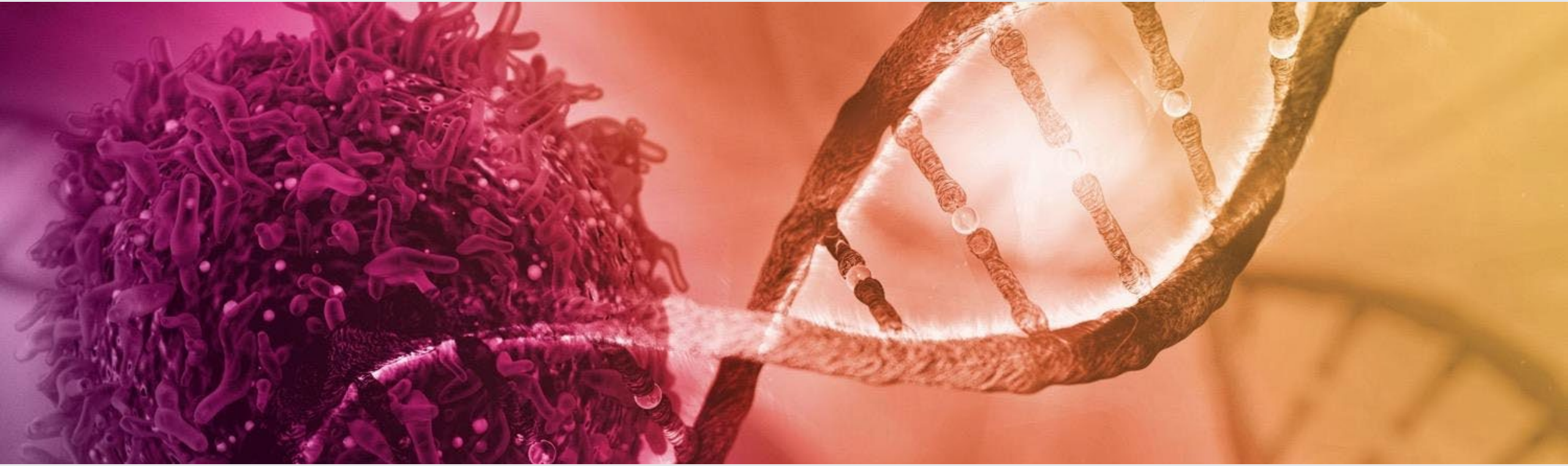


Achilles Therapeutics

AI-Powered Precision Cell Therapy Targeting All Tumor Cells

March 2023

Forward-Looking Statements / Disclaimers

This presentation contains “forward-looking statements,” including statements regarding the proposed development plans and timelines for the Company’s product candidates and the success, cost and timing of its research activities and clinical trials. Forward-looking statements can generally be identified by the use of words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “project,” “potential,” “seek,” “should,” “think,” “will,” “would” and similar expressions, or they may use future dates.

Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. These and other risks which may impact management's expectations are described in greater detail under the heading "Risk Factors" in the Company's quarterly report on Annual Report on Form 20-F and in any subsequent periodic or current report that the Company files with the SEC.

All forward-looking statements reflect the Company's estimates only as of the date of this release (unless another date is indicated) and should not be relied upon as reflecting the Company's views, expectations or beliefs at any date subsequent to the date of this release.

Transforming the treatment of solid tumors with precision T cell therapy

Company founded 2016

Nasdaq IPO: ACHL 2021

Early clinical proof of concept 2022

Clinical update 2023

Global Headquarters
London, UK

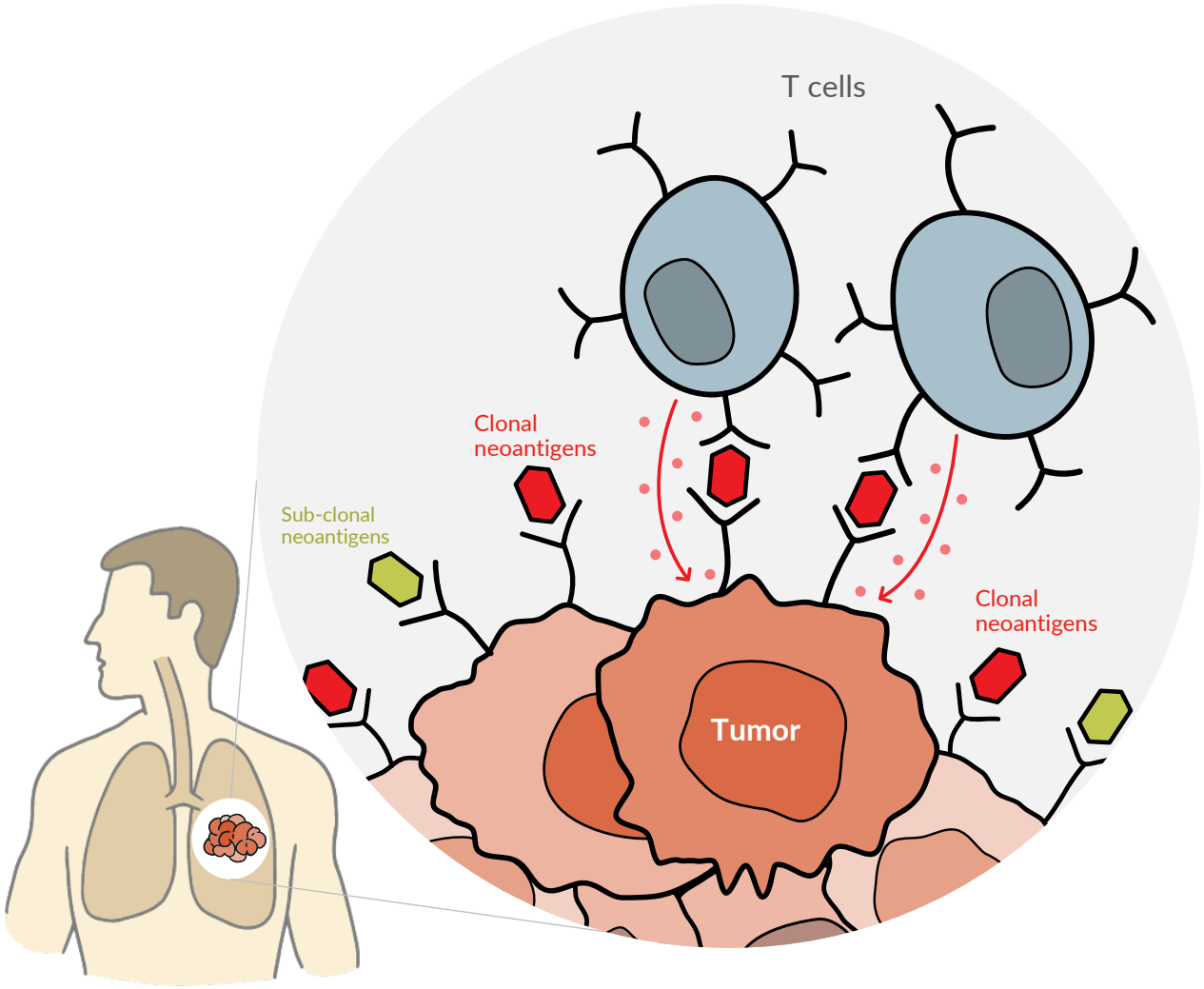
Two active clinical programs

~200 employees

$173M cash

U.S. Headquarters
Philadelphia, PA

Targeting clonal neoantigens with patented technology, linking mechanism and potency



Clonal neoantigens: a novel and ideal cancer target → **Only target present on all cancer cells, absent from healthy tissue**

Unique and world leading capability to identify clonal neoantigens → **Only neoantigen platform validated on real world data**

World class scientific platform → **Demonstrated target engagement supporting mechanism of action**

Clinical-stage precision targeting for solid tumors using clonal neoantigen-reactive T cells (cNeT)

Targeting clonal neoantigens: a novel class of cancer target present on all tumor cells

We have developed a proprietary patent protected AI platform (PELEUS®) that is validated on real world patient data (TRACERx) and which can be used to identify personal clonal neoantigens

Controlled precision therapy

Scientific platform that can quantify, characterize and track tumor reactive T cells, target engagement and mechanism of action

