Syncona

Investing to extend and enhance human life

Interim results 2021

synconaltd.com

***Image** Freeline labs, Stevenage*

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Progress in the half

Continued focus on hands-on, active engagement with a maturing portfolio with key milestones ahead

Strong clinical progress across our diversified portfolio

- New cell therapy company, Clade Therapeutics, taking the portfolio to 12 companies
- Five clinical stage companies with Anaveon dosing first patients
- Seven clinical data read-outs year to date[1]: Autolus, Gyroscope, Freeline and Achilles
- Quell and SwanBio set to enter the clinic in CY2022

Portfolio

NAV of £1,152.8m, 171.7p per share, total return of (11.4)%

- (21.3)% return from life science portfolio
- Performance predominantly driven by valuation declines from two listed holdings, Freeline and Achilles
- Portfolio companies on track to deliver 15 clinical milestones by the end of CY2022
- Syncona remains confident in long-term potential of portfolio to deliver value

Performance

Decisive actions taken by our portfolio companies

- Syncona CIO and Freeline Chair, Chris Hollowood closely engaged with the Freeline Board as it updated executive leadership team and appointed new CEO
- Syncona CEO, Martin Murphy took on the role of Chair of Autolus as company focused on the delivery of the AUTO1 pivotal study; new Chair John H. Johnson now appointed
- Supporting portfolio companies to hire world-class teams (Purespring), develop manufacturing capabilities (Quell) and progress into the clinic (Anaveon)

Operational

Positive momentum with companies accessing capital from high quality investors

- $397m committed to portfolio companies year to date[1] with $30m committed by Syncona
- Three financings year to date[1]
- £50.8m deployed in the period, current capital position of £534.9m
- Continue to expect to deploy between £100-£175m into our existing companies and new opportunities this year

Investment

1 From 31 March to 10 November 2021

Syncona model in action: a partnership approach to building global leaders

Found, Build, Fund model enables strategic influence to address and navigate issues as they arise in clinical development

Expert Syncona team

Found
Strong relationships with academic founders and management teams

18 companies founded or invested in early

Build
Syncona team works closely with management teams to bring expertise to bear as company navigates clinical and regulatory processes

10 companies where we have had operational roles and 17 current board seats

Fund
Significant, strategic ownership positions enable influence

£832m invested since foundation

- Five clinical stage companies with 12 clinical trials
- Intensive period of hands-on involvement with maturing portfolio
- Decisive action taken by our portfolio companies to manage challenges as they've arisen
- 15 clinical milestones anticipated by the end of CY2022 with potential to deliver value

Portfolio update

Bringing our expertise to bear across our clinical portfolio

A maturing portfolio with five clinical-stage companies navigating the risks inherent in clinical development

Autolus — CAR-T cell therapy: Pivotal study

Focus on progressing pivotal trial for AUTO1 (obe-cel)

- Published positive durability data for AUTO1 in r/r adult ALL
- Appointed experienced biopharma Chair, John H. Johnson and strengthened senior team
- Up to $250m commitment from Blackstone post period end; now very well funded to deliver AUTO1 pivotal study

Syncona engagement

- Martin Murphy took the role of Chair as company focused on the delivery of AUTO1 (obe-cel) pivotal study

FREELINE — Systemic gene therapy: Phase I/II

Clinical progress and focus on accelerating value creation

- Reinitiated clinical programmes post COVID
- Dosed second patient in Fabry; enrolling for run-in study for lead programme in Haemophilia B
- Change of leadership, new CEO and redefined strategic priorities to accelerate value creation

Syncona engagement

- Chris Hollowood, as Chair of Freeline, engaged with its board to implement executive leadership team changes and appoint new CEO

1 Including Phase I/II and pivotal study

Bringing our expertise to bear across our clinical portfolio

A maturing portfolio with five clinical-stage companies navigating the risks inherent in clinical development

GYROSCOPE Retinal gene therapy: Phase I/II

Continued positive data generation in FOCUS trial

- Additional positive interim data in Phase I/II trial for the treatment of Geographic Atrophy (GA) secondary to dry AMD
- Decision made in May to postpone IPO in light of challenging market conditions
- Up to $60m Sanofi equity investment post period end to support Phase II trials

Syncona view

- Recent data from Apellis Phase III trials in GA validate complement system as mechanism for treatment

ACHILLES THERAPEUTICS TIL cell therapy: Phase I/II

Good momentum across two Phase I/II trials

- Continued patient enrolment across Phase I/II trials for non-small cell lung cancer (NSCLC) and melanoma
- Continued data generation supports move to the higher dose process for Phase I/II trials by end of CY2021
- Continued to strengthen the Board

Syncona view

- Business executing well; share price performance impacted by wider cell and gene therapy market context

ANAVEON Selective IL-2 agonist: Phase I/II

Dosed first patient in a Phase I/II study of ANV419

- Initiated clinical programme to develop a selective IL-2 agonist
- Making good progress dosing patients
- Expect to release initial data in Q1 CY2022

Syncona view

- Business executing well and progressing clinical programme; potential for differentiated agent

Generation 3 poised for clinical entry with Generation 4 progressing at pace

Syncona

Significant momentum and progress across pre-clinical companies led by strong management teams

QuellTX

- Set for clinical entry in Q1 CY2022 with CTA filed[1]
- Progressing pipeline of programmes focused on engineered Tregs
- Expanded team with Dominik Hartl (CMO) and Tracey Lodie (CSO)

SwanBio THERAPEUTICS

- Initiated a natural history study in AMN
- Published encouraging pre-clinical data on lead programme
- On track for clinical entry in lead programme in CY2022

RTx

- Progressing pre-clinical development for lead programme assessing the use of macrophage therapy in end stage liver disease
- Data in early study maturing and due in CY2022

Generation 3 companies approaching clinical entry or demonstrating significant pre-clinical progress

OMass THERAPEUTICS

- Progressing exciting pipeline of small molecules (MC2, Gasdermin D, GPR65)
- Focus on immunological and orphan diseases

neogene THERAPEUTICS

- Appointment of top class leaders Brent Pfeiffenberger (COO) and Han Lee (CFO)
- On track to file CTA by end of CY2021

purespring

- Further strengthened leadership team with Ronny Renfurm (CMO), Julian Hanak (CDO)
- Building out operations and pre-clinical pipeline

Clade Therapeutics

- World-class founding team, Chad Cowan in the role of CEO (ex CRISPR and Sana)
- Progressing pre-clinical development and identifying pipeline targets

Generation 3/4 companies stewarded by world-class teams progressing pre-clinical development and building out operations

1. CTA: clinical trial application

15 milestones by the end of CY2022 with the potential to drive value

Syncona

- Clinical stage
- Pre-clinical stage

Upcoming clinical milestones

Q4 CY2021

Autolus – initial Phase Ib pivotal data in AUTO1

Autolus - data in AUTO1/22 Phase I trial

Freeline - expect to publish durability data in Haemophilia B Phase I/II study; Gaucher trial site initiation in Phase I/II trial

CY2022

Autolus – deliver Phase I data on AUTO4 in H1 and pivotal data in AUTO1 mid CY2022

