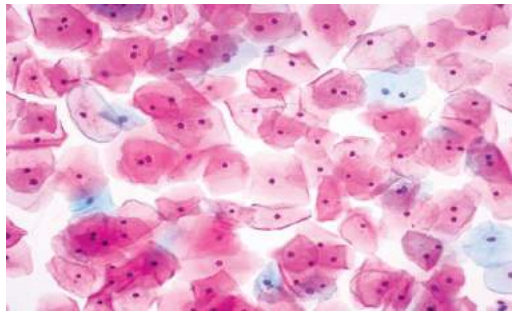

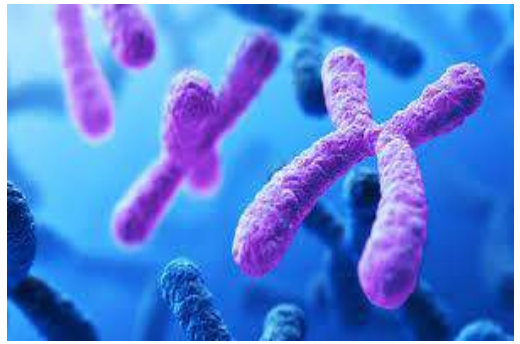

Welcome

Cells, Genes and Vaccines: Developing the Treatments of Tomorrow

London Bioscience Innovation Centre

Tuesday 15th November 2022

London BioScience Innovation Centre

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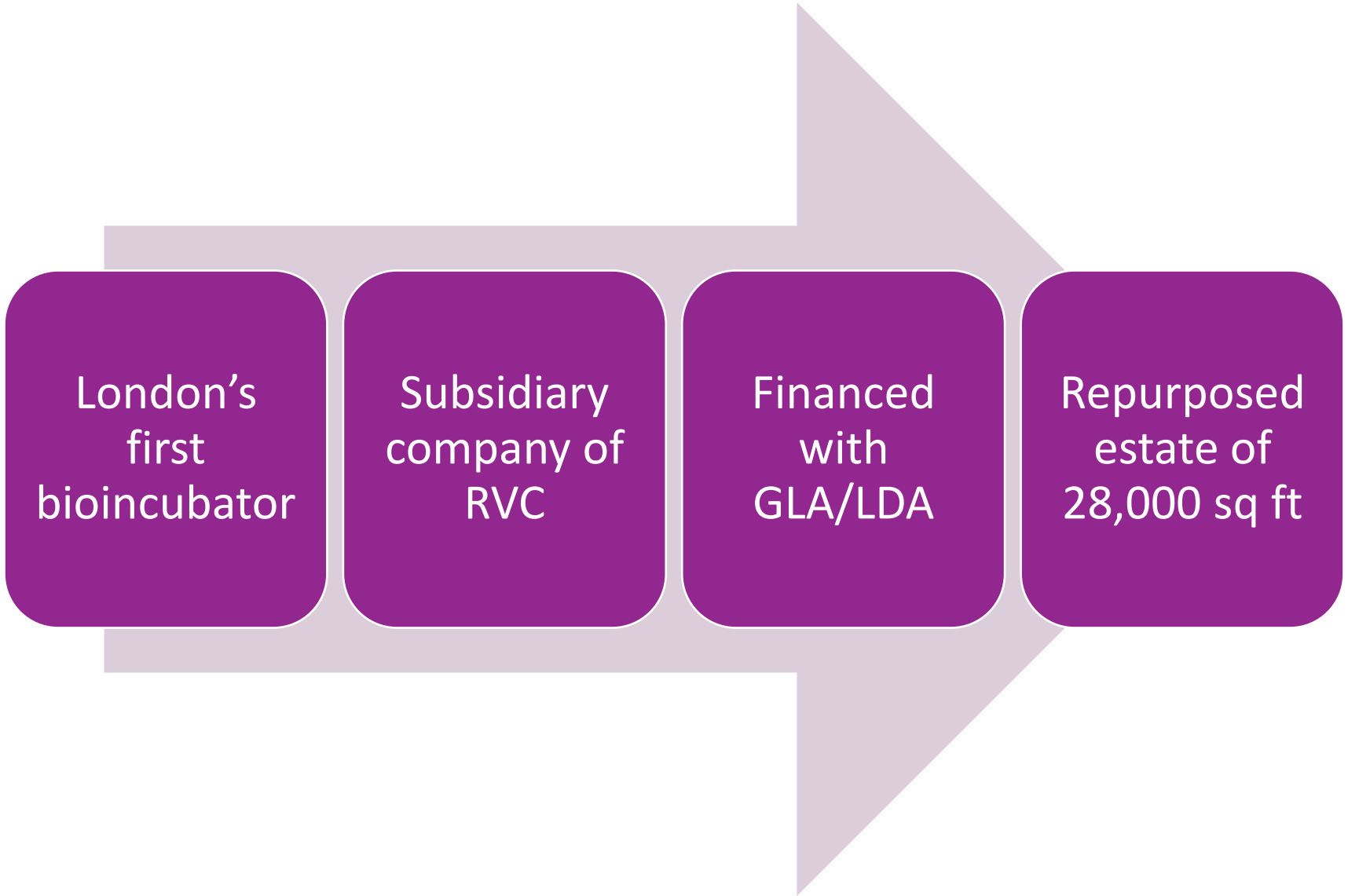
LBIC – 22 years of Leadership in Bioinnovation



