SYNCONA

Synconaltd.com

Interim Results

November 2023

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In particular, many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many companies in the Syncona Limited portfolio have yet to commercialise a product and their ability to do so may be affected by operational, commercial and other risks.

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Syncona Limited seeks to achieve returns over the long term. Many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many companies in the Syncona Limited portfolio have yet to commercialise a product and their ability to do so may be affected by operational, commercial and other risks. The timing of positive or negative outcomes is uncertain and investors should be aware that over shorter periods our returns are likely to be volatile. The price of shares in Syncona Limited is determined by market supply and demand, and may be volatile in response to changes in demand and different to the net asset value.

Executive summary

Overview of the half

Rigorous capital allocation and active portfolio management to deliver key value inflection points

NAV return of (4.2)% reported in the half

- Driven by the write-off of the risk adjusted and discounted value of the Gyroscope milestone payments

Rigorous capital allocation

- Macroeconomic environment continues to be challenging for biotech companies both in terms of cost and access to capital, bringing both opportunity and financing risk
- Proactively managing the portfolio to ensure companies with clinical data reach late-stage clinical development
- Focus of capital allocation on clinical opportunities across the portfolio - >80% of capital deployed in the period into clinical or near clinical assets
- Board believes share price undervalues portfolio and prospects, launch of £40m share buyback

Strength of our balance sheet continues to be a key differentiator

- Supporting portfolio companies to navigate the cycle, driving new opportunities in innovation and selectively adding clinical-stage deals

Continued build out the senior leadership team, now well embedded to deliver long-term targets

- Appointments of Roel Bulthuis as Managing Partner and Head of Investments and John Tsai as Executive Partner
- Martin Murphy stepping down as Chair of SIML with Chris Hollowood becoming Interim Chair and CEO

Six value inflection points over the next 12-36 months that have the potential to drive significant value

Market and opportunity

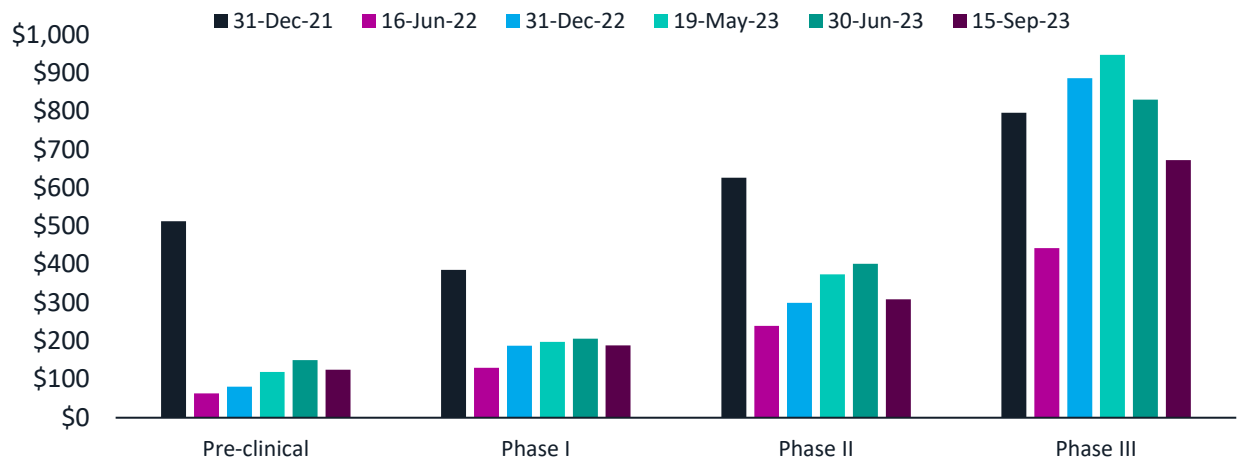
Market conditions remain challenging but value returning to late stage

Grounds for optimism for companies with high quality late-stage assets

Private and public financing environment remains challenging

- Valuations are recovering in companies developing late-stage assets in the public markets
- Financing challenges remain for clinical and pre-clinical companies – reflecting the importance of focusing on commercial opportunity
- Within the private market, down-rounds across Series A-C more common
- High quality assets will continue to win out
  - Public markets continue to put a premium on late stage, high quality assets
  - Pharma continues to be reliant on biotech for product development, with over $200bn in large pharma revenue at risk of patent expiry over the next six years[1]
  - Number of recent late-stage deals where big pharma have acquired biotech companies at attractive multiples

Average Enterprise Value of a Biotech listed on US exchanges by stage of development[2]



Recent $1bn+ deals with big pharma

1. Lazard. 2. Stifel. Note that the recent sales of Prometheus, Chinook Therapeutics, Bellus Health, Dice Therapeutics and Iveric Bio have reduced the average value of Phase III companies for June and September 2023. Syncona categorises Phase I assets as being clinical stage, with assets from Phase II onwards being late clinical

Continuing to develop our clinical-stage portfolio

Clinical-stage opportunities presented in the current market can be aligned with Syncona's strategy and model

Clinical-stage assets with opportunities to drive growth

- Targeting clinical assets which align with Syncona's model and provide the opportunity for significant returns
- Leveraging Syncona's expertise in identifying attractive late-stage opportunities and driving them towards approval
- The current market is providing more opportunities to acquire clinical-stage assets at attractive prices

Syncona investment model in action

BLUE EARTH DIAGNOSTICS
A Bracco Company

- Purchased Axumin asset from GE Healthcare in 2014, product approved in 2016
- Company sold for **$476m** at **9.9x** MOIC[1] in 2019

beacon therapeutics

- Acquired late-stage asset in XLRP from take-private of AGTC
- Syndicated **£96 million** Series A with Oxford Science Enterprises

1. Multiple on Invested Capital

Actively managing the portfolio

A framework for delivering NAV growth

Significant value accessed at late-stage development

Operational build

- Clearly defined strategy and business plan
- Leading management team established

Emerging efficacy data

- Pre-clinical companies with clinical strategy defined
- Clinical companies with initial efficacy data from Phase I/II

Current market environment

Capital access still driven by delivery of these expected milestones

Definitive data

- Significant clinical data shows path to marketed product
- Moving to pivotal trial and building out commercial infrastructure

On the market

- Commercialising product
- Revenue streams

Current market environment

Uplifts for late-stage assets are achievable

Actively managing our maturing portfolio

Rigorous capital allocation and proactive management across a portfolio with 71% of value in clinical stage

Prioritising capital allocation

- Funding de-risking clinical data to late stage
- Focus on execution of expected milestones that can drive capital access, recognising that in some cases we may need to prioritise assets with strong return opportunities
- Focus on funding 'first- and best-in-class' therapies in cell therapy and assets that can reach late stage in the near and medium term in gene therapy

Driving capital discipline within the portfolio

- Extending cash runways across the portfolio - rationalising budgets across all companies and reviewing and prioritising pre-clinical pipelines
- Widening financing syndicates and exploring creative sources of finance

Upcoming key value inflection points

With the potential to drive NAV growth

- **15 expected milestones** across the portfolio over the **next 12 months** which have the potential to enable capital access
- **Six value inflection points** which have the potential to drive significant NAV growth over **the next 12-36 months**
- These are not without risk, particularly given the importance of delivering de-risking clinical data in the current market environment

	CY2024	CY2025	CY2026
On the market Autolus		Traction in Autolus' commercial launch of obe-cel in Adult ALL, dependent on FDA regulatory approval in **CY2025**	
Definitive data beacon therapeutics	Beacon to present 24-month data from its Phase II trial in XLRP in **H2 CY2024**		
FREELINE	Freeline to release additional data from its Phase I/II trial in Gaucher disease in **CY2024**		
RTx			Resolution to complete Phase I/II trial in liver cirrhosis in **CY2026**
Emerging data QuellTx		Proof of concept data from Quell's liver transplant study in **CY2025**	
ANAVEON			Anaveon to publish data from its next generation ANV600 asset in **CY2026**

