SYNCONA

Syncona Full Year Results

12 months ended 31 March 2025

June 2025

Synconaltd.com

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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.

Overview

Financial performance impacted by challenging markets; strong portfolio execution and strategic update

Financial performance impacted by public market volatility

- NAV of £1.05bn, 170.9p per share, a return of (9.5%)
- (17.0)% return from the life science portfolio, with performance impacted by:
  - Significant decline in Autolus share price
  - Partial write-downs in the valuations of Resolution and Biomodal
  - Partially offset by valuation uplifts from financings of Beacon and Forcefield

Maturing portfolio of 14 companies making significant progress

- 78.5% of strategic portfolio is now in eight clinical-stage and commercial companies; two at late-stage
- Further two companies expected to enter the clinic in the next 12 months
- Delivered 10 capital access milestones and three key value inflection points (KVIP)
- Broader strategic progress, notably Mosaic in-licensing transaction
- Seven financings attracting £310.6m of capital - £175.5m of this from leading life sciences investors

Comprehensive review of options to maximise value for a diverse shareholder base

- Syncona's share price continues to be impacted by headwinds in the markets it operates
- Board has undertaken a comprehensive review of options and extensive shareholder engagement
- Proposed change to investment objective and policy to maximise value for shareholders over the medium term
- Exploring options to provide shareholders with accelerated cash returns
- Seeking to provide alternative opportunities for shareholders who wish to retain exposure to early-stage companies, via a private investment fund to be managed by SIML

Strategy update

Strategy update

The Board has been reviewing options to maximise shareholder value; these have progressed materially, with a number of anticipated future steps but definitive terms not yet agreed

Proposed Changes to Investment and Capital Allocation Policies

- Move to orderly realisation of portfolio assets – balance between returning cash in a timely manner and maximising value
- Continue to support existing portfolio companies to deliver KVIPs and preserve value in financings
- Net proceeds from realisations of private companies to be returned to shareholders
- Subject to FCA and shareholder approval
- Suspension of 2032 targets

Potential Acceleration of Cash Returns

- Exploring options to accelerate realisations
- May include sale of minority interests in certain portfolio companies at a modest premium to current share price, and a discount to NAV[1]
- Absent near-term realisations, Board to seek to accelerate cash returns in light of new strategy

Alternative Opportunities for Shareholders

- Seeking to offer certain shareholders opportunity to roll interests into a new independent private fund managed by SIML
- Discussions ongoing with several investors and London based university and research partners (LRPs)
- New private fund's strategy would be to build world class companies from ground breaking science sourced from LRPs and elsewhere

Governance

- Potential for SIML to be separated to continue managing Syncona's portfolio and new private fund
- Subject to approval of investment policy, expected reduction in Board size to reflect new strategy

1. If the new private fund is successful in raising new capital, it would enter into such transaction. There can be no certainty that new capital will be raised.

Market environment

Markets remain challenging for biotech

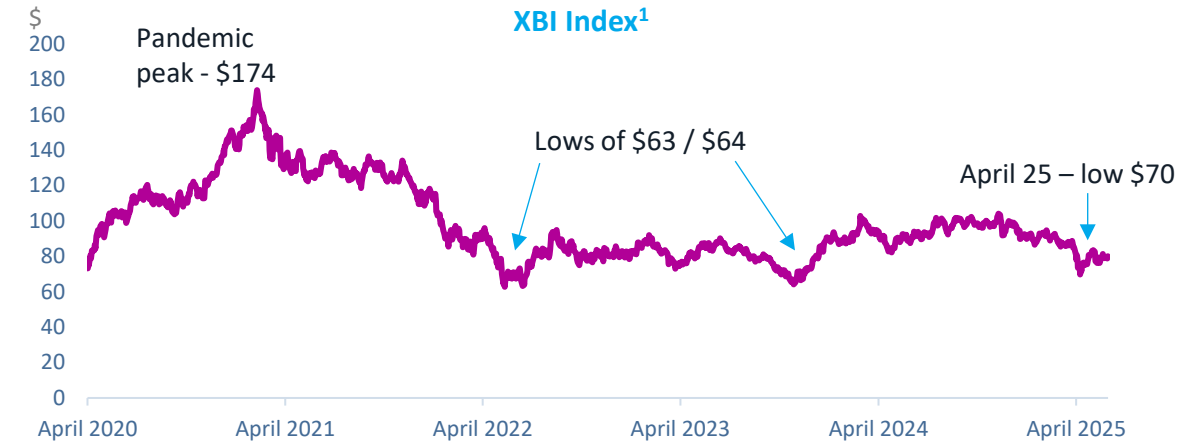
XBI is still >50% below its peak in 2021, but biotech market coming to the end of a significant period of restructuring, consolidation and rationalisation

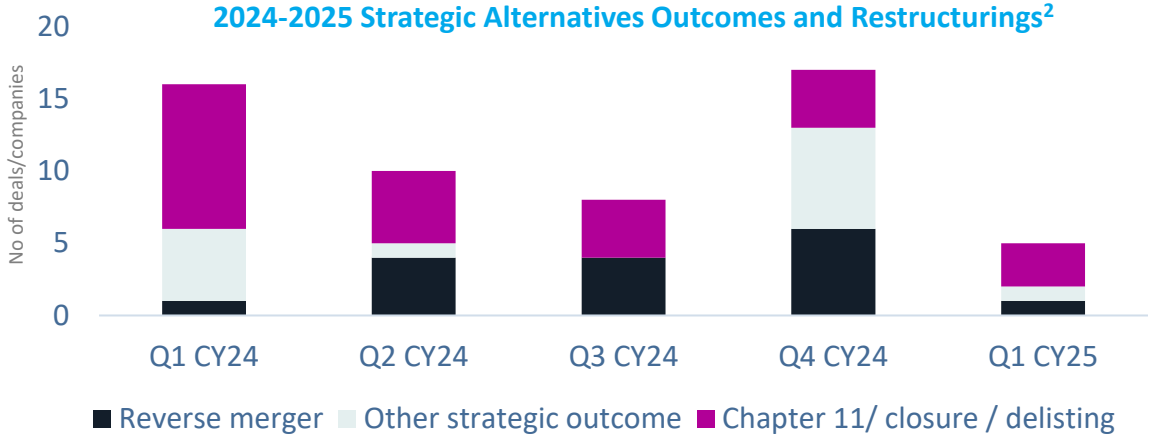
Rising inflation prompted central banks to increase interest rates, materially impacting the cost of capital

- Between March 2022 and July 2023, the Fed raised rates by more than five percentage points

Prompted a significant period of restructuring, consolidation and rationalisation

- c.28% of US listed biopharma companies trading at negative EVs – >50% have market caps below $100m – c. 43% of these are early stage[2]
- Strategic alternatives outcomes have slowed in Q1 CY2025
- Overall result will be healthier fundamentals, higher quality companies positioned for future growth





1. Source: Bloomberg as at 29 May 2025 2. William Blair The Quarterly Rx: Q1 2025 U.S. Biopharma Recap.

Other dynamics are delaying recovery

Biopharma facing several regulatory and policy headwinds in the US, with majority priced in amidst bearish sentiment

NIH[1] cuts

- Reduced federal research funding to foundational scientific discovery and early translational research
- Some smaller biotech firms reliant on NIH backed science grants

FDA staffing and policy shifts

- Large disruptions at the FDA and Department of Health and Human Services
- Shift in stance on vaccines and uncertainty on accelerated approvals and priority reviews

Pharmaceutical tariffs

- Renewed or expanded tariffs on pharmaceutical inputs could raise costs across the supply chain

Pricing reform

- Broad reaching Most Favored Nations executive order signed with potential impact on innovation

