
SPEAR-heading
THE CANCER
REVOLUTION
1st LIVE VIRTUAL EVENT –
OUR ALLOGENEIC PLATFORM
Thursday, September 9, 2021
Adaptimmune
TRANSFORMING T CELL THERAPY

Disclaimer

This presentation contains “forward-looking statements,” as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect” and other words of similar meaning. These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials; our ability to submit an IND and successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates; the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates; government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates; and our ability to protect our proprietary technology and enforce our intellectual property rights; amongst others. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Annual Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2021 and our other SEC filings.

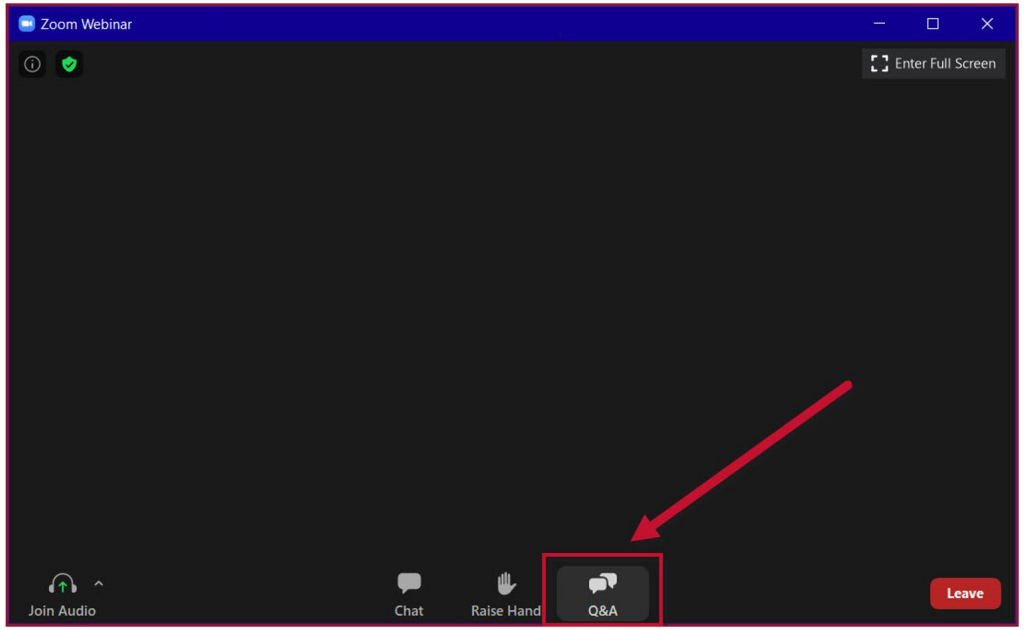
We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

Q&A

- Please send your questions – throughout the presentation – using the Q&A function (see screen grab below)

- The questions will be answered at the end of the presentation



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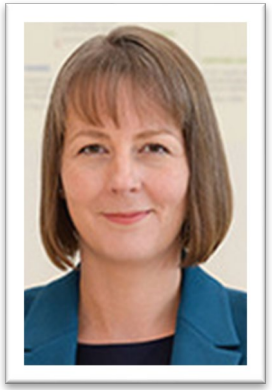
TRANSFORMING T CELL THERAPY

Agenda

Adrian (Ad) Rawcliffe
Chief Executive Officer



Joanna (Jo) Brewer, Ph.D.
SVP, Allogeneic Research

Helen Tayton-Martin, Ph.D., M.B.A.
Chief Business Officer

William (Bill) Bertrand
Chief Operating Officer

Topic	Presenter	Duration ~60 mins
Introduction	Ad Rawcliffe	10 mins
Adaptimmune's allogeneic platform	Jo Brewer	20 mins
Overview of Genentech deal	Helen Tayton-Martin	5 mins
Q&A	Bill Bertrand	20 mins
Closing remarks	Ad Rawcliffe	3 mins

Five-year strategic “2-2-5-2” plan towards curative and mainstream cell therapies

Allogeneic therapy is a key part of our future

Two

marketed SPEAR T-cell products targeting MAGE-A4

- Synovial sarcoma and MRCLS
- Esophageal and EGJ cancers

Two

additional BLAs for SPEAR T-cell products

- Additional indications for MAGE-A4 targeted products
- ADP-A2AFP

Five

autologous products in the clinic

- HiT
- Next-gen TILs
- New targets
- Broader HLA coverage

Two

allogeneic products entering the clinic

- SPEAR T-cell product targeting MAGE-A4
- HiT mesothelin partnered with Astellas