Emerging PoC for cNeT in NSCLC

Durable disease control achieved with cNeT monotherapy, 71% (5/7) NSCLC patients (including 1 PR and 4 SDs) with encouraging safety and tolerability

Near-term clinical milestones

Clinical and translational updates in 2023: 15-20 new patients across NSCLC (CHIRON) monotherapy and melanoma (THETIS) monotherapy and in combination with check-point inhibitor (anti-PD-1)

Strong cash position supports all planned operations into mid-2025

Cash runway of $173M (£143M) as of December 31, 2022

Experienced leadership with decades in cell therapy drug development

Sergio Quezada
CSO

UCL · CANCER RESEARCH UK · Memorial Sloan Kettering Cancer Center

Karl Peggs
CMO

UCL · NIHR National Institute for Health Research · Memorial Sloan Kettering Cancer Center

Robert Coutts
CFO

KPMG · Syncona

Iraj Ali
CEO

Syncona · McKinsey&Company

Daniel Hood
General Counsel

Intercept · GILEAD

Shree Patel
EVP, Patient Supply Operations

Cell Medica

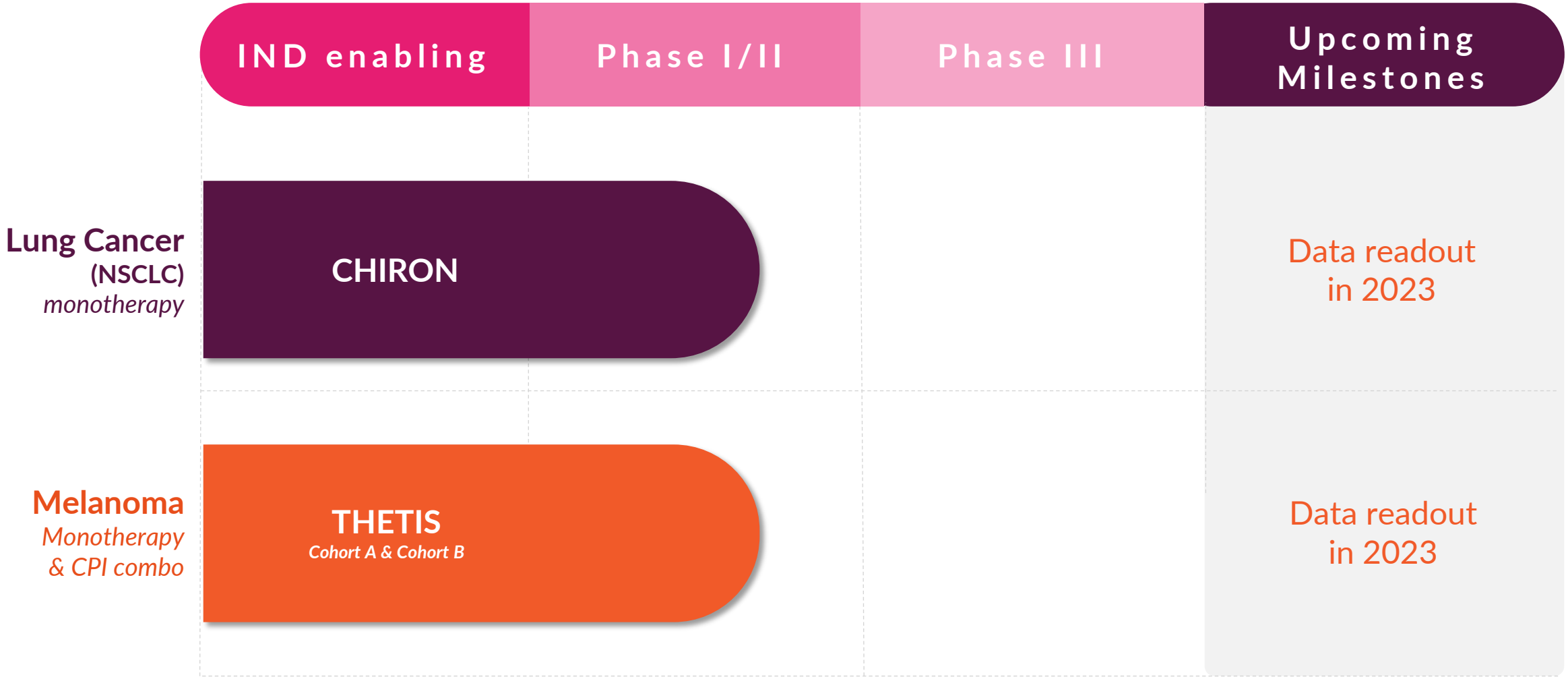
Jim Taylor
CBO

sosei HEPTARES · GSK

Ed Samuel
EVP, Technical Operations

Orchard therapeutics · COGNATE BIOSERVICES

Differentiated pipeline of precision T cell therapies across multiple solid tumors



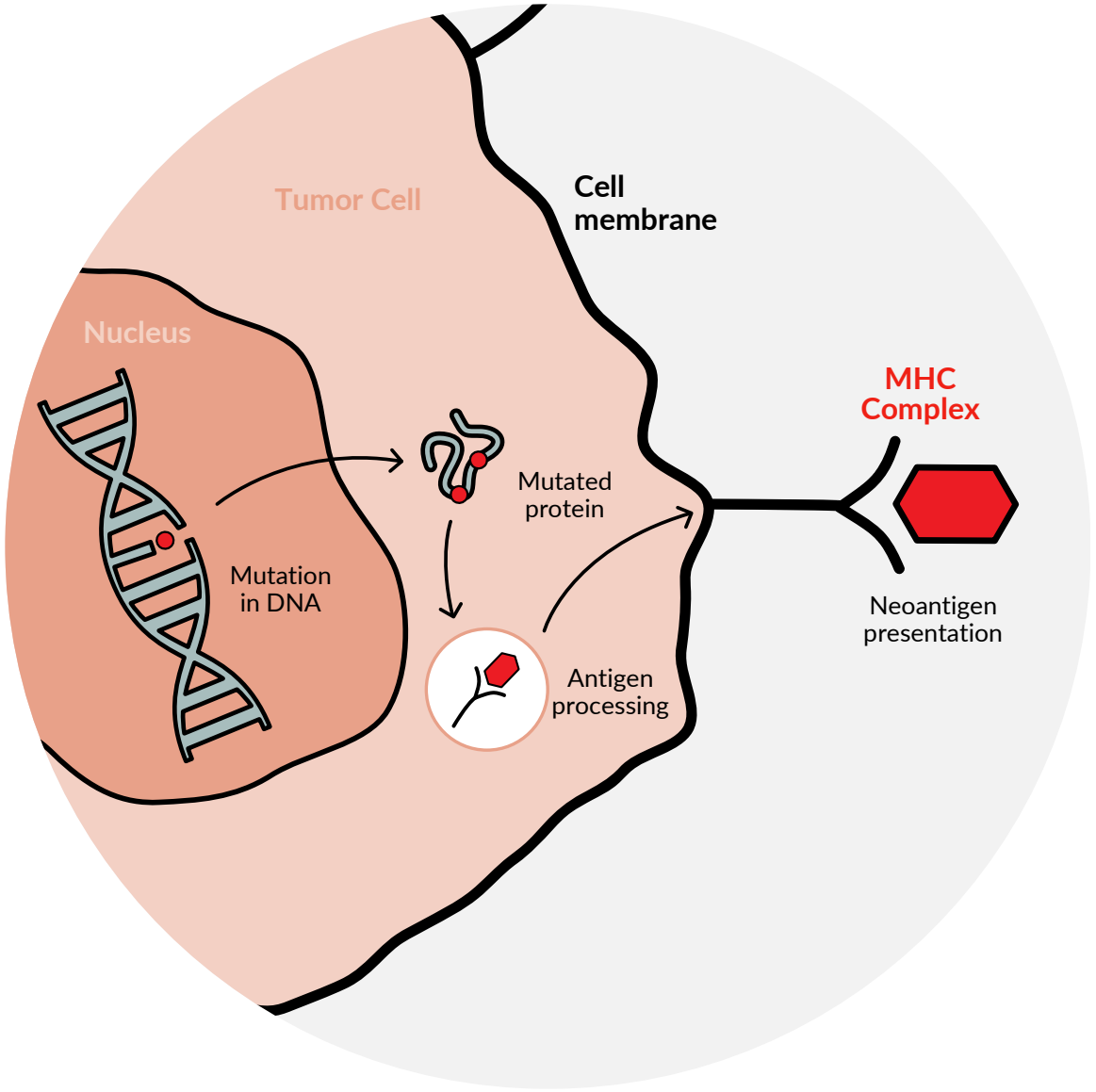
Cancer is driven by mutations to DNA which create targets for the immune system

