

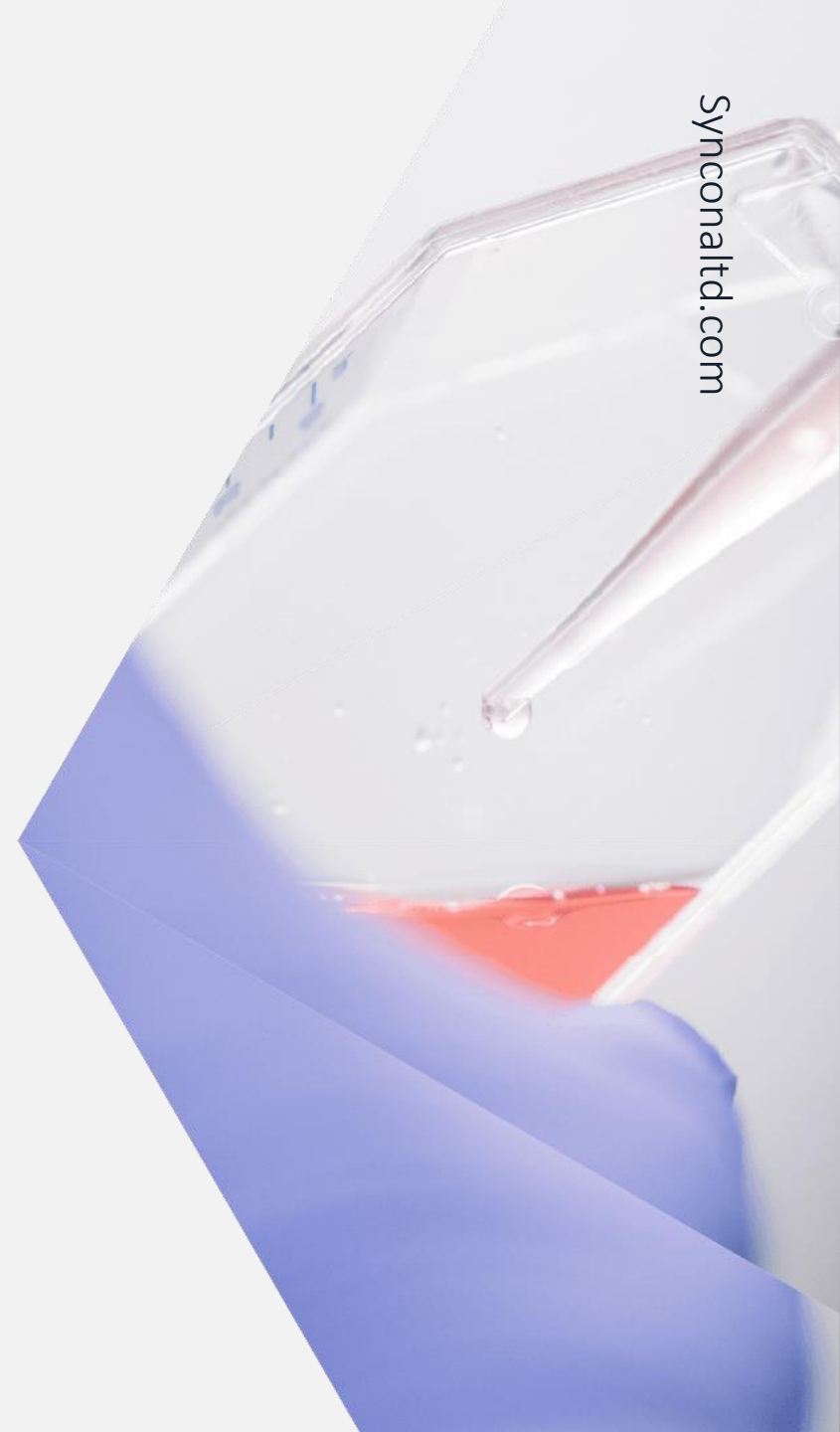


# Syncona Interim Results

Six months ended 30 September 2025

November 2025

Synconatd.com



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# Highlights

Mature portfolio well-positioned to deliver shareholder value as market conditions in biotech improve

## Financial performance

- NAV of £1.0bn, 167.9p per share, a return of (1.7)%
- (1.7)% return from the life science portfolio, with performance impacted by:
  - Decline of £15.9m from CRT Pioneer Fund, a legacy holding in a private, oncology-focused investment fund
  - CRT Pioneer Fund is a non-core holding in Life Science Portfolio, which is not managed by SIML
  - Positive financial performance across the remainder of the Life Science Portfolio (+£9.2m)

## Maturing portfolio of 14 companies making strong clinical progress

- 76.8% of Life Science Portfolio is in eight clinical-stage and commercial companies; two at late-stage
- Continued positive clinical progress, notably multiple clinical data read-outs from Beacon and iOnctura continues to execute on its clinical plans
- Strong strategic, operational and financial execution at several portfolio companies, notably, Quell, OMass, Mosaic and Yellowstone
- Four capital access milestones delivered
- Five key value inflection points (KVIP), that have the potential to drive significant NAV growth, expected in CY2026

## Strategy update

- Undertaken extensive engagement with shareholders
- Seeking shareholder approval for a change in investment objective and policy with an initial focus on the return of £250m of proceeds
- After £250m has been returned, the SIML team will continue to build out Syncona's portfolio to 20-25 companies
- The SIML team is seeking to establish a new private fund, independent from Syncona to diversify its funding sources
- Intention to reduce Board size to five to reflect new strategy
- Intention to optimise the cost base across the group to align with the proposed investment objective and policy