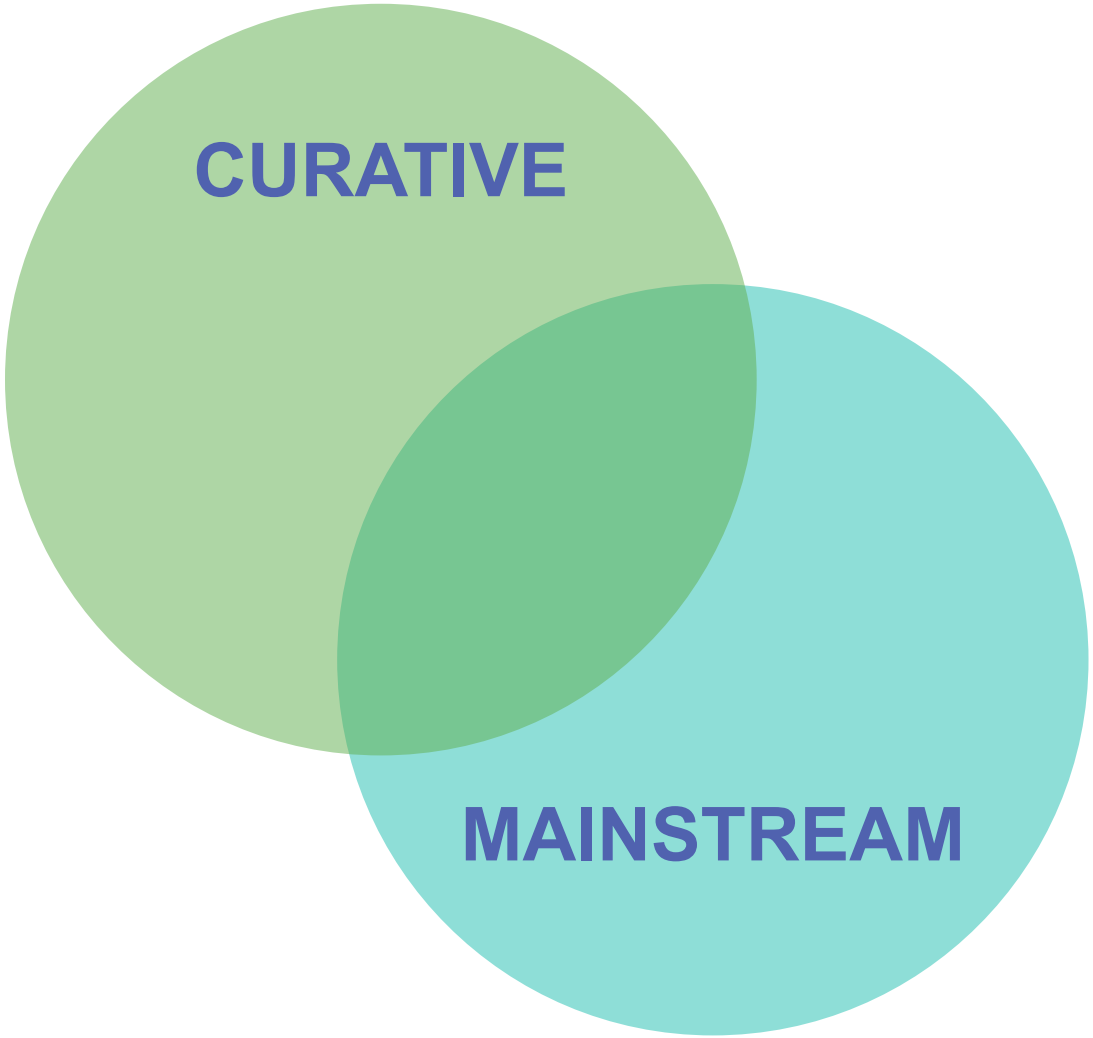
Integrated Cell Therapy Capabilities

Research | Preclinical | Translational | Clinical | CMC | Regulatory | Commercial

EGJ: esophagogastric junction cancer; HiT: HLA-independent T-cell receptor (TCR); TIL: tumor infiltrating lymphocyte; CMC: chemistry, manufacturing, and controls

Five-year strategic “2-2-5-2” plan towards curative and mainstream cell therapies

Allogeneic therapy is a key part of our future



Two

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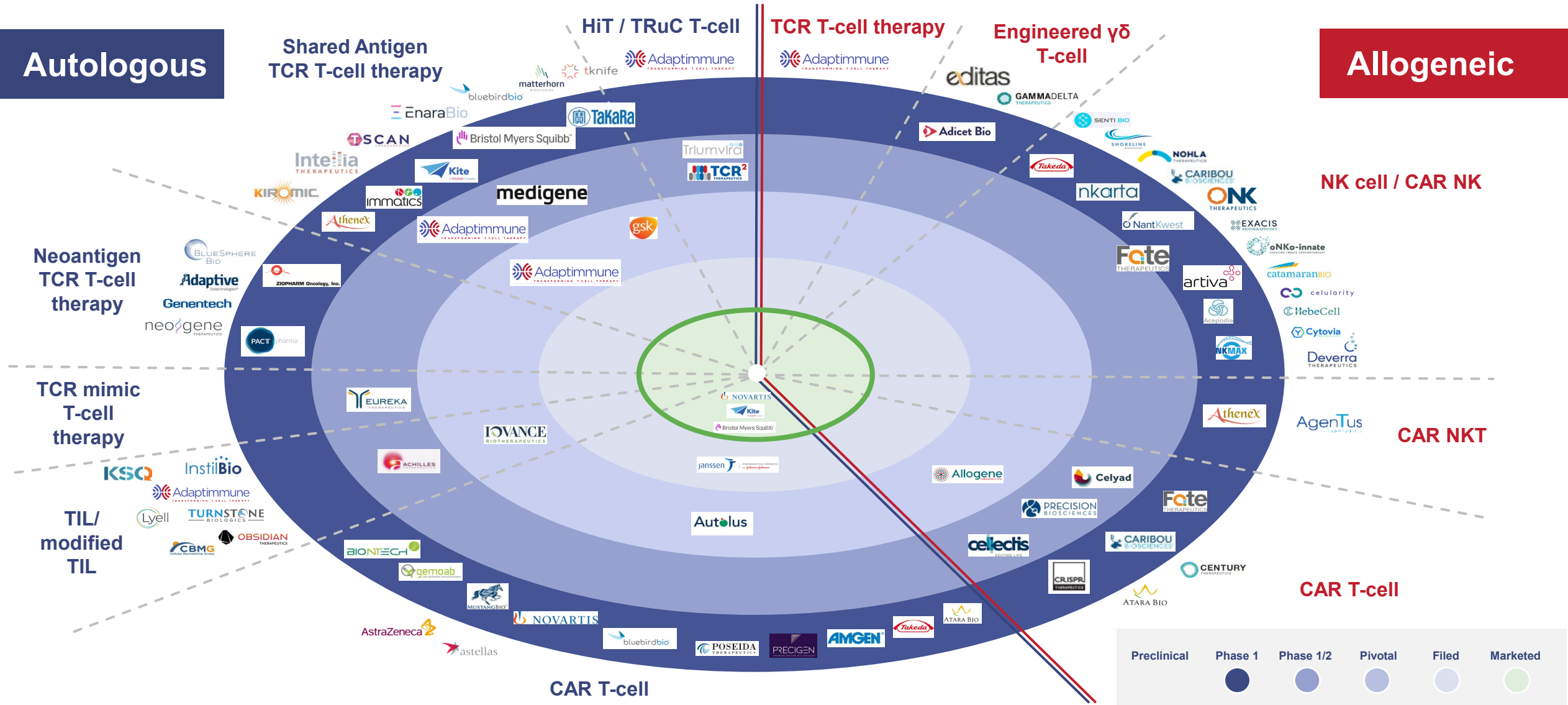
EGJ: esophagogastric junction cancer; HiT: HLA-independent T-cell receptor (TCR); TIL: tumor infiltrating lymphocyte; CMC: chemistry, manufacturing, and controls

Cell Therapy Landscape

Overview of select approaches and players



Adaptimmune TRANSFORMING T CELL THERAPY

Adaptimmune is positioned to deliver allogeneic cell therapy for people with cancer