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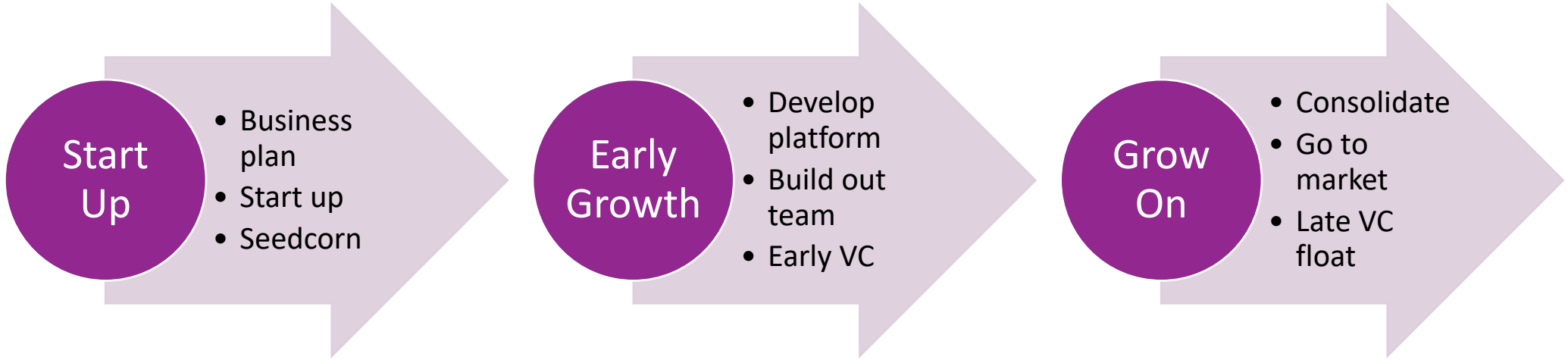
Our Approach



Virtual presence Hot desks Personal Occupancy Desks	Labs 250sf – 1100 sq ft Offices 100sf – 790 sq ft Lab operations services	Labs 3000 sq ft Office suites / boardrooms Lab operations services

Business Support Network, Events, Networking, Seminars, Clinics

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LBIC Impacts

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Innovation Centre

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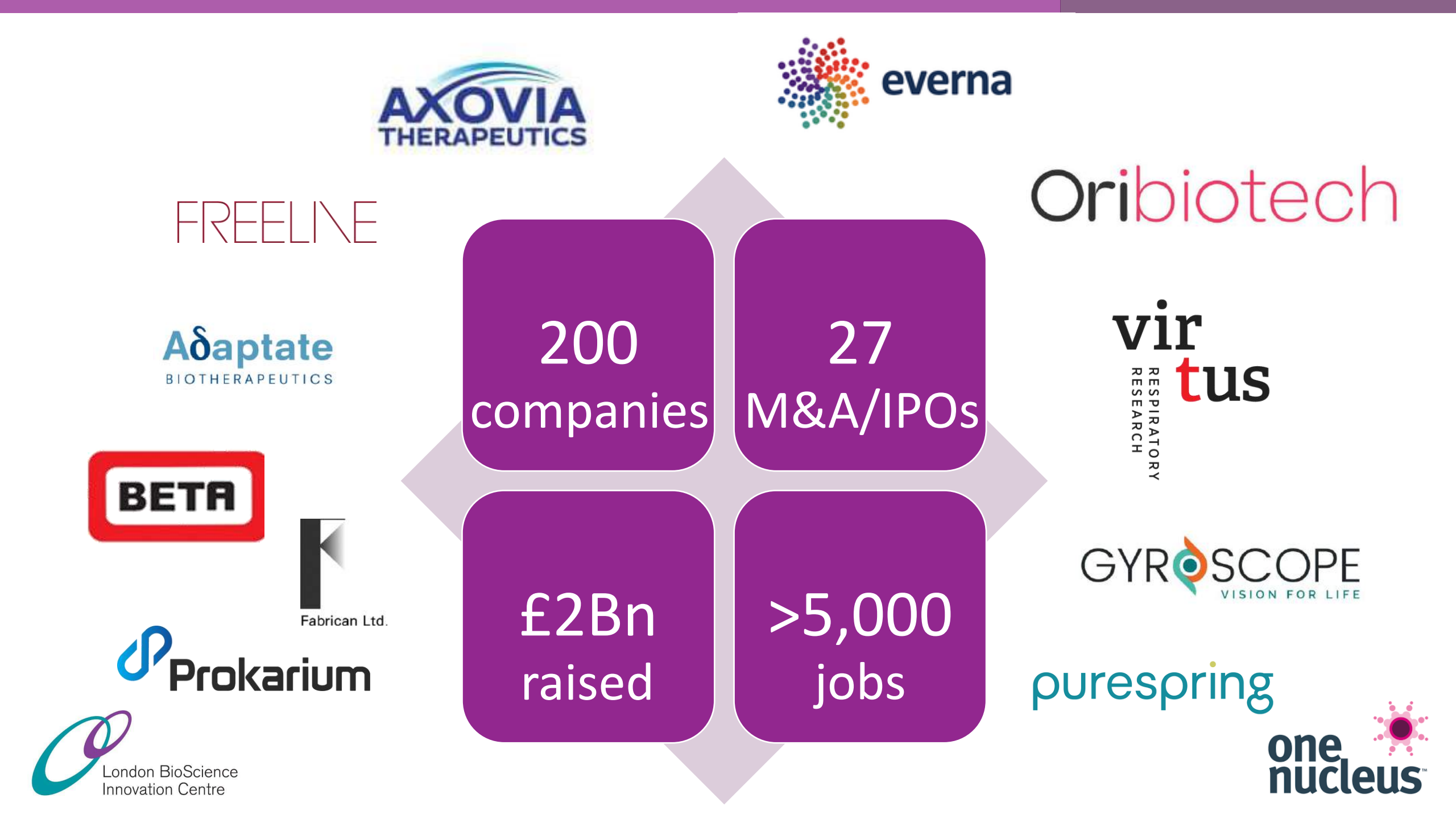
AXOVIA THERAPEUTICS
everna
FREELINE
Oribiotech
Adaptate BIOTHERAPEUTICS
200 companies
27 M&A/IPOs
vir tus RESPIRATORY RESEARCH
BETA
Fabrican Ltd.
£2Bn raised
>5,000 jobs
GYROSCOPE VISION FOR LIFE
Prokarium
purespring
London BioScience Innovation Centre
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Future Plans

