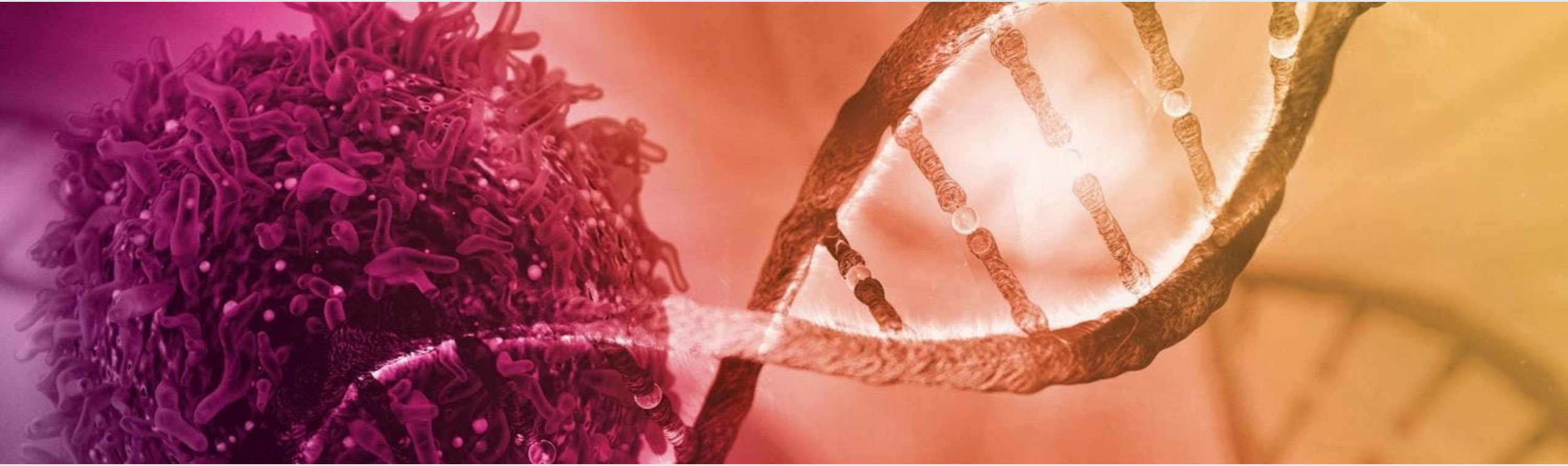

Achilles Therapeutics

Targeting Clonal Neoantigens to Treat Solid Tumors with AI-Powered Precision Cell Therapy

January 2023

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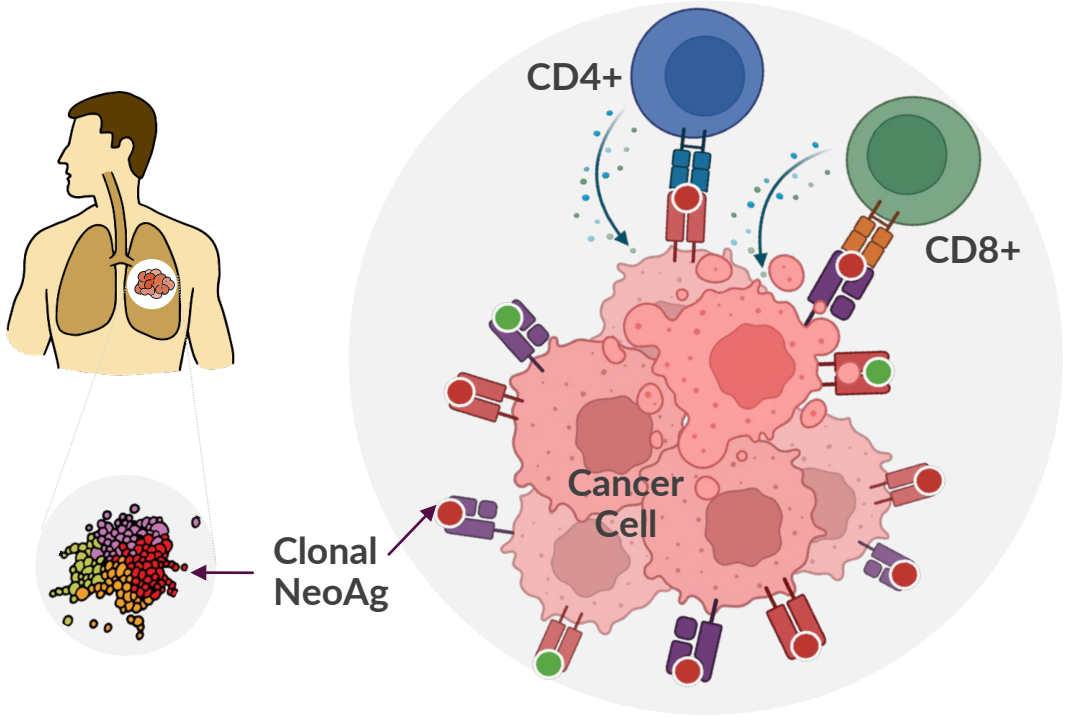
Certain graphics within were created with BioRender.com.

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

Transforming the treatment of solid tumors with precision T cell therapy by:

- targeting clonal neoantigens present on all cancer cells
- linking mechanism of action and potency with our translational science platform



Global Headquarters
London, UK

U.S. Headquarters
Philadelphia, PA

Founded 2016

Nasdaq IPO 2021

Early PoC 2022

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

Emerging PoC for cNeT in NSCLC

Durable disease control achieved with cNeT monotherapy through 12 weeks

71% (5/7) NSCLC patients (including 1 PR and 4 SDs); encouraging safety and tolerability

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

Developed a proprietary patented AI platform (PELEUS®) validated on real world patient data (TRACERx)

Controlled precision therapy

Scientific platform that can quantify, characterize and track the tumour reactive component to deconvolute mechanism of action, define potency and drive process improvements

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

Cash runway of £161M* as of September 30, 2022 supports all planned operations into mid-2025

