SYNCONA

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Interim Results

For the six months ended 30 September 2024

November 2024

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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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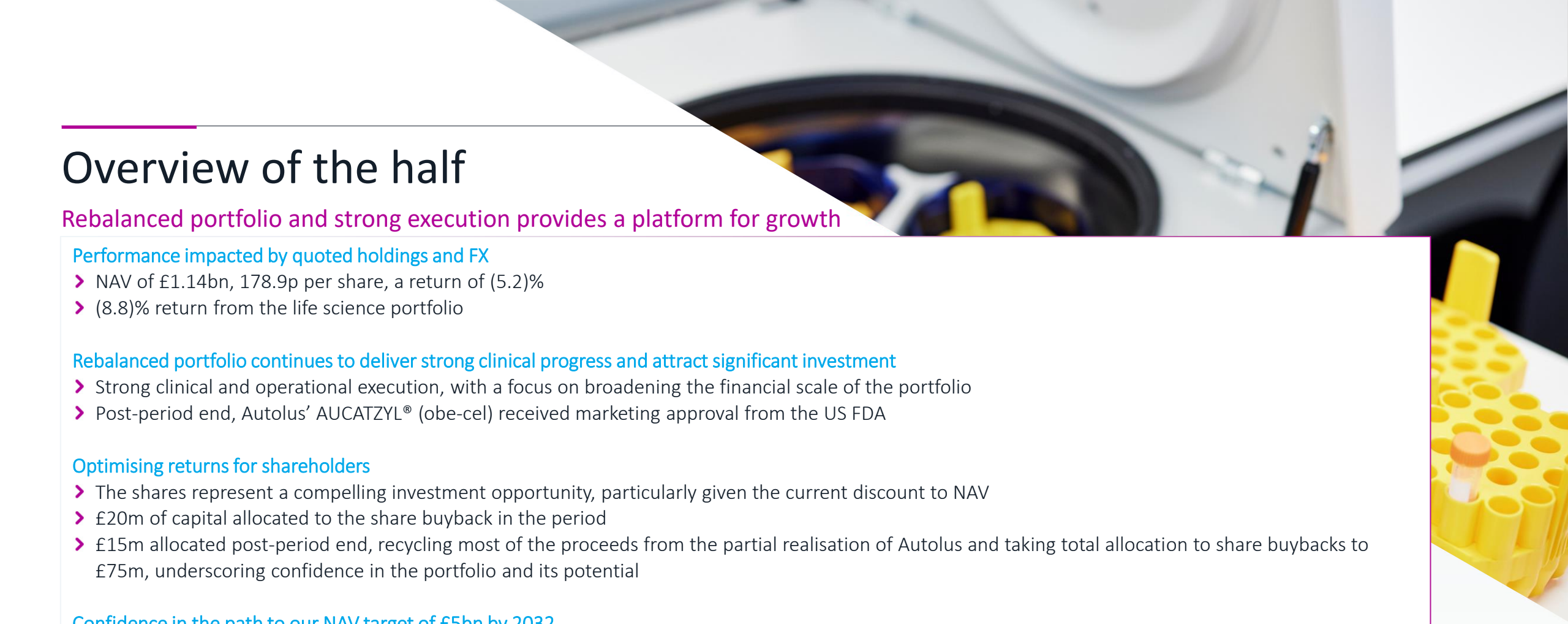
Syncona Limited seeks to achieve returns over the long term. Many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many 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.



Overview of the half

Rebalanced portfolio and strong execution provides a platform for growth

Performance impacted by quoted holdings and FX

- NAV of £1.14bn, 178.9p per share, a return of (5.2)%
- (8.8)% return from the life science portfolio

Rebalanced portfolio continues to deliver strong clinical progress and attract significant investment

- Strong clinical and operational execution, with a focus on broadening the financial scale of the portfolio
- Post-period end, Autolus' AUCATZYL® (obe-cel) received marketing approval from the US FDA

Optimising returns for shareholders

- The shares represent a compelling investment opportunity, particularly given the current discount to NAV
- £20m of capital allocated to the share buyback in the period
- £15m allocated post-period end, recycling most of the proceeds from the partial realisation of Autolus and taking total allocation to share buybacks to £75m, underscoring confidence in the portfolio and its potential

Confidence in the path to our NAV target of £5bn by 2032

- Delivery of expected key value inflection points by the end of CY2027 has the potential to drive significant NAV growth

Well positioned for improving market conditions

- Macro environment is improving with softening inflation and interest rate cuts

Kenneth Galbraith appointed as Chair of SIML

- He brings 35 years of experience across biotechnology and venture capital to further support Syncona's growth ambitions[1]

1. Kenneth Galbraith's appointment as Chair of SIML will take effect following regulatory approval

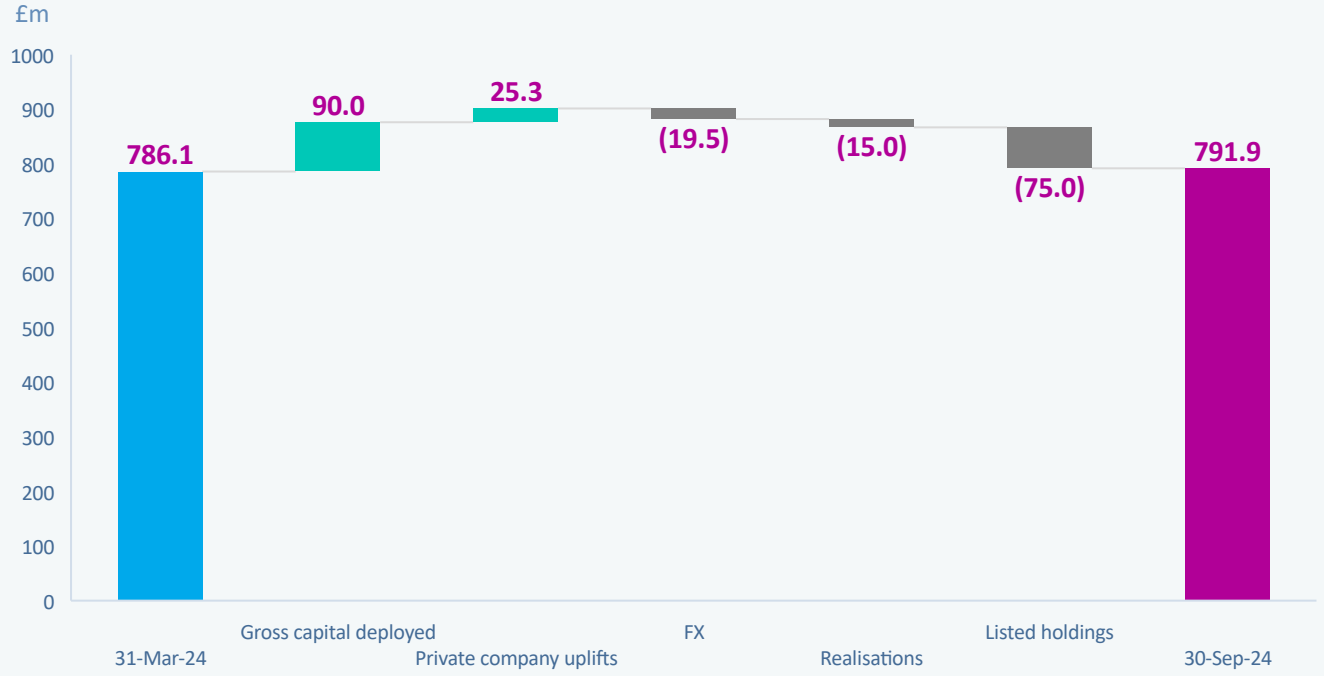
NAV performance

Net assets of £1.14bn, 178.9p per share – a return of (5.2)% in the six-month period

Life science portfolio valued at £791.9m – a return of (8.8)%

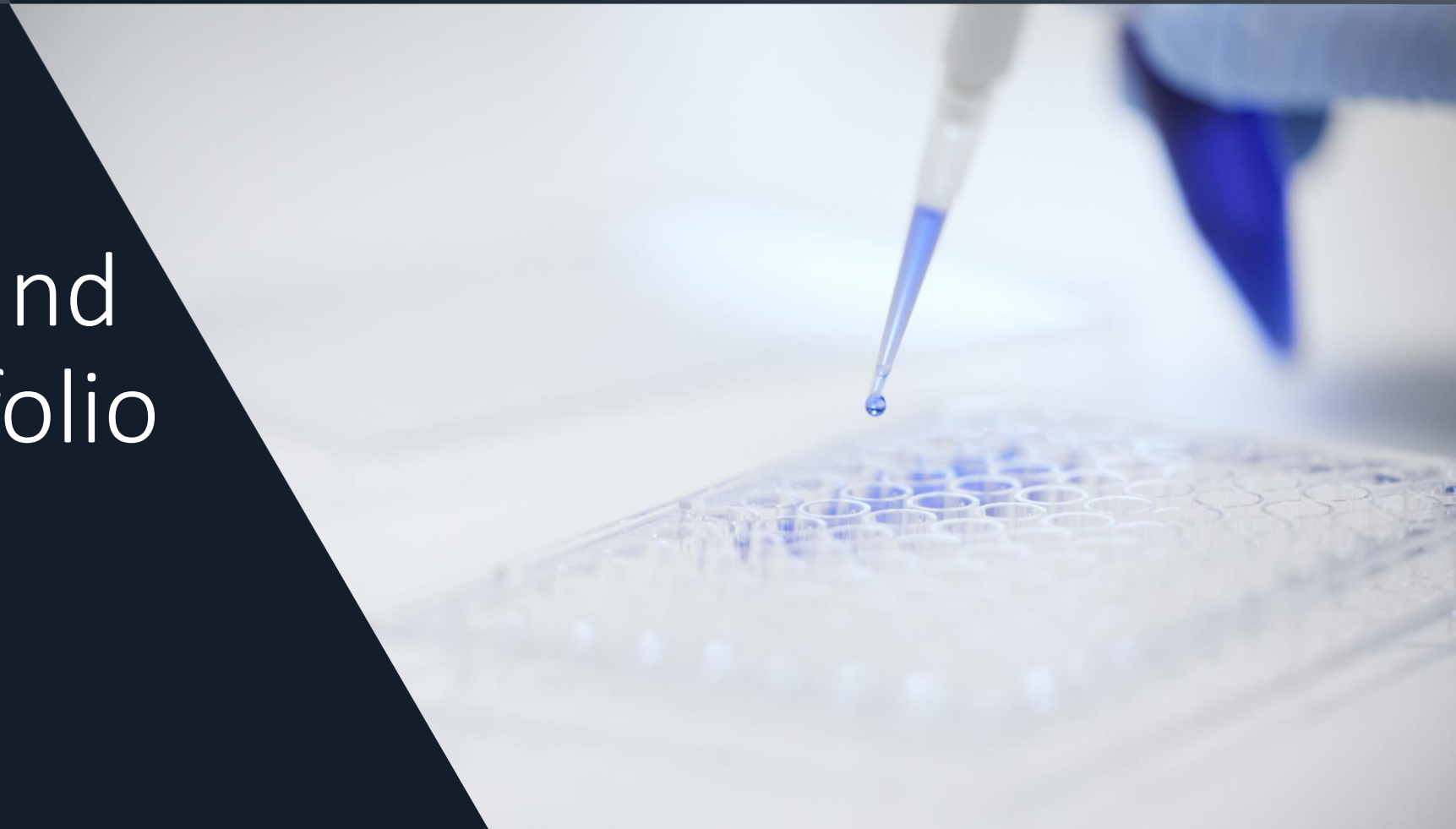
- £25.3m in valuation uplifts from private portfolio, including from financings
- Offset by £75.0m decline in value of listed holdings, as well as foreign exchange headwinds and realisations
  - 43% fall in the share price of Autolus
  - £(19.5)m impact from foreign exchange, primarily due to the 5.9% weakening of the Dollar versus Sterling
  - Sale of Clade and partial realisation of Autolus in the period
- Exposure to Autolus rebalanced as it transitions from a development stage to a commercial biotech, generating proceeds of £9.7m in the period, and £6.6m post-period end[2]