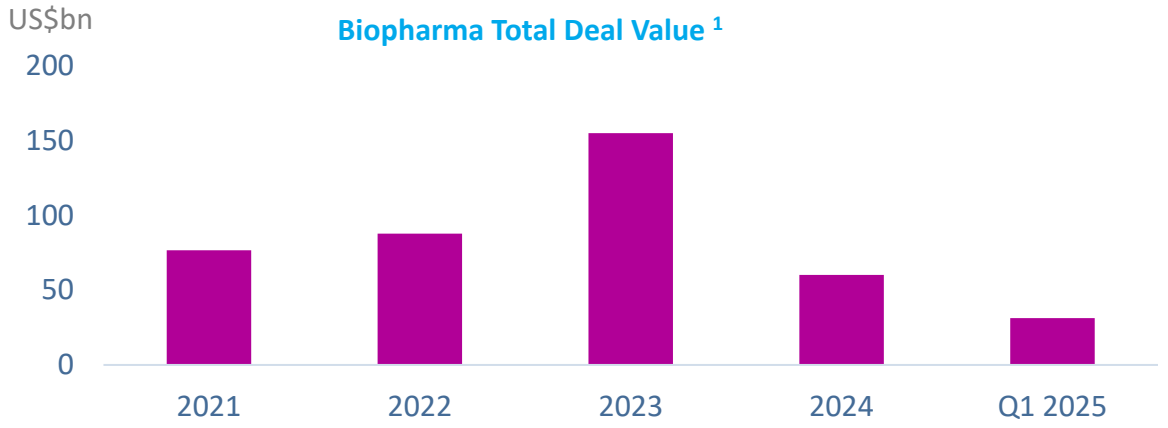
1. US National Institutes of Health

Fundamentals for the biotech sector are strong

Inflation and interest rates have been trending in the right direction, providing a tailwind for the sector

Pick up in M&A with market focused mainly on late-stage assets

- Total M&A deal value rebounded in Q1 2025 to $31 billion, largely driven by J&J's $14.6 billion acquisition of Intra-Cellular[1]
- In Q1 2025, 100% of public M&A and 60% of all M&A focused on companies with approved products or upcoming PDUFA[4] dates[1], aligned with Syncona's strategy



Biotech is the source of innovation for pharmaceutical companies

- Pharma is facing a patent cliff of over $350bn[2] by 2030 and has >$1.5tn in deal capacity[3]
- Pharma needs to replenish its pipeline and this will drive M&A and in-licencing activity to recycle capital into the biotech sector

Optimistic that once a more stable policy environment emerges, the combination of a healthier, restructured biotech market and pharma's need for innovation will catalyse a recovery

1. William Blair The Quarterly Rx: Q1 2025 U.S. Biopharma Recap 2. Evaluate Pharma / Stifel Healthcare: Biopharmaceutical Outlook for 2025 3. https://www.iqvia.com/locations/emea/blogs/2025/01/biopharma-m-and-a-outlook-for-2025 ; 4 A PDUFA date is the date by which the FDA aims to approve or reject a new medication

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Life science portfolio

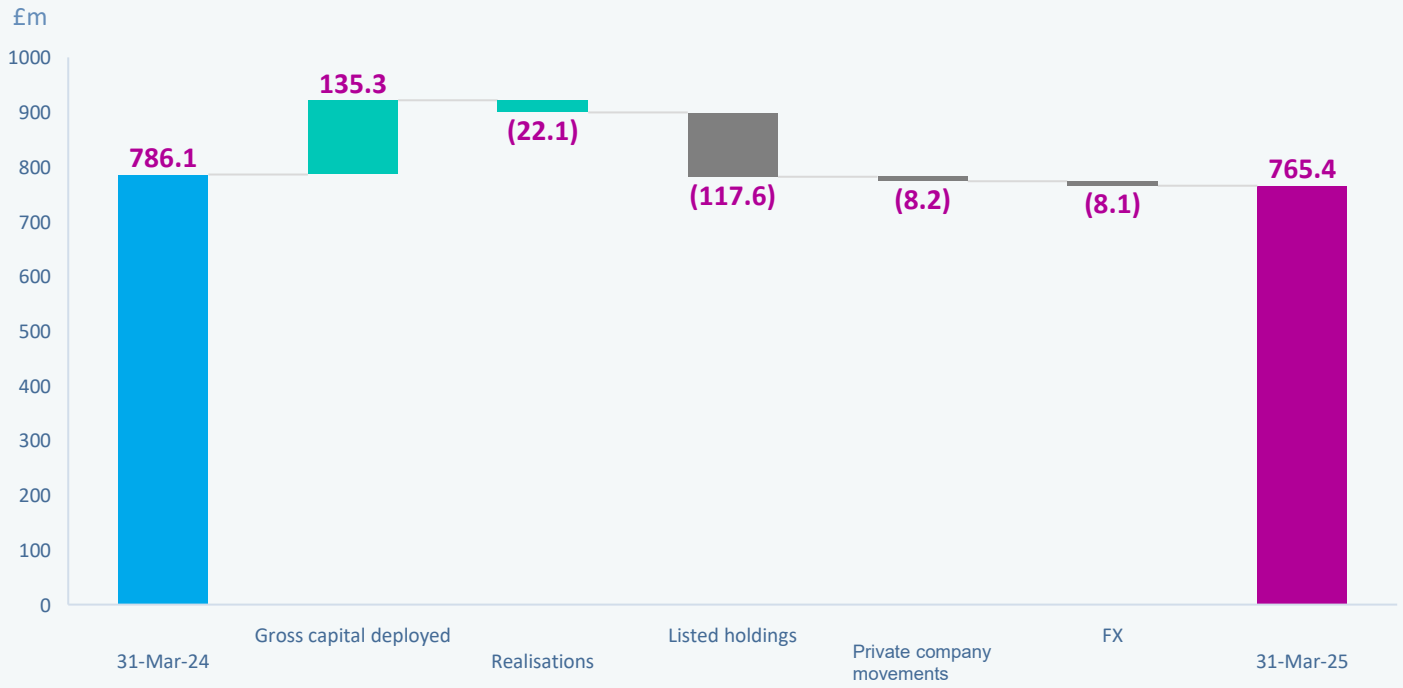
Performance impacted by challenging market and financing conditions

Net assets of £1.05bn, 170.9p per share – a return of (9.5)%

Life science portfolio valued at £765.4m – a return of (17.0)%

- £17.8m in valuation uplifts from financings of Beacon and Forcefield
- Outweighed by fall in Autolus share price, and partial write downs to Resolution and Biomodal
  - 76% fall in the share price of Autolus, despite FDA approval of AUCATZYL®
  - Private portfolio valuations broadly stable despite partial write downs of:
    - Resolution, following material third party interest in Series B syndication
    - Biomodial, reflecting the anticipated value of a future financing round. Syncona has not invested in Biomodial since its Series B in 2015
- Sale of Clade and partial realisation of Autolus at $4.50

Life science NAV bridge[1]

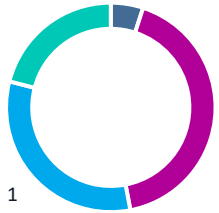


1. Realisations include proceeds from the partial realisation of Autolus, sale of Clade and distributions from the CRT Pioneer fund.

A well diversified portfolio weighted towards clinical-stage assets

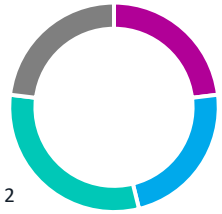
Portfolio maturing, well positioned to deliver value over the medium term

79% of strategic portfolio is clinical, late-stage clinical or commercial stage



1

- **5%** Commercial
- **42%** Late-stage clinical
- **32%** Clinical stage
- **21%** Pre-clinical