# Improving market conditions



# Market conditions improving across the biotech sector

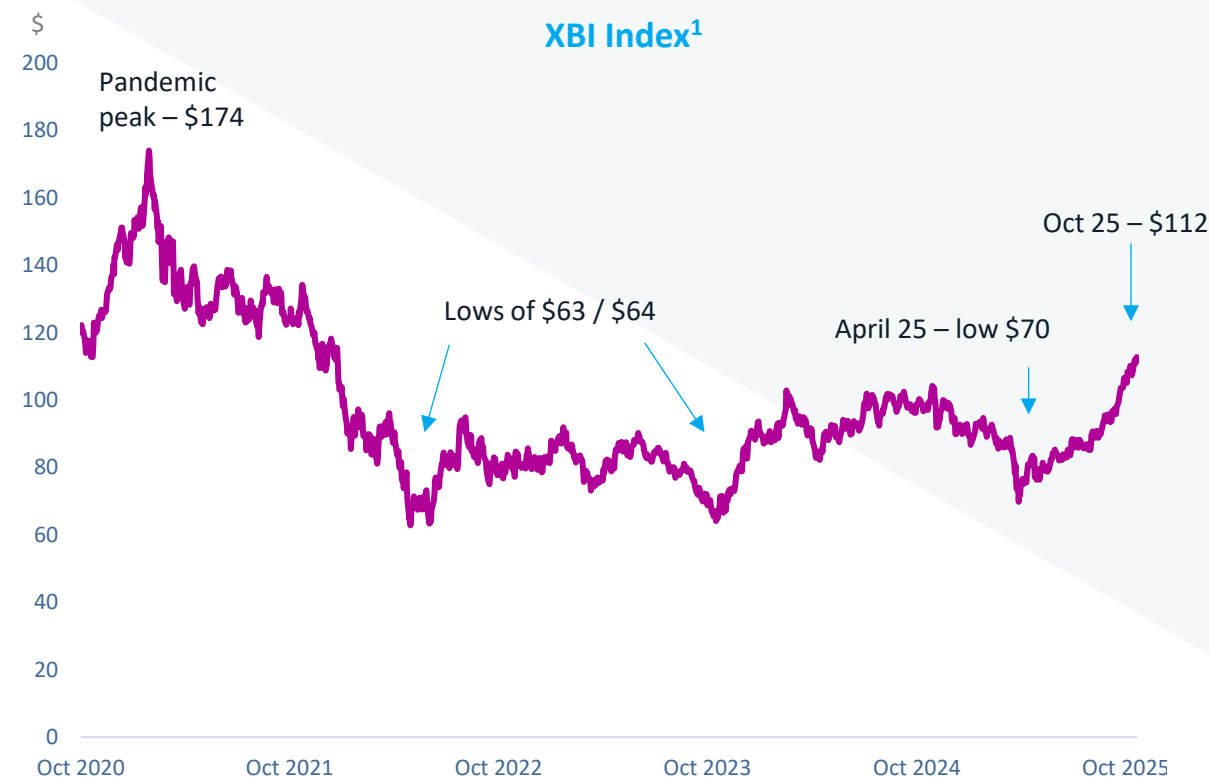
Sector is showing signs of positive momentum

Sector has undergone a significant period of restructuring, consolidation and rationalisation

- Biotech markets have been depressed for approaching five years
- Driven initially by Fed raising interest rates and need for sector consolidation; prolonged by ongoing sector-specific uncertainty (NIH cuts, FDA changes, tariffs)

Now seeing positive change

- Cost of capital is coming down and nearing the end of a sector-wide restructuring
  - Decreasing number of US listed biopharma companies trading at negative EVs, 31% with <12 months cash runway remaining<sup>2</sup>
- XBI is trading at levels not seen since 2021<sup>3</sup>
- Companies and investors are being rewarded for positive clinical data, with average 1-day stock reaction of +40%, the highest since Q3 2023<sup>2</sup>



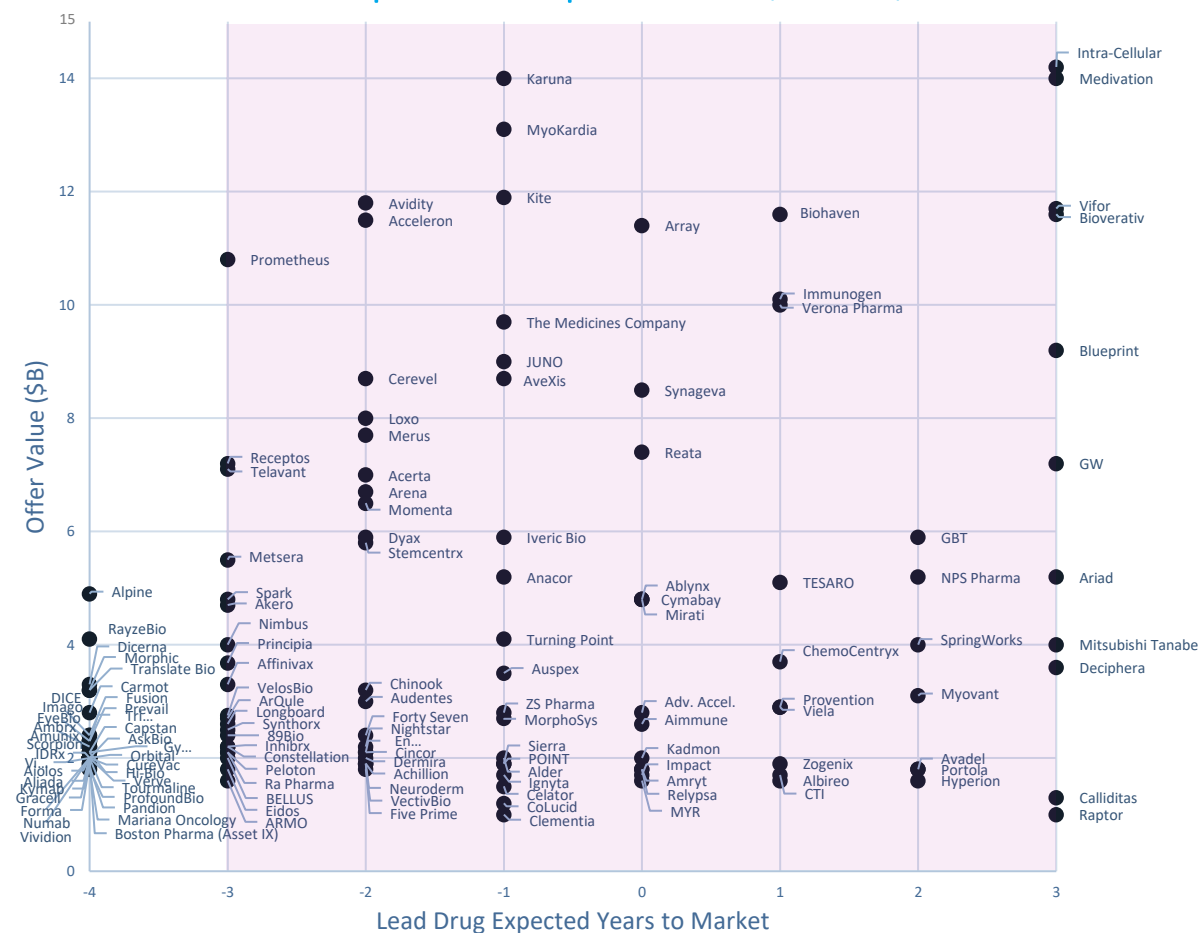
# Underlying Healthcare sector fundamentals remain strong