TECHNOLOGY PLATFORM

iPSC derived

Serum free and feeder free

Virtually unlimited genetic enhancements

+

CELL THERAPY EXPERTISE

SPEAR T-cells
HiTs
Next-gens
Multiple HLAs

Research, translational and clinical insight

Vast potential pipeline

Adaptimmune
astellas
Genentech
A Member of the Roche Group

+

CMC CAPABILITIES

Experienced CMC capability

Integrated process development team

Scalable mass production

EFFECTIVE

CONSISTENT

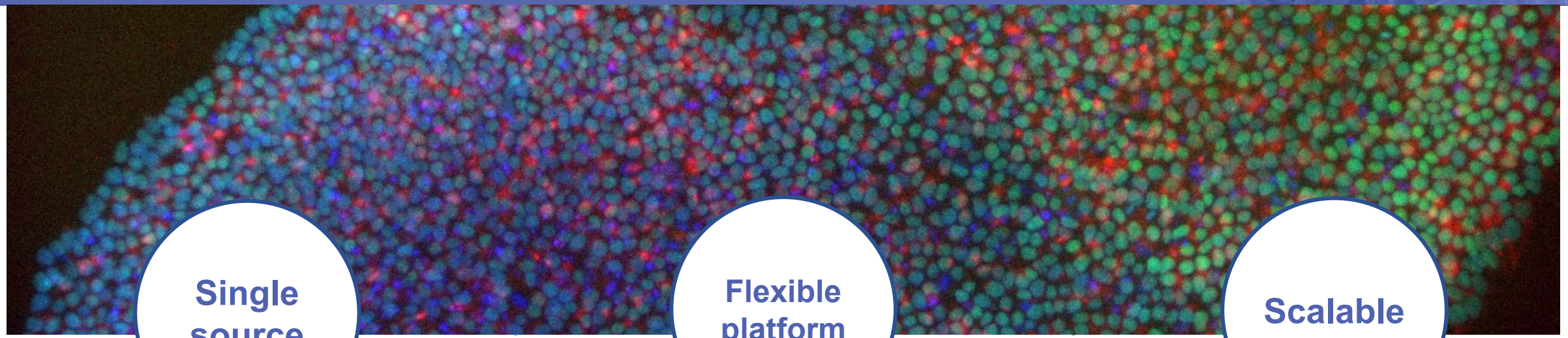
AVAILABLE ON DEMAND

Internally aggregated data based on public information

Our allogeneic platform and recent progress

iT-cell platform provides controlled, consistent off-the-shelf products

How we will deliver one product suitable for multiple patients on demand



Single source

- iPSCs from single donor stem cells
- High proliferative potential
- **Reproducible** starting material

Flexible platform

- Overcomes lentivector capacity limit
- **Flexibility** to add multiple next-gens or edits

Scalable

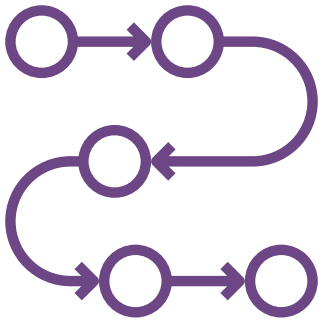
- Single cell line for characterization
- Defined media composition
- **No serum or feeder lines**

Steps to make our allogeneic iT-cells ready for the clinic

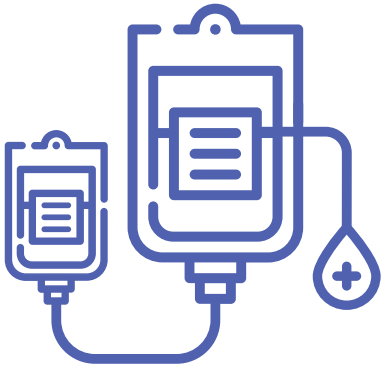
Focusing on the right steps to make safe and effective allogeneic cell therapies

1 → 2 → 3

Gene editing



Differentiation process



Scale up

Gene editing enables us to tailor effective and safe iT-cells

Learning from our autologous trials and preclinical research to make the best allogeneic cell therapies

1 → 2 → 3

Gene editing

Differentiation process

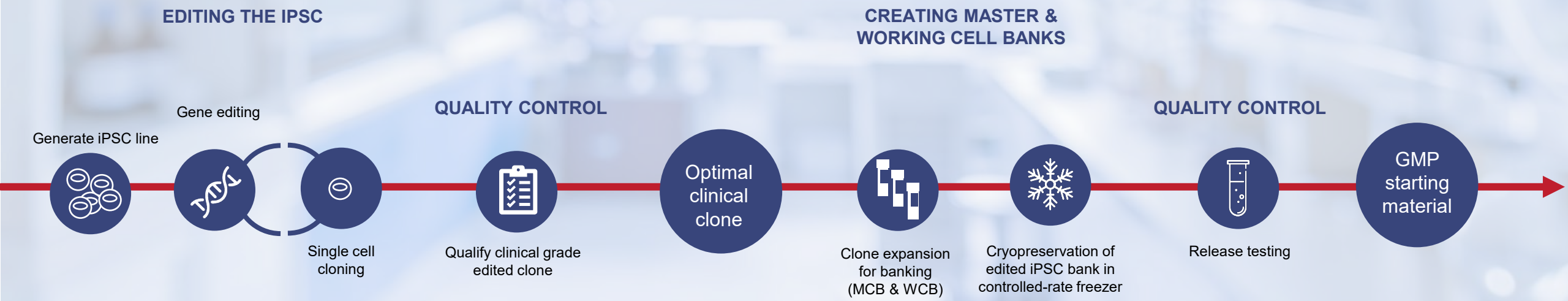
Scale up

Reproducible starting material reduces allogeneic product variability

Large cell banks can be made from edited iPSC so that each batch of product starts from the same cells

1

GETTING TO GMP STARTING MATERIAL



A single iPSC can be expanded to make 100s or 1,000s vials in master and working cell banks

MCB: master cell bank; WCB: working cell bank

Making the right gene edits for safe and effective allogeneic products

Precision engineering and single-cell cloning allow for fine tuning of product characteristics

1

POTENCY	• TCR or CAR insertion • Other next-gen or editing modifications
SAFETY	• Remove natural TCR to prevent GvHD • Knockout RAG gene to prevent native TCR expression
PERSISTENCE	• Gene edits to hide iT-cells from the patent's immune system

Cloning ensures every cell has every edit

RAG: recombination activating gene; responsible for recombining VDJ elements to make native TCR
GvHD: graft versus host disease; a phenomenon when engrafted cells (such as iT-cells) attack the host's tissues

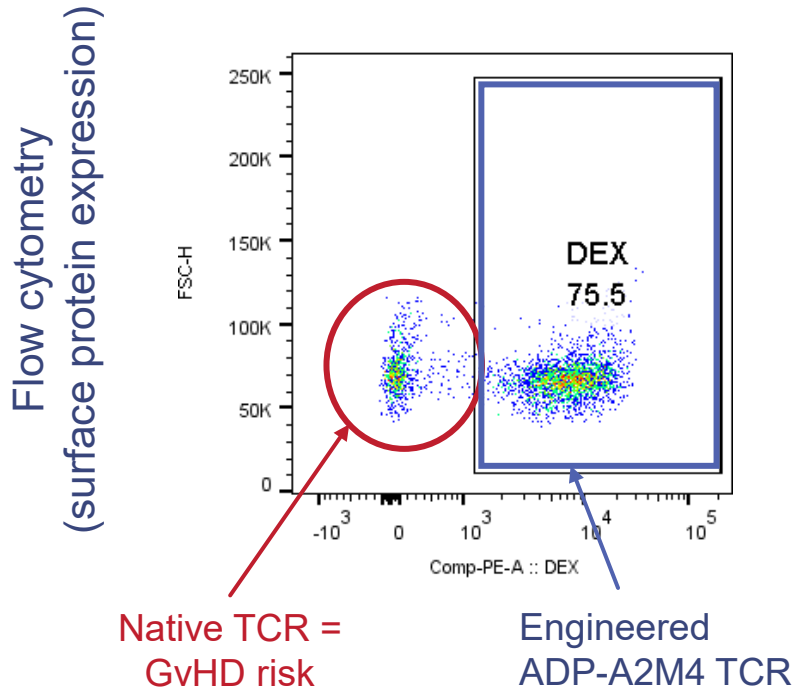
Removing RAG gene eliminates native TCR to prevent GvHD