- Commit to operate and upgrade our primary site at Camden
- Operate new SME space at CVRM Hawkshead
- Launch new grow-on space in the APEX Building
- Grow from 28,000 sq ft to 68,000 sq ft

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Contact Details

rferrie@rvc.ac.uk

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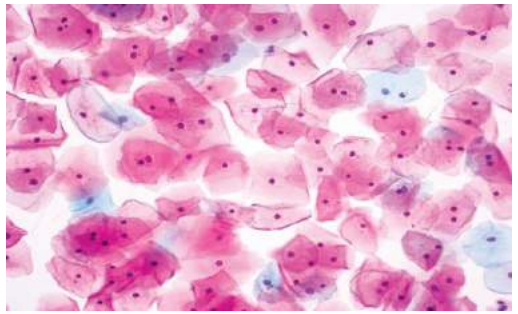

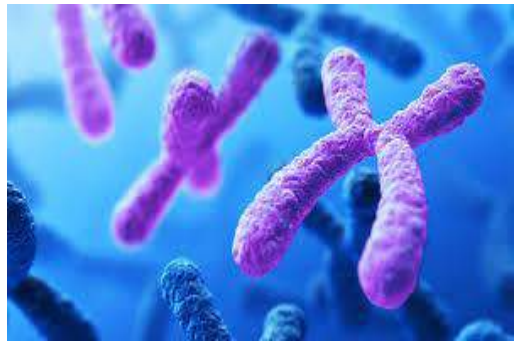

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Royal Veterinary College
University of London

Dirk Werling, BVetMed, DrMedVet, PhD

- Professor of Molecular Immunology
- Director, Centre for Vaccinology and Regenerative Medicine (CVRM)
- @WerlingLab
- https://www.rvc.ac.uk/about/our-people/dirk-werling

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Translational and Early Clinical Development Issues in Cell and Gene Therapy Drug Development

Bams Abila, MSc, MD, PhD, FFPM
Professor of Biologics and ATMPs
Centre for Pharmaceutical Medicine Research
Faculty of Life Sciences and Medicine
King's College London.