M&A is a constant driving force in the industry

## 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<sup>1</sup>
- ▶ Focused on restocking their pipelines with later-stage assets
- ▶ Late-stage/marketed assets make up ~74% of transactions in the period 2015-2025<sup>2</sup>
- ▶ Possess balance sheets to invest heavily, with over \$1 trillion in M&A firepower<sup>3</sup>
- ▶ Biotech M&A 2025 YTD already surpassing 2024, with \$96bn of transactions announced<sup>4</sup>

## 2015 – 2025 Biopharma Acquisitions: ~\$1bn – \$15bn Offer Value<sup>5</sup>



1. Evaluate Pharma, World Preview 2024 Report. 2. Syncona analysis, by number of deals, as of November 2025. 3. EY, firepower defined as a company's capacity to do M&A based on the strength of its balance sheet. 4. William Blair Q3 2025 U.S. Biopharm Recap, as of 30 September 2025. 5. Centerview analysis; Public filings, Wall Street research and FactSet as of November 2025. Dollars in billions. Excludes specialty pharma, animal health, generics, OTC, and consumer healthcare transactions.

# Life science portfolio



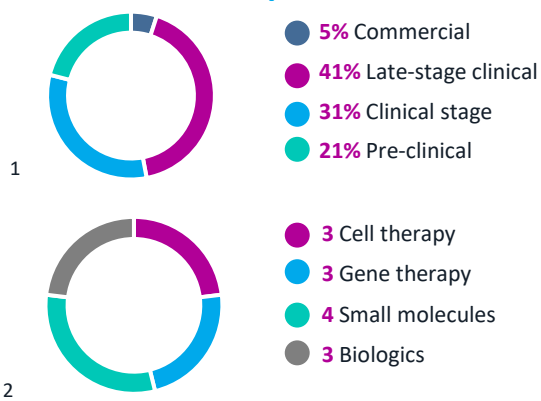
# A well-diversified portfolio weighted towards clinical-stage assets

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

## Delivery against milestones

- Four capital access milestones delivered
- Updated milestones at Anaveon, Autolus and Quell

**76.8% of Life Science Portfolio value in commercial, late-stage clinical and clinical-stage companies**



1. Remaining portfolio is held in Syncona Investments  
 2. Number of companies and excludes Slingshot, the Syncona Accelerator

On the market (4.7%)

Moving towards the market (41.4%)

Moving towards definitive data (11.4%)

Moving towards emerging efficacy / completed operational build (37.1%)

Moving towards operational build (3.8%)

	Best ideas	Pre-clinical	Clinical	Late-stage clinical	BLA	Commercial	KVIP
<b>Autolus</b>	●	—————	—————	—————	—————	—————	★ CY2026
<b>beacon therapeutics</b>			●	—————			★ H2 CY2026
<b>SPUR</b>	●	—————	—————	—————			★ H1 CY2028
<b>IONCTURA</b>			●	—————			★ H2 CY2026
<b>RTx</b>	●	—————					★ H2 CY2026
<b>QuellTX</b>	●	—————	—————				★ CY2026
<b>ANAVEON</b>		●	—————				
<b>MosaicTX</b>	●	—————	—————				
<b>purespring</b>	●	—————	—————				★ H1 CY2027
<b>OMass THERAPEUTICS</b>	●	—————	—————				★ CY2027
<b>forcefield</b>	●	—————	—————				
<b>Yellowstone BIOTECHNOLOGIES</b>	●	—————	—————				
<b>Kesmalea THERAPEUTICS</b>	●	—————	—————				
<b>slingshot</b>	●	—————	—————				

★ KVIP

# Potential from our most mature private portfolio companies

Beacon, Spur and iOnctura to deliver KVIPs by the end of 2028

## 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<sup>1</sup>
- › Once metastasised (50% of patients) median overall survival is approximately one year<sup>2</sup>
- › Data released to date from the Phase Ib trial demonstrates long-term safety and emerging efficacy
- › Continues to execute on its clinical plans - five studies running in parallel to explore the full potential of its lead asset

Data readout from its Phase II clinical trial in H2 CY2026

## SPUR

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

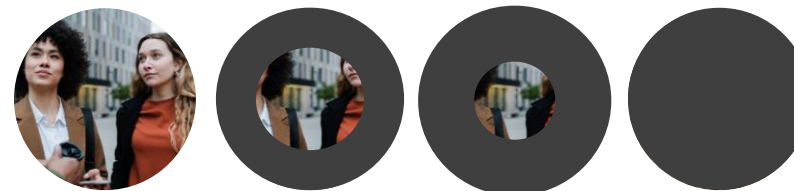
- › Gaucher disease is a disorder caused by the build-up of fatty substances in certain organs, particularly the spleen and liver
- › c.18,000 Gaucher disease type 1 patients in the US, UK, EU and Israel<sup>3</sup>
- › No substantial advances in treatment in the last two decades
- › Presented positive data in October demonstrating long-lasting potential of FLT201 up to 23 months post-dosing

Completion of the pivotal stage of its Phase III trial expected in H1 CY2028

## 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<sup>4</sup>
- › Patients are legally blind by a median age of 45
- › Presented positive 36-month safety and efficacy data from its Phase II SKYLINE trial in September, demonstrating durable efficacy profile of AGTC-501
- › Pivotal trial fully recruited in July 2025



