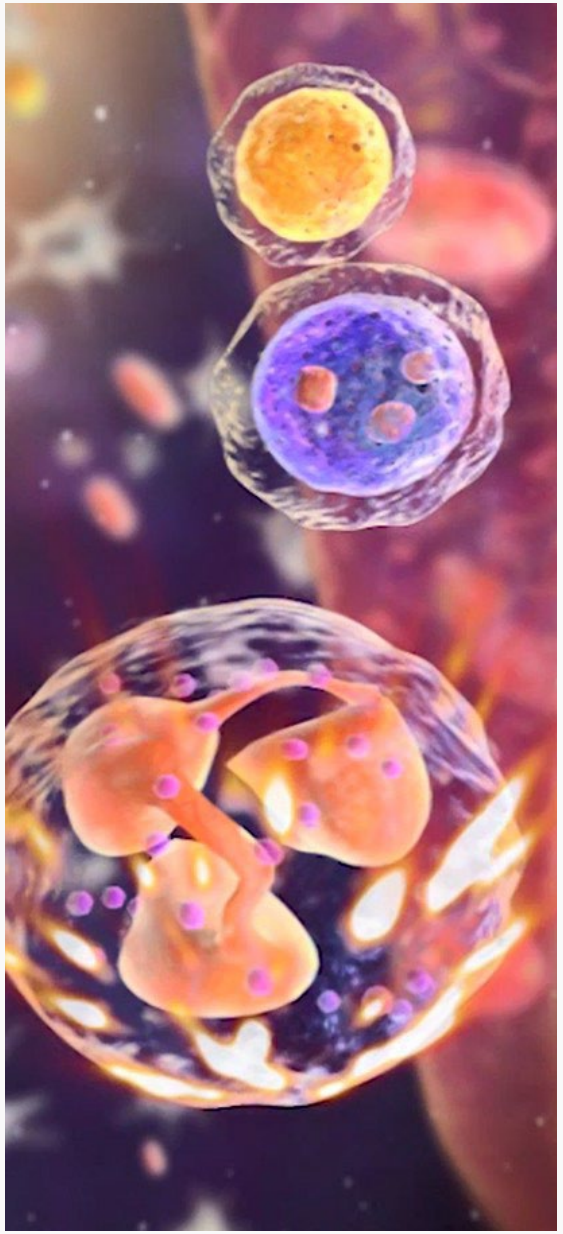
LIfT BioSciences

Innately curing cancer

Introducing The world's only neutrophil based cell therapy platform

Nov 22 – summary



LIfT Biosciences is developing a new-to-world transformative allogeneic innate cell therapy for the treatment of solid tumours

Founded / 1st Patent Filing
2016

Technology
Immuno-Modulatory Alpha Neutrophil progenitors (IMANp) produced using the N-LIfT and CAR iN-LIfT Platforms