* £1.000 = $1.116 for 9/30/2022 reporting of GBP balances in USD

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

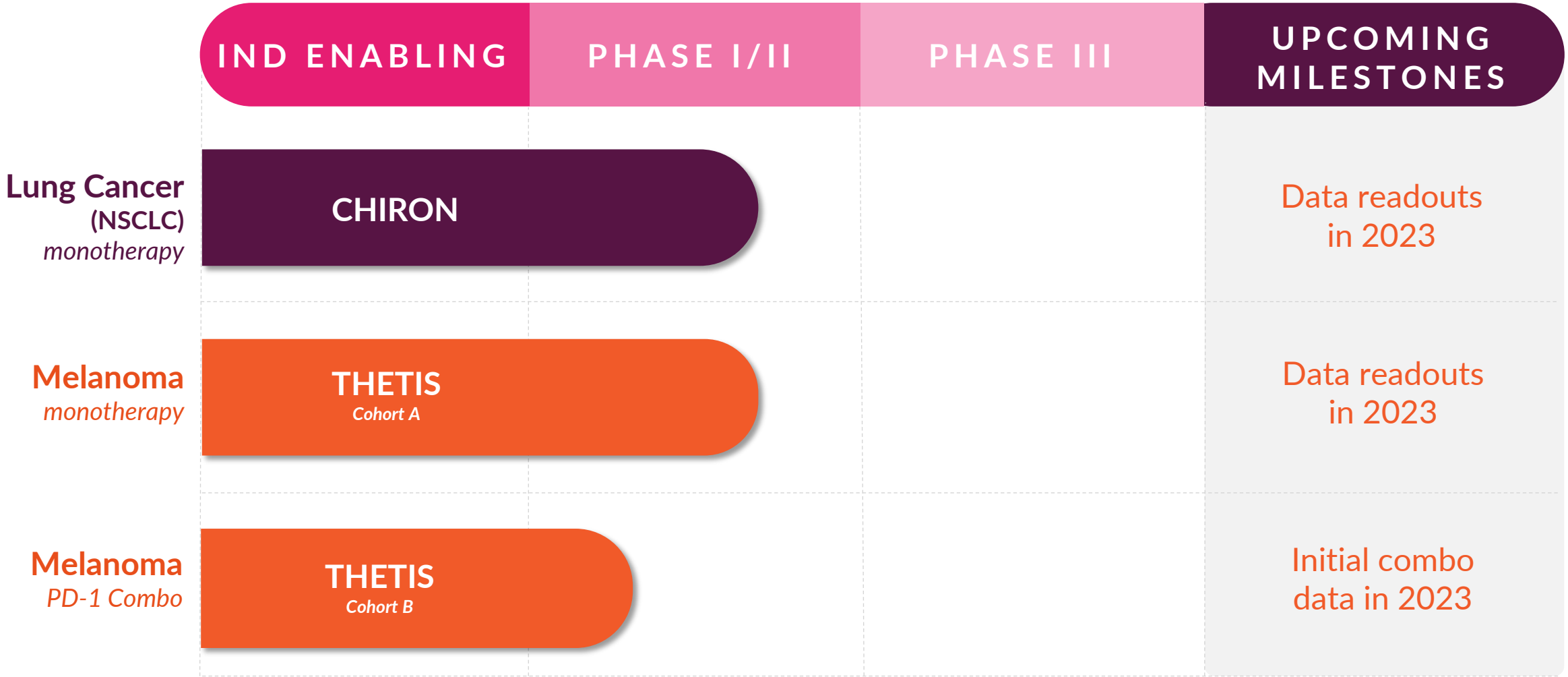
Jim Taylor
CBO

sosei HEPTARES · GSK

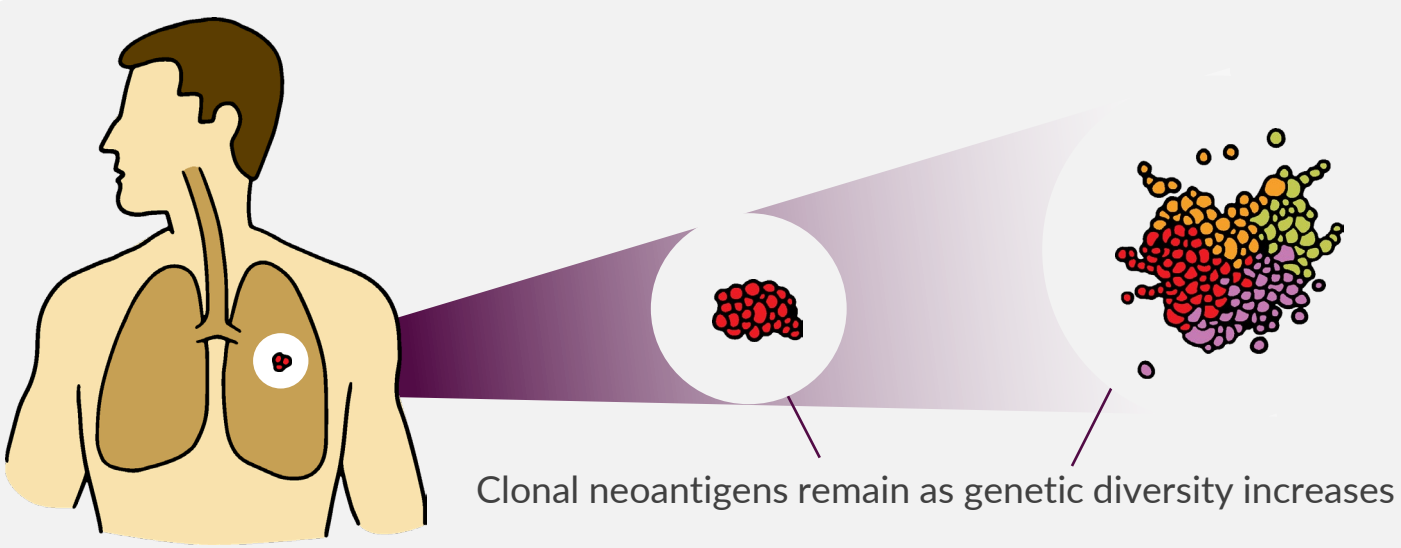
Ed Samuel
EVP, Technical Operations

Orchard therapeutics · COGNATE BIOSERVICES

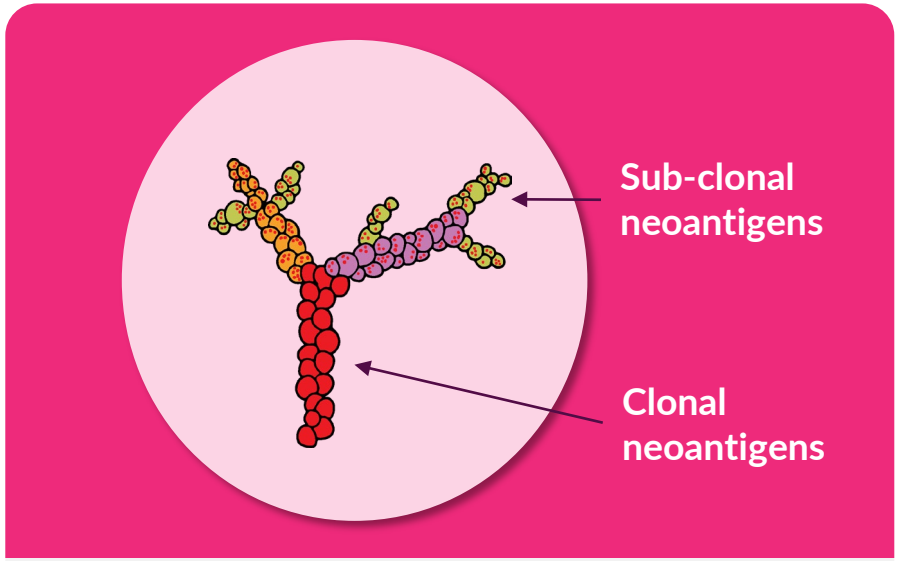
Differentiated pipeline of precision T cell therapies across multiple solid tumors



Ideal cancer targets: clonal neoantigens present on all tumor cells and absent from healthy tissue



- Tumors are constantly evolving and acquiring new mutations
- Genetic diversity enables tumors to develop resistance to standard therapies which leads to disease relapse
- Despite increased genetic diversity the original mutations (clonal neoantigens) always remain[1]