Freeline - interim Phase I/II data expected in Haemophilia B, Fabry and Gaucher

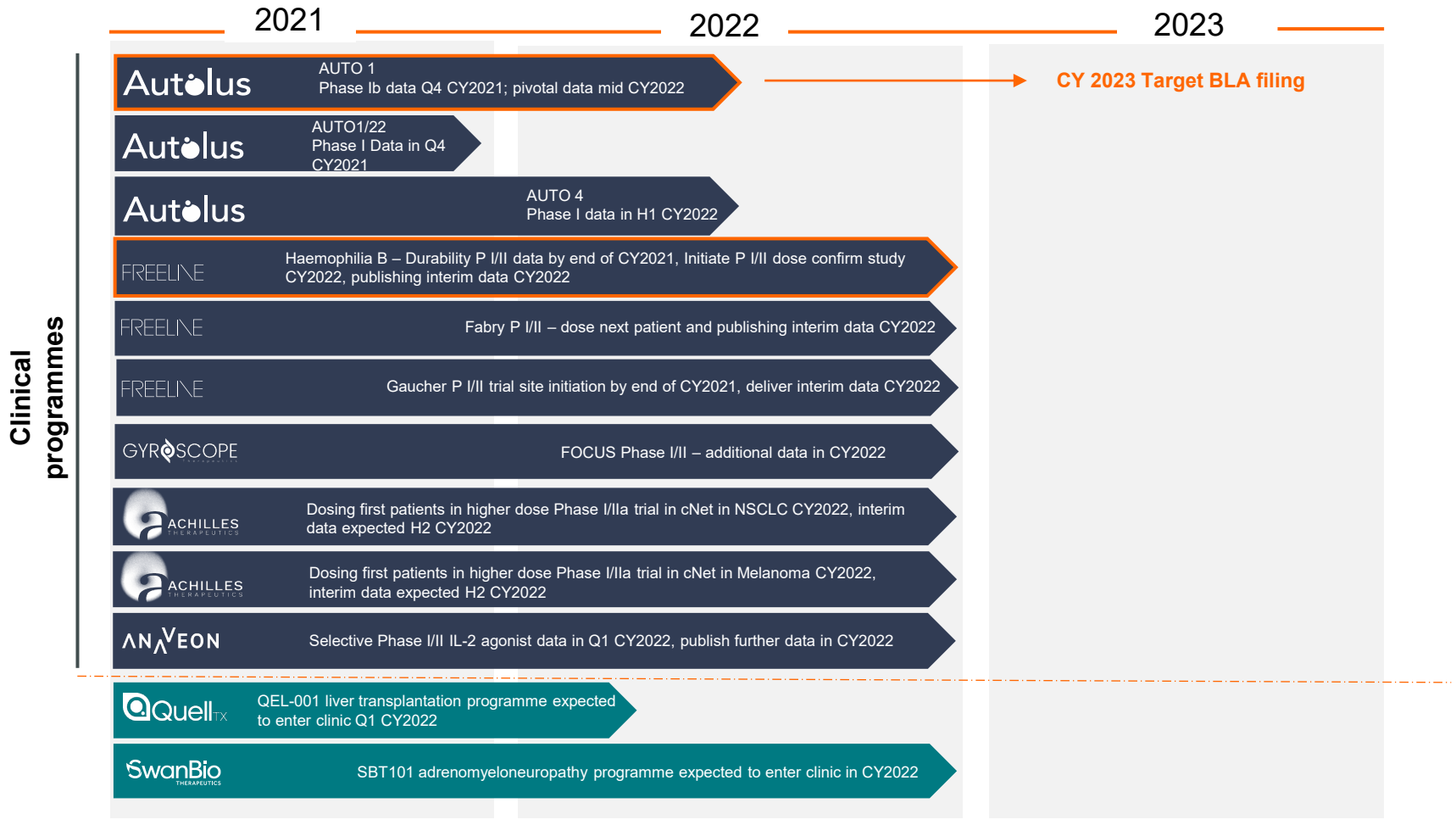
Gyroscope - additional data from Phase I/II trial

Achilles – interim data in higher dose process in NSCLC and Melanoma Phase I/II studies

Anaveon – data from ANV419 Phase I/II study expected in Q1

Quell – expected to enter clinic Q1

SwanBio – expected to enter clinic



Clade Therapeutics

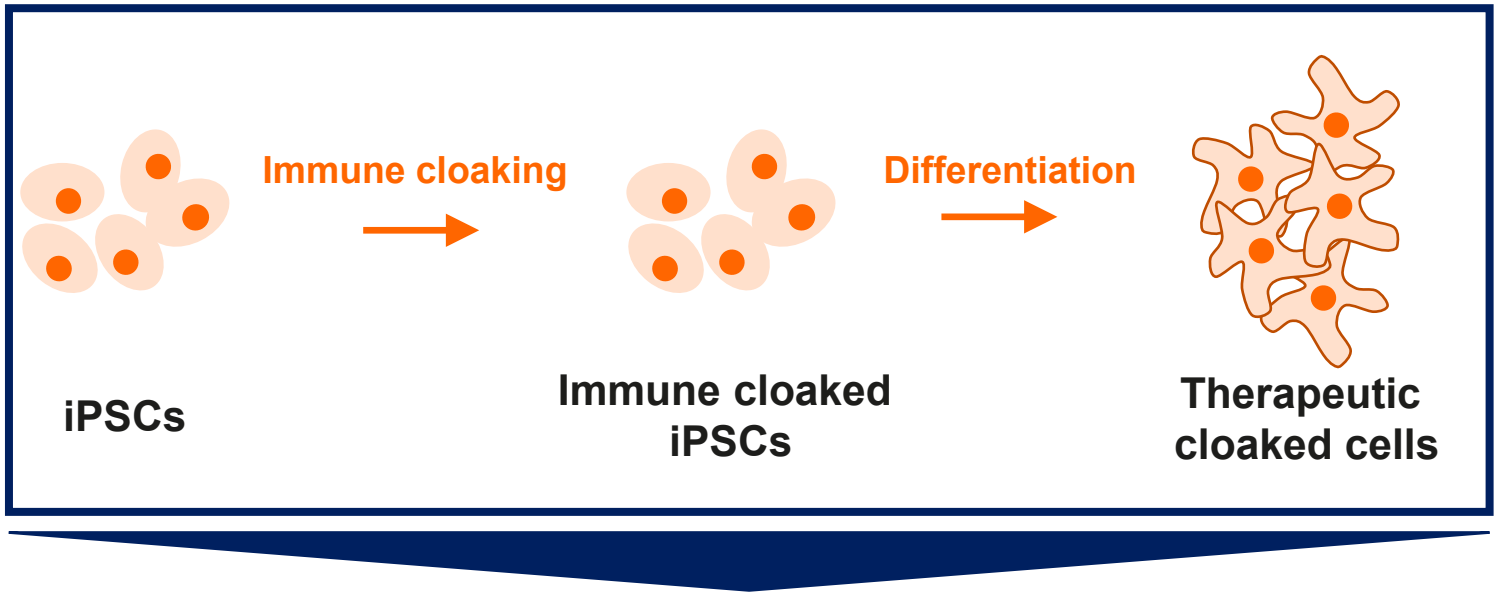
Harnessing iPSC immune cloaking and differentiation platform technology to deliver 'off-the-shelf' cell therapies

Founded by CEO Dr. Chad Cowan, a scientific co-founder of CRISPR Therapeutics and former Associate Professor at Harvard University

- Syncona led the Series A committing $30m in a $87m financing
- Seeking to deliver scalable next generation induced pluripotent stem cell (iPSC) derived medicines
- Combining two proprietary platforms: immune cloaking technology, and differentiated technology to generate target cell types
- Syncona has deep domain expertise in cell therapy – proactively seeking opportunity to diversify exposure across modalities
- Syncona CEO Martin Murphy has joined the Clade Board as a Director, with Michael Kyriakides acting as a Board observer

Syncona

Clade was founded by a world-class team of company builders and scientific innovators with an unparalleled expertise in generating stem cell derived immune therapies



The company will develop iPSC derived adult T, NK and B cells with an initial focus on developing "cloaked" immune cells for cancer treatment

Financing strategy

Optimising our financing approach to deliver on our strategy

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

Our financing approach involves supporting our companies to take one of two core strategies:

1 **Solely fund companies through pre-clinical stage**

Bring external investors in before the point of clinical validation

- Maintain significant ownership position
- Provides company with a broader set of investors to support them as they scale (with public market an option)

2 **Solely funding companies to clinical validation**

Sole ownership or syndicate to investors and maintain significant ownership

- Risk based decision on whether to syndicate to external investors (with public market an option)

Strategy in action

- $87m raised in syndicated Clade Series A
- Autolus commitment of up to $250m from Blackstone
- Gyroscope commitment of up to $60m from Sanofi

Pre-clinical → Phase I/II → Phase III/Pivotal → BLA[1] → Launch

Ken Galbraith, our Executive in Residence, brings critical expertise that will be instrumental in helping us to continue to optimise our financing approach

1 Biologics License Application

Financial review

Financial review

NAV of £1,152.8m, 171.7p per share, (11.4%) return in the period; capital base of £534.9m

