Syncona

Corporate presentation

March 2023

synconaltd.com

***Image** Freeline labs, Stevenage*

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A long-term vision:10 years of Syncona

Co-founded in 2012 with the Wellcome Trust, our purpose is to invest to extend and enhance human life

Building global leaders

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

Our track record

24%	IRR since 2012; 1.5x multiple on cost across whole portfolio[1]
£1.01bn	Syncona capital deployed since 2012
£948m	Generated from four successful exits; 4.3x multiple of cost[2]

Patient impact

165k	Patients benefitting from Blue Earth's Axumin™
3	Products to pivotal trial, with 18 programmes progressed into the clinic[3]
383k	Total Addressable Market (TAM) for the clinical-stage portfolio[4]

Current financials

£1.29bn	Net Asset Value (192.6p per share)
£654m	Capital pool
£150m-250m	Capital deployment guidance for 2022/3

1- Includes sales of Nightstar, Blue Earth, Gyroscope and Neogene and closure of 14MG and Azeria. 38% of the portfolio held at cost. Reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
2 - Includes sales of Nightstar, Blue Earth, upfront proceeds from sale of Gyroscope and upfront proceeds from Neogene, reflects original Syncona Partners capital invested where applicable. All IRR and multiple on cost figures are calculated on a gross basis
3 – Includes lead AGTC programme in XLRP. 4 - Total addressable market calculated from estimated new patients diagnosed per annum in lead indications of clinical stage portfolio companies, as defined by the company or the Syncona investment team estimate
With the exception of proceeds generated from Neogene acquisition completed in January 2023, all financial data at 31 December 2022, employee figures as at 31 March 2022

Performance in FY2022/3

Financial performance has been impacted by share prices of listed holdings against a challenging market backdrop for biotech

Market context	- Financing environment in public and private markets remains challenging with a continued absence of generalist investors in the sector - Sector specialists continue to prioritise existing investments; balance sheet strength a key differentiator
NAV performance	- Net assets of £1,294.9m, 192.6p per share, a NAV return of (5.1)% in the quarter and (1.0)% in the nine months to 31 December 2022 - Performance in the quarter impacted by declines in the valuations of the listed portfolio and negative movement in FX
Listed portfolio	- Listed portfolio impacted by market environment and in some cases, operational delays - Important milestone for Autolus where it has met it primary endpoint in its pivotal study in adult ALL; further data to follow in CY2023 with further data also expected from Freeline and Achilles
New investments	- Addition of late stage clinical asset to the portfolio with acquisition of AGTC; Kesmalea, a small molecule discovery platform, also added to the portfolio
Continued interest from pharma	- Sale of Neogene to AstraZeneca shows the continued interest of pharma in our portfolio - Fourth sale of a Syncona portfolio company in the last four years, generating total potential proceeds £1.2bn, and a multiple of cost of 4.3x on upfront proceeds

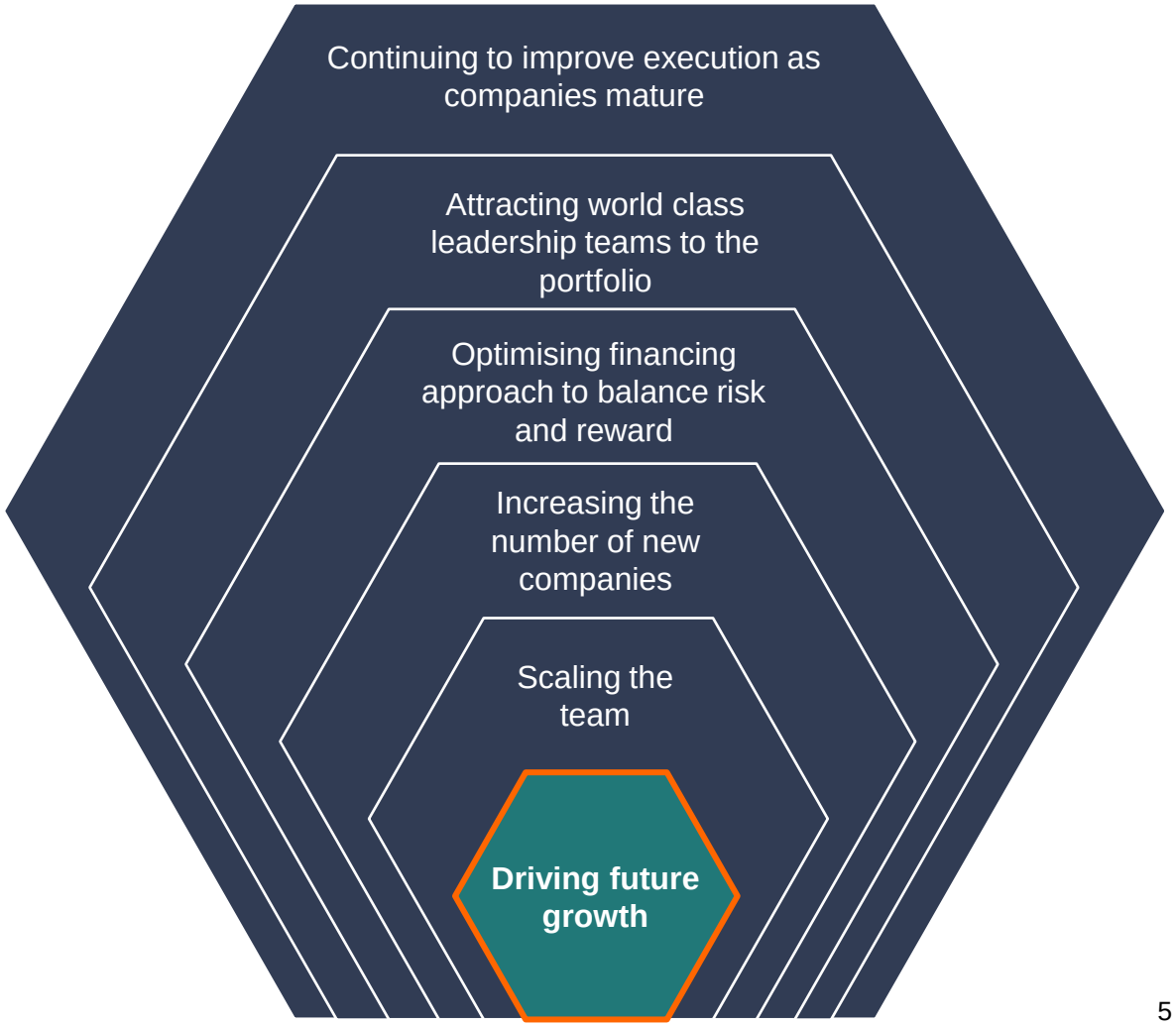
Building on our success

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

The Syncona model

- Core team skill is to identify science and create companies with the potential to deliver transformational treatments
- We scale these businesses and their teams to be globally competitive
- Strength of balance sheet provides a differentiated market position through the cycle

Lessons learnt



The opportunity in the next 10 years

Well positioned to capture strong market opportunity

Syncona

Syncona believes the out return in life science is weighted towards late development and product approval