Stage
Pre-clinical

Focus
Solid Tumours with high unmet medical need e.g. PDAC

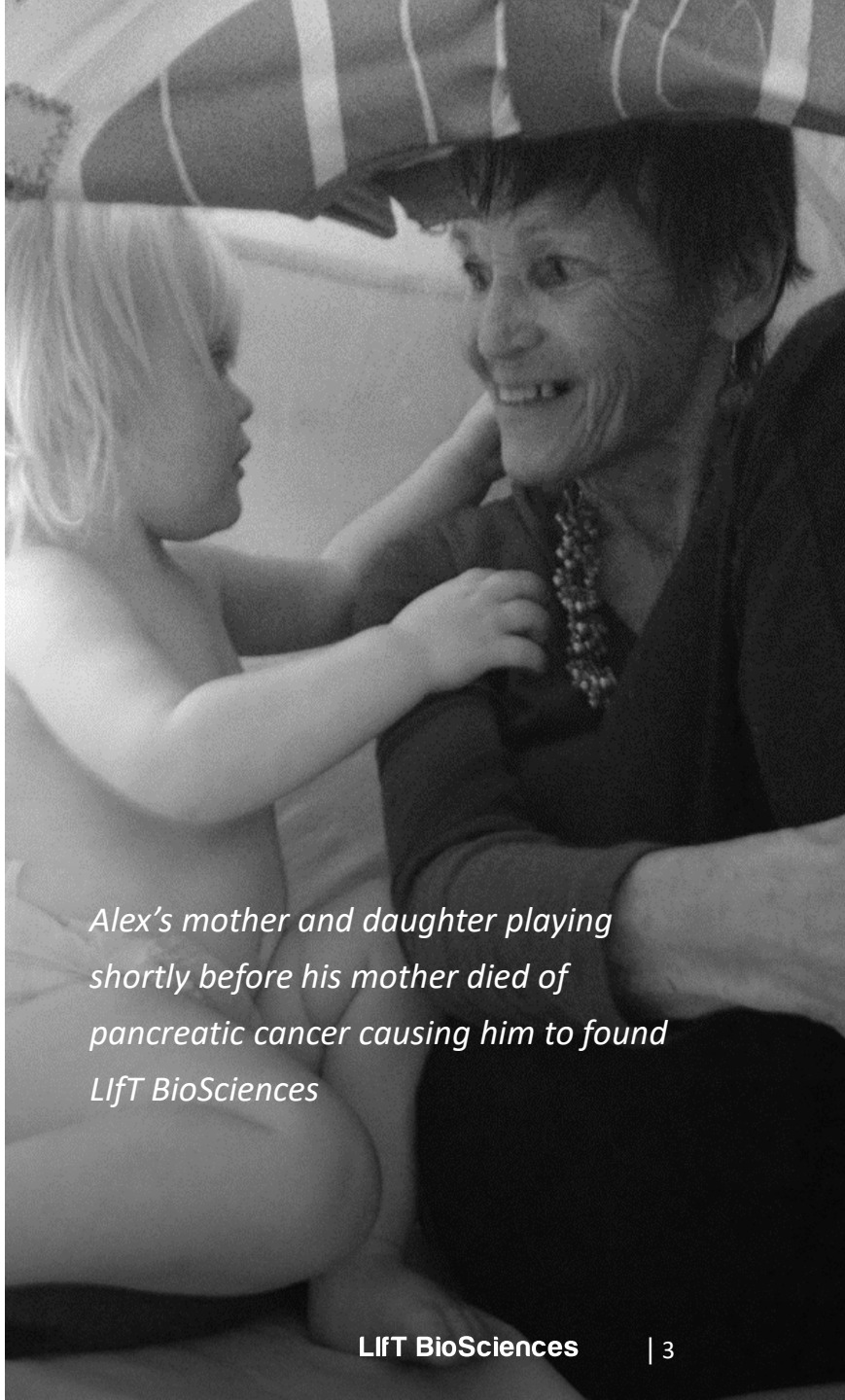
IP/FTO
6 Patents with FTO

- LIfT Biosciences is a pre-clinical stage biotech with **The World's only Neutrophil based Cell Therapy Platform**
- The LIfT platform is allogeneic and can be used to produce different **Immuno-Modulatory Alpha Neutrophils (IMANs)** for treating a range of different therapeutic indications, including solid tumours
- The LIfT Platform is being used to produce N-LIfT, our first-to-market anti-cancer innate cell therapy that **overcomes many of the issues current therapies struggle with**
- N-LIfT has an **antigen independent mechanism of action**. N-LIfT cells have a superior to T-cell ability to infiltrate tumours, retain function in a tumour microenvironment and can recruit the host immune system
- LIfT is able to demonstrate the **scalable** and **cost-effective** production of N-LIfT
- **Exceptional efficacy** demonstrated in multiple ex vivo PDX tumouroid models showing **>90% lysis**
- **Raising a further $50m in H1 2023** to fund moving into **clinical trials by Q1 2024**
- Core team includes members behind two major successful exits in immuno-oncology
- Investors include Jonathan Milner (abcam) and VCs like Downing & Kizoo. Advisors include leading oncologists, scientists and leaders in cell therapy (BMS, AZ, Novartis)

LIfT BioSciences was established to set-up an adaptable cell therapy with a broad killing mechanism that continues to kill even as the tumour adapts

"Targeted therapies often fail because tumours adapt, and they don't. We are developing N-LIfT to destroy all solid tumours irrespective of where the tumour is or how it adapts. So there will be no escape. That is why N-LIfT is different!"

- Alex Blyth, CEO

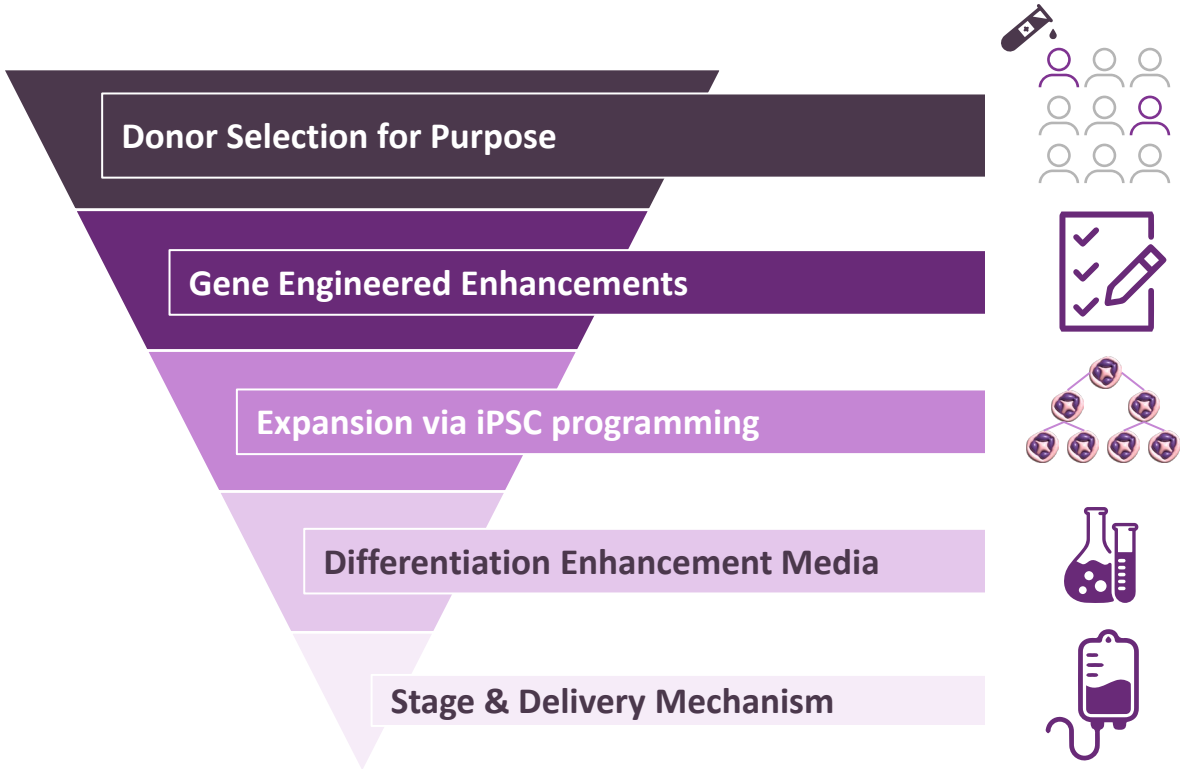


Alex's mother and daughter playing shortly before his mother died of pancreatic cancer causing him to found LIfT BioSciences

The World's 1st Neutrophil based Cell Therapy Platform

A Flexible Unique Platform

The N-LIfT Cell Therapy Platform allows us to produce different types of Immuno-Modulatory Alpha Neutrophils (IMANs) for a wide range of different purposes.



Therapeutic Application Specific IMANs

e.g. Cancer type, Bacteria, Fungi, Autoimmune disease, senescent cell, microbiome etc

COMPANY

LIfT Team

Alex Blyth
Chief Executive Officer & Founder

Entrepreneur with 18 years experience of commercialising novel biopharma assets, built & sold two companies.

Cell Therapy Specialist from concept to clinic. From GSK to Gamma Delta Therapeutics & founded Adaptate. Two major exits.

Oxana Polyakova
Chief Scientific Officer

Panteli Theocharous
Chief Medical Officer

Andrew Willis
Chief Regulatory & Development Officer

35 years experience, brought multiple cell therapies to market in Biotech, including ReNeuron & IO Biotech

Martin Woodward
Principal Scientist
Pre-Clinical Lead

Urvi Thacker
Process Development Lead

Sam Florence
Senior Scientist
Assay Dev & Lab Manager

Mihil Patel
Principal Scientist
CAR-iN-LIfT Lead

Lugein Al Khashlok
Research Associate & Clinical Coordinator

Jakub Lich
Associate Scientist

Aoife McGinley
MOA/Translational Lead

Advisers

Professor David Pinato
Oncologist, Director of Cancer Thera. Imperial College

Professor James Spicer
Oncologst, Head of Experimental Cancer Med, KCL

Mark Treherne
Monument, Talisman, CDD

Rachel Humphrey
Former VP Immuno-Oncology Lilly, Az

Holger Korsunky
Ex-Cellerant

Professor Mark Lowdell
Founder InMuneBio

Professor John Campbell
Dir SNBTS, Resolution Tx

Amir Hefni
Global Head of Novartis Cell & Gene

LIfT Board

Alex Blyth

CEO & Founder

CCL, Takeda, Cello (Takeda, AbbVie, Allergan), Huron

Patrick Burgermeister

Kizoo, BioMed Partners, Novartis

Jonathan Milner

Meltwind, Abcam Founder

Founder of Abcam plc (£2bn). Major Biotech investor, assisted three technology companies to IPO on AIM.