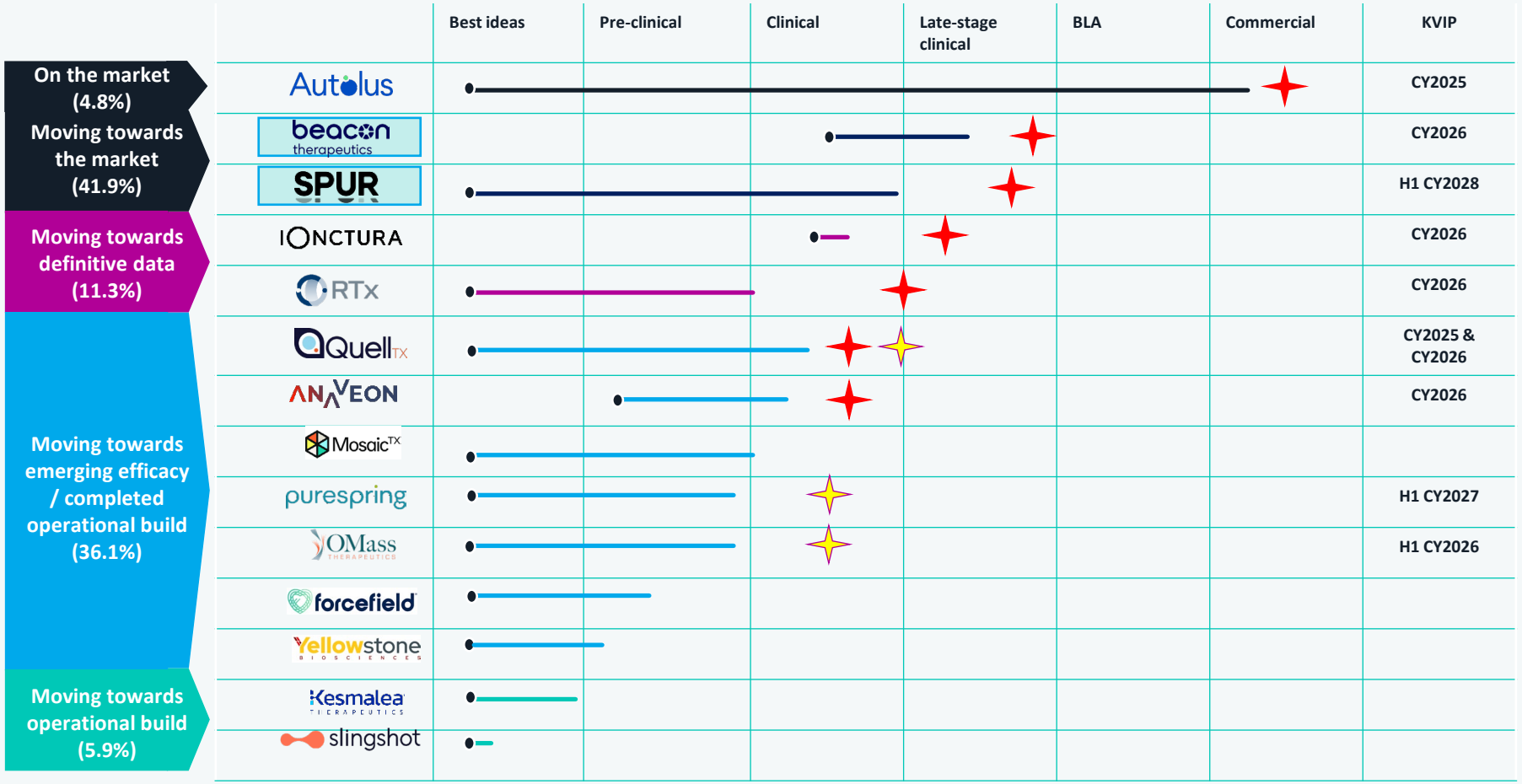


2

- **3** Cell therapy
- **3** Gene therapy
- **4** Small molecules
- **3** Biologics

£310.6m

Raised by portfolio companies; £175.5m from leading life science investors



1. By value of strategic portfolio
2. Number of companies and excludes Slingshot, the Syncona Accelerator

Building a world leader in targeted oncology combinations

Syncona drives transformational transaction, accelerating path to potential approval

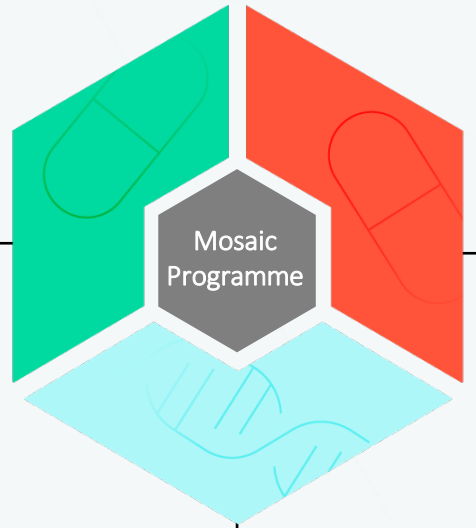
Adopting a new approach to target and drug discovery to identify novel biomarker-stratified medicines

Combinations are needed to increase response rates and durations for cancer patients in areas of high unmet medical need. Mosaic has developed a large-scale, agonistic approach to identify synergistic combinations and biomarkers that predict patient response

- To accelerate clinical entry, SIML sourced two clinical assets to in-license from Astex Pharmaceuticals, each of which will be combined with marketed medicines to enable proprietary programmes identified by the Mosaic platform
- Time to potential approval is reduced by c.50%, and potential probability of success increased by using clinically-experienced molecules

Mosaic Development Candidate

- Targeted small molecule
- Prior clinical exposure in >100 pts
- Safety / tolerability differentiation
- On-target clinical activity
- IP protection



Potential approved Drug

- Potential approved targeted small molecule
- Extensive clinical data enables streamlined development in combination setting

Mosaic-Identified Genetic Stratification Biomarker

Enables identification of patients most likely to benefit from treatment through a companion diagnostic strategy

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Capital deployment and allocation

Capital deployment weighted to later stage companies

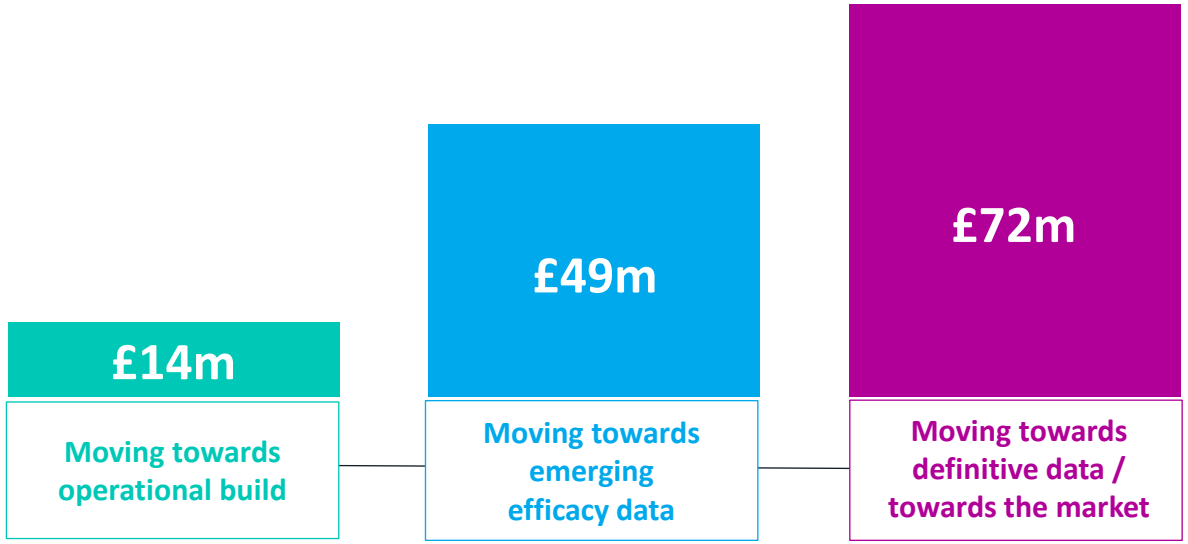
69% of capital deployed into portfolio has been to clinical or late-stage clinical companies

£135.3m deployed into the life science portfolio in the year

- Below guidance driven by disciplined capital allocation and success in raising external capital
- One new company added to the portfolio in the year, Slingshot, the Syncona Accelerator
  - £2.1m invested in Slingshot's first asset,Apini, a small molecule therapeutic aimed at treating inflammatory diseases

£43.0m deployed into share buybacks

- 40m shares repurchased at an average 37.4% discount to NAV per share; +4.96p accretion to NAV per share