DNA damage causes genetic alterations which can lead to cancer

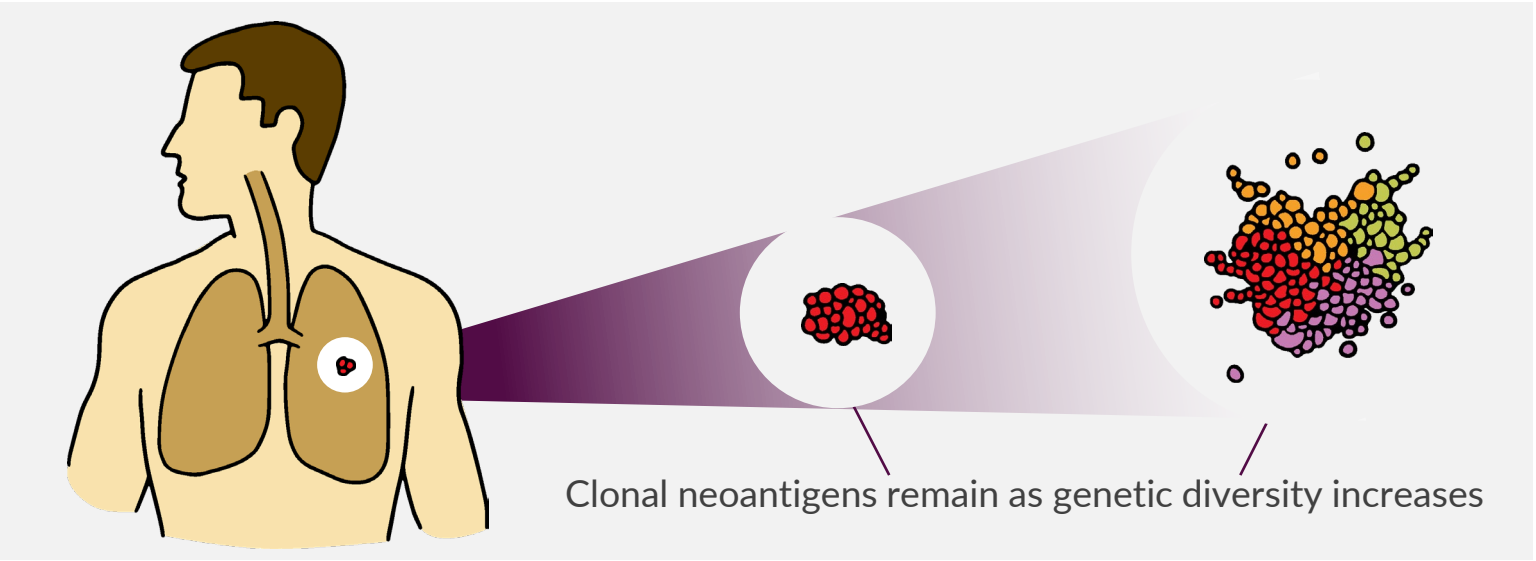
Mutated proteins from these alterations create antigens for the immune system

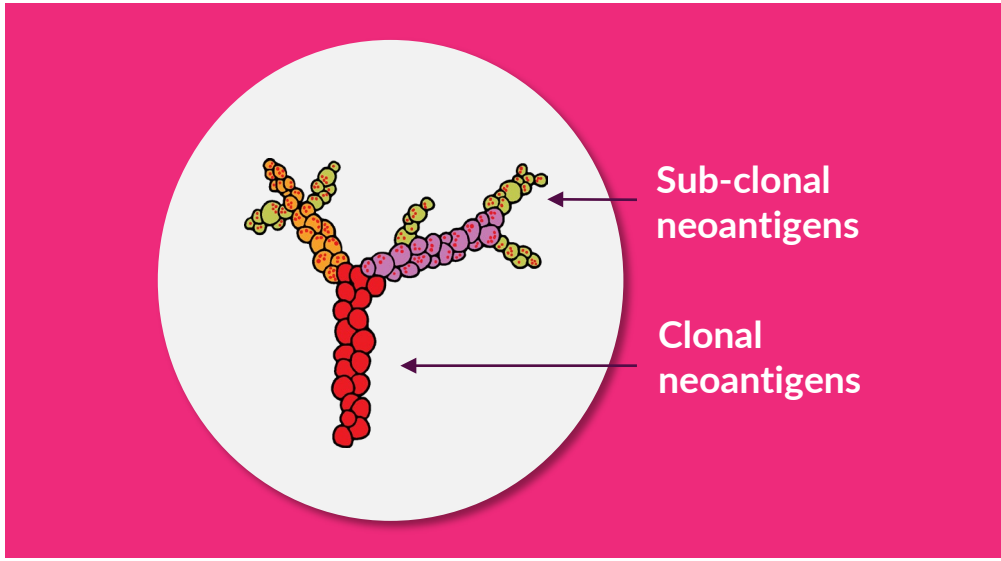
Neoantigens presented on cell surface via MHC molecules recognized by T cells

T cells will recognize neoantigens as foreign and destroy the tumor cell



A landmark study (TRACERx) demonstrated that a specific group of neoantigens (clonal neoantigens) are present on all tumor cells in cancers



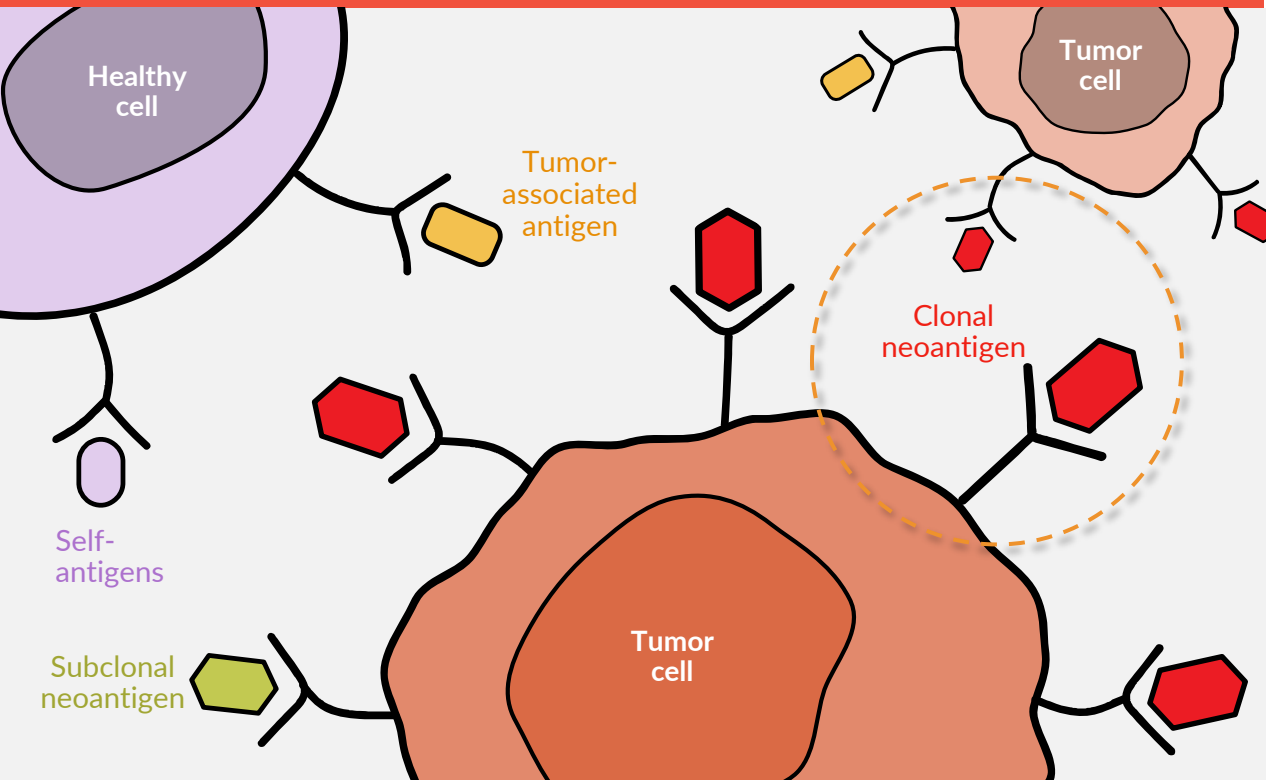


- Tumors are constantly evolving and acquiring new mutations
- This genetic diversity enables tumors to develop resistance to standard therapies
- However, original mutations (clonal neoantigens) are passed down and remain present in all tumor cells[1-4]
- We can identify the original clonal mutations for each patient and so can target multiple antigens present only on tumor cells[2-4]