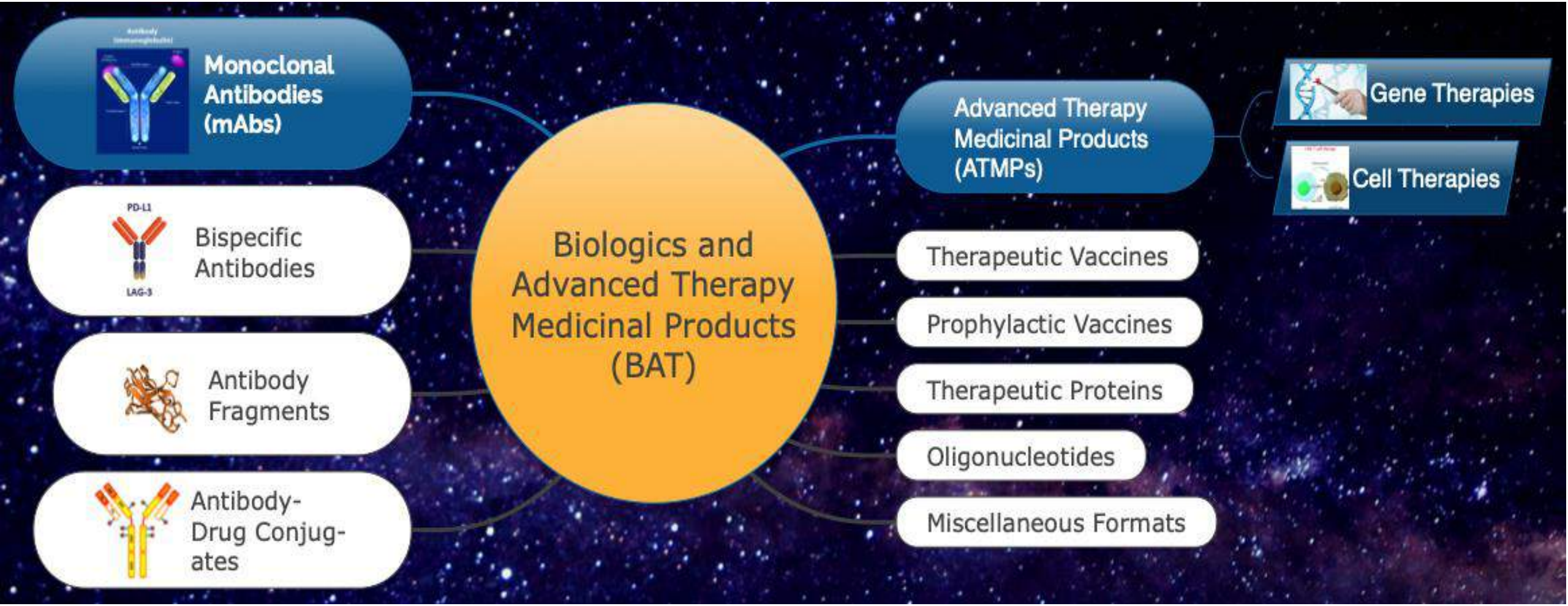
- Professor Bams Abila is a UK-registered physician and clinical scientist with specialisms in clinical pharmacology and pharmaceutical medicine. He has over 15 years' experience of academic medical research and 35 years' experience of pharmaceutical medicine in global drug development leadership roles in Aventis, Pfizer, Astellas, AstraZeneca and GSK among others.

- Since 2017, Prof Abila has provided drug development consultancy services to a wide variety of Pharma, Biotech and CRO companies in the UK and Europe.

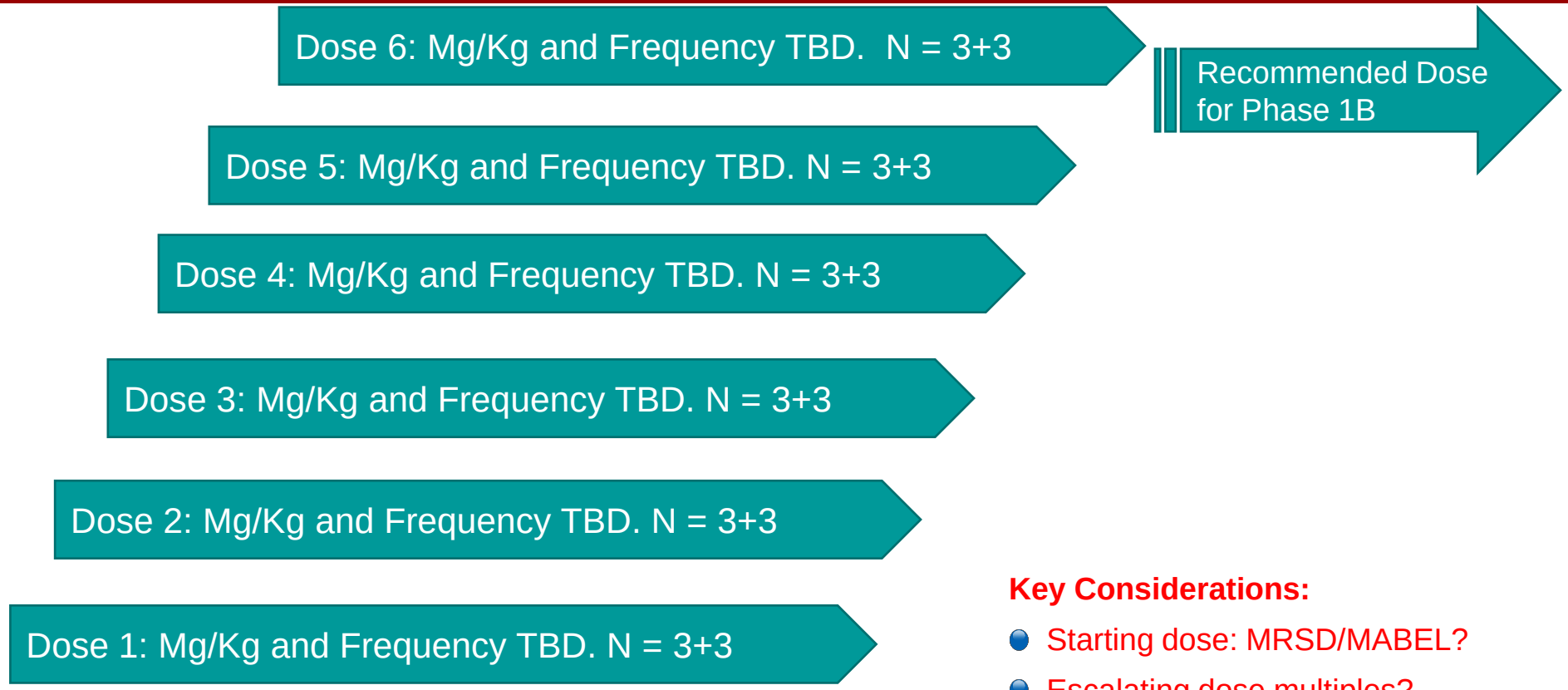
- During his first 15 years in the Pharmaceutical Industry, Prof Abila worked mostly on developing small molecule drugs in various therapy areas. In the last 20 years, Professor Abila's focus has been the development of biologics and advanced therapy medicinal products (ATIMPs) in several therapy areas including oncology, immuno-inflammation, neurology and respiratory disorders.