Antonin De Fougerolles

CEO Evox, former CSO Moderna, Ablynx

Harvard Immunologist. CEO, Evox Therapeutics. Former CSO for three billion dollar Biotechs incl. Ablynx & Moderna.

Oliver Sims

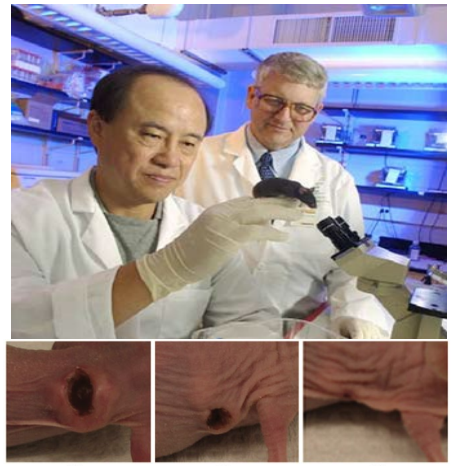
Meltwind

Matt Pierce

Downing Ventures

The right neutrophils kill cancer

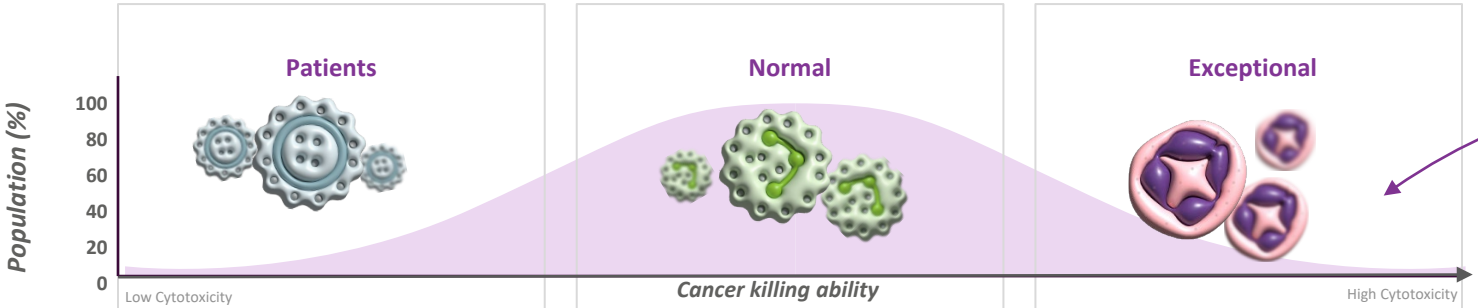
- Neutrophils can have potent antitumour function, while others can have protumour function
- Neutrophils traffic and penetrate the tumour (extravasation, chemotaxis, and stromal tissue penetration in superior in myeloid cells). Myeloid cells are present even in cold tumours
- CD177+ neutrophils suppress epithelial cell tumourigenesis in colitis-associated cancer and predict good prognosis in colorectal cancer
- Neutrophils are associated with a good response to chemotherapy in patients with gastric, colorectal or high-grade ovarian cancer
- Chemotherapy drugs like cabozantinib triggers a neutrophil-mediated anticancer innate immune response, resulting in tumor clearance
- Neutrophils co- localise with CD8 in CRC lesions and support antitumor adaptive immunity
- Adoptive transfer of neutrophil progenitors from mice with exceptional immunity has been found to cause complete tumour remission in mice with compromised immunity
- Adoptive transfer of neutrophils & neutrophil progenitors from HLA mismatched young healthy donors was found to be safe and induced upto 80% necrosis in patients in palliative care



Heliyon

Young donor white blood cell immunotherapy induces extensive tumor necrosis in advanced-stage solid tumors

N-LIfT gives patients the immune killing of donors with exceptional immunity



Pro-tumourgeneic Neutrophils

- Large (FSC-A^{high})
- Low density
- Appear immature
- Banded/circular nuclei
- RB-CD11b^{low}
- Anti-inflammatory
- Proangiogenic
- No T cell stimulation
- Antiapoptotic
- Negative Charge

Normal Anti-Cancer Neutrophils

- Small (FSC-A^{low})
- High density
- Mature
- Segmented nuclei
- RB1+
- Cytotoxic (CD11b^{high})
- Proinflammatory
- Antiangiogenic
- T cell stimulatory
- Proapoptotic
- Less Negative Charge

N-LIfT Alpha Neutrophils, Exceptional Cancer Killing

- Extreme of healthy neutrophils
- Exceptional selective cancer cytotoxicity
- Granules and cationic peptide (>50% mass)
- Very high density
- Positive net cell charge when activated

UNDER PATENT

Patent P47950EP priority filing Oct 2016

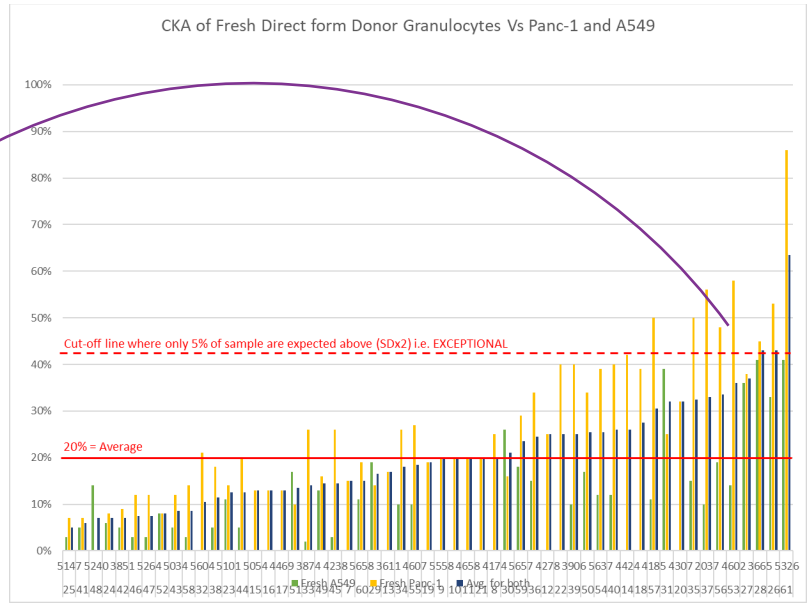
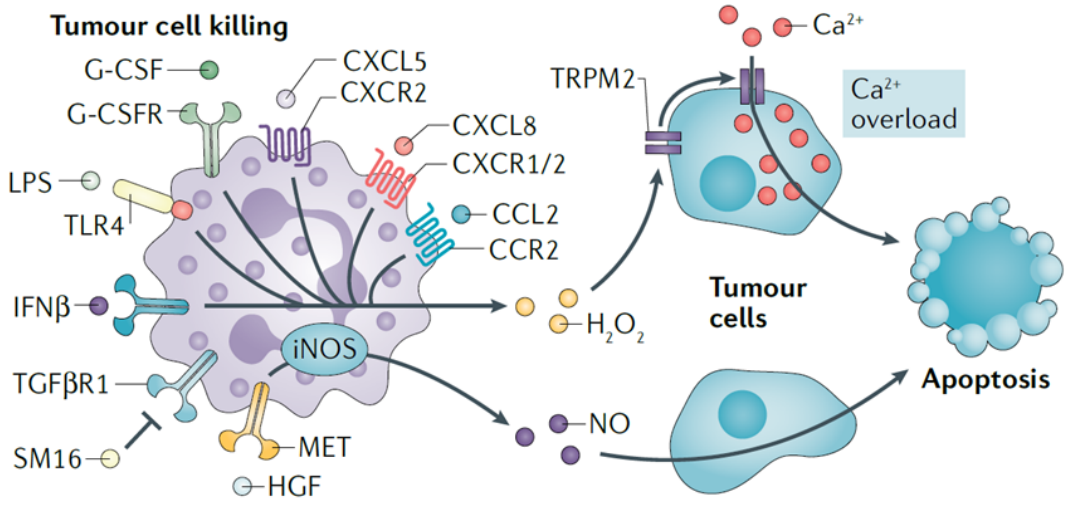