1. Gerlinger et al., NEJM, 2012
2. Jamal-Hanjani et al., Plos Biol, 2014
3. Jamal-Hanjani et al. NEJM,
4. Abbosh et al., Nature, 2017

Multiple lines of clinical evidence support neoantigens as relevant cancer targets and clonal neoantigens as the predominant predictive biomarker for positive clinical outcome

Clonal neoantigens: the only known target present on all tumor cells and absent from healthy tissue



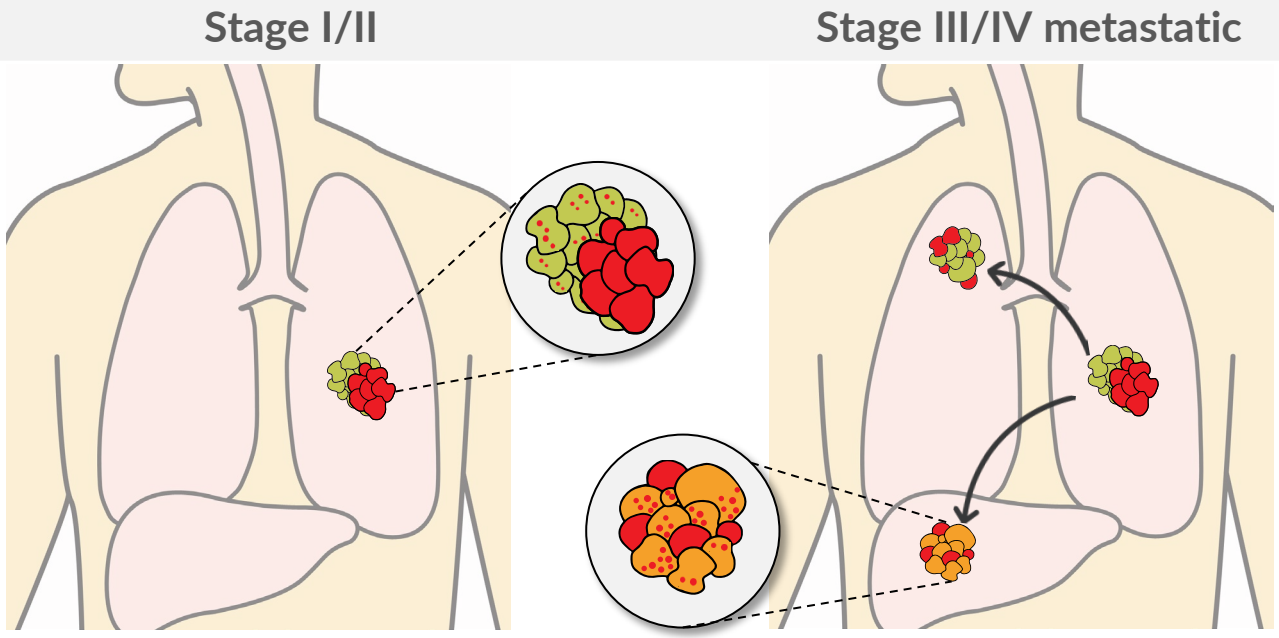
Multiple lines of evidence link neoantigens with positive clinical outcomes

- Neoantigen-reactive T cells are correlated with **improved outcomes** for **CPI and TIL** therapy[1-3]
- **Disease-free survival** is driven by the presence of **clonal neoantigens** in untreated NSCLC[4]
- Evidence that clonal neoantigens are the driver of **overall survival** in **checkpoint (CPI) therapy**[5-7]
- **mRNA vaccines targeting neoantigens** now clinically validated showing **recurrence-free survival benefit** vs anti-PD-1 alone[8]

1. *Litchfield et al. Cell 2021*
2. *Lauss et al. Nat Commun. 2017 Nov 23;8(1):1738*
3. *Kristensen et al. J Clin Invest. 2022 Jan 18;132(2):e150535*
4. *Rosenthal et al. Nature. 2019. 567 479–485*
5. *Rizvi et al. 2015 Cancer Immuno 348(6230):124-8*
6. *McGranahan et al. 2016 Science 351:1463-1469*
7. *Litchfield et al. Cell 2021*
8. *https://clinicaltrials.gov/ct2/show/NCT03897881*

TRACERx is a unique asset that enables Achilles' neoantigen identification capability

TRACERx: patients (815) enrolled with early stage to advanced NSCLC and followed over several years with extensive tumor sampling, DNA sequencing and neoantigen analysis



- Biopsies taken over five years tracking disease progression
- DNA sequencing and bioinformatic analysis confirm which neoantigens (clonal) are conserved at all tumor sites (red)

TRACERx

- TRACERx is the **largest longitudinal real-world patient data** set of its kind[1-4]
- **Unique asset** with a network of 15 NHS hospital sites using a harmonised protocol
- Extensive sequencing data (>4,000 biopsy samples across 815 patients) **identify clonal neoantigens** at **primary and metastatic sites**[1-4]
- Clonals neoantigens proven to be present in **all tumor sites, at all time points**[4]
- Clonal neoantigens can be identified by their specific sequence "signatures" using our **patent protected** PELEUS platform

1. Jamal-Hanjani et al., Plos Biol, 2014
2. Jamal-Hanjani et al. NEJM, 2017
3. Abbosh et al., Nature, 2017
4. Rosenthal et al., Nature, 2019

PELEUS: Patented AI-driven neoantigen prediction model built and validated on real-world data

AI-powered neoantigen prediction

- Neoantigen identification requires an advanced computational approach
- AI and machine learning developed to enable reliable and rapid processing of complex patient DNA data
- Our neoantigen prediction method is patented and validated with real-world patient data

Compares tumor DNA to healthy DNA to differentiate clonal and subclonal neoantigens

Method for identification of clonal neoantigens can be applied to multiple tumor types

PELEUS: An industry leading neoantigen platform

- Uniquely positioned to validate our clonal neoantigen predictions (>10,000 predicted clonal neoantigens validated with human patient data)
- Our AI-platform can predict neoantigen immunogenicity based on real world T cell reactivity data
- Our extensive real-world patient datasets can be mined for targetable mutations and associated TCRs

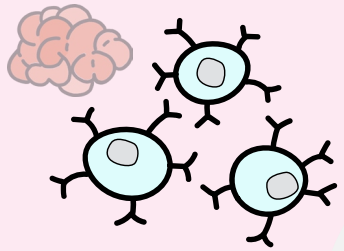
1. Jamal-Hanjani et al., Plos Biol, 2014
2. Jamal-Hanjani et al. NEJM, 2017
3. Abbosh et al., Nature, 2017
4. Rosenthal et al., Nature, 2019