- His special research interest is in the development and use of ***translational biomarkers*** for decision-making during drug development and for differentiation of medicines in the market.

Kings College London MSc Courses in Pharmaceutical Medicine
Biologics and ATMP (BAT) Module



Typical Example of Biologic Oncology Phase 1 Study



Key Considerations:

- Starting dose: MRSD/MABEL?
- Escalating dose multiples?
- Each patient dosed repeatedly until occurrence of unacceptable AEs or disease progression
- Max tolerated dose (from MID)
- If not MTD, then MFD
- **Biomarkers** for Entry and PD effect.

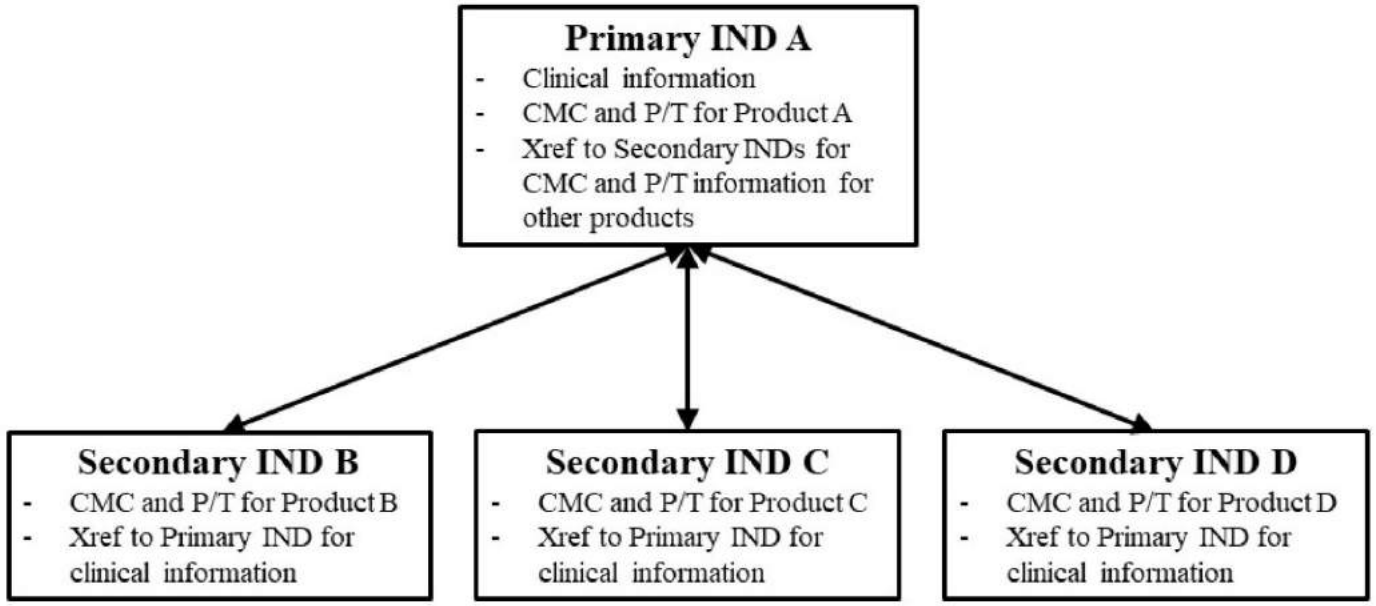
Some Regulatory Challenges in Early Oncology Studies

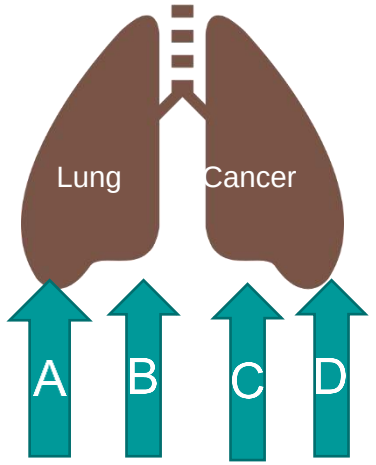
- Insufficient pre-clinical data for clinical protocol decision making
- Ambiguous dose selection decisions (e.g. No MABEL?)
- Personalised manufacturing for individual patients
- Management of severe AEs – e.g. cytokine release syndrome

New FDA Guidance on 'Umbrella' Studies for Early Clinical Dev't of Cell and Gene Therapies (Nov 2022)

- https://www.fda.gov/regulatory-information/search-fda-guidance-documents/studying-multiple-versions-cellular-or-gene-therapy-product-early-phase-clinical-trial
- **Enables testing of different versions of CGT in same disease in one IND (protocol)**

Figure 1: Schematic Representation of the Primary and Secondary IND Framework[6]



