Syncona

Investing to extend and enhance human life

Full year results 2022

synconaltd.com

Image Freeline labs, Stevenage

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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

A decade of building global leaders

- Built 18 companies since foundation with 11 in the portfolio
- Operating in areas of high unmet medical need
- Vision to deliver treatments to patients
- 1,200+ employees across the Syncona portfolio

Portfolio

Our growing track record

- £905.7m deployed since foundation
- 27% IRR and 1.6x multiple on cost across whole portfolio*
- £932.7m generated from three successful exits
- Exits have delivered a 4.6x multiple on cost**

Returns

15 programmes taken into the clinic; 1 marketed product

- Three products taken to pivotal trial
- One product to market (Blue Earth's Axumin®)
- Exciting pipeline across our diversified portfolio of 11 companies

Patients

Vision set out in 2012, to build globally leading life science companies that have the potential to deliver transformational outcomes for patients, further validated during the year

*Includes sales of Nightstar, Blue Earth, upfront proceeds from sale of Gyroscope 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

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Progress in the year

Delivering a return in a challenging market; growing track record of successfully building globally competitive businesses

Delivered a return against a challenging market backdrop	– NAV of £1.3bn, 194p per share, return of 0.3% – 0.8% return from life science portfolio; aggregate uplift in value of private companies of £274.8m, led by uplift from Gyroscope sale, offset by declines in value of listed holdings
Strong clinical progress across our portfolio	– Four clinical stage companies; 12 clinical data read-outs across portfolio – Anaveon entered the clinic and reported promising initial data in April 2022
Multiple financings ensuring portfolio is funded to deliver on key upcoming milestones	– $712.2m committed across seven financings; $126.4m by Syncona – Our portfolio companies are well funded in challenging market conditions
Strengthened capital base provides greater flexibility	– £325.8m received from sale of Gyroscope to Novartis – £784.9m capital pool at 31 March 2022
Progress on sustainability	– £4.2m donated to charity – Responsible Investment Policy rolled out across the portfolio – Diversity and Inclusion initiatives successfully launched

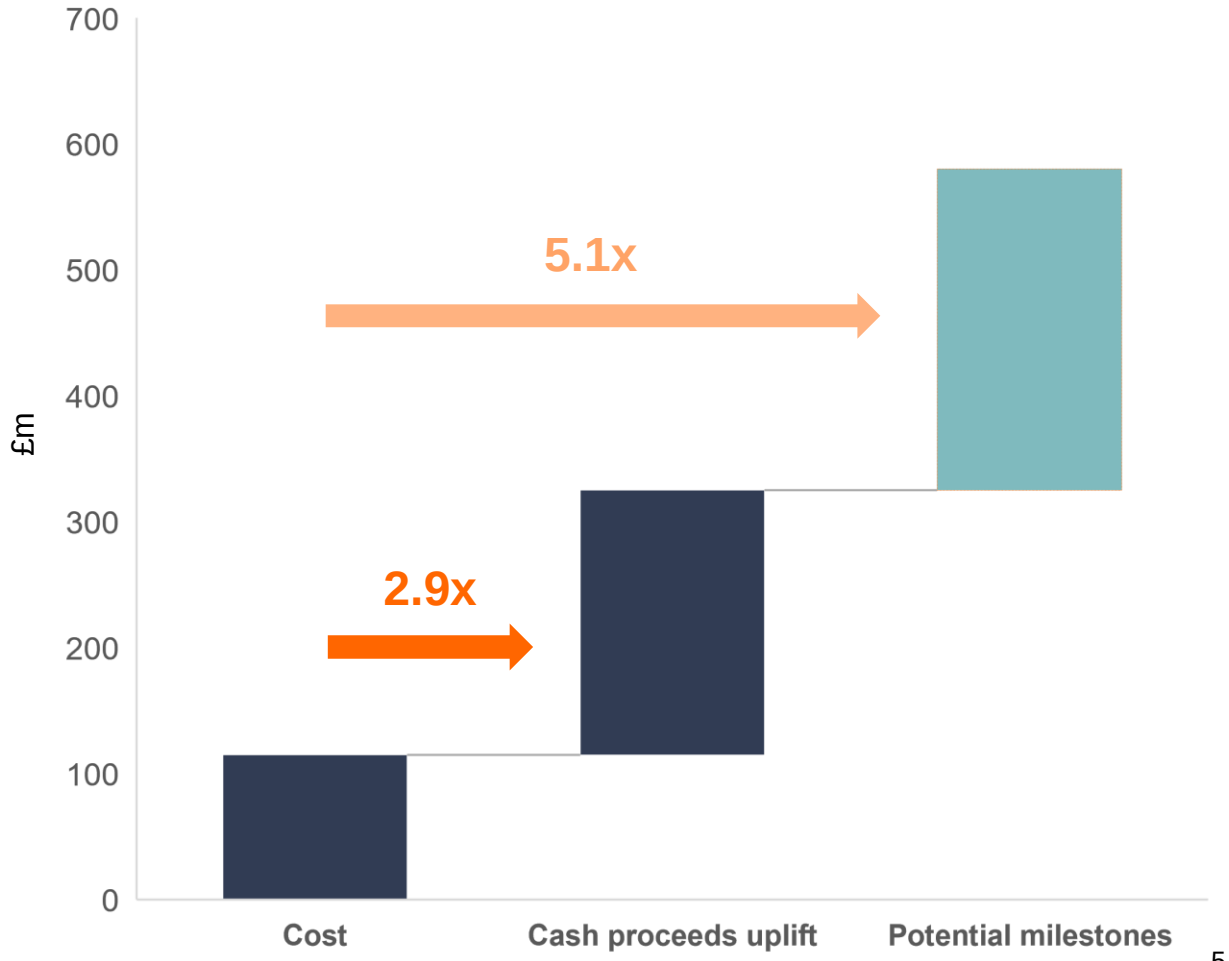
Gyroscope is third successful exit for Syncona

Drives significant value for Syncona shareholders; continued interest from pharma for Syncona companies

Gyroscope was co-founded by Syncona in 2016

- Novartis agreed to acquire Gyroscope in December 2021 for up to $1.5bn
- Upfront proceeds of $800m with a further $700m linked to milestones
- Upfront proceeds to Syncona of £325.8m; 2.9 multiple of cost and 50% IRR*
  - Upfront proceeds and discounted risk-adjusted valuation of milestones provide a £225.5m uplift to previous holding value
  - Milestones have potential to deliver a further £255.3m to Syncona
- Realisation of all milestones could lead to an overall 5.1 multiple of original cost*

