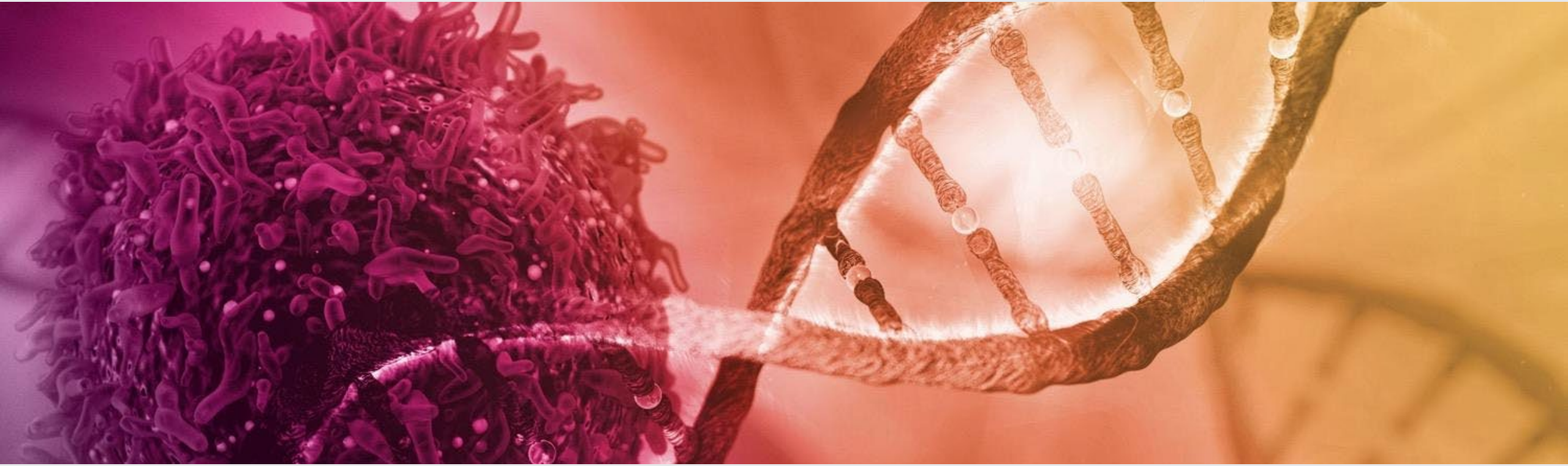


Achilles Therapeutics

PI/IIa CHIRON & THETIS Interim Update

ESMO Immuno-Oncology Congress 2022 | December 6, 2022

Forward-Looking Statements

This presentation contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements.

In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other facts, which are, in some cases, beyond our control and which could materially affect results. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this presentation and the documents that we reference in this presentation completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. This presentation also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events, or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research, surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this presentation, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors

AI-powered precision targeting for solid tumors using clonal neoantigen-reactive T cells (cNeT)

Emerging PoC for cNeT in NSCLC

Data now generated on 14 patients dosed with cNeT monotherapy across NSCLC and melanoma, with durable clinical benefit observed through 12 weeks in 71% (5/7) NSCLC patients including 1 PR and 4 SDs

Two additional patients dosed since data cut-off including first patient in THETIS Cohort B (not included here)

THETIS Cohort B will evaluate the combination of cNeT with a PD-1 checkpoint inhibitor to treat melanoma

US Patent Issued for the Achilles Clonality Engine

Patented method for determining clonality of patient-specific mutations that drives our AI-powered PELEUS™ platform which is built and validated on real-world data

Near-term milestones

Multiple clinical updates planned for 2023

Strong cash position

Cash runway of $180M (September 30, 2022) supports all planned operations into 2Q 2025

PELEUS is a 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 have been 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 tumour types