Fig. 1 | Spread of cancer cytotoxicity in donors tested by LIfT. 2020. To qualify as an Alpha Donor we need to see cytotoxicty at two standard deviations above the average in the population

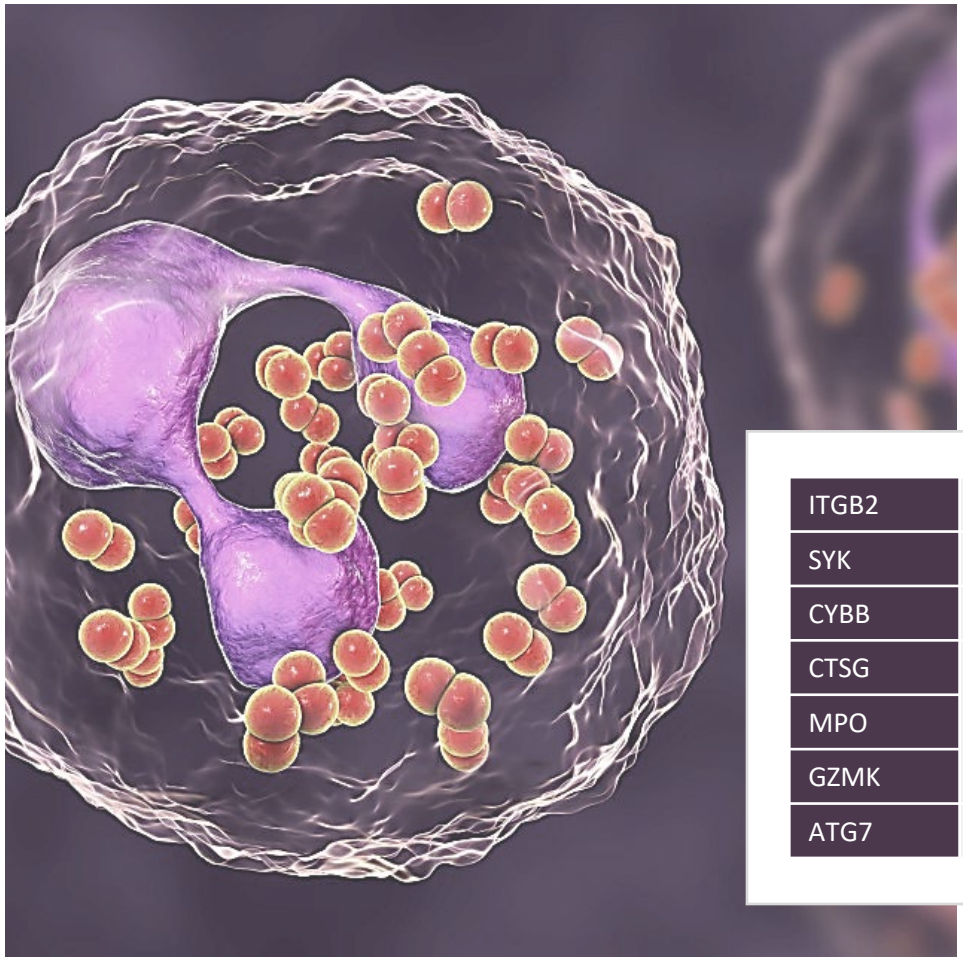
Alpha Neutrophils Cancer Killing Mechanism of Action

- Neutrophils migrate to cancer cells via chemotaxis, and are activated by chemotactic ligands (e.g. IL-8, TGFβ)
- Neutrophils are then attracted towards threats in a non-antigen specific way and works irrespective of tumour burden or mutation and so can work across multiple solid tumour types
- The primary killing mechanism is a lethal influx of calcium (Ca2+) into cancer cells via H202 release with SYK and IP3-mediated Ca2+-exocytosis
- The superior killing seen in IMANs over other neutrophils correlates with the larger granules found in IMANs and upregulated peptides associated to this killing mechanism (e.g. CTSG, MPO, GZMK)



Source: Jaillon. Neutrophil diversity and plasticity in tumour progression and therapy. Nature Reviews Oncology Sept 2020.

HSC derived Neutrophils from exceptional donors (alpha neutrophils) are different to normal neutrophils

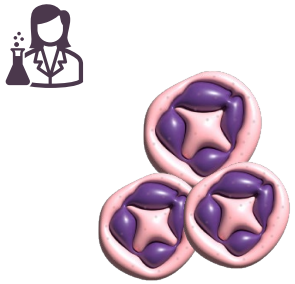
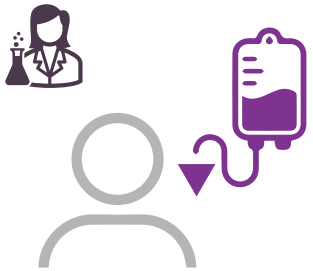


Cluster analysis of exceptional vs. normal donors shows that the proteins involved in alpha neutrophils **migration, activation** and **cytotoxicity** are **upregulated** in neutrophils from **exceptional donors** versus normal neutrophils (proteomics analysis by LC-MS/MS).