Strong returns from investment in Gyroscope



*All IRR and multiple on cost figures are calculated on a gross basis. Includes original Syncona Partners capital invested where applicable

Challenging market backdrop for listed companies

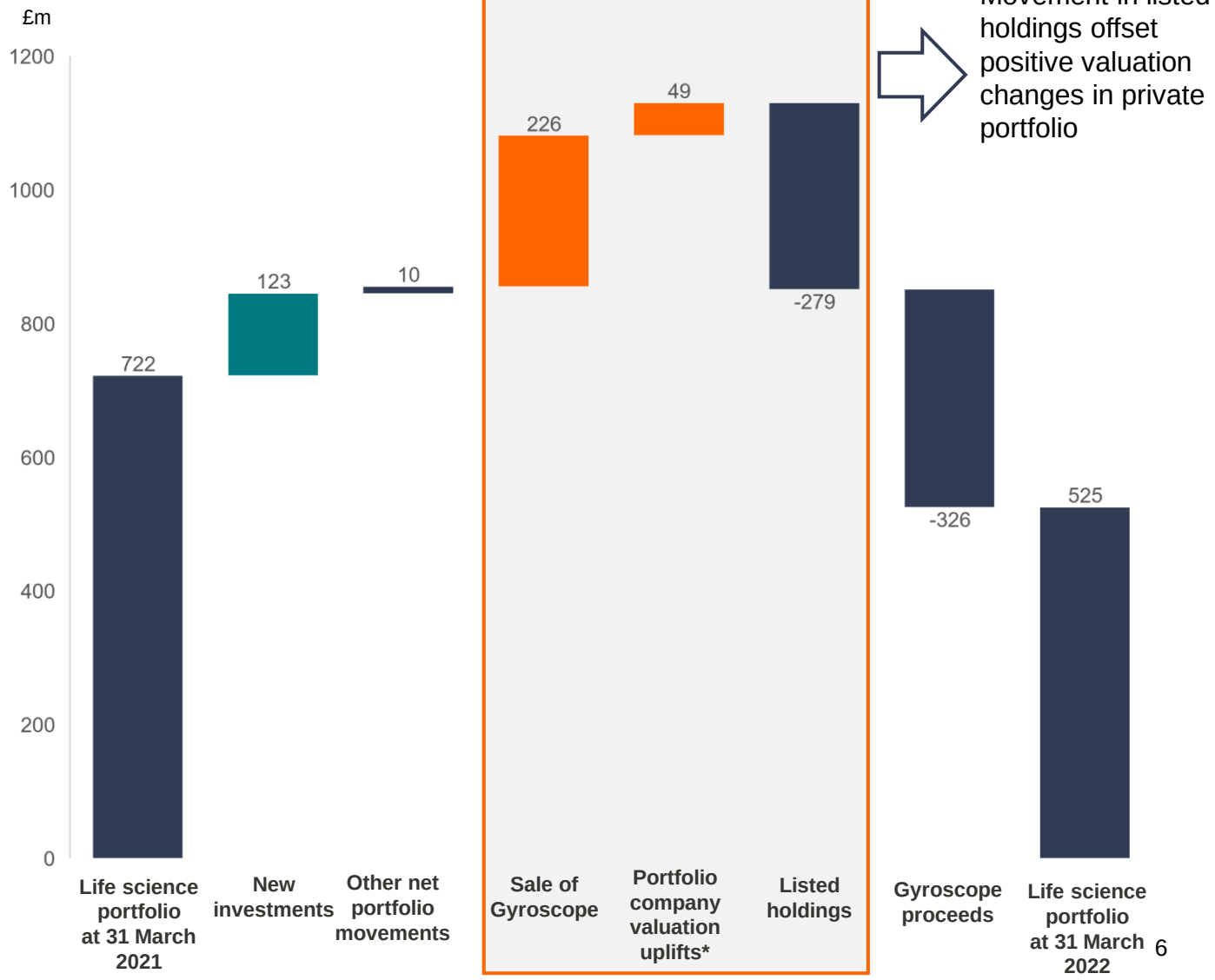
Sentiment towards cell and gene therapy companies continues to impact listed holdings

Public markets continue to be challenging for smaller biotech stocks

- On average, share prices of lower 50% of NASDAQ Biotech Index, weighted by market cap, down by 41% during the year
- Negative market sentiment has impacted share prices of listed companies in our portfolio
- There have been delays to clinical trials and operational challenges at Freeline; new management team in place with renewed focus on clinical and operational execution

Syncona companies well funded to deliver on key data catalysts in the next 12 months

*Includes uplifts from Series B financings in Quell, Anaveon and OMass



Promise of cell and gene therapy remains

Public market sentiment impacted by industry challenges as field matures;
field remains exciting with significant untapped potential

Curative potential of the products with significant commercial opportunity

- Cell and gene therapies seeking to target diseases in areas of high unmet medical need
- Potential for single dose cure in intractable diseases
- We believe patients will opt for best-in-class products

Growing understanding of manufacturing process in cell therapy and safety in gene therapy

- Cell therapy companies increasing manufacturing footprints and more local infrastructure available – regulators providing more information on manufacturing requirements
- Concerns about dose safety in the gene therapy field; our companies are able to navigate appropriately – Syncona gene therapy strategy has been to limit potential exposure to toxicity

Positive data in the space is translating into product approvals

- Nine FDA-approved cell and gene therapies to date, with 60 expected to be approved by 2030*
- Number of products in late stage development, expected to receive regulatory feedback in 2022/3**

* https://www.sciencedirect.com/science/article/pii/S2329050121000668, Syncona team analysis
** https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-gene-therapy-pipeline-2021-may.pdf

Portfolio update

Clinical stage companies

Maturing clinical pipelines, with multiple upcoming data read-outs and Autolus' obe-cel in pivotal trial

Cash runways / funds raised in 2021/2

Gen 1

Autolus

Research | Target ID | Pre-Clinical | Clinical

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

- Published further data in lead obe-cel programme in adult ALL; meaningful data read-out in H2 CY2022
- Encouraging clinical data published at EHA across pipeline, inc. AUTO4
- Strengthened cash runway following $250.0m commitment from Blackstone