- Life science portfolio valued at £617.9m, a return of (21.3)% in the period:
  - Performance driven by a fall in share prices of Achilles and Freeline
  - Syncona continues to be confident in longer term potential of listed portfolio
  - New company, Clade Therapeutics, added to the portfolio
  - Life science investments; CEGX £15.4m write up following Series D financing post period end
- Capital base of £534.9m; £50.8m of capital deployment in the period

☐ Clinical ☐ Pre-clinical ■ Drug discovery

Syncona

Portfolio company	Fully diluted ownership %	31 March 2021 value £m (fair value)	Net invested/returned in the period £m	Valuation change	FX movement	30 Sep 2021 value £m (fair value)	Valuation basis (fair value)	% of NAV
GYROSCOPE VISION FOR LIFE	54	150.1	-	-	3.4	153.5	PRI	13.3
Autolus	24	81.2	-	11.6	2.1	94.9	Quoted	8.2
ACHILLES THERAPEUTICS	27	133.1	-	(70.4)	1.4	64.1	Quoted	5.6
FREELINE	45	167.9	-	(121.0)	1.1	48.0	Quoted	4.2
ANAVEON	51	18.5	-	-	0.7	19.2	Cost	1.7
SwanBio THERAPEUTICS	75	53.7	7.6	-	1.5	62.8	Cost	5.4
QuellTx	74	35.1	10.1	-	-	45.2	Cost	3.9
purespring	84	3.9	14.6	-	-	18.5	Cost	1.6
neogene THERAPEUTICS	9	11.0	-	-	0.4	11.4	Cost	1.0
Clade Therapeutics	23	-	10.8	-	0.4	11.2	Cost	1.0
RTx	79	7.4	-	-	-	7.4	Cost	0.6
OMass THERAPEUTICS	49	16.4	5.1	-	-	21.5	Cost	1.9
Investments[1]		43.8	1.0	15.3	0.1	60.2		
Total		**722.1**	**49.2**	**(164.5)**	**11.1**	**617.9**		

1 Investments include CEGX Series D, closed post period end

Balance sheet: a competitive advantage

Provides flexibility and control to take long-term approach

Capital pool of £534.9m
- £50.8m of capital deployed into the portfolio during the period

£103.4m uncalled commitments across the portfolio at the period end

$397m of capital committed to Syncona companies year to date[1] with $30m committed from Syncona[2]
- Three financings year to date

Capital pool predominantly held in cash and cash equivalents
- 85% held in cash and cash equivalents with the remainder in legacy funds

- Continue to expect to deploy £100m-£175m this financial year
- As our companies enter the clinic, we expect them to conduct new financings, bringing in specialist global external investors to invest alongside us
- Our balance sheet enables us to fund portfolio companies to deliver next key milestones and found new companies

1 31 March 2021 to 10 November 2021
2 Includes Series A financing in Clade during the period and post period financings in Gyroscope and Autolus

Market context

Development of the cell and gene therapy field

Public market sentiment towards cell and gene therapy impacted by inevitable industry challenges in innovative fields of medicine; Syncona view is that field's promise remains

Industry challenge	Syncona platform	Portfolio position
Safety in AAV gene therapy	- Potential to deliver transformational treatments - Gene therapy strategy has been to limit potential exposure to toxicity – tissue compartment led - Continued to develop know-how in managing toxicity	- Companies publishing encouraging clinical data - Freeline differentiated from peer set by low dosing strategy
Manufacturing in cell therapy	- Developed experience in manufacturing - Continuing to build manufacturing capacity across the portfolio	- First investment in cell therapy space in 2014 - Capability developed at Autolus led by its strong team - Lessons learnt being applied to: Quell, Resolution and Achilles
Increasing regulatory focus	- Early focus and investment in manufacturing to meet regulatory requirements - Targeting areas of high unmet medical need - FDA gene therapy advisory committee met to discuss field and supportive of continued development protocols	- Investing in and developing commercial manufacturing platforms early, i.e. SwanBio – with knowledge of expected regulatory standard - Six orphan drug designations year to date

Potential to transform the lives of patients

Designed to halt a disease or reverse its progress

Approved products and data to date have shown the transformational impact and potential of these products

Cell therapy

- Potential for profound efficacy - to date mainly oncology focused

Gene therapy

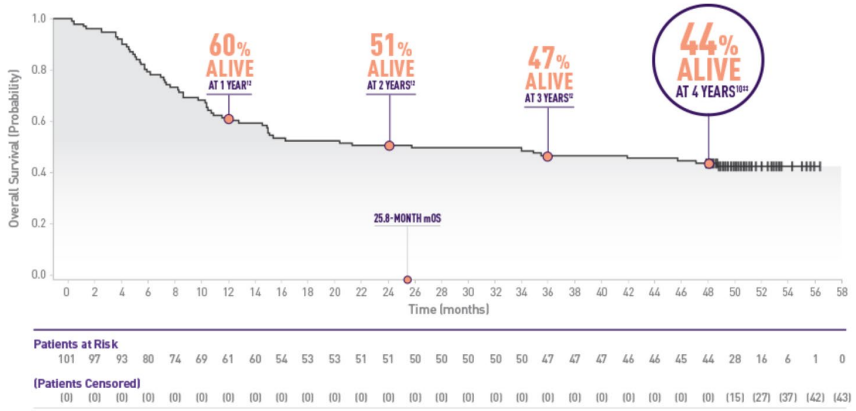
- The potential for one-time treatments vs conventional medicines which are taken on a continual basis

Significant number of diseases where cell and gene therapy are potentially applicable

Kite/Gilead: engineered CAR-T cell therapy for adult relapse / refractory Diffuse Large B-cell Lymphoma (DLBCL)

- DLBCL is an aggressive cancer of the lymphatic system
- >18k people diagnosed with DLBCL annually[1]
- Yescarta was approved in 2017 for use in relapse / refractory patients
- Disruptive efficacy seen, with 4x more patients responding to treatment[3]

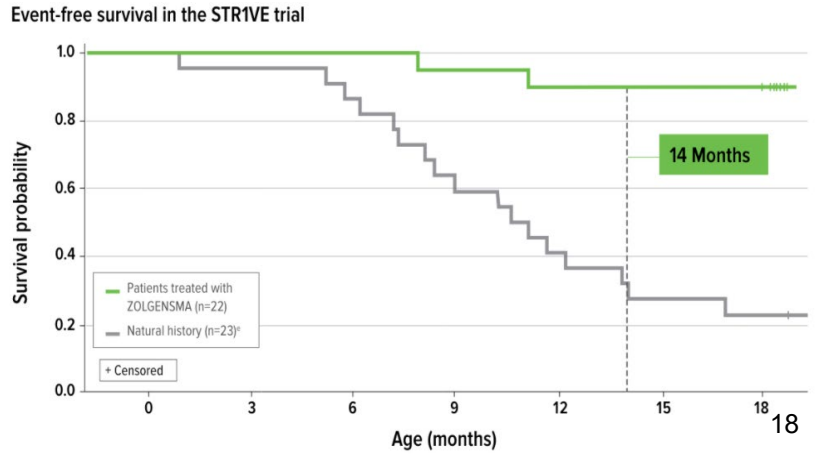
44% of patients alive at four years post treatment[2]
3x overall survival rate of current standard of care at 12 months[3]



Novartis/AveXis: one-time therapy addressing spinal muscular atrophy (SMA)

- SMA is a genetic disease caused by a lack of a functional survival motor neuron 1 gene, resulting in the rapid and irreversible loss of motor neurons
- Most often impacts babies and children
- Zolgensma now an approved product based on profound data

91% (20/22) of patients were alive and free of permanent ventilation at 14 months of age[4]



1 https://lymphoma.org/aboutlymphoma/nhl/dlbcl/
2 https://www.yescartahcp.com/large-b-cell-lymphoma/efficacy
3 https://www.ncbi.nlm.nih.gov/books/NBK552022/
4 https://www.zolgensma-hcp.com/aboutzolgensma/efficacy/str1ve/

Cell and gene therapies have the potential to disrupt the market

Approved cell and gene therapies are expected to increase significantly in the coming years, Syncona believes the growth could be similar to antibody therapies