10 years

Progression of sight over time

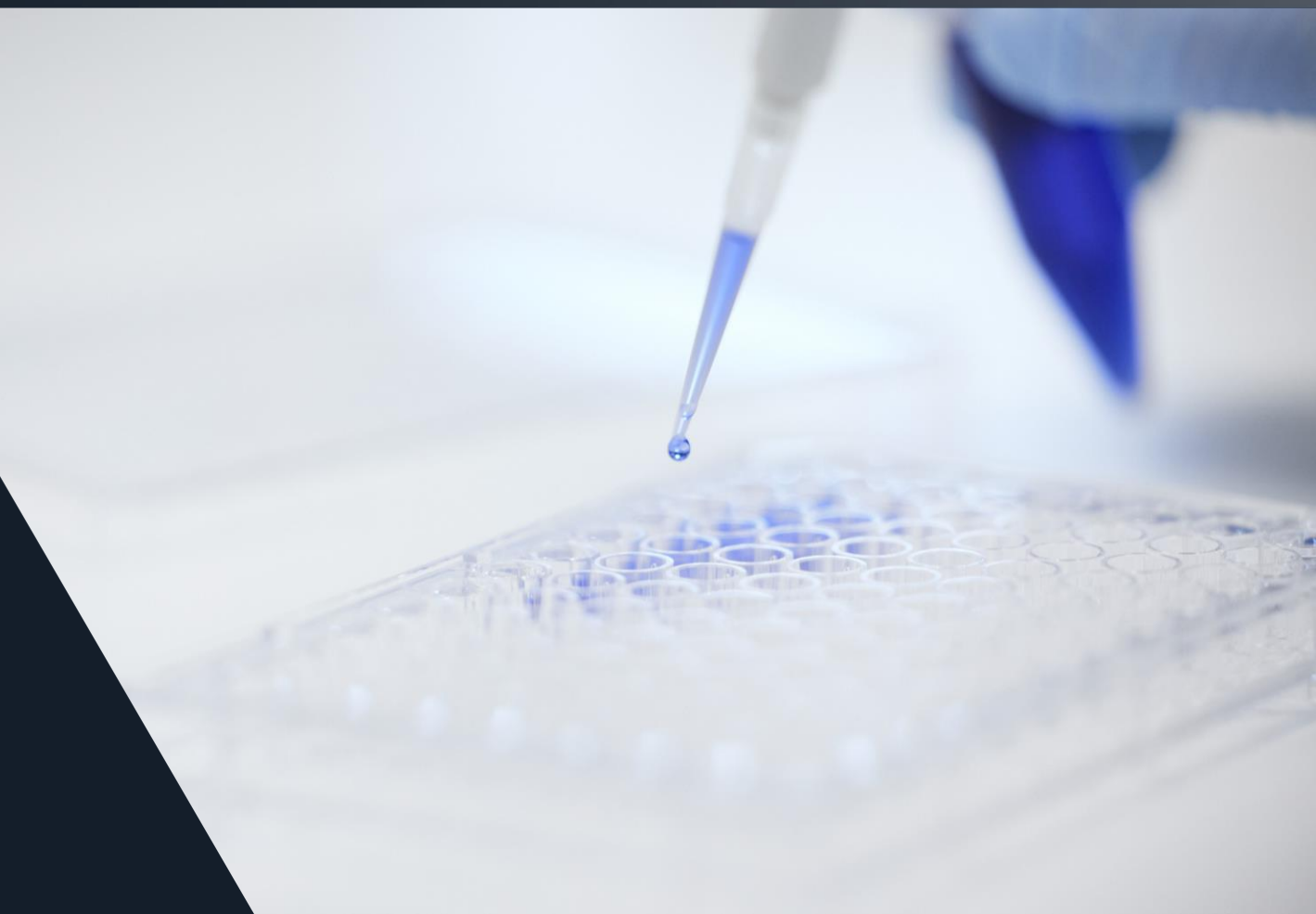
30-40 years

Data readout from Phase II/III pivotal trial in H2 CY2026

Clinical

Late-stage clinical

# Capital deployment



# Capital deployment weighted towards late stage and clinical stage assets

## Continue to apply a rigorous approach to capital allocation

### £17.2m deployed<sup>1</sup> into the life science portfolio in the period

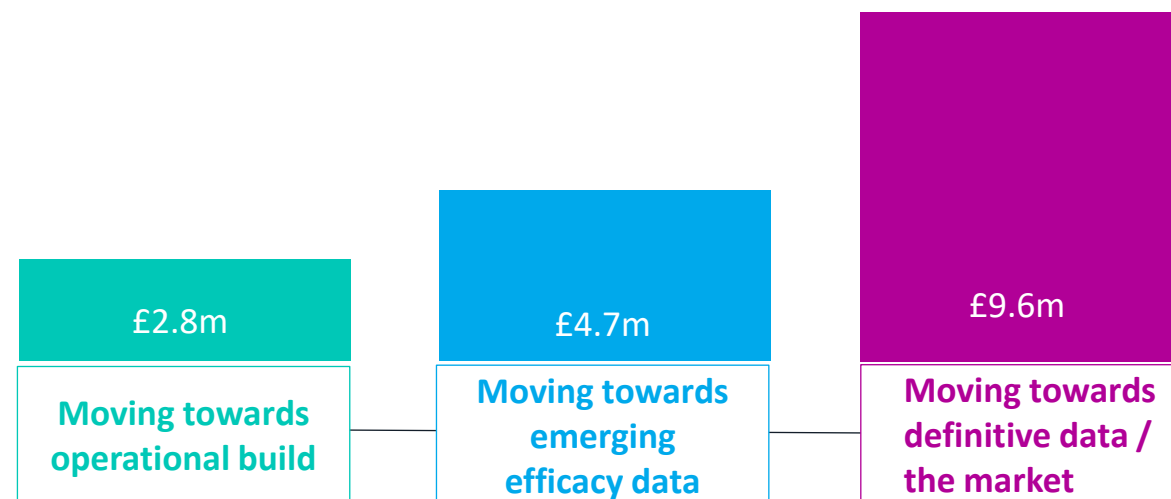
- › 56% into late-stage and clinical-stage assets

### £6.8m deployed into share buybacks

- › 7.8m shares repurchased at an average discount of 49.8%, resulting in 1.2p accretion per share

### Capital pool of £270.7m

- › 42% held in cash and cash equivalents, with the remainder predominantly held in multi-assets and credit funds<sup>2</sup>
- › 24% of capital pool held in US\$ as a natural hedge against short term US\$ cashflows
- › Continued disciplined allocation of capital across the maturing portfolio, in line with proposed new Capital Allocation Policy



Syncona is funded to deliver all eight KVIPs across the portfolio

# Strategy update



# Strategy update

Following extensive shareholder consultation set of refined proposals which seek to maximise value for shareholders and to create a sustainable longer-term structure

## Proposal to return £250m to shareholders

- › Return of £250m of net proceeds from sales of mature private portfolio companies in a timely manner
- › Portfolio will continue to be proactively managed - portfolio companies will only be sold when it is in the best interests of shareholders
- › After £250m has been returned, the SIML team will continue to build out Syncona's portfolio to 20-25 companies

## Proposed changes to Investment and Capital Allocation Policies

- › Seeking shareholder approval for a change of investment objective and policy
- › Updated Capital Allocation Policy ensuring Syncona is funded to KVIPs and can protect portfolio company value in third-party financing
- › Continue to make small selective investments to underpin future growth with a prudent and sustainable approach; amount to be invested will be capped at 5% of NAV<sup>1</sup>
- › Will consult regarding a new Capital Allocation Policy in advance of the return of £250m