- We can identify the original (clonal) mutations and so target multiple antigens present only on tumor cells



Clonal neoantigens are

- Original mutations formed early in tumor evolution
- Expressed on all cancer cells[1] and absent from healthy tissue
- Found in multiple tumor types as tumor evolution principles apply across multiple solid cancers

1. Gerlinger et al., NEJM, 2012

PELEUS is a 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

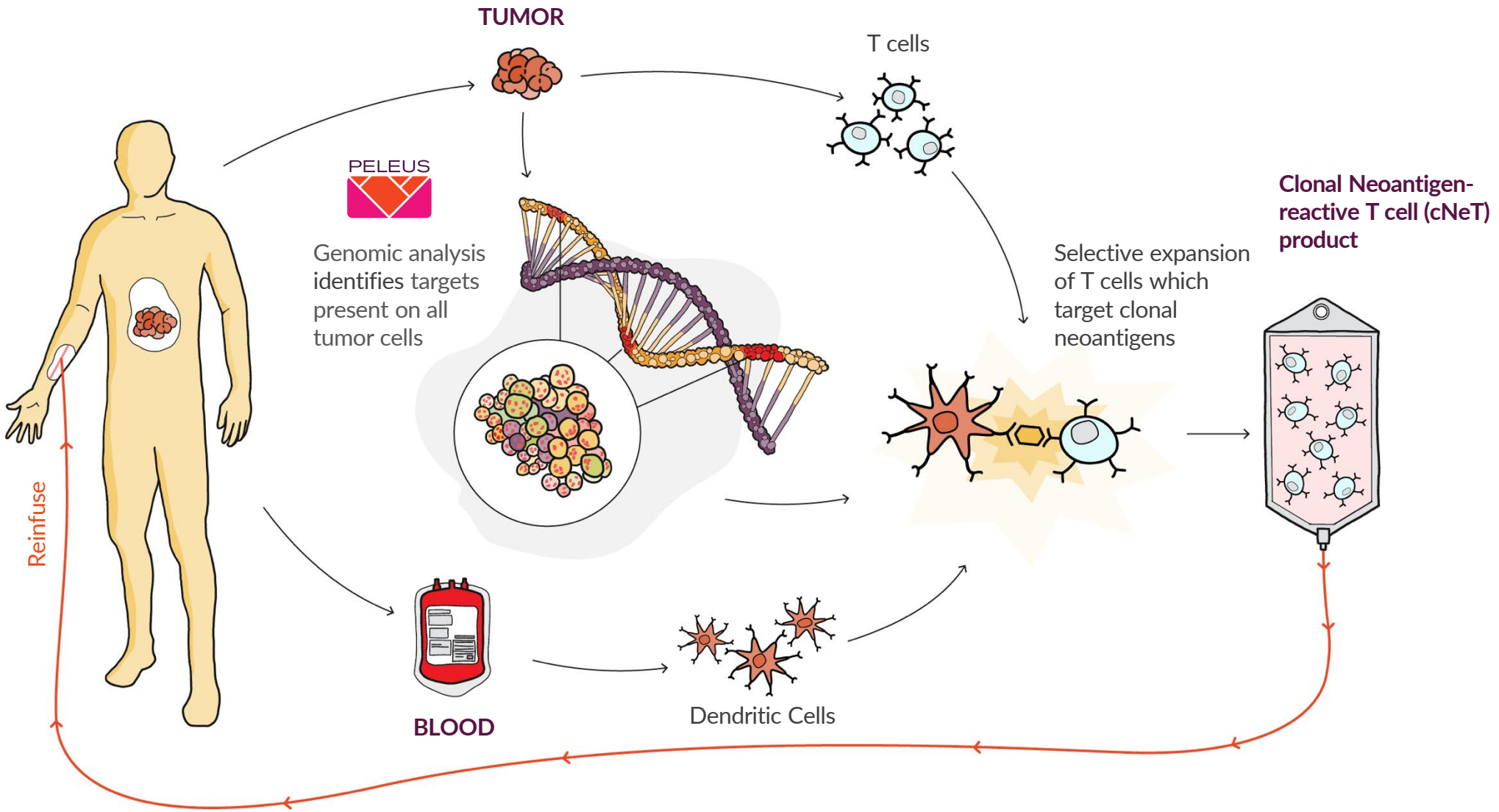
Trained and validated on TRACERx data

- TRACERx is the largest longitudinal patient data set[1-4] of its kind
- Unparalleled network of 15 NHS sites
- 3,200 tumor regions collected from over 800 NSCLC patients over 5 years
- Multi-region data from primary & metastatic sites used to confirm clonal status

