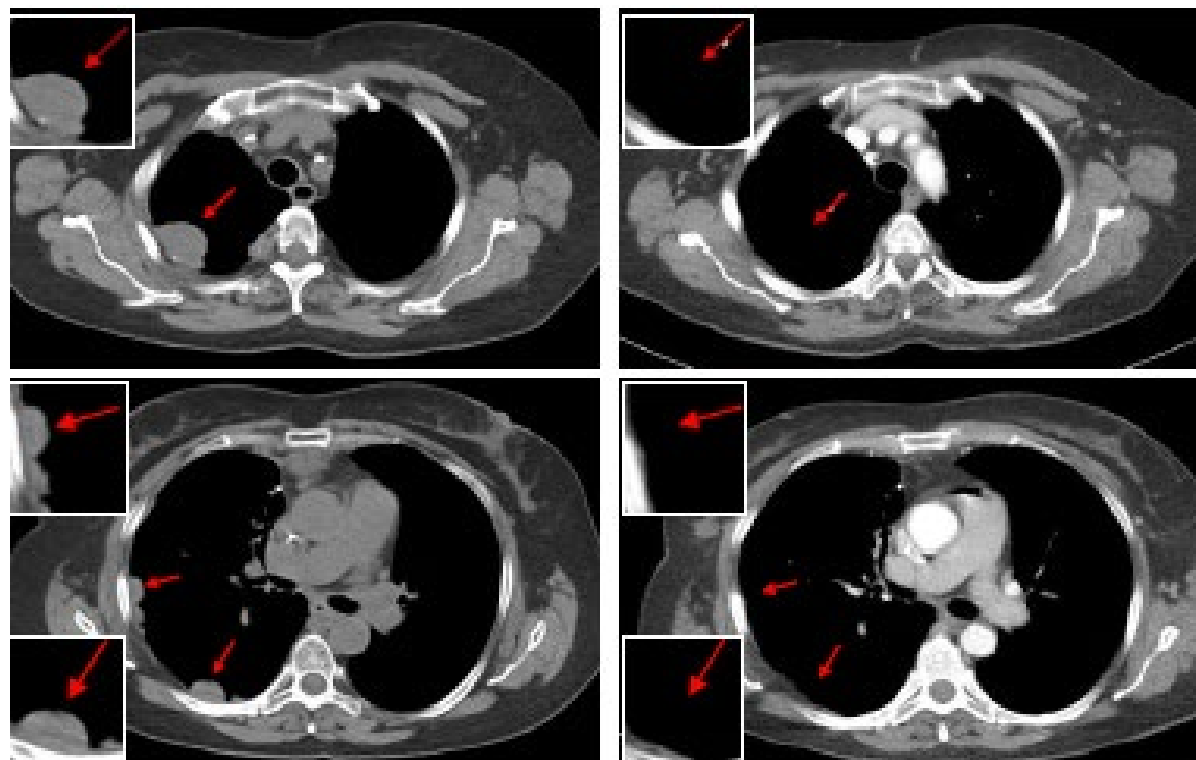
Positive clinical data demonstrating the potential for best-in-class agent

- ANV419 therapy currently in Phase I/II dose escalation study
- All patients in the trial have advanced solid tumours with disease progression in at least the last three months
- Data presented recently underlines strong safety and efficacy potential of the drug
- 66% of patients achieving at least disease stabilisation at ≥ 108 $\mu\text{g/kg}$ dose level

NSCLC patient, who continues ANV419 treatment, shows sustained and deepening response with 56% reduction in sum of diameter of target lesions, at 12 weeks after treatment initiation

11 May 2022

08 August 2022



SITC poster 631. Patient shown is 63 year old female with relapsed refractory non small cell lung cancer (NSCLC). Cut off date 20th September 2022

Financial performance

NAV performance driven by positive impact of foreign exchange across the portfolio and capital pool

**Net assets of £1.37bn (203p)
+4.3%**

- NAV performance driven by £112.6m positive impact of foreign exchange across the portfolio and capital pool
- 3.9% return from life science portfolio, (£49.2m) decline in share prices of listed outweighed by positive foreign exchange movements
- Performance of listed portfolio continues to be impacted by the challenging market backdrop