All data at 31 March 2025

We are funded to deliver current KVIPs over the next three years

Disciplined capital allocation with focus on funding companies to drive KVIPs

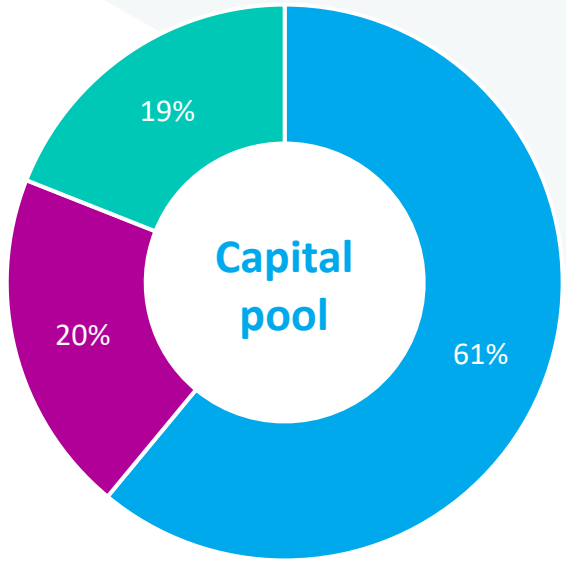
Capital pool of £287.7m

- c.80% of capital pool allocated to commitments and underwriting current KVIPs
- Remaining capital allocated to driving broader portfolio company milestones and protecting value in future third party financings

£35m allocated to share buybacks in the year

- Taking total committed to share buyback to £75m

As at 31 March 2025



- Committed to portfolio companies, operational costs and share buybacks
- Underwriting key value inflection points
- Driving broader portfolio company milestones, protecting value in third party financings

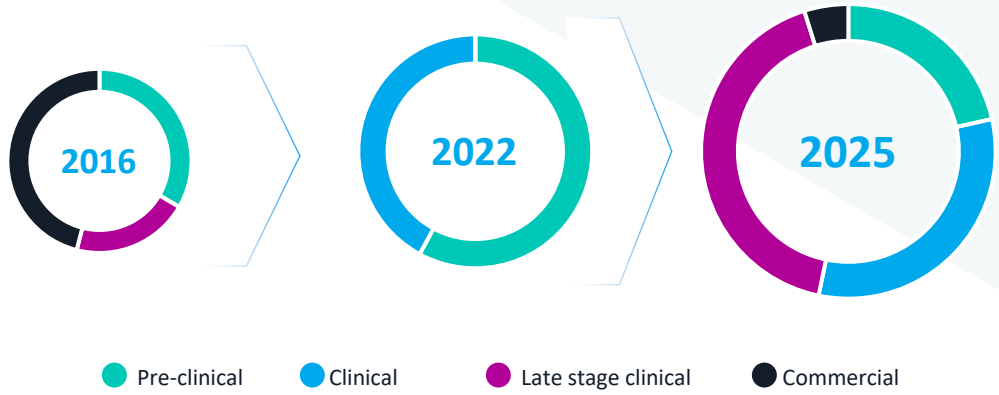
Summary and outlook

Leveraging the UK’s world class science

Strong risk-adjusted returns in life science weighted towards late-stage development; SIML's create, build, scale model is operationally intensive and is centred on enabling our shareholders to access this value

- Founded in 2012 with a model focused on creating and building world class companies around exceptional UK scientific research
- Maturing portfolio of seven companies at the time of merger with BACIT in 2016
  - Exits from this portfolio drove returns between 2018 – 2021
- As we entered 2022, the portfolio was weighted towards pre-clinical companies
- Against a challenging backdrop, SIML rebalanced and restructured the portfolio

Syncona’s portfolio over time[1]



Today, portfolio is maturing and is again weighted towards clinical and commercial companies with a rich set of KVIPs

1 By life science portfolio / strategic portfolio value

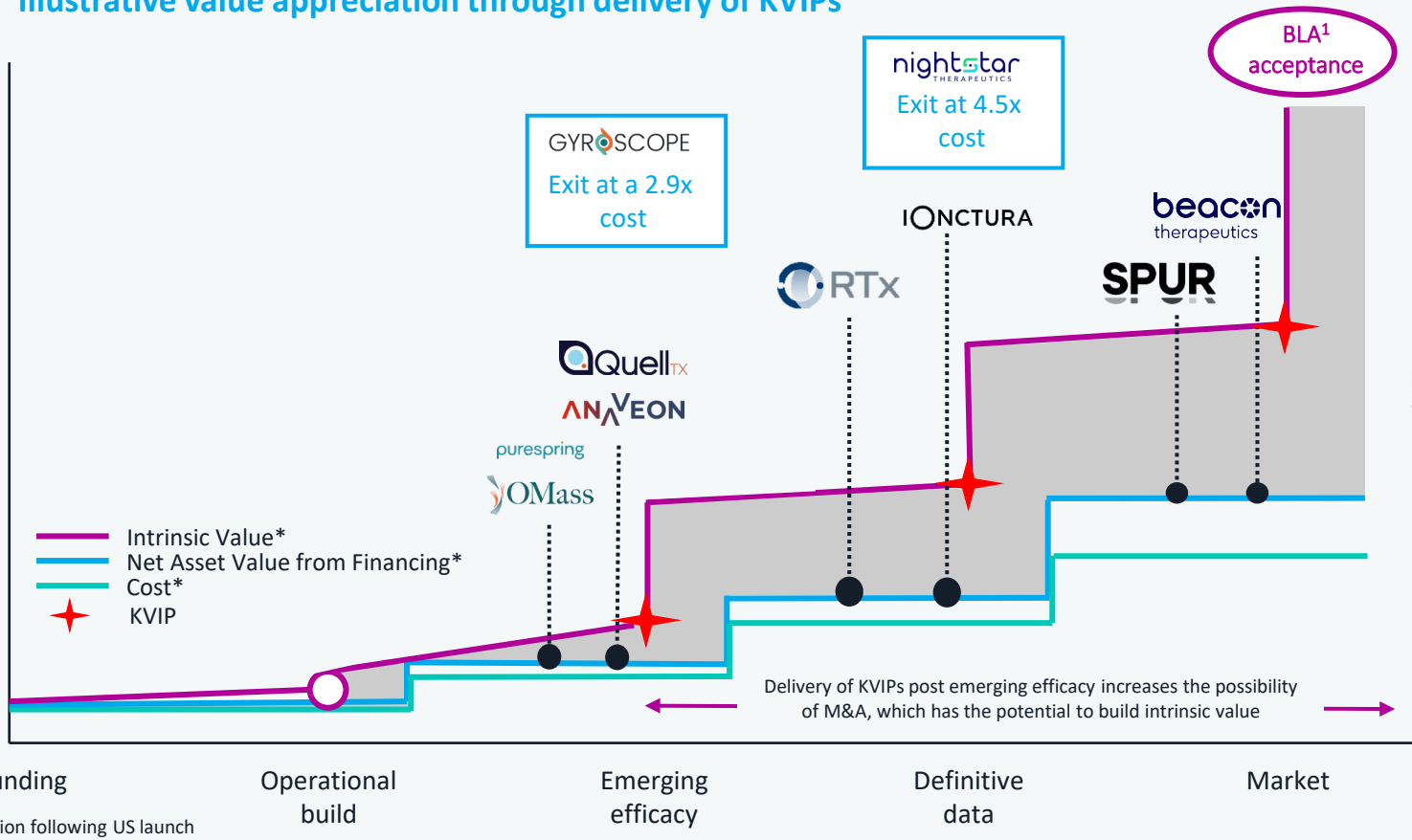
Driving value through the delivery of KVIPs

Portfolio has a rich set a key value inflections points that are expected to be delivered over the next three years, each with the potential to drive significant NAV growth through M&A and liquidity events

- 10 KVIPs across the portfolio over the next three years
- Including two, Beacon and Spur, both of which have the potential to underpin a BLA filing for FDA approval
- The successful delivery of each KVIP derisks the clinical thesis, making the companies more attractive for M&A or liquidity events

We are resolutely focused on delivery of KVIPs

Illustrative value appreciation through delivery of KVIPs



3.9x
Aggregate multiple of cost from Syncona's five exits[2]

Note Autolus is now a commercial company, with KVIP in 2025 for commercial traction following US launch

1. Biologics License Application * illustrative 2. Includes sales of Nightstar, Blue Earth, upfront proceeds from sale of Gyroscope, upfront proceeds from Neogene and upfront consideration of Clade. Reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis.