Recent gene editing progress ensures only MAGE-A4 targeted TCR is present – cloning ensures all iT-cells have edit

1

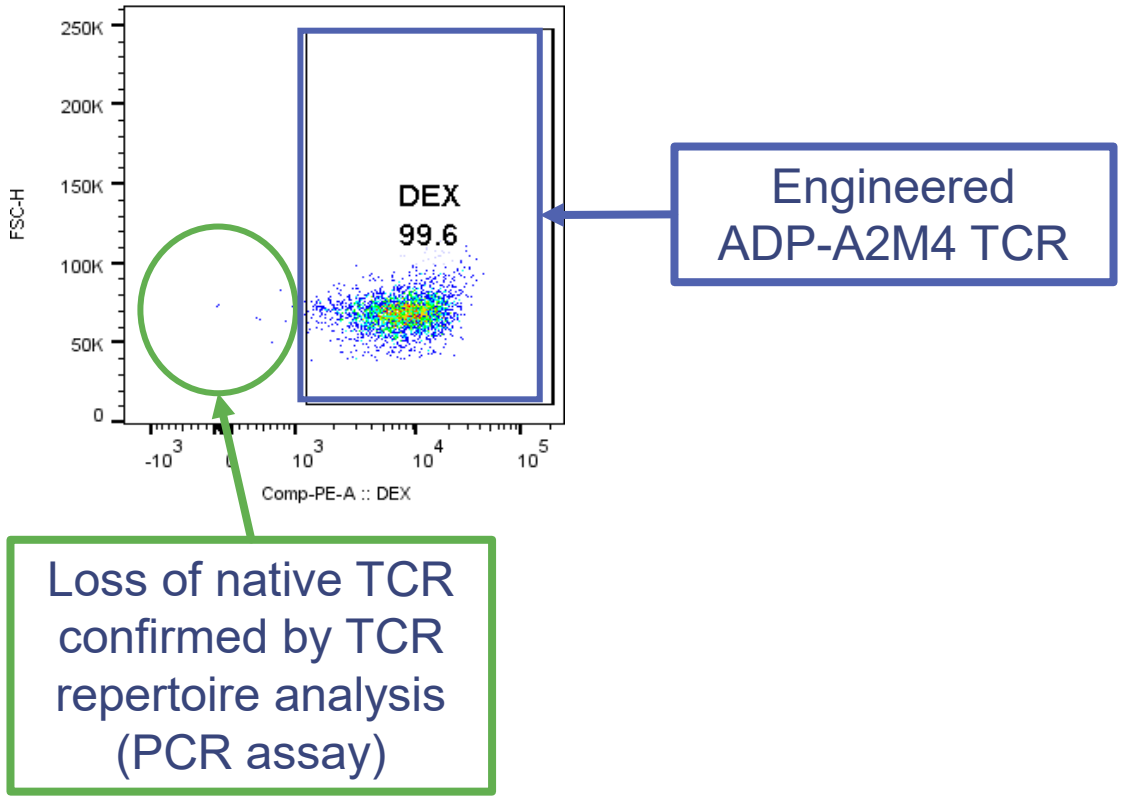
Clone 1 – RAG intact

Both native TCR and
engineered ADP-A2M4 TCR present



Clone 2 – RAG knockout

Only engineered
ADP-A2M4 TCR present



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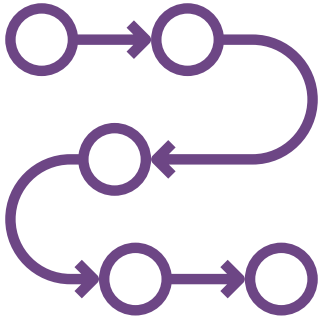
Proprietary differentiation process to produce functional iT-cells

1 → **2** → 3

Gene editing



Differentiation process

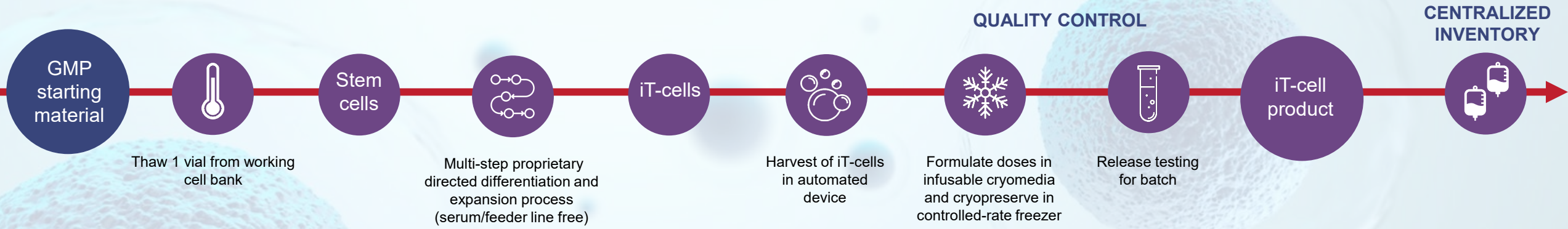
Scale up

From edited iPSC banks of cells to centralized inventory of on demand product

Clonal starting material for consistent iT-cell therapies ready for patients

2

CREATING BATCHES OF DIFFERENTIATED CELLS



A single vial of iPSC clones will make multiple patient doses depending on scale up