Portfolio spotlight: Freeline Therapeutics

Potential to deliver a company to late-stage development

Clinical stage

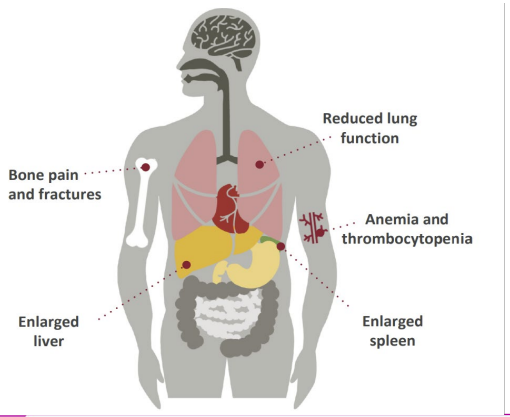
Initial investment	2015
Value	£8.8m
Financing stage	NASDAQ
Stage of lead programme	Phase I/II

Investment thesis

- Freeline has a **potential first- and best-in-class** lead programme
- **Highly differentiated** gene therapy candidate FLT201 for Gaucher disease type 1
- Published **compelling initial data** demonstrating robust enzyme activity and favourable safety and tolerability in first two patients treated with FLT201
- Experienced management team **executing well**
- Potential to extend innovation into Parkinson's disease

Targeting an area of high unmet need

- Gaucher disease type 1 is a **debilitating, chronic and progressive** disorder
- Affects multiple organs, leading to wide range of symptoms and shortening life span



Market opportunity

- Freeline estimates that Gaucher Disease Type 1 has approximately **18,000** patients[1]
- Annual Gaucher market size is **$1.5bn**[2]
- Syncona's shareholding is 49.7% with a **current valuation of £8.8m**

1. Freeline Corporate Presentation. Note: The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy 2. Global Gaucher's Disease Treatment Market Report and Forecast 2023-2031, Research and Markets. Note: this includes enzyme replacement therapy and substrate replacement therapy

Driving growth

The next frontier of science

Syncona sees significant opportunity across the scientific landscape to create the next wave of biotech leaders

"First Wave"

1950's

Small Molecule drugs, dominated by large pharmaceutical companies

"Second Wave"

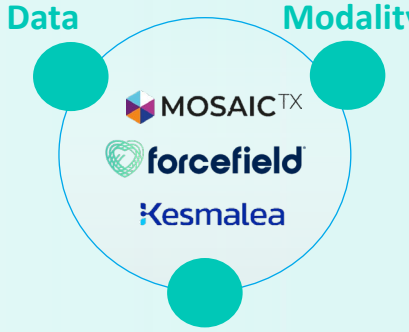
1990's

Large Molecule (antibody therapies, enzyme replacement therapies)

"Third Wave"

2010's

Advanced Biologics and genetic medicines such as gene therapy and cell therapy and DNA/RNA medicines



- Syncona was an early mover in the Third Wave, particularly in gene and cell therapy
- Starting to see a new frontier of science come to the fore
- Data generated from scientific advances unlocks new insights
- Increased understanding of genetics enables us to understand more about what is causing diseases
- Wide range of modalities across Second and Third Waves, provide flexibility in disease intervention
- We can then better pair the right modality to suit the disease context – huge opportunity for impact

Syncona aims to drive innovation in this frontier, further increasing portfolio diversification

Forcefield Therapeutics

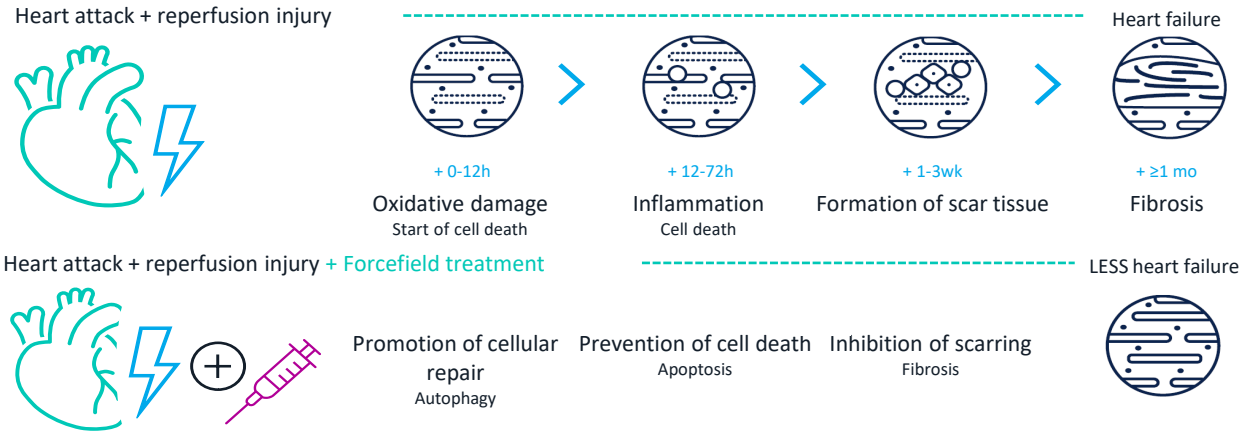
Pioneering therapeutics to retain heart function; moving from a seed investment to Series A launch

Unmet need in heart disease

- Heart disease is the **leading cause of death** worldwide
- Acute myocardial infarction (AMI), **affects 3 million people worldwide annually**
- There has been **no significant pharmacological advancement** in the treatment for AMI in the past two decades
- **25% of cells** in an area of heart containing up to 2-4 billion cells die after heart attack and reperfusion treatment
- Cells are not replaced, **leading to further heart attacks, heart failure or death**

Forcefield Therapeutics

- Pioneer of best-in-class therapeutics to retain heart function via protection of cardiomyocytes
- Discovered first-in-class cardioprotective proteins that Forcefield is progressing to target AMI
- Appointed Syncona Executive Partner, John Tsai MD, as Chief Executive Officer



Source: Global Awareness of Myocardial Infarction Symptoms in General Population; Korean Circulation Journal. Forcefield investment thesis to date based upon pre-clinical data