Beacon Therapeutics

Clinical data demonstrates improvements in visual sensitivity sustained for 36 months

beacon therapeutics

Beacon has a highly attractive gene therapy programme targeting X-linked retinitis pigmentosa (XLRP), a blinding disease

Beacon's potentially first and 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

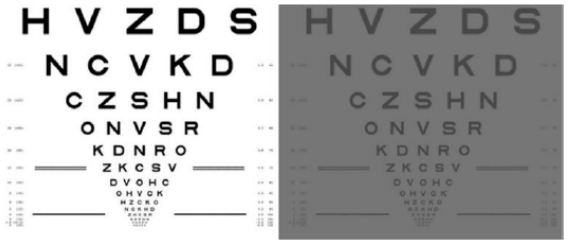
Targeting an area of high unmet need, with no current treatment options

- XLRP is a severe, aggressive, inherited retinal disease that causes blindness in men

Market opportunity

- >20,000 patients in US/Europe[1]

Low Luminance Visual Acuity (LLVA)



Positive data in an improving competitive environment

- Six-month Phase II DAWN data showed early improvements in LLVA with a greater number of two- and three-line improvements in the study eyes
- Enrolling patients in its Phase II/III pivotal trial, with data expected in CY2026
- In May 25, J&J announced that MeiraGtx's LUMEOS Phase III trial in XLRP did not meet its primary endpoint

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

Summary and outlook

Portfolio well positioned to deliver value in the medium term

Portfolio maturing and increasingly later stage

- 78.5% of strategic portfolio value is in eight clinical and commercial stage companies
- Expect a further two companies to enter the clinic in next 12 months
- Significant clinical, operational and strategic progress across the portfolio

Portfolio is well financed, with a rich set of KVIPs that are expected to be delivered over the next three years

- We are funded to KVIPs with capital focused on opportunities that are clinical stage or close to clinical entry

Uncertainty has delayed the biotech market recovery, but fundamentals remain strong

- Portfolio well positioned to generate value over the medium term

SIML team is focused on delivering key value inflection points to maximise value for shareholders

Strategy update

- **Proposed Changes to Investment and Capital Allocation Policies**
- **Potential Acceleration of Cash Returns**
- **Alternative Opportunities for Shareholders**
- **Governance**

Appendix 1 – Syncona team and track record

SIML platform

Our organisational operating model supports the delivery of our strategy

Senior investment team


Chris Hollowood
CEO


Roel Bulthuis
Managing Partner


Ed Hodgkin
Managing Partner


Elisa Petris
Partner


Magdalena Jonikas
Partner

Broader investment team


Alex Hamilton
Principal


Alessio D'addabbo
Analyst


Gonzalo Garcia
Principal


Melina Hoffmann
Associate


Michael Kyriakides
Principal


Nathaniel Dahan
Senior Associate


Pierre Joffrin
Senior Associate


Raghd Rostom
Senior Associate


Sarah Qian
Associate

Executive Partner group


John Tsai
Experienced clinical leader


Hitesh Thakrar
Experienced life sciences fund manager


Richard Wooster
Extensive drug discovery experience


Kenneth Galbraith
Chair of SIML
Commercial leader

A platform for…

- New opportunities
- Company launch
- Clinical approach
- Regulatory plan
- Commercial strategy

… delivering long-term growth

SIML leadership team comprises experience from across the business

Responsible for the operational delivery of Syncona's strategic priorities

Chris Hollowood
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

Kate Butler
CFO

- Balance sheet management
- Strategic leadership

Edward Hodgkin
Managing Partner

- Executive leadership
- Company building

Marc Perkins
General Counsel

- Leads legal team
- Supports Board on all governance and company secretary matters

Harriet Gower Isaac
Chief People Officer

- Process optimisation
- People leadership
- Employee engagement

John Tsai
Executive Partner

- Executive leadership
- Support life science portfolio

Annabel Clark
Head of Corporate Affairs and ESG

- Shareholder relations
- Media communications
- Responsible investment

A track record of significant value creation from exits

£1.4 billion invested to date, generating an IRR of 14.5%, 1.3x invested capital[1]

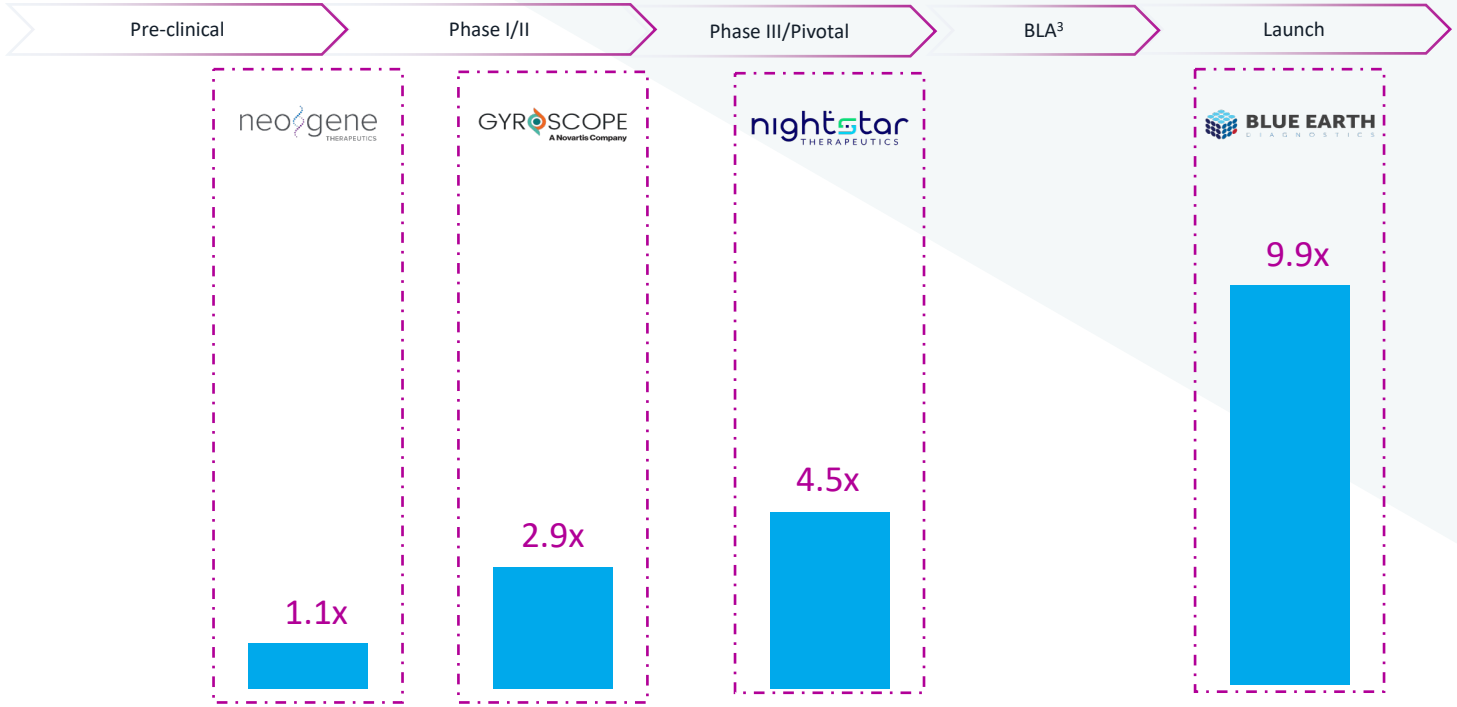
Full exits generated £955m of proceeds, at an aggregate IRR of 73.6% and a 3.9x cost[2]

Blue Earth
- First invested 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 2019, sold to AstraZeneca in 2023
- 3% IRR – 1.1x cost on £15.3m upfront proceeds



All financial data at 31 March 2025

Returns since Syncona merged with BACIT in December 2016, are: Neogene 1.1x, Gyroscope 2.9x, Nightstar 3.5x, Blue Earth 3.9x.