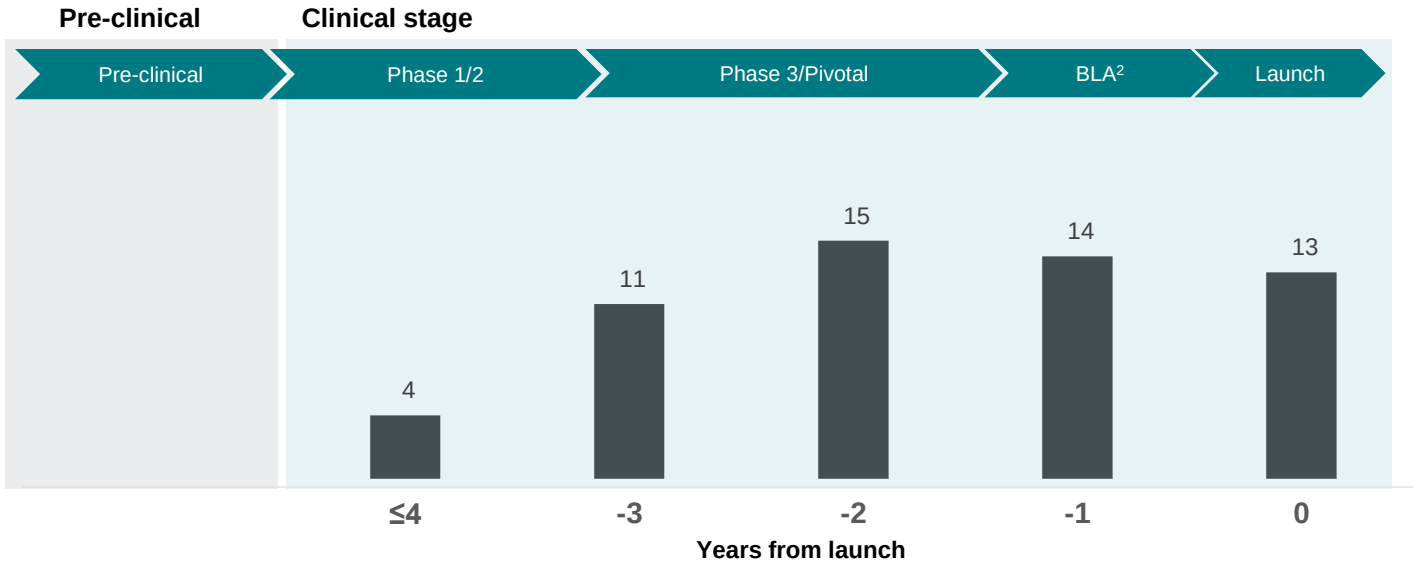
Leveraging a world-class scientific research base

- Syncona is located within the richest concentration of life science research universities and also has a global network

Building companies capable of seizing the commercial opportunity of translating science to products

- Syncona has demonstrated a differentiated company building capability
- Underpinned by a strong capital base, Syncona is able to bridge the gap between scientific research and commercial opportunity

Global transaction volume by expected years to market; Number of global biopharma deals greater than $1bn[1] from 2005 to 2021



1 Source Centerview, BCIQ, Syncona analysis
2 Biologic license application

Scaling the business to continue to deliver strong returns

Growing NAV by increasing the size of the life science portfolio reduces cash impact for shareholders

		Key metrics
Expanding the portfolio is central to growing NAV to £5bn	– Historically, we have added 1-2 new companies p.a to the portfolio – To grow NAV, we believe we need to add 3 new companies p.a to deliver an expanded life science portfolio of 20-25 companies – We will be targeting top quartile returns for the life science portfolio – Financing strategy will support our expanded portfolio	**Companies founded per year**
Capital base underpins the delivery of strategy	– Runway of 2-3 years of capital provides the investing confidence to build and scale companies strategically to deliver long-term value – As a result a minimum amount of balance sheet capital is required – Growing the NAV by increasing the size of the life science portfolio reduces impact of cash for shareholders	**No. of years funding**
Progressing to self-sustainable financing	– Ambition to fund companies on sole basis to proof-of-concept on a selective basis – Optimised financing strategy with syndicated options has the potential to deliver more frequent NAV uplifts and improve risk profile of portfolio – Recycling of exit proceeds into the portfolio will support us in maintaining a runway of 2-3 years of capital and deliver further growth	**Risk-adjusted returns**

Embedding a differentiated model

An expert team, with the skill set, track record and strategic capital base to build a sustainable, diverse, high-quality portfolio

Create

Proactively source **world-class** science – bringing commercial vision

Focus on dramatic impact for patients in areas of high unmet need

Select products a biotech company can credibly take to approval

Build

Leverage expertise and track record to drive success

Take **long-term decisions** consistent with a company taking product to approval independently

Attract and retain the best global talent

Early decision taken on financing approach for these companies to **ensure level of capital necessary** with appropriate risk profile for Syncona

Scale

Scale ambitiously, maintain significant ownership positions through the clinic; option to fund to market

Ownership position provides **strategic influence**; flexibility and control

Selective approach to funding companies to market on a sole basis (1-2 over a cycle)

Strength of our balance sheet protects against risk of being a forced seller

Evolving and leveraging the investment team

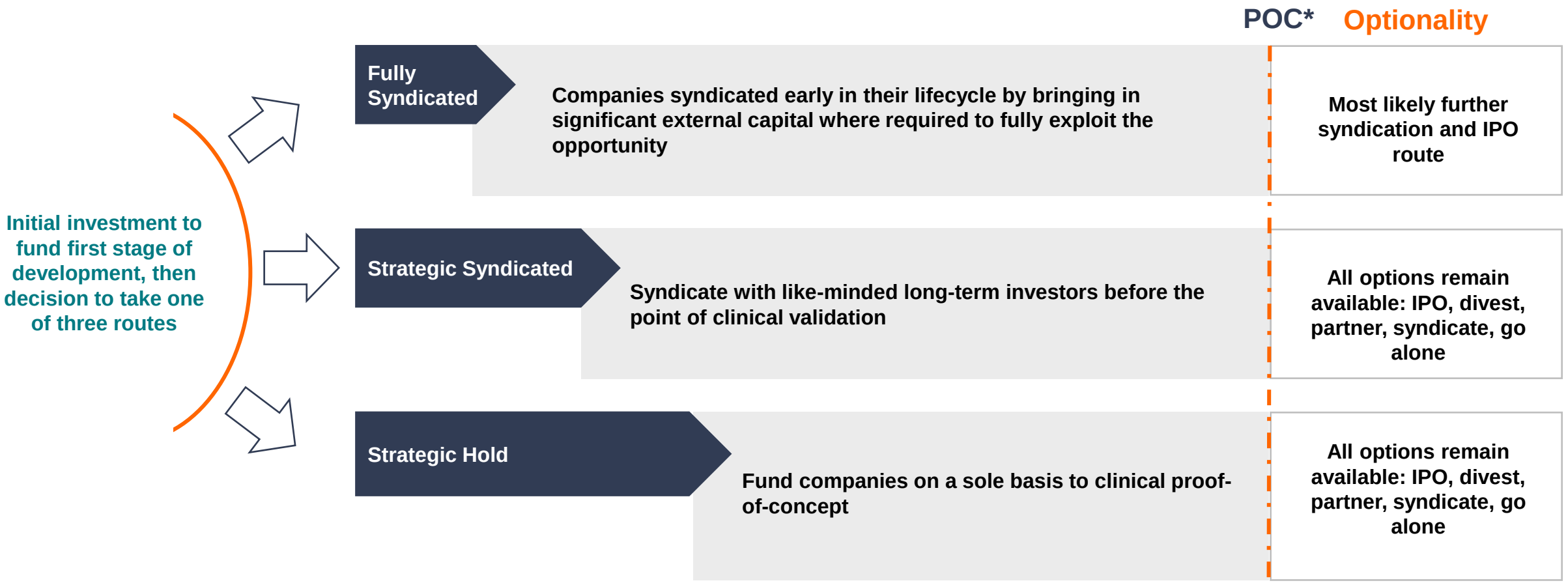
Reviewed the company's organisational structure to enable the business to scale

- Chris Hollowood has stepped up into the role of CEO, leading delivery of growth plans for next 10 years and managing team, alongside creating new companies and managing portfolio companies
- Martin Murphy has become Chair of SIML, continuing to source and drive the creation of new companies, alongside managing portfolio companies
- Ed Hodgkin has been promoted to the role of Senior Partner, with Magdalena Jonikas and Elisa Petris promoted to Lead Partners
- Will be further expanding the team to support growth
- Company launch team and advisory team now formed

Team behind the investment process delivering 3 new deals p.a.