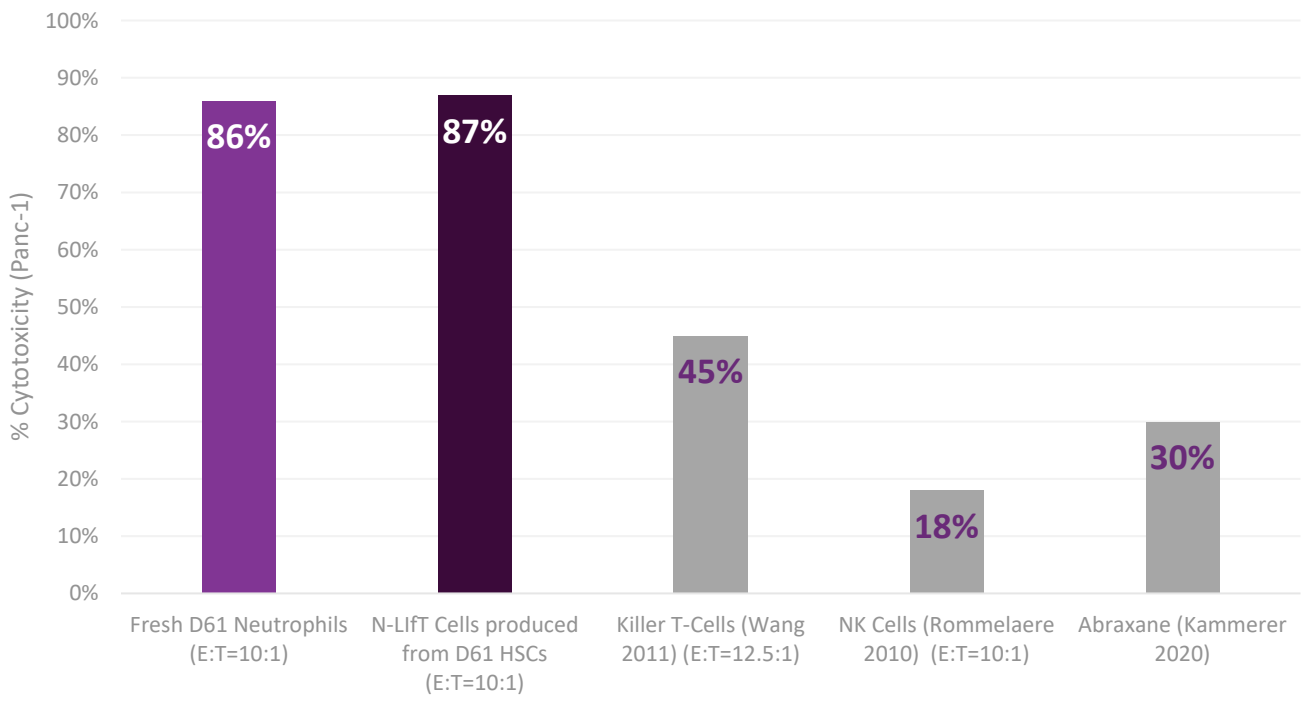
It is also evident under microscope that alpha neutrophils have larger and more plentiful granules (fire power)

ITGB2	leukocyte trafficking and activation
SYK	signalling
CYBB	ROS production
CTSG	effector function and cytotoxicity
MPO	
GZMK	
ATG7	autophagy

N-LIfT simply overcomes the challenges of other cell therapies

PROCESS	 Exceptional Donors Identification through FUNCTIONAL screening	 Stem Cell Harvest	 Manufacturing of Exceptional Neutrophils from Stem Cells	 Clinical Application
CHALLENGE	Sufficient Cell Sourcing	Simple Extraction & Storage of Cells	Scalable Manufacture	Safe & Efficacious in Solid Tumours
SOLUTION	Selection of donors with best anticancer activity >1M donor poll to select from iPSC for unlimited supply	Donor mobilisation with G-SCF and apheresis of HSC Bank of frozen CD34+	Straightforward protocol No Feeder cells or complex supplements No purification steps	No excessive activation or uncontrolled expansion of IMANp cells Time limited engraftment. TME is not a barrier to trafficking, infiltration, cytotoxicity & recruitment Non-Antigen specific killing

N-LIfT platform reliably emulates exceptional donor immunity

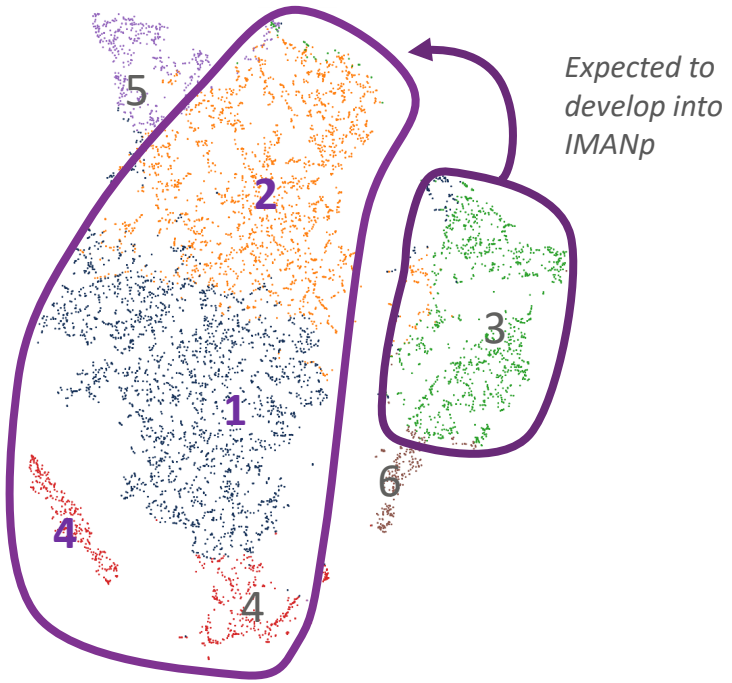


Sources: Killer T-Cells (Wang 2011) (E:T=12.5:1), NK Cells (Rommelaere 2010) (E:T=10:1), Abraxane (Kammerer 2020)

N-LIfT produced from Donor 61 HSCs shows comparable killing of Panc-1 cells to the original donor's fresh neutrophils.

N-LIfT is >90% comprised of progenitor cells that are committed (IMANp) or expected to become alpha neutrophils (IMANs)