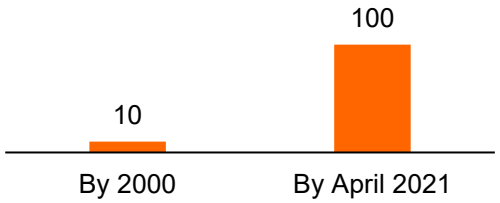
"… By 2025, we predict that the FDA will be approving 10 to 20 cell and gene therapy products a year based on an assessment of the current pipeline and the clinical success rates of these products …"

Scott Gottlieb, ex-FDA commissioner

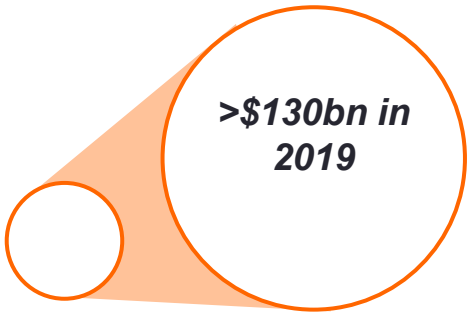
Monoclonal antibodies

FDA approved products[1]

100



Annual sales ($bn)[2]

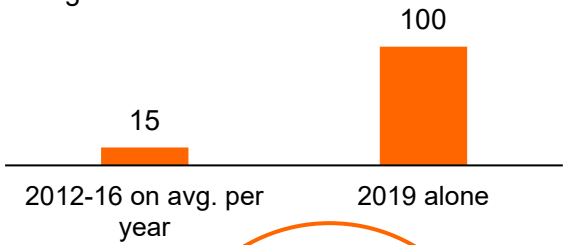


Cell and gene therapy

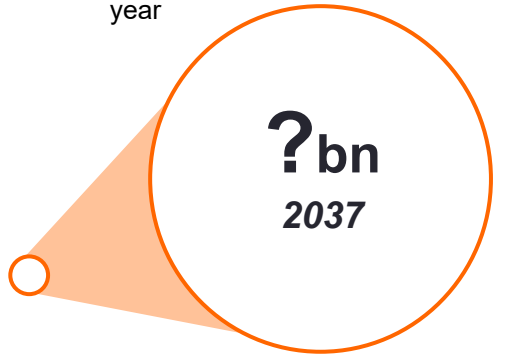
FDA approved products[4]

8

New Investigational New Drug applications to begin clinical trials[3]



Annual sales ($bn)[5]

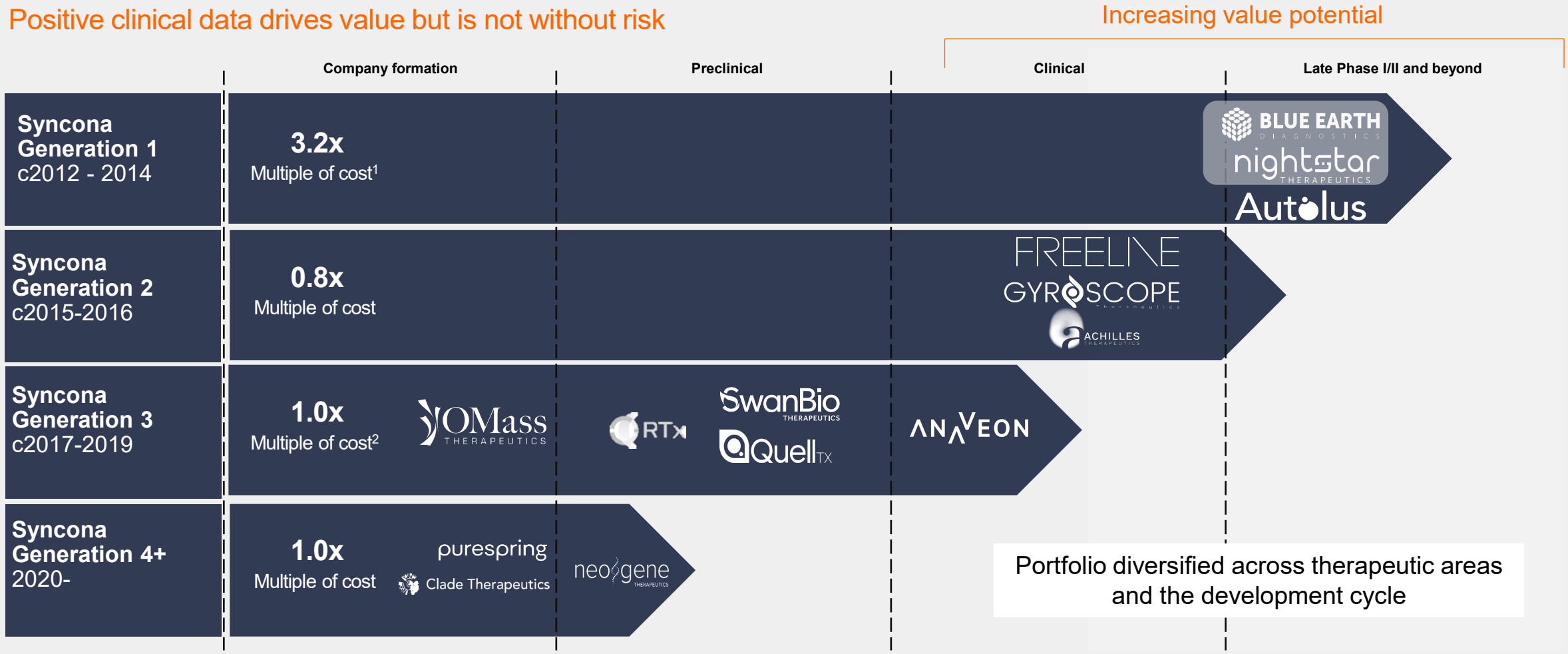


1 Nature Reviews Drug Discovery article published on 5 May 2021; 2 Lu, RM., Hwang, YC., Liu, IJ. *et al.* Development of therapeutic antibodies for the treatment of diseases. *J Biomed Sci* **27,** 1 (2020); 3 Lapteva L, Purohit-Sheth T, Serabian M, Puri RK. Clinical Development of Gene Therapies: The First Three Decades and Counting. Mol Ther Methods Clin Dev. 2020 Oct 10;19:387-397; 4 FDA Office of Tissues and Advanced Therapies: Includes engineered cell therapies and gene therapies only; 5 https://bisresearch.com/industry-report/cell-gene-therapy-market.html,

Summary

Significant value creation opportunity ahead

Positive clinical data drives value but is not without risk



All data as at 30 September 2021; multiples based on original Syncona Partners cost invested
Nightstar and Blue Earth realised in 2019
1 Includes capital invested in CEGX and write off of 14MG
2 Includes write off of Azeria

Summary

Syncona's platform creates value from the commercialisation of life science innovation

Period of intensive management of the portfolio supporting companies to navigate clinical development