£603m
Value of life
science
portfolio

**Continue to expect deployment to
be £150m-250m in the financial
year**

- £58.6m deployed in the first half; majority of investment expected to come in the second half in existing and new companies
- £69.0m of uncalled commitments to portfolio at 30 September
- Continue to target 2-3 years' minimum capital required, as we look to increase the cadence of new deal creation
- Strength of the balance sheet a strategic advantage in this environment

£763m
Capital pool

Managing our capital pool and cost base

Continue to balance liquidity and access to capital pool to ensure we are able to fund our life science portfolio

Disciplined and rigorous financial approach

- Primary focus is on liquidity, continue to hold 12-24 months of liquidity in cash and treasuries; benefitting from yields on treasuries
- To manage inflationary risk, we have introduced a number of low risk, low volatility multi-asset funds with daily liquidity to the capital pool
- Approximately £200m has been invested in these funds, managed by three separate managers
- 36% of capital pool in foreign denominated currencies, predominantly USD with this resulting in an unrealised gain of £48.8m in the capital pool during the half
- We continue to closely monitor the macro environment to ensure that the capital pool is appropriately managed
- Growing our team and expanding our advisory capabilities in the next two years will mean a modest corresponding increase to our cost base
 - Costs will continue to be managed prudently - expect SIML costs for FY2022/3 to be £12.5m-£13.5m (c1% of NAV)

£763m

In the capital pool

36%

Of capital in foreign
denominated
currencies

12-24

Months of liquidity in cash
and treasuries

Summary

Scaling for the next phase of growth

Ambitious growth plans underpinned by a strong track record and continued strong progress across the portfolio

Our track record

£965m

Invested in life science portfolio since foundation in 2012

26%

Gross IRR since inception²

19

Portfolio companies founded or invested in¹

1.6x

Gross MOIC²

15

Programmes into the clinic

£41m

Donated to charity



3

New companies p.a



20-25

Portfolio of leading life science companies



3-5

Companies to product approval where Syncona has a majority shareholding

Rolling ten year targets

Our vision for 2032

£5bn

Net Assets

1 - Includes sales of Blue Earth, Nightstar and Gyroscopic, closure of 14MG and Azeria, merger of Orbit and Gyroscopic; CEGX now an investment
2 - Includes sales of Nightstar, Blue Earth, and Gyroscopic, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
All financial data at 30 September 2022

Appendix 1 – Syncona team

An expert multi-disciplinary investment team



Our unique skill set



Scientific



Commercial



Company creation



Investment

Martin Murphy ^{1,2}
Co-founder, CEO
and Chair, SIML
PhD

Quellx ANVEON
neogene Autolus CLADE
21 years' experience YOMass



Chris Hollowood ¹
CIO, SIML
PhD

FREELINE purspring
20 years' experience SwanBio



Investment
Committee

92%
of investment
team with PhDs

150+
Years of
experience in life science

Edward Hodgkin ^{1,2}
Senior Partner
PhD

RTx
YOMass

31 years' experience



Elisa Petris ²
Lead Partner
PhD

neogene Quellx
ACHILLES

14 years' experience



Magda Jonikas ²
Lead Partner
PhD

YOMass Kesmalea

11 years' experience



Alex Hamilton ²
Investment Partner
PhD

ANVEON SwanBio

8 years' experience



Michael Kyriakides ²
Investment Partner
PhD

FREELINE purspring
CLADE
THERAPEUTICS

6 years' experience



Gonzalo Garcia ²
Investment Partner
PhD

RTx

7 years' experience



Alice Renard ²
Investment Partner
PhD

ANVEON purspring
6 years' experience



Raghd Rostom ²
Associate Partner
PhD

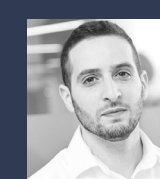
Kesmalea

3 years' experience



Nathaniel Dahan
Associate Partner
PhD

3 years' experience



Hitesh Thakrar
Partner
BChem

28 years' experience



Investment team supported by experts in life sciences and company building



Markus John

- Joined in July 2021
- Former Global Medical Affairs Franchise Head at Roche

Lisa Bright

- Joined in January 2022
- Most recently President International and Chief Commercial and Corporate Affairs Officer for Intercept Pharmaceuticals