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. 2. To 12 November 2024

A rebalanced and maturing portfolio



Our NAV Growth Framework

Significant value can be accessed at late-stage clinical development

Operational build

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

Emerging efficacy data

- Clinical strategy defined
- Initial efficacy data from Phase I/II in patients

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

Key exits[1]

neogene THERAPEUTICS
1.1x
£15m proceeds
(2023)

GYROSCOPE A Novartis Company
2.9x
£325m proceeds
(2022)

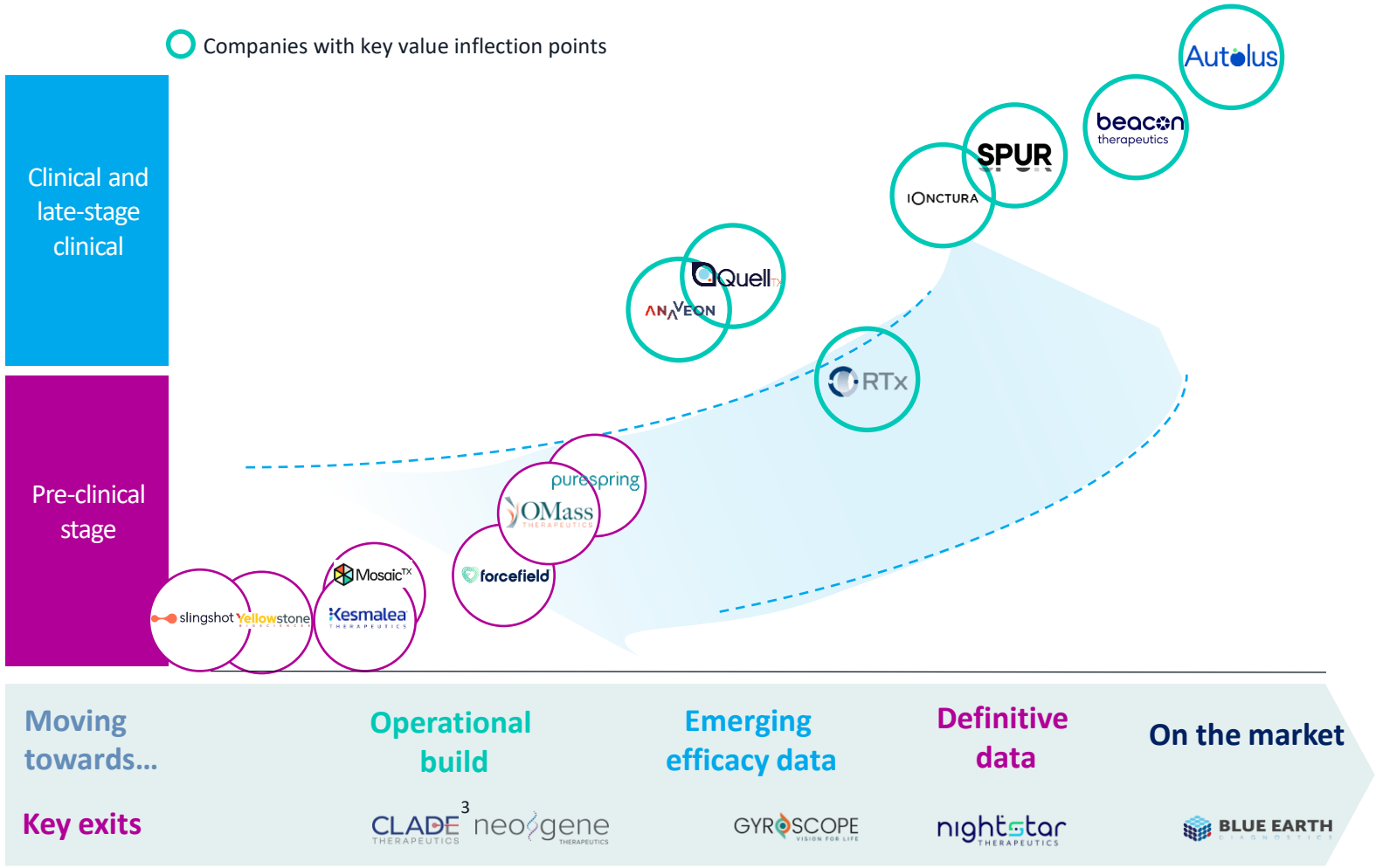
nightstar THERAPEUTICS
4.5x
£256m proceeds
(2019)

BLUE EARTH DIAGNOSTICS
9.9x
£351m proceeds
(2019)

1. Returns since 2012, reflects original Syncona Partners capital invested where applicable. Returns since Syncona merged with BACIT in December 2016, are: Neogene 1.1x, Gyroscope 2.9x, Nightstar 3.5x, Blue Earth 3.9x. All multiples reflect up front proceeds. Exits excludes Clade which has not been fully realised, with Syncona continuing to hold shares in Century

We have rebalanced to a more mature portfolio

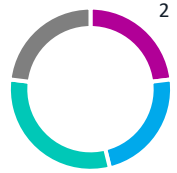
We have a strategic portfolio of 14 companies at different stages of the clinical development pathway



Portfolio rebalanced towards later-stage companies with increased diversification

- **27%** Late-stage clinical (2 companies)[1]
- **41%** Clinical stage (4 companies)
- **32%** Pre-clinical (8 companies)

- **27%** Moving towards the market
- **34%** Moving towards definitive data
- **31%** Moving towards emerging efficacy data
- **8%** Moving towards operational build



[2]

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

68.1% of portfolio is clinical or late-stage clinical companies

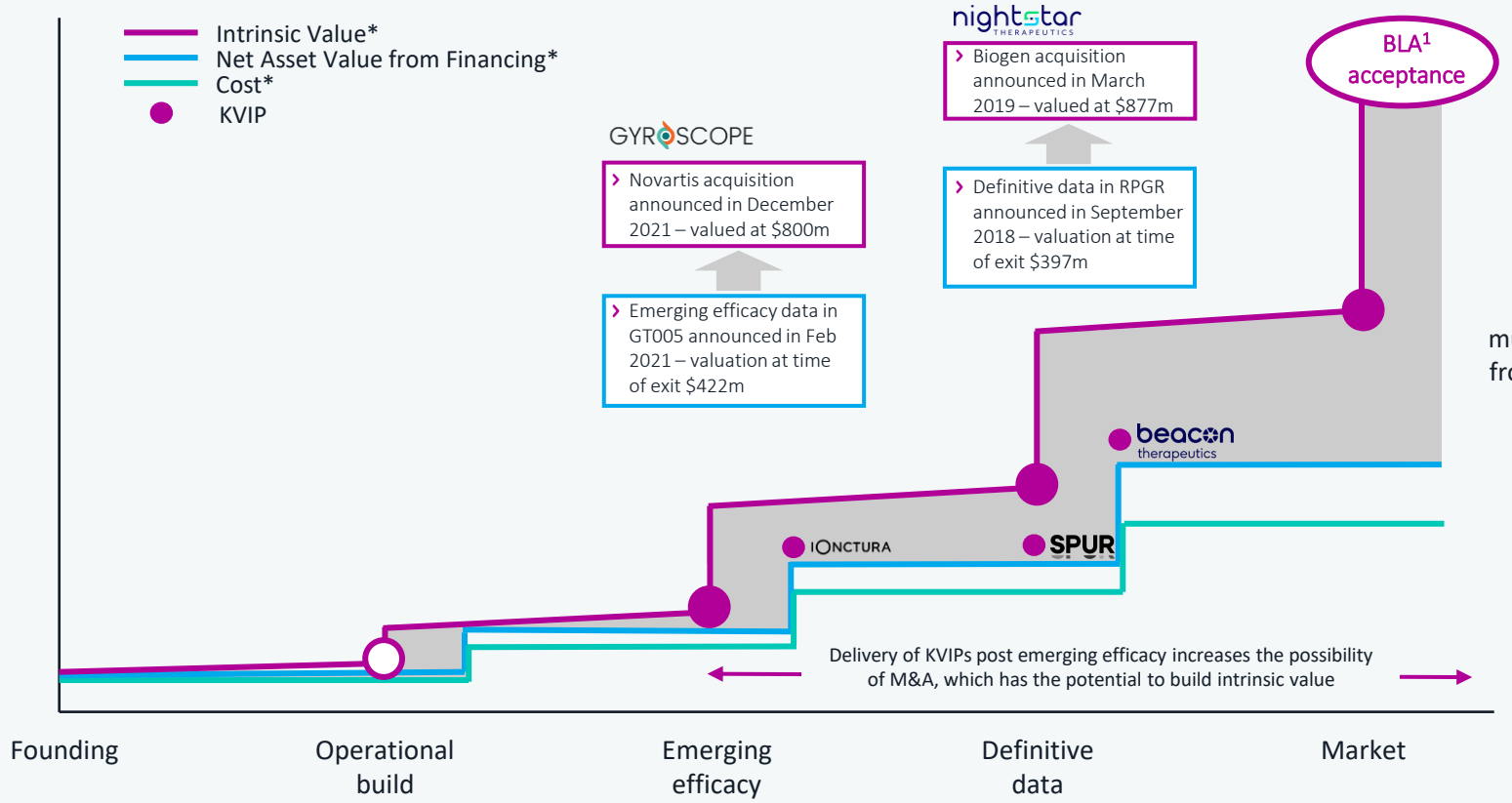
1. This includes Autolus, which was a late-stage clinical company at 30 September 2024. 2. Excluding Slingshot, the Syncona Accelerator. 3. Clade is not yet fully realised, with Syncona retaining shares in Century Therapeutics as part of the acquisition