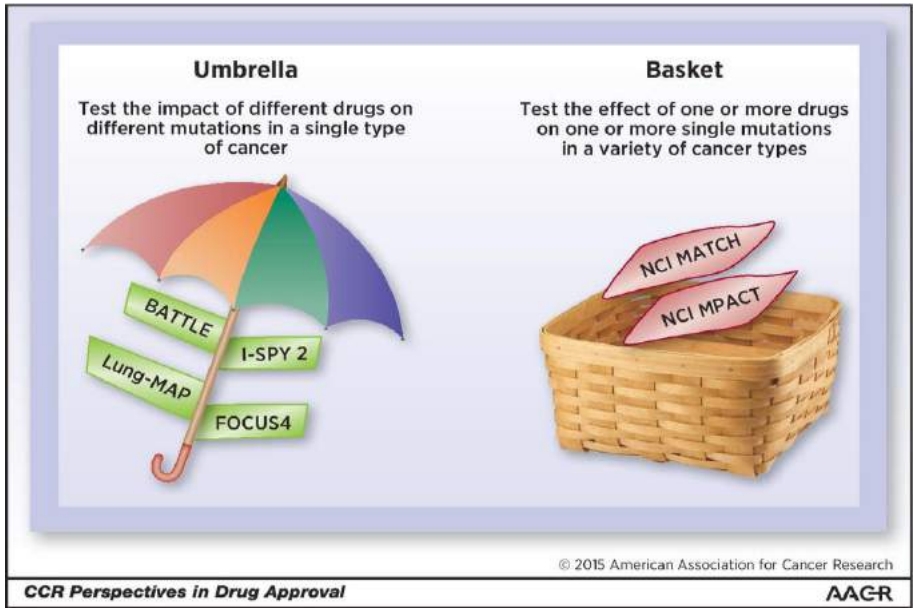


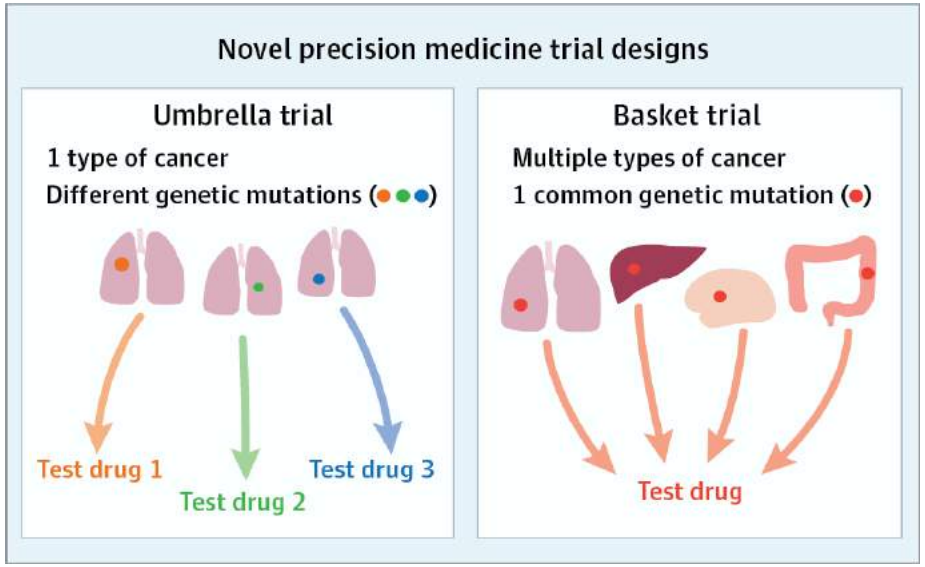
Where A, B, C & D are different versions of the same CGT being studied in the same protocol

Novel Precision Medicine Clinical Study Designs: Umbrella and Basket Design Studies in Oncology

Important Reference: Howard West, JAMA Oncology, March 2017, Volume 3, Number 3, p.423

- **Traditional Ph1 oncology studies involved inclusion of all patients with all types of cancer.**
- **Development of precision mutation diagnostic methods ➔ *precision medicine*: targeting specific drugs for specific mutations in cancer.**
- **Two novel study designs gaining traction are: *umbrella and basket study d*esigns.**
- **Example of Umbrella Design = *PRECISION-Panc* Master Protocol –** Ref: Dreyer SB et al., *PRECISION-Panc*: the Next Generation Therapeutic Development Platform for Pancreatic Cancer; Clinical Oncology, https://doi.org/10.1016/j.clon.2019.07.011