Gwenaelle Pemberton

- Joined in July 2022
- Former Vice President of International Regulatory Affairs at Gilead

Ben Woolven

- Joined in February 2022
- Former Senior Director Medical, Regulatory, and Quality, Global Head of Transformation Operations, GSK

Leveraging the strength of clinical and operational experts



Scientific



Commercial



Regulatory



Business strategy

Markus John
CMO, Head of R&D
MD



21 years' experience

Lisa Bright¹
Commercial Advisor
BSc



33 years' experience

Gwenaelle Pemberton
Regulatory Advisor
MSc



33 years' experience

Ben Woolven
Business Strategy
and Operations Partner
PhD



20 years' experience

100+












Years of
experience in
life science

Appendix 2 – Portfolio companies

Portfolio company outlook

Upcoming milestones across the portfolio



Company	Status of pipelines	Next steps
	Five ongoing clinical trials	<ul style="list-style-type: none">– Progress pivotal study obe-cel / adult ALL, with initial results in Q4 CY2022 with data expected in H1 CY2023. Longer term follow up from ALLCAR19 Phase I trial expected Q4 CY2022– Publish longer term follow up data in obe-cel in B-NHL, AUTO1/22 in paediatric ALL, and AUTO4 in PTCL in Q4 CY2022
	Lead Fabry programme in Phase I/II trial	<ul style="list-style-type: none">– Initial safety and efficacy data from the second cohort of the Fabry study expected in H1 CY2023– Dosing in Gaucher study expected in Q4 CY2022, with initial data in H1 CY2023
	Two lead programmes in Phase I/IIa trials	<ul style="list-style-type: none">– Expect to publish interim data from VELOS™ Process 2 manufacturing in its Phase I/IIa NSCLC and melanoma therapies at ESMO IO in December 2022
	Nominated lead programme in the clinic	<ul style="list-style-type: none">– Publish further data from Phase I/II trial in Q3 CY2023, following data released at a conference in November 2022
	Lead programme in pre-clinical development	<ul style="list-style-type: none">– Expect to dose first patient in lead programme targeting liver transplant in H1 CY2023
	Lead programme in pre-clinical development	<ul style="list-style-type: none">– Expects to enter the clinic with lead programme targeting AMN in Q4 CY2022
	Lead programme in pre-clinical development	<ul style="list-style-type: none">– Expect to enter the clinic in H1 CY2023
	Pre-clinical development of lead programme	<ul style="list-style-type: none">– Company and leadership team build out
	Pre-clinical development	<ul style="list-style-type: none">– Company and leadership team build out, identify lead programme
	Pre-clinical development	<ul style="list-style-type: none">– Company and leadership team build out, identifying pipeline targets
	Five programmes identified for pre-clinical development	<ul style="list-style-type: none">– Progress of lead programme into lead optimisation

Financial review



Clinical



Pre-clinical



Drug discovery



Portfolio company	Fully diluted ownership %	30 March 2022 value £m (fair value)	Net invested/returned in the period £m	Valuation change	FX movement	30 September 2022 value £m (fair value)	Valuation basis (fair value) ^{1,2}	% of NAV
ANAEON	40.7%	59.8	-	-	6.0	65.8	PRI	4.8%
Autolus	18.9%	62.0	-	(30.2)	5.6	37.4	Quoted	2.7%
FREELINE	51.3%	32.3	-	(12.3)	3.5	23.5	Quoted	1.7%
ACHILLES THERAPEUTICS	24.5%	24.8	-	(5.7)	3.3	22.4	Quoted	1.6%
SwanBio THERAPEUTICS	79.9%	75.1	15.6	0.7	14.3	105.7	Cost	7.7%
QuellTX	39.0%	81.4	-	-	14.4	95.8	PRI	7.0%
purespring	82.9%	18.5	16.6	-	-	35.1	Cost	2.6%
RTx	77.4%	10.4	12.6	-	-	23.0	Cost	1.7%
neogene THERAPEUTICS	7.9%	14.5	-	-	2.6	17.1	Cost	1.3%
CLADE THERAPEUTICS	16.4%	11.4	-	-	2.0	13.4	Cost	1.0%
YOMass THERAPEUTICS	34.4%	34.7	9.0	-	-	43.7	PRI	3.2%
Kesmalea	37.1%	-	4.0	-	-	4.0	Cost	0.3%
Investments		100.0	(0.4)	4.0	12.1	115.7		8.5%
Capital pool		784.9	(68.5)	(1.9)	48.8	763.3		55.9%
Total		1,309.8				1,365.9		100.0%