Our financing strategy

Providing our shareholders with exposure to a set of high-growth companies, both private and public



* Proof of concept. Syncona view is that this is the point when a company has generated a maturing clinical data set that validates its investment thesis

Scaling Syncona to £5bn

We are updating our 10 year targets with increased ambition

3

New companies created p.a

20-25

Portfolio of leading life science companies

3-5

Companies to product approval where Syncona has a majority shareholding

£5bn

Net Assets

Market context

The promise of precision medicine

Enables faster development, smaller, more capital efficient clinical trials and targeted commercial roll-out

- Traditional drug development can lead to ineffective drug development; it assumes all patients respond similarly
- Precision medicine can enable more effective therapies; genetics revolution has enabled greater insight into choosing low risk targets and selecting patients that will respond
- Many chronic diseases impacting millions of patients have genetic sub-drivers, permitting targeted drug development

30-60%

A traditional drug may only be 30-60% effective[1]

>2x

Drugs with genetically supported targets more likely to be successful in Phases II & III and the use of human genetic evidence increases approval by greater than two-fold[2]

46%

Estimated reduction in the cost of the development of a precision medicine versus conventional medicine[3]

1 https://www.england.nhs.uk/healthcare-science/personalisedmedicine/
2 https://pubmed.ncbi.nlm.nih.gov/31830040/
3 McKinsey & Co Report Precision Medicine Opening the aperture Feb 2019

An exciting investment landscape

Creating commercial concepts around ground-breaking science has always been a point of differentiation for Syncona

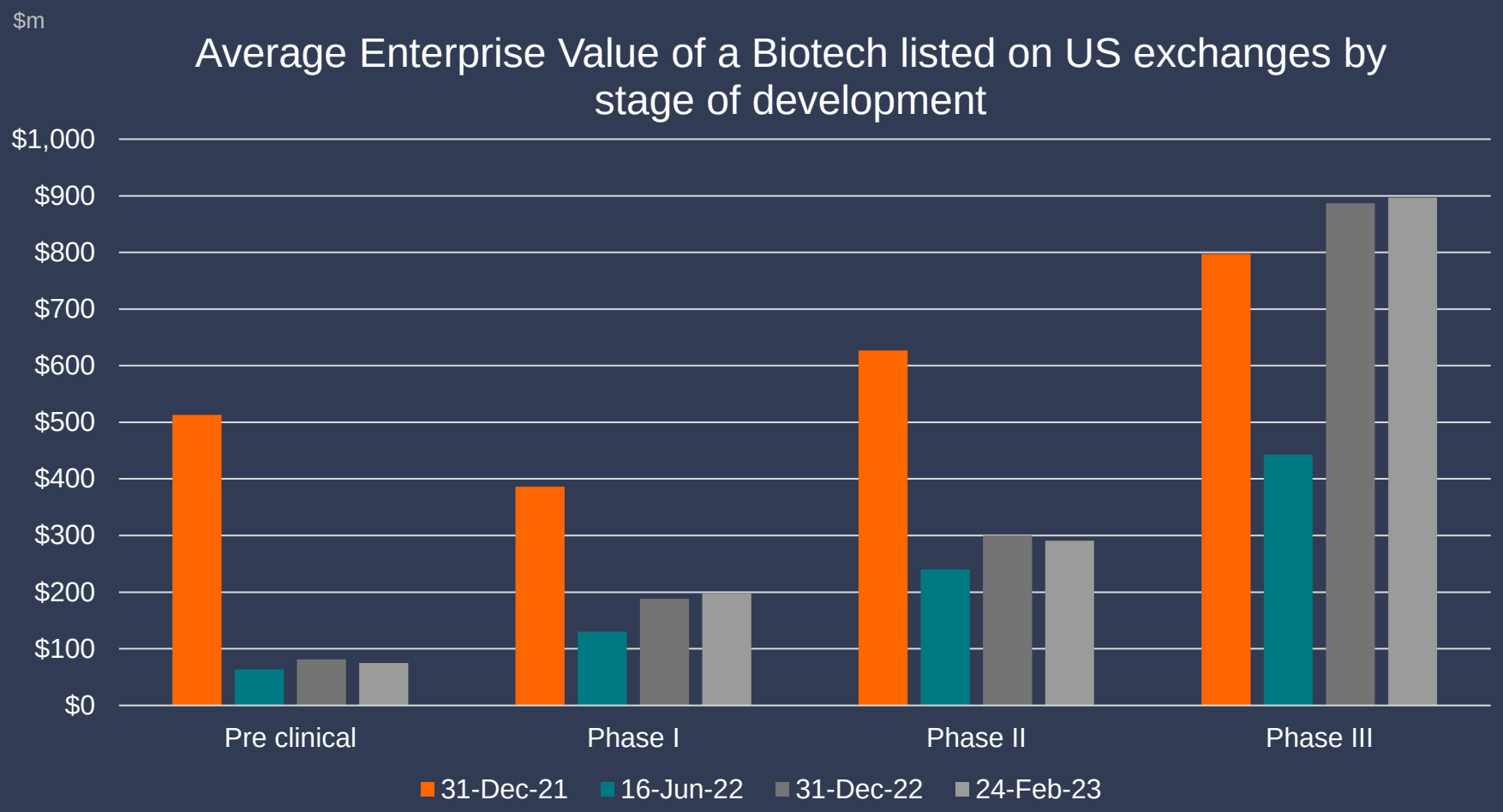
- Over the last 10 years, we have been an early mover in a significant technology disruption (cell and gene therapy)
- The technology disruption meant that there were often no incumbents where we were operating – now institutionalising best practice for pace is critical
- We are focused on targets that have been de-risked by genetics or data - lots of opportunities to apply this position across biologics and small molecules
- Significant opportunity in cell and gene therapy remains

Syncona identifies science that will make a difference for patients in areas of high unmet need

Current biotech landscape

Market conditions improving for clinical assets

- Market is responding to good data again – it is all about a great product
- Valuations have recovered in companies developing later stage assets
- Financing challenges remain for pre clinical companies – reflecting the importance of focusing on commercial opportunity



Source: Capital IQ and Torreya Analysis
Syncona Team View

Portfolio and the capital pool

A differentiated portfolio of leading life science companies

Syncona

Diversified across modality and therapeutic area

Cell therapy

- Focused on key cell types and T-cell biology backed by leading academics
- In areas of high unmet medical need

CAR-T

Autolus

TILs

Achilles

T-Reg

QuellTX

Macrophage

RTx

iPSC cells

Clade Therapeutics

- Two clinical stage companies (Autolus and Achilles)
- Quell expects to dose first patient in H1 CY2023

Gene therapy

- Operating in key tissue compartments backed by leading academics
- In areas of high unmet medical need

Systemic

FREELINE

Renal

purespring

CNS

SwanBio THERAPEUTICS

Retina

agtc

- Two clinical stage companies (Freeline and AGTC)
- SwanBio now expects to dose first patient in H1 CY2023

Biologics

- T-cell immunotherapy - selective IL-2 agonist, wide potential utility across multiple oncology indications

Selective IL-2 Agonist

ANAVEON

Small molecule

- Small molecule and drug discovery platform focused on hard to drug targets in immunological and orphan diseases