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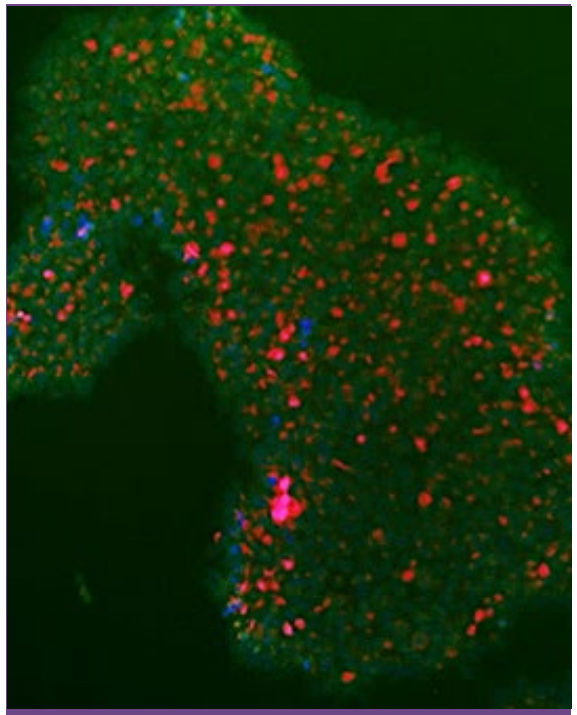
Proprietary iPSC differentiation process mimics early T-cell development in a dish

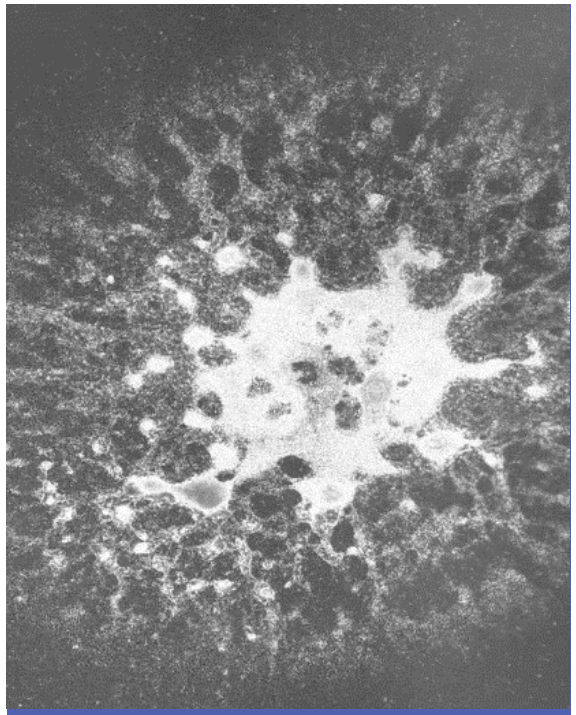
Stem cells form organoids with complex 3-D structure to support iT-cell development

2



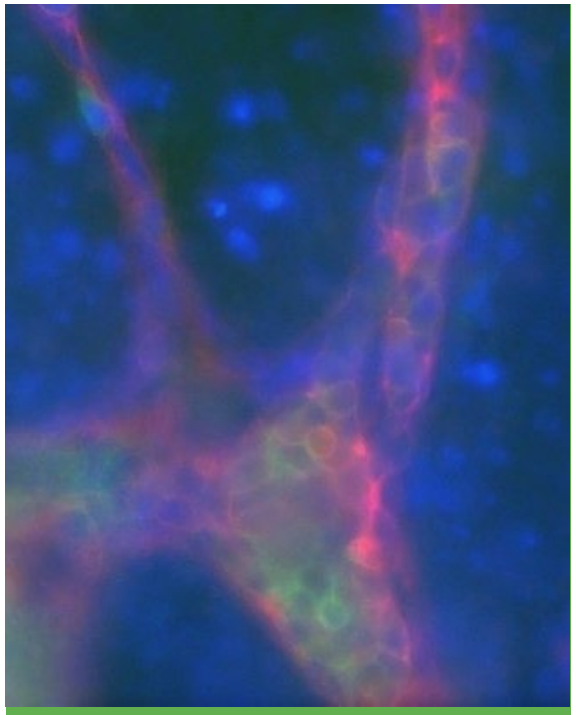
Stem cells (starting material)