Clonal neoantigens can be targeted with a range of therapeutic modalities

Current Achilles approach

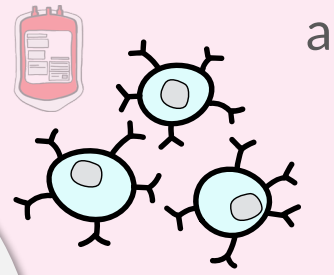
TIL-based cNeT

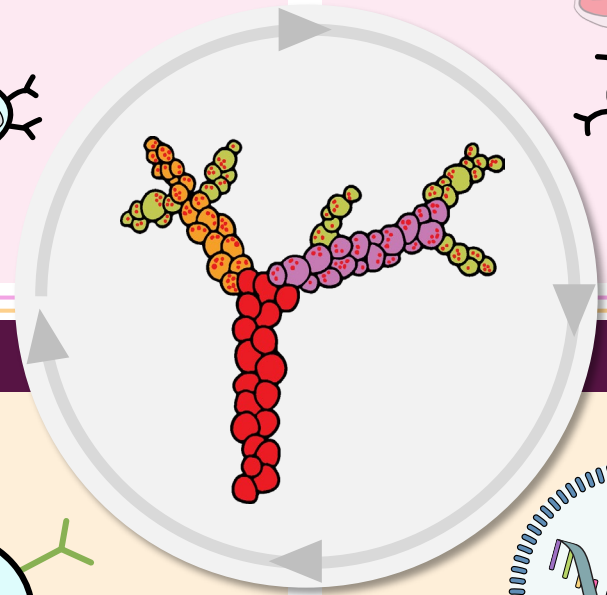
Sourcing cNeT from TIL – a clinically validated approach across multiple solid tumor settings



Blood-based cNeT (cNeT)

Investigational approach exploring use of blood as source of cNeT, without the need for surgery

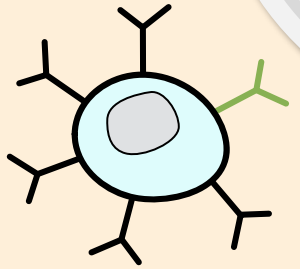




Alternative modalities

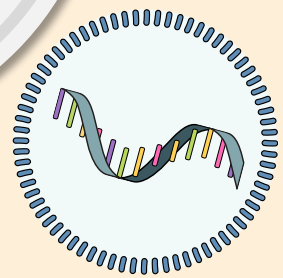
TCR-therapy for shared neoantigens

Engineered TCR therapy equips activated T cells with specific receptors that can target shared neoantigens



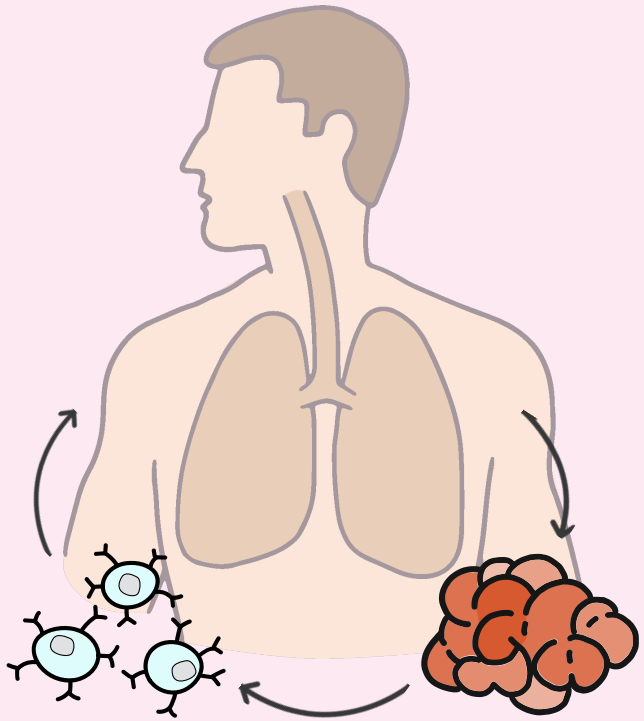
Clonal neoantigen vaccines (mRNA)

Instruct cells in the body to translate RNA to make clonal neoantigens, which activate an immune response



Compelling clinical data support TIL based approaches, but a significant opportunity remains

TIL: impressive clinical responses seen in multiple late-stage settings



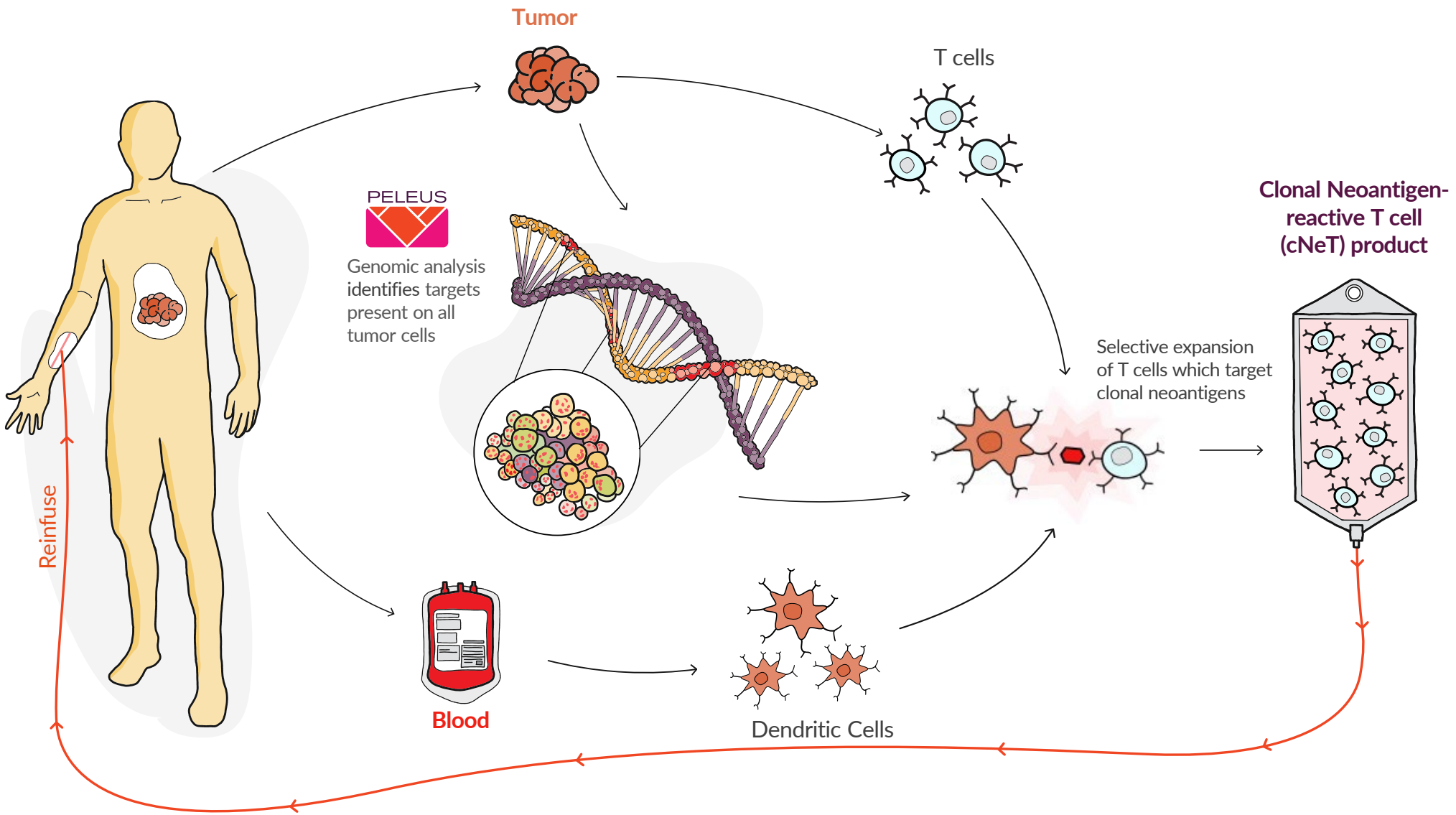
- 31% ORR TIL monoTx in PD-1 refractory **melanoma** (n=153)[1]
- 21% ORR TIL monoTx in PD-1 refractory **NSCLC** (n=28)[2]
- 44% ORR TIL monoTx in pre-treated **cervical cancer** (n=27)[3]

- TIL therapy uses uncontrolled expansion that will enrich both sub-clonal and clonal neoantigen reactive T cells and can result in T cell exhaustion
- Opportunity to **build on and improve traditional TIL** therapy: by prospectively targeting clonal neoantigens we aim to enrich the tumor reactive component and deliver a **more potent product**

[1] *Chesney et al. Journal for ImmunoTherapy of Cancer 2022;10:e005755;* [2] *IOVANCE Cohort 3B*
[3] *IOVANCE ASCO abstract May 2019*