Small molecule therapeutics

OMass THERAPEUTICS

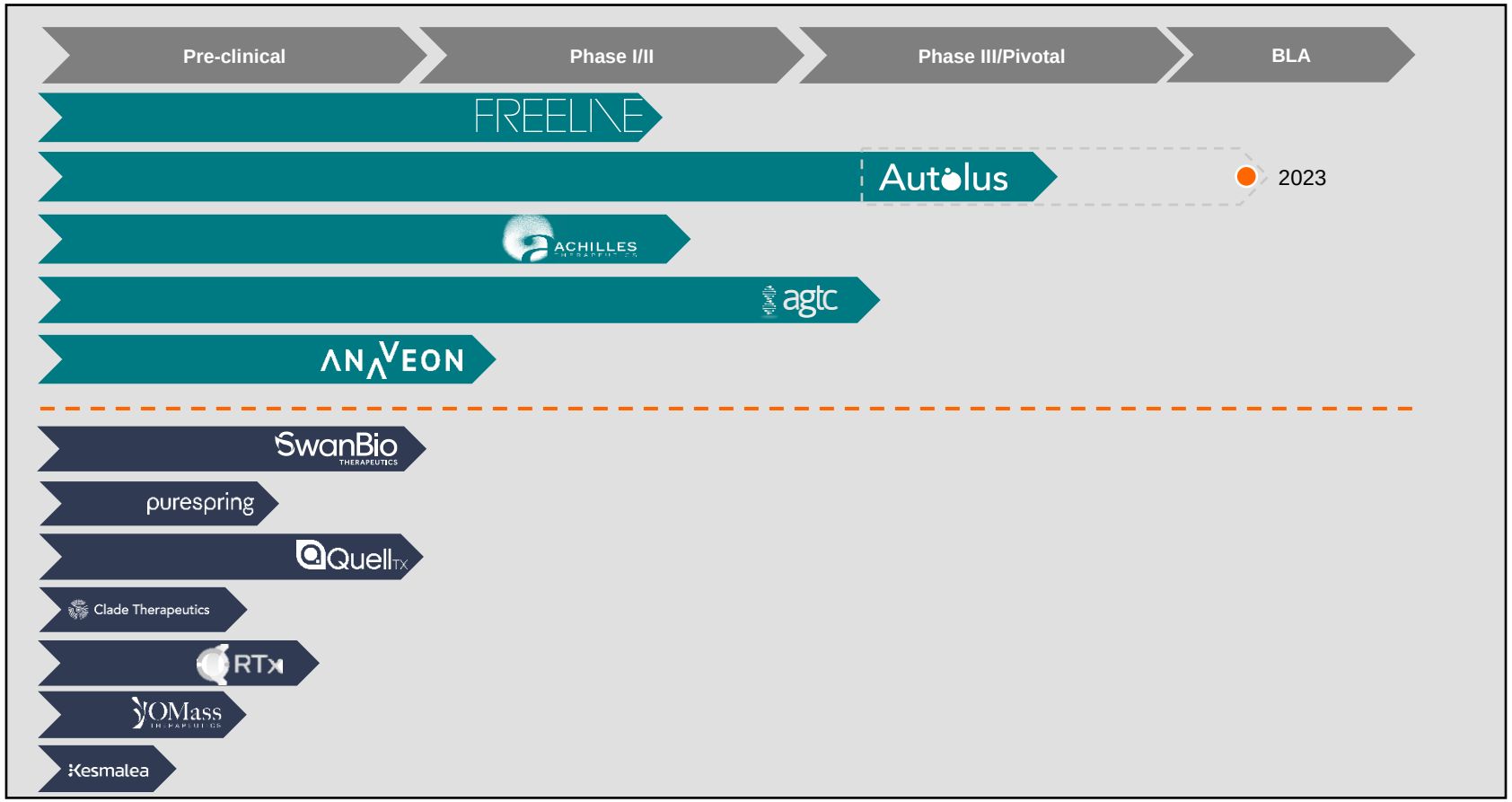
Kesmalea

- Anaveon is clinical stage, with two further Phase I/II trials in ANV419, now having entered the clinic

Portfolio diversified with a number of late stage assets

Five clinical stage companies in the portfolio

- Syncona portfolio diversified across pre-clinical and clinical stage
- Addition of AGTC to the portfolio means we have five clinical stage companies, with Quell and SwanBio soon also to dose their first patients
- Autolus has recently announced exciting data from its pivotal trial in adult ALL, and is expected to file a BLA in 2023
- Freeline's Gaucher programme soon to enter the clinic, a potentially first-in-class and best-in-class asset
- Seven data read outs expected in CY2023



Managing our capital pool and cost base

Continue to balance liquidity and access to capital pool to ensure we are able to fund our life science portfolio

Disciplined and rigorous financial approach

- Primary focus is on liquidity, continue to hold 12-24 months of liquidity in cash and treasuries; benefitting from yields on treasuries
- To manage inflationary risk, we have introduced a number of low risk, low volatility multi-asset funds with daily liquidity to the capital pool
- Approximately £200m has been invested in these funds, managed by three separate managers
- 27% of capital pool in foreign denominated currencies, predominantly USD with this resulting in a foreign exchange gain of £30.6m in the capital pool during the year to date
- We continue to closely monitor the macro environment to ensure that the capital pool is appropriately managed
- Growing our team and expanding our advisory capabilities in the next two years will mean a modest corresponding increase to our cost base
    - Costs will continue to be managed prudently - expect SIML costs for FY2022/3 to be £12.5m-£13.5m (c1% of NAV)

£654m
In the capital pool

27%
Of capital in foreign denominated currencies

12-24
Months of liquidity in cash and treasuries

Summary

Scaling for the next phase of growth

Leveraging our strategic capital base and institutional capability as we enter our next phase of growth

- Focused on optimising returns for shareholders by growing our portfolio whilst retaining a minimum level of balance sheet capital
- Strong deal flow with three investments in the year to date
- Performance within the listed portfolio has been disappointing; upcoming clinical catalysts in CY2023 with potential to drive value

Rolling ten year targets

20-25

Portfolio of leading life science companies

3

New companies p.a

3-5

Companies to product approval where Syncona has a majority shareholding

Our vision for 2032

£5bn

Net Assets

Appendix 1 – Syncona team

An expert multi-disciplinary investment team

Syncona

Our unique skill set

Scientific | Commercial | Company creation | Investment

Martin Murphy [1,2]
Co-founder and Chair, SIML
PhD

QuellTx · ANVEON · Autolus · CLADE THERAPEUTICS · YOMass · Kesmalea · ACHILLES

22 years' experience

Chris Hollowood [1]
CEO, SIML
PhD

FREELINE · SwanBio · purespring · agtc

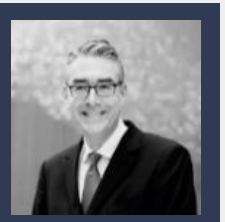
21 years' experience

Investment Committee

92%
of investment team with PhDs

170
Years of experience in life science

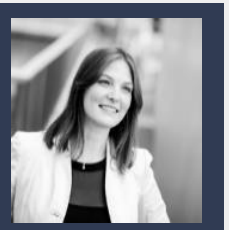
Edward Hodgkin [1,2]
Senior Partner
PhD



RTx · YOMass

32 years' experience

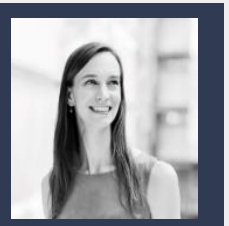
Elisa Petris [2]
Lead Partner
PhD



QuellTx · ACHILLES · agtc

15 years' experience

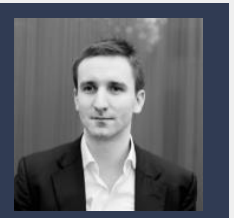
Magda Jonikas [2]
Lead Partner
PhD



YOMass · Kesmalea

12 years' experience

Alex Hamilton [2]
Investment Partner
PhD



ANVEON · SwanBio

9 years' experience

Michael Kyriakides [2]
Investment Partner
PhD

FREELINE · purespring · CLADE THERAPEUTICS · agtc

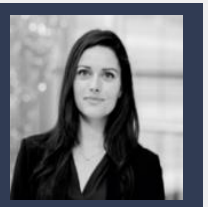
7 years' experience

Gonzalo Garcia [2]
Investment Partner
PhD

RTx

8 years' experience

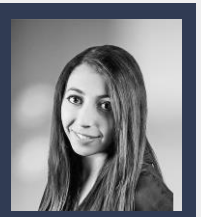
Alice Renard [2]
Investment Partner
PhD



ANVEON · purespring

7 years' experience

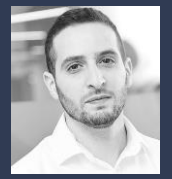
Raghd Rostom [2]
Associate Partner
PhD



Kesmalea

4 years' experience

Nathaniel Dahan
Associate Partner
PhD



agtc

4 years' experience

Hitesh Thakrar
Partner
BChem

29 years' experience

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

Investment team supported by experts in life sciences and company building

Markus John

- Joined in July 2021
- Former Global Medical Affairs Franchise Head at Roche

Lisa Bright

- Joined in January 2022
- Most recently President International and Chief Commercial and Corporate Affairs Officer for Intercept Pharmaceuticals

Gwenaelle Pemberton

- Joined in July 2022
- Former Vice President of International Regulatory Affairs at Gilead

Ben Woolven

- Joined in February 2022
- Former Senior Director Medical, Regulatory, and Quality, Global Head of Transformation Operations, GSK

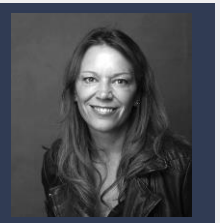
Leveraging the strength of clinical and operational experts