Driving value through the delivery of KVIPs

Material de-risking events with the potential to drive significant NAV growth

- Key value inflection points are material de-risking events for a portfolio company that have potential to drive significant NAV growth for Syncona
- These milestones can also enable companies to access significant capital, including through financings and IPOs, which may take place at valuation uplifts
- Primarily, key value inflection points are the delivery of emerging efficacy or definitive data, with the latter typically being more valuable
- The delivery of emerging efficacy data and subsequent milestones increasingly builds intrinsic value in a company

Illustrative value appreciation through delivery of KVIPs



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

1. Biologics License Application 2. Reflects upfront proceeds

*Illustrative

Potential from our most mature private portfolio companies

Beacon, Spur and iOnctura to deliver KVIPs by the end of 2027

iONCTURA

Lead programme (roginolisib – first-in-class asset)

- Uveal melanoma is the most common form of eye tumour, with over 7,000 new cases of uveal melanoma annually globally[1]
- Once metastasised (50% of patients) median overall survival is approximately one year[2]
- Data released to date from the Phase Ib trial demonstrates long-term safety and emerging efficacy

Expected to enter Phase II trial in CY2024

SPUR

Lead programme (FLT201 – first-in-class asset)

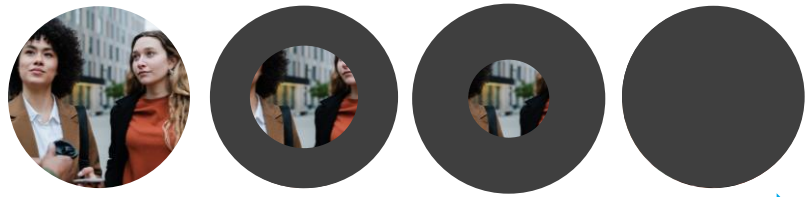
- Gaucher disease is a disorder caused by the build-up of fatty substances in certain organs, particularly the spleen and liver
- c.18,000 Gaucher disease type 1 patients in the US, UK, EU and Israel[3]
- No substantial advances in treatment in the last two decades
- Presented positive data in October demonstrating long-lasting potential of FLT201 up to 15 months post-dosing (KVIP)

Expected to enter Phase III trial in CY2025

beacon therapeutics

Lead programme (AGTC-501 – first-in-class asset)

- XLRP is a genetic disease that causes blindness in men
- >20,000 XLRP patients in US/Europe[4]
- Patients are legally blind by a median age of 45
- Presented positive 24-month interim safety and efficacy data from its Phase II SKYLINE trial in October, demonstrating durable efficacy profile of AGTC-501 (KVIP)

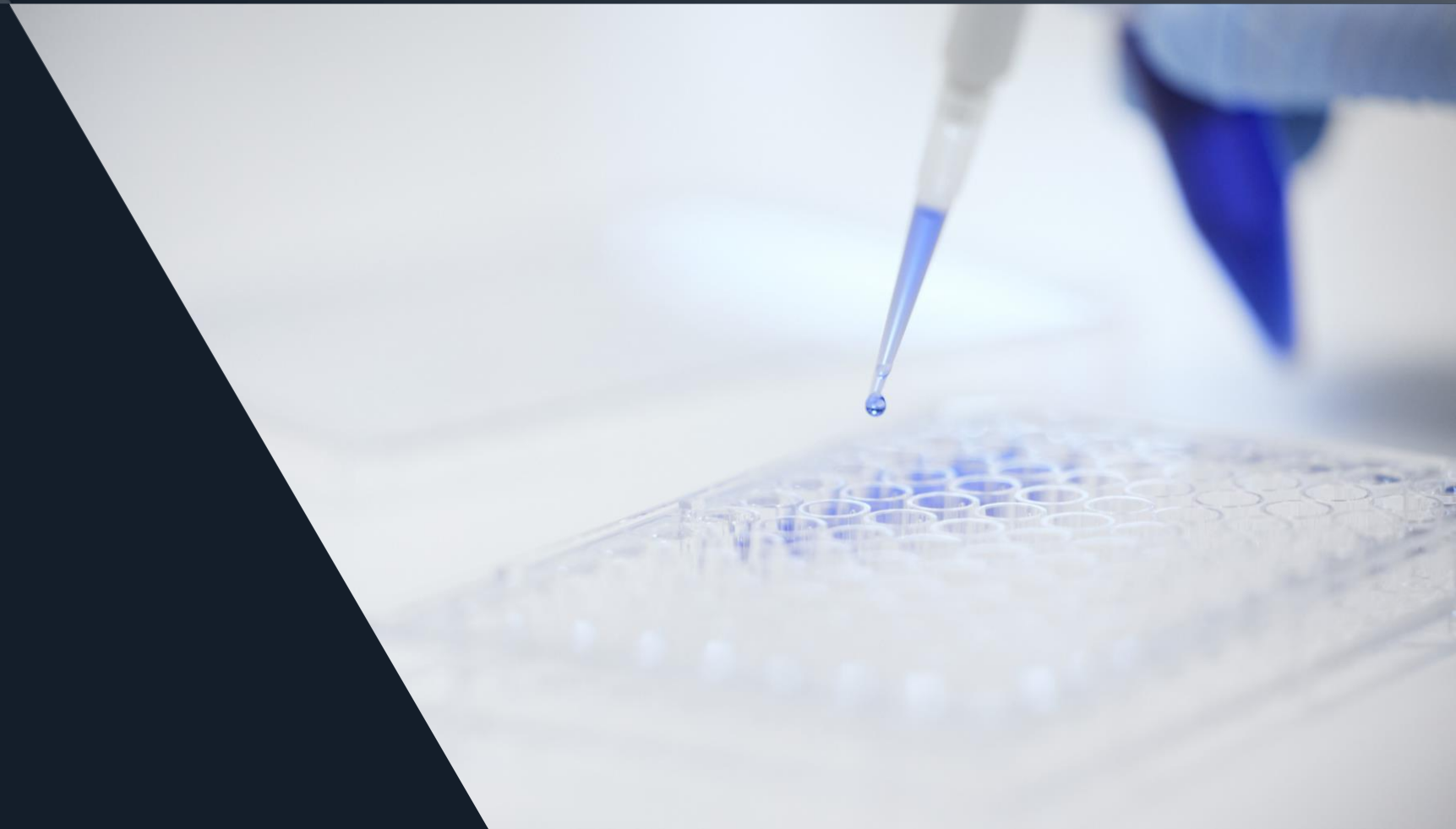


Entered Phase II/III trial in CY2024

Clinical → **Late-stage clinical**

1. GLOBOCAN 2020. 2. Rantala, 2019. 3. Company estimate. 4. Daiger SP. Perspective on genes and mutations causing retinitis pigmentosa. Arch Ophthalmol

Market environment

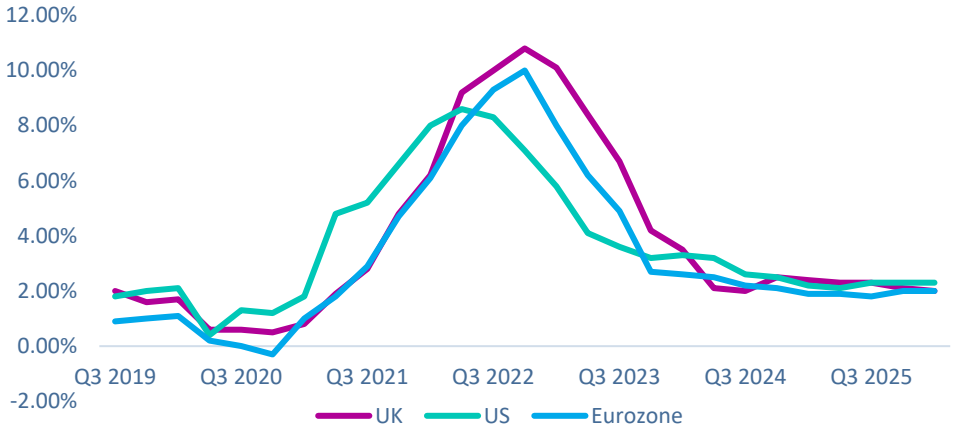


Biotech markets are recovering

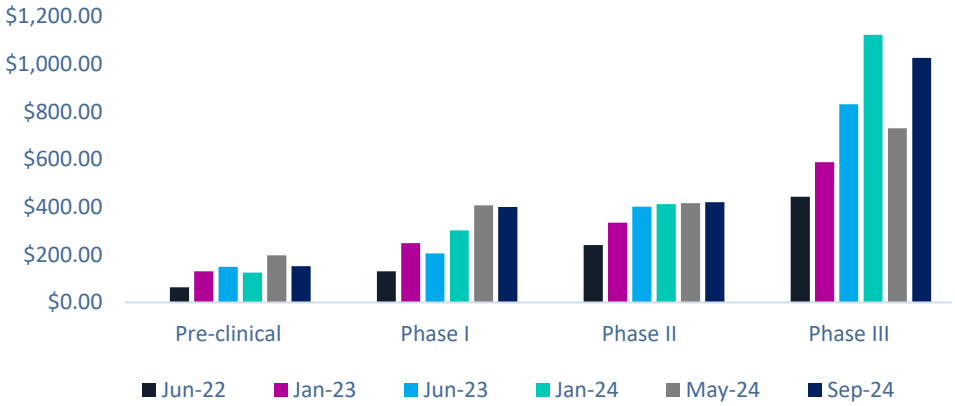
Sentiment and outlook improving

- Macro trends such as softening inflation and falling interest rates have the potential to act as tailwinds for our sector
- We are seeing improvements in the private financing environment, underlined by the recent delivery of a number of successful syndicated financings across the Syncona portfolio
- More broadly the IPO market continues to recover following a first half where more capital was raised in IPOs than in the whole of 2022 or 2023[1]
- Late-stage assets continue to lead the recovery in both the public and private markets, and in terms of financings, IPOs and M&A
- Pharma is focused on these de-risked assets and they are willing to pay a premium for the nearer-term value they bring

Inflation rates across EU/UK/US (2014-2024)[2]



Average Enterprise Value of a biotech listed on US exchanges by stage of development ($ millions)[3]