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

VELOS™ 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, EU 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, expanding to EU & US

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

Early PoC in NSCLC

- Disease control >12 weeks in 71% patients, including one PR (>36 weeks)
- 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)

Lymphodepletion & IL-2 well tolerated

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

World Class Translational Science

- Proprietary platform identifies product features associated with clinical response
- Driving development of the VELOS manufacturing process and potency assay

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

Heavily pretreated patients with advanced cancer

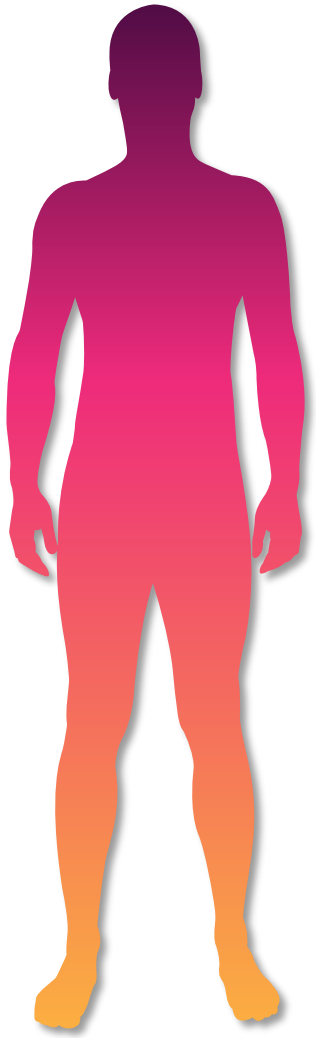
- Eight advanced unresectable or metastatic NSCLC patients (CHIRON)
- Six relapsed/refractory melanoma patients (THETIS)
- Two median lines of prior therapy, all patients refractory to checkpoint inhibitor (CPI)
- All patients had progressive disease at time of lymphodepletion
- Process improvements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

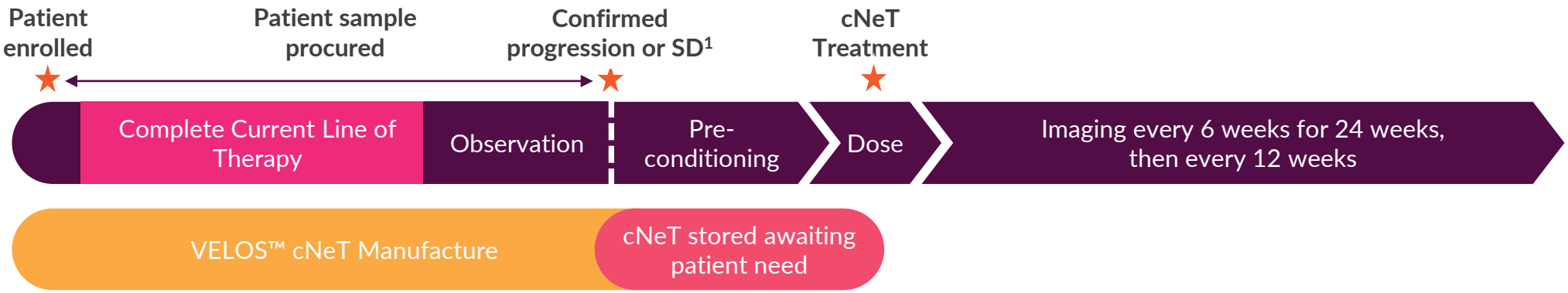
cNeT tolerability profile[1]

- Tolerability similar to standard TIL
- No new cNeT-related SAEs or dose-limiting toxicities since last report (SITC 2021)
- 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
- One previously reported ICANS event deemed to be possibly related to cNeT treatment

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

cNeT therapies can be readily delivered within standard treatment pathways





Manufacturing

Manufactured and cryopreserved for infusion

Tolerable pre-conditioning

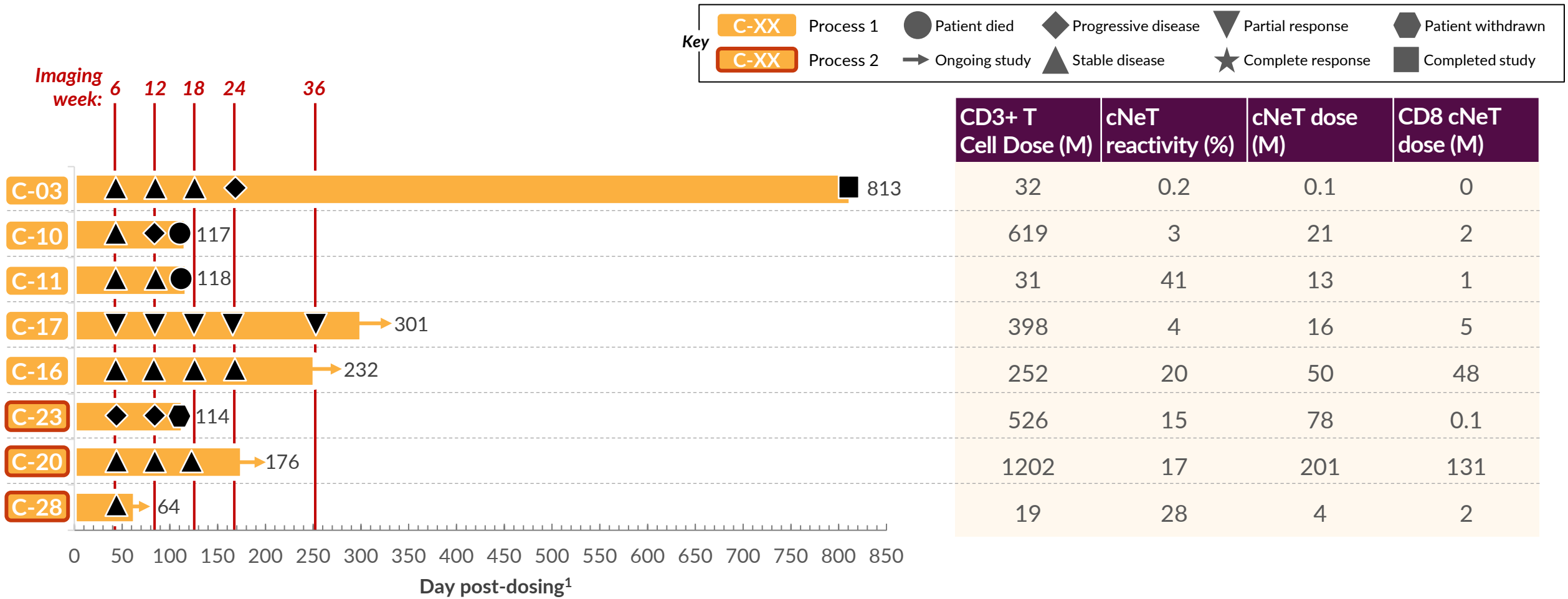
Lower, more tolerable pre-conditioning (cy/flu)