Scientific | Commercial | Regulatory | Business strategy

Markus John
CMO, Head of R&D
MD

22 years' experience

Lisa Bright[1]
Commercial Advisor
BSc



34 years' experience

Gwenalle Pemberton
Regulatory Advisor
MSc

34 years' experience

Ben Woolven
Business Strategy
and Operations Partner
PhD

21 years' experience

110+

Years of experience in life science

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

Appendix 2 – Portfolio

Portfolio company outlook

Upcoming milestones across the portfolio

Company	Status of pipelines	Next steps
Autolus	Five ongoing clinical trials	– Progress pivotal study obe-cel / adult ALL, with full data expected in H1 CY2023
FREELINE	Lead Fabry programme in Phase I/II trial	– Initial safety and efficacy data from the second cohort of the Fabry study expected in H1 CY2023 – Initial data from Gaucher programme in H1 CY2023
ACHILLES THERAPEUTICS	Two lead programmes in Phase I/IIa trials	– Progress Phase I/IIa NSCLC and melanoma trials, with data readouts expected in CY2023
agtc	Lead programme AGTC-501 in XLRP in Phase II/III trial	– Progress Phase II trial in XLRP
ANAVEON	Nominated lead programme in the clinic	– Progress Phase I/II trials of ANV419 in multiple myeloma and advanced melanoma, following recent entry to the clinic
QuellTX	Lead programme in pre-clinical development	– Expects to dose first patient in lead programme targeting liver transplant in H1 CY2023
SwanBio THERAPEUTICS	Lead programme in pre-clinical development	– Expects to dose first patient with lead programme targeting AMN in H1 CY2023
RTx	Pre-clinical development of lead programme	– Company and leadership team build out
purespring	Pre-clinical development	– Company and leadership team build out, identify lead programme
CLADE THERAPEUTICS	Pre-clinical development	– Company and leadership team build out, identifying pipeline targets
Kesmalea	Drug discovery	– Company and leadership team build out
OMass	Five programmes identified for pre-clinical development	– Progress of lead programme into lead optimisation

Clinical | Pre-clinical | Drug discovery

Portfolio company	Fully diluted ownership %[3]	30 Sep 2022 value £m (fair value)	Net invested/returned in the period £m	Valuation change	FX movement	31 Dec 2022 value £m (fair value)	Valuation basis (fair value)[1,2]	% of NAV
ANAVEON	37.9%	65.8	-	-	(0.9)	64.9	PRI	5.0%
Autolus	17.9%	37.4	23.0	(5.3)	(2.4)	52.7	Quoted	4.1%
agtc	100.0%	-	40.8	-	-	40.8	Cost	3.1%
FREELINE	51.3%	23.5	-	(7.4)	(1.2)	14.9	Quoted	1.1%
ACHILLES THERAPEUTICS	24.5%	22.4	-	(13.5)	(0.6)	8.3	Quoted	0.6%
SwanBio THERAPEUTICS	80.0%	105.7	8.5	-	(8.5)	105.7	Cost	8.2%
QuellTx	37.4%	95.8	-	-	(7.3)	88.5	PRI	6.8%
purespring	84.0%	35.1	-	-	-	35.1	Cost	2.7%
CLADE THERAPEUTICS	22.6%	13.4	12.4	-	(0.9)	24.9	Cost	1.9%
RTx	81.1%	23.0	-	-	-	23.0	Cost	1.8%
neogene THERAPEUTICS	*7.9%*	*17.1*	-	*2.1*	*(1.3)*	*17.9*	*Sale proceeds*	*1.4%*
Syncona NewCo	52.8%	-	7.3	-	-	7.3	Cost	0.6%
OMass THERAPEUTICS	30.9%	43.7	-	-	-	43.7	PRI	3.4%
Kesmalea	57.5%	4.0	-	-	-	4.0	Cost	0.3%
Investments		115.7	(0.6)	0.5	(6.2)	109.4		8.5%
Capital pool		763.3	(91.7)	1.4	(19.2)	653.8		50.5%
Total		**1,365.9**				**1,294.9**		100.0%

1 The basis of valuation is stated to be "Cost", this means the primary input to fair value is capital invested (cost) which is then calibrated in accordance with our Valuation Policy. 2 The basis of valuation is stated to be "PRI", this means the primary input to fair value is price of recent investment which is then calibrated in accordance with our Valuation Policy
3 Sale of Neogene to AstraZeneca completed in January 2023. Valuation is based on proceeds of $19 million and a discounted valuation of the milestone payments

Anaveon: harnessing the power of IL-2 for patients with solid tumours

Syncona

Initial investment	2019
Cost	£39.9m
Financing stage	Series B

Specialising in the development of treatments for diseases with immune system dysfunction

Anaveon is a clinical stage company developing biologics to modulate the function of “cytokines” with the potential to provide substantial therapeutic benefit to cancer patients

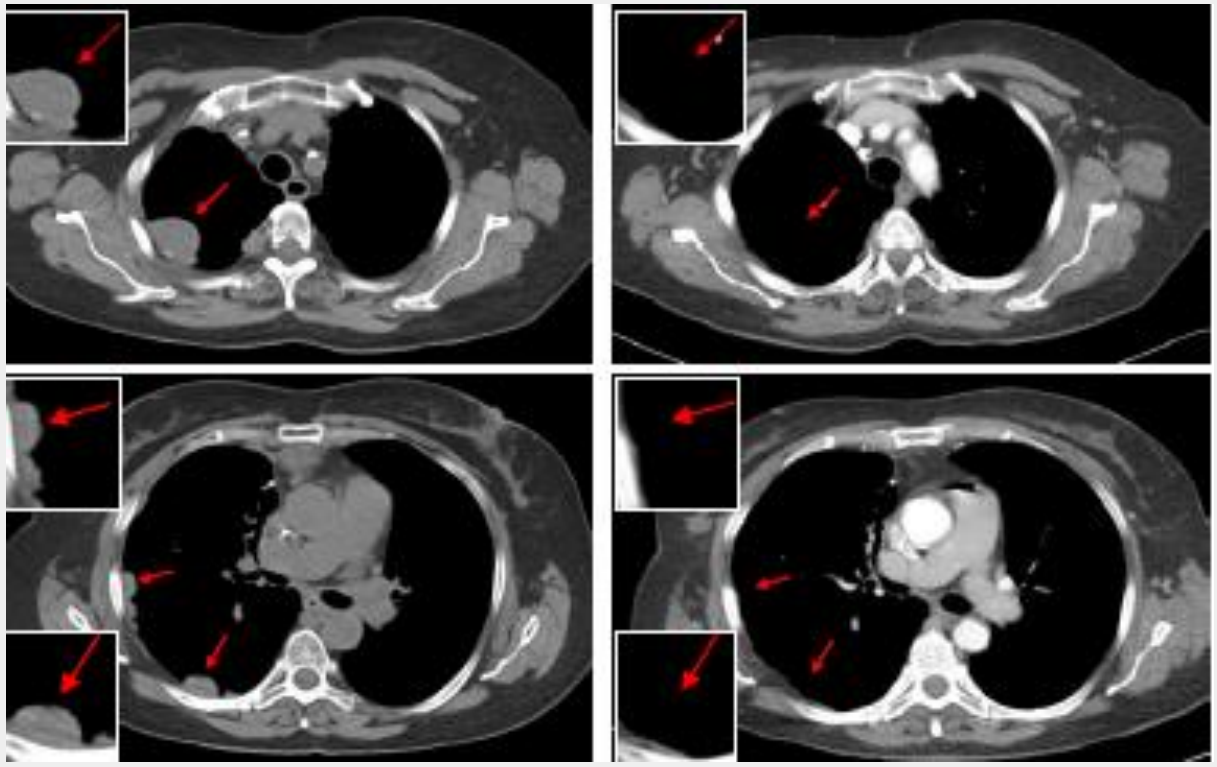
Its vision is to develop novel immune therapies benefiting patients suffering from a wide variety of diseases with immune pathology

Positive clinical data demonstrating the potential for best-in-class agent

- ANV419 therapy currently in Phase I/II dose escalation study; all patients in the trial have advanced solid tumours with disease progression in at least the last three months
- Data presented recently underlines strong safety and efficacy potential of the drug
- 66% of patients achieving at least disease stabilisation at ≥108 µg/kg dose level

NSCLC patient, who continues ANV419 treatment, shows sustained and deepening response with 56% reduction in sum of diameter of target lesions, at 12 weeks after treatment initiation

11 May 2022 **08 August 2022**



SITC poster 631. Patient shown is 63 year old female with relapsed refractory non small cell lung cancer (NSCLC). Cut off date 20th September 2022