1 The basis of valuation is stated to be "Cost", this means the primary input to fair value is capital invested (cost) which is then calibrated in accordance with our Valuation Policy. 2 The basis of valuation is stated to be "PRI", this means the primary input to fair value is price of recent investment which is then calibrated in accordance with our Valuation Policy

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	£124.0m
No. of employees	350+

Competitor Landscape



Key risks

- Highly competitive environment
- Differentiated product required
- Complex manufacturing and supply chain

Clinical pipeline

Research | Target ID | Pre-Clinical | Clinical

Obe-cel – aALL
AUTO4 – TCL
AUTO1/22 – pALL
Obe-cel – B-NHL
Obe-cel – PCNSL



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)

Edgar Braendle, Chief Development Officer (formerly CMO at Sumitomo Dainippon Pharma Oncology)

Lucinda Crabtree, Chief Financial Officer (formerly Woodford, Panmure Gordon and Goldman Sachs)

Founder

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 financials at Sep 2022, employee numbers March 2022

* Source; Autolus Corporate Presentation August 2022

Key competitors and risks: Syncona team view



Investment thesis

- Syncona believes obe-cel has a differentiated safety profile and improved persistence to address limitations of current T cell therapies
- AUTO4 targeting T-cell lymphoma, a setting where there are currently no approved T cell therapies and substantial unmet clinical needs

Unmet medical need

- In lead programme of obe-cel, only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care*

Market opportunity*

- 8,400 patients p.a. in lead programme of adult ALL (estimated new patients globally diagnosed per annum)
- Estimated relapsed refractory adult ALL patient population, US/EU: 3,000

Anaveon Therapeutics

Exploiting the power of cytokines to orchestrate immune responses by using protein engineering with the potential to create safe and effective treatments for various diseases

Board Seat	2 (inc. Chair)
Date of Founding	2017
Date of Syncona investment	2019
Valuation basis	Series B
Stage	Clinical
Syncona capital invested	£39.9m
No. of employees	20

Competitor Landscape



Key risks

- Multiple players and highly competitive
- Strategy for differentiation and clinical / commercial positioning
- Clinical risk

Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical

ANV419 – multiple tumour types



Key management team

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

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

Gary Phillips, Chief Business Officer (previously President and CEO, OrphoMed)

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

Co-founder

Andreas Katopodis (as above)

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

Unless stated all financials at Sep 2022, employee numbers March 2022

Key competitors and risks: Syncona team view

* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4938354/>

** <https://www.cancernetwork.com/view/managing-toxicities-high-dose-interleukin-2>



Investment thesis


- Developing a selective IL-2 agonist with improved administration and toxicity burden
- Wide potential utility across multiple oncology indications in wider markets*

Unmet medical need

- Human Interleukin 2 “IL-2” approved as a medicine for the treatment of metastatic melanoma and renal cancer, but with a cumbersome administration schedule and significant toxicity**

Freeline Therapeutics

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

Board Seat	1 (Chair)
Date of Founding	2015
Date of Syncona investment	2015
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£183.1m
No. of employees	c.200
Competitor Landscape	
Key risks	<ul style="list-style-type: none"> - Highly competitive environment - Differentiated product required - Complex manufacturing



Key management team

Michael Parini, CEO (former Chief Administrative, Legal and Business Development Officer at Vertex)

Pamela Foulds, CMO (formerly CMO of Aegerion Pharmaceuticals)

Henning Stennicke, CSO (formerly Vice President of Global Development, Biorpharm, Novo Nordisk)

Alison Long, SVP, Head of Clinical Development (formerly Head of Clinical Research and Development, Spark Therapeutics)

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)

James Bircher, Chief Technical Operations Officer (formerly CTO at Abeona Therapeutics Inc.)