Michael Kyriakides

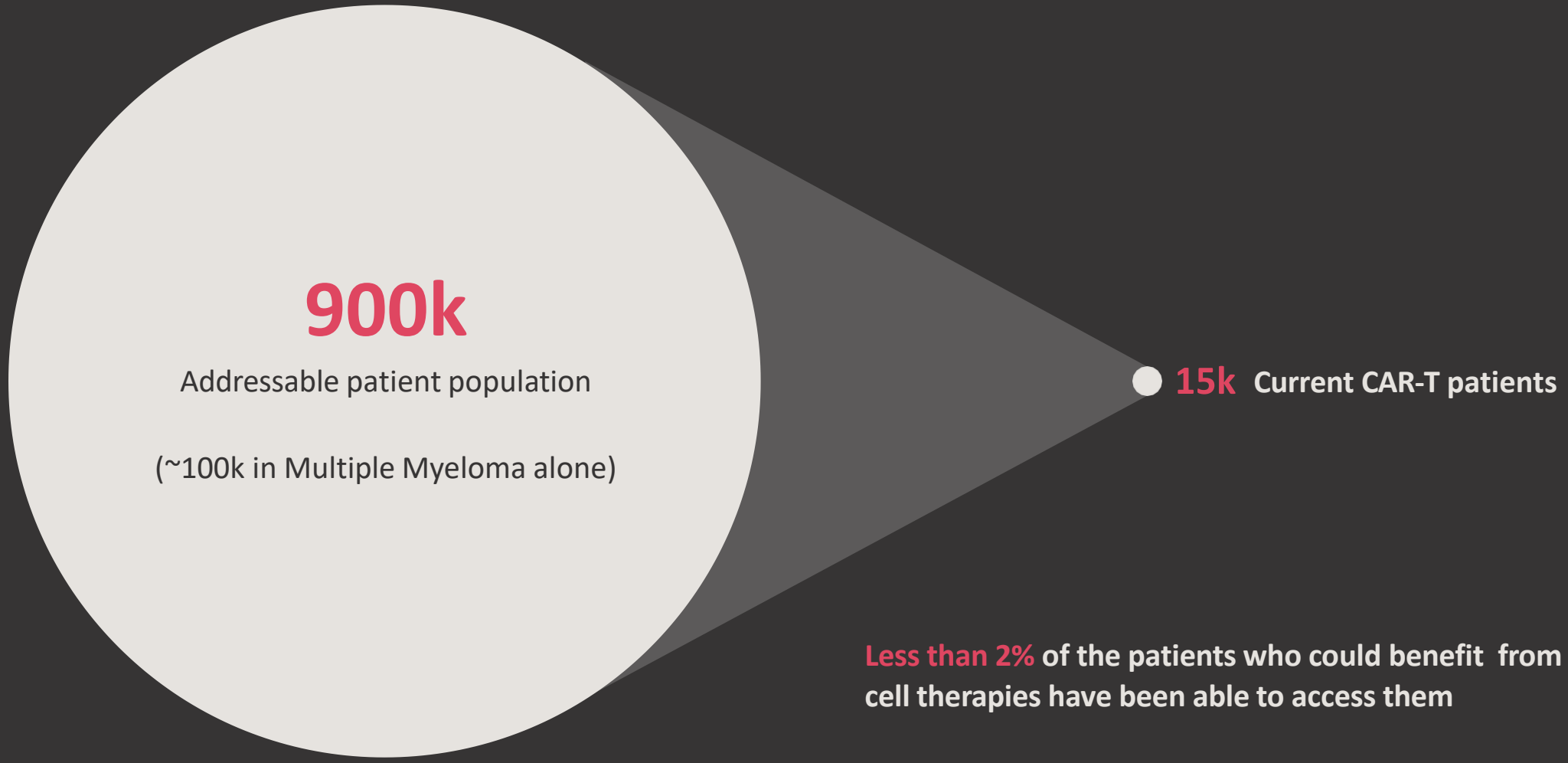
- Investment partner at Syncona, joined in 2018
- Non-executive director of Purespring Therapeutics, observer to the board of Clade Therapeutics. also supporting Freeline Therapeutics and previously supported Azeria, Gyroscope and Nightstar Therapeutics
- Previously Senior Life Sciences Specialist at L.E.K. Consulting and programme / NMR manager at Imperial College London
- PhD in toxicology and metabolic profiling at Imperial College London

Oribiotech

William Raimes
Head of Process Development

A new generation of personalized, living medicines have been clinically proven to have curative potential.

small fraction receive curative treatments.



Less than 2% of the patients who could benefit from cell therapies have been able to access them

Source: McKinsey, Statnews

Manufacturing problems threaten the future of CGTs

Therapy developers and regulators continue to feel the pain of manufacturing challenges

Cost of Goods Is Crucial for the Future of Regenerative Medicine: CAR-T Cell Therapy Provides a Case Study in Perspective

Manufacturing Delays Set Back Autolus' CAR-T Programs by Five Months

Breakthrough Cancer Therapy Stalls in Manufacturing Bottleneck

Novartis still hasn't solved its CAR-T manufacturing issues

Gilead's Second CAR-T Treatment Suffers the Same Issues as Yescarta

Gene therapy costs, manufacturing keeping CBER head 'up at night'

Delays in CAR T-Cell Treatment Cost Patients, Society

Bluebird delays gene therapy launch to 2020, citing manufacturing tweaks

Bluebird Bio delays Zynteglo launch as manufacturing trips up another gene therapy