H1 2024

Gen 2

FREELINE

Research | Target ID | Pre-Clinical | Clinical

- FLT180a – Haemophilia B[1]
- FLT190 – Fabry disease
- FLT201 – Gaucher disease

- Positive data read-outs in FLT180a in haemophilia B and FLT190 in Fabry disease
- Gaucher programme on track to become third programme in the clinic
- Extended cash runway following $26.1m direct offering, led by Syncona

H2 2023

ACHILLES THERAPEUTICS

Research | Target ID | Pre-Clinical | Clinical

- cNeT – Melanoma
- cNeT – NSCLC

- Further positive data from lower dose cohort in Phase I/II studies in melanoma and non-small cell lung cancer (NSCLC)
- Data from higher dose processes expected in H2 CY2022

H2 2024

Gen 3

ANAVEON

Research | Target ID | Pre-Clinical | Clinical

- ANV419 – Multiple tumour types

- Raised CHF 110.0m (£89.8m) in Series B financing in December 2021
- First clinical data from lead programme, ANV419, published post period end, underlining safety and selectivity profile of the drug
- Further data from ANV419 expected in H2 CY2022

CHF 110m

1 Including B-AMAZE and B-LIEVE trials

Pre-clinical companies

Syncona

Significant momentum across pre-clinical companies; well funded to deliver key clinical milestones

Gen 3

	Funds raised in 2021/2
QuellTX - CTA approval for lead QEL-001 programme - Oversubscribed $156.3m (£116.6m) Series B alongside leading syndicate	$156.3m
SwanBio Therapeutics - Fast Track and Orphan Drug designations for lead programme, SBT101 in AMN - Post period, $55.9m (£45.3m) Series B	$55.9m*
RTx - Expanding allogeneic programme - Extended Series A financing provides £10.0m of additional funding	£10.0m

Gen 4

	Funds raised in 2021/2
purespring - Continuing to build out senior leadership team - Strong progress across pre-clinical pipeline - Positioned to be a leader in AAV renal gene therapy	-
neogene therapeutics - Continued build out of world class leadership team - Post period, CTA approval for lead candidate in the Netherlands	-
OMass - Strong pipeline of five candidates across immunological and orphan diseases - Post period, £75.5m Series B	£75.5m*
CLADE Therapeutics - Syncona led $87.1m (£63.0m) Series A financing in November 2021 - Building out team under world class leadership of Chad Cowan and Jim Glasheen	$87.1m

*Financing completed post period end

Diversified portfolio set to deliver key upcoming milestones

Four at clinical stage, with a further three expected to enter the clinic in the next 12 months

Upcoming clinical milestones

Autolus – Meaningful read-out from obe-cel in r/r adult ALL expected in H2 CY2022; further data in AUTO1/22

Freeline – Data expected across haemophilia B, Fabry, and Gaucher Type 1 programmes in H2 CY2022

Achilles – Interim data in higher dose process in NSCLC and melanoma Phase I/II studies expected in H2 CY2022

Anaveon – Further data from ANV419 Phase I study expected later in CY2022

Quell – Expect to dose first patient in H2 CY2022

SwanBio – Expect to enter clinic in H2 CY2022

Neogene – Expect to enter clinic in H1 CY2023

*Biologics Licence Application

An exciting pipeline of opportunities

Genetic medicines are unlocking diseases and streamlining drug development

Cell and gene therapies have demonstrated transformative potential; significant opportunity ahead

Cell therapy

- Continue to be active within cell therapy, as shown by $30.0m Series A investment in Clade during the year
- Field has focused on oncology to date, now broadening out to focus on other areas

Gene therapy

- Currently being applied in small number of diseases, opportunity in chronic degenerative conditions
- Significant expertise and success in gene therapy (Gyroscope and Nightstar); opportunity to leverage this expertise to treat other conditions

Genetic revolution enabling more targeted drug development

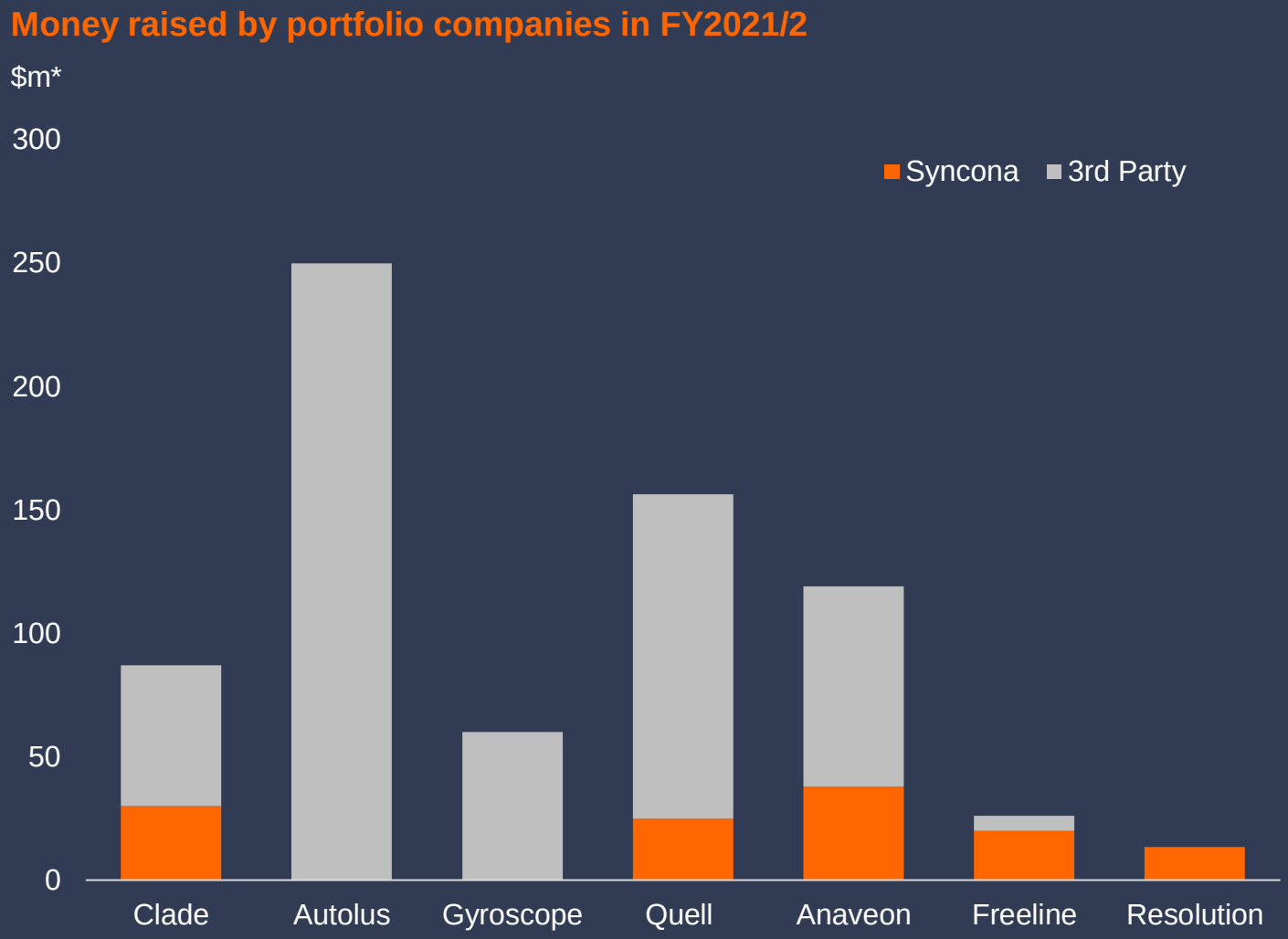
Syncona has the expertise to apply the right modality to the relevant disease setting across small molecules, biologics, antibodies, cell therapy, gene therapy and other Third Wave modalities such as nucleic acids