1. Nature 2. Bloomberg. Based on consumer prices 3. Stifel

Continued focus from pharma on late-stage M&A

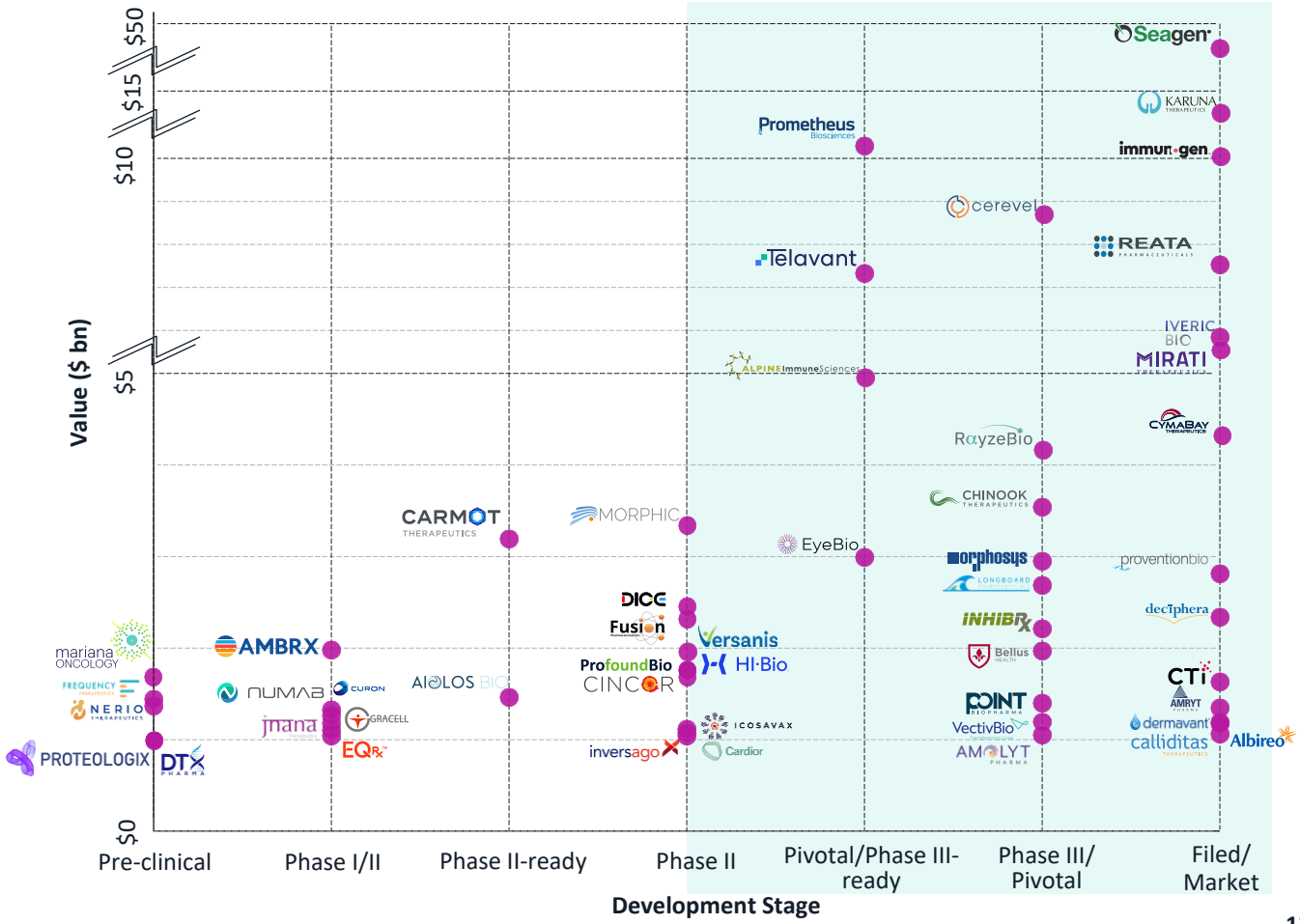
Larger deals weighted to late-stage companies

Pharma facing upcoming patent cliff

- Pharma are facing a patent cliff with over $300 billion of revenue from medicines at risk of patent expiry by 2030[1]
- Focused on restocking their pipelines with later-stage assets
- Late-stage/marketed assets make up ~75% of transactions since 2022[2]
- Possess balance sheets to invest heavily, with over $1 trillion in M&A firepower[3]

Biopharma deals ~$1bn - $50bn since 2022[2]

Out-return is weighted toward later stage development



1. Evaluate Pharma, World Preview 2024 Report 2. Syncona analysis; data as at October '24. 3. EY, firepower defined as a company's capacity to do M&A based on the strength of its balance sheet

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Proactive portfolio management

Diversified and maturing portfolio

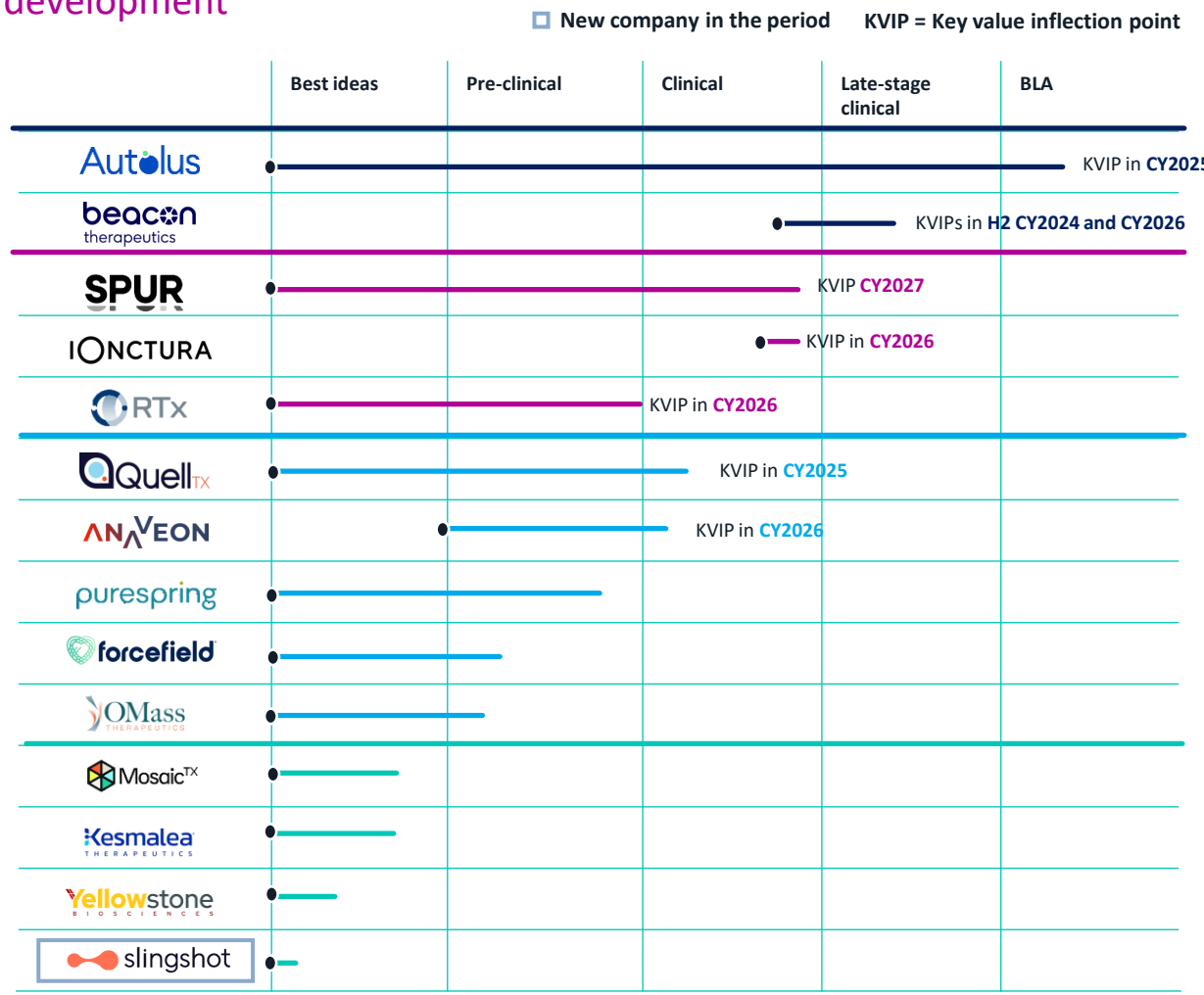
14 strategic portfolio companies at different stages of development

Portfolio increasingly weighted towards clinical and late-stage clinical development

- Beacon has commenced its pivotal Phase II/III trial whilst Spur will be entering a Phase III trial in CY2025

Significant period of execution across the portfolio

- Six capital access milestones achieved in the financial year to date with two key value inflection points delivered post-period end
  - Beacon 24-month data from Phase II SKYLINE trial in XLRP
  - Spur data from Phase I/II Gaucher disease trial
- Post-period end, Autolus received marketing approval from the US FDA for AUCATZYL® (obe-cel)
- Anaveon entered the clinic in the period with its ANV600 programme



1. At 30 September 2024 Autolus was classified as a company moving towards being on the market

slingshot

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Slingshot - The Syncona Accelerator

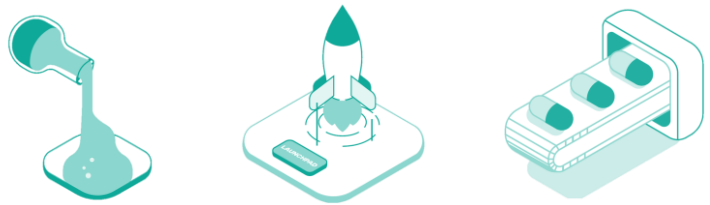
A capital efficient way to invest in the next frontier of innovation

Accelerating exceptional academic science towards clinical development with £12.5m commitment

- Slingshot will accumulate and develop multiple pre-clinical programmes under one pipeline
- These programmes will be accelerated along the development pathway towards the clinic
- High quality management team with Syncona Managing Partner Edward Hodgkin appointed Executive Chair, with Executive Partner Richard Wooster appointed as Slingshot's Chief Scientific Officer
- First pipeline programme, Apini, is a small molecule programme focused on inflammatory disease identified from the University of Manchester
- This structure provides a capital efficient and de-risked way to gain more exposure to the returns available from translating highly innovative science into promising biotech assets

The Slingshot model

- Programmes are identified from world-leading academic institutions in the UK, US and Europe
- Academics are then able to access development expertise that is rarely available for singular early-stage programmes, alongside centralised resource, funding and operational support
- This creates a variety of paths to take medicines to the clinic and ultimately to patients



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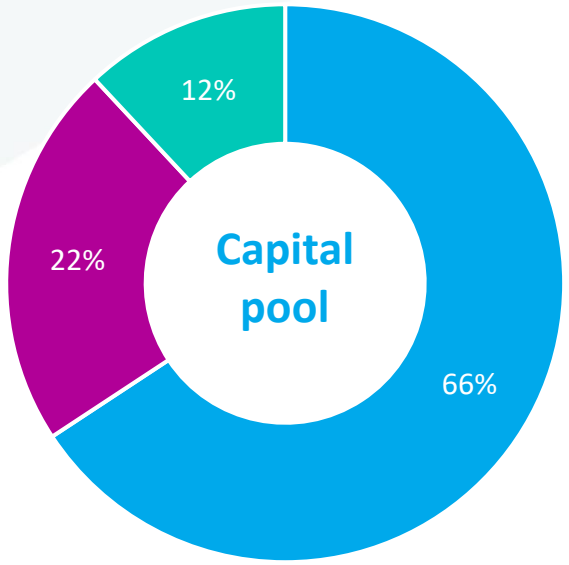
Rigorous approach to capital allocation