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Capital management

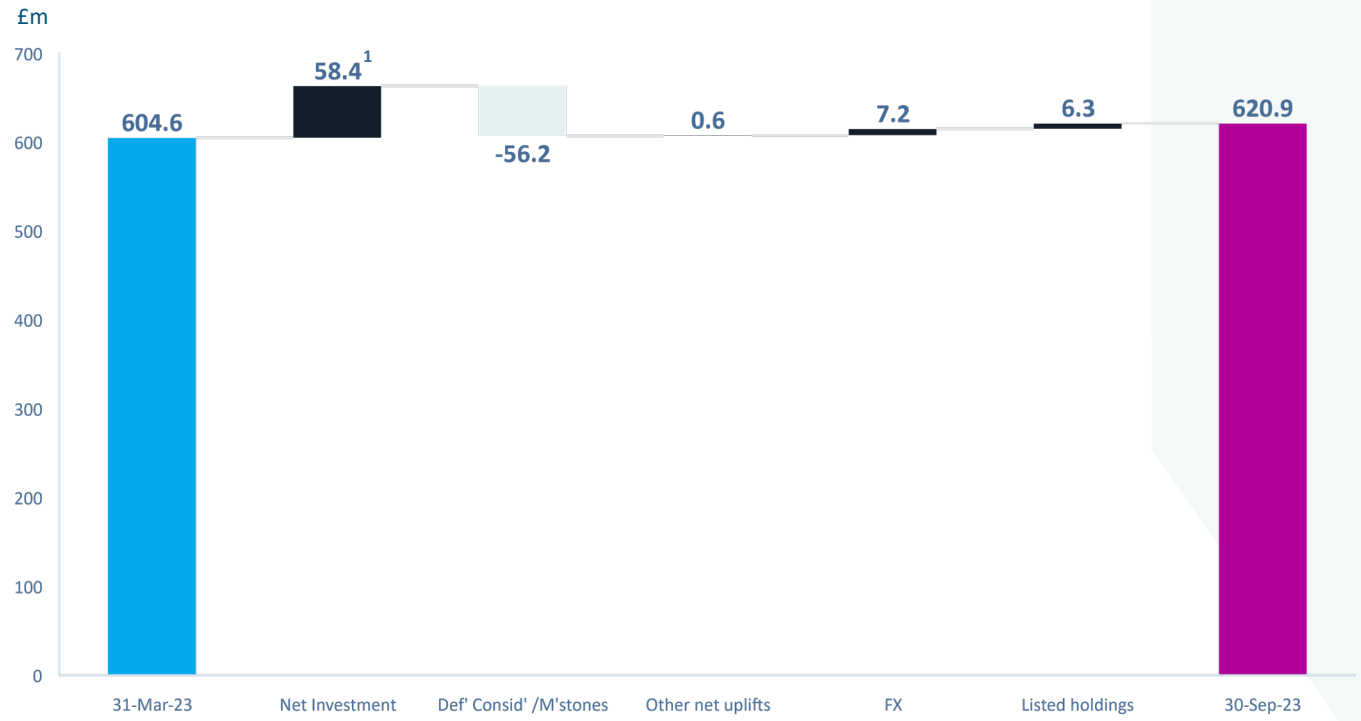
Performance in the half

Net assets of £1.2bn – a return of (4.2)% in the period

Performance primarily driven by Novartis' decision to discontinue development of GT005 and the subsequent £56.4 million write-off of the Gyroscope milestone payments

- Life science portfolio valued at £620.9m, a return of (7.0)%
- GT005 impact partially offset by net gain in the listed holdings of £6.3m
  - 27% increase in Autolus share price (+£12.4m), partially offset by declines in share prices of Freeline and Achilles
- £7.2 million gain from positive foreign exchange movements in the life science portfolio

Life science NAV bridge



1. £58.4m net investment in the period; £58.6m total capital deployed in the period is gross of £0.2m in distributions from the CRT Pioneer Fund.

Capital deployment in the half

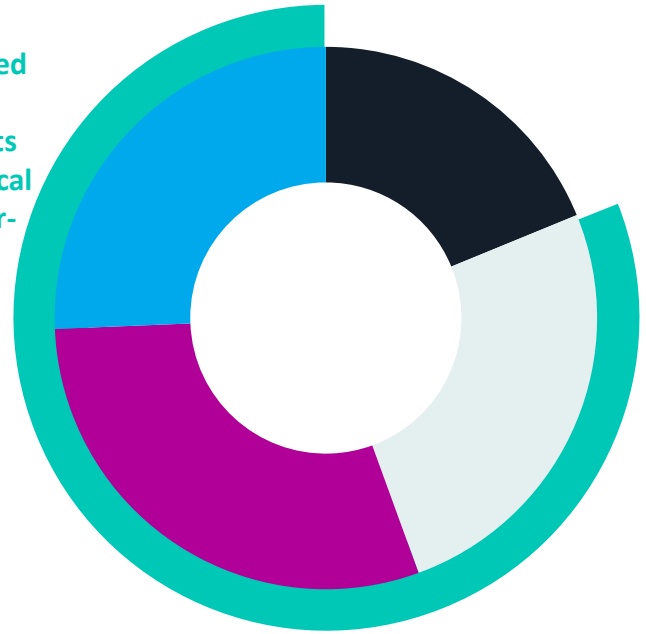
Continuing to prioritise investing in assets with the potential to drive near term growth

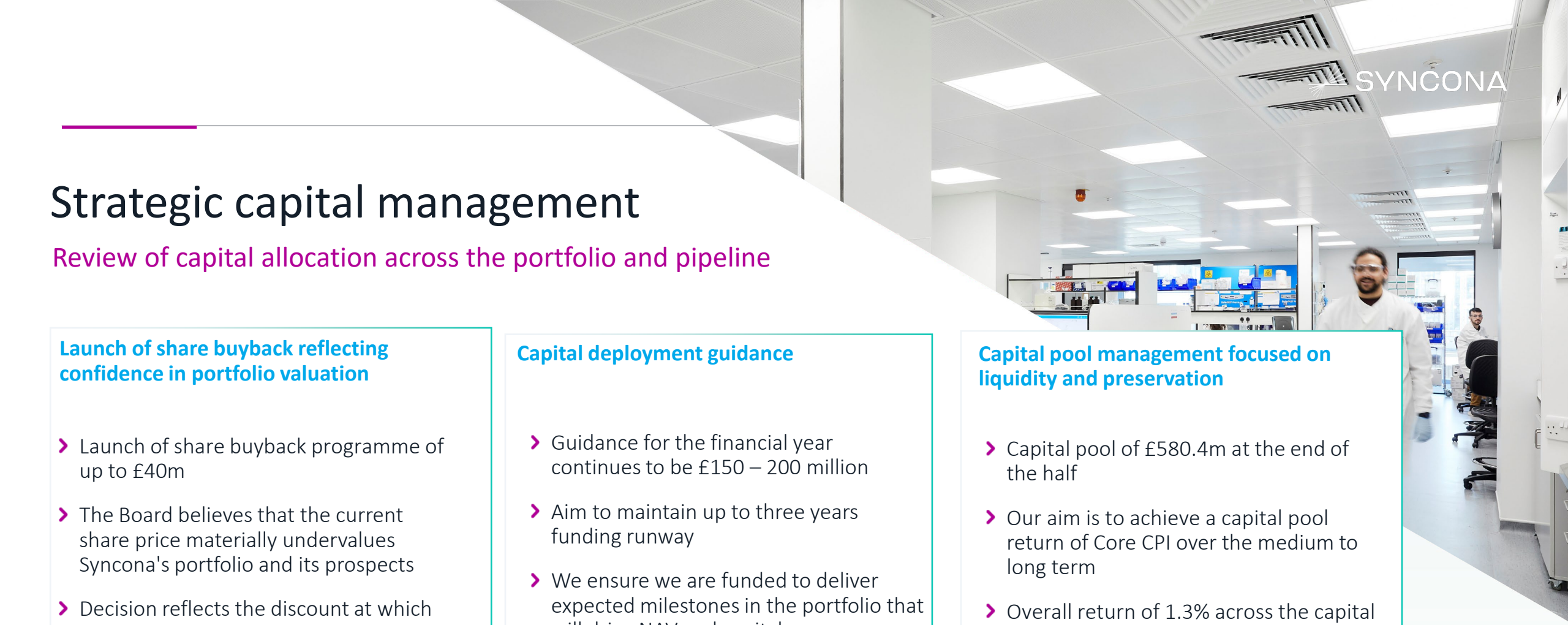
Capital deployment in the period

- Continued focus on allocating capital towards clinical assets
- Our priority remains driving optionality across the portfolio in a capital constrained environment whilst leveraging our expertise in driving assets through late-stage towards approval
- £58.6m capital deployed in the half - >80% has been into clinical-stage assets and assets approaching clinical entry in the near-term
- 26% of capital deployed into Beacon Therapeutics – an opportunity with the potential to progress to pivotal study
- Disciplined investment carefully tranched into pre-clinical opportunities
- More broadly, continue to tranche capital allocation across the portfolio to completion of key milestones

Capital deployment during the period (£m)

>80%
of capital deployed into clinical assets and assets approaching clinical entry in the near-term





Strategic capital management

Review of capital allocation across the portfolio and pipeline

Launch of share buyback reflecting confidence in portfolio valuation

- Launch of share buyback programme of up to £40m
- The Board believes that the current share price materially undervalues Syncona's portfolio and its prospects
- Decision reflects the discount at which the shares are trading and the near-term NAV per share accretion available
- Share price continues to represent a compelling investment opportunity

Capital deployment guidance

- Guidance for the financial year continues to be £150 – 200 million
- Aim to maintain up to three years funding runway
- We ensure we are funded to deliver expected milestones in the portfolio that will drive NAV and capital access
- If realisations from portfolio take us significantly above 3 years financing runway, the Board would look to return excess capital to shareholders, subject to an assessment of investment opportunities at the time

Capital pool management focused on liquidity and preservation

- Capital pool of £580.4m at the end of the half
- Our aim is to achieve a capital pool return of Core CPI over the medium to long term
- Overall return of 1.3% across the capital pool in the period
- 12-24 months of funding in cash and Treasury Bills