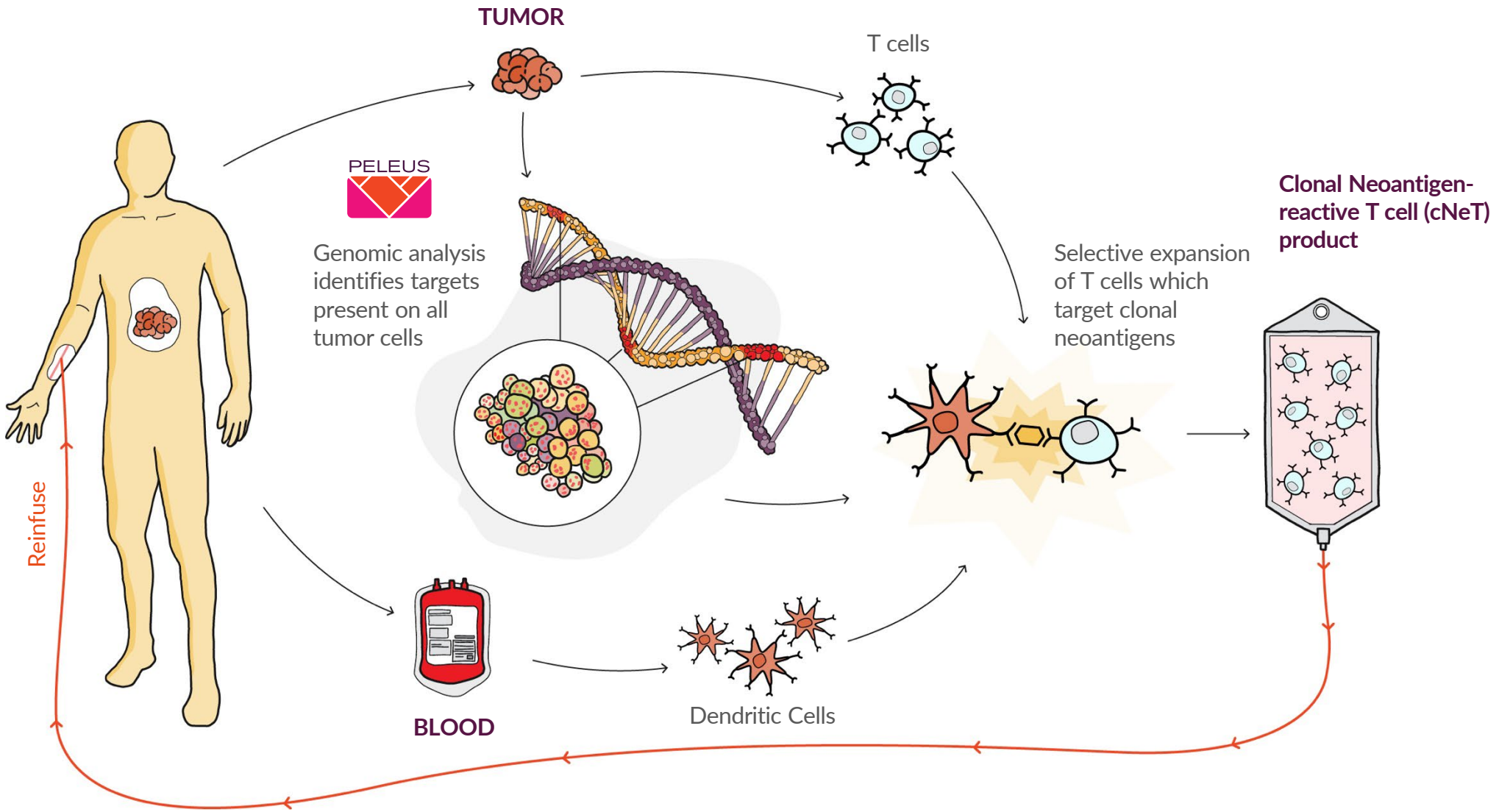
Trained and validated on TRACERx data

- 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)

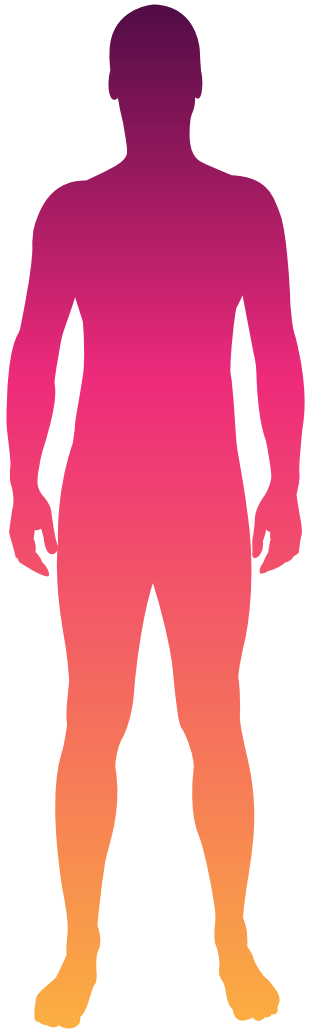
Cutting edge personalized genomics and machine learning enable targeting of all cancer cells