Capital pool central to delivery of strategy

We are funded to the delivery of all of our expected key value inflection points

Capital pool of £352.7m

- 66% of capital pool committed to our existing portfolio and operational costs (including share buybacks), with 22% allocated to underwriting further KVIPs
- Additional capital is allocated to driving broader portfolio milestones and new investments
- 12-24 months of funding allocated to cash and Treasury Bills, with the capital pool returning 1.0%
- A further £20m allocated to the share buyback in the period, with an additional £15m allocated post-period end, taking total allocation to £75m
- We remain funded to deliver on our KVIPs, whilst retaining capital to drive the broader strategy
- £46.3m shares have now been repurchased at an average 34.7% discount resulting in 3.66p accretion[1]



- Committed to portfolio companies, operational costs and share buybacks
- Underwriting key value inflection points
- Driving broader portfolio milestones and new investments

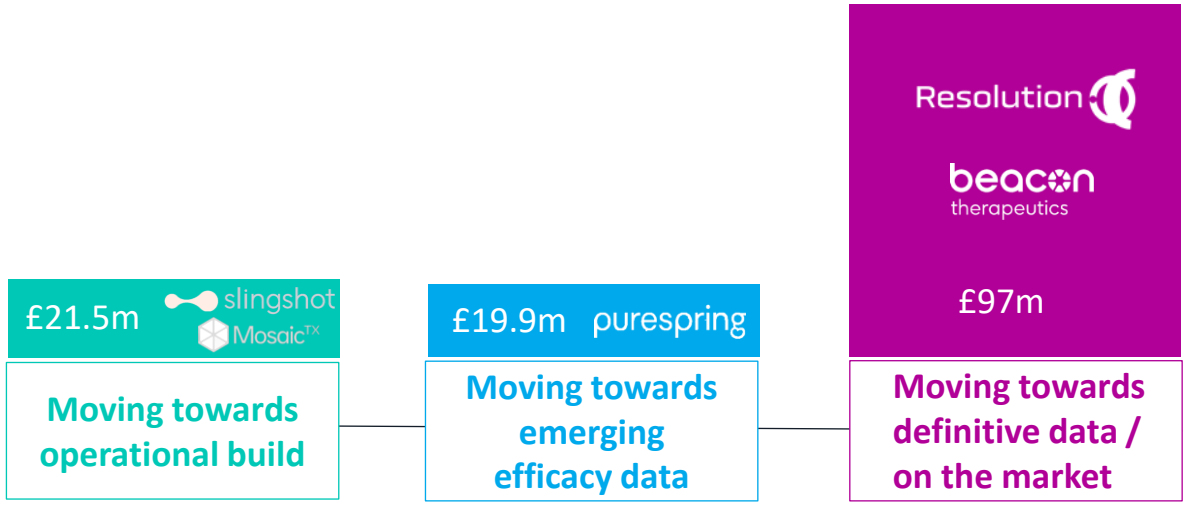
1. As at 13 November 2024

Capital commitments weighted to clinical assets and assets approaching clinical entry

Continue to apply a rigorous approach to capital allocation

- £90m deployed[1] into the life science portfolio in the period into the current portfolio and new opportunities
- Six financings closed in the period, with five commitments from Syncona
  - £63.5m committed to Resolution Series B financing
  - £33.5m committed to Beacon in £134m Series B financing
  - £19.9m committed to Purespring in £80m Series B financing
  - Additional £9m committed to Mosaic's Series A financing
  - Launch of Slingshot with £12.5m commitment
- Also secured an additional £10m commitment from Roche Venture Fund to Forcefield's Series A financing

Capital deployment guidance for FY2024/5 remains unchanged at £150-200m



Capital commitments weighted towards clinical-stage assets or assets approaching the clinic

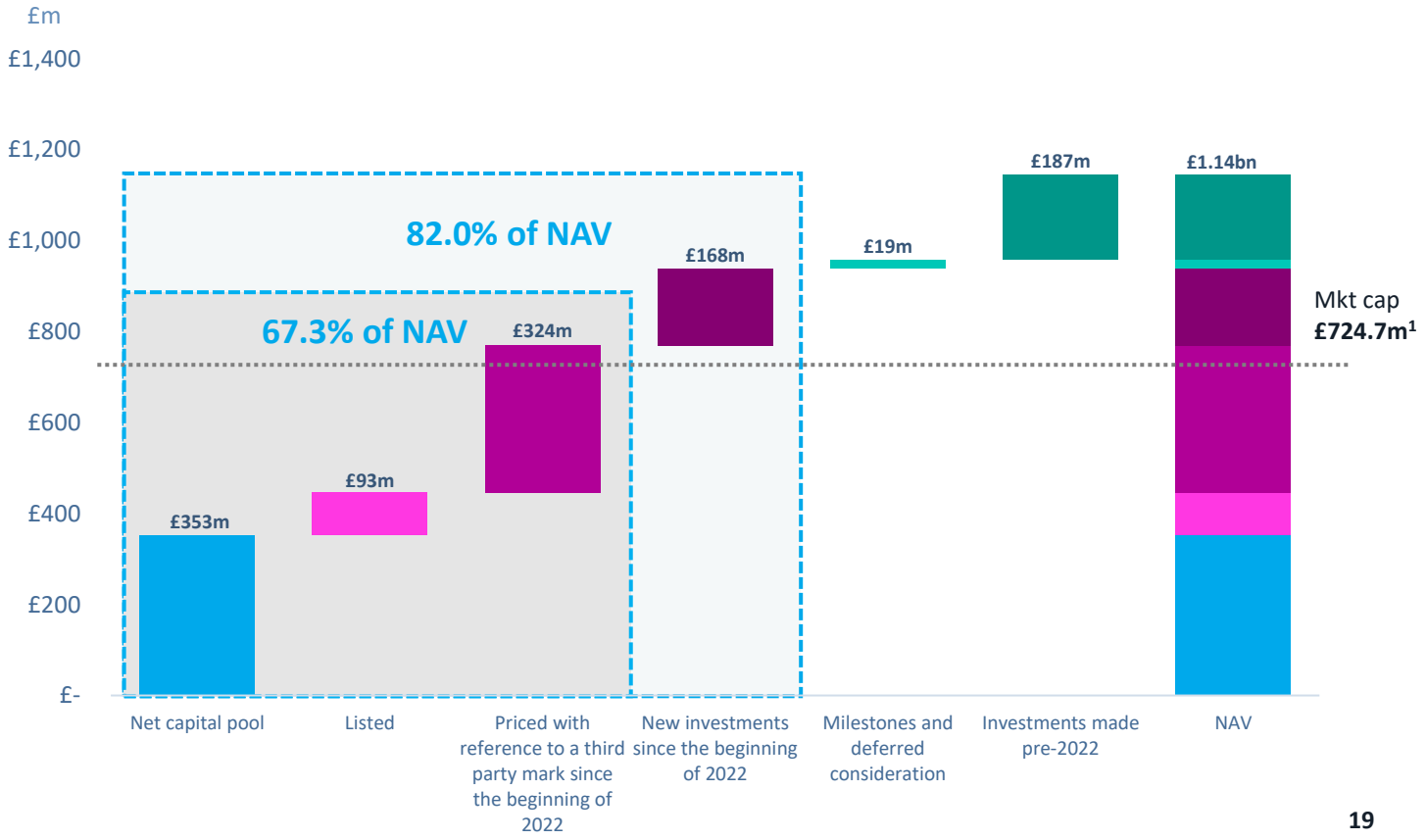
Note - A portion of the capital committed to financings in Resolution, Beacon and Purespring in the period was deployed pre-period through convertible loan notes. 1. Capital deployment refers to capital invested (rather than committed) in the period.

Attracting external investment to the portfolio

NAV is robust following recent syndicated financings

Portfolio is now substantially refinanced

- £305.6m of capital raised by portfolio companies in the period, with £170.5m raised from external investors
- Including the capital pool, £770.1m (67.3%) of NAV has been priced with reference to a third-party mark since the start of 2022, when the market downturn had fully set in
- Our NAV is robust, providing a strong platform for growth



1. As at 30 September 2024

A strong platform for growth

A number of expected key value inflection points

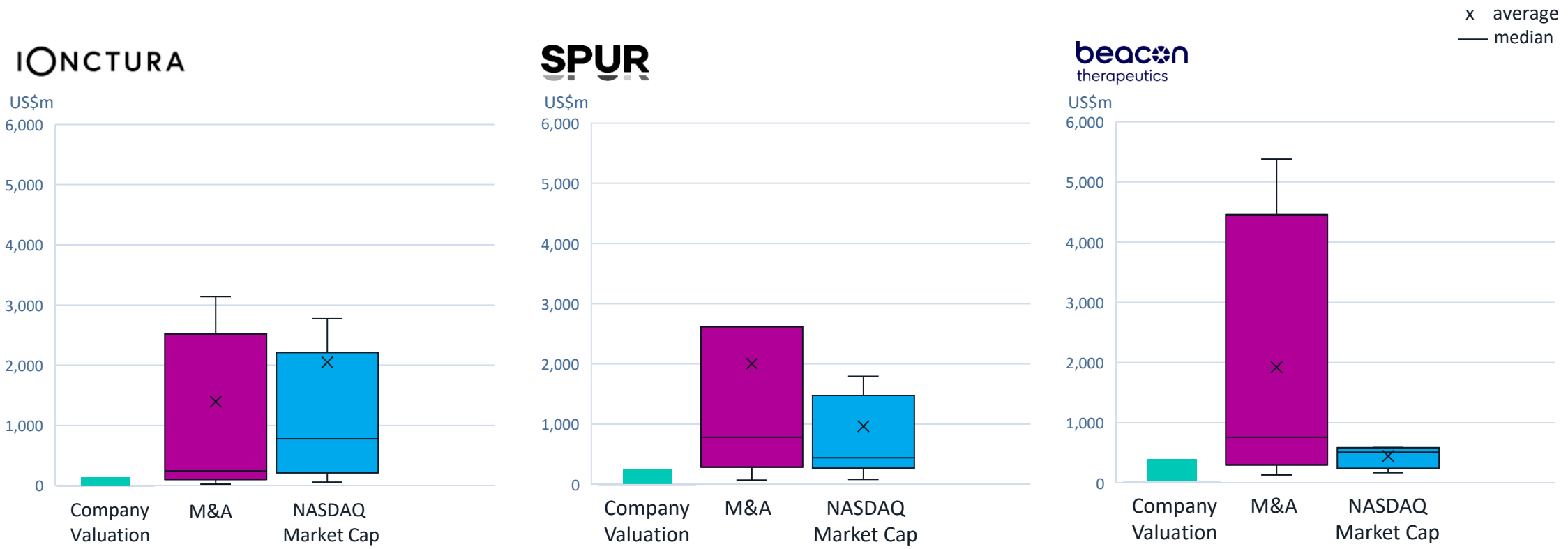
Key de-risking events with the potential to drive significant NAV growth