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People

Operating model embedded across Syncona team

The evolution of our team and structure will support delivery against our long-term targets

Senior investment team


Chris Hollowood
CEO


Roel Bulthuis
Managing Partner


Ed Hodgkin
Managing Partner


Elisa Petris
Lead Partner


Magdalena Jonikas
Lead Partner

Executive Partner Group


John Tsai
Experienced clinical leader and former CMO of Novartis


Ken Galbraith
Experienced biotech executive, Chair/CEO of multiple companies


Lisa Bright
Commercial leader with experience launching innovative medicines

Senior investment team supported by Executive Partner Group in driving delivery across the portfolio

- Expanded our Senior Investment and Executive Partner team with key personnel now embedded in a new structure
- Structure leverages the strengths and expertise of senior investment team members and enables business to further scale
- Supported by our Executive Partner Group who are working with portfolio companies as they scale
- Launch Team operational in companies that are in late-stage diligence

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Summary

Scaling our net assets

Committed to delivering our long-term strategy against a challenging market backdrop

3 new companies a year

We expect this target to incorporate late-stage opportunities or a significant transaction

Portfolio of 20-25 leading life sciences companies

Portfolio increasingly diversified by stage, therapeutic area and modality

3-5 companies to late-stage development where Syncona is a significant shareholder

Bringing in aligned co-investors, while maintaining strategic influence

Targets

3 new companies p.a.

20-25

companies

3-5 products to late-stage development

£5bn

Net Assets by 2032

Summary

Opportunity to deliver value in our portfolio and pipeline remains compelling

- The macroeconomic environment has been and remains challenging for biotech companies both in terms of the cost of and access to capital
- We remain resolutely focused on disciplined capital allocation and active portfolio management to drive NAV growth
- We have six potential value inflection points across the portfolio over the next 12-36 months and are funded to deliver these
- Our balance sheet will also enable us to continue to start new companies on the frontier of science that will lead the industry over the next decade
- We are focused on delivering our strategy to create, build and scale a portfolio of 20-25 leading life science companies and organically grow net assets to £5 billion by 2032
- We are well positioned to emerge from the current environment in an exciting position and deliver strong risk-adjusted returns for shareholders

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Appendix 1 - Team

Leadership team incorporates experience from across the business

Responsible for the operational delivery of Syncona's strategic priorities

Chris Hollowood
Chair and CEO

- M&A
- Biotech investing
- Board leadership
- Strategy development

Roel Bulthuis
Managing Partner, Head of Investments

- Deal generation and delivery
- Investment banking, VC and business development

Rolf Soderstrom
CFO

- Balance sheet management
- Strategic leadership

Edward Hodgkin
Managing Partner

- Executive leadership
- Company building

Alasdair Moodie
General Counsel

- Governance and compliance
- Company Secretary matters

Lisa Bright
Executive Partner

- Commercial launch and strategy
- Board leadership

Annabel Clark
Head of IR & Comms

- Shareholder relations
- Media communications
- Responsible investment

Andrew Cossar
Executive Partner, Head of Strategic Transactions

- Corporate and portfolio transactions

Fiona Langton-Smith
Chief Human Resources Officer

- Process optimisation
- People leadership
- Employee engagement

Strong senior investment team embedded

Responsible for leading the investment team and building the next generation of Syncona companies

Chris Hollowood[1]
Chair and CEO
PhD

FREELINE purespring beacon therapeutics

21 years' experience

Roel Bulthuis
Managing Partner, Head of Investments
MSc, MBA

23 years' experience

Edward Hodgkin[2]
Managing Partner
PhD

RTx OMass THERAPEUTICS

32 years' experience

Elisa Petris[2]
Lead Partner
PhD

QuellTX beacon therapeutics

15 years' experience

Magdalena Jonikas[2]
Lead Partner
PhD

Kesmalea THERAPEUTICS
OMass THERAPEUTICS
MOSAICTX

12 years' experience

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

Appendix 2 – Performance and track record

A track record of significant value creation from successful exits

£1.1 billion invested to date, generating an IRR of 20%, 1.4x invested capital[1]

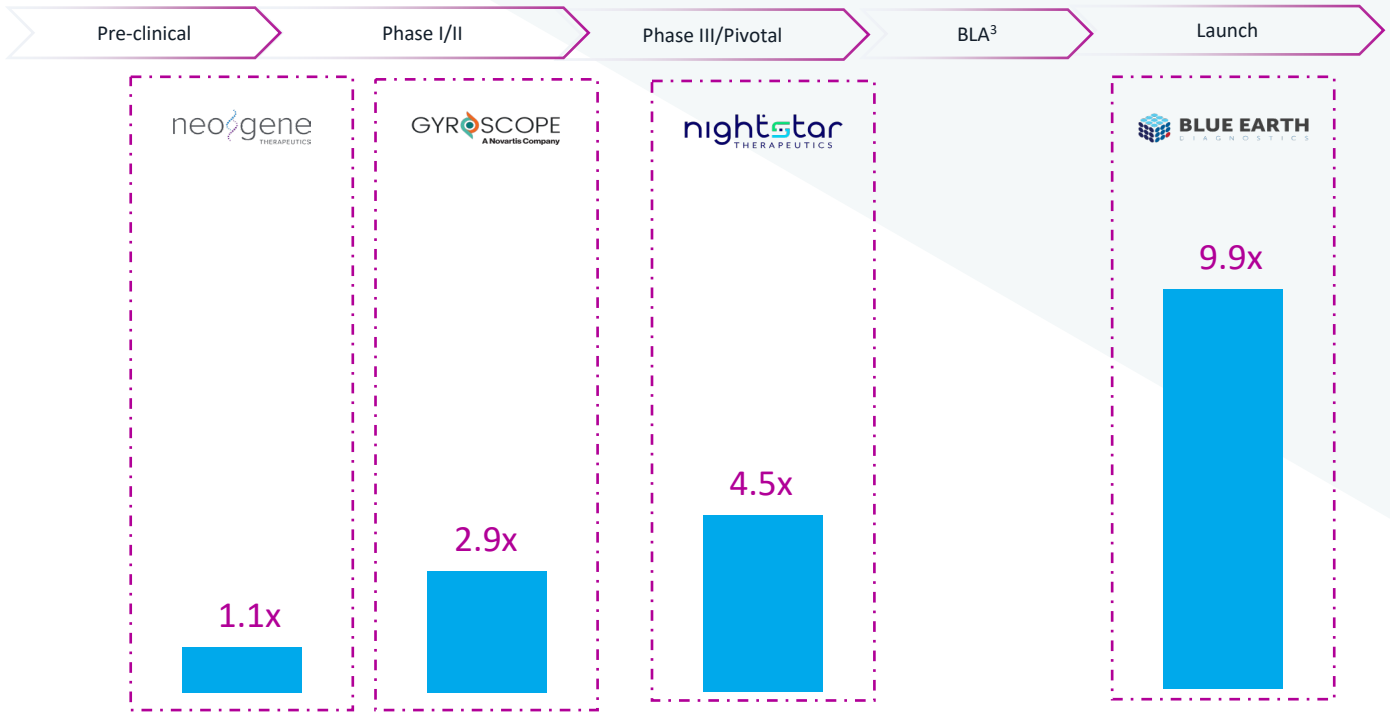
Four exits generated £948m of proceeds, at an aggregate IRR of 74% and a 4.3x cost[2]

Blue Earth
- First invested in the company in 2014, sold to Bracco Imaging in 2019
- 83% IRR – 9.9x cost on £351.0m proceeds

Nightstar
- Founded company in 2013, sold to Biogen in 2019
- 71% IRR – 4.5x cost on £255.7m proceeds

Gyroscope
- Founded company in 2016, sold to Novartis in 2022
- 50% IRR – 2.9x cost on £325.3m proceeds

Neogene
- First invested in the company in 2019, sold to AstraZeneca in 2022
- 3% IRR – 1.1x cost on £15.3m upfront proceeds