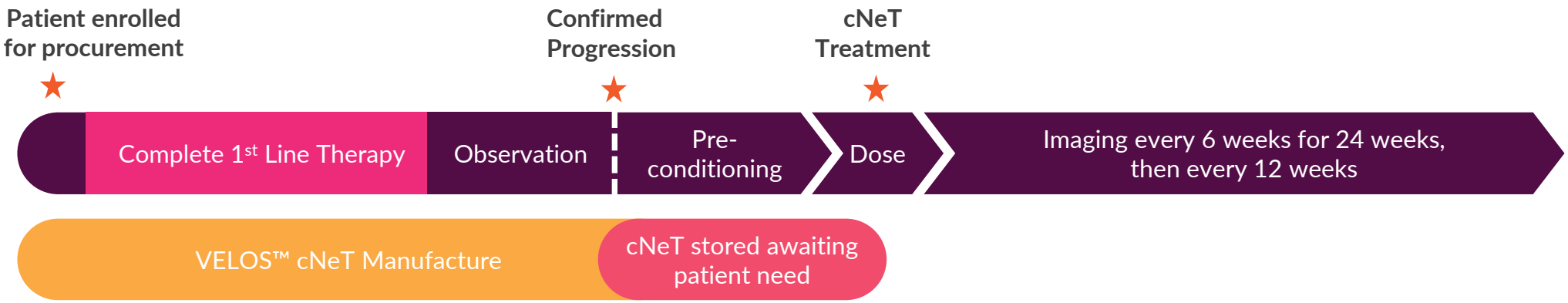


Durable clinical benefit in NSCLC and encouraging safety and tolerability data with cNeT monotherapy

- **Early proof-of-concept has been demonstrated in NSCLC with disease control at >12 weeks observed in 5 of 7 evaluable patients (71%), including one PR (>36 weeks)**
  - Potential for deep and durable clinical responses in solid tumours with low doses of cNeT and reduced dose lymphodepletion and IL-2
- **T cell engraftment and cytokine profiles are supportive of cNeT driving anti-tumour activity in the PR**
  - Functionally active cNeT display peak expansion at day 21 coincident with peak in IL-6 (cytokine associated with T cell activity)
  - Durable cNeT engraftment is demonstrated by tracking T cell receptors, extending beyond week 12
- **Lower dose lymphodepletion and IL-2 regimes (versus standard TIL therapies) were well tolerated, supporting potential for wider applicability of cNeT, including in an ambulatory setting**
  - 95% of IL-2 doses were delivered with no dose-limiting toxicities
- **Ongoing development of our proprietary translational platforms will allow further understanding of parameters associated with clinical response and inform development of the VELOS manufacturing process and potency assay**

cNeT therapies can be readily delivered within standard treatment pathways





Manufacturing

Manufactured and cryopreserved for infusion after patient progression

Tolerable pre-conditioning

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

Low IL-2

Lower dose IL-2 vs existing TIL therapies

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

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

Heavily pretreated patients with advanced cancer

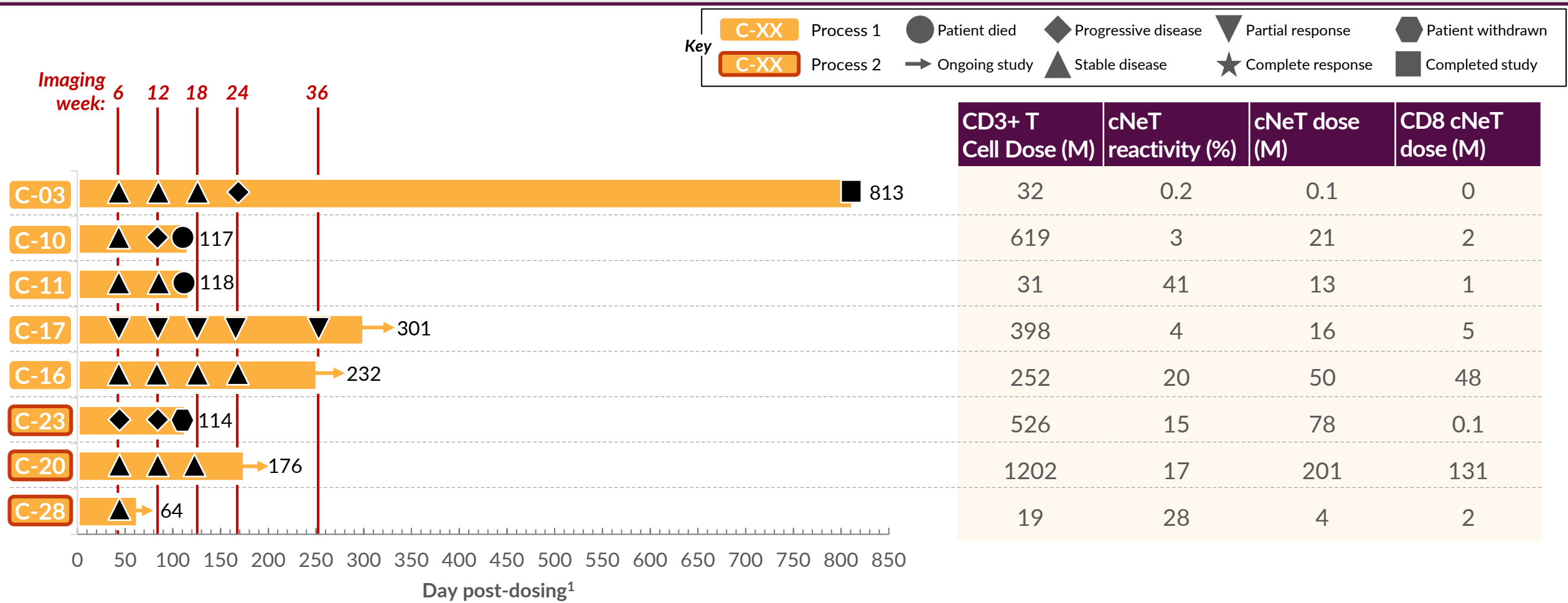
- Eight advanced unresectable or metastatic NSCLC patients (CHIRON)
- Six relapsed/refractory melanoma patients (THETIS)
- Two median lines of prior therapy, all patients refractory to checkpoint inhibitor (CPI)
- All patients had progressive disease at time of lymphodepletion
- Median cNeT dose 47M in last six patients since SITC 2021 and 78M in first three Process 2 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*