1. 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, Gyroscope, upfront proceeds from Neogene and upfront consideration of Clade. 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

Appendix 2 – Portfolio

Portfolio making strong clinical, operational and strategic progress

10 capital access milestones, and three key value inflection points in the year

- Beacon – data from both DAWN and SKYLINE Phase II trials (KVIPs)
- Spur – data from its Phase I/II trial in Gaucher disease (KVIP)

Seven financings with significant capital attracted to the portfolio

- £310.6m of capital raised by portfolio companies, with £175.5m raised from leading external investors

Strong clinical progress across the portfolio

- Autolus' AUCATZYL® launched in US following FDA approval; post period end received conditional marketing authorization from UK MHRA, and a positive opinion from EMA's CHMP
- Beacon commenced Phase II/III pivotal trial in XLRP
- Alignment with FDA on design of Spur's Phase III trial for Gaucher, expected to initiate pivotal trial in CY2026
- iOnctura commenced Phase II trial in uveal melanoma. Post-period end dosed the first patient in its Phase II trial in NSCLC and sites are screening patients for a Phase II trial in myelofibrosis
- Resolution entered the clinic with its lead programme in end-stage liver disease

Broader strategic progress through in-licencing and commercial milestone achievements

- Quell received $10m of milestones from AstraZeneca for its type 1 diabetes programme; a further $10m received post period end for IBD programme
- Mosaic in-licenced two clinical assets, significantly accelerating clinical pathway

3

KVIPs delivered

£310.6m

Raised by portfolio companies across seven financing

8

Clinical and commercial companies, including two late stage clinical companies

	31 March 2024	Net investment in the period	Valuation change	FX movement	31 March 2025[1]	% of Group NAV	Valuation Basis [2, 3, 4]	Fully diluted ownership stake[5]	Focus area
	(£m)	(£m)	(£m)	(£m)	(£m)			(%)	
Strategic portfolio companies									
On the market									
Autolus	169.5	(16.3)	(116.2)	(2.4)	34.6	3.3	Quoted	9.9	Cell therapy
Late-stage clinical									
Spur	135.6	43.8	2.8	-	182.2	17.3	Cost	79.2	Gene therapy
Beacon	94.7	9.6	15.4	(2.2)	117.5	11.2	PRI	41.0	Gene therapy
Clinical									
Quell	84.7	2.8	-	(2.1)	85.4	8.1	PRI	33.7	Cell therapy
Resolution	50.0	19.0	(13.5)	-	55.5	5.3	Adj Cost	82.6	Cell therapy
Anaveon	35.7	-	-	(0.1)	35.6	3.4	PRI	36.9	Biologics
Mosaic	7.3	18.2	-	-	25.5	2.4	Cost	54.3	Small molecules
iOnctura	25.6	-	-	(0.5)	25.1	2.4	PRI	21.9	Small molecules
Pre-clinical									
Purespring	45.3	5.0	0.9	-	51.2	4.9	PRI	41.7	Gene therapy
OMass	43.7	6.0	-	-	49.7	4.7	PRI	29.0	Small molecules
Kesmalea	12.0	8.0	-	-	20.0	1.9	Cost	59.7	Small molecules
Yellowstone	1.0	15.5	-	-	16.5	1.6	Cost	60.9	Biologics
Forcefield	6.5	1.7	2.4	-	10.6	1.0	PRI	49.6	Biologics
Slingshot	0.0	5.6	-	-	5.6	0.5	Cost	100.0	Accelerator
Investments and milestone payments									
Neogene milestone payment	2.2	-	4.0	(0.1)	6.1	0.6	DCF	-	Cell therapy
Clade milestone payment	0.0	0.7	0.1	-	0.8	0.1	DCF	-	Cell therapy
CRT Pioneer Fund	33.9	(1.3)	(5.3)	-	27.3	2.5	Adj Third Party	64.1	Oncology
Biomodal	18.0	-	(15.0)	(0.3)	2.7	0.3	Adj PRI	5.5	Epigenetics
Achilles	11.0	-	2.4	(0.3)	13.1	1.2	Expected proceeds	22.7	Cell therapy
Century	0.0	4.3	(3.8)	(0.1)	0.4	0.0	Quoted	1.3	Cell therapy
Clade	9.4	(9.4)	-	-	0.0	0.0	-	-	Cell therapy
Total Life Science Portfolio	786.1	113.2	(125.8)	(8.1)	765.4	72.7			
Capital pool	452.8	(177.8)	12.4	0.3	287.7	27.3			
TOTAL	1,238.9				1,053.1	100			

1 Portfolio valuations reflect Syncona's total interest in a company or investment 2. Primary input to fair value of equity holding. 3. 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. 4. 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. 5. Percentage holding reflects Syncona's ownership stake at the point full current commitments are invested.

SYNCONA

Commercial

Autolus Therapeutics

Leading cell therapy company with lead programme in adult ALL granted approval by the US FDA

Initial investment	2014
Value	£34.6m
Financing stage	NASDAQ
Stage of lead programme	Approved

Investment thesis and company update

- Lead product candidate, for AUCATZYL® (obe-cel), a 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
- AUCATZYL launched in US following FDA approval; received conditional marketing authorization from UK MHRA in April 2025, and a positive opinion from EMA's CHMP in May 2025
- Product generated $9m of revenue in first quarter of launch
- Advanced in-house manufacturing facility supporting commercial launch

Targeting an area of high unmet need

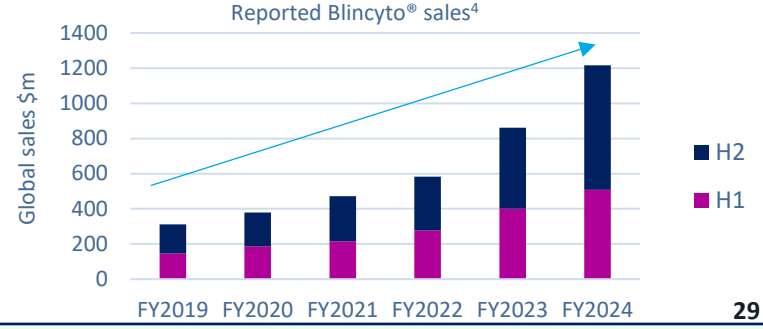
- Only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care[1]
- obe-cel has the potential to be a best-in-class curative therapy in adult ALL
- Launched a Phase I trial in systemic lupus erythematosus (SLE) in H1 CY2024, a multi-organ systemic autoimmune disease that affects approximately 160K - 320K patients in the US[2]. Initial data from the trial in April 2025 support further development in lupus nephritis and initiation of a trial in multiple sclerosis

Key data

- Data has demonstrated at 21.5 months median follow up 40% of B-cell ALL patients treated with obe-cel were in ongoing remission without Stem Cell Transplant (SCT) or other therapy[1]

Market opportunity for lead programme

- Over 8,000 new cases of adult ALL annually worldwide[1]
- Obe-cel has launched into an expanding ALL market and is now being commercialised across key target geographies
- Tecartus® (approved in 2022) is expected to establish CAR-T in adult ALL; sales increased 9% to $403m in 2024[3]
- Blincyto®, current market leader, sales increased 41% year-over-year to $1,216 in 2024[4]



1. Autolus corporate presentation 2. 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 3. Gilead 4. Amgen

Late-stage clinical

Spur Therapeutics

Developing transformative gene therapies for patients suffering from chronic debilitating diseases

Initial investment	2015
Value	£182.2m
Financing stage	Taken private
Stage of lead programme	Phase I/II

Investment thesis

- Spur is driving forward a potentially first- and best-in-class gene therapy candidate for Gaucher disease type 1, FLT201
- Published positive data from Phase I/II trial of FLT201 demonstrating continued safety and tolerability and robust enzyme activity
- Preclinical programme focused on GBA1 Parkinson's disease that leverages the same novel transgene as FLT201

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

- Spur estimates that Gaucher disease type 1 has approximately 18,000 patients[1]
- Annual Gaucher market size is $2bn[2]

1. Company estimate 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

Late-stage clinical

Beacon Therapeutics

Progressing its pivotal study in X-linked retinitis pigmentosa

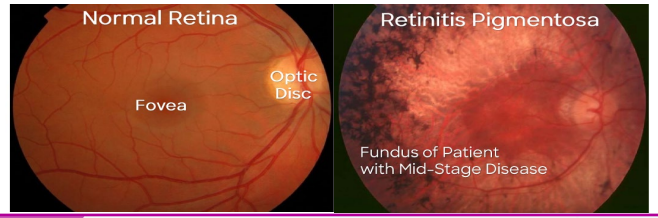
Initial investment	2022
Value	£117.5m
Financing stage	Series B
Stage of lead programme	Phase II/III

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 36 months
- Pivotal VISTA trial initiated in H1 CY2024, with data readout expected in CY2026
- Retinal gene therapy is an area where Syncona has significant expertise and XLRP is a disease setting the team knows well from the Nightstar Therapeutics experience