- Antibodies have had great success in immunological and inflammatory diseases – new technologies are providing real insight as to how unaddressed conditions could be tackled
- Targeted small molecules have been successful in oncology but are limited by lack of technologies that:
  - Allow identification of the right setting
  - Develop the right molecular therapy for a known cancer target

Capital pool

Supporting our portfolio companies as they scale

- Our balance sheet is a strategic and competitive advantage; gives us flexibility to bring in specialist institutional investors at the right time and price
- $712.2m committed across seven financings, of which $126.4m was committed by Syncona



*FX rates at date of closing of financings
Figures reference maximum levels of committed funding and in places are subject to the achievement of milestones

Strengthened capital pool

Our strengthened capital base provides us with a strategic advantage, particularly in the current market environment

Capital deployment to increase in FY2022/3

- £123.2m deployed into portfolio in the year
- Expect to deploy £150-£250m of capital in FY2022/3 as we found new companies, invest in our existing portfolio, and hold a select number of companies privately for longer

£150-£250m

Expected FY2022/3 capital deployment

Capital pool asset allocation

- Aim to maintain a minimum of 12-24 months in cash and treasuries
- FX exposure – will hold US dollars to match expected future requirements on an ongoing basis (current levels ~40% of capital pool)
- Selectively introducing a small number of low-risk, multi-asset funds to offer some inflation protection over time

£784.9m

Capital pool to fund growing life science portfolio and found new companies

Outlook

Building on our success

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

Where we are today

Operating at scale

- NAV of £1.3bn
- Capital pool of £785m
- 1,200+ employed at Syncona and its portfolio companies
- Strong pipeline of opportunities

How we got here

Leveraging our success

- Core team skill is to identify science and leverage it to create a company that has the potential to deliver transformational treatments
- Demonstrated we can build these businesses and their teams to be globally competitive
- Strength of balance sheet provides a differentiated market position – increasingly important in the current market environment

Key learnings

Driving future growth

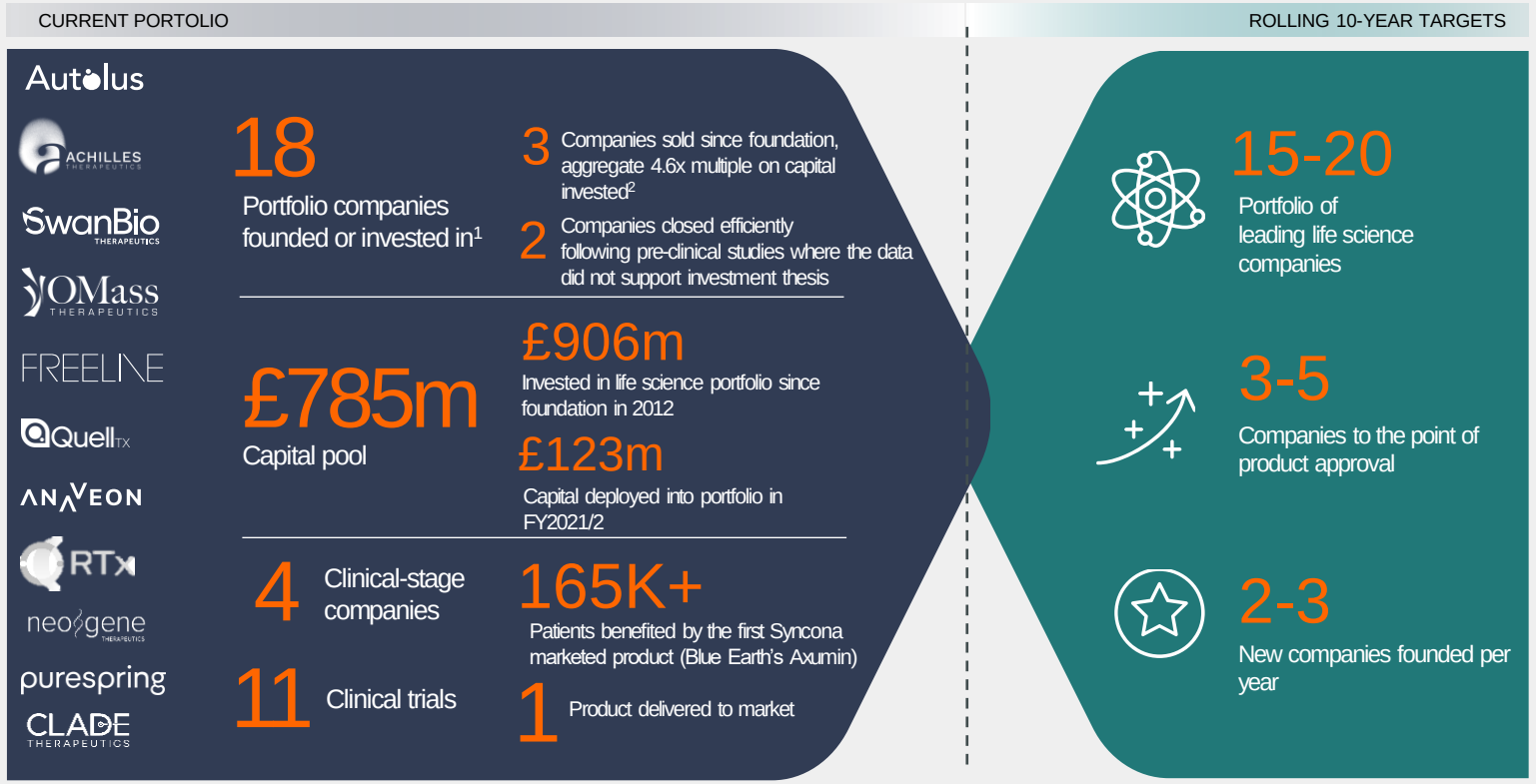
- Optimising financing approach to manage risk and reward across diversified portfolio
- Attracting world-class teams to lead our portfolio companies from an early stage
- Continuing to improve execution as companies mature and progress through the clinic