Mark Baldry, Chief Commercial Officer (formerly Senior VP of Global Marketing & Commercial Operations at Amicus Therapeutics Inc)

Paul Schneider, CFO (former SVP Finance, Exo Therapeutics)

Founders

Professor Amit Nathwani. Professor of Hematology at UCL since November 2011

Markus Hörer, as above, brought the Rentschler manufacturing platform to Freeline

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

Investment thesis

- To deliver therapies for a broad pipeline of systemic diseases which require the delivery of high protein expression levels, with the aim of curing and transforming patients' lives.

Unmet medical need

- Significant number of systemic diseases with genetic drivers which have poor or no treatment options
- Current standard of care in Fabry disease is Enzyme Replacement Therapy (ERT); requires regular administration with protein activity remaining unstable

Market opportunity*

- 16,000 patients in Fabry disease
- 18,000 patients in Gaucher disease

Unless stated all financials at Sep 2022, employee numbers March 2022

*Source: Freeline Corporate Presentation August 2022. The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy

Key competitors and key risks: Syncona team view

Achilles Therapeutics

Differentiated cell therapy approach targeting solid tumours utilising AI-enabled bioinformatics and precision Tumour Infiltrating Lymphocytes to target clonal neoantigens for personalised treatments

Board Seat	-
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£60.7m
No. of employees	250+

Competitor Landscape



Key risks

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

Clinical pipeline

Research | Target ID | Pre- Clinical | Clinical



1 Clonal neoantigen T cell

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, Dr Ben Creelan, Dr Markwin Velders, Dr Cassian Yee

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

Unless stated all financials at Sep 2022, employee numbers March 2022

Key competitors and risks: Syncona team view

* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131487/pdf/nihms286994.pdf>

** <https://seer.cancer.gov/statfacts/html/lungb.html>

*** <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2022/2022-cancer-facts-and-figures.pdf>



Investment thesis

- TILs have shown convincing efficacy in solid tumours*
- Leveraging clonal neoantigens to develop patient specific immunotherapies to increase response rates and reduce risk of relapse

Unmet medical need

- Lung cancer has limited treatment options and is the leading cause of cancer deaths

Market opportunity

- Over 236,000 patients expected to be diagnosed with lung cancer in the United States in 2022**
- Over 197,000 patients are expected to be diagnosed with melanoma in the US in 2022***

Quell Therapeutics

Engineered cell therapy company addressing immune dysregulation

Board Seat	2 (inc. Chair)
Date of Founding	2019
Date of Syncona investment	2019
Valuation basis	Series B
Stage	Pre-Clinical
Syncona capital invested	£61.4m
No. of employees	110+

Competitor Landscape



Key risks

- Highly innovative concept in emerging space
- Complex manufacturing

Key management team

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

Tracey Lodie, CSO (former CSO at Gamida Cell)

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)

Marc Martinez-Llordella Founder and Vice President Biology (former Senior Lecturer at King's College London)

Founders

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

Marc Martinez-Llordella, (as above)

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

- Potential pipeline to treat serious, chronic conditions mediated by the immune system
- Potential to be first-in-class in CAR-Tregs; an early mover in the space

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 significantly impacting patient quality of life*

Market opportunity

- 15,000 liver transplants p.a across US and Europe**

Unless stated all financials at Sep 2022, employee numbers March 2022

Key competitors and risks: Syncona team view

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

** Source: OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015

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 B
Stage	Pre-Clinical
Syncona capital invested	£90.7m
No. of employees	50+

Competitor Landscape



Key risks

- Slowly progressing disease
- Complex manufacturing
- Clinical risk

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 and VP of R&D at RegenX)

David Weiner– Chief Medical Officer (founder of Bend Therapeutics)

Scott McMillan, Chief Technical Officer, (formerly Chief Executive Officer of Saliogen Inc. and Chief Operating Officer at UniQure)