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



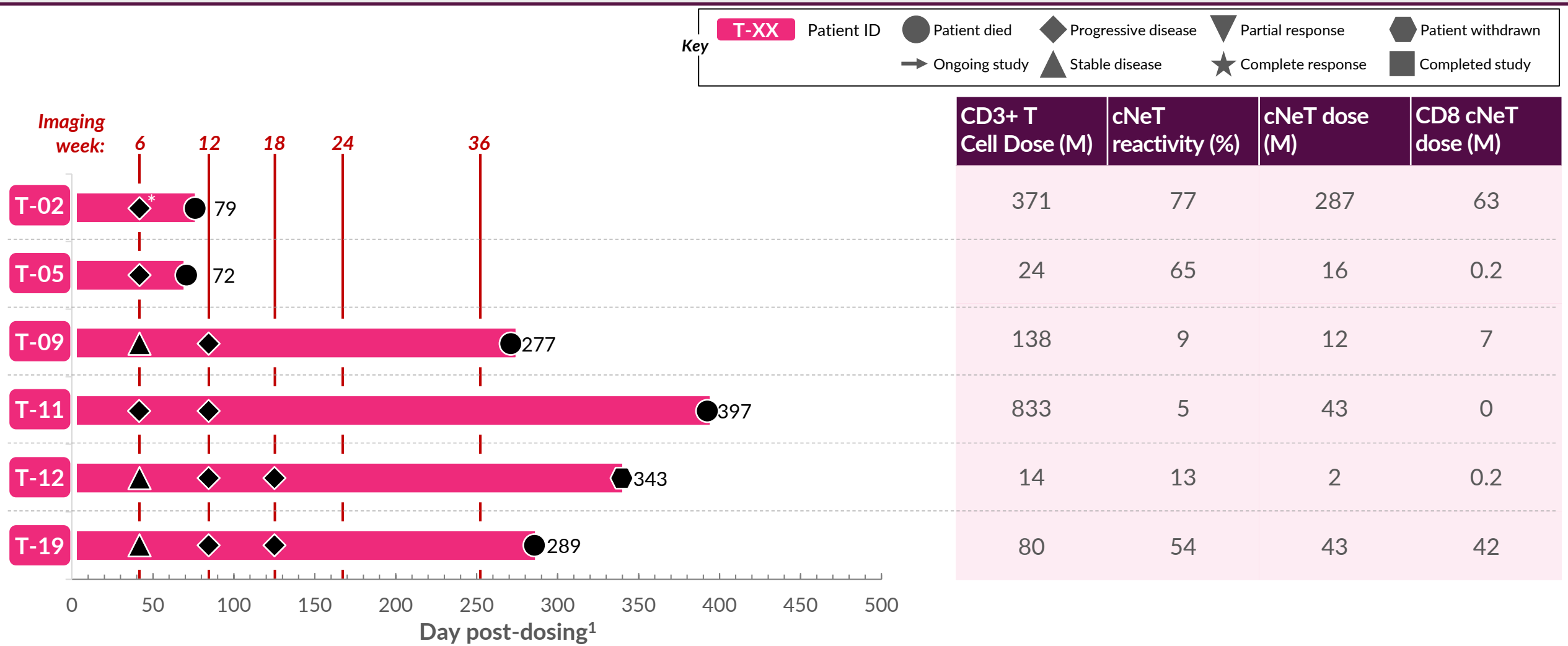
CD3+ T Cell Dose (M)	cNeT reactivity (%)	cNeT dose (M)	CD8 cNeT dose (M)
32	0.2	0.1	0
619	3	21	2
31	41	13	1
398	4	16	5
252	20	50	48
526	15	78	0.1
1202	17	201	131
19	28	4	2

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 15/11/2022*

THETIS: Six patients dosed to date