Summary

Syncona's platform seeks to create value from the commercialisation of life science innovation

Syncona team has shown it can effectively manage the portfolio and deliver a return through the cycle

- **Up to $1.5bn sale of Gyroscope to Novartis** further validated the Syncona model
- **0.8% life science portfolio return** during a period of significant volatility for biotech
- Maturing portfolio well funded to deliver on upcoming key clinical milestones with **potential to create value in CY2022**
- **Strengthened capital base** positions Syncona for long-term success



1 Includes sales of Blue Earth, Nightstar and Gyroscope, closure of 14MG and Azeria, merger of Orbit and Gyroscope; CEGX now an investment
2 Includes sales of Blue Earth, Nightstar and Gyroscope, reflects original Syncona Partners capital invested where applicable. Includes upfront proceeds from sale of Gyroscope. All IRR and multiple on cost figures are calculated on a gross basis

Appendix 1 – Syncona team

An expert multi-disciplinary investment team

Syncona

Our unique skill set

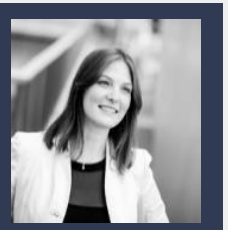
Scientific | Commercial | Company creation | Investment

Martin Murphy [1,2]
Co-founder, CEO and Chair, SIML
PhD
QuellTx ANAVEON neogene Autolus CLADE THERAPEUTICS YOMass ACHILLES
21 years' experience

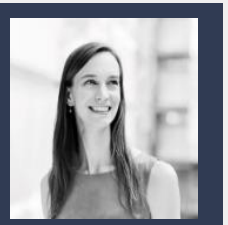
Chris Hollowood [1]
CIO, SIML
PhD
FREELINE SwanBio purespring
20 years' experience

Markus John
CMO, Head of R&D
MD
21 years' experience

Edward Hodgkin [1,2]
Senior Partner
PhD
RTx YOMass
31 years' experience

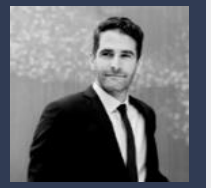


Elisa Petris [2]
Lead Partner
PhD
neogene QuellTx ACHILLES
14 years' experience



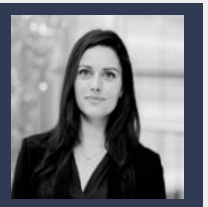
Magda Jonikas [2]
Lead Partner
PhD
YOMass
11 years' experience

Alex Hamilton [2]
Investment Partner
PhD
ANAVEON SwanBio
8 years' experience

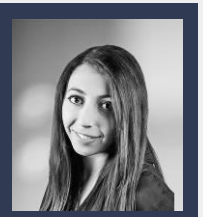


Michael Kyriakides [2]
Investment Partner
PhD
FREELINE purespring CLADE THERAPEUTICS
6 years' experience

Gonzalo Garcia [2]
Investment Partner
PhD
RTx
7 years' experience

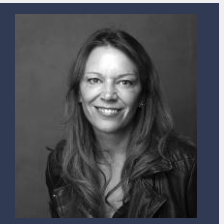


Alice Renard [2]
Investment Partner
PhD
ANAVEON purespring
6 years' experience



Raghd Rostom [3]
Associate Partner
PhD
3 years' experience

Hitesh Thakrar
Partner
BChem
28 years' experience



Lisa Bright [2]
Commercial Advisor
BSc
RTx
33 years' experience

Ben Woolven
Business Strategy and Operations Partner
PhD
RTx
20 years' experience

Full team details: https://www.synconaltd.com/about-us/our-people/
1 Portfolio company chairman, 2 Portfolio company board member/observer 3 – Joined post period end

Appendix 2 – Market context

Potential to transform the lives of patients

Designed to halt a disease or reverse its progress

Approved products and data to date have shown the transformational impact and potential of these products

Cell therapy

- Potential for profound efficacy – to date mainly oncology focused

Gene therapy

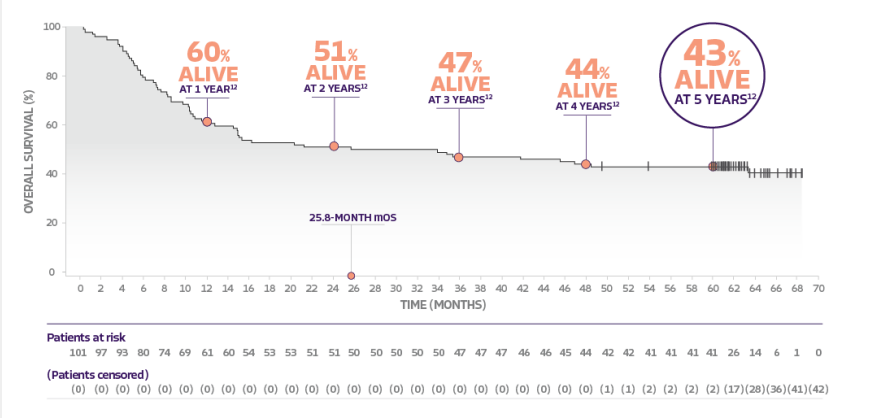
- The potential for one-time treatments vs conventional medicines which are taken on a continual basis

Significant number of diseases where cell and gene therapy are potentially applicable