Hoescht blue, OCT4 green,TRA160 red



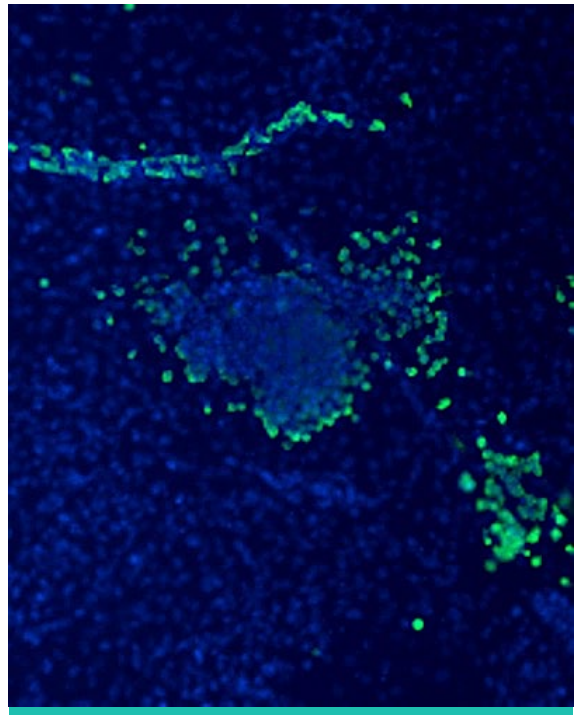
Complex 3D structures self assemble

Brightfield



Hemogenic endothelium forms

Hoescht blue, CD45 green,CD34 red



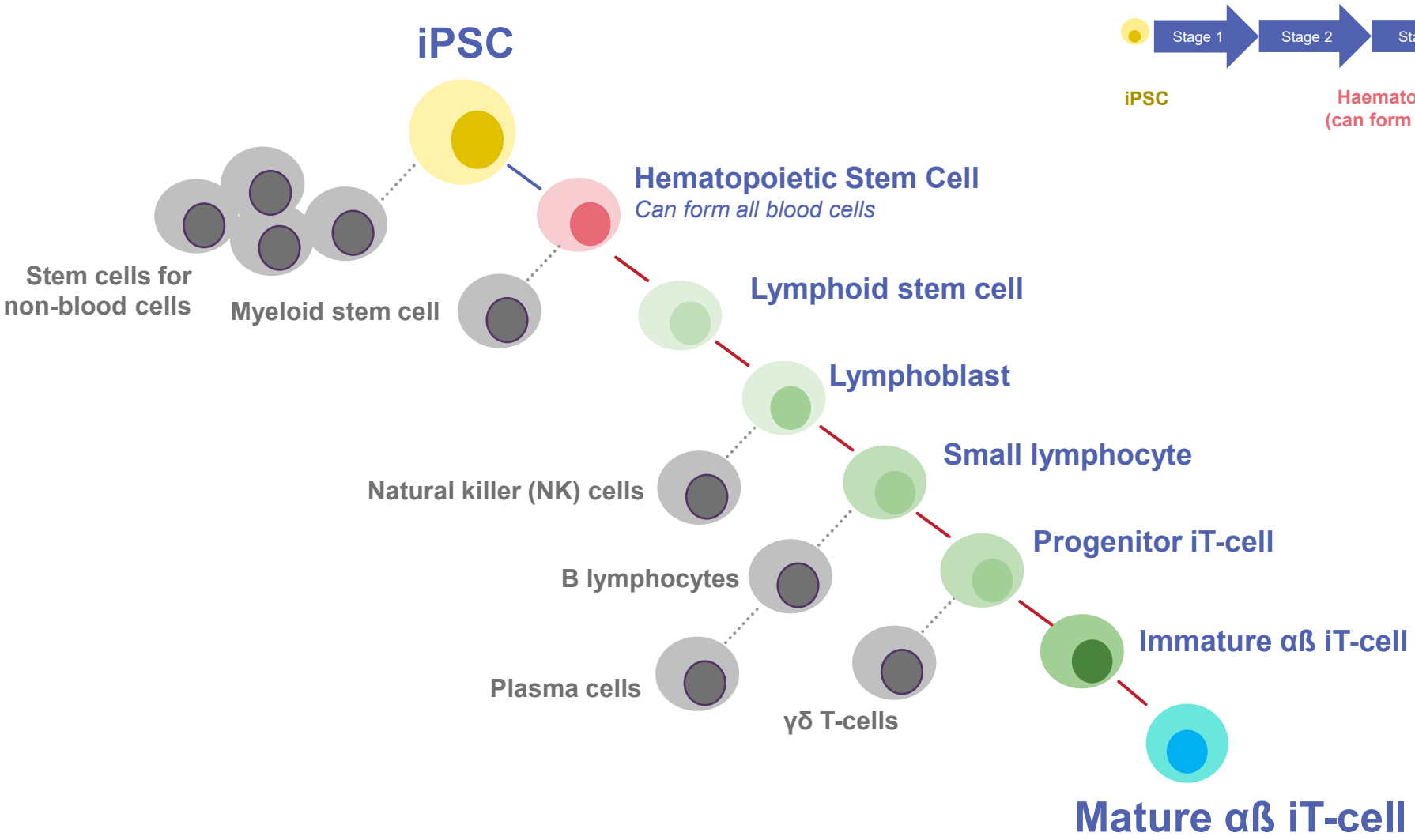
T-cells form

Hoescht blue, CD3 green

We chose to make αß T-cells from stem cells because they work in solid tumors

Differentiation path to mature αß T-cells is one of the longest for any lymphoid cells

2



Our proprietary differentiation process produces functional, mature iT-cells

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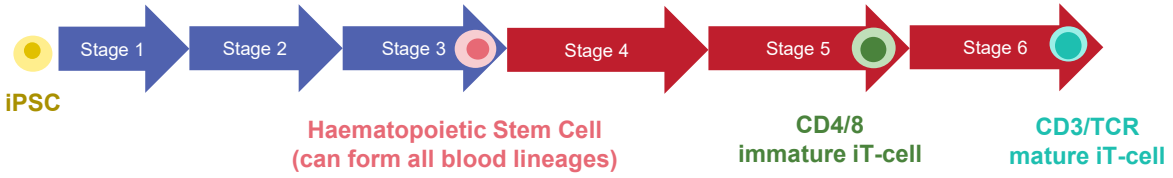
Autologous product sets the standard for making functional allogeneic iT-cells

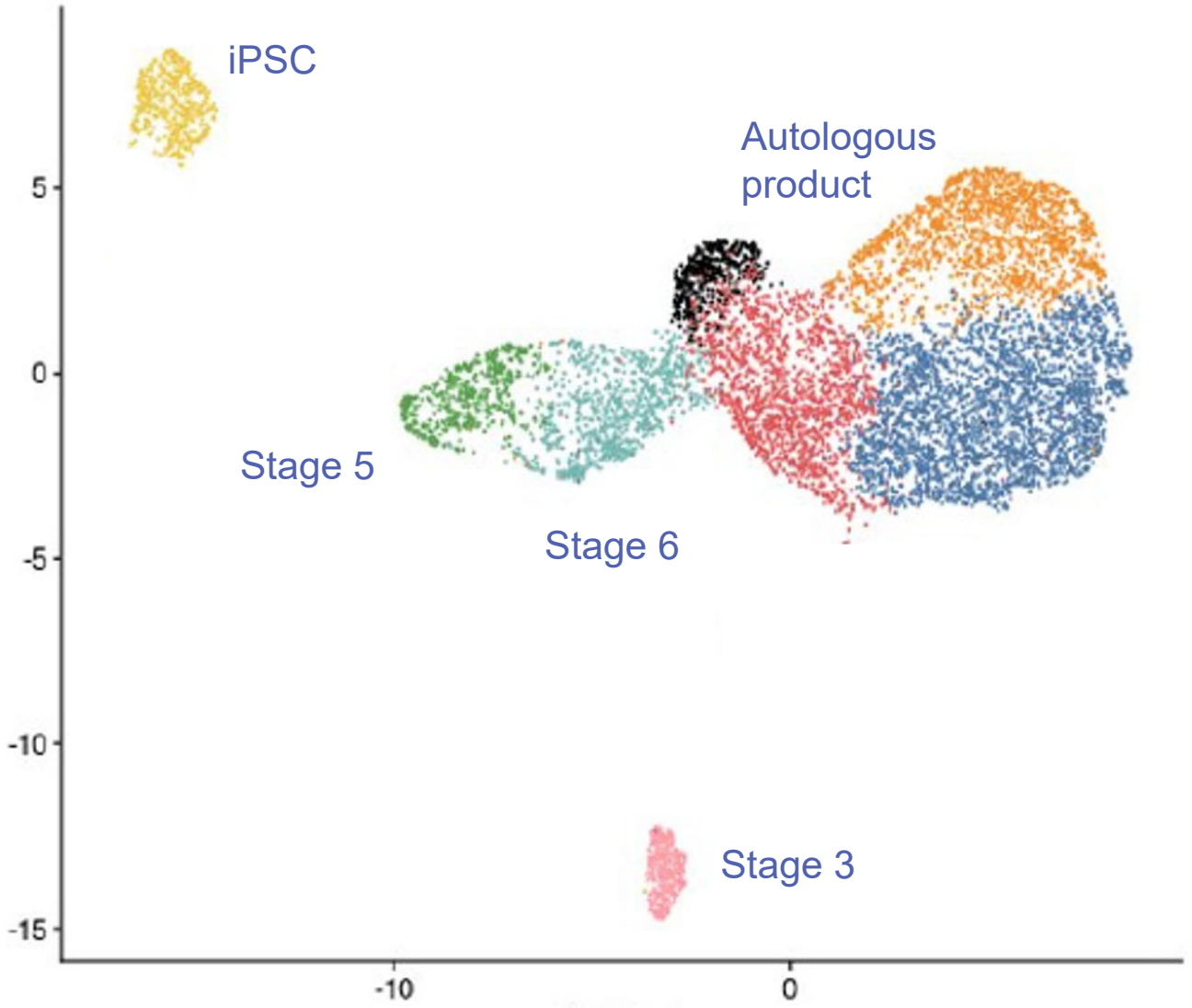
Proprietary differentiation process produces mature iT cells approaching genetic phenotype of autologous product