- Two key value inflection points recently achieved by Beacon and Spur which provide strong momentum
- Eight key value inflection points across the porfolio, with three expected before the end of CY2025
- These key value inflection points are not without risk
- In addition, nine expected capital access milestones across the portfolio, including seven expected by the end of CY2025

		CY2024	CY2025	CY2026	CY2027
On the market	Autolus		Commercial traction following Autolus' US launch of obe-cel in **CY2025**, following FDA regulatory approval		
Definitive data	beacon therapeutics	3-month data from Beacon's Phase II DAWN trial in XLRP in **H2 CY2024 (formerly CAM)**		Data readout from Beacon's pivotal VISTA trial in XLRP in **CY2026**	
	IONCTURA			Data readout from iOnctura's Phase II trial in uveal melanoma in **CY2026**	
	SPUR				Completion of the pivotal stage of its Phase III trial in Gaucher disease in **CY2027 (new)**
	RTx			Data readout from Resolution's Phase I/II trial in end-stage liver disease in **CY2026**	
Emerging data	QuellTX		Data readout from Quell's Phase I/II trial in liver transplantation in **CY2025**		
	ANAVEON			Data readout from Anaveon's Phase I/II trial of ANV600 in **CY2026**	

Peer groups for most mature private companies

Beacon, Spur and iOnctura expected to publish key value inflection points by end of CY2027



Small molecule oncology peer group
Company Valuation = US$145.0m
Syncona ownership = 23.0%
Syncona holding value = US$33.4m (£25.0m)

Rare genetic medicines peer group
Company Valuation = US$254.0m
Syncona ownership = 82.9%
Syncona holding value = US$210.6m (£157.5m)

Ophthalmology genetic medicines peer group
Company Valuation = US$375.0m
Syncona ownership = 41.5%
Syncona holding value = U$151.1m (£113.0m)[1]

Syncona team analysis, data does not represent a forecast. Outliers are excluded from the graphs but included in the calculations. Peer set included on slide 51. 1 – Also includes discounted valuation of Beacon milestone payments

Summary and outlook

Focused on delivering our strategy and driving NAV growth for our shareholders

- Later stage and diversified portfolio continues to execute well and has attracted significant external capital
- Continue to focus capital towards opportunities which are clinical stage or close to clinical entry
- Eight key value inflection points expected by the end of CY2027 with the potential to drive significant NAV growth
- We believe there is substantial latent value in the portfolio which will support the delivery of £5bn of NAV by 2032
- We are well positioned to benefit from an improving macro environment

Rebalanced portfolio provides a strong platform for growth and underpins confidence in achieving our ten-year targets

10-year targets

Creating or adding

3

new companies a year

based on exceptional science

20-25

companies

targeting top quartile returns

3-5 companies to late-stage development with significant ownership positions

£5bn

Net Assets by 2032

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Appendix 1 – Team

Evolving and expanding our platform

Embedding a new organisational operating model to support the delivery of our strategy

Senior investment team


Chris Hollowood
CEO


Roel Bulthuis
Managing Partner


Ed Hodgkin
Managing Partner


Elisa Petris
Lead Partner


Magdalena Jonikas
Lead Partner

Broader investment team


Alex Hamilton
Investment Partner


Alessio D'addabbo
Analyst


Alice Renard
Investment Partner


Gonzalo Garcia
Investment Partner


Michael Kyriakides
Investment Partner


Nathaniel Dahan
Associate Partner


Pierre Joffrin
Associate Partner


Raghd Rostom
Associate Partner

Executive Partner group

- Supports the investment team in their review process and **work with portfolio companies as they scale**
- Provide insight and experience through the identification and review process, ensuring only the best opportunities are progressed

Scale

Expertise

Support

A platform for…

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

… delivering long-term growth

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

Harriet Gower Isaac
Head of People

- 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

Strong senior investment team

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

Chris Hollowood[1]
CEO
PhD

SPUR
Yellowstone BIOSCIENCES
beacon therapeutics

22 years' experience

Roel Bulthuis[2]
Managing Partner, Head of Investments
MSc, MBA

ANAVEON
RTx
IONCTURA

24 years' experience

Edward Hodgkin[2]
Managing Partner
PhD

RTx
OMass THERAPEUTICS
slingshot
Mosaic[TX]

33 years' experience

Elisa Petris[2]
Lead Partner
PhD

QuellTX
beacon therapeutics
forcefield

16 years' experience

Magdalena Jonikas[2]
Lead Partner
PhD

Kesmalea THERAPEUTICS
OMass THERAPEUTICS
Mosaic[TX]

13 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 exits

£1.3 billion invested to date, generating an IRR of 17%, 1.3x invested capital[1]

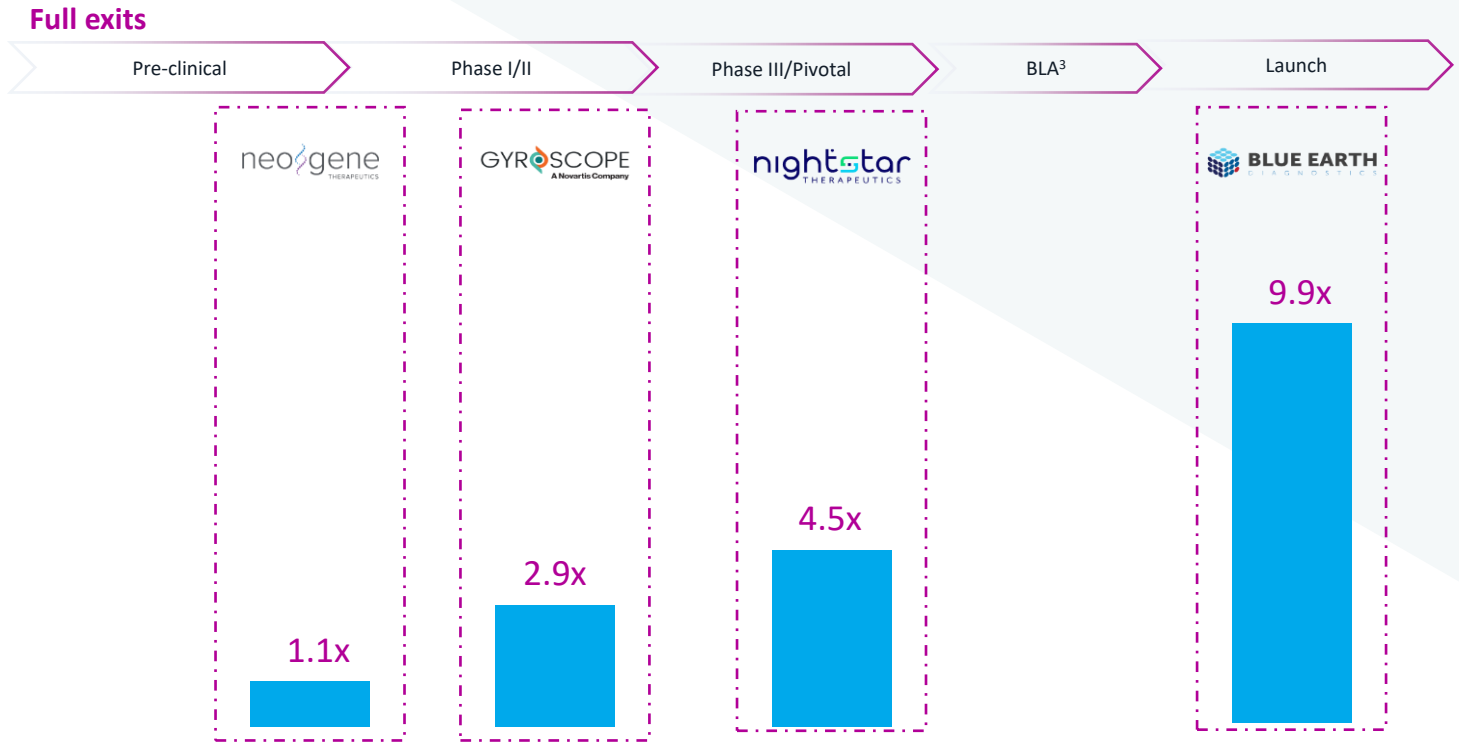
Exits generated £955m of proceeds, at an aggregate IRR of 73.6% and a 3.9x cost[2]

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



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

All financial data at 30 September 2024

1. Includes sales of Nightstar, Blue Earth, Gyroscope and Neogene, upfront consideration of Clade and closure of 14MG and Azeria. Reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
2. Includes sales of Nightstar, Blue Earth, upfront proceeds from sale of 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

Building companies with impact

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

Building global leaders

26 Syncona portfolio companies since 2012 foundation

14 Number of companies in the portfolio today

1,000+ Number of employees across Syncona portfolio

Our track record

17% IRR since 2012; 1.3x multiple on cost across whole portfolio[1]

£1.3bn Syncona capital deployed since 2012

£955m Generated from five successful exits; 3.9x multiple of cost[2]

Clinical progress

4 Late-stage clinical companies across the portfolio since inception

29 Clinical-stage programmes across the portfolio since inception

20 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[3]

6 Diseases with high unmet need targeted by lead programmes in clinical portfolio

1. Includes sales of Clade, Nightstar, Blue Earth, Gyroscope and Neogene and closure of 14MG and Azeria. Reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis. Since 2016, Syncona's NAV per share has increased from 127.9p to 178.9p, a total return of 5.0% per annum, and the Syncona life science portfolio has delivered an IRR of 12.9% and a 1.3 multiple of cost
2. Includes sales of Clade, 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. Calculated from our original 2012 founding
3. Autolus corporate presentation

All financials as at 30 September 2024, employee numbers as of March 2024

Appendix 3 - Portfolio

Scaling our net assets

Committed to delivering our long-term strategy

3 new companies a year

Late-stage opportunities or significant transactions included in this target

Portfolio of 20-25 leading life science companies

Portfolio increasingly diversified by development 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

10-year targets to 2032

Creating or adding

3

new companies a year

based on exceptional science

20-25

companies

targeting top quartile returns

delivering 3-5 companies to late-stage development with significant ownership positions

£5bn

Net Assets by 2032

Ensuring execution in the portfolio

Strong delivery since introduction of NAV Growth Framework

- Six capital access milestones and two key value inflection points delivered since FY2023/4, including post-period end
- Includes data readouts from Beacon's Phase II SKYLINE trial in XLRP and Spur's Phase I/II trial in Gaucher disease
- Beacon's three-month data readout from its Phase II DAWN trial in XLRP now expected in H2 CY2024