Kite/Gilead: engineered CAR-T cell therapy for adult relapse / refractory Diffuse Large B-cell Lymphoma (DLBCL)

- DLBCL is an aggressive cancer of the lymphatic system
- >18k people diagnosed with DLBCL annually[1]
- Yescarta was approved in 2017 for use in relapse / refractory patients
- Disruptive efficacy seen, with 4x more patients responding to treatment[3]

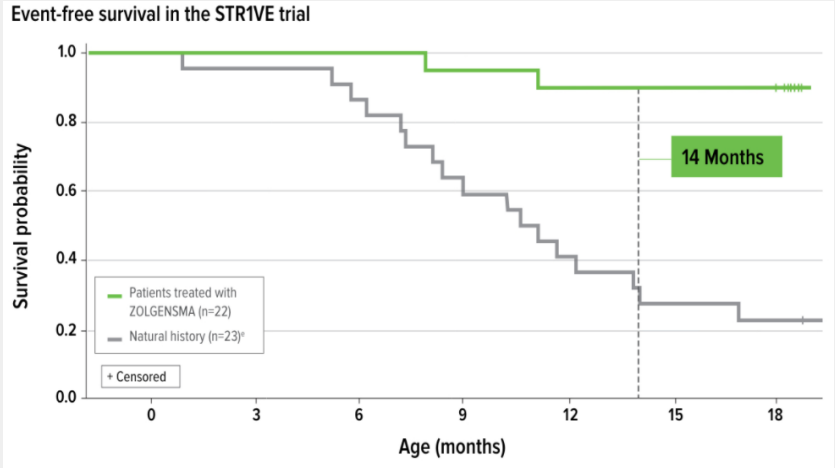
43% of patients alive at five years post treatment[2]
3x overall survival rate of current standard of care at 12 months[3]



Novartis/AveXis: one-time therapy addressing spinal muscular atrophy (SMA)

- SMA is a genetic disease caused by a lack of a functional survival motor neuron 1 gene, resulting in the rapid and irreversible loss of motor neurons
- Most often impacts babies and children
- Zolgensma now an approved product based on profound data

91% (20/22) of patients were alive and free of permanent ventilation at 14 months of age[4]



1 https://lymphoma.org/aboutlymphoma/nhl/dlbcl/
2 https://www.yescartahcp.com/large-b-cell-lymphoma/efficacy
3 https://www.ncbi.nlm.nih.gov/books/NBK552022/
4 https://www.zolgensma-hcp.com/aboutzolgensma/efficacy/str1ve/

Cell and gene therapies have the potential to disrupt the market

Approved cell and gene therapies are expected to increase significantly in the coming years, Syncona believes the growth could be similar to antibody therapies

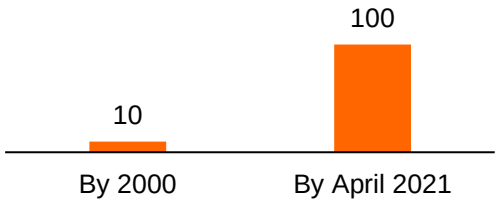
"… By 2025, we predict that the FDA will be approving 10 to 20 cell and gene therapy products a year based on an assessment of the current pipeline and the clinical success rates of these products …"

Scott Gottlieb, ex-FDA commissioner

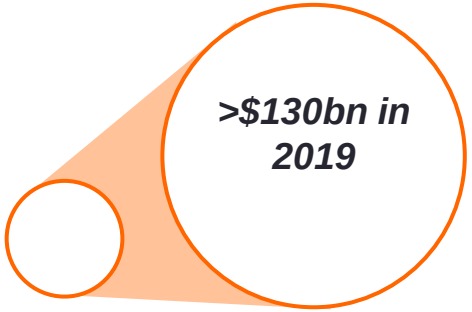
Monoclonal antibodies

FDA approved products[1]

100



Annual sales ($bn)[2]

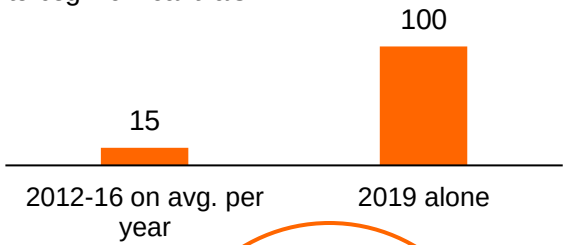


Cell and gene therapy

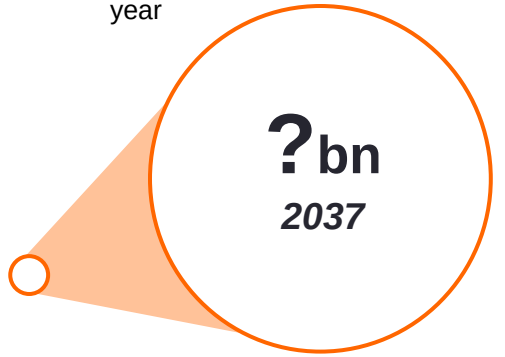
FDA approved products[4]

9

New Investigational New Drug applications to begin clinical trials[3]



Annual sales ($bn)[5]



1 Nature Reviews Drug Discovery article published on 5 May 2021; 2 Lu, RM., Hwang, YC., Liu, IJ. *et al.* Development of therapeutic antibodies for the treatment of diseases. *J Biomed Sci* **27,** 1 (2020); 3 Lapteva L, Purohit-Sheth T, Serabian M, Puri RK. Clinical Development of Gene Therapies: The First Three Decades and Counting. Mol Ther Methods Clin Dev. 2020 Oct 10;19:387-397; 4 FDA Office of Tissues and Advanced Therapies: Includes engineered cell therapies and gene therapies only, Syncona team analysis; 5 https://bisresearch.com/industry-report/cell-gene-therapy-market.html,