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/>



Investment thesis

- Gene therapy has the potential to be transformational in neurology
- Lead programme targeting AMN*, 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 no treatment options
- Lead programme targeting one of the most common monogenic neurological disorders, a severely debilitating progressive movement disorder with no available therapies

Market opportunity**

- AMN impacts 8,000-10,000 patients in the US and EU5

Unless stated all financials Sep 2022, employee numbers March 2022


* Adrenomyeloneuropathy

** SwanBio analysis

Key competitors and risks: Syncona team view

Purespring

Advancing gene therapies for the treatment of chronic renal diseases that are currently poorly addressed with existing treatments

Board Seat	2 (inc. Chair)
Date of Founding	2020
Date of Syncona investment	2020
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£35.1m
No. of employees	20+
Competitor landscape	
Key risks	<ul style="list-style-type: none">- Highly innovative concept in emerging space- Clinical risk by addressing non-monogenic disorders

Key management team

Richard Francis, CEO (previously CEO of Sandoz, and a member of the Executive Committee of Novartis)

Moin Saleem, CSO and Founder (leader of Bristol Renal, a glomerular research group of approximately 45 researchers)

Alice Brown, CSO (former Senior Director, Cell Therapy Innovation, Takeda Pharmaceuticals)

Julian Hanak, CDO (formerly of Biogen, Nightstar)

Founders

Moin Saleem (see above)

Mauro Giacca, Professor of Cardiovascular Sciences at the School of Cardiovascular Medicine & Sciences, King's College London

For more information see: <https://purespringtx.com/>






Investment thesis

- A number of chronic kidney diseases are poorly addressed by existing therapies, which are primarily based around the lowering of blood pressure and often progress to dialysis and kidney transplantation
- Purespring is developing disease-modifying therapies for a number of monogenic and non-monogenic kidney diseases

Neogene

Pioneering the development of next-generation, fully personalised engineered T cell therapies for a broad spectrum of cancers

Board Seat	1
Date of Founding	2018
Date of Syncona investment	2020
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£14.3m
No. of employees	100+
Competitor landscape	  
Key risks	<ul style="list-style-type: none">- Complex early stage technology- Complex manufacturing- Highly competitive field

Key management team

Carsten Linneman, CEO (formerly co-founder of T-Cell Factory B.V.)

Christopher Wilfong, Chief Business Officer (co-founder of Two River Consulting)

Brent Pfeifferberger, COO (former senior Vice President, U.S. Oncology, Bristol Myers Squibb)

Raphael Rousseau, CMO (former CMO at Gritstone Bio)

Gavin Bendle, Vice President R&D (former Senior Director of Cell Therapy at Kite Pharma)

Mauro Avanzi, Vice President Clinical Development (former Executive Medical Director, Kite Pharma)

Han Lee, Chief Financial Officer (formerly of Arcellx)

Founders

Ton Schumacher, Principal Investigator at The Netherlands Cancer Institute, Onco Institute member, and Professor of Immunotechnology at Leiden University Medical Center

Carsten Linneman (see above)

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



Investment thesis

- The company is developing an engineered T Cell Receptor (TCR) therapeutic approach for solid tumours based on a patient's own neoantigens (personalised autologous cell therapy)

Unmet medical need



- Limited treatment options for relapsed/refractory patients with advanced solid tumours that have progressed through front line therapies.
- Cell therapies offer the potential for deep and durable responses in the populations as evidenced by lovance's Tumor Infiltrating Lymphocyte therapy. We believe Neogene's approach should result in a more efficacious product that can address a larger number of patients

Market opportunity

- The company has not yet announced its target indications within the solid tumour field

Resolution

Developing macrophage cell therapies to repair inflammatory organ damage, including treatment of end-stage chronic liver disease.