Low IL-2

Lower dose IL-2 vs existing TIL therapies

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

CHIRON: 5 of 7 (71%) evaluable patients showed durable clinical benefit ≥12 weeks

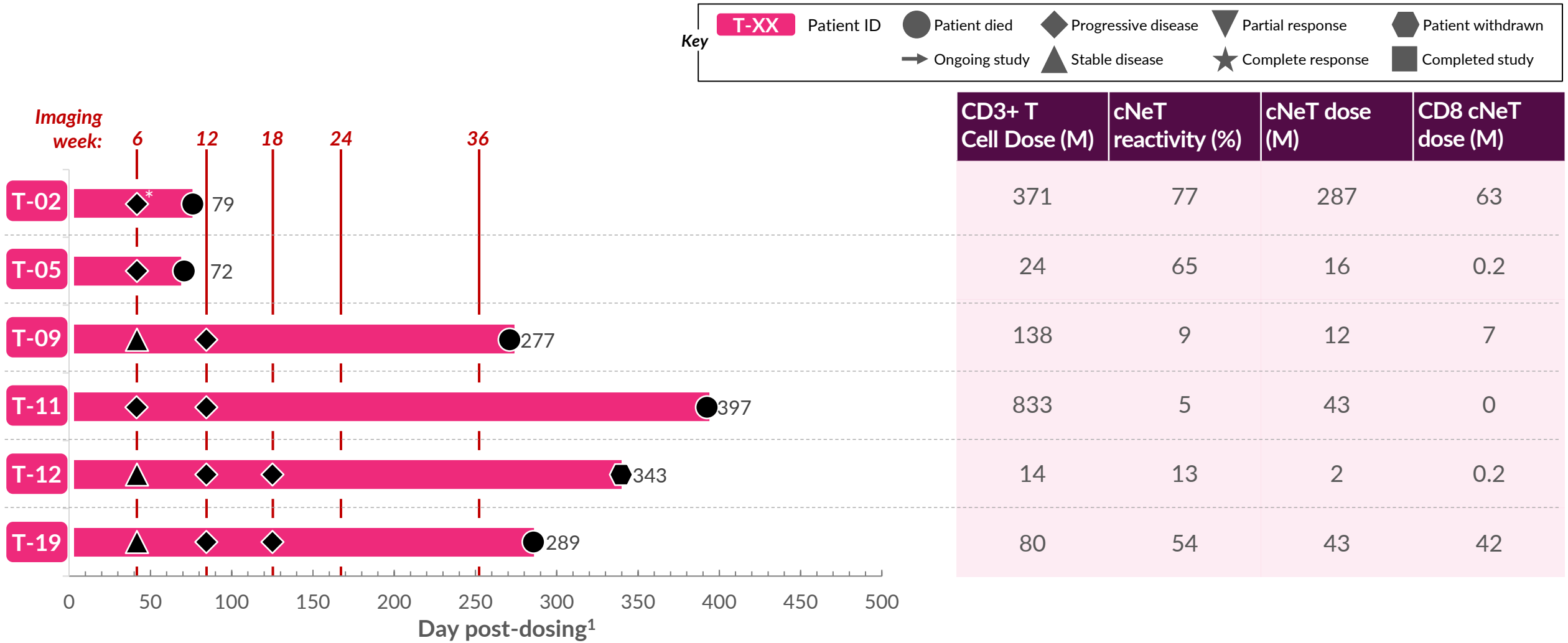


CD3+ T Cell Dose (M)	cNeT reactivity (%)	cNeT dose (M)	CD8 cNeT dose (M)
32	0.2	0.1	0
619	3	21	2
31	41	13	1
398	4	16	5
252	20	50	48
526	15	78	0.1
1202	17	201	131
19	28	4	2

Best response to cNeT monotherapy: one PR, six SD and one PD
5 of 7 (71%) evaluable patients showed clinical benefit (SD or PR) at 12 weeks with 4 of 7 (57%) out to >18 weeks

1. As of November 15, 2022

THETIS: Six patients dosed to date

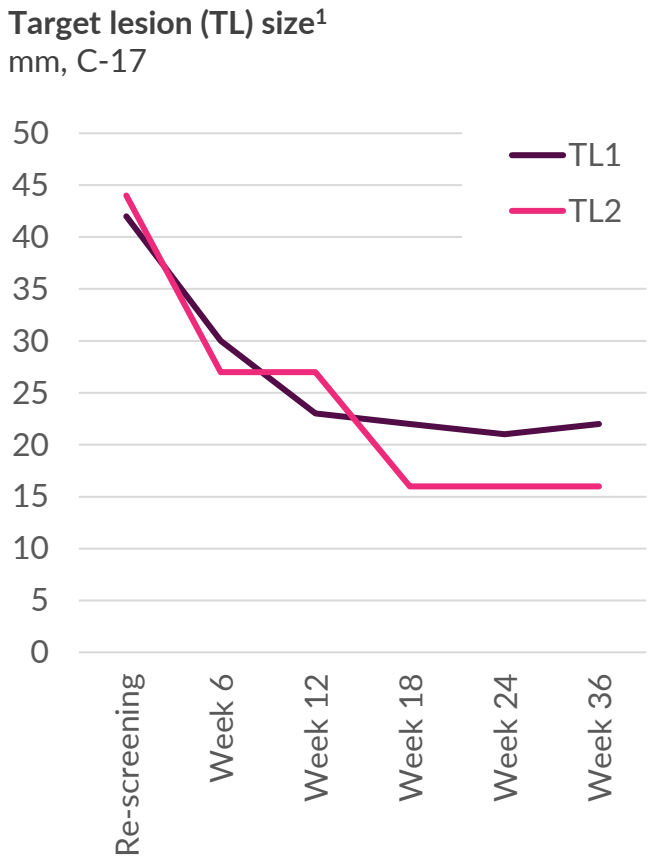


CD3+ T Cell Dose (M)	cNeT reactivity (%)	cNeT dose (M)	CD8 cNeT dose (M)
371	77	287	63
24	65	16	0.2
138	9	12	7
833	5	43	0
14	13	2	0.2
80	54	43	42