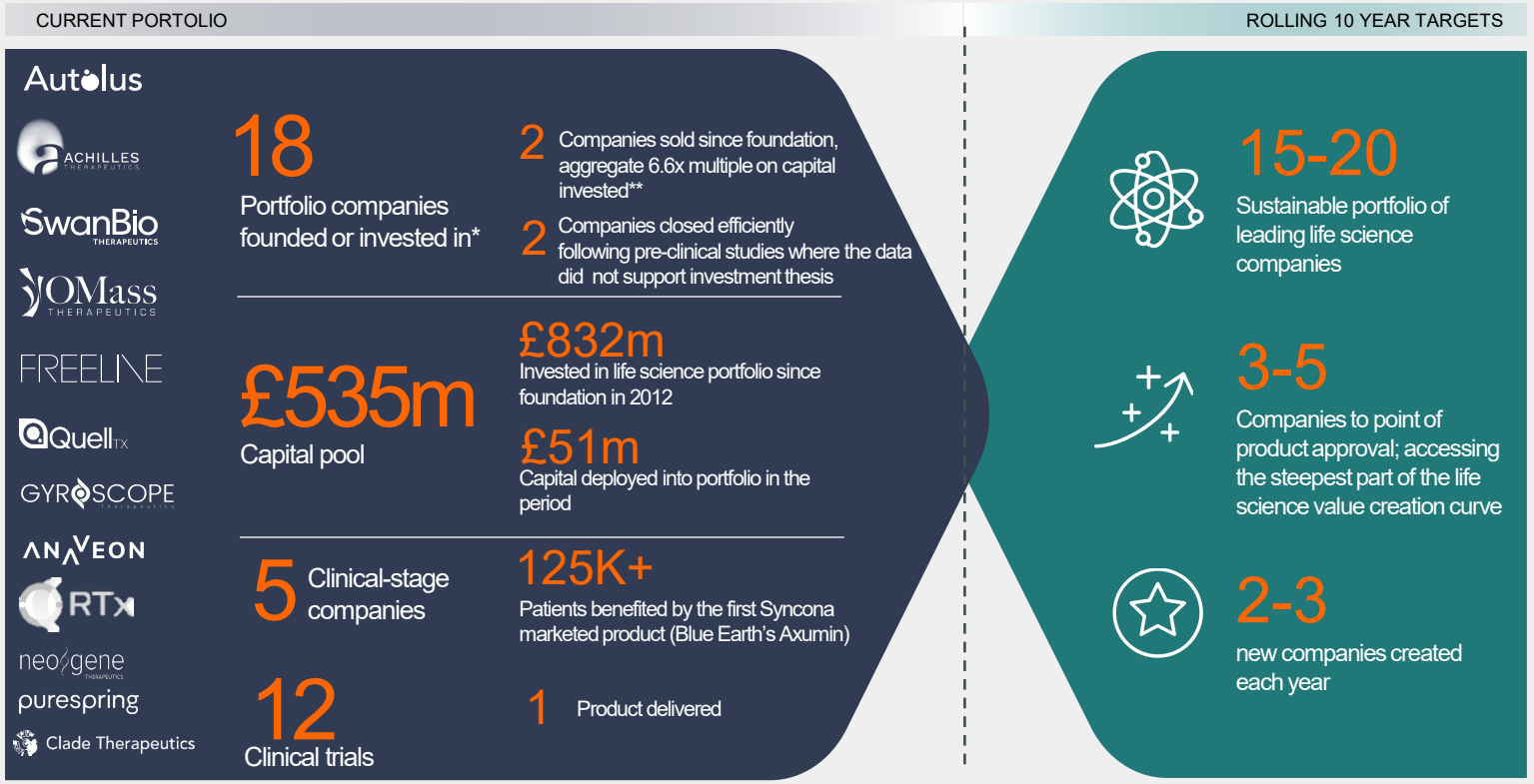
Maturing portfolio with companies set to read out clinical data in the next 12-24 months with the potential to drive value

- Five clinical stage companies and 12 trials in the clinic

Optimised financing approach, aiming to deliver long-term strategy and value

Untapped promise of cell and gene therapy remains

We have experienced volatility in our NAV but retain conviction that a long-term approach to building globally competitive businesses has the potential to deliver significant value to shareholders



- *Includes sales of Blue Earth and Nightstar, closure of 14MG and Azeria, merger of Orbit and Gyroscope; CEGX now an investment
- **Sales of Nightstar and Blue Earth, original Syncona Partners capital invested

Appendix 1 – Syncona team

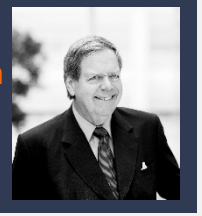
An expert multi-disciplinary team

Our unique skill set

Scientific | Commercial | Company creation | Investment

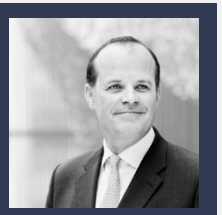
Investment committee

Nigel Keen
Co-founder and Chairman
FIET, FCA



- Commercial and company creation
- Chairman of Oxford University Innovation, Oxford Academic Health Network, MedAccess

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



- Scientific, commercial, company creation and investment
- PhD in Biochemistry
- 20 years in venture capital and management consultancy

Chris Hollowood [1]
CIO
PhD

- Scientific, commercial, company creation and investment
- PhD in Organic Chemistry
- 19 years in healthcare investing, of which 17 were in venture capital

Markus John
CMO and Head of R&D
M.D.

20 years' experience

Elisa Petris [2]
Partner
PhD

13 years' experience

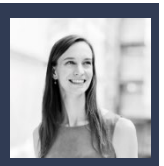
Edward Hodgkin [1,2]
Partner
PhD

30 years' experience

Dominic Schmidt [2]
Partner
PhD

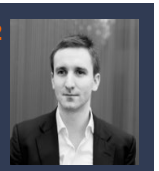
9 years' experience

Magda Jonikas [2]
Partner
PhD



10 years' experience

Alex Hamilton [2]
Partner
PhD



7 years' experience

Ken Galbraith
Executive in Residence
BComm

33 years' experience

Michael Kyriakides
Partner
PhD

5 years' experience

Freddie Dear [2]
Partner
BSc

4 years' experience

Alice Renard [2]
Partner
PhD

5 years' experience

Gonzalo Garcia [2]
Partner
PhD

6 years' experience

Hitesh Thakrar
Partner
BChem

27 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 – Portfolio companies

Portfolio company outlook

Strong momentum in the portfolio with near term catalysts

Company	Status of pipelines	Next steps
Autolus	Three programmes across four clinical trials	– Progress pivotal study AUTO1 / Adult ALL, Phase Ib data update in Q4 CY2021 with pivotal data in mid CY2022 – Publish clinical data on AUTO1/22 / paediatric ALL in Q4 CY2021 – Publish Phase I interim data on AUTO4 in H1 CY2022
FREELINE	Two lead programmes in Phase I/II clinical trials, set for trial site initiation for Phase I/II trial for Gaucher Type 1 by end of CY2021	– Progress Haemophilia B study, long-term durability data in Q4 CY2021 with further interim data in CY2022 – Dose next Fabry patient in Q1 CY2022, present interim data in CY2022 – Gaucher study to publish interim data in CY2022
GYROSCOPE VISION FOR LIFE	Lead programme in Phase II trials	– Additional data from Phase I/II trial – Progress Phase II trials; final read out expected CY2023
ACHILLES THERAPEUTICS	Two lead programmes in Phase I/IIa trials	– Expect to begin enrolling patients for higher dose VELOS™ Process 2 manufacturing in its Phase I/IIa NSCLC and melanoma therapies before end of CY2021; dosing in H1 CY2022, interim data in H2 CY2022
ANAVEON	Nominated lead programme in the clinic	– Publish initial data from Phase I/II trial in Q1 CY2022; with further data later in CY2022
QuellTx	Nominated clinical candidate in lead programme	– Phase I/II initiation of lead programme targeting liver in Q1 CY2022
SwanBio THERAPEUTICS	Lead programme in pre clinical development	– Phase I/II initiation of lead programme targeting AMN in CY2022
RTx	Pre-clinical development of lead programme	– Company and leadership team build out
neogene THERAPEUTICS	Pre-clinical development of lead programme	– Company and leadership team build out; plan to file CTA by end of CY2021
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
OMass	Five programmes identified for pre-clinical development	– Progress of lead programme into lead optimisation

Autolus Therapeutics

Applying a broad range of technologies to build a pipeline of precisely targeted T cell therapies designed to better recognise and attack cancer

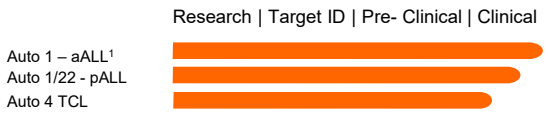
Board Seat	1
Date of Founding	2014
Date of Syncona investment	2014
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£124.0m
No. of employees	c.330

Competitor Landscape

GILEAD NOVARTIS Fate THERAPEUTICS

Key risks
- Highly competitive environment
- Differentiated product requirement
- Complex manufacturing and supply chain

Clinical pipeline



1 including Phase I/II and pivotal study

Key management team

Christian Itin, Chief Executive (formerly CEO of Micromet)
Martin Pule, Founder and Chief Scientific Officer
David Brochu, Chief Technical Officer (formerly VP of Technical Operations at Kedrion SpA)
Edgar Braendle, Chief Development Officer (formerly CMO at Sumitomo Dainippon Pharma Oncology)