Appendix 3 – Portfolio companies

Financial review

☐ Clinical ☐ Pre-clinical ■ Drug discovery

Syncona

Portfolio company	Fully diluted ownership %	30 March 2021 value £m (fair value)	Net invested/returned in the period £m	Valuation change	FX movement	31 March 2022 value £m (fair value)	Valuation basis (fair value)[1,2]	% of NAV
Autolus	18.8%	81.2	-	(22.1)	2.9	62.0	Quoted	4.7%
ANAVEON	37.9%	18.5	20.4	17.9	3.0	59.8	PRI	4.6%
FREELINE	53.4%	167.9	15.4	(151.6)	0.6	32.3	Quoted	2.5%
ACHILLES THERAPEUTICS	25.3%	133.1	-	(109.5)	1.2	24.8	Quoted	1.9%
GYROSCOPE A Novartis Company	0.0%	150.1	(325.8)	168.3	7.4	-	Sold	0.0%
QuellTx	37.4%	35.1	26.3	18.5	1.5	81.4	PRI	6.2%
SwanBio THERAPEUTICS	75.4%	53.7	17.7	0.5	3.2	75.1	Cost	5.7%
purespring	84.0%	3.9	14.6	-	-	18.5	Cost	1.4%
neogene THERAPEUTICS	7.9%	11.0	2.9	-	0.6	14.5	Cost	1.1%
CLADE THERAPEUTICS	22.6%	-	10.8	-	0.6	11.4	Cost	0.9%
RTx	81.1%	7.4	3.0	-	-	10.4	Cost	0.8%
OMass THERAPEUTICS	49.3%	16.4	10.0	8.3	-	34.7	PRI	2.6%
Investments		43.8	1.7	54.0	0.5	100.0		
Total		**722.1**	**(203.0)**	**(15.7)**	**21.5**	**524.9**		

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

Portfolio company outlook

Syncona

Upcoming milestones across the portfolio

Company	Status of pipelines	Next steps
Autolus	Five ongoing clinical trials	– Progress pivotal study in obe-cel / adult ALL, with meaningful data in H2 CY2022 with full data expected in H1 CY2023 – Publish longer term follow-up data in AUTO1/22 / paediatric ALL in H2 CY2022
FREELINE	Two lead programmes in Phase I/II clinical trials, first trial site initiated for Phase I/II trial for Gaucher Type 1	– Progress haemophilia B study, initial data from dose-confirmation study in July 2022 – Programme update expected in Fabry study in H2 CY2022 – Gaucher study to publish initial data in H2 CY2022
ACHILLES THERAPEUTICS	Two lead programmes in Phase I/IIa trials	– Expect to publish interim data from VELOS™ Process 2 manufacturing in its Phase I/IIa NSCLC and melanoma therapies in H2 CY2022
ANAVEON	Nominated lead programme in the clinic	– Publish further data from Phase I trial in H2 CY2022
QuellTx	Lead programme in pre-clinical development	– Expect to dose first patient in lead programme targeting liver transplant in H2 CY2022
SwanBio THERAPEUTICS	Lead programme in pre-clinical development	– Expects to enter the clinic with lead programme targeting AMN in H2 CY2022
neogene THERAPEUTICS	Lead programme in pre-clinical development	– Expect to enter the clinic in H1 CY2023
RTx	Pre-clinical development of lead programme	– Company and leadership team build out
purespring	Pre-clinical development	– Company and leadership team build out, identify lead programme
CLADE THERAPEUTICS	Pre-clinical development	– Company and leadership team build out, identifying pipeline targets
OMass	Five programmes identified for pre-clinical development	– Progress of lead programme into lead optimisation

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

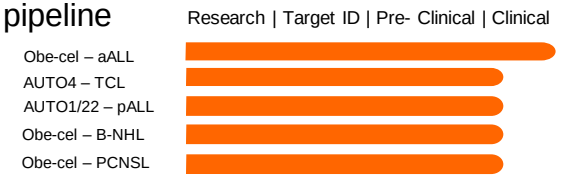
Board Seat	1
Date of Founding	2014
Date of Syncona investment	2014
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£124.0m
No. of employees	350+

Competitor Landscape

GILEAD NOVARTIS Fate THERAPEUTICS

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

Clinical pipeline



Key management team

Christian Itin, Chief Executive Officer (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)
Brent Rice, Chief Commercial Officer (formerly Head of Managed Markets at Juno Therapeutics)
Christopher Vann, Chief Operating Officer (formerly Roche)

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

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

Unless stated all financials at March 2022
* Source; Autolus Corporate Presentation May 2022
**Key competitors and risks: Syncona team view

Anaveon

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

Roche, SANOFI, Alkermes, neoleukin

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 Officer and Founder (formerly 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)

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

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**

Unless stated all financials at 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

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

uniQure, Spark, 4DMT, Roche, AVROBIO, Pfizer, Sanofi/Regeneron

Key risks
- Highly competitive environment
- Differentiated product required
- Complex manufacturing

Clinical pipeline

1 Including B-AMAZE and B-LIEVE trials

Key management team

Michael Parini, Chief Executive Officer (formerly Chief Administrative, Legal and Business Development Officer at Vertex)
Pamela Foulds, Chief Medical Officer (formerly CMO of Aegerion Pharmaceuticals)
Henning Stennicke, Chief Scientific Officer (20 years of leadership positions across the R&D value chain at Novo Nordisk)
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, Chief Financial Officer (formerly SVP Finance, Exo Therapeutics)

Founders

Amit Nathwani, Founder, Clinical and Scientific Adviser and Director, Prof. Nathwani is renowned for his pioneering work on gene therapy for haemophilia B, and was first to show successful correction of bleeding diathesis in patients with severe haemophilia B
Markus Hörer, as above, brought the Rentschler manufacturing platform to Freeline
For more information see: https://www.freeline.life

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 clinical programmes of Haemophilia B and Fabry disease is Enzyme Replacement Therapy (ERT); requires regular administration with protein activity remaining unstable

Market opportunity*

- 15,000 patients in lead programme in haemophilia B
- 16,000 patients in Fabry's disease
- 18,000 patients in Gaucher disease

Unless stated all financials at March 2022
*Source: Freeline Corporate Presentation May 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

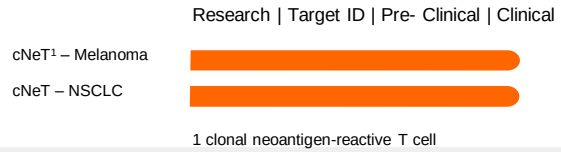
Board Seat	-
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£60.7m
No. of employees	250+

Competitor Landscape

gritstone · IOVANCE BIOTHERAPEUTICS · InstilBio · TURNSTONE BIOLOGICS

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

Clinical pipeline



Key management team

Iraj Ali, Chief Executive Officer (formerly Syncona Partner)
Karl Peggs, Founder and Chief Medical Officer
Sergio Quezada, Founder and Chief Scientific Officer
Robert Coutts, Chief Financial Officer