Achilles process delivers precision clonal neoantigen targeting T cell therapy (cNeT)

Cutting edge personalized genomics and machine learning enable targeting of all cancer cells



Two studies open in advanced NSCLC and melanoma

CHIRON
Advanced NSCLC

Monotherapy

- Advanced unresectable or metastatic Stage III-Stage IV NSCLC
- Never-smokers and EGFR/ALK/Ros-1 mut excluded
- Open-label
- n = up to 40
- Option to open Cohort B in combination with a PD-1 inhibitor

Evaluating safety, tolerability and activity (RECIST) and biomarkers of clinical activity

Ongoing in UK, Europe and US

THETIS
Melanoma

Cohort A – Monotherapy

- Recurrent or metastatic malignant melanoma (n = up to 40); Open-label
- Acral, uveal and mucosal melanoma excluded

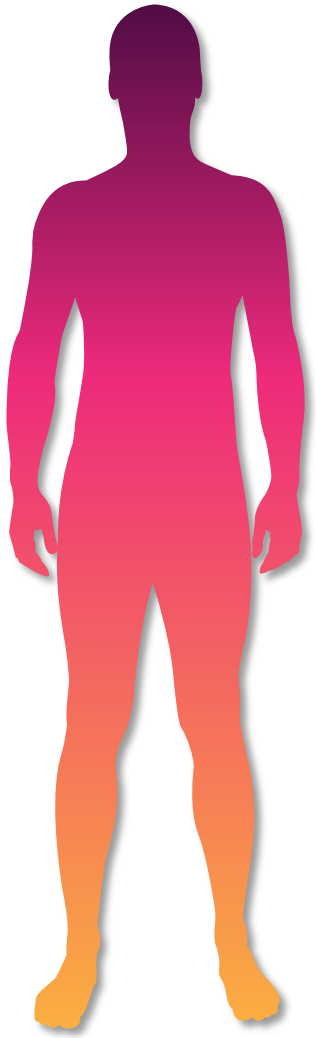
Cohort B – Combination with PD-1 inhibitor (nivolumab)

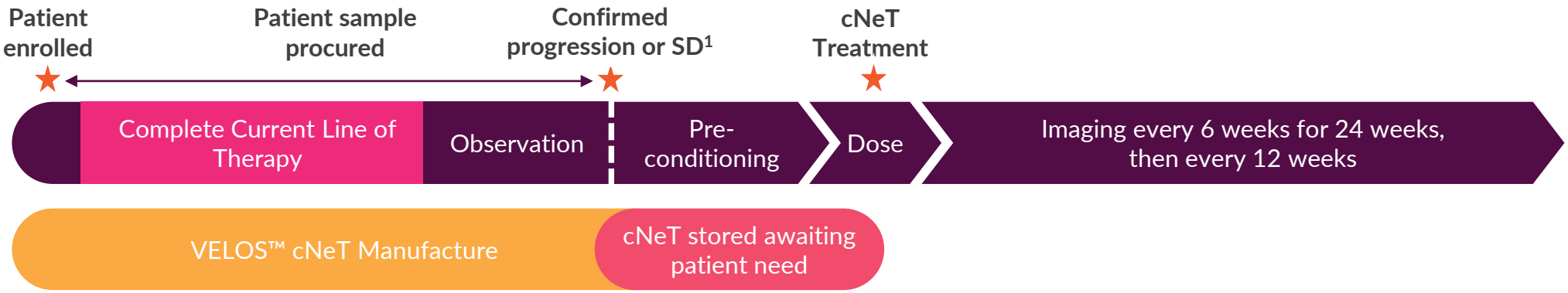
- n = up to 20 checkpoint refractory patients; Open-label
- CPI dosed 7-13 days prior to cNeT and restarted day 14 post-cNeT

Evaluating safety, tolerability and activity (RECIST) and biomarkers of clinical activity

Ongoing in UK and Europe, expanding to US

cNeT therapies will be readily delivered within standard treatment pathways





Manufacturing

Manufactured and cryopreserved for infusion

Tolerable pre-conditioning

Lower, more tolerable pre-conditioning (cy/flu)

Low IL-2

Lower dose IL-2 vs existing TIL therapies

1. Begin treatment process with confirmed stable disease or progression per site protocol

cNeT were generally well tolerated in the fourteen patients treated in CHIRON & THETIS

Heavily pretreated patients with advanced cancer

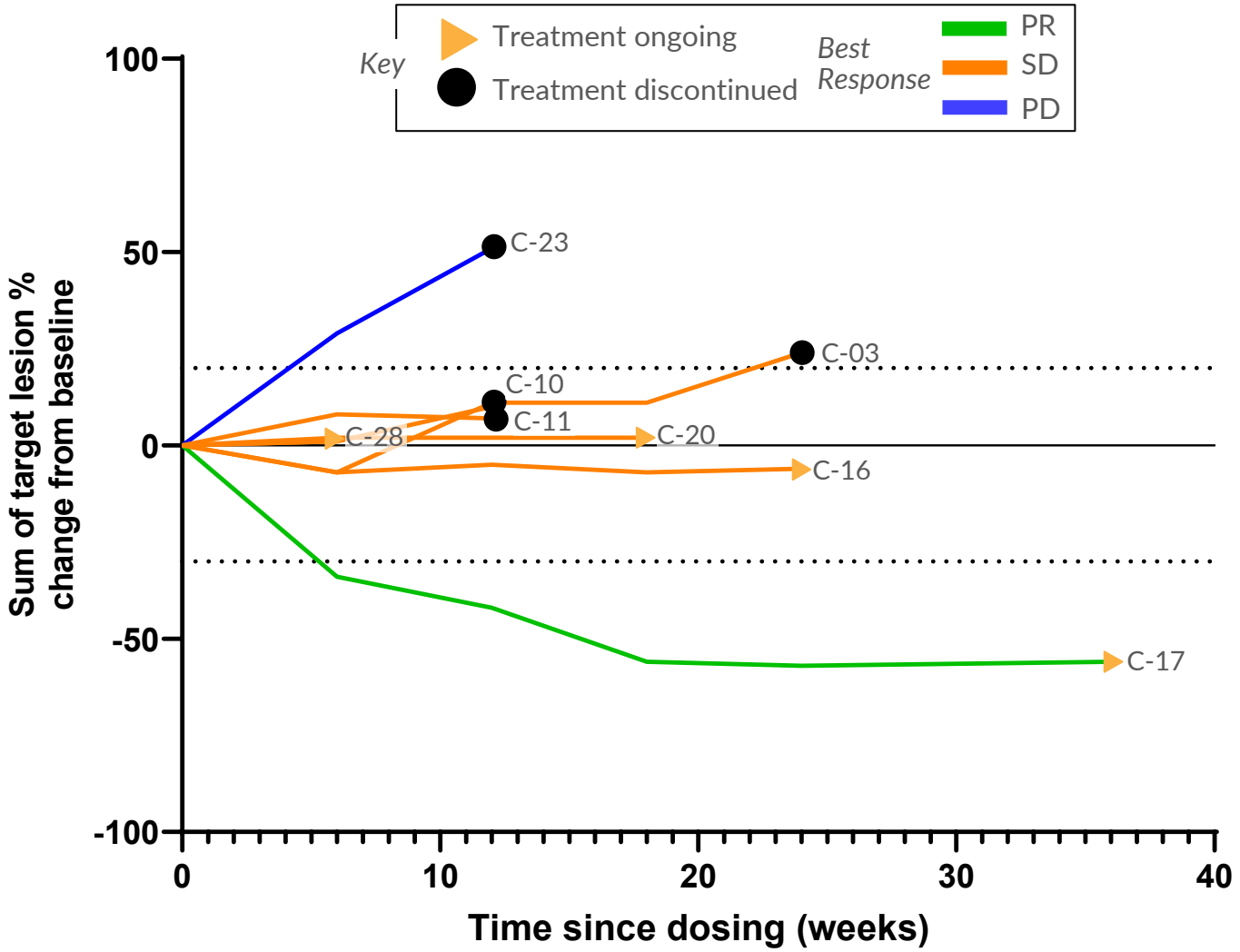
- Eight advanced unresectable or metastatic NSCLC patients (CHIRON)
- Six relapsed/refractory melanoma patients (THETIS)
- Two median lines of prior therapy, all patients refractory to checkpoint inhibitor (CPI)
- All patients had progressive disease at time of lymphodepletion
- Process improvements delivering median cNeT dose of 78M (n=3 dosed patients)

cNeT tolerability profile[1]