## Raising a private fund

- › SIML team is seeking to establish a new private fund<sup>2</sup>, independent from Syncona
- › Fund will diversify SIML's funding sources
- › Discussions ongoing with several investors
- › New private fund's strategy would be to build world class companies from groundbreaking science predominantly sourced from the UK

## Governance

- › Consultation with shareholders on the new long-term incentive arrangements to align SIML's interest with new investment objective and policy
- › Intention to reduce Board size to five to reflect new strategy; two board members stepping down in coming months
- › Intention to optimise the cost base across the group
- › Change of investment objective and policy, and the new long-term incentive arrangements will be put to shareholder vote in due course
- › Potential for SIML to be separated to continue managing Syncona's portfolio and new private fund

# Summary and outlook











# A number of expected key value inflection points

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

Eight key value inflection points across the portfolio, five expected before the end with of CY2026

- › Beacon’s data readout in CY 2026, if positive, will support a BLA filing
- › iOnctura’s data readout in CY 2026 has the potential to underpin a Phase III pivotal trial
- › These key value inflection points are not without risk

	CY2026	CY2027	CY2028	
	Further commercial traction following Autolus’ US launch of AUCATZYL® (obe-cel) in CY2026			On the market
	Data readout from Phase II/III pivotal VISTA trial in XLRP in H2 CY2026			
			Completion of the pivotal stage of Phase III trial in Gaucher disease in H1 CY2028	Definitive data
	Data readout from Phase II trial in uveal melanoma in H2 CY2026			
	Interim data readout from Phase I/II trial in end-stage liver disease in H2 CY2026			
	Data readout from Phase I/II trial in liver transplantation in CY2026			Emerging data
		Complement biomarker clinical data in H1 CY2027		
		Data from Phase I trial of MC2 programme in CY2027		

# Summary and outlook

## Portfolio well positioned to deliver value in the medium term

### Portfolio maturing and increasingly later stage

- 76.8% of Life Science Portfolio value is in eight clinical and commercial stage companies
- 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 have five KVIPs expected in CY2026

### Market conditions improving across the biotech sector

- Public market conditions are improving for biotech companies in line with cost of, and access to, capital
- Significant period of restructuring, consolidation and rationalisation across the sector largely complete

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



# Q&A

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# Appendix 1 – Syncona team and track record

# An experienced team to deliver quality at scale

Senior team of corporate leaders and experienced investment team to deliver the Fund's investment strategy

## Leadership Team



Chris Hollowood  
CEO



Roel Bulthuis  
Managing Partner



Kate Butler  
CFO



Edward Hodgkin  
Managing Partner



Marc Perkins  
General Counsel



Harriet Gower Isaac  
Head of People



John Tsai  
Executive Partner



Annabel Clark  
Head of Corporate Affairs and ESG

## Senior Investment Team

A strong track record of origination and company creation, portfolio management, team building and realising significant value



Chris Hollowood  
CEO



Roel Bulthuis  
Managing Partner



Edward Hodgkin  
Managing Partner



Elisa Petris  
Managing Partner



Magda Jonikas  
Partner



Gonzalo Garcia  
Partner



>145  
years of  
combined  
relevant  
experience

85%  
of the  
investment  
team have  
PhDs

## Broader Investment Team



Michael Kyriakides  
Principal



Raghd Rostom  
Snr. Associate



Pierre Joffrin  
Snr. Associate



Nathaniel Dahan  
Snr. Associate



Melina Hoffmann  
Associate



Sarah Qian  
Associate



Alessio D'addabbo  
Analyst

# Leading executive partner team established to support scaling the model

Provides leadership and insight across the portfolio for all strategic issues, as well as delivering executive functions to early-stage portfolio



**John Tsai**  
Executive Partner  
Clinical expert  
**25+ years experience**

Previously **President, Global Drug Development & CMO at Novartis**

Prior roles as **CMO and SVP Global Medical Affairs at Amgen** and several senior medical roles at BMS



**Richard Wooster**  
Executive Partner  
Drug discovery expert  
**30+ years experience**

Most recently **CSO at Translate Bio**; acquired by Sanofi 2021 for \$3.2bn

Prior roles as **CSO & President of R&D at Tarveda**, and senior roles at **GSK**

Began in academia at ICR where he discovered the BRCA2 gene, and as founder of the Cancer Genome Project at Wellcome Sanger Institute



**Kenneth Galbraith**  
SIML Chair  
Commercial leader  
**30+ years experience**

Currently **Chair and CEO of Zymeworks**. Previously **CEO, CFO, Exec. Chair, director, investor and advisor** in both private and NASDAQ-listed companies from an **early-stage through commercialisation**

Also worked with AnorMED, Alder Pharma (sold to Lundbeck), Celator Pharma (sold to Jazz Pharma), Novadaq (sold to Stryker), Fairhaven Pharma (sold to Liminal Bio) among others



**Gwenaelle Pemberton**  
Executive Partner  
Regulatory expert  
**30+ years experience**

Most recently **VP International Regulatory Affairs at Gilead**, leading the International Regulatory Group responsible for regulatory activities worldwide, ex-US

Previous roles at **Pfizer, Pharmacia and AstraZeneca**

Chair of the **BIA Regulatory Affairs Advisory Committee**



## A platform to scale...



New opportunities



Company launch



Clinical approach



Regulatory plan



Commercial strategy

... delivering long-term growth

# A track record of significant value creation from exits

£1.4 billion invested to date, generating an IRR of 13.1%, 1.3x invested capital<sup>1</sup>

Full exits generated £961m of proceeds, at an aggregate IRR of 73.6% and a 4.0x cost<sup>2</sup>