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 Jaffee, Dr Scott Antonia, Dr Christopher Klebanoff, Dr Ben Creelan, Dr Alena Gros, Dr Markwin Velders

For more information, please see https://achillestx.com

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

- 234,000 patient opportunity in non-small cell lung cancer**
- In 2022, over 197,000 patients are expected to be diagnosed with melanoma in the US***

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view
* https://www.nature.com/articles/s41416-021-01353-6
** https://pubmed.ncbi.nlm.nih.gov/33600992/
*** 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

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	SONOMA, gentibio, abata, Sangamo, Kyverna, MOZART

Key risks
- Highly innovative concept in emerging space
- Complex manufacturing

Key management team

Iain McGill, Chief Executive Officer (formerly on the Executive Committee and as Head of Europe and Rest of World for Jazz Pharmaceuticals)
Dominik Hartl, Chief Medical Officer (formerly Therapeutic Area Head at Novartis Institutes for Biomedical Research)
Tracey Lodie, Chief Scientific Officer (formerly CSO at Gamida Cell)
Nathalie Belmonte, SVP Research & Translation (formerly Chief Operating Officer at Promethera Biosciences)
Luke Henry, Chief Business Officer (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 (formerly 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 Sánchez-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

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 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	£75.1m
No. of employees	50+

Competitor Landscape

TAYSHA, Alcyone Lifesciences Inc., Novartis, Voyager Therapeutics, PassageBio, Lilly, NeuroGene

Key risks
- Slowly progressing disease
- Complex manufacturing
- Clinical risk

Key management team

Tom Anderson, Chief Executive Officer (formerly Chief Commercial Strategy Officer at Sage Therapeutics)
Karen Kozarsky, Chief Scientific Officer and Founder (formerly President of Vector BioPartners and VP of R&D at RegenX)
Steven Zelenkofske, Chief Medical Officer (formerly Chief Medical Officer of Achillion Pharmaceuticals and uniQure)
Scott McMillan, Chief Technical Officer, (formerly Chief Executive Officer of Saliogen Inc. and Chief Operating Officer at uniQure)
Marita James, Chief Financial Officer

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, formerly 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 March 2022
* Adrenomyeloneuropathy
** SwanBio analysis
Key competitors and risks: Syncona team view

Purespring Therapeutics

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	£18.5m
No. of employees	20+
Competitor landscape	NOVARTIS, calliditas, REATA, SANOFI, OMEROS, TRAVERE THERAPEUTICS, Apellis

Key risks
- Highly innovative concept in emerging space
- Clinical risk by addressing non-monogenic disorders

Key management team

Richard Francis, Chief Executive Officer (previously CEO of Sandoz, and a member of the Executive Committee of Novartis)
Moin Saleem, Chief Scientific Officer and Founder (leader of Bristol Renal, a glomerular research group of approximately 45 researchers)
Julian Hanak, Chief Development Officer (formerly of Biogen, Nightstar)

Founders

Moin Saleem (as 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

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view

Neogene Therapeutics

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

PACT, Adaptive, TCR cure

Key risks
- Complex early stage technology
- Complex manufacturing
- Highly competitive field

Key management team

Carsten Linnemann, Chief Executive Officer and Founder (formerly co-founder of T-Cell Factory B.V.)
Christopher Wilfong, Chief Business Officer (co-founder of Two River Consulting)
Brent Pfeiffenberger, Chief Operating Officer (formerly senior Vice President, U.S. Oncology, Bristol Myers Squibb)
Gavin Bendle, Senior Vice President, R&D (formerly Senior Director of Cell Therapy at Kite Pharma)
Mauro Avanzi, Vice President, Clinical Development (formerly Executive Medical Director, Kite Pharma)
Han Lee, Chief Financial Officer (formerly of Arcellx)
Raphaël Rousseau, Chief Medical Officer (formerly CMO at Gritstone bio)

Founders

Ton Schumacher, Principal Investigator at The Netherlands Cancer Institute, Oncode Institute member, and Professor of Immunotechnology at Leiden University Medical Center
Carsten Linnemann (as 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 Iovance's tumour 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

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view

Resolution Therapeutics

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	£10.4m
No. of employees	c.20

Competitor landscape

carisma THERAPEUTICS

SHORELINE biosciences

Key risks

- Highly innovative concept in an emerging space
- Future competition

Key management team

Edward Hodgkin, Chair & Chief Executive Officer (Syncona Partner)

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

Alex Armesilla, Director, Cell Engineering (formerly of Censo Biotechnologies and GSK)

Philip Starkey Lewis, Director, Pharmacology (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 (Cell Therapy & Business Development Consultant at eXmoor pharma)

Founders

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

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

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view

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	£26.4m
No. of employees	40+
Competitor landscape Crinetics Pharmaceuticals	
Key risks - Attrition of potential drugs	

Key management team

Rosamond Deegan, Chief Executive Officer (formerly 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, Platforms and Founder; worked with Carol Robinson on developing mass spectrometry
Idlir Liko, Director of Technology and Founder; 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: https://www.omass.com

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

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view

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

CRISPR THERAPEUTICS · Bristol Myers Squibb · CENTURY THERAPEUTICS

Key risks

- 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 (as above)
Jim Glasheen (as above)
Leandro Vetcher (as above)
Deepta Bhattacharya, PhD, (Professor, Department of Immunobiology, University of Arizona, College of Medicine, Tuscon)
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://cladetx.com/

Syncona

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

Unless stated all financials at March 2022
Key competitors and risks: Syncona team view

Appendix 4 – Sustainability

Delivering positive and sustainable impact

Our social impact

- £4.2m donated to charity
- 19 portfolio company clinical trial sites across the UK
- 900+ people employed by Syncona and its portfolio in the UK

Responsible investor and partner

- Became a signatory to the UN Principles for Responsible Investment
- Responsible Investment Policy rolled out to full portfolio
- 9 out of 11 Syncona portfolio companies now reporting Scope 1 to 3 carbon emissions to Syncona

Inspiring and empowering our people

- First Windsor Fellowship intern completes six-month placement at Syncona
- First Generating Genius cohort begin studies
- Developing family-friendly policies

Responsible and ethical business

- First TCFD 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

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
Donations to charity since 2012[1]

30
Charities supported

0.35%
Of Syncona’s NAV donated to charity on an annual basis

1 Includes FY2021/2 donation (to be paid in July 2022)