Founder

Martin Pule, Clinical Senior Lecturer in the Dept. of Haematology at UCL Cancer Institute and Honorary Consultant in Haematology at University College London Hospital

For more information see https://www.autolus.com/about-us/executive-team

Unless stated all financials at September 2021, employee numbers March 2021
* Source; Autolus Corporate Presentation August 2021
**Key competitors and risks: Syncona team view

UCL Syncona

Investment thesis

- No CAR-T therapy approved for adult ALL patients
- AUTO1 has a differentiated safety profile and improved persistence to address limitations of current T cell therapies
- AUTO4 targeting T-cell lymphoma, a setting where there are currently no approved T cell therapies and substantial unmet clinical needs

Unmet medical need

- In lead programme of AUTO1, only 30-40% of patients with aALL achieve long term remission with combination chemotherapy, the current standard of care*

Market opportunity*

- 8,400 patients p.a. in lead programme of aALL (estimated new patients globally diagnosed per annum)
- Estimated relapsed refractory adult ALL patient population, US/EU: 3,000

Freeline Therapeutics

Seeking to deliver constant high protein expression levels with curative potential across a broad pipeline of systemic diseases; opportunity to deliver curative gene therapy

Board Seat	1 (Chair)
Date of Founding	2015
Date of Syncona investment	2015
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£167.7m
No. of employees	250+

Competitor Landscape

uniQure, Spark, 4DMT, Roche, AVROBIO, Pfizer, Sanofi/Regeneron

Key risks
- Highly competitive environment
- Differentiated product required
- Complex manufacturing

Clinical pipeline

Rentschler Biotechnologie | UCL | Syncona

Key management team

Michael Parini, CEO (former Chief Administrative, Legal and Business Development Officer at Vertex)
Pamela Foulds, CMO (formerly CMO of Aegerion Pharmaceuticals)
Alison Long SVP, Head of Clinical Development (formerly Head of Clinical Research and Development, Spark Therapeutics)
Professor Amit Nathwani, Founder and interim Chief Scientific Officer. Prof. Nathwani is renowned for his pioneering work on gene therapy for Haemophilia B, and was first to show successful correction of bleeding diathesis in patients with severe Haemophilia B
Markus Hörer, Founder and Chief Technology Officer (over 30 years' experience working in AAV biology, as well as over 23 years' experience in industrial vaccine and biologics development)
James Bircher, Chief Technical Operations Officer (Formerly CTO at Abeona Therapeutics Inc.)
Mark Baldry, Chief Commercial Officer (formerly Senior VP of Global Marketing & Commercial Operations at Amicus Therapeutics Inc)

Founders

Professor Amit Nathwani, as above
Markus Hörer, as above, brought the Rentschler manufacturing platform to Freeline

For more information see: https://www.freeline.life/about-us/our-team/

Investment thesis

- To deliver therapies for a broad pipeline of systemic diseases which require the delivery of high protein expression levels, with the aim of curing and transforming patients' lives.

Unmet medical need

- Significant number of systemic diseases with genetic drivers which have poor or no treatment options
- Current standard of care in clinical programmes of Haemophilia B and Fabry disease is Enzyme Replacement Therapy (ERT); requires regular administration, protein activity does not remain stable

Market opportunity*

- 9,000 patient opportunity in lead programme in Haemophilia B
- 9,000 patient opportunity in Fabry's disease
- 6,000 patient opportunity in Gaucher's
- 38,000 patient opportunity in Haemophilia A

Unless stated all financials at September 2021, employee numbers March 2021
*Source: Freeline Corporate Presentation August 2021
Key competitors and key risks: Syncona team view

Gyroscope Therapeutics

Global clinical-stage company developing gene therapy beyond rare disease

Board Seat	1 (as Chair)
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	Series C
Stage	Clinical
Syncona capital invested	£113.1m
No. of employees	160+

Competitor Landscape

gemini, Apellis, janssen, IVERIC BIO

Key risks
- Highly innovative concept
- Biological link to clinical outcome

Clinical pipeline

Key management team

Khurem Farooq, Chief Executive (formerly SVP of Immunology and Ophthalmology at Genentech)
Nadia Waheed, Chief Medical Officer (formerly Director of the Boston Image Reading Center and Consultant at the New England Eye Center, Tufts University School of Medicine)
Jane Hughes, Chief Scientific Officer (formerly Senior Director of Integrated Drug Discovery at Charles River)
Ian Pitfield, SVP, Technical Operations (formerly project leadership in GSK's cell and gene therapy CMC platform)
Jessica Stitt, CFO (formerly Vice President of Finance and Operations, MyoKardia)
Ed Lang, Chief Business Officer (formerly Corporate Affairs Adviser, Sana Biotechnology)

Founders

Peter Lachmann, former Sheila Joan Smith Professor of Immunology at the University of Cambridge (deceased)
David Kavanagh, Professor Of Complement Therapeutics at National Renal Complement Therapeutics Centre
Andrew Lotery, Professor of Ophthalmology within Medicine at the University of Southampton

Scientific Advisory Board

Keith Peters, David Kavanagh, Douglas Fearon, Jean Bennett, Alberto Auricchio, Pete Coffey, Claire Harris, Robert Maclaren, Matthew Pickering, David Steel and Timothy Stout
For more information see: https://www.gyroscopetx.com/scientific-advisory-board/

Investment thesis

- Seeking to take application of gene therapy beyond rare diseases to treat dry AMD sub-retinally

Unmet medical need

- AMD is one of the leading causes of permanent vision impairment for people aged 65 and older with no approved treatments

Market opportunity*

- Initial population of an estimated 3.5 million people in the US & EU5 with GA, late stage dry AMD

Unless stated all financials at September 2021, employee numbers March 2021
*Gyroscope analysis
Key competitors and key risks: Syncona team view

Achilles Therapeutics

Differentiated cell therapy approach targeting solid tumours utilising bioinformatics and TILs to target clonal neoantigens for personalised treatments

Board Seat	N/A
Date of Founding	2016
Date of Syncona investment	2016
Valuation basis	NASDAQ
Stage	Clinical
Syncona capital invested	£60.7m
No. of employees	150+

Competitor Landscape

gritstone IOVANCE BIOTHERAPEUTICS InstilBio TURNSTONE BIOLOGICS

Key risks
- Highly innovative concept in emerging space
- Complex manufacturing
- Increasing competition

Clinical pipeline

Key management team

Iraj Ali, Chief Executive (former Syncona Partner)
Karl Peggs, Founder and Chief Medical Officer
Sergio Quezada, Founder and Chief Scientific Officer
Edwin Moses, Chair (formerly CEO at Ablynx)

Founders

Karl Peggs, Professor of Transplant Science and Cancer Immunotherapy at UCL Cancer Institute, Scientific Director of the NIHR Blood and Transplant Research Unit for Stem Cells and Immunotherapies, and Clinical and Scientific Director of the Sir Naim Dangoor Centre for Cellular Immunotherapy at UCLH
Mark Lowdell, Director of the Centre for Cell, Gene & Tissue Therapeutics at the Royal Free and Professor of Cell & Tissue Therapy at UCL
Charles Swanton, Royal Society Napier Professor of Cancer and consultant thoracic oncologist at UCL Hospitals, Chief Clinician at Cancer Research UK (CRUK) and Group Leader of the Cancer Evolution and Genome Instability Laboratory at CRUK and the Francis Crick Institute
Sergio Quezada, Professor of Cancer Immunology and Immunotherapy at University College London Cancer Institute and CRUK senior research fellow

Scientific Advisory Board

Dr Elizabeth M. Jaffee, Dr Scott Antonia and Dr Christopher A. Klebanoff

For more information, please see https://achillestx.com/about-us

Investment thesis

- TILs have shown convincing efficacy in solid tumours*
- Leveraging clonal neoantigens to develop patient specific immunotherapies to increase response rates and reduce risk of relapse

Unmet medical need

- Lung cancer has limited treatment options and is the leading cause of cancer deaths

Market opportunity

- 234,000 patient opportunity in non-small cell lung cancer**
- In 2021, over 207,000 patients are expected to be diagnosed with melanoma in the US***