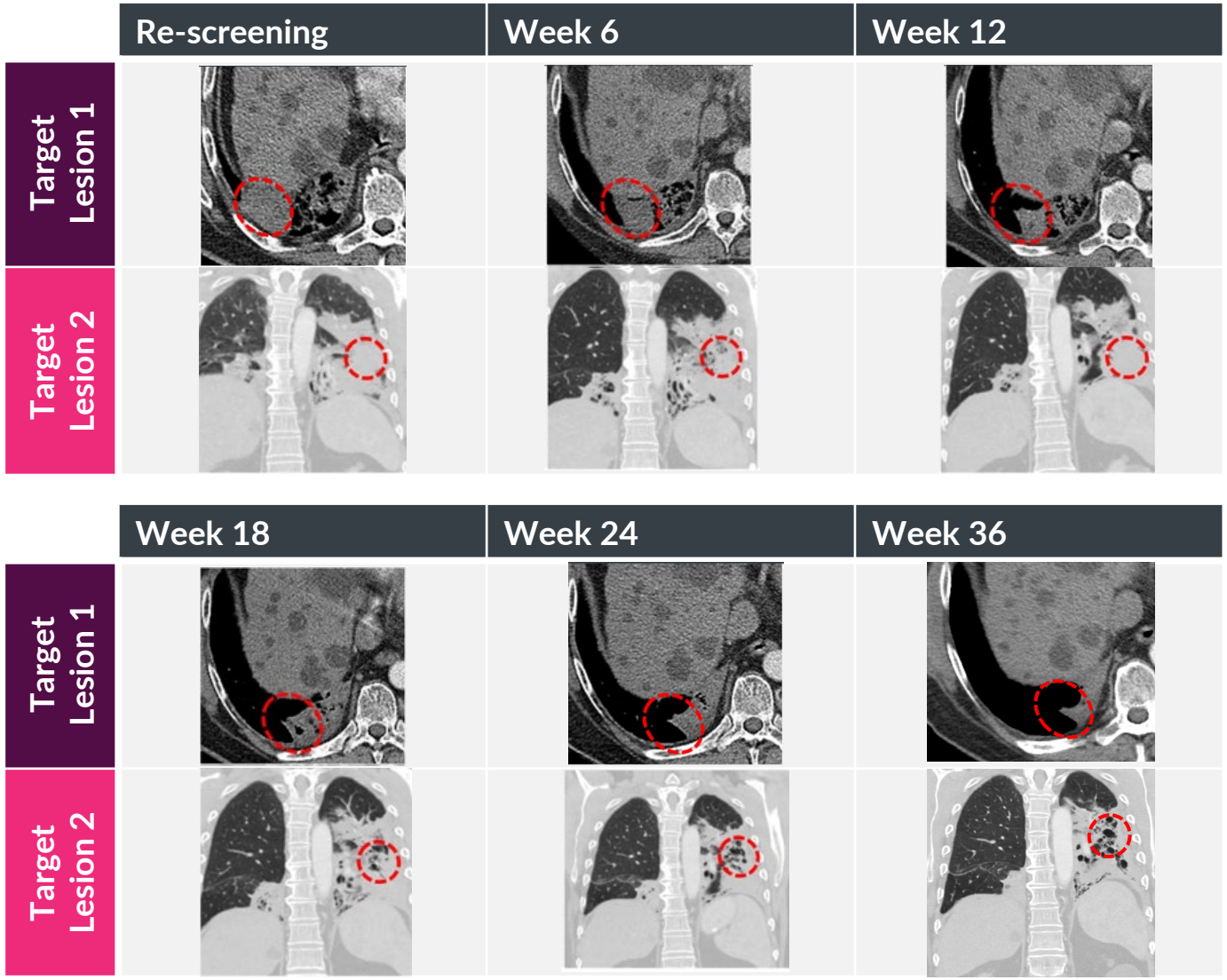
Best response to cNeT of the six patients dosed: three SD, three PD

1. As of November 15, 2022
*Mixed response – reduction in size of 2 of 4 target lesions

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



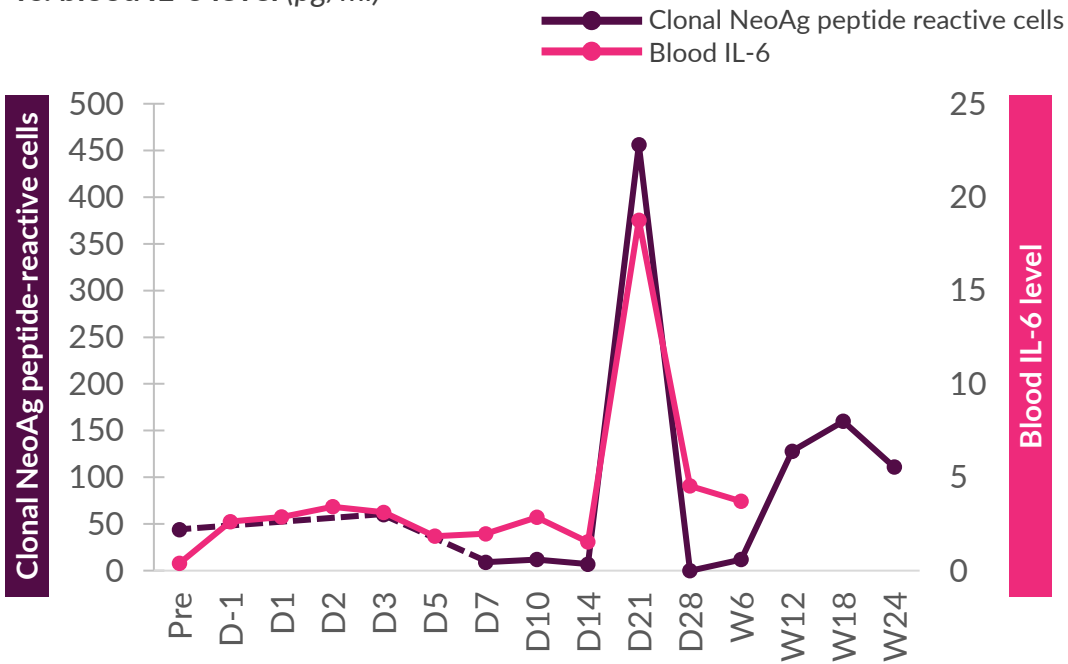
Total target lesion reduction of 56% at wk 36, with a 64% reduction in Target Lesion 2