- Tolerability similar to standard TIL
- No new cNeT-related SAEs or dose-limiting toxicities since last report (ESMO 2022)
- Lower dose lymphodepletion and lower dose IL-2 well tolerated
  - 124/130 (95%) scheduled IL-2 doses delivered
- Lymphopenia and neutropenia the most common AEs

1. Safety data cut-off on September 7th 2022, at which point 13 of the 14 pts had been dosed

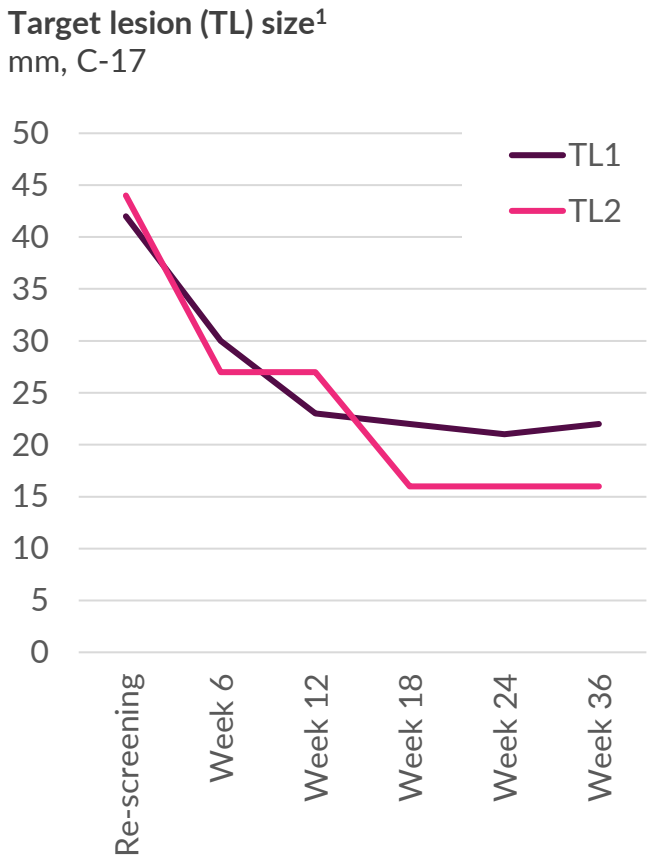
8 CHIRON (NSCLC) patients dosed with Best Response of PR and SD[1]



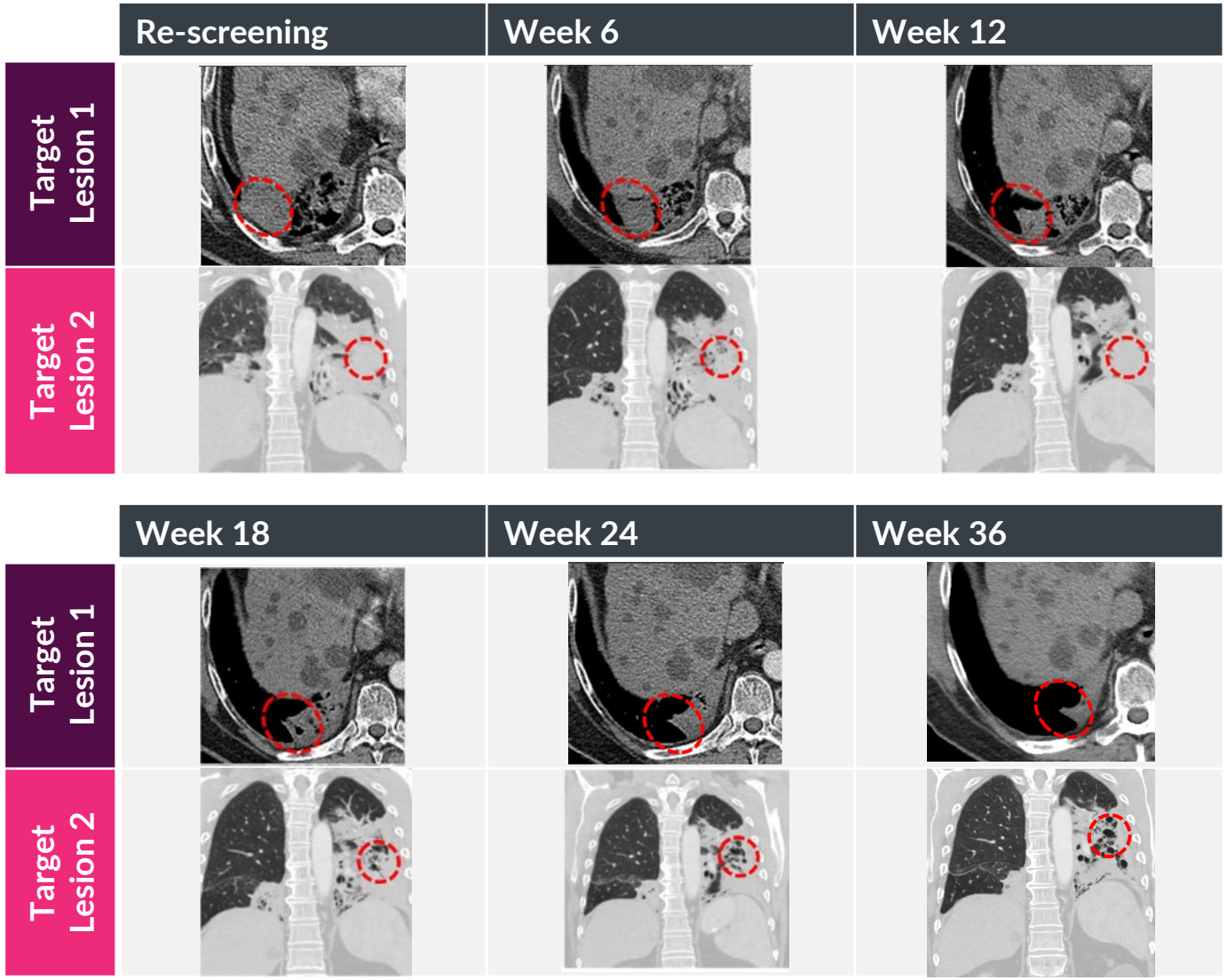
- **Early proof-of-concept demonstrated in NSCLC**
  - Disease control at >12 weeks observed in 5 of 7 evaluable patients (71%), including one PR (>36 weeks)
  - 4 of 7 (57%) out to >18 weeks
- **PR/SD with lower dose lymphodepletion and IL-2**
  - Supports potential for wider applicability of cNeT, including in an ambulatory setting

1. *As reported at ESMO IO 2022*

Patient C-17: 56% reduction in total target lesion size vs. baseline at week 36



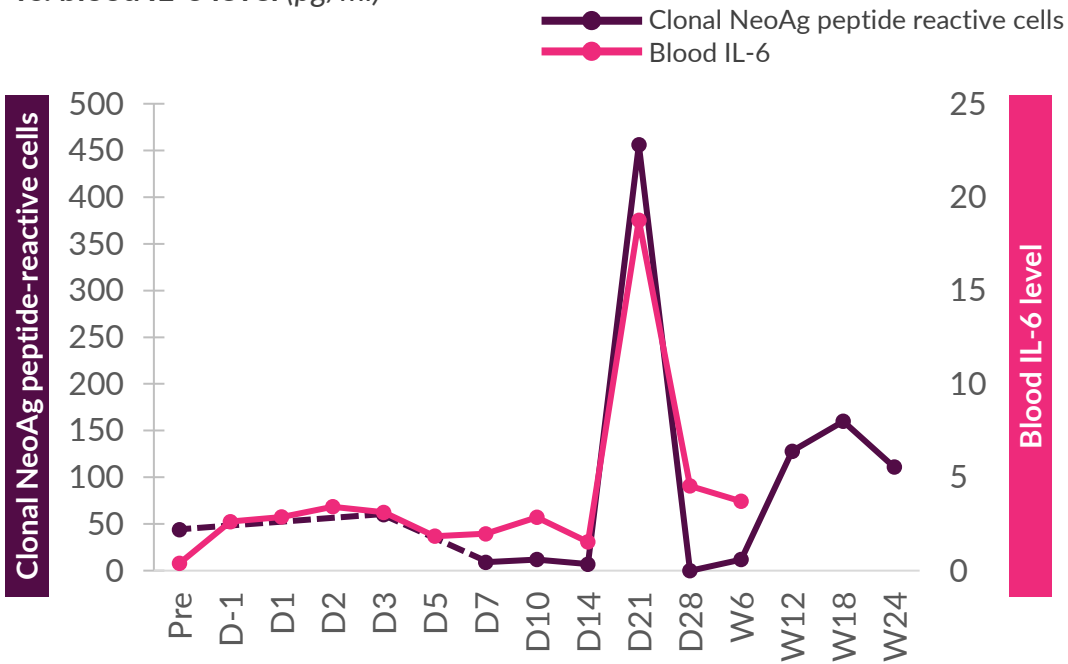
Total target lesion reduction of 56% at wk 36, with a 64% reduction in Target Lesion 2