Note: Please see slide 46 for key risks

Autolus Therapeutics: building a fully integrated CAR-T cell therapy company

Initial investment	2014
Cost	£147.0m
Financing stage	NASDAQ

Lead clinical programme: Obe-cel, a standalone, potentially best-in-class CD19 CAR T cell therapy candidate

- Lead product candidate, obe-cel, potentially best-in-class for relapsed refractory for adult acute lymphoblastic leukaemia (ALL) and has a competitive profile in B-cell Non-Hodgkin's Lymphoma (B-NHL)
- Pipeline built on modular innovation targeting cancers with limited treatment options
- In house cell manufacturing for clinical trial supply
- Commercial fit-for-purpose manufacturing facility running through validation process
- Strong cash position, year end: $382.7m

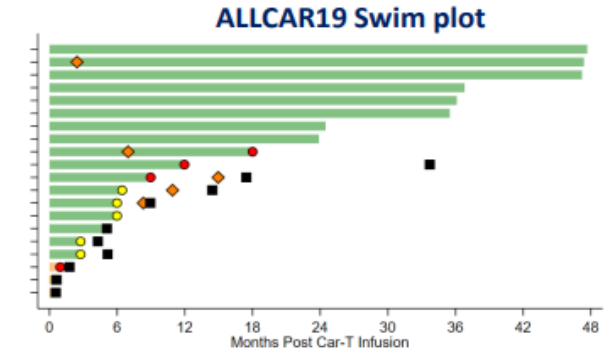
Lead programme

Obe-cel

- Pivotal Phase 2 trial in ALL met primary endpoint, full readout in mid 2023
- Potential best-in-class efficacy and safety profile relative to other CAR T cell therapies, with high overall remission rate (ORR)*,**
- 35% of patients with long-term remission, without any further therapy**
- Target engagement with fast off-rate drives unique product properties

Filing of BLA planned by end of 2023

Key data***



Collaboration:

- $250m with Blackstone Life Sciences, of which $220m already received to develop obe-cel in adult ALL
- Established technology collaborations with Moderna and BMS
- Opportunity for partnering of pipeline programmes

* FELIX pivotal study **ALLCAR19 academic study, *** Source: Autolus corporate presentation January 2023.

AGTC

Opportunity to apply Syncona's differentiated strategy to a late-stage asset and drive value for shareholders

Initial investment	2022
Cost	£40.8m
Financing stage	Series A

A clinical-stage gene therapy business in an area where Syncona has unique expertise

- Acquired all outstanding shares of Applied Genetic Technologies Corporation (AGTC) for $0.34 per share, valuing AGTC at $23.3m
- We believe AGTC's X-Linked Retinitis Pigmentosa (XLRP) programme has the potential to be a best-in-class product
- XLRP programme has orphan drug designations from the FDA and European Commission
- Experienced management team with CEO David Fellows (ex Nightstar) and CMO Nadia Waheed (ex Gyroscope)

Syncona's ideal characteristics for a scientific asset	
Defined patient segments / target market	✓
Defined, commercial lead programme with commercial potential	✓
Therapeutic areas where Syncona has deep domain expertise	✓
Transformational efficacy in area of high unmet need	✓
Accelerated development and regulatory pathways	✓
No current incumbent	✓

Discovery | IND enabling | Phase I/II | Phase II/III

XLRP programme

Freeline Therapeutics: developing transformative gene therapies for inherited systemic debilitating diseases

Potential to treat a wide range of chronic diseases

Initial investment	2015
Cost	£183.1m
Financing stage	NASDAQ

- Clinical stage company, with two programmes targeting diseases with high unmet medical need
- World class founder and leading management team, with extensive experience in gene therapy and clinical translation
- Leveraging differentiated platform based on validated capsid to deliver high protein expression at low doses

Lead programmes

Fabry disease

- Inherited deficiency in α-Gal A enzyme
- Progressive organ damage
- Reduced life expectancy despite existing treatments
- Renal failure and cardiac disease most common causes of premature death

Freeline's FLT190 has the potential to be best-in-class gene therapy

Patient population: ~16,000**

Gaucher disease

- Inherited deficiency in GCaseenzyme
- Leads to enlarged spleen and liver, low platelets and red blood cells, and bone and lung dysfunction
- Existing treatments cannot penetrate all tissues, poorly addressing certain aspects of disease

Freeline's FLT201 has the potential to be first and best-in-class gene therapy

Patient population: ~18,000**

Source Freeline Corporate Presentation. ** Note: The* seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients currently not eligible for gene therapy

Achilles Therapeutics: developing novel cancer immunotherapies targeting clonal neoantigens

Focus on the treatment of solid tumors with precision T cell therapy by targeting multiple clonal neoantigens that are present on all cancer cells

Initial investment	2016
Cost	£60.7m
Financing stage	NASDAQ

- Lead product is a precision tumor-derived T cell therapy targeting clonal cancer neoantigens.
- High unmet need in lead indications, advanced non-small cell lung cancer and recurrent metastatic melanoma
- Achilles uses DNA sequencing data from each patient, together with a proprietary bioinformatics platform, to identify clonal neoantigens specific to that patient and to potentially enable the development of personalised cell therapies
- In order for Achilles to be competitive in the space it is operating, it is critical that the company can manufacture at scale

Lead programmes

Data from 14 heavily pre-treated patients across its Phase I/IIa clinical trials in advanced non-small cell lung cancer (NSCLC) and recurrent or metastatic melanoma presented in December 2022

- Data reported on eight patients with advanced NSCLC and six patients in recurrent or metastatic melanoma
- Safety and tolerability observations of cNeT compare favorably to standard tumor infiltrating lymphocytes (TIL) due to less IL-2 related toxicity
- Durable partial response and stable disease achieved in heavily pre-treated NSCLC patients dosed with cNeT monotherapy
- The best clinical response was a partial response (ongoing at week 33) in a NSCLC patient that showed an investigator reported 57% total tumor reduction at week 24, with response ongoing at 33 weeks.
- Stable disease was observed in five NSCLC patients at week 12, with two patients remaining stable beyond weeks 15 and 26

Source: https://polaris.brighterir.com/public/syncona_limited/news/rns/story/xqg9e2w

SwanBio: focus on gene therapy for spinal cord related disorders

Syncona

Initial investment	2018
Cost	£99.2m
Financing stage	Series B

A gene therapy company developing leading-edge medicines to potentially deliver dramatic clinical efficacy for the treatment of genetically defined neurological conditions

Gene therapy

- Gene therapy has the potential to be transformational in neurology
- Focus on the spine – an uncrowded space and only tissue with proven transduction and clinical efficacy
- Potential to target diseases across three distinct classifications – Spastic Paraplegias (AMN), Monogenic Neuropathies, Polygenic Neuropathies

Lead opportunity

- Lead programme targeting AMN*, an inherited neurodegenerative disease in which the causative gene is definitively known and well characterised
- A devastating disease with no current treatments
- AMN impacts 8,000-10,000 male patients in the US and EU5[1]

The company

- World class scientific founders and management team
- Efficacy proof of concept established pre-clinically
- Patients enrolled in the CYGNET natural history study to assess disease progression in patients with AMN to inform the research and development of potential treatments
- SwanBio now expects to dose first patient in H1 CY2023

1 SwanBio analysis
* Adrenomyeloneuropathy

Quell Therapeutics: developing engineered T-regulatory cell therapies

Syncona

Initial investment	2019
Cost	£61.4m
Financing stage	Series B

On track to be the first company to potentially present transformative data in the engineered Treg-field in the liver transplant setting

Treg Cells

- "Master modulators" of the immune system:
  - Multiple mechanisms of suppressive activity
  - Bystander suppression in the local environment
- Natural Tregs are the optimal starting cell to demonstrate Treg therapeutic potential – stability and potency

Lead opportunity

- 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
- 15,000 liver transplants per year in US/EU5

The company

- Broad, proprietary Treg engineering toolkit
- GMP manufacturing capacity on-line in Quell facilities
- Clinical study to be initiated in 2023 with goal to demonstrate a durable full tolerance
- World class management team (Ian McGill, CEO, formerly Jazz)
- Funded through key datasets with premier investor syndicate (inc Jeito, Ridgeback, SV Health)