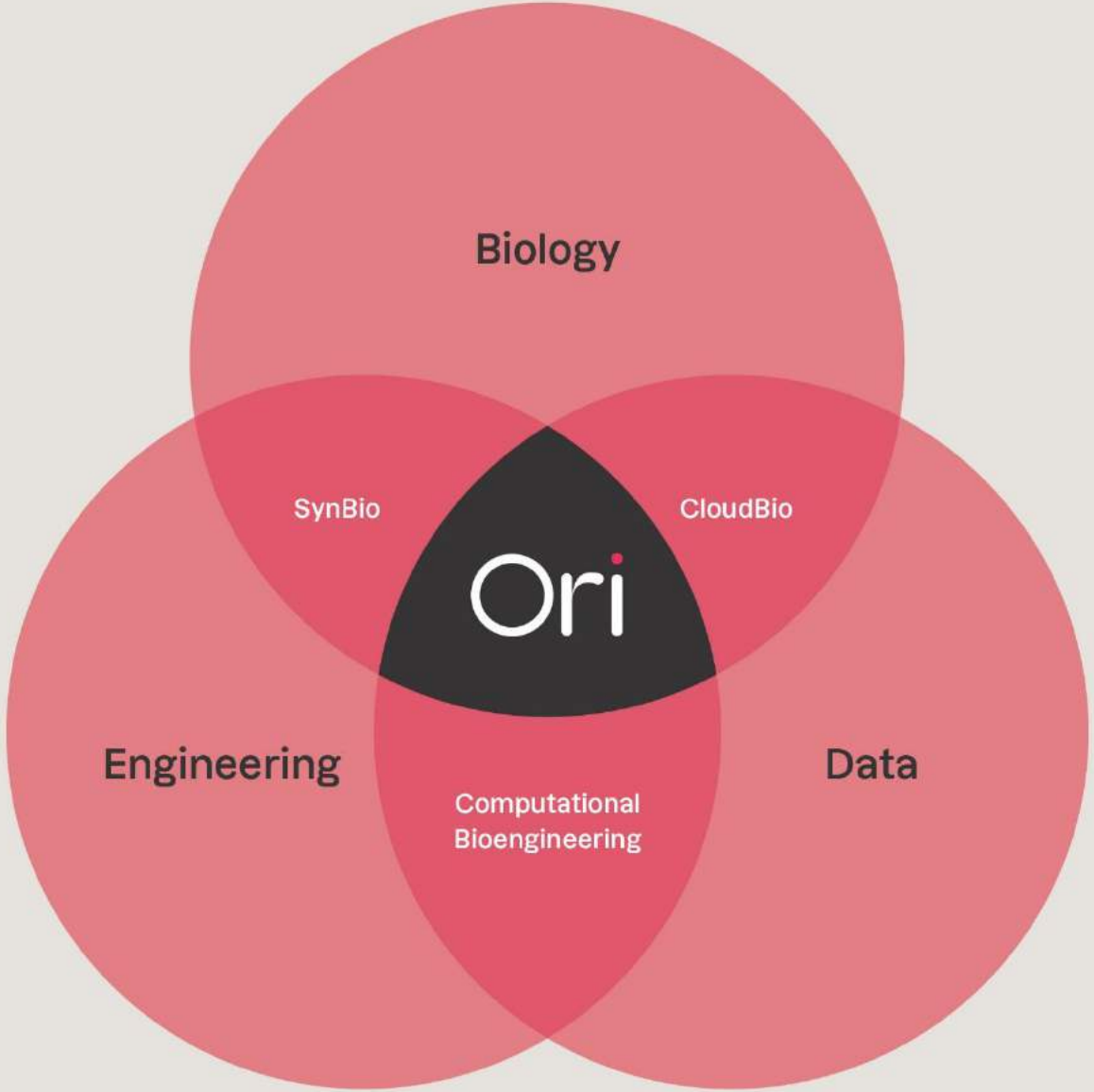
Pfizer, Novartis lead $2 billion spending spree on gene therapy production

Manufacturing difficulties arise for Novartis' CAR-T therapy

For CAR-Ts to be successful, figuring out manufacturing is key

Ori is bringing together a full stack platform combining Biology Engineering and Data to Industrialize Precision Medicines

The current model of fragmented, inflexible, disconnected hardware solutions will not solve this challenge



Current solutions available are not fit for purpose

Ori technology enables a future state of high throughput cell and gene therapy manufacturing

From the Status Quo of Manufacturing		To the Future State of Manufacturing
Large, expensive facilities that are heavily under utilized and require individual regulatory approvals	Production of 30 doses simultaneously per 1000ft^2, seamless tech transfer	Smaller, cheaper, highly utilized facilities with network approval and standardized technology transfer between sites
Highly skilled workforce performing multiple manual fluid transfers and sterile connections	Consumable is fully automatable and designed for full robotic manipulation	Fewer, cheaper people monitoring processes with fully automated sterile connections and fluid handling
Technology borrowed from other industries that is unscalable and inflexible to the needs of CGT products	Bellows-based bioreactor is flexible and can be used across many process steps	Flexible manufacturing technology adapting to the needs of multiple products from clinical to commercial scale
No data integration with paper-based manufacturing execution and manual batch release	Secure connectivity to the Ori Cloud allows real-time process data utilization	Digital integration across cloud native platform enabling full product traceability and continuous process validation

Manufacturing Brighter Futures

Oribiotech Ltd
London Biosciences Innovation Centre
2 Royal College Street London, NW1 0NH

Cells, Genes and Vaccines: Developing the Treatments of Tomorrow

Q&A

Networking reception

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