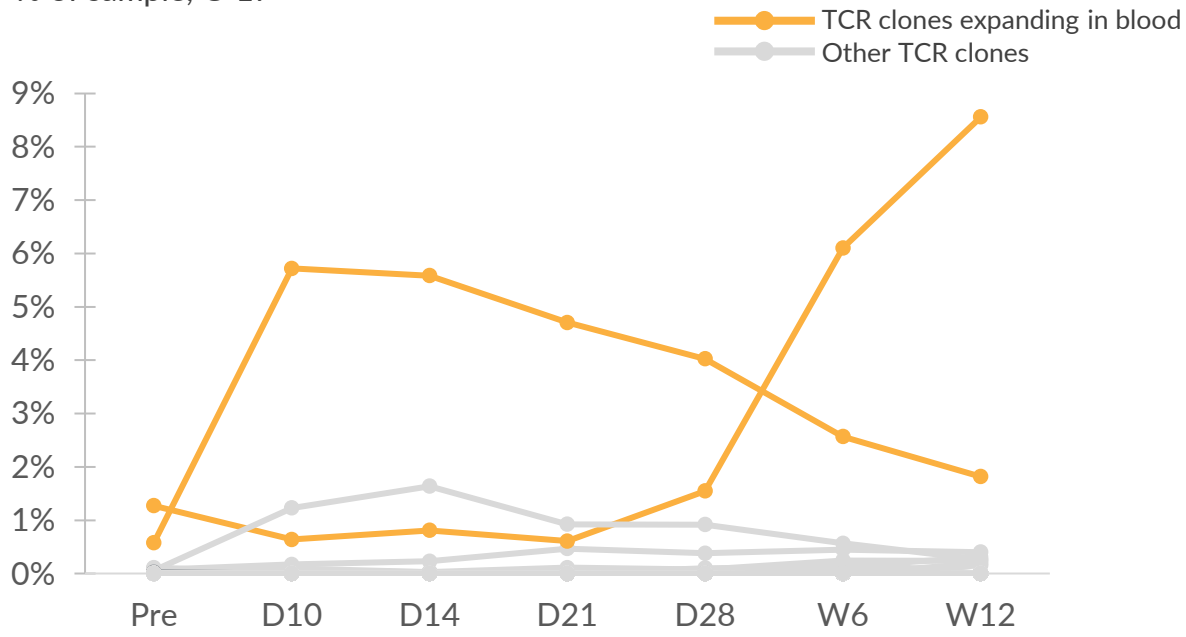
1. Site-reported lesion size
NB C-17 known to have polycystic liver disease

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

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



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

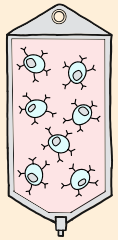


Cytokine-secreting clonal NeoAg reactive cells detected in blood-post dosing, with peak at Day 21 – coincident with peak in serum cytokine associated with T cell activity (IL-6)

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

World class translational science to drive rational process design

We will optimize our process to deliver product features that have been shown to deliver clinical activity

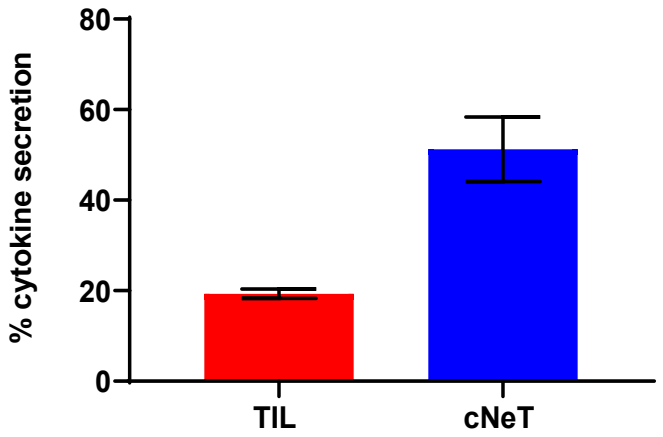
	Questions addressed	Analysis platform
Patient 	Clinical history	
	Tumor mutational burden	PELEUS
	Tumor status (e.g., hot, cold or immune-resistant)	RNA and Exome Seq
Product 	cNeT composition by T cell sub-type (e.g., CD4 & CD8 dose, central and effector memory)	Flow cytometry
	cNeT phenotype (exhaustion & activation markers)	Flow cytometry
	Gene expression signatures	Single cell RNA sequencing
Performance 	Presence of functional cNeTs in patient's blood	ELISpot (engraftment of IFN-γ producing cNeT)
	Diversity and frequency of clonally reactive TCRs (in product and patient's blood)	TCR sequencing (cNeT persistence independent of function)
	Changes in markers in blood indicative of anti-tumor response or cNeT engraftment	Immune reconstitution

Targeting clonal neoantigens allows characterization of the cNeT (tumor reactive) component of each product which provides the basis for a potency assay

T cell fitness

% cytokine secretion, patient data, *n=5*

Natural dendritic cell-driven expansion improves T cell fitness

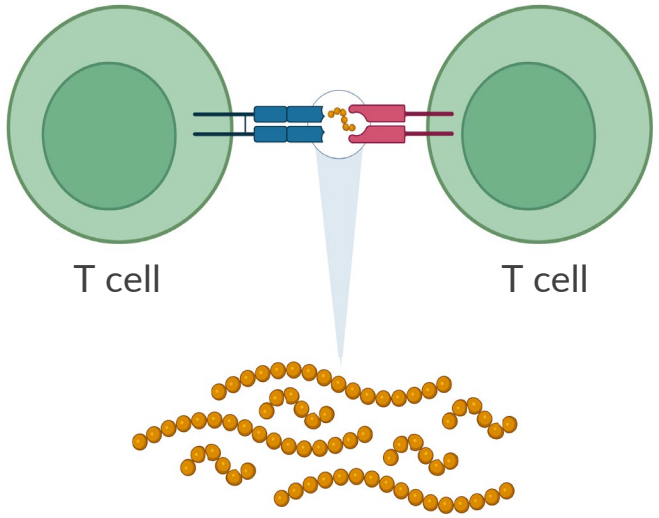


Ability of T cells to produce inflammatory cytokines in response to the same polyclonal stimulation