All financial data at 30 September 2023

1. Includes sales of Nightstar, Blue Earth, Gyroscope and Neogene and closure of 14MG and Azeria. 20% of the life science portfolio (including investments) held at cost, with 12% (SwanBio) held at calibrated cost. 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 Gyroscope and upfront proceeds from Neogene, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
3. Biologics License Application

Building companies with impact

Syncona has generated significant impact across its portfolio since being founded in 2012

Building global leaders

22	Syncona portfolio companies since 2012 foundation
13	Number of companies in the portfolio today
1,200+	Number of employees across Syncona portfolio

Our track record

20%	IRR since 2012; 1.4x multiple on cost across whole portfolio[1]
£1.1bn	Syncona capital deployed since 2012
£948m	Generated from four successful exits; 4.3x multiple of cost[2]

Clinical progress

3	Companies progressed to late-stage development since inception
22	Programmes progressed to clinical stage since inception
14	Number of clinical trials in the portfolio

Patient impact

165k	Patients diagnosed by Blue Earth's product Axumin
8,400	Annual cases of Adult ALL, disease targeted by Autolus' obe-cel[4]
7	Diseases with high unmet need targeted by lead programmes in clinical portfolio

1. Includes sales of Nightstar, Blue Earth, Gyroscope and Neogene and closure of 14MG and Azeria. 20% of the life science portfolio (including investments) held at cost, with 12% (SwanBio) held at calibrated cost. 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 Gyroscope and upfront proceeds from Neogene, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
3. Includes lead Beacon programme in XLRP. 4. Autolus corporate presentation
All financials as at 30 September 2023, employee numbers as of March 2023

Appendix 3 - Portfolio

Late-stage clinical | Clinical | Pre-clinical

Portfolio company	Fully diluted ownership %	31 Mar 2023 value £m (fair value)	Net invested/returned in the period £m	Valuation change £m	FX movement £m	30 Sep 2023 value £m (fair value)	Valuation basis (fair value)[1,2]	% of NAV
beacon therapeutics	67.8%	60.0	15.0	-	-	75.0	PRI	6.2%
Autolus	17.5%	50.0	-	12.4	1.6	64.0	Quoted	5.3%
QuellTX	35.0%	86.7	-	-	1.0	87.7	PRI	7.3%
SwanBio THERAPEUTICS	80.0%	58.2	17.5	0.5	1.2	77.4	Adjusted cost	6.4%
ANAVEON	37.9%	64.2	-	-	0.7	64.9	PRI	5.4%
FREELINE	49.7%	14.1	-	(5.4)	0.1	8.8	Quoted	0.7%
ACHILLES THERAPEUTICS	24.5%	8.6	-	(0.4)	0.1	8.3	Quoted	0.7%
OMass THERAPEUTICS	28.9%	43.7	-	-	-	43.7	PRI	3.6%
RTx	78.8%	23.0	14.9	-	-	37.9	Cost	3.2%
purespring	84.0%	35.1	-	-	-	35.1	Cost	2.9%
CLADE THERAPEUTICS	22.3%	24.3	-	-	0.3	24.6	Cost	2.1%
Kesmalea	71.8%	4.0	8.0	-	-	12.0	Cost	1.0%
MOSAICTX	52.4%	7.3	-	-	-	7.3	Cost	0.6%
Milestones and deferred consideration		70.4	-	(56.2)	2.0	16.2	DCF	1.4%
Syncona Investments		55.0	3.0	(0.2)	0.2	58.0		4.9%
Capital pool		650.1	(79.4)	10.4	(0.7)	580.4		51.7%
Total		**1,254.7**				**1,201.3**		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

Clinical portfolio company outlook

Strategic portfolio companies	Next expected milestones with the potential to enable capital access	Syncona view of potential value inflection points across the portfolio
Autolus	H2 CY2023 - Further long-term follow up data from its pivotal study in obe-cel in adult r/r B-ALL - BLA submission for obe-cel to the FDA H1 CY2024 - Initiate a Phase I study of obe-cel in refractory systemic lupus erythematosus (SLE), extending the use of obe-cel into autoimmune diseases H2 CY2024 - Provide initial data from the Phase I trial in SLE CY2024 - Commence the US commercial launch of obe-cel, dependent on FDA regulatory approval	CY2025 - Traction in the US commercial launch of obe-cel, dependent on FDA regulatory approval
Achilles Therapeutics	Q1 CY2024 - Provide further data from its Phase I/IIa clinical trial in NSCLC - Provide further data from its Phase I/IIa clinical trial in melanoma	
QuellTx	H2 CY2023 - Complete dosing of the safety cohort in its Phase I/II trial in liver transplantation	CY2025 - Proof of concept data from its Phase I/II trial in liver transplantation
beacon therapeutics	H1 CY2024 - Publish 12-month data from its Phase II trial in XLRP - Initiate its Phase II/III trial in XLRP	H2 CY2024 - Present 24-month data from its Phase II trial in XLRP
FREELINE	CY2024 - Release of additional data from its Phase I/II trial in Gaucher disease	CY2024 - Release of additional data from its Phase I/II trial in Gaucher disease
SwanBio Therapeutics	H1 CY2024 - Initial safety readout on higher dose cohort from its Phase I/II trial in AMN	
RTx	H2 CY2024 - Enter the clinic in a Phase I/II trial in liver cirrhosis	CY2026 - Completion of Phase I/II trial in liver cirrhosis in CY2026
ANAVEON	H2 CY2024 - Publish initial data from its Phase I/II trial of ANV419 in metastatic melanoma - Initiate a Phase I/II trial of ANV600, the company's next generation compound	CY2026 - Clinical data readout from its Phase I/II trial of its next generation asset ANV600

SYNCONA

Late-stage clinical

Beacon Therapeutics

Progressing to pivotal study in X-linked retinitis pigmentosa programme

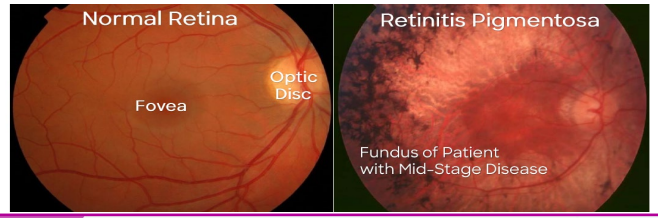
Initial investment	2022
Value	£75.0m
Financing stage	Series A
Stage of lead programme	Phase II

Investment thesis

- Beacon has a highly attractive gene therapy programme targeting X-linked retinitis pigmentosa (XLRP), a blinding disease
- Clinical data generated by the company so far has been encouraging demonstrating improvements in visual sensitivity sustained for 24+ months
- Pivotal study initiation in H1 CY2024
- Retinal gene therapy is an area where Syncona has significant expertise and XLRP is a disease setting the team knows well from Nightstar experience
- Business has an integrated gene therapy manufacturing platform and leading management team

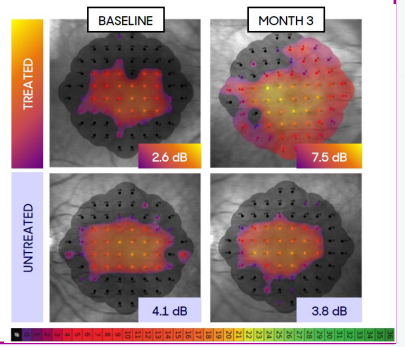
Targeting an area of high unmet need

- XLRP is a severe, aggressive, inherited retinal disease
- Disease progression – moves from night blindness to central vision loss and legally blind by median age 45
- No treatment options
- Beacon's potentially best-in-class programme is the only late-stage clinical programme that can deliver the full-length missing protein, important for function of both rods and cones



Market opportunity

- >20,000 patients in US/Europe[1]
- Although XLRP accounts for 15% of all cases of retinitis pigmentosa (RP), it is characterised to have the most severe vision loss - with XLRP patients four times more likely to have visual acuity ≤20/200 (legally blind), than those with autosomal dominant RP