Board Seat	2 (inc. Chair)
Date of Founding	2020
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£23.0m
No. of employees	c.20
Competitor landscape	 
Key risks	<ul style="list-style-type: none">- Highly innovative concept in an emerging space- Future competition

Key management team

Ed Hodgkin, CEO (Syncona Partner)

Amol Ketkar, Chief Development Officer (formerly of GSK)

Lara Campana, VP Macrophage Biology (visiting scientist at the University of Edinburgh)

Victor Dillard, VP Corporate Development (founder of Desktop Genetics)

Lorna Peers, VP Finance (formerly of Censo Biotechnologies)

Evelien Stalmeijer, VP Translation (formerly of eXmoor pharma concepts)

Damian Marshall, VP Analytical Development (formerly of Achilles Therapeutics and C> Catapult)

Founders

Professor Stuart Forbes, Professor of Transplantation and Regenerative Medicine at the University of Edinburgh. Professor Forbes has pioneered the research of macrophage cell therapy for liver disease.

Professor John Campbell, Director of Tissues, Cells, and Advanced Therapeutics at the Scottish National Blood Transfusion service. Professor Campbell has worked on the therapeutic use of immune cells for 30 years.

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



Investment thesis

- An opportunity to create the leading inflammation-focused macrophage cell therapy business, focusing initially on treatment of liver cirrhosis. The goal is to repair the livers of patients sufficiently to reduce the risk of decompensation. Future opportunity lies in lung and kidney repair in chronic fibrotic disease

Unmet medical need


- Chronic inflammatory organ damage represents a major burden to patients. If left untreated, liver cirrhosis will often progress to decompensation through significant loss of liver function. Today there are no efficacious treatments to prevent deterioration in the latter stages of the disease, thus leaving costly and burdensome liver transplantation often as the only option

Market opportunity

- New diagnoses of liver cirrhosis affect hundreds of individuals per million of population

OMass Therapeutics

Using novel biochemistry techniques, native mass spectrometry and custom chemistry to deliver novel medicines against highly validated but inadequately drugged targets, with a focus on immunological and rare diseases

Board Seat	2 (inc. Chair)
Date of Founding	2016
Date of Syncona investment	2018
Valuation basis	Series B
Stage	Drug discovery
Syncona capital invested	£35.4m
No. of employees	40+
Competitor landscape	
Key risks	<ul style="list-style-type: none">- 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

Idlir Liko, **Director of Technology**, has a wealth of experience in mass spectrometry across biotech and pharma

Founders

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

Hsin-Yung Yen, Principal Investigator at the Institute of Biological Chemistry, Academia Sinica in Taiwan

Jonathan Hopper, (as above)

Idlir Liko, (as above)

For more information see: www.omass.com/team

Unless stated all financials at Sep 2022, employee numbers March 2022
Key competitors and risks: Syncona team view



Investment thesis







- Opportunity to develop differentiated small molecule drugs leveraging a world-leading Native Mass Spectrometry platform which enables unique insights into membrane proteins and protein complexes such as GPCRs and Solute Carriers – classes of targets that have been historically difficult to drug in spite of high clinical relevance and unmet need

Unmet medical need

- Programmes are all in indications with significant unmet medical need

Clade Therapeutics

Harnessing iPSC immune cloaking and differentiation platform technology to deliver 'off-the-shelf' cell therapies

Board Seat	1
Date of Founding	2021
Date of Syncona investment	2021
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£10.8m
No. of employees	20+
Competitor landscape	     
Key risks	<ul style="list-style-type: none"> - Highly innovative concept in emerging space

Key management team

Chad Cowan, PhD, Chief Executive Officer, Co-Founder (previously Co-founded and CSO, Sana Biotechnology, Co-Founder, Head of Research CRISPR Therapeutics)

Jim Glasheen, PhD, President / Chief Business Officer, Co-Founder (previously, co-founder and founding President and CEO of Atalanta Therapeutics, Executive Vice Chancellor at UMASS Medical School, co-lead of Life Science Practice at Technology Partners Venture Capital)

Leandro Vetcher, Chief Operating Officer, Co-Founder (previously VP of Research Operations at Sana Biotechnologies, business development lead for the Blavatnik Biomedical Accelerator at Harvard University, co-founder of Green Pacific Biologicals and Keclon SA)

Derek Hei, PhD, Chief Technology Officer (previously SVP of Preclinical and Clinical Manufacturing, Cell and Gene Therapies at Vertex Pharmaceuticals, SVP of Manufacturing, Quality, and Regulatory at BlueRock Therapeutics as well as BlueRock's Chief of Manufacturing and Technical Operations)