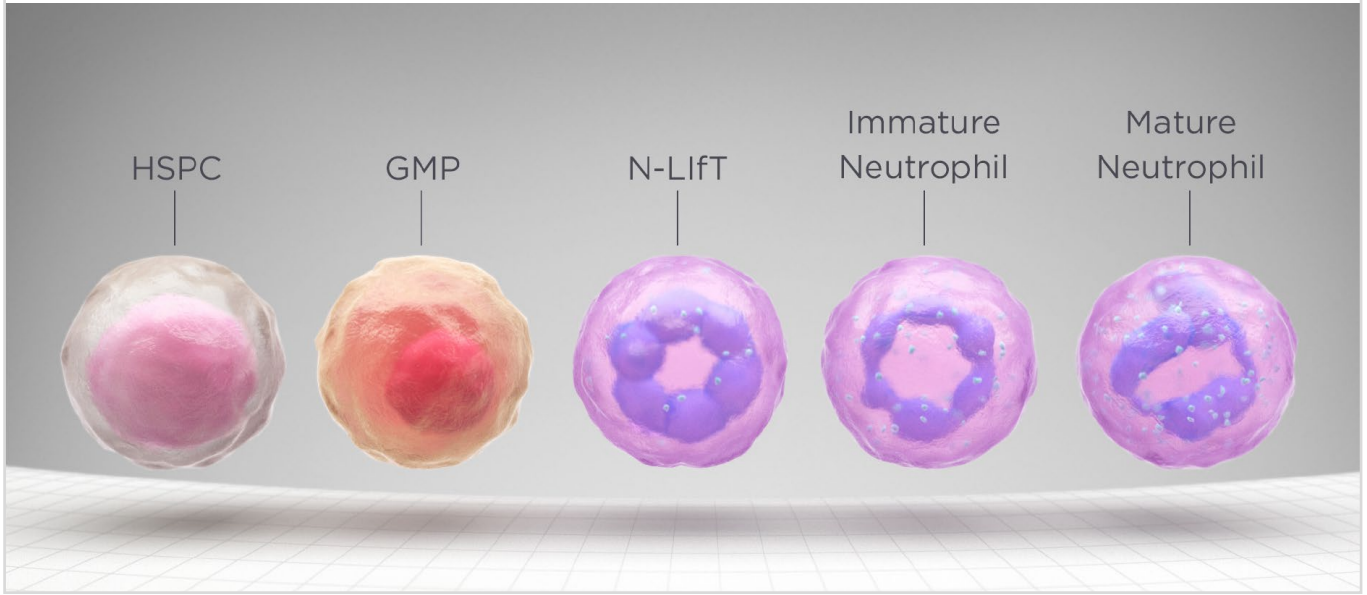
scRNAseq (10X Genomics)



Expected to develop into IMANp

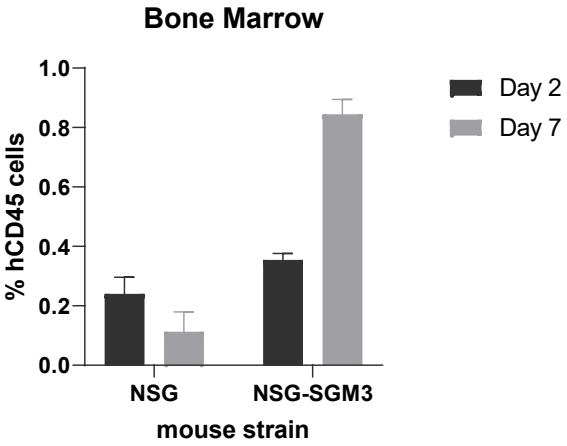
1, 2, 4, IMANp Neutrophil Progenitors (74%)
3. Earlier Progenitors expected to become IMANp (17%)
5. CD14+ (6%)
6. Platelets -3%

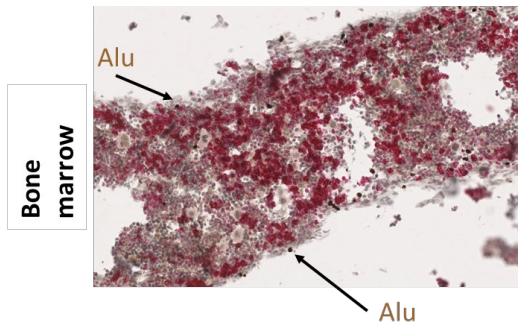
- scRNAseq analysis identified neutrophils progenitors as a main component of HSC derived product
- Flowcytometry analysis confirmed that IMANp cells are CD15+, CD66b-, CD177- , CD10- and mature in vitro into IMAN: CD15+, CD66b+, CD177+ and CD10+

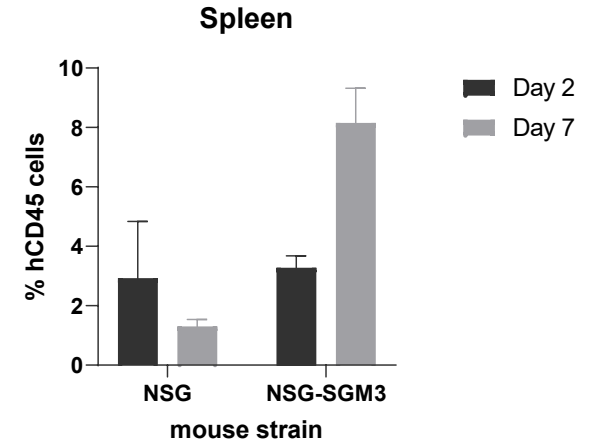


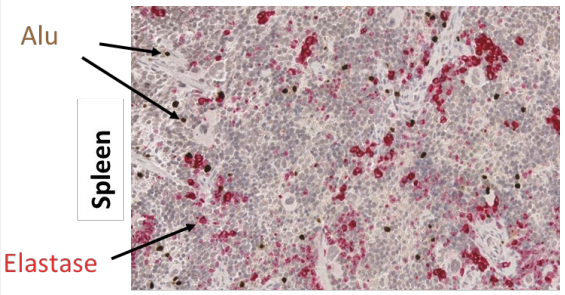
N-LIfT is safe, well tolerated and travels to immunologically relevant sites

- N-LIfT progenitors survive and safely biodistribute to immunologically relevant sites when intravenously injected (tail-vein) into NSG and NSG-SGM3 “Gold Standard” mice strains
- The increase in cell number shown on day 7 vs. day 2 suggests successful progenitor proliferation in the NSG-SM3 mouse, which is not apparent in the NSG mouse
- NSG-SGM3 mice constitutively express a trio of human myeloid-supporting cytokines, presumably acting to support N-LIfT maintenance and survival.
- Further fate and efficacy studies are now underway in the NSG-SGM3 mouse



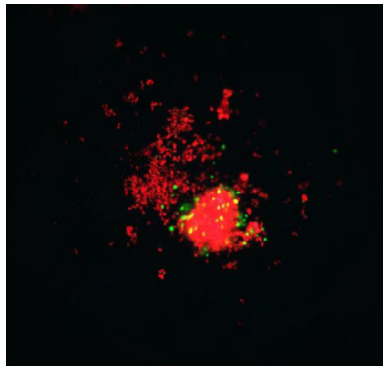




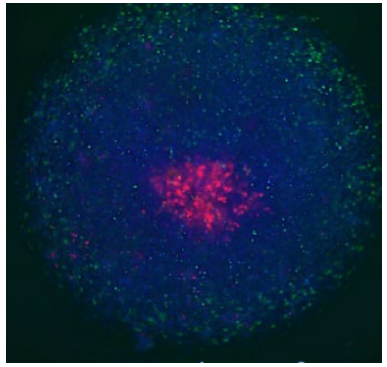


IMANs demonstrate exceptional efficacy in a patient derived organoid model for NSCLC Squamous Cell Carcinoma