Potency Assay

Cytokine secretion in response to stimulation by patient-specific peptide pools and T cell-T cell antigen presentation

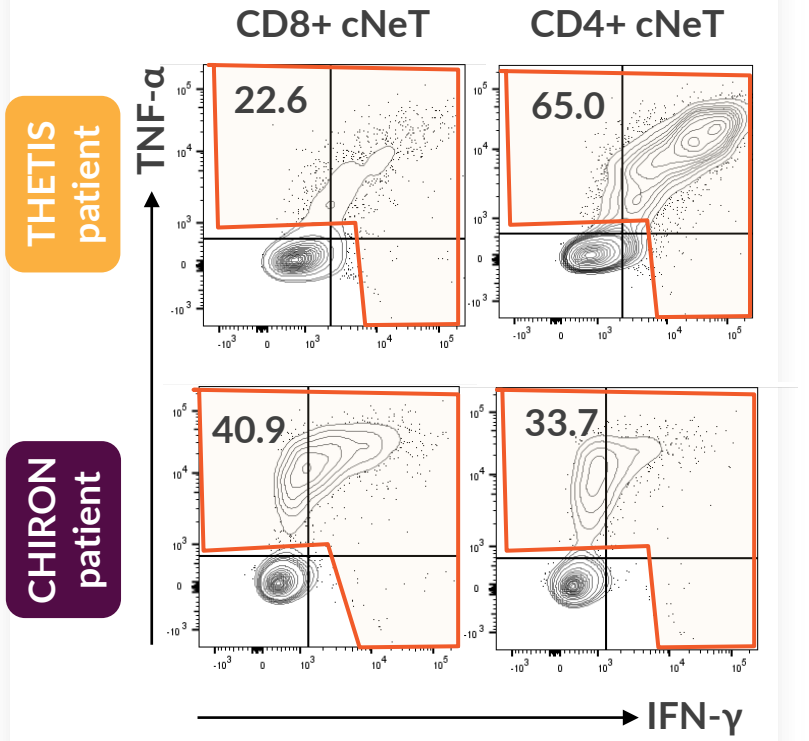
Precise readout of the tumour reactive component (cNeT) of each product



Peptide-specific peptide pools

Clonal neoantigen reactive T cells

Cytokine secretion measured through flow cytometric analysis, n=2



Translational science evaluates key features to deconvolute mechanism and inform rational process design

Range: Upper / Middle / Lower

CHIRON patients dosed as of December 2022

				Cell Fitness Markers			
Dosed Product	cNeT dose	cNeT Reactivity	#CD8 reactive cNeTs	Tumor migration	Low exhaustion (PD-1, TIGIT, etc.)	Engraftment	Best Clinical Activity
C-17	16M	4%					PR
C-03	0.1M	0.2%					Durable SD
C-16	50M	20%					Durable SD
C-20	201M	17%					Durable SD
C-10	21M	3%					SD
C-11	13M	41%					SD
C-23	78M	15%					PD

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 and Catapult currently support global clinical trial manufacturing
- Identified and initiated tech-transfer to CDMO in Greater Philadelphia in preparation for expansion
- Design work complete for GMP modular facility to support late stage clinical and commercial supply

Royal Free Hospital

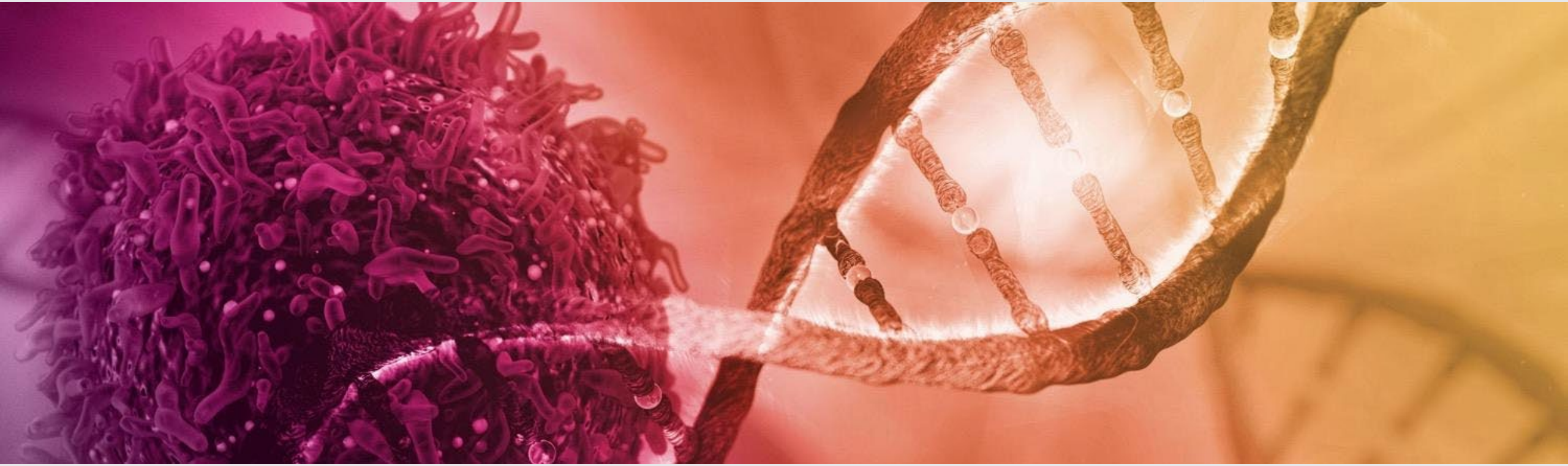
Cell & Gene Therapy Catapult

Center for Breakthrough Medicine

Additional Capacity

Focus for CHIRON and THETIS data readouts in 2023

- Dose & deliver data from 15-20 additional patients with cNeT monotherapy (lung & melanoma) and CPI combo (melanoma)
- Leverage translational science platform to define true features of response
- Drive additional confirmed responses in CHIRON and THETIS patients
- Continue VELOS manufacturing evolution and increase cNeT doses



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