	CY2023	Status	CY2024	Status
On the market Autolus	Further long-term follow up data from its pivotal study in obe-cel in adult r/r B-ALL	Delivered	Initiate a Phase I study of obe-cel in refractory systemic lupus erythematosus (SLE), extending the use of obe-cel into autoimmune diseases	Delivered
	BLA submission for obe-cel to the FDA	Delivered	Initial data from Phase I trial in SLE	Now expected in H1 CY2025
			Commence the US commercial launch of obe-cel, dependent on anticipated FDA regulatory approval	Delivered
Definitive data beacon therapeutics			Publish 12-month data from its Phase II trial in XLRP	Delivered
			Initiate its Phase II/III trial in XLRP	Delivered
			Publish 24-month data from its Phase II SKYLINE trial in XLRP	Delivered
			Three-month data readout from the Phase II DAWN trial in XLRP	Now expected in H2 CY2024
SPUR			Release of additional data from its Phase I/II trial in Gaucher disease	Delivered
			Initial safety readout in higher dose cohort from its Phase I/II trial in AMN	Expected H1 CY2025[2]
			Data readout from its Phase I/II trial in Gaucher disease	Delivered
ACHILLES[1]			Provide further data from its Phase I/IIa clinical trial in NSCLC	Delivered
			Provide further data from its Phase I/IIa clinical trial in melanoma	Delivered
Emerging data QuellTX			Publish initial safety data in Phase I/II trial in liver transplantation	Delivered
			Complete dosing of the safety cohort in its Phase I/II trial in liver transplantation	Delivered
ANAVEON			Publish initial data from its Phase I/II trial of ANV419 in metastatic melanoma	ANV419 programme deprioritised
			Initiation of Phase I/II trial of ANV600	Delivered

1. Achilles is now a Syncona investment and not part of the strategic life science portfolio. 2. In the Q3 Update in February 2024, Syncona updated its guidance for the SBT101 programme to report that it expected its safety read-out to be published in H2 CY2024

KVIP On time/ early Delayed/ deprioritised

Late-stage clinical | Clinical | Pre-clinical

Portfolio company	Fully diluted ownership %[4]	31 Mar 2024 value £m (fair value)	Net invested/returned in the period £m	Valuation change £m	FX movement £m	30 Sep 2024 value £m (fair value)	Valuation basis (fair value)[1,2,3]	% of NAV
beacon therapeutics	41.5%	94.7[5]	9.6	15.1	(6.4)	113.0	PRI	9.9%
Autolus	10.6%	169.5	(9.7)	(70.3)	(6.1)	83.4	Quoted	7.3%
SPUR	82.9%	135.6	20.8	1.1	-	157.5	Cost	13.8%
QuellTX	33.7%	84.7	-	-	(4.7)	80.0	PRI	7.0%
ANAVEON	36.9%	35.7	-	-	0.2	35.9	PRI	3.1%
IONCTURA	23.0%	25.6	-	-	(0.6)	25.0	Cost	2.2%
RTx	82.6%	50.0	10.0	3.6	-	63.6	Cost	5.6%
purespring	38.1%	45.3	5.0	0.9	-	51.2	PRI	4.5%
OMass THERAPEUTICS	28.9%	43.7	6.0	-	-	49.7	PRI	4.3%
Kesmalea THERAPEUTICS	59.7%	12.0	8.0	-	-	20.0	Cost	1.7%
Yellowstone BIOSCIENCES	60.9%	1.0	15.5	-	-	16.5	Cost	1.4%
MosaicTX	76.6%	7.3	7.7	-	-	15.0	Cost	1.3%
forcefield	62.6%	6.5	1.7	2.4	-	10.6	PRI	0.9%
slingshot	100.0%	0.0	5.6	-	-	5.6	Cost	0.5%
Milestones and deferred consideration		2.2	0.7	2.2	(0.3)	4.8	DCF	0.5%
Syncona Investments		72.3	(5.9)	(4.7)	(1.6)	60.1		5.2%
Capital pool		452.8	(104.7)	8.4	(3.8)	352.7		30.8%
Total		**1,238.9**				**1,144.6**		100.0%

1. Primary input to fair value of equity holding. 2. 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. 3. 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. 4. Percentage holding reflects Syncona's ownership stake at the point full current commitments are invested. 5. Total investment interest related to Beacon at 31 March 2024 includes the value of equity held in the company and deferred consideration

Clinical portfolio company outlook

Strategic portfolio companies	Next expected milestones with the potential to enable capital access	Syncona view of potential key value inflection points across the portfolio[1]
Autolus	H1 CY2025 - Initial data from Phase I trial in SLE	CY2025 - Commercial traction following US launch of AUCATZYL® (obe-cel), after FDA approval
beacon therapeutics		H2 CY2024 - Three-month data readout from the Phase II DAWN trial in XLRP (formerly a Capital Access Milestone) CY2026 - Data readout from its Phase II/III pivotal VISTA trial in XLRP
IONCTURA	CY2024 - Initiation of Phase II trial in uveal melanoma	CY2026 - Data readout from its Phase II trial in uveal melanoma
SPUR	H2 CY2024 - Select development candidate for GBA1 Parkinson's disease programme H1 CY2025 - Initial safety readout in higher dose cohort from its Phase I/II trial in AMN H1 CY2025 (new) - Additional data readout from its Phase I/II trial in Gaucher disease CY2025 - Initiation of Phase III trial in Gaucher disease	CY2027 (new) - Completion of the pivotal stage of its Phase III trial in Gaucher disease
RTx	H2 CY2024 - Initiation of Phase I/II trial in end-stage liver disease	CY2026 - Data readout from its Phase I/II trial in end stage liver disease
QuellTx		CY2025 - Data readout from its Phase I/II trial in liver transplantation
ANAVEON		CY2026 - Data readout from its Phase I/II trial of ANV600
purespring	CY2026 - Initiation of Phase I/II trial in complement mediated kidney disease	
OMass THERAPEUTICS	CY2025 - Initiation of Phase I trial of its MC2 programme	

1. Key value inflection points across the portfolio also have the potential to enable capital access.

SYNCONA

Late-stage clinical

Beacon Therapeutics

Progressing its pivotal study in X-linked retinitis pigmentosa

Initial investment	2022
Value	£113.0m
Financing stage	Series B
Stage of lead programme	Phase II/III

Investment thesis

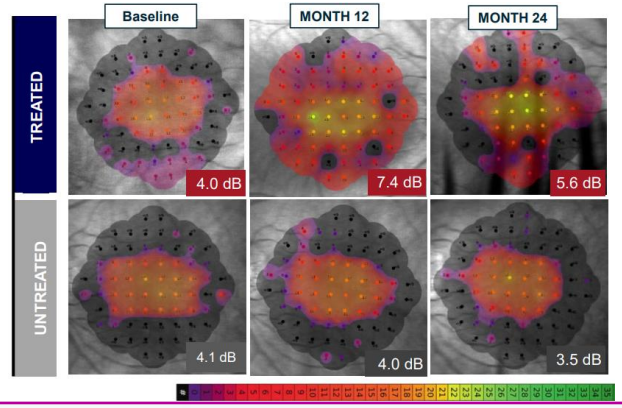
- Beacon has a highly attractive gene therapy programme targeting X-linked retinitis pigmentosa (XLRP), a blinding disease
- Clinical data generated by the company so far has been encouraging demonstrating improvements in visual sensitivity sustained for 36 months
- Registrational VISTA trial initiated 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 Nightstar 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

SYNCONA

Late-stage clinical

Autolus Therapeutics

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

Initial investment	2014
Value	£83.4m
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
- Granted marketing approval by the US FDA in November 2024
- Advanced in-house manufacturing facility ready for commercial launch
- Autolus expects to publish initial data from its Phase I trial of obe-cel in SLE in H1 CY2025

Targeting an area of high unmet need

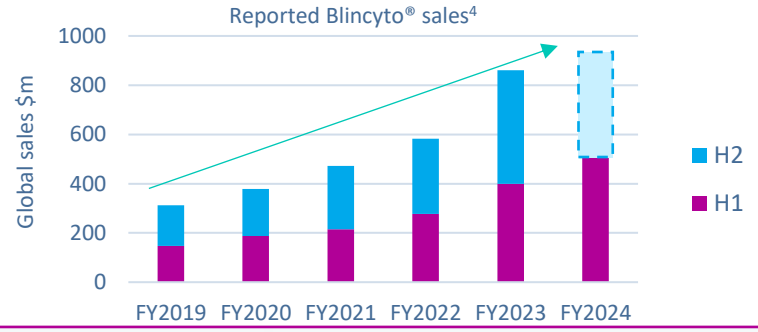
- Only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care[1]
- obe-cel has the potential to be a best-in-class curative therapy in adult ALL
- Launched a Phase I trial in systemic lupus erythematosus (SLE) in H1 CY2024, a multi-organ systemic autoimmune disease that affects approximately 160K - 320K patients in the US[2]. Initial data from the trial is expected in H1 CY2025

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 could launch into an expanding ALL market with commercial rollout planned for 2024
- Tecartus® (approved in 2022) is expected to establish CAR-T in adult ALL; sales increased 21% to $107m in the second quarter 2024[3]
- Blincyto®, current market leader, sales increased 28% year-over-year to $264m in the second quarter of 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

Spur Therapeutics

Developing transformative gene therapies for patients suffering from chronic debilitating diseases

Clinical stage

Initial investment	2015
Value	£157.5m
Financing stage	Taken private
Stage of lead programme	Phase I/II

Investment thesis

- Spur is driving forward two potentially first-in-class gene therapy assets towards late-stage development, including a highly differentiated gene therapy candidate for Gaucher disease type 1, FLT201
- Published compelling initial data demonstrating robust enzyme activity and favourable safety and tolerability

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
- Second clinical-stage gene therapy programme in adrenomyeloneuropathy (AMN)
- AMN is a devastating inherited neurodegenerative disease with **no approved treatment**

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

Clinical stage

Initial investment	2019
Value	£80.0m
Financing stage	Series B
Stage of lead programme	Phase I/II

Quell Therapeutics

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

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 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

Anaveon

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

Clinical stage

Initial investment	2019
Value	£35.9m
Financing stage	Series B
Stage of lead programme	Phase I/II

Investment thesis

- Developing a selective IL-2 receptor agonist with improved administration and toxicity burden
- Company's lead asset ANV600 is in a Phase I/II dose escalation trial
- Pre-clinical data suggests potential of ANV600 to be a best in class agent

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 will have potential application in a range of solid tumours resistant to existing therapies

Market opportunity

- Wide potential utility across multiple oncology indications in wider markets[2]

1. OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015 2. https://seer.cancer.gov/statfacts/html/melan.html 4. GLOBOCAN 2020

iOnctura

Innovative small molecule company developing transformative cancer therapies

Clinical stage

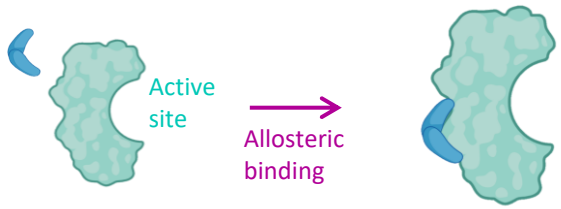
Initial investment	2024
Value	£25.0m
Financing stage	Series B
Stage of lead programme	Phase Ib