1. Daiger SP. Perspective on genes and mutations causing retinitis pigmentosa. Arch Ophthalmol

SYNCONA

Late-stage clinical

Autolus Therapeutics

Leading cell therapy company preparing for commercial launch of its lead programme in adult ALL

Initial investment	2014
Value	£64.0m
Financing stage	NASDAQ
Stage of lead programme	Pivotal

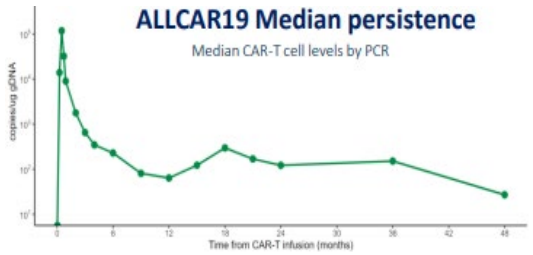
Investment thesis and company update

- Chimeric Antigen Receptor (CAR) T cell therapies have been shown to be effective in some haematological malignancies and may have wide applications as a cancer treatment, with the potential for cure in some patients
- Lead product candidate, obe-cel, potentially best-in-class therapy for relapsed refractory for adult acute lymphoblastic leukaemia (ALL), has a competitive profile in B-cell non-Hodgkin's lymphoma (B-NHL) and has potential in autoimmune diseases
- BLA filing for obe-cel in adult ALL planned by end of CY2023
- Advanced in-house manufacturing facility ready for commercial launch

Targeting an area of high unmet need

- Only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care[1]
- If approved, obe-cel has the potential to be a best-in-class curative therapy in adult ALL and expanding use beyond academic transplant centres

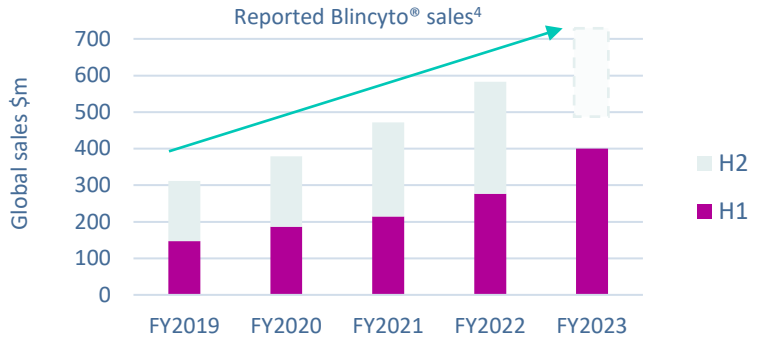
Key data[2]



- Launching a Phase I trial in systemic lupus erythematosus (SLE) in H1 2024, a multi-organ systemic autoimmune disease that affects approximately 160K - 320K patients in the US[3]

Market opportunity for lead programme

- Over 8,000 new cases of adult ALL annually worldwide
- Obe-cel could launch into an expanding ALL market if approved with commercial rollout planned for 2024
- Tecartus® (approved in 2022) is expected to establish CAR-T in adult ALL
- Blincyto®, current market leader, sales increased 48% year-over-year to $206 million for the second quarter 2023[4]



1. Autolus corporate presentation 2. ALLCAR19 academic study 3. Mackensen et al., Nat Med. 2022, Mougiakakos et al. N Engl J Med. 2021, Müller et al. Lancet. 2023, Bergmann et al. Ann Rheum Dis. 2023, Taubman et al. Rheumatology (Oxford). 2023 4. As per Amgen quarterly SEC filings

Quell Therapeutics

On track to be the first company to deliver engineered Tregs in the liver transplant setting

Clinical stage

Initial investment	2019
Value	£87.7m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Potential to durably reset immune dysregulation with a single treatment, in transplantation, auto-immunity and inflammation
- On track to be the first trial in liver transplantation – a de-risked setting with significant unmet need for patients
- Collaboration with AstraZeneca with $85m upfront (cash and equity) and potential payments of over $2bn
- Dosing in 2023 with goal to demonstrate a durable full tolerance
- Funded through key datasets with strong investor syndicate

Targeting an area of high unmet 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[1]
- Immunosuppression leaves the patient open to attack by pathogens which cause serious infections
- Immunosuppression can also leave a patient susceptible to develop cancer due to it not being recognised and cleared by the body
- Quell's Treg therapy could save patients from needing life-long immunosuppression

Market opportunity

- 15,000 liver transplants per year across US and Europe[2]
- GMP manufacturing capacity on-line in Quell facilities

1. https://www.ema.europa.eu/en/clinical-investigation-immunosuppressants-solid-organ-transplantation 2. OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015

Anaveon

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

Clinical stage

Initial investment	2019
Value	£64.9m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Developing a selective IL-2 agonist with improved administration and toxicity burden
- Clinical data demonstrating the potential for a best-in-class agent
- In Phase I dose escalation study, data presented to date underlines strong safety and efficacy potential of the drug – this is key in human IL-2 where other drugs have had a high toxicity burden and require burdensome infusions
- In its Phase I/II study, 66% of patients achieved at least disease stabilisation at ≥108 µg/kg dose level
- A Phase I/II trial of the drug in metastatic melanoma began in FY2022/3
- Company's pre-clinical ANV600 programme also has potential as a targeted therapeutic

Targeting an area of high unmet 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[1]
- Metastatic melanoma suffers from a very poor prognosis, with the 5-year survival rate estimated to be 10%[2]

Market opportunity

- Wide potential utility across multiple oncology indications in wider markets[3]
- In 2022, 97,610 patients in the US are expected to be diagnosed with melanoma, 13% have disease which can't be managed by removal of the tumour alone[3]
- NSCLC accounts for around 80% of lung cancers, the leading cause of global cancer incidence and mortality, accounting for an estimated 2 million diagnoses and 1.8 million deaths[4]

1. OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015 2. https://www.ncbi.nlm.nih.gov/books/NBK470358/ 3. https://seer.cancer.gov/statfacts/html/melan.html 4. GLOBOCAN 2020

SYNCONA

Clinical stage

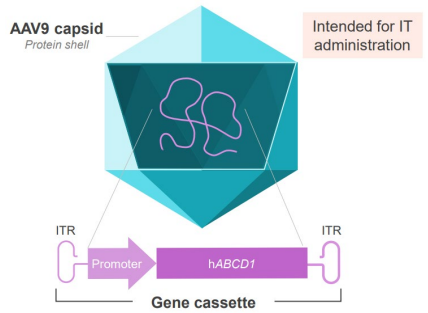
SwanBio Therapeutics

Developing AAV-based therapies for the treatment of devastating, inherited neurological conditions

Initial investment	2018
Value	£77.4m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Gene therapy has the potential to be transformational in neurology
- Focus on the spine – an uncrowded space and only tissue with proven transduction and clinical efficacy
- In lead adrenomyeloneuropathy (AMN) programme, have completed dosing of low-dose cohort, and initiated dosing of high-dose cohort
- Efficacy proof of concept established pre-clinically



Targeting an area of high unmet need

- AMN is an inherited neurodegenerative disease in which the causative gene is definitively known and well characterised
- AMN is a devastating disease characterised by progressive muscle weakness, leading to loss of mobility, incontinence and debilitating pain
- As the disease progresses and becomes more debilitating, most people with AMN require a wheelchair
- There are no current treatments and few in development

Market opportunity

- AMN impacts 8,000-10,000 male patients in the US and EU5[1]
- Zolgensma, a gene therapy which treats spinal muscular atrophy, has a reported list price of £1.79m per dose[2]

1. SwanBio analysis. 2. https://www.england.nhs.uk/2021/03/nhs-england-strikes-deal-on-life-saving-gene-therapy-drug-that-can-help-babies-with-rare-genetic-disease-move-and-walk/

SYNCONA

Clinical stage

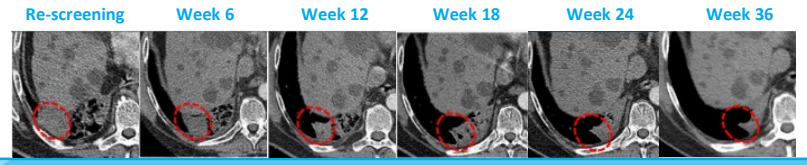
Initial investment	2016
Value	£8.3m
Financing stage	NASDAQ
Stage of lead programme	Phase I/II