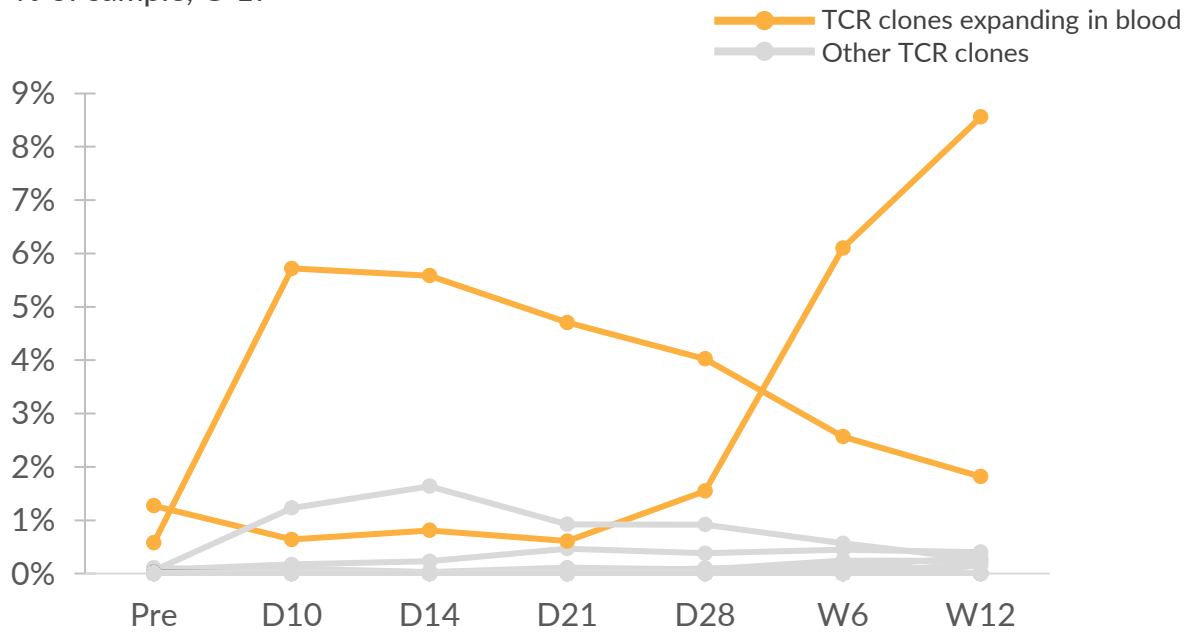
1. Site-reported lesion size
NB C-17 known to have polycystic liver disease

Patient C-17: cNeTs expand and persist beyond week 12 coincident with tumor regression

Clonal neoantigen peptide-reactive cells in blood *(normalized spot count)* **vs. blood IL-6 level** *(pg/ml)*



Detection of T cell receptors from the product
% of sample, C-17



Clonal neoantigen reactive T cells detected in blood-post dosing, with peak at Day 21 – coincident with peak in serum cytokine associated with T cell activity (IL-6)

T cell clones that are clonal neoantigen-specific are identified expanding in the patient beyond 12 weeks and to a greater extent than other patients

Durable clinical benefit and encouraging safety and tolerability data with cNeT therapy

Lymphodepletion & IL-2 well tolerated

- Lower dose lymphodepletion and IL-2 and 95% of IL-2 doses well tolerated
- Supports potential for wider applicability of cNeT, including in an ambulatory setting

Early PoC in NSCLC

- Disease control >12 weeks in 71% patients, including one PR (>36 weeks[1])
- Potential for deep, durable clinical responses with reduced lymphodepletion and IL-2

cNeT Driving Anti-tumor Activity

- Engraftment & cytokine profiles supportive of cNeT driving anti-tumor activity
- Active cNeT peak expansion at day 21 coincides with peak in IL-6 (marker of activity)

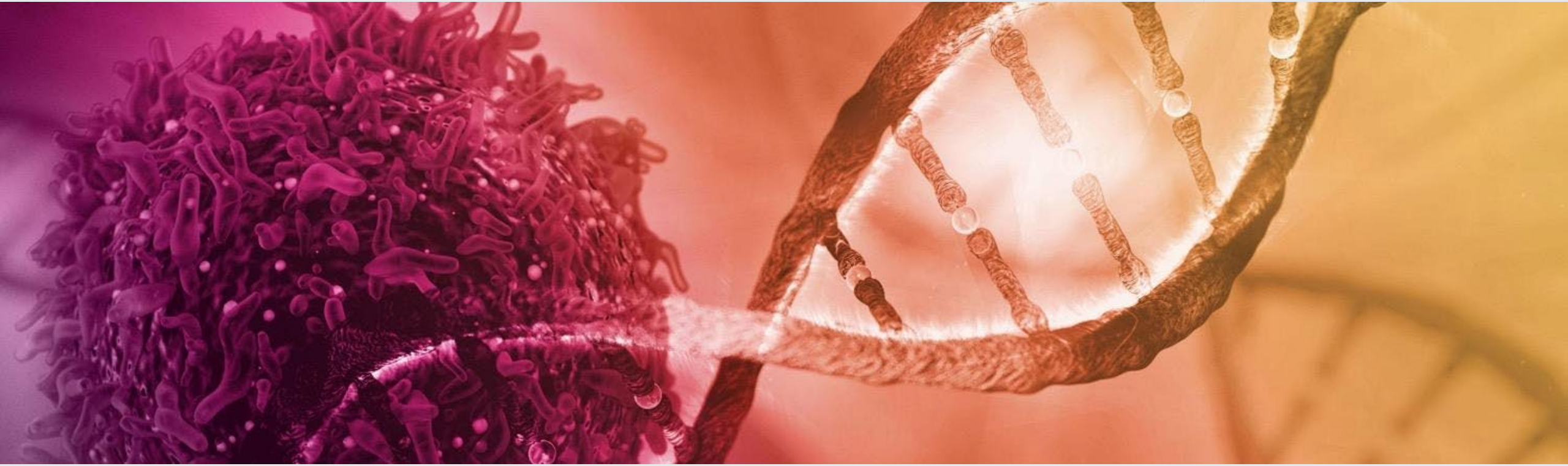
1. *As reported at ESMO IO 2022*

Efficient scale-up of GMP manufacturing to align with clinical and commercial need

- Flexible manufacturing allows efficient alignment of scale-up
- GMP facilities at Royal Free Hospital in London and Catapult site in Stevenage, UK currently support global clinical trial manufacturing
- Identified and initiated tech transfer to CDMO in Philadelphia, USA, in preparation for expansion
- Design work complete for GMP modular facility to support late stage clinical and commercial supply

Focus for CHIRON and THETIS data readouts in 2023

Clinical	Dose & deliver data from 15-20 additional patients with cNeT monotherapy (lung & melanoma) and CPI combo (melanoma)
	Drive additional confirmed responses in CHIRON and THETIS patients with higher cNeT doses
Translational	Leverage world-class translational science platform to define actionable cNeT features of response
Process	Continue PELEUS™ and process development to optimize dose and identify new sources of clonal neoantigens



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AI-Powered Precision Cell Therapy Targeting All Tumor Cells

March 2023