Investment thesis

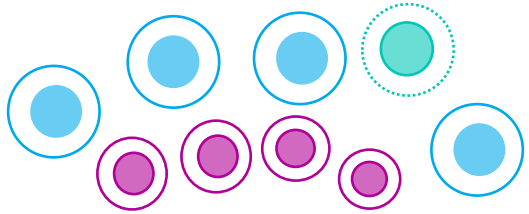
- iOnctura represented an opportunity to invest in a clinical-stage company that has published promising emerging data to date
- Opportunity to drive lead programme through late-stage clinical development
- The PI3K signalling pathway is one of the most commonly dysregulated pathways in cancer
- iOnctura's lead programme, roginolisib, is a **first-in-class, highly selective allosteric inhibitor** 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

- Over **7,000** new cases of uveal melanoma annually worldwide[2]

1. Rantala, 2019. 2. GLOBOCAN 2020

SYNCONA

Pre-clinical stage

Initial investment	2018
Value	£63.6m
Financing stage	Series B

Resolution Therapeutics

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

Investment thesis

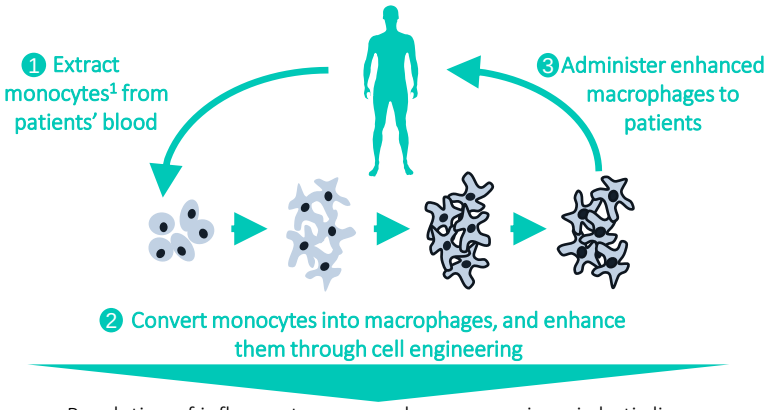
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries[1]
- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest fibrotic scar, modulate the inflammatory response and 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

- 1-2 million people estimated to be affected by liver cirrhosis across major Western markets[2]
- The global liver transplantation market in 2023 was $1.5 billion in 2023[3]



1. Resolution analysis 2. Scaglione et al., Journal of Clinical Gastroenterology, 2015 3. Liver Transplantation Market, Persistence Market Research

SYNCONA

Pre-clinical stage

Initial investment	2020
Value	£51.2m
Financing stage	Series B

Purespring Therapeutics

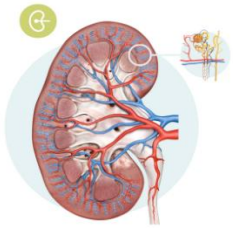
First company to treat kidney diseases by directly targeting the podocyte with AAV gene therapy

Investment thesis

- 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

- 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]

1. https://www.nature.com/articles/s41581-022-00542-7 2. Purespring analysis

SYNCONA

Pre-clinical stage

Initial investment	2018
Value	£49.7m
Financing stage	Series B

OMass Therapeutics

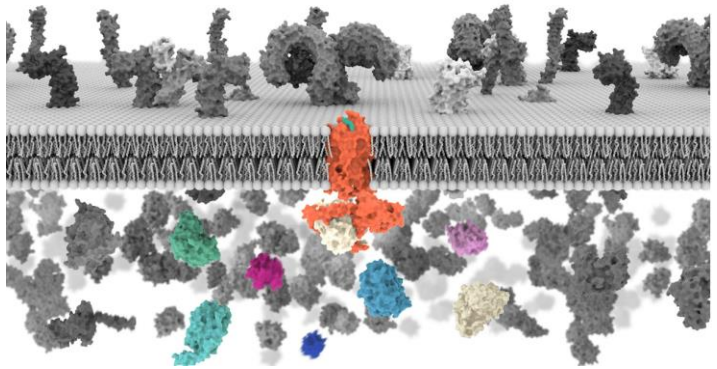
A platform built to unlock highly validated but inadequately drugged targets, with a focus on immunological and rare diseases

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 ACTH-dependent Cushing's syndrome
- CAH occurs in about 1 in 13,000-15,000 births[1], and presents a $450m global market opportunity[2]
- Pituitary ACTH-dependent Cushing causes 65 to 70 percent of Cushing syndrome[3].

1. https://www.ncbi.nlm.nih.gov/books/NBK278953/ 2. https://www.marketresearchfuture.com/reports/congenital-adrenal-hyperplasia-market-4946 3. Endocrinol Metab Clin North Am. 1988;17(3):445.

SYNCONA

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

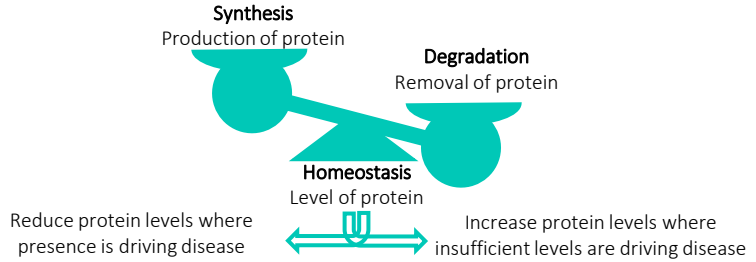
- Small molecule drug discovery platform focused on protein homeostasis
- Protein homeostasis is the system of maintaining the equilibrium of proteins in the human body. This intricate system is in a constant state of change, with the body continuously synthesising and regulating proteins, whilst removing 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



Yellowstone Biosciences

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

Pre-clinical stage

Initial investment	2024
Value	£16.5m
Financing stage	Series A

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 Syncona launch team has enabled the company to operationalise at pace, accelerating its early development

Targeting an area of high unmet need

- AML represents a significant unmet need with **overall median survival of 8.5 months**; AML accounts for 62% of all leukaemia deaths[2]
- 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

- **44,000** new cases of AML annually across the US and Europe[3]
- **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[3]
- 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. https://www.who.int/news-room/fact-sheets/detail/cancer 2. https://www.sciencedirect.com/science/article/abs/pii/S0268960X18301395?via%3Dihub 3. Yellowstone analysis

SYNCONA

Pre-clinical stage

Initial investment	2022
Value	£15.0m
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
- Drug development is hampered by a 90% clinical failure rate[1]

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

1. Sun D, et al. Why 90% of clinical drug development fails and how to improve it?

Forcefield Therapeutics

Pioneering therapeutics to retain heart function

Pre-clinical stage

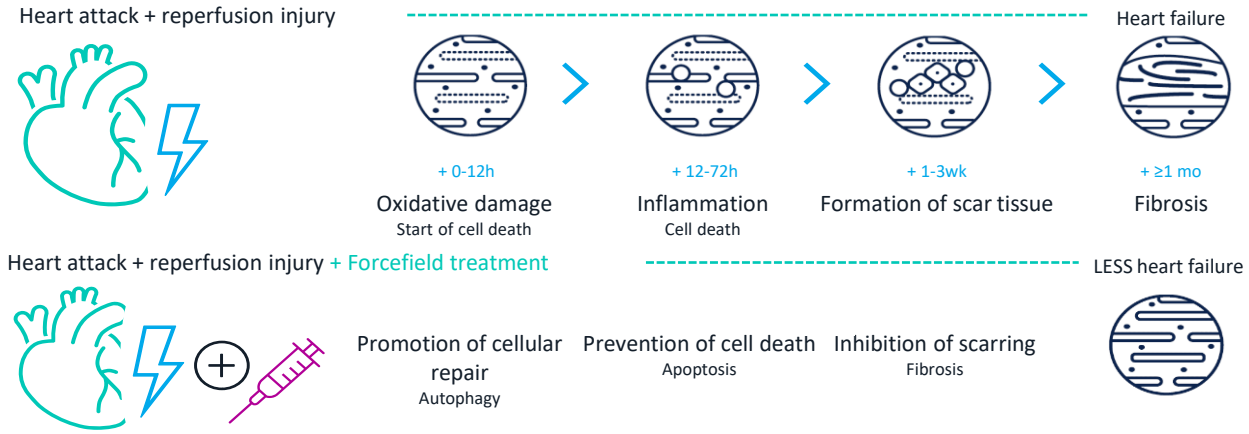
Initial investment	2022
Value	£10.6m
Financing stage	Series A

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

Pre-clinical stage

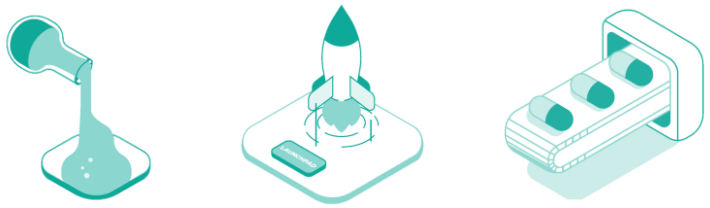
Initial investment	2024
Value	£5.6m

Slingshot Therapeutics

Bridging the gap from academia to drug development

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

Appendix 4 – Additional information

Further information - Peer groups for most mature private companies (slide 22)

Company	Constituents of trading peer group	Constituents of M&A peer group
IONCTURA	Revolution Medicines, Nuvalent, IDEAYA Biosciences, Nurix Therapeutics, Recursion, Relay Therapeutics, Tyra, Monte Rosa Therapeutics, Foghorn Therapeutics, C4 Therapeutics, Acrivon Therapeutics, Nuvectis Pharma, Black Diamond Therapeutics, Prelude Therapeutics, Immuneering	AnHeart Therapeutics, Kinnate Biopharma, Theseus Pharmaceuticals, ORM-6151, Kinnjiu Biopharma, Turning Point, Oncoceutics, Forbius, ArQule, Peloton Therapeutics, Loxo Oncology, Ignyta, Tolero, Acerta Pharma
SPUR	Crispr, Intellia, Rocket, Neurogene, RegenxBio, Verve, Taysha, Voyager, UniQure, Editas, Lexeo, Solid Bio, Bluebird Bio	Orchard Therapeutics, Decibel Therapeutics, Akouos, Prevail Therapeutics Inc, AskBio, Audentes Therapeutics, AveXis
beacon therapeutics	RegenxBio, Meira GTx, 4D Molecular Therapeutics, Adverum Biotechnologies	Bota-vec (MeiraGTx), Iveric Bio, Gyroscope Therapeutics, Nightstar Therapeutics, Spark Therapeutics, Ocata