## Blue Earth

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

## Nightstar

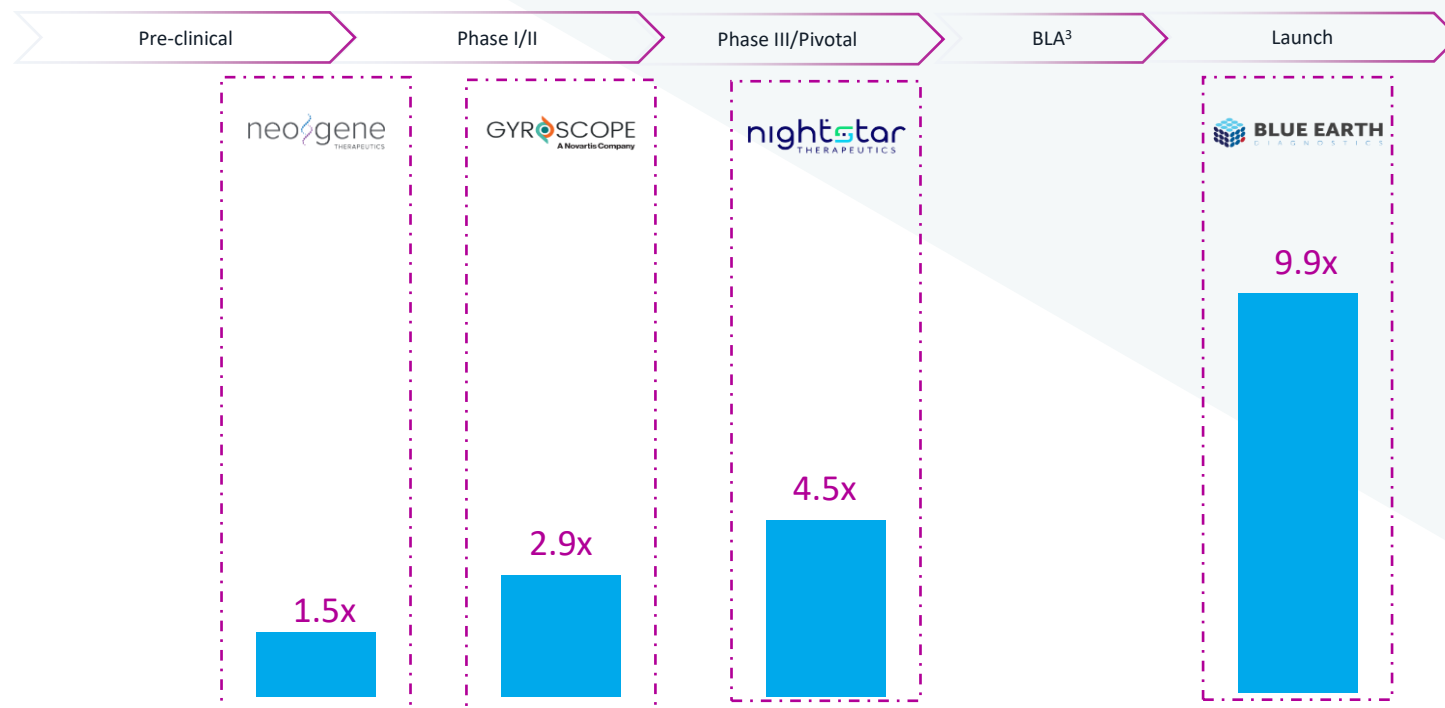
- Founded company in 2013, sold to Biogen in 2019
- 71% IRR – 4.5x cost - £255.7m proceeds

## Gyroscope

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

## Neogene

- First invested in 2019, sold to AstraZeneca in 2023
- 3% IRR – 1.5x cost - £21.3m proceeds



Returns since Syncona merged with BACIT in December 2016, are: Neogene 1.5x, Gyroscope 2.9x, Nightstar 3.5x, Blue Earth 3.9x.

All financial data at 30 September 2025

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, 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

	31 March 2025	Net investment in the period	Valuation change	FX movement	30 September 2025 <sup>1</sup>	% of Group NAV	Valuation Basis <sup>2, 3, 4</sup>	Fully diluted ownership stake <sup>5</sup>	Focus area
	(£m)	(£m)	(£m)	(£m)	(£m)	(%)		(%)	
<b><u>Strategic portfolio companies</u></b>									
<b>On the market</b>									
Autolus	34.6	-	1.2	(0.9)	34.9	3.4	Quoted	9.6	Cell therapy
<b>Late-stage clinical</b>									
Spur	182.2	-	2.7	-	184.9	18.1	Cost	79.1	Gene therapy
Beacon	117.5	6.6	6.1	(4.6)	125.6	12.3	PRI	43.9	Gene therapy
<b>Clinical</b>									
Quell	85.4	-	-	(3.3)	82.1	8.0	PRI	33.7	Cell therapy
Resolution	55.5	3.0	0.4	0.0	58.9	5.8	Cost	81.2	Cell therapy
Anaveon	35.6	-	-	2.3	37.9	3.7	PRI	36.9	Biologics
Ionctura	25.1	-	-	1.1	26.2	2.6	PRI	21.9	Small molecules
Mosaic	25.5	-	-	-	25.5	2.5	Cost	59.2	Small molecules
<b>Pre-clinical</b>									
Purespring	51.2	2.5	(0.3)	-	53.4	5.2	PRI	46.3	Gene therapy
OMass	49.7	-	-	-	49.7	4.9	PRI	28.9	Small molecules
Kesmalea	20.0	-	-	-	20.0	2.0	Cost	59.7	Small molecules
Yellowstone	16.5	-	-	-	16.5	1.6	Cost	60.9	Biologics
Forcefield	10.6	2.2	0.1	-	12.9	1.3	PRI	73.7	Biologics
Slingshot	5.6	2.8	-	-	8.4	0.8	Cost	100.0	Accelerator
<b><u>Investments and milestone payments</u></b>									
Neogene milestone payments	6.1	(6.0)	-	(0.1)	0.0	0.0	-	-	Cell therapy
Clade/Century milestone payments	0.8	-	-	(0.1)	0.7	0.1	DCF	-	Cell therapy
CRT Pioneer Fund	27.3	(1.5)	(15.9)	-	9.9	1.0	Adj Third Party	64.1	Oncology
Achilles	13.1	(12.0)	(0.8)	(0.3)	0.0	0.0	-	22.7	Cell therapy
Biomodal	2.7	-	(0.3)	(0.2)	2.2	0.2	PRI	3.0	Epigenetics
Century	0.4	-	0.1	-	0.5	0.0	Quoted	1.3	Cell therapy
<b>Total Life Science Portfolio</b>	<b>765.4</b>	<b>(2.4)</b>	<b>(6.7)</b>	<b>(6.1)</b>	<b>750.2</b>	<b>73.5</b>			
<b>Capital pool</b>	<b>287.7</b>	<b>(21.4)</b>	<b>6.7</b>	<b>(2.3)</b>	<b>270.7</b>	<b>26.5</b>			
<b>TOTAL</b>	<b>1,053.1</b>				<b>1,020.9</b>	<b>100.0</b>			

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

# Autolus Therapeutics

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

Initial investment	2014
Value	£34.9m
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
- ▶ Commercial launch in the US is progressing on track, with 46 centres fully activated as of 12 August 2025 and coverage secured for approximately 90% of total US medical lives
- ▶ Advanced in-house manufacturing facility supporting commercial launch