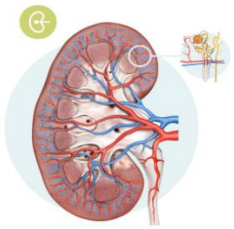
Purespring: one of the first gene therapy companies focused on the kidney globally

Syncona

Initial investment	2020
Cost	£35.1m
Financing stage	Series A

Seeking to advance gene therapies for the treatment of chronic renal diseases that are currently poorly addressed with existing treatments

- Gene therapy targeting the podocyte, allowing it to potentially 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.
  - The podocyte is implicated in 60% of renal disease[1]
- Purespring was founded around the seminal work of Professor Moin Saleem, Director of Bristol Renal; the originator of the gold-standard human podocyte cell lines
- The company is developing a proprietary platform to potentially enable kidney gene therapy



Each kidney is divided into individual functional units called nephrons

The glomerulus is a key element of the nephron where important filtration mechanisms happen

The Podocyte is one of the key cell types responsible for the filtration of blood

- Regulation of Filtration
- Maintenance of renal function
- Immune/inflammation regulation – complement modulation
- Metabolic Sensing/regulation and Insulin sensing

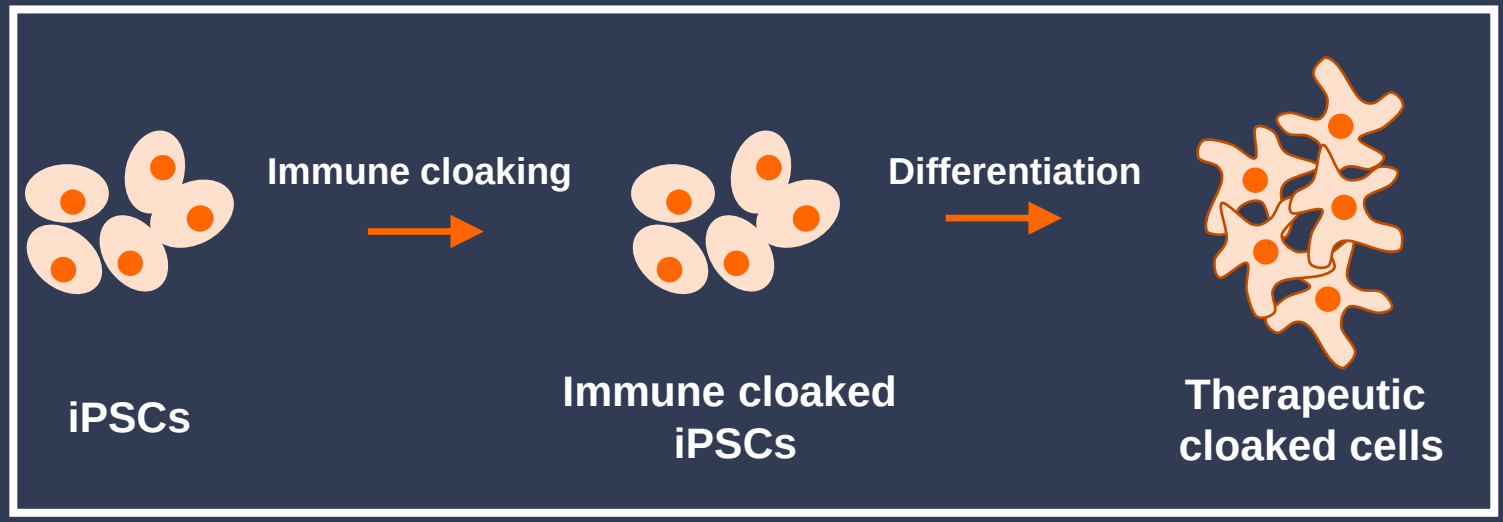
1 Source: Purespring analysis

Clade Therapeutics: developing the next-generation off-the-shelf cell therapies

Initial investment	2021
Cost	£23.2m
Financing stage	Series A

Advancing cell therapy beyond haematological malignancies to solid tumours and enabling access to a greater number of patients

- Delivery of scalable next generation induced pluripotent stem cell (iPSC) derived medicines that address the supply and cost challenges of autologous cell therapy, and the efficacy challenge of allogeneic cell therapy
- Combining two leading proprietary platforms:
  - Advanced immune cloaking technology to increase persistence
  - Differentiation to key target cell types in a reproducible and scalable manner
- Founded by CEO Dr. Chad Cowan, scientific co-founder of CRISPR Therapeutics, who is supported by leading experts of the field



Initial focus on cancer treatment but platform can be applied to other cell types

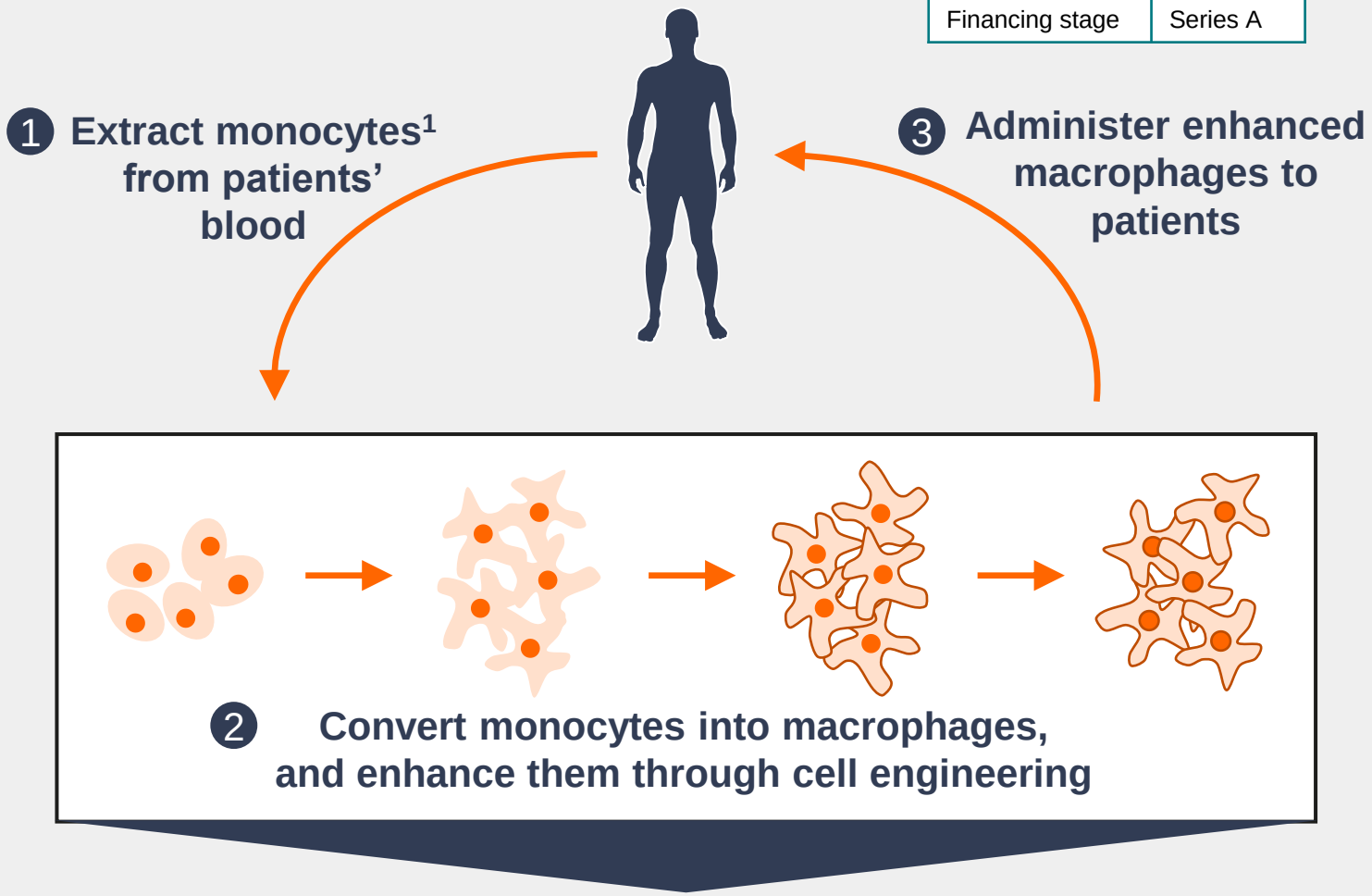
Resolution Therapeutics: macrophage cell therapy company in inflammatory diseases