2



Our autologous T-cell products work in solid tumors

Single-cell gene analysis and clinical data provide map to ideal allo iT-cell



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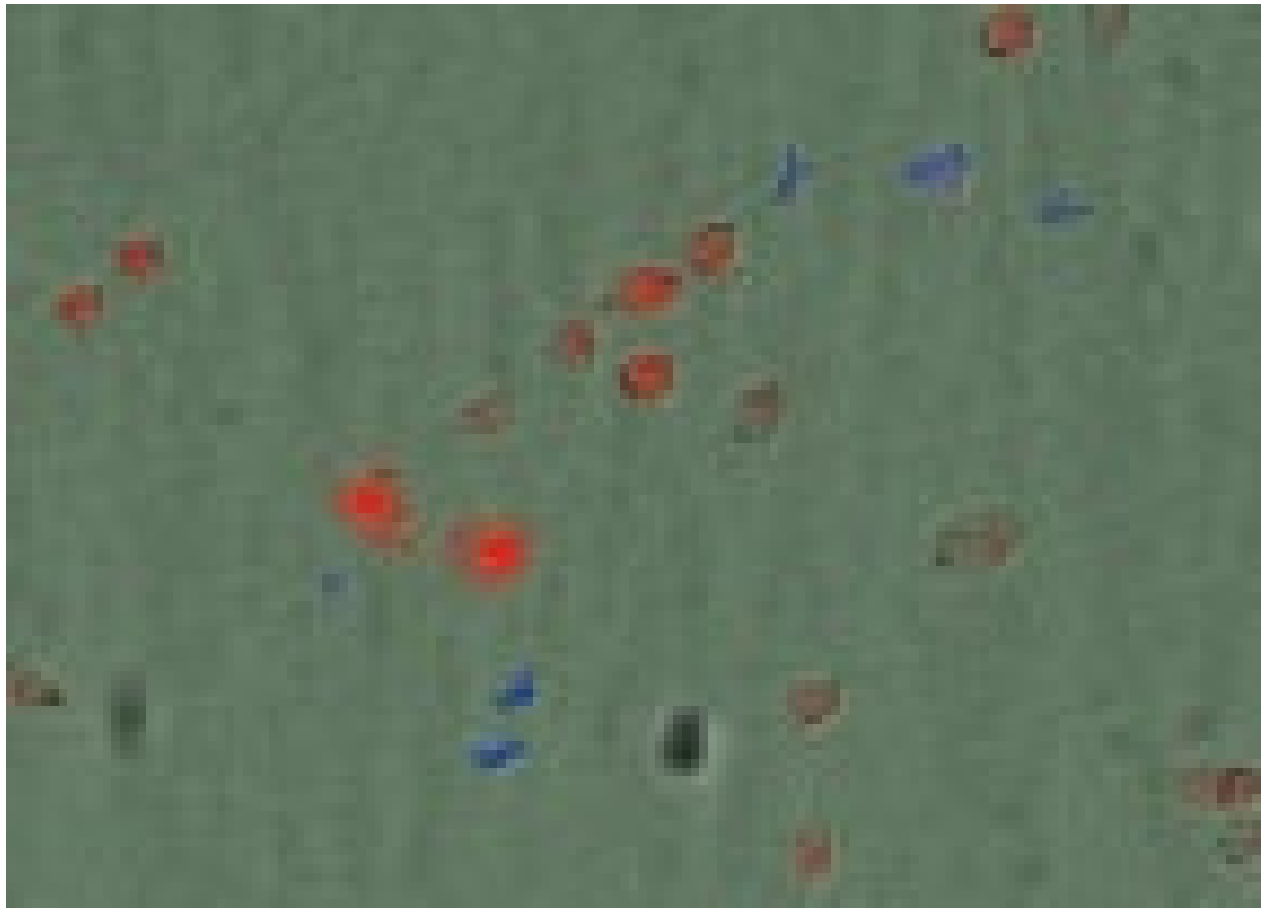
iT-cells can kill target more than once; the type of activity needed to treat solid tumors

Serial killing of tumor cells is a hallmark of mature, functional, effector T-cells

2



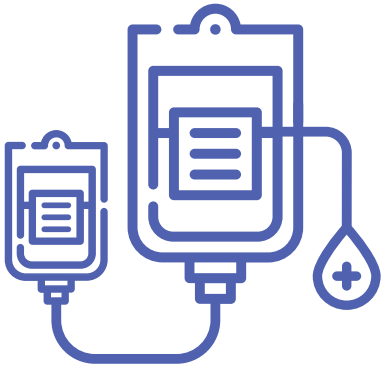
Scalability is a key requirement to make cell therapies more mainstream

Scale up informed by our in-house expertise in autologous T-cell therapy production

1 → 2 → 3

Gene editing

Differentiation process



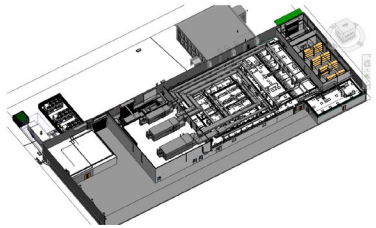
Scale up

Our fully integrated cell production expertise puts us on quick path to allogeneic scale up

We know how to build world-class manufacturing facilities to supply products for the clinic

Allogeneic facilities at Milton Park, UK

- Research
- Process development



- Allogeneic manufacturing

To be open by end of 2022

Leveraging successful build out of two autologous facilities in last 4 years

Navy Yard, US

Stevenage, UK

Providing a consistent “off-the-shelf” product for multiple patients on demand

Reduced hospital time, no apheresis, simplified patient journey

DELIVERING TO THE PATIENT

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Our allogeneic pipeline for the near future

Making allogeneic cell therapies curative and mainstream for people with cancer

Platform	Product	Discovery	Preclinical
Adaptimmune	Allogeneic T-cells targeting MAGE-A4		
	Other TCRs (inc. next-gen)		
astellas	HiT mesothelin		
	Target 2 (unnamed)		
Genentech	"Off-the shelf" TCR therapy target 1		
	Personalized cell therapy platform		

Adaptimmune

- MAGE-A4 targeted TCR
  - Validated target
  - Broad range of indications
- "Plug and play" platform
  - All wholly owned receptors
  - Next-gen and other enhancements

astellas

- Mesothelin HiT as first product
- Second target nominated but not named

Genentech

- Off-the-shelf T-cell therapies
  - Up to five targets
- Personalized medicine platform
  - Unique targets and receptors based on individual patient tumors