## Targeting an area of high unmet need

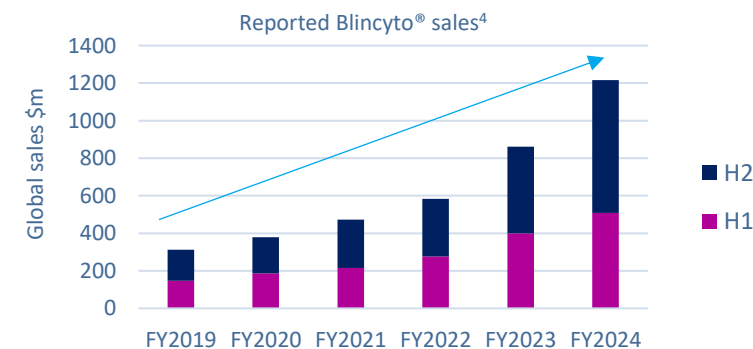
- ▶ Only 30-40% of patients with adult ALL achieve long-term remission with combination chemotherapy, the current standard of care<sup>1</sup>
- ▶ obe-cel has the potential to be a best-in-class curative therapy in adult ALL
- ▶ Launched a Phase I trial in systemic lupus erythematosus (SLE) in H1 CY2024,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

## Market opportunity for lead programme

- ▶ Over 8,000 new cases of adult ALL annually worldwide<sup>1</sup>
- ▶ Obe-cel has launched into an expanding ALL market and is now being commercialised across key target geographies
- ▶ Blincyto®, current market leader, sales increased 41% year-over-year to \$1,216 in 2024<sup>3</sup>



# Spur Therapeutics

Developing transformative gene therapies for patients suffering from chronic debilitating diseases

Initial investment	2015
Value	£184.9m
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, with four patients seeing sustained benefit at 19 to 23 months as of August 2025
- › 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<sup>1</sup>
- › Annual Gaucher market size is \$2bn<sup>2</sup>

# Beacon Therapeutics

Progressing its pivotal study in X-linked retinitis pigmentosa

Late-stage clinical

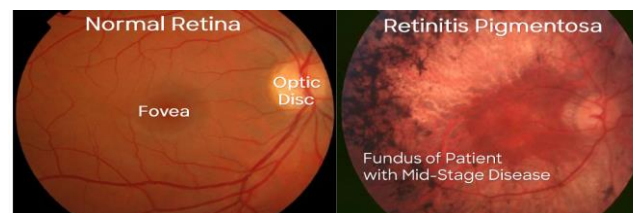
Initial investment	2022
Value	£125.6m
Financing stage	Series B
Stage of lead programme	Phase II/III

## 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

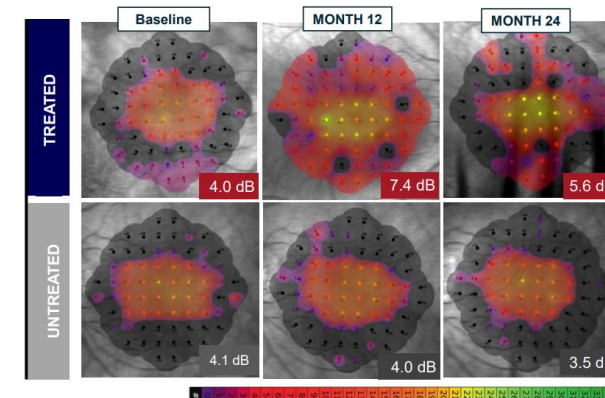
## Targeting an area of high unmet need

- 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<sup>1</sup>
- 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  $\leq 20/200$  (legally blind), than those with autosomal dominant RP



# Quell Therapeutics

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

Initial investment	2019
Value	£82.1m
Financing stage	Series B
Stage of lead programme	Phase I/II

## Investment thesis

- Potential to durably control 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; two milestone payments received to date - \$10 million for Type 1 Diabetes programme and \$10m for inflammatory bowel disease programme
- 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<sup>1</sup>
- 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

## Market opportunity

- 15,000 liver transplants per year across US and Europe<sup>2</sup>

# Resolution Therapeutics

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

Initial investment	2018
Value	£58.9m
Financing stage	Series B
Stage of lead programme	Phase I/II

## Investment thesis

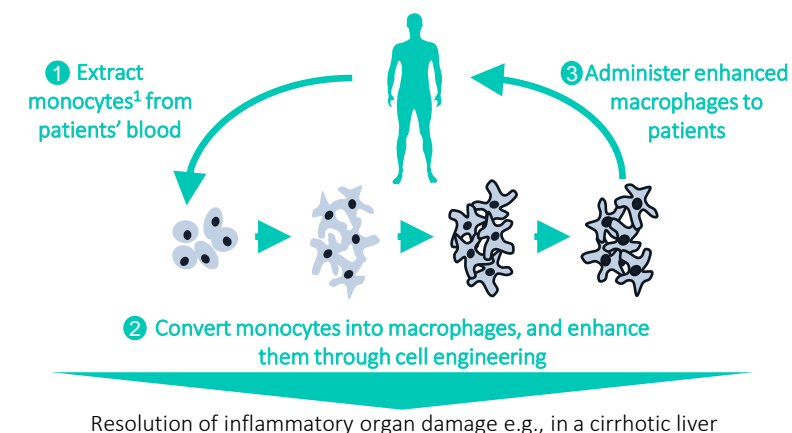
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries<sup>1</sup>
- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest fibrotic scar, modulate the inflammatory response 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<sup>2</sup>



# Anaveon

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

Initial investment	2019
Value	£37.9m
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 and file an IND for its Phase I/II trial in ANV200, both in CY 2026

## 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<sup>1</sup>
- ▶ 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<sup>2</sup>

# iOnctura

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

Clinical stage

Initial investment	2024
Value	£26.2m
Financing stage	Series B
Stage of lead programme	Phase II

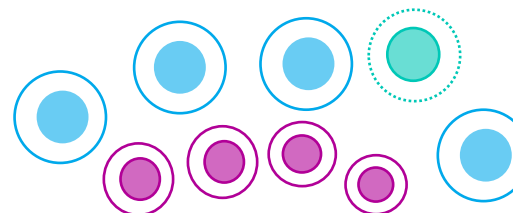
## Investment thesis

- › iOnctura represented an opportunity to invest in a clinical-stage company that has published promising emerging data to date
- › 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 PI3K $\delta$ , with a unique chemical structure and binding mode
- › The Syncona team worked closely with iOnctura to consider the broader application of roginolisib
- › Opportunity to drive lead programme through late-stage clinical development in multiple indications, including uveal melanoma and NSCLC