Syncona

Initial investment	2018
Cost	£23.0m
Financing stage	Series A

Encouraging clinical data already obtained in lead indication with earlier generation programme

- Studies have identified a prominent role for macrophages in tissue repair. Pro-restorative macrophages can digest scar tissue, switch off inflammatory response and promote organ repair
- Resolution is focused on the treatment of chronic liver disease, the only chronic disease still on the rise in Western countries
- Built over a three-year partnership between Syncona and the University, with £37m committed to date
- Company is developing both an autologous and allogeneic platform
- Based on the research of Prof. Stuart Forbes and Prof. John Campbell from the University of Edinburgh



Resolution of inflammatory organ damage
e.g., in a cirrhotic liver

1. Monocytes are precursor cells of macrophages

OMass: a platform built to unlock highly validated but inadequately drugged targets

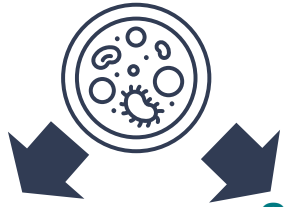
With a focus on immunological and rare diseases

Syncona

Initial investment	2018
Cost	£35.4m
Financing stage	Series B

- 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, we need 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
- Platform is based on work initiated by its scientific founders in the laboratory of Professor Carol Robinson at Oxford University

Today, researchers are forced to make trade-offs:



Cell-based systems

Researchers know that biology is observed with high fidelity. However, **there is a disconnect between what is measured and the drug's action** resulting in **false leads and missed opportunities.**

Cell-free approaches

Confounding factors have been stripped away giving precise data on how tightly or how quickly a drug binds to its target. However, the target protein **no longer faithfully represents its living counterpart** and endogenous biomolecules are absent

OMass' platform retains biological relevance at high resolution, delivering cell-system fidelity with cell-free precision.

Kesmalea Therapeutics

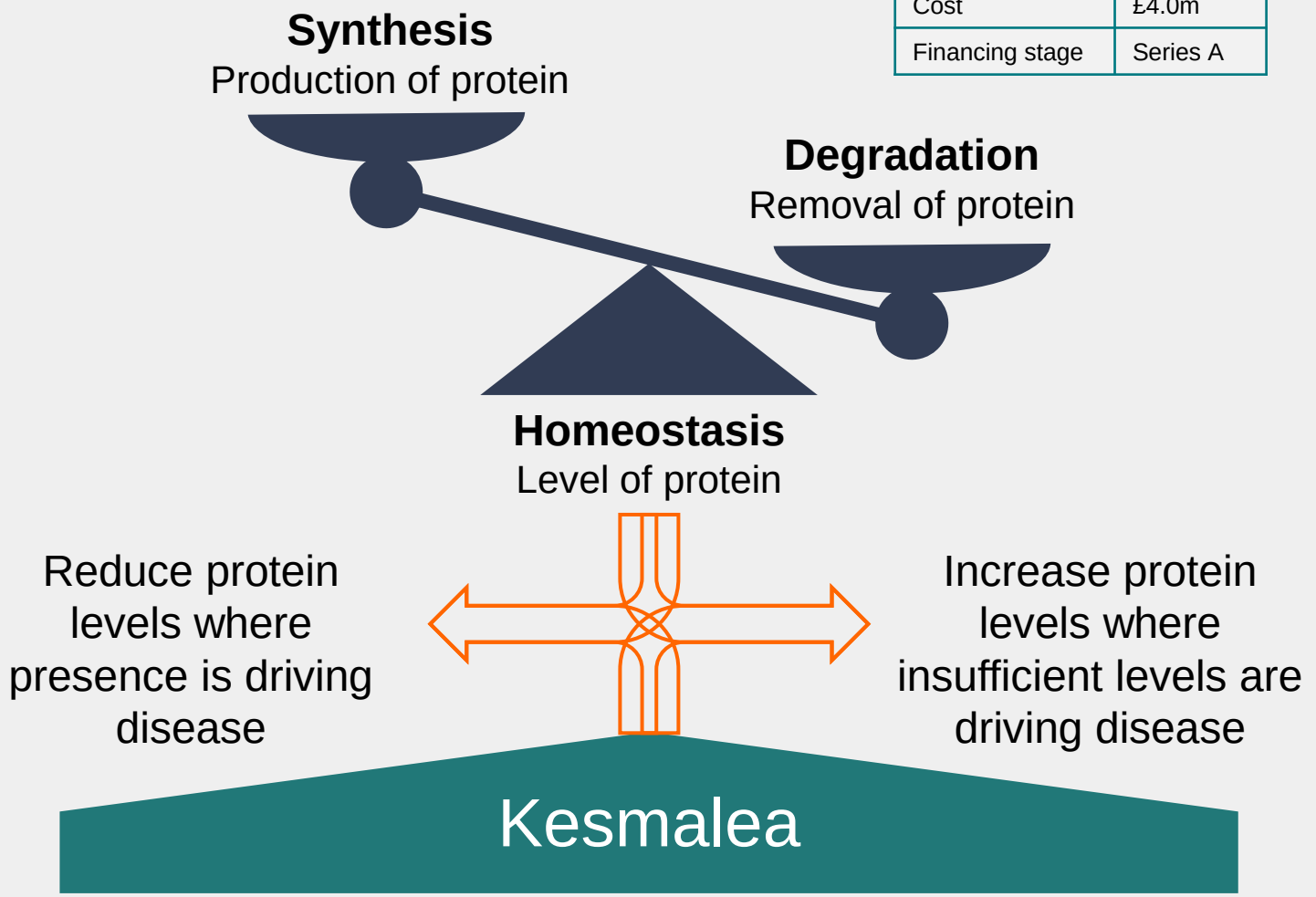
Small molecule drug discovery platform focused on protein homeostasis

Syncona

Initial investment	2022
Cost	£4.0m
Financing stage	Series A

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

- Founded by Dr Harry Finch, a world-class chemist and co-inventor of GSK's Serevent™
- Protein homeostasis company which 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
- Syncona Lead Partner Magdalena Jonikas led the launch of the company and has joined the Board of Directors



Appendix 3 – Sustainability

Continuing to show a strong commitment to ESG

Our social impact

- £4.2m donated to charity in FY2021/2, ongoing commitment to donate 0.35% of NAV per year
- 19 portfolio company clinical trial sites across the UK
- 1200+ people employed by Syncona and its portfolio
- Total addressable market of c.383k patients across clinical stage portfolio companies[1]

Responsible investor and partner

- Responsible Investment Policy recently rolled out to full portfolio
- Launched project to integrate ESG into ongoing priorities of newly formed company launch team
- Continue to work closely with portfolio companies to develop ESG reporting

Inspiring and empowering our people

- Second Windsor Fellowship intern begins six-month placement at Syncona[2]
- Generating Genius scholars begin second year of studies at university[3]
- Updated family-friendly policies

Responsible and ethical business

- First TCFD report published in FY22 Annual Report
- Net zero aspiration on a full portfolio basis by 2050
- Intend to publish full portfolio carbon footprint in FY2022/3
- Intend to become a signatory to the Net Zero Asset Managers (NZAM) initiative

1 - Total addressable market calculated from estimated new patients diagnosed per annum in lead indication/s of clinical stage portfolio companies, as defined by the company or the Syncona investment team estimate
2 – The Windsor Fellowship aims to design and deliver personal development and leadership programmes, with the goal of supporting minority communities in science, technology, engineering and maths (STEM) subjects
3 – Generating Genius supports low-income students across the UK to obtain places at top universities in STEM subjects. The Syncona Foundation has provided a donation of £301,500 over three years, to provide five of Generating Genius's students with scholarships to go to university, covering all their university fees as well as most living expenses when there

The Syncona Foundation

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

Focused on cancer, neuro-degenerative diseases, gene therapy. Alongside other health and society related areas including mental health, bereavement and diversity

“The Syncona Foundation plays an incredibly important role in helping us make discoveries and improve cancer patients’ lives.”

Professor Kristian Helin
CEO of the Institute for Cancer Research (ICR)

£40.6m
Syncona donations to charity since 2012[1]

26
Charities supported

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

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

1 Includes FY2021/2 donation