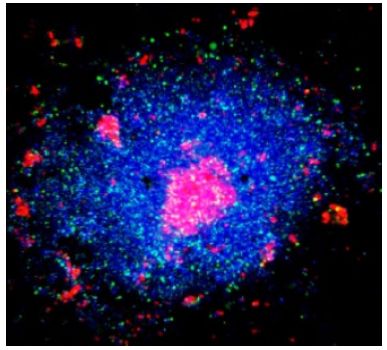
"N-LIfT gave the most comprehensive killing we have seen in this model and would clinically represent complete tumour destruction"
– Champions Oncology



Organoid only



Organoid + N-LIfT



Organoid + Keytruda + Autologous TILs

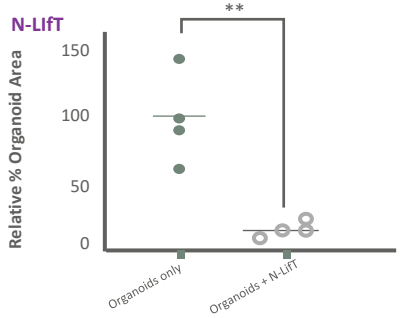
Channels

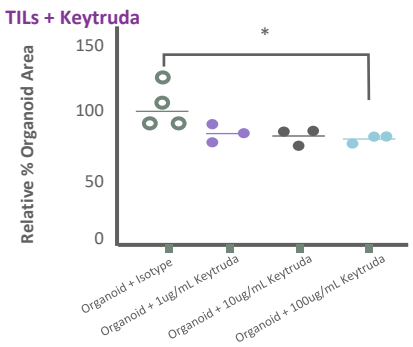
- Tumor Cells
- TIL Cells or N-LIfT Cells
- **Dead Cells**