## Targeting an area of high unmet need

- › Once metastasised (50% of patients) overall survival of uveal melanoma patients drops to one year<sup>1</sup>

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<sup>2</sup>
- › NSCLC accounts for approximately 85% of all lung cancer cases and is the most common type of lung cancer<sup>3</sup>

# Mosaic Therapeutics

Building the world leader in targeted oncology combinations

Initial investment	2022
Value	£25.5m
Financing stage	Series A

## 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<sup>1</sup>
- ▶ 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

# Purespring Therapeutics

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

Pre-clinical stage

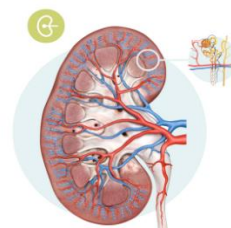
Initial investment	2020
Value	£53.4m
Financing stage	Series B

## 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
- Purespring received FDA IND and UK CTA approval for its Phase I/II clinical trial in IgA nephropathy (IgAN)

## 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<sup>1</sup>
- More than 840 million people globally suffer from chronic kidney disease<sup>2</sup>
- The podocyte is implicated in 60% of renal disease<sup>2</sup>
- 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<sup>3</sup>

# OMass Therapeutics

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

Pre-clinical stage

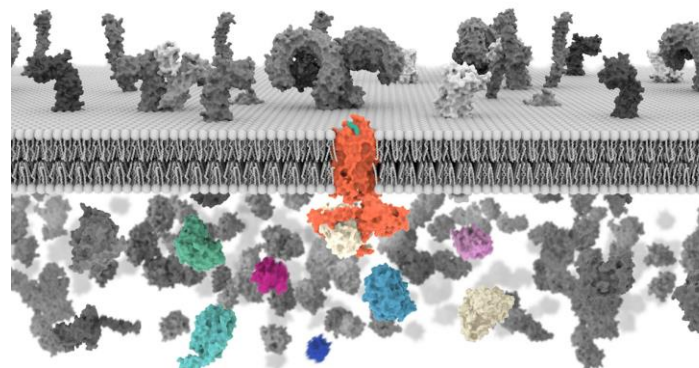
Initial investment	2018
Value	£49.7m
Financing stage	Series B

## 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 adrenocorticotrophic hormone (ACTH) excess, including congenital adrenal hyperplasia (CAH) and ACTH-dependent Cushing's
- CAH occurs in about 1 in 13,000-15,000 births<sup>1</sup>
- Pituitary ACTH-dependent Cushing causes 65 to 70 percent of Cushing syndrome<sup>2</sup>

# Kesmalea Therapeutics

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

Pre-clinical stage

Initial investment	2022
Value	£20.0m
Financing stage	Series A

## Investment thesis

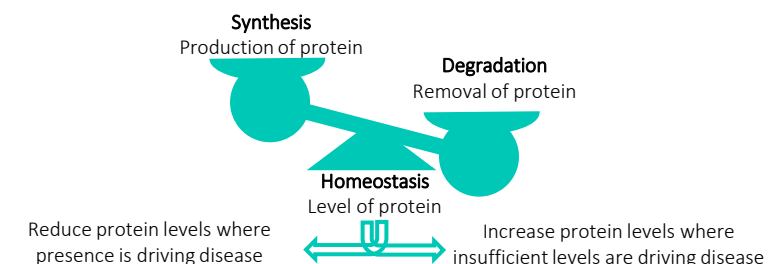
- ▶ Small molecule drug discovery platform focused on protein homeostasis, initially targeted protein degraders (TPDs)
- ▶ Protein homeostasis is the system of maintaining the equilibrium of proteins in the human body. This intricate system is in a constant state of change, with the body continuously 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

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

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 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<sup>1</sup>
- ▶ 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<sup>1</sup>
- ▶ 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

# Forcefield Therapeutics

Pioneering therapeutics to retain heart function

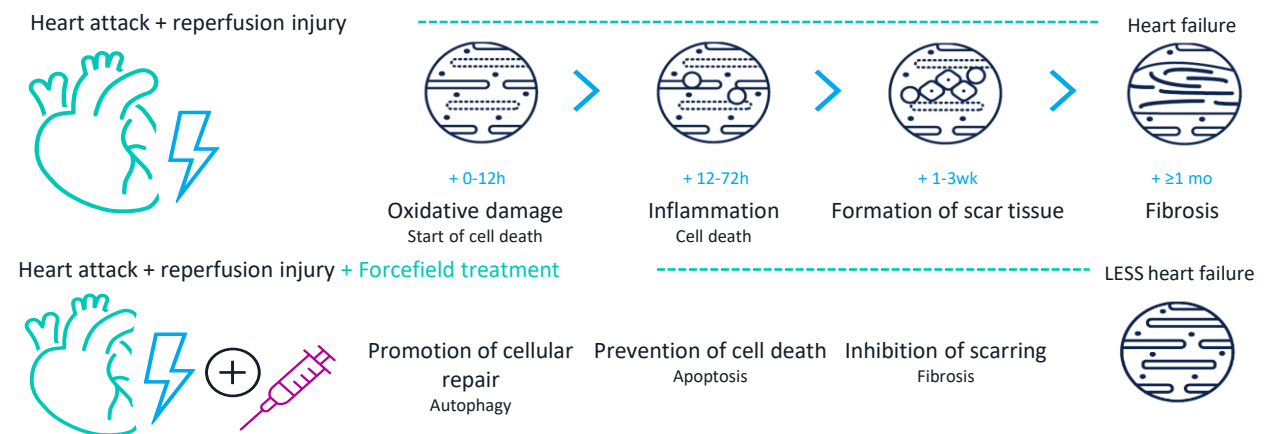
Initial investment	2022
Value	£12.9m
Financing stage	Series A

## Unmet need in heart disease

- ▶ Heart disease is the leading cause of death worldwide
- ▶ Acute myocardial infarction (AMI), affects 3 million people worldwide annually<sup>1</sup>
- ▶ 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<sup>1</sup>
- ▶ 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

# Slingshot Therapeutics

Bridging the gap from academia to drug development

Initial investment	2024
Value	£8.4m

## 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
- ▶ Led by Syncona Managing Partner, Edward Hodgkin, as Executive Chair, with a highly experienced management team
- ▶ 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