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view
* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131487/pdf/nihms286994.pdf
** https://pubmed.ncbi.nlm.nih.gov/33600992/
*** https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf

Anaveon Therapeutics

Exploiting the power of cytokines to orchestrate immune responses by using protein engineering with the potential to create to create safe and effective treatments for various diseases

Board Seat	2 (inc. Chair)
Date of Founding	2017
Date of Syncona investment	2019
Valuation basis	Series A
Stage	Clinical
Syncona capital invested	£19.5m
No. of employees	10+

Competitor Landscape

Roche SANOFI Alkermes NEKTAR neoleukin

Key risks
- Multiple players and highly competitive
- Strategy for differentiation and clinical / commercial positioning
- Clinical risk

Clinical pipeline

Key management team

Andreas Katopodis, Chief Executive and Founder (former Director in the Autoimmunity, Transplantation & Inflammation group at the Novartis Institutes for BioMedical Research)
Christoph Bucher, Chief Medical Officer (Previously at Roche pRED Immunology, where he led the transition to the late-stage development of Crovalimab)
Christoph Huber, Chief Scientific Officer (previously held leadership positions at Roche, Pfizer and COI Pharmaceuticals)

Co-founder

Andreas Katopodis (as above)

Scientific Advisory Board

Jane K. Osbourn, **Wolf H. Fridman and Robert Hawkins**

For more information see: https://anaveon.com/board/

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view
* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4938354/
** https://www.cancernetwork.com/view/managing-toxicities-high-dose-interleukin-2

Syncona

Investment thesis

- Developing a selective IL-2 agonist with improved administration and toxicity burden
- Wide potential utility across multiple oncology indications in wider markets*

Unmet medical 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**

SwanBio Therapeutics

Developing leading-edge gene therapies to deliver dramatic clinical efficacy for the treatment of neurological diseases

Board Seat	2 (inc. Chair)
Date of Founding	2018
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-Clinical
Syncona capital invested	£65.1m
No. of employees	40+

Competitor Landscape

Key risks
- Slowly progressing disease
- Complex manufacturing

Key management team

Tom Anderson, Chief Executive (formerly Chief Commercial Strategy Officer at Sage Therapeutics)
Karen Kozarsky – Chief Scientific Officer (former President of Vector BioPartners and VP of R&D at RegenX)
Steven Zelenkofske – Chief Medical Officer (former Chief Medical Officer of Achillion Pharmaceuticals and UniQure)
Scott McMillan, Chief Technical Officer, (formerly Chief Executive Officer of Saliogen Inc. and Chief Operating Officer at UniQure)

Founders

Florian Eichler, Director of the Leukodystrophy Service and of the Center for Rare Neurological Diseases at Massachusetts General Hospital and Associate Professor of Neurology, Harvard Medical School
Rachel Salzman, Former Chief Science Officer of The Stop ALD Foundation
Karen Kozarsky, (as above)

For more information see: https://www.swanbiotx.com/

Unless stated all financials at September 2021, employee numbers March 2021
* Adrenomyeloneuropathy
** SwanBio analysis
Key competitors and risks: Syncona team view

Investment thesis

- Gene therapy has the potential to be transformational in neurology
- Lead programme targeting AMN*, an inherited neurodegenerative disease in which the causative gene is definitively known and well characterised
- One-off delivery mechanism and multiple tractable pipeline programmes

Unmet medical need

- Hundreds of single gene disorders with poor or no treatment options
- Lead programme targeting one of the most common monogenic neurological disorders, a severely debilitating progressive movement disorder with no available therapies

Market opportunity**

- AMN impacts 8,000-10,000 patients in the US and EU5

Quell Therapeutics

Engineered cell therapy company addressing immune dysregulation

Board Seat	2 (inc. Chair)
Date of Founding	2019
Date of Syncona investment	2019
Valuation basis	Series A
Stage	Pre-Clinical
Syncona capital invested	£45.2m
No. of employees	70
Competitor Landscape	SONOMA, gentibio, abata, Sangamo, Kyverna, MOZART

Key risks
- Highly innovative concept in emerging space
- Complex manufacturing

Key management team

Iain McGill, CEO (formerly on the Executive Committee and as Head of Europe and Rest of World for Jazz Pharmaceuticals)
Dominik Hartl, CMO (former Therapeutic Area Head at Novartis Institutes for Biomedical Research)
Tracey Lodie, CSO (Former CSO at Gamida Cell)
Nathalie Belmonte, SVP Research & Translation (formerly Chief Operating Officer at Promethera Biosciences)
Luke Henry, VP Operations & Corporate Development (formerly Senior Director of Business Development & Strategy at Neon Therapeutics)
Bernd Schmidt, VP Product Delivery (formerly MPD Leader at GSK Stevenage with overall accountability for the CMC development, governance and end to end supply chain)
Marc Martinez-Llodella Founder and Vice President Biology (former Senior Lecturer at King's College London)

Founders

Giovanna Lombardi, Professor of Human Transplant Immunology at King's College London
Marc Martinez-Llodella, (as above)
Alberto Sanchez-Fueyo, Head of the Liver Sciences Department at King's College London
Hans Stauss, Director of the Institute of Immunity & Transplantation at UCL
Emma Morris, Professor of Clinical Cell and Gene Therapy at UCL
Elmar Jaeckel, Co-Leader Liver Transplant program MHH and Group Leader "Immune tolerance" in the Department of Gastroenterology, Hepatology and Endocrinology at Hannover Medical School.
For more information see: https://quell-tx.com/about/

Investment thesis

- 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*
- Potential pipeline to treat serious, chronic conditions mediated by the immune system
- Potential to be first-in-class in CAR-Tregs; an early mover in the space

Unmet medical need

- First programme addressing solid organ transplant; current standard of care to prevent transplant rejection is life-long immunosuppression, resulting in long-term side effects which materially impact quality of life and long-term survival

Market opportunity

- 15,000 liver transplants p.a across US and Europe**

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view
* https://www.ema.europa.eu/en/clinical-investigation-immunosuppressants-solid-organ-transplantation
** Source: OPTN/SRTR 2016 Annual Data report: Liver; EDQM Volume 20 2015

OMass Therapeutics

Using novel biochemistry techniques, native mass spectrometry and custom chemistry to deliver novel medicines against highly validated but inadequately drugged targets, with a focus on immunological and rare diseases

Board Seat	2 (inc. Chair)
Date of Founding	2016
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Drug discovery
Syncona capital invested	£21.5m
No. of employees	30+
Competitor landscape Crinetics Pharmaceuticals	
Key risks - Attrition of potential drugs	

Key management team

Rosamund Deegan, Chief Executive (former Chief Business Officer at Bicycle Therapeutics, where she established the company's Boston-based subsidiary)
Ali Jazayeri, Chief Scientific Officer (Previously Chief Technology Officer at Heptares)
Jonathan Hopper, VP of Platforms and Founder; worked with Carol Robinson on developing mass spectrometry

Founders

Professor Dame Carol Robinson, Founder and Scientific Adviser; recognised for using mass spectrometry to further research into the 3D structure of proteins and their complexes and is the first female Professor in Chemistry at the University of Cambridge
Jonathan Hopper, (as above)

For more information see: https://omass.com/our-team/

Investment thesis

- Opportunity to develop differentiated small molecule drugs leveraging a world-leading Native Mass Spectrometry platform which enables unique insights into membrane proteins and protein complexes such as GPCRs and Solute Carriers – classes of targets that have been historically difficult to drug in spite of high clinical relevance and unmet need.

Unmet medical need

- Programmes are all in indications with significant unmet medical need

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view

Resolution

Developing macrophage cell therapies to repair inflammatory organ damage, including treatment of end-stage chronic liver disease.