N-LIfT cells demonstrate complete superiority over autologous TILs + Keytruda

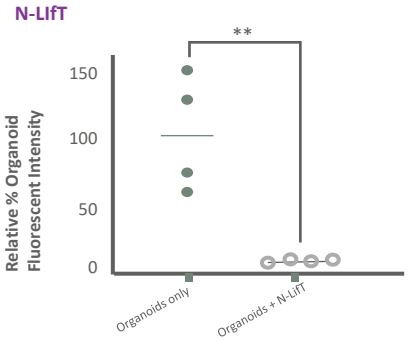
CTG-3493 PDX Tumouroid Model

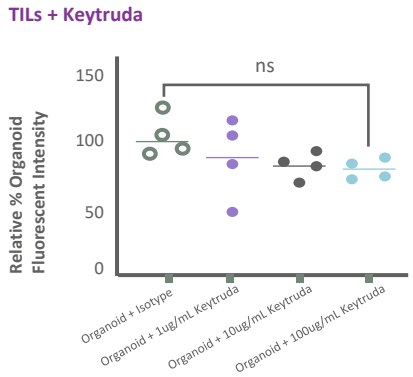
Tumouroid Area



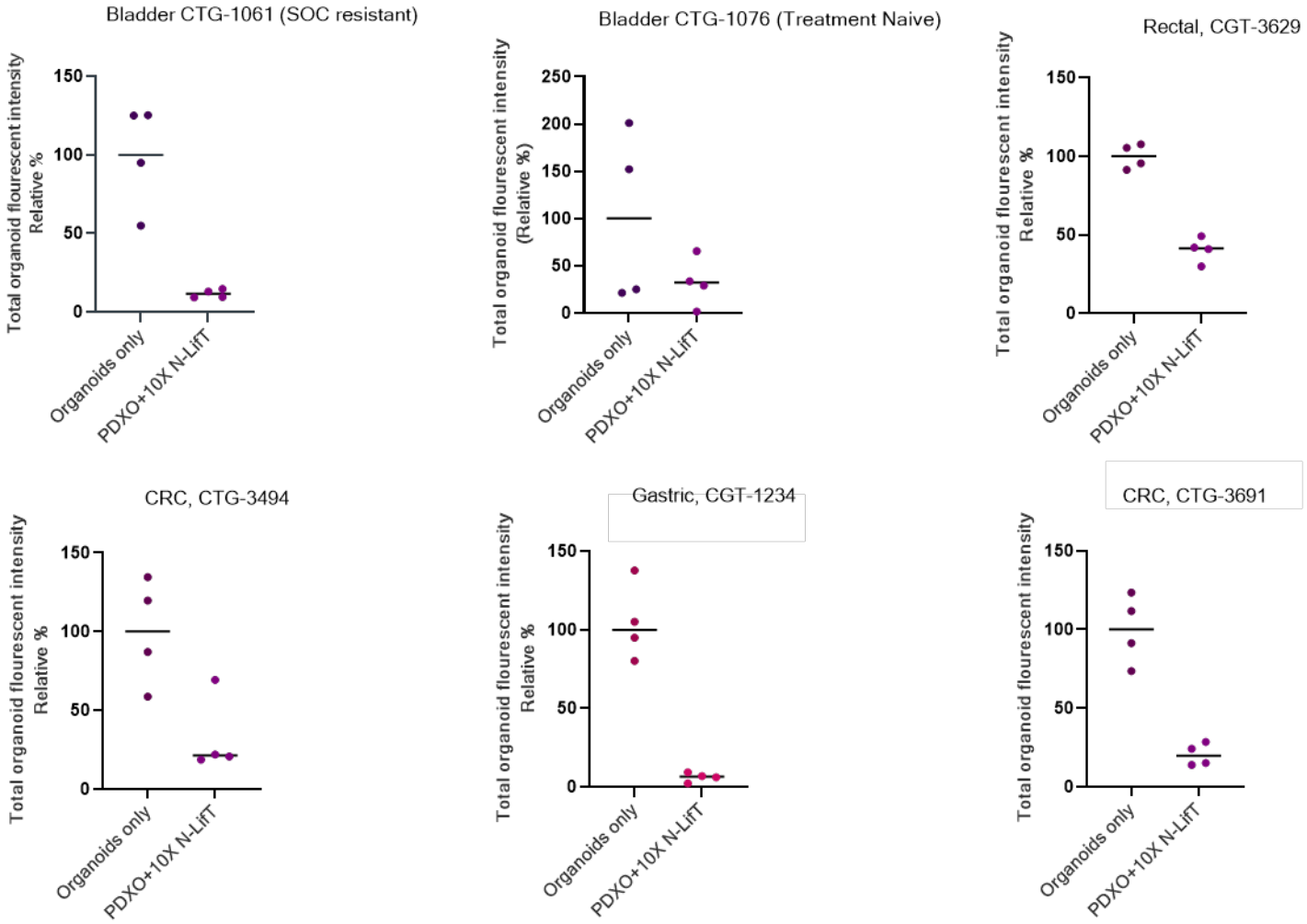


Fluorescence Intensity





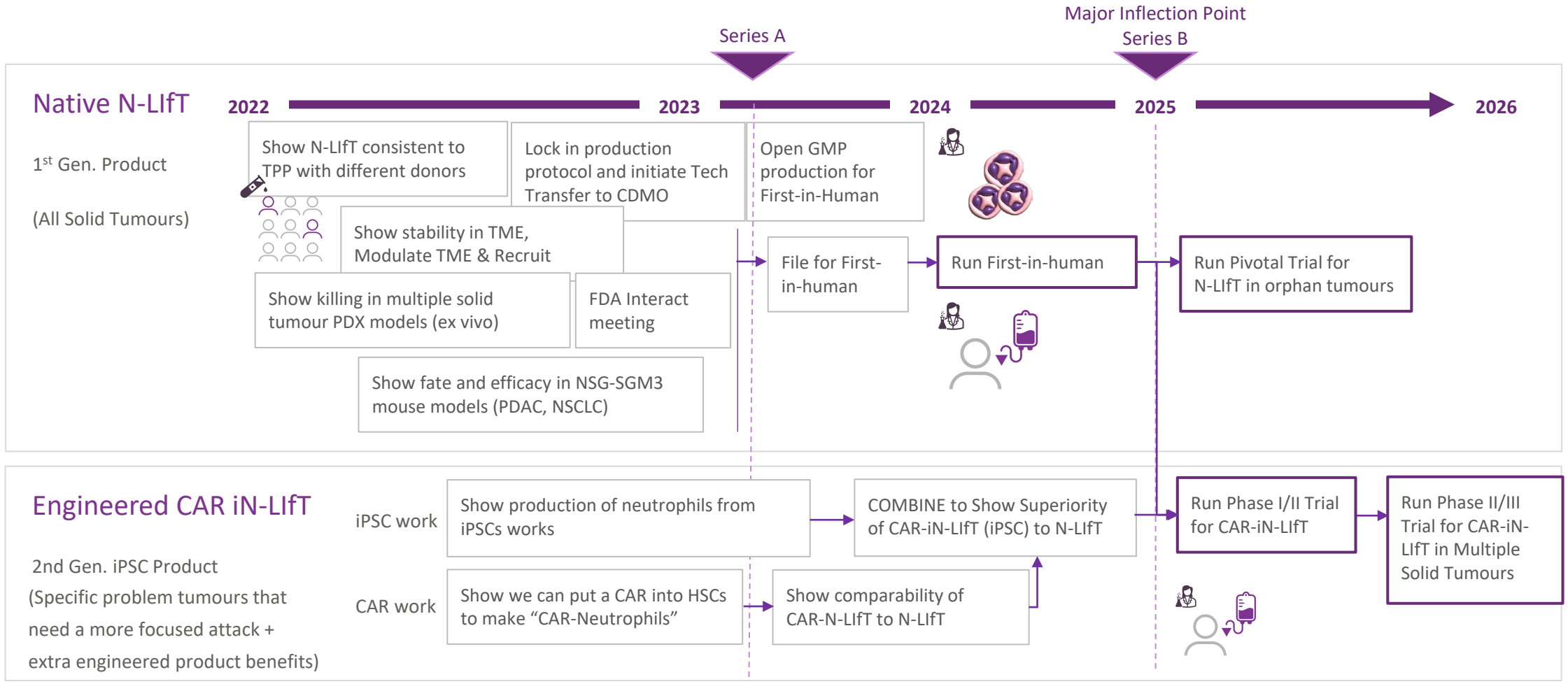
N-LIfT shows potency across multiple solid tumour types in ex vivo PDX-O models



- Efficacy of IMANs demonstrated in Bladder, CRC/Rectal and Gastric PDX-O models (combinations of treatment naïve (Bladder 1076) and SOC resistant tumours (Bladder 1061 and Gastric 1234)
- PDX model runs for 4 days off a single dose without immune cells to recruit (direct killing only). Note: in clinic repeat weekly dosing with immune system recruitment for additional cytotoxicity.
- Neck, Liver and Pancreatic models are under development
- Neck, Liver, Pancreatic and NSCLC will be used for IND enabling studies e2022

R&D Plan Overview

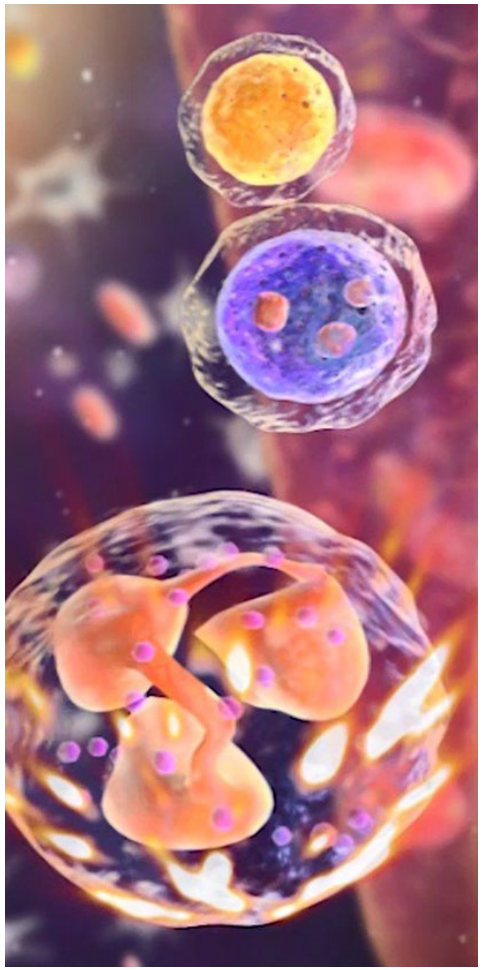
Moving into clinical trials by Q1 2024



Summary: A New Class of Innate Allogeneic Cell Therapy

- Neutrophils have long been recognised as crucial mediators of innate immunity and the first line of defence that mobilises innate and adaptive responses to return to homeostasis.
- At LIfT Biosciences, we are harnessing the innate properties of Immuno-Modulatory Alpha Neutrophils (IMANs) that exhibit exceptional cytotoxic and immunomodulatory capacity for the treatment of solid tumour indications.
- LIfT is the only Biotech company in the world with a Neutrophil Based Cell Therapy Platform that has potential across not just all solid tumours but many other therapy areas
- N-LIfT cells differentiate in vivo into Immuno-Modulatory Alpha Neutrophils (IMANs) that have the potential to overcome hurdles encountered by other cell therapies in the treatment of solid tumours, by being:
    - Allogeneic, straightforward to scale, cost effective and off-the-shelf
    - Innate antigen-independent mechanism-of-action
    - Actively recruited into the tumour micro-environment
    - Stable and capable of overcoming immunosuppressive tumour microenvironments
    - Capable of orchestrating patients own anti-tumour immune responses

- We will be looking to raise a further $50m in H1 2023 to fund moving into clinical trials by Q1 2024



LIfT BioSciences

We are now seeking

1. Research collaborations with partners
2. Funds to join our Series A Round in early 2023

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Learn More about us
LIfTBioSciences.com