Achilles Therapeutics

Developing AI-powered precision T cell therapies targeting clonal neoantigens to treat solid tumours

Investment thesis

- Lead product is a precision tumour-derived T cell therapy targeting clonal cancer neoantigens
- Uses DNA sequencing data from each patient, together with a proprietary bioinformatics platform, to identify clonal neoantigens specific to that patient and to potentially enable the development of personalised cell therapies
- Focusing on treating solid tumours with precision T cell therapy by targeting multiple clonal neoantigens present on all cancer cells
- NSCLC patient with a 56% reduction in total target lesion size vs. baseline at week 36



Targeting an area of high unmet need

- High unmet need in lead indications, advanced NSCLC and recurrent metastatic melanoma
- Of all NSCLC patients, 65% are diagnosed with advanced disease (stage III/IV)[1], of which less than 10% survive for 5 years or more[2]
- Metastatic melanoma suffers from a similarly poor prognosis, with the 5-year survival rate estimated at 10%[3]

Market opportunity

- Lung cancer is the leading cause of global cancer incidence and mortality, accounting for an estimated 2 million diagnoses and 1.8 million deaths[4]
- NSCLC accounts for around 80% of lung cancers, which has limited treatment options and is the leading cause of cancer deaths[4]
- In 2022, 97,610 patients in the US were expected to be diagnosed with melanoma, 13% have disease which can't be managed by removal of the tumour alone[5]

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7867742/#:~:text=As%20pointed%20out%20above%2C%20NSCLC,as%20stage%20III%20(6). 2. https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.24871 3. https://www.ncbi.nlm.nih.gov/books/NBK470358/ 4. GLOBOCAN 2020 5. https://seer.cancer.gov/statfacts/html/melan.html

SYNCONA

Pre-clinical stage

Initial investment	2018
Value	£43.7m
Financing stage	Series B

OMass Therapeutics

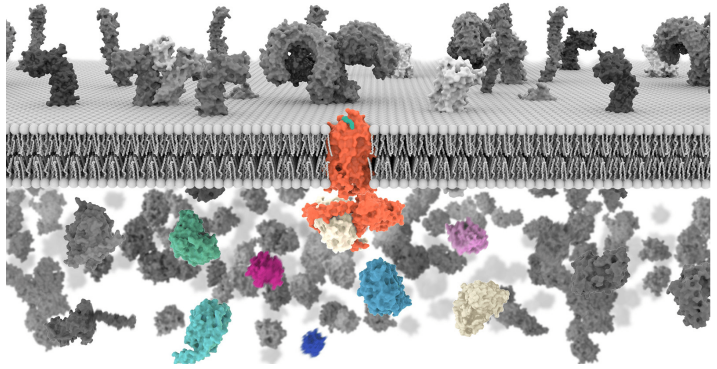
A platform built to unlock highly validated but inadequately drugged targets, with a focus on immunological and rare diseases

Investment thesis

- Historically, small molecule drug discovery has focused on targets that operate in relative isolation
- Many of the best targets operate within a membrane or an intracellular complex
- To drug these targets, it is necessary to interrogate their full spectrum of physical interactions within the native ecosystem
- OMass' platform seeks to interrogate not just the target, but how it interacts with its native ecosystem to identify new medicines against highly validated but inadequately drugged targets
- Pipeline of small molecule therapeutics including five programs in rare diseases and immunological conditions

Targeting an area of high unmet need

- All of OMass' programmes are in indications with significant unmet medical need
- Programmes include: orphan endocrine disorders, lupus and other IFN-opathies, immunology, inflammatory bowel disease and epilepsy



Market opportunity

- Most advanced programme in orphan endocrine disorders could potentially include several indications with large market sizes
- These include, congenital adrenal hyperplasia (CAH) and in Polycystic Ovary Syndrome (POS)
- CAH occurs in about 1 in 13,000-15,000 births[1], and presents a $450m global market opportunity[2]
- POS affects around 8-13% of women of reproductive age worldwide[3], presenting a $3.54bn global market opportunity[4]

1. https://www.ncbi.nlm.nih.gov/books/NBK278953/ 2. https://www.marketresearchfuture.com/reports/congenital-adrenal-hyperplasia-market-4946 3. https://www.who.int/news-room/fact-sheets/detail/polycystic-ovary-syndrome#:~:text=PCOS%20a%20significant%20public%20health,70%25%20of%20cases%20are%20undiagnosed.

4. https://www.insightaceanalytic.com/report/global-polycystic-ovary-syndrome-pcos-treatment-market/1455#:~:text=The%20Polycystic%20Ovary%20Syndrome%20(PCOS,PCOS)%2C%20a%20hormonal%20disorder.

SYNCONA

Pre-clinical stage

Initial investment	2020
Value	£35.1m
Financing stage	Series A

Purespring Therapeutics

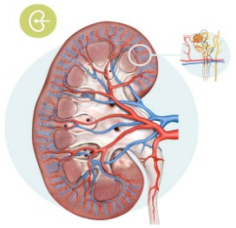
First company to treat kidney diseases by directly targeting the podocyte with AAV gene therapy

Investment thesis

- Developing a proprietary platform to enable kidney gene therapy
- Targeting the podocyte allows it to directly treat a significant portion of kidney diseases
- We only have a finite number of podocytes in our kidneys: unlike other human cells such as liver cells or skin cells, podocytes do not regenerate over our lifetime
- Injuries to the podocytes lead to issues in the filtration barrier, reducing the kidney's filtration capacity, causing kidney diseases

Targeting an area of high unmet need

- There are currently no curative or disease-modifying therapies
- Current standard of care for end-stage renal disease relies on either dialysis or kidney transplant
- Haemodialysis can cause low blood pressure and leave patients at risk of infection, whilst kidney transplant patients will still need to take lifelong immunosuppression



Market opportunity

- 4m patients are on renal replacement therapy[1]
- Kidney diseases are common. Around 10% of the population suffers from chronic kidney diseases[2]
- More than 840m people globally suffer from chronic kidney disease, including 3m in the UK and more than 37m in the US
- The podocyte is implicated in 60% of renal disease[3]

1. https://www.nature.com/articles/s41581-022-00542-7 2. Health Survey for England, 2016; CDC, Chronic Kidney Disease in the US, 2021; GBD Chronic Kidney Disease Collaboration. Nephrol Dial Transplant (2019) 34: 1803–1805 3. Purespring analysis

SYNCONA

Pre-clinical stage

Initial investment	2021
Value	£24.6m
Financing stage	Series A

Clade Therapeutics

Seeking to dramatically broaden the impact of cell therapy by establishing a more robust cellular platform

Investment thesis

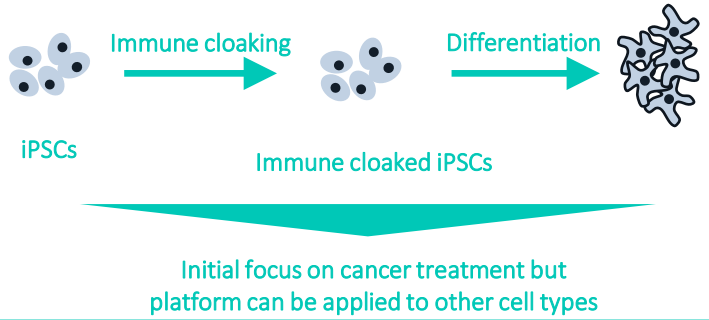
- Building the foundation for engineerable, off-the-shelf, scalable, and consistent cell medicines
- Delivery of scalable next generation induced pluripotent stem cell (iPSC) derived medicines that address the supply and cost challenges of autologous cell therapy, and the efficacy challenge of allogeneic cell therapy
- Combining three leading proprietary platforms:
  - Advanced immune cloaking technology to increase persistence
  - Differentiation to key target cell types in a reproducible and scalable manner
  - Universal targeting discovery platform