Board Seat	2 (inc. Chair)
Date of Founding	2020
Date of Syncona investment	2018
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£7.4m
No. of employees	10+
Competitor landscape	carisma THERAPEUTICS, SHORELINE biosciences, BlueRock THERAPEUTICS

Key risks
- Highly innovative concept in an emerging space
- Future competition

Key management team

Ed Hodgkin, Chair & CEO (Syncona Partner)
Evelien Stalmeijer, Vice President of Translation (formerly of eXmoor Pharma)
Lara Campana, Director of Macrophage Biology (visiting scientist at the University of Edinburgh)
Alex Armesilla, Director of Cell Engineering (formerly of Censo Biotechnologies and GSK)
Philip Starkey Lewis, Director of Pharmacology (visiting scientist at the University of Edinburgh)
Gonzalo Garcia, Chief of Staff (Syncona Partner)

Founders

Professor Stuart Forbes, Professor of Transplantation and Regenerative Medicine at the University of Edinburgh. Professor Forbes has pioneered the research of macrophage cell therapy for liver disease.
Professor John Campbell, Director of Tissues, Cells, and Advanced Therapeutics at the ScottishNational Blood Transfusion service. Professor Campbell has worked on the therapeutic use ofimmune cells for 30 years.

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view

For more information see: https://resolution-tx.com/

Investment thesis

- An opportunity to create the leading inflammation-focused macrophage cell therapy business, focusing initially on treatment of liver cirrhosis. The goal is to repair the livers of patients sufficiently to reduce the risk of decompensation. Future opportunity lies in lung and kidney repair in chronic fibrotic disease.

Unmet medical need

- Chronic inflammatory organ damage represents a major burden to patients. If left untreated, liver cirrhosis will often progress to decompensation through significant loss of liver function. Today there are no efficacious treatments to prevent deterioration in the latter stages of the disease, thus leaving costly and burdensome liver transplantation often as the only option.

Market opportunity

- New diagnoses of liver cirrhosis affect hundreds of individuals per million of population.

Purespring

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

Board Seat	2 (inc. Chair)
Date of Founding	2020
Date of Syncona investment	2020
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£18.5m
No. of employees	c.10
Competitor landscape	NOVARTIS, calliditas THERAPEUTICS, REATA PHARMACEUTICALS, SANOFI, OMEROS, TRAVERE THERAPEUTICS, Apellis

Key risks
- Highly innovative concept in emerging space
- Clinical risk by addressing non-monogenic disorders

Key management team

Richard Francis, CEO (previously CEO of Sandoz, and a member of the Executive Committee of Novartis)
Moin Saleem, CSO and Founder (leader of Bristol Renal, a glomerular research group of approximately 45 researchers)
Ronny Renfurm, CMO (former Executive Director at Astellas Pharma)
Julian Hanak, CDO (formerly of Biogen, Nightstar)

Founders

Moin Saleem (see above)
Mauro Giacca, Professor of Cardiovascular Sciences at the School of Cardiovascular Medicine & Sciences, King's College London

University of BRISTOL Syncona

Investment thesis

- A number of chronic kidney diseases are poorly addressed by existing therapies, which are primarily based around the lowering of blood pressure and often progressing to dialysis and kidney transplantation
- Purespring is developing disease-modifying therapies for a number of monogenic and non-monogenic kidney diseases

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view

Neogene

Building a differentiated small molecule portfolio based on a unique drug discovery platform leveraging native Mass Spectrometry.

Board Seat	1
Date of Founding	2018
Date of Syncona investment	2020
Valuation basis	Series A
Stage	Pre-clinical
Syncona capital invested	£11.4m
No. of employees	40+
Competitor landscape	PACT, Adaptive, TCR cure

Key risks
- Complex early stage technology
- Complex manufacturing
- Highly competitive field

Key management team

Carsten Linneman, CEO (formerly co-founder of T-Cell Factory B.V.)
Christopher Wilfon, Chief Business Officer (co-founder of Two River Consulting)
Brent Pfeiffenberger, COO (former senior Vice President, U.S. Oncology, Bristol Myers Squibb)
Gavin Bendle, Vice President R&D (former Senior Director of Cell Therapy at Kite Pharma)
Mauro Azanzi, Vice President Clinical Development (former Executive Medical Director, Kite Pharma)
Han Lee, Chief Financial Officer (formerly of Arcellx)

Founders

Ton Schumacher, Principal Investigator at The Netherlands Cancer Institute, Oncode Institute member, and Professor of Immunotechnology at Leiden University Medical Center
Carsten Linneman (see above)

For more information see: https://www.neogene.com/

Investment thesis

- The company is developing an engineered T Cell Receptor (TCR) therapeutic approach for solid tumours based on a patient's own neoantigens (personalised autologous cell therapy)

Unmet medical need

- Limited treatment options for relapsed/refractory patients with advanced solid tumours that have progressed through front line therapies.

- Cell therapies offer the potential for deep and durable responses in the populations as evidenced by Iovance's Tumor Inflitrating Lymphocyte therapy. We believe Neogene's approach should result in a more efficacious product that can address a larger number of patients

Market opportunity

- The company has not yet announced its target indications within the solid tumour field

Unless stated all financials at September 2021, employee numbers March 2021
Key competitors and risks: Syncona team view

Appendix 3 – Sustainability

Sustainability

Syncona

Signatory of:

PRI Principles for Responsible Investment

Progress in year so far

- PRI signatory from October 2021
- Responsible Investment Policy rolled out to majority of portfolio

Ongoing priorities for FY22

- Syncona Ltd emissions target to be published
- First year of TCFD alignment
- Responsible Investment Policy roll-out to full portfolio

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 has been critical in equipping us with the ability to respond to emergencies. By allowing us to use donations flexibly, our frontline services have been able to respond quickly and effectively to the pandemic.”

Marie Curie

£36.4m

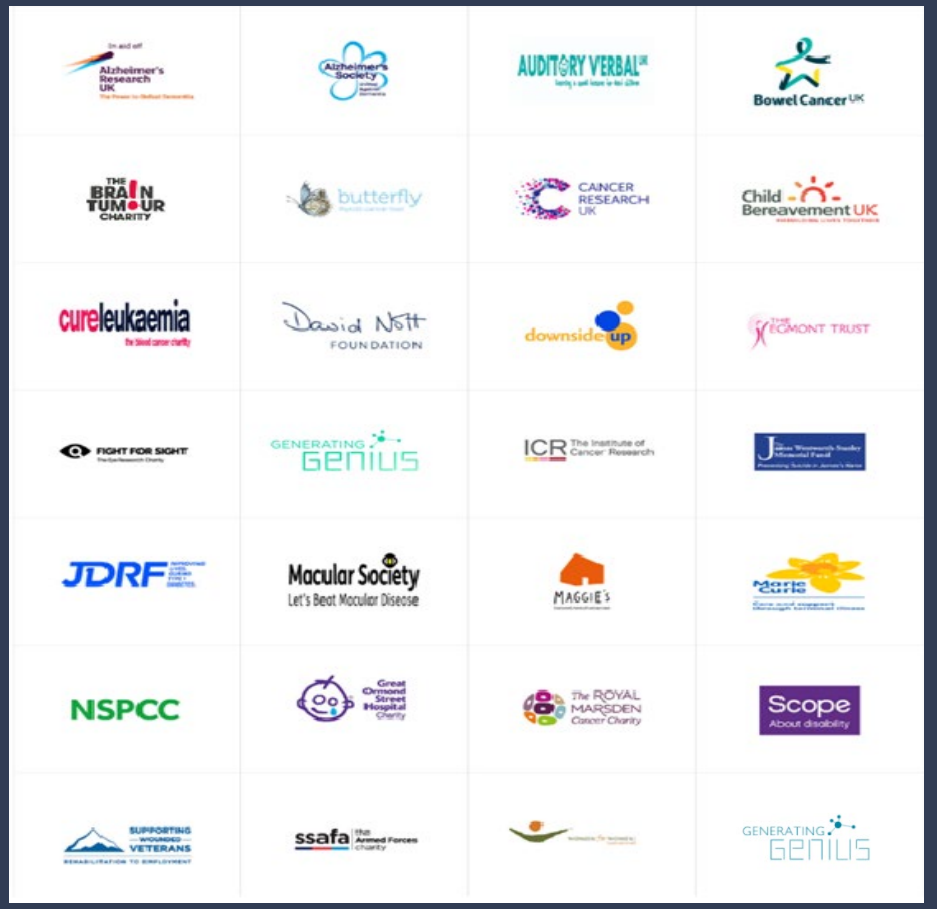
Donations since 2012[1]

28

Charities supported

0.35%

of Syncona’s NAV donated on an annual basis



1 – Includes FY21 donation