Overview of the strategic collaboration with Genentech

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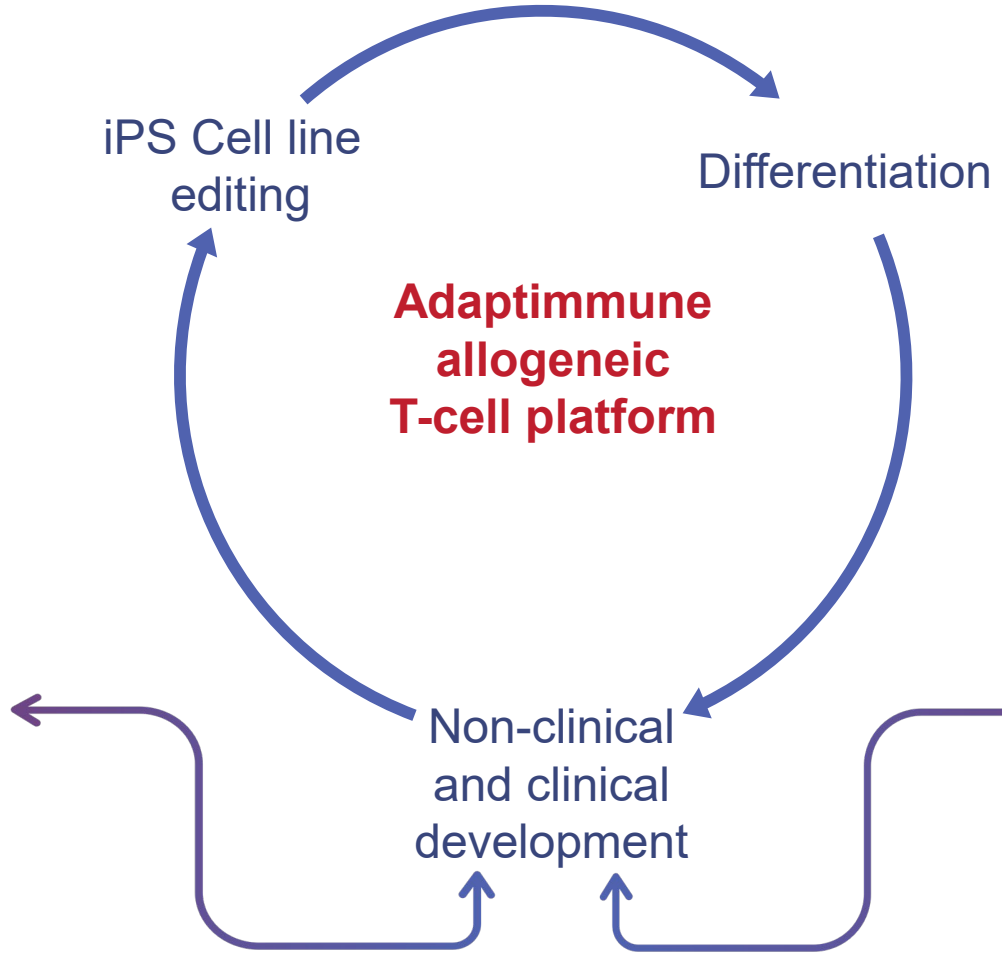
Combining Adaptimmune and Genentech cell therapy expertise

To deliver allogeneic cell therapies for people with cancer



Component 1:
Off the Shelf Products

Knock-in of Genentech provided TCRs specific to 5 targets including scope for next-gen modifications

Component 2:
Personalized Therapy

Real-time identification and knock-in of patient-specific TCRs; scope for next-gen modifications

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Financials

- Under the terms of the agreement*, Adaptimmune will receive:
  - Upfront payment of $150 million
  - $150 million in additional payments over the next 5 years*
- In addition, Adaptimmune may be eligible to receive research, development, regulatory and commercial milestones payments potentially exceeding $3 billion in aggregate value
- Adaptimmune will receive tiered royalties on net sales in the mid-single to low-double digits
- Adaptimmune has the right to opt in to a 50/50 U.S. profit/cost share on "off-the-shelf" products
  - If Adaptimmune elects to opt in, then Adaptimmune will be eligible to share 50 percent of profits and losses from U.S. sales on such products and is eligible to receive ex-U.S. regulatory and sales-based milestone payments, as well as royalties on ex-U.S. net sales

- *The effectiveness of the agreement is subject to clearance under the Hart-Scott-Rodino Antitrust Improvements Act.*

*unless agreement is earlier terminated

Q&A moderated by Bill Bertrand

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Q&A

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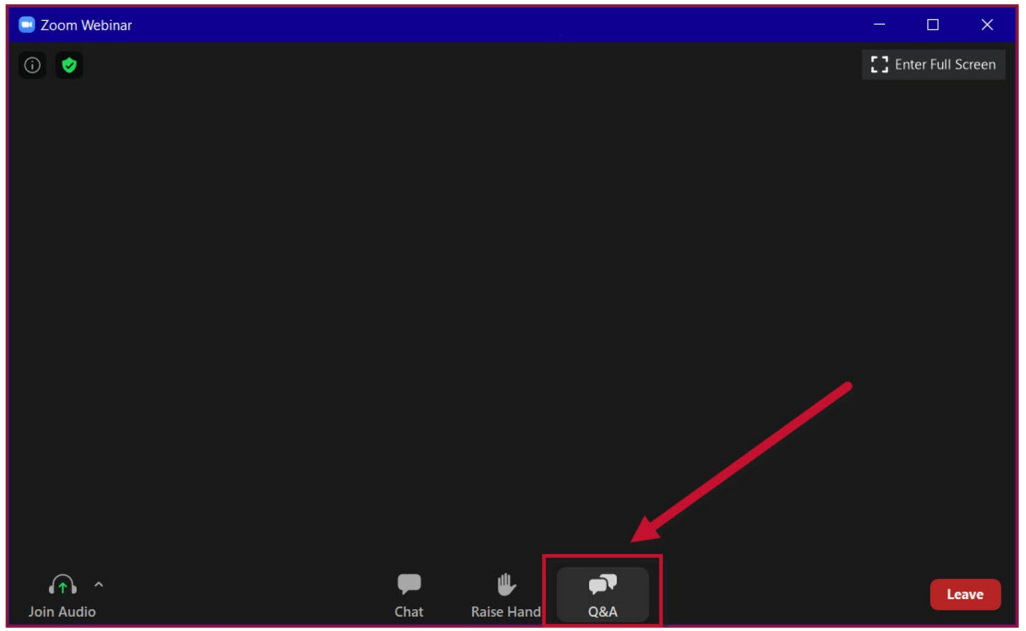

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Closing remarks

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Our vision and mission

Arming cells.
Against cancer.
For Good.

To transform the lives of people with cancer
by designing and delivering cell therapies

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