Targeting an area of high unmet need

- Replicating the benefits of the autologous CAR-T products, while addressing their profound limitations – inconsistent quality, challenging patient logistics, cost, and lack of scalability
- Broadening the applicability of cell therapies, e.g., for solid tumour indications, where cell therapies have had underwhelming impact due to the limited engineerability of autologous cells
- Significant potential for best-in-class iPSC-derived therapies for applications outside of oncology

Market opportunity

- 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



SYNCONA

Pre-clinical stage

Initial investment	2018
Value	£37.9m
Financing stage	Series A

Resolution Therapeutics

Seeking to extend the impact of cell therapy into chronic inflammatory liver disease

Investment thesis

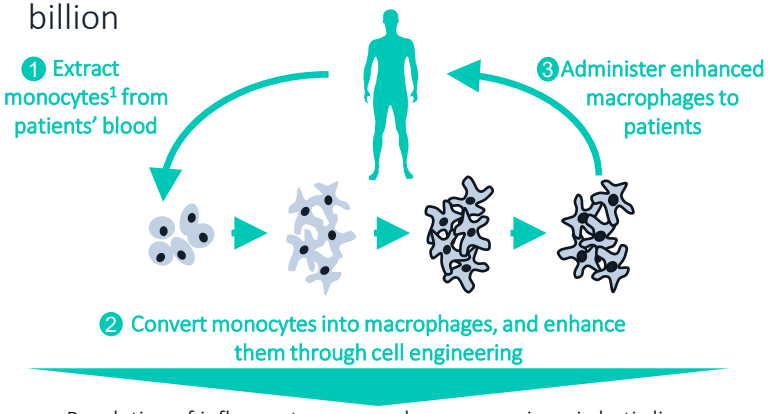
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries
- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest scar tissue, switch off the inflammatory response and promote organ repair
- Encouraging clinical data already obtained in cirrhotic patients with earlier generation (academic) programme
- Company's lead program is an engineered, autologous macrophage product

Targeting an area of high unmet need

- Cirrhotic patients experience severe "decompensation" episodes as a result of failing liver function
- Decompensation episodes include life-threatening GI bleeding, ascites and coma, all of which contribute to a high cost of treatment and the need for liver transplantation
- Liver transplant, the only therapeutic treatment for chronic liver failure, is associated morbidity, mortality and cost, and requires lifetime immunosuppression

Market opportunity

- 1-2 million people estimated to be affected by liver cirrhosis across major Western markets[1]
- The all-in cost of a liver transplant today is several $100k, yielding a total annual market size across the US and EU5 in the region of c.$10 billion



1. Scaglione et al., Journal of Clinical Gastroenterology, 2015

SYNCONA

Pre-clinical stage

Initial investment	2022
Value	£7.3m
Financing stage	Series A

Mosaic Therapeutics

Leveraging the unprecedented insights of the genomic revolution to develop targeted therapies for cancer

Investment thesis

- Tumour agnostic drug discovery based upon deep biological understanding of target-disease association, seeking precision oncology drug combinations for biomarker-stratified populations
- Differentiated platform technology leveraging machine learning, patient tumour material and existing chemical matter provides opportunity for improved success rates and potential for accelerated clinical entry

Targeting an area of high unmet need

- Mosaic platform and proprietary technology enables large scale CRISPR and drug screens, supporting drug development against genetically informed targets
- Mean 5-year survival across all cancer types remains at 51%
- Oncology drug development is hampered by a 93% clinical failure rate

Market opportunity

- Testing all potential drug, target and therapeutic hypotheses is too time consuming and costly; there are over 800 known cancer fitness genes, over 200 cancer types, and over 2,000 known genetic biomarkers

SYNCONA

Pre-clinical stage

Initial investment	2022
Value	£12.0m
Financing stage	Series A

Kesmalea Therapeutics

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

Investment thesis

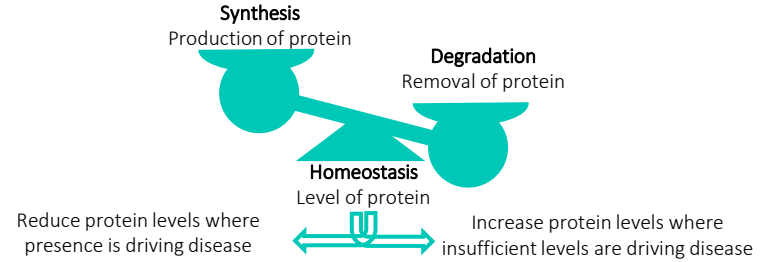
- Small molecule drug discovery platform focused on protein homeostasis
- Protein homeostasis is the system of maintaining the equilibrium of proteins in the human body. This intricate system is in a constant state of change, with the body continuously synthesising and regulating proteins, whilst removing those which are no longer required (or have mutated) through controlled degradation.
- 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
- Founded by Dr Harry Finch, a world-class chemist and co-inventor of GSK's Serevent™

Targeting an area of high unmet need

- Small perturbations of the human body's natural control mechanism that result in an excess or absence of certain proteins can drive the progression of disease
- Kesmalea aims to counter this dysregulation with novel treatments which restore balance through effective protein degradation or stabilisation
- Its novel approach allows it to overcome the challenges of existing protein degradation and stabilisation technologies, opening the door to previously unavailable oral therapeutics in areas of high unmet medical need

Market opportunity

- Protein degradation has the potential to be broadly applicable across of range of therapeutic areas, including but not limited to oncology, immunology and neurology indications
- Kesmalea will take a targeted approach as it develops its pipeline to ensure its programmes are addressing indications with significant clinical unmet need and ability to leverage Kesmalea's differentiation in oral therapeutics



Appendix 4 - Sustainability

Continuing to show a strong commitment to ESG

Our social impact

- £4.6m donated to charity in FY2022/3, ongoing commitment to donate 0.35% of NAV per year
- 18 portfolio company clinical trial sites across the UK[1]
- 1200+ people employed by Syncona and its portfolio
- Autolus' lead therapy, obe-cel, approaching BLA filing
  - Opened its 70k sq. foot UK manufacturing facility in Stevenage during the period

Inspiring and empowering our people

- Top 10 Firm in the FTSE 250 for appointing women to Board and leadership positions following FTSE Women Leaders Review
- Launched first D&I Framework
- Implementing results from first employee engagement survey across company
- Welcomed our third Windsor Fellowship intern to Syncona
- Continue to sponsor the Bio-spark programme, working with five fellows who will work on two Syncona-defined projects

Responsible investor and partner

- 11 Portfolio companies reporting Scope 1 to 3 carbon emissions to Syncona
- Integrating responsible investment approach into Launch Team processes
- Submitted first UN PRI questionnaire

Responsible and ethical business

- Signatory to the Net Zero Asset Managers (NZAM) initiative with draft target in development
- Published full portfolio carbon footprint
- Net zero aspiration on a full portfolio basis by 2050

1 - Sites which are active and at which patients are enrolled

The Syncona Foundation

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

Focused on the prevention, treatment, cure and ultimately eradication of cancer and other diseases — as well as other charitable activities

"I am incredibly proud of the support we continue to provide our charities. They are all working hard to assist those people who are in real need."

Tom Henderson
Chair of the Board of Trustees of the Syncona Foundation

£45m

Syncona donations to charity since 2012[1]

27

Charities supported

0.35%

Of Syncona's NAV donated to charity annually

In aid of Alzheimer's Research UK	Alzheimer's Society	Auditory Verbal UK	The Brain Tumour Charity
Brain Waves	butterfly thyroid cancer trust	Child Bereavement UK	cureleukaemia
David Nott Foundation	downside up	The Egmont Trust	Fight for Sight
Generating Genius	ICR The Institute of Cancer Research	James' Place	JDRF
Great Ormond Street Hospital Charity	the listening place	Macular Society	Maggie's
Marie Curie	NSPCC	Place 2Be	The Royal Marsden Cancer Charity
Supporting Wounded Veterans	ssafa the Armed Forces charity	Ella Project	

1 Includes FY2022/3 donation