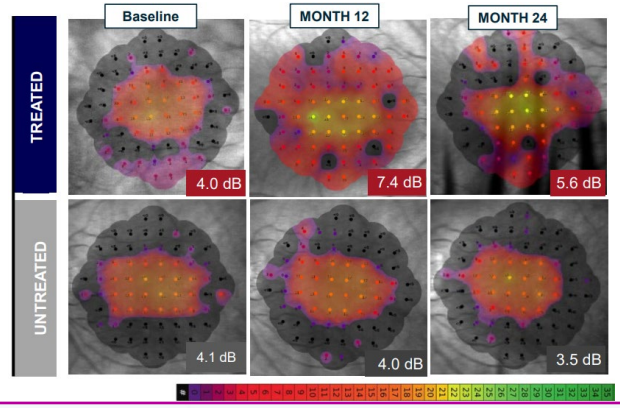
Targeting an area of high unmet need

- 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
- Currently no approved 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

Quell Therapeutics

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

Clinical stage

Initial investment	2019
Value	£85.4m
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
- First engineered Treg trial in liver transplantation – a de-risked setting with significant unmet need for patients
- Collaboration with AstraZeneca announced in 2023 with $85m upfront (cash and equity) and potential payments of over $2bn
- Funded through key datasets with strong investor syndicate
- Presented clinical data demonstrates QEL-001 to be safe and well tolerated

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 developing 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]

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

Clinical stage

Resolution Therapeutics

Seeking to extend the impact of cell therapy into inflammatory and fibrotic diseases

Initial investment	2018
Value	£55.5m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

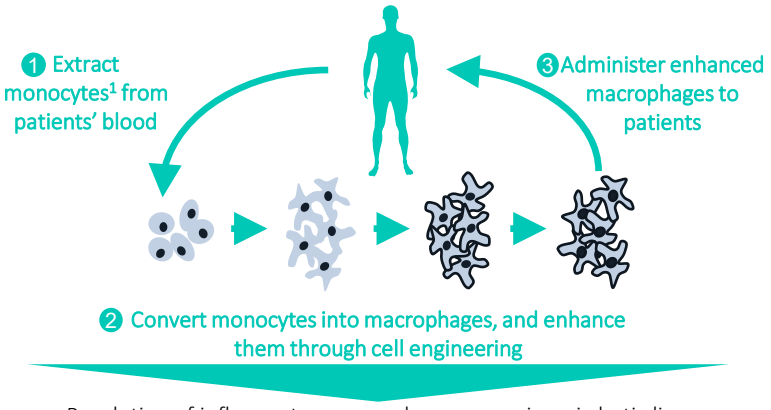
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries[1]
- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest fibrotic scar, modulate the inflammatory response and promote organ repair
- Encouraging clinical data 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 with high morbidity, mortality and cost, and requires lifetime immunosuppression

Market opportunity

- >500k individuals in the US alone with end stage liver disease[2]



1. Resolution analysis 2. GBD 2017 Cirrhosis Collaborators, Lancet Gastroenterol Hepatol., 2020; Ladner DP., et al. PLoS One, 2024; LEK analysis

Anaveon

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

Clinical stage

Initial investment	2019
Value	£35.6m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Developing a selective IL-2 receptor agonist, ANV600, with improved administration and toxicity burden, currently in a Phase I/II dose escalation trial
- Anaveon expects to publish data from its trial in ANV600 in CY2026

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]
- Anaveon anticipates targeting cells expressing PD-1 with ANV600 will have potential application in a range of solid tumours resistant to existing therapies

Market opportunity

- We believe that ANV600, if approved, would potentially have wide utility in oncology, across multiple settings, including but not limited to melanoma, and in combination with several advanced therapies or more traditional agents[2]

1. OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015 2. https://seer.cancer.gov/statfacts/html/melan.html

SYNCONA

Clinical stage

Initial investment	2022
Value	£25.5m
Financing stage	Series A

Mosaic Therapeutics

Building the world leader in targeted oncology combinations

Investment thesis

- Combinations are needed to increase response rates and durations for cancer patients in areas of high unmet medical need, however the current standard industry approach is opportunistic and ineffective
- Mosaic has developed a large-scale, agonistic approach to identify synergistic combinations and biomarkers that predict patient response
- Extensive screening in the Mosaic platform has identified developable hypotheses of combinations in solid tumors. This pipeline of programmes is enabled through the in-license of 2 clinically experienced targeted small molecules

Targeting an area of high unmet need

- Large patient subgroups within oncology, such as microsatellite stable (MSS) colorectal cancer (CRC), continue to elude therapeutic advances and large unmet need remains
  - Only ~25% of CRC patients have tumours with biomarkers that allow for targeted therapies
  - The remaining ~75% have a high unmet medical need with median Progression-Free Survival (mPFS) on Standard of Care (chemo combinations) of ~10 mo (1L) and 4-6 mo (2L)

Market opportunity

- Mosaic's lead programme has the potential to address an eligible patient population of ~86k pts, including in CRC, breast and prostate cancer
- This represents a revenue potential of up to $3.3bn peak year sales for the lead programme
- Further programmes in the Mosaic pipeline aim to address similar sizes of patients, all in areas of high medical need

iOnctura

Clinical-stage precision oncology company combating neglected and hard-to-treat cancers

Clinical stage

Initial investment	2024
Value	£25.1m
Financing stage	Series B
Stage of lead programme	Phase II

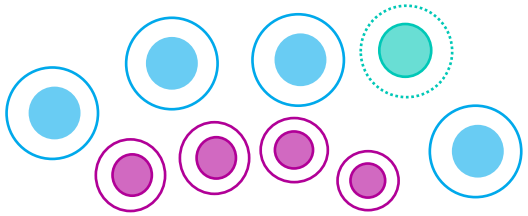
Investment thesis

- iOnctura represented an opportunity to invest in a clinical-stage company that has published promising emerging data to date
- Opportunity to drive lead programme through late-stage clinical development
- The PI3K signalling pathway is one of the most commonly dysregulated pathways in cancer
- iOnctura's lead programme, roginolisib, is a first-in-class, highly selective allosteric modulator of PI3Kδ, with a unique chemical structure and binding mode
- The Syncona team has worked closely alongside iOnctura to consider the broader application of roginolisib

Targeting an area of high unmet need

- Once metastasised (50% of patients) overall survival of uveal melanoma patients drops to one year[1]

Roginolisib boosts **tumour targeting cells** and reduces levels of **tumour protecting** cells to boost the fight against **cancer cells**



Market opportunity

- There are over 7,000 new cases of uveal melanoma annually worldwide[2]
- NSCLC accounts for approximately 85% of all lung cancer cases and is the most common type of lung cancer.[3]

1. Rantala, 2019. 2. GLOBOCAN 2020; 3. Medscape Registration. Last accessed 17.06.2025

SYNCONA

Pre-clinical stage

Initial investment	2020
Value	£51.2m
Financing stage	Series B

Purespring Therapeutics

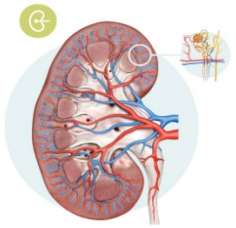
First company to treat kidney diseases by directly targeting the podocyte with AAV gene therapy

Investment thesis

- 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, and can eventually lead to kidney failure

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

- c.4 million patients are on renal replacement therapy[1]
- More than 840 million people globally suffer from chronic kidney disease[2]
- The podocyte is implicated in 60% of renal disease[2]
- The lead programme is targeting IgA nephropathy, a disease caused by pathogenic antibodies, and is estimated to affect more than 100,000 people in the US[3]

1. https://www.nature.com/articles/s41581-022-00542-7 2. Purespring analysis 3. https://www.kidneymedicinejournal.org/article/S2590-0595(23)00111-5/fulltext