Founders

Chad Cowan, PhD, (as above), **Jim Glasheen**, PhD, (as above) **Leandro Vetcher**, (as above)

Deepta Bhattacharya, PhD, (Professor, Department of Immunobiology, University of Arizona, College of Medicine, Tucson)

Chris Sturgeon, PhD, (Associate Professor at the Icahn School of Medicine at Mount Sinai)

Gustavo Mostoslavsky, MD PhD (Associate Professor of Medicine in the Section of Gastroenterology in the Department of Medicine at Boston University School of Medicine)

For more information see: <https://cladetxt.com/>



Investment thesis

- Clade has been established with the aim of discovering and delivering scalable next generation induced pluripotent stem cell (iPSC)-derived medicines

Unmet medical need

- Syncona believes Clade's technology has the potential to deliver greater efficacy than the first generation of allogeneic cell therapies
- "Off the shelf" stem cell-based therapies have potential to deliver practical and commercial benefits in cell therapeutics

Appendix 4 – Sustainability

Delivering positive and sustainable impact

Our social impact

- £4.2m donated to charity in FY2021/2, ongoing commitment to donate 0.35% of NAV per year
- 19 portfolio company clinical trial sites across the UK
- 1200+ people employed by Syncona and its portfolio
- Total addressable market of c.383k patients across clinical stage portfolio companies¹



Responsible investor and partner

- Responsible Investment Policy rolled out to full portfolio
- Launched project to integrate ESG into ongoing priorities of newly formed company launch team
- Continue to work closely with portfolio companies to develop ESG reporting



Inspiring and empowering our people

- Second Windsor Fellowship intern begins six-month placement at Syncona²
- Generating Genius scholars begin second year of studies at university³
- Updated family-friendly policies



Responsible and ethical business

- First TCFD report published in FY22 Annual Report
- Net zero aspiration on a full portfolio basis by 2050
- Intend to publish full portfolio carbon footprint in FY2022/3
- Intend to become a signatory to the Net Zero Asset Managers (NZAM) initiative



¹ - Total addressable market calculated from estimated new patients diagnosed per annum in lead indication/s of clinical stage portfolio companies, as defined by the company or the Syncona investment team estimate

² – The Windsor Fellowship aims to design and deliver personal development and leadership programmes, with the goal of supporting minority communities in science, technology, engineering and maths (STEM) subjects

³ – Generating Genius supports low-income students across the UK to obtain places at top universities in STEM subjects. The Syncona Foundation has provided a donation of £301,500 over three years, to provide five of Generating Genius's students with scholarships to go to university, covering all their university fees as well as most living expenses when there

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 plays an incredibly important role in helping us make discoveries and improve cancer patients’ lives.”

Professor Kristian Helin
CEO of the Institute for Cancer Research (ICR)

£40.6m

Syncona donations to charity since 2012¹

26

Charities supported

0.35%

Of Syncona’s NAV donated to charity on an annual basis

 In aid of Alzheimer's Research UK The Power to Defeat Dementia	 Alzheimer's Society	 AUDITORY VERBAL UK Creating a world where everyone can hear	 THE BRAIN TUMOUR CHARITY
 BRAIN WAVES	 butterfly thyroid cancer trust	 Child Bereavement UK REBUILDING LIVES TOGETHER	 cureleukaemia the blood cancer charity
 David Nott FOUNDATION	 downside up	 THE EGMONT TRUST	 FIGHT FOR SIGHT The Eye Research Charity
 GENERATING GENIUS	 ICR The Institute of Cancer Research	 JAMES' PLACE www.jamesplace.org.uk	 JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.
 Great Ormond Street Hospital Charity	 the listening place	 Macular Society Beating Macular Disease	 MAGGIE'S Everyone's home of cancer care
 Marie Curie Care and support through terminal illness	 NSPCC	 Place 2Be	 The ROYAL MARSDEN Cancer Charity
 SUPPORTING WOUNDED VETERANS REHABILITATION TO EMPLOYMENT	 ssafa the Armed Forces charity		