OMass Therapeutics

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

Pre-clinical stage

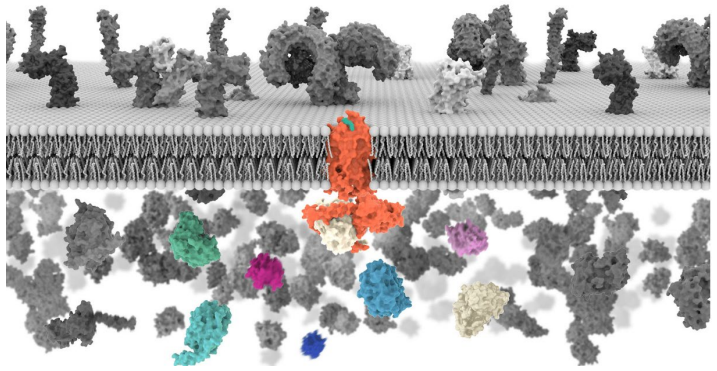
Initial investment	2018
Value	£49.7m
Financing stage	Series B

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 four programs in endocrinology and immunology

Targeting an area of high unmet need

- All of OMass' programmes are in indications with significant unmet medical need
- Programmes include: congenital adrenal hyperplasia, lupus and inflammatory bowel disease



Market opportunity

- Most advanced programme is in diseases associated with adrenocorticotropic hormone (ACTH) excess, including congenital adrenal hyperplasia (CAH) and ACTH-dependent Cushing's
- CAH occurs in about 1 in 13,000-15,000 births[1]
- Pituitary ACTH-dependent Cushing causes 65 to 70 percent of Cushing syndrome[2]

1. https://www.ncbi.nlm.nih.gov/books/NBK278953/ 2. Endocrinol Metab Clin North Am. 1988;17(3):445.

Pre-clinical stage

Initial investment	2022
Value	£20.0m
Financing stage	Series A

Kesmalea Therapeutics

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

Investment thesis

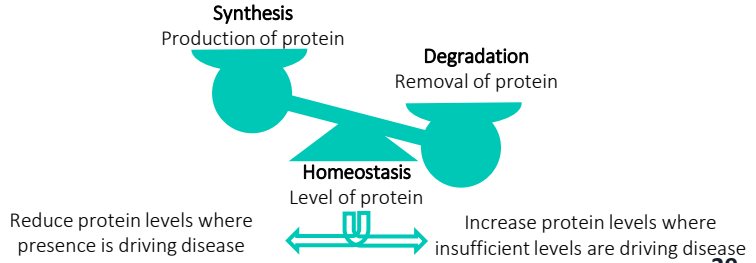
- Small molecule drug discovery platform focused on protein homeostasis, initially targeted protein degraders (TPDs)
- Protein homeostasis is the system of maintaining the equilibrium of proteins in the human body. This intricate system is in a constant state of change, with the body continuously synthesising and regulating proteins, whilst removing those which are no longer required through controlled degradation, however this can become dysregulated
- Kesmalea aims to counter this dysregulation with novel treatments which restore balance through effective protein degradation or stabilisation
- Founded by Dr Harry Finch, a world-class chemist and co-inventor of GSK's Serevent™

Targeting an area of high unmet need

- Some of the most validated protein targets are difficult to address with traditional small molecule approaches
- TPD is a promising approach for these challenging high-value targets, as relatively modest binding has the potential to translate into a clinically significant degradation of the target protein. The concept has the potential to be promising and has been clinically tested. However, technical challenges have limited the ability to rapidly discover and develop oral TPDs
- Kesmalea's novel approach has the potential to overcome the challenges of existing TPD technologies, opening the door to previously unavailable oral and CNS-penetrant therapeutics in areas of high unmet need

Market opportunity

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



Yellowstone Biosciences

Pre-clinical stage

Initial investment	2024
Value	£16.5m
Financing stage	Series A

Pioneering soluble bispecific T-cell receptor (TCR)-based therapies to unlock a new class of cancer therapeutics

Investment thesis

- Developing treatments for oncology indications with a high unmet patient need that presents a significant commercial opportunity
- Advancing its lead programme in acute myeloid leukaemia (AML), with pipeline potential across a range of other cancers
- Spun out from the University of Oxford around the pioneering work of Prof. Paresh Vyas, a world leader in haematological oncology
- Support of SIML launch team has enabled the company to operationalise at pace, accelerating its early development

Targeting an area of high unmet need

- 80% of all AML patients progress to relapsed/refractory (r/r) status which has median survival of 3-6 months, and no universally agreed standard of care for the majority of patients[1]
- An ongoing challenge for the industry has been identifying frequently expressed antigens that can be targeted therapeutically across patients, a challenge that Yellowstone's platform overcomes

Market opportunity

- >40,000 new cases of AML annually across the US and Europe[1]
- Yellowstone's class of therapeutics has the potential to address unmet clinical need in a broader set of cancers beyond AML, expanding the market opportunity significantly

1. Yellowstone analysis

Forcefield Therapeutics

Pioneering therapeutics to retain heart function

Pre-clinical stage

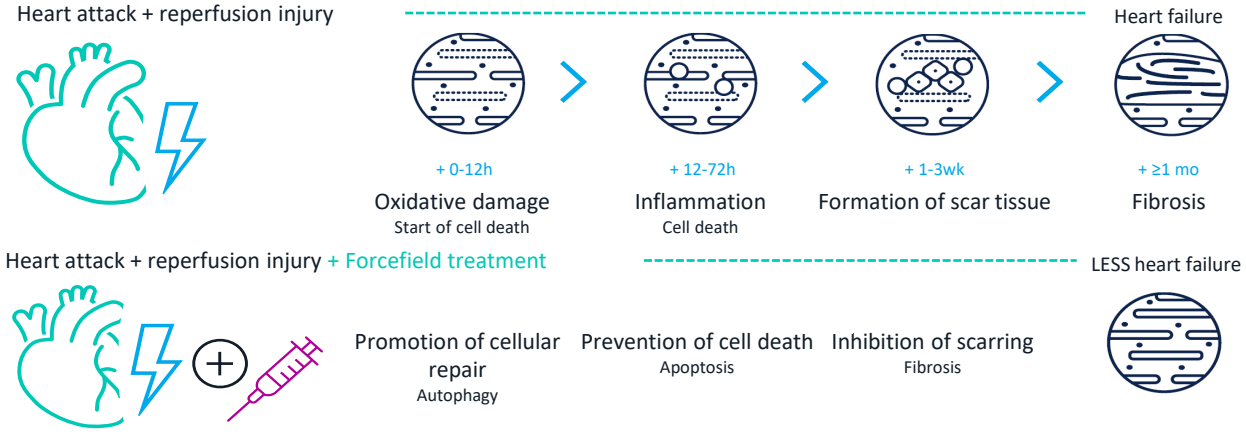
Initial investment	2022
Value	£10.6m
Financing stage	Series A

Unmet need in heart disease

- Heart disease is the leading cause of death worldwide
- Acute myocardial infarction (AMI), affects 3 million people worldwide annually[1]
- 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[1]
- Cells are not replaced, leading to further heart attacks, heart failure or death
- Initially a seed investment with Syncona committing £20.0m in a Series A financing, with Roche Venture Fund subsequently committing a further £10m

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



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

1. Forcefield analysis

Slingshot Therapeutics

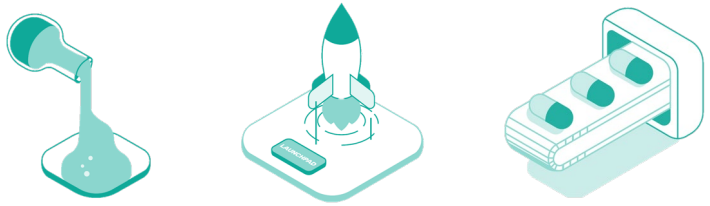
Bridging the gap from academia to drug development

Pre-clinical stage

Initial investment	2024
Value	£5.6m

Slingshot model

- Successful programmes are identified from world-leading academic institutions in the UK, US and Europe
- Programmes are supported along the development pathway towards the clinic, leveraging Syncona's expertise creating and building companies from early-stage science
- Creates a variety of paths to take medicines to the clinic



Investment thesis

- A compelling and capital efficient way to gain exposure to the returns available from translating highly innovative science into promising biotech assets
- Allowing Syncona to accelerate exceptional academic science towards clinical entry in a capital efficient way
- Syncona Managing Partner, Edward Hodgkin is Executive Chair, and Executive Partner, Richard Wooster is Slingshot's Chief Scientific Officer
- Advance multiple pre-clinical programmes under one pipeline, supporting the early and efficient de-risking of leading science before clinical entry
- First pipeline programme: Apini, a small molecule inflammatory disease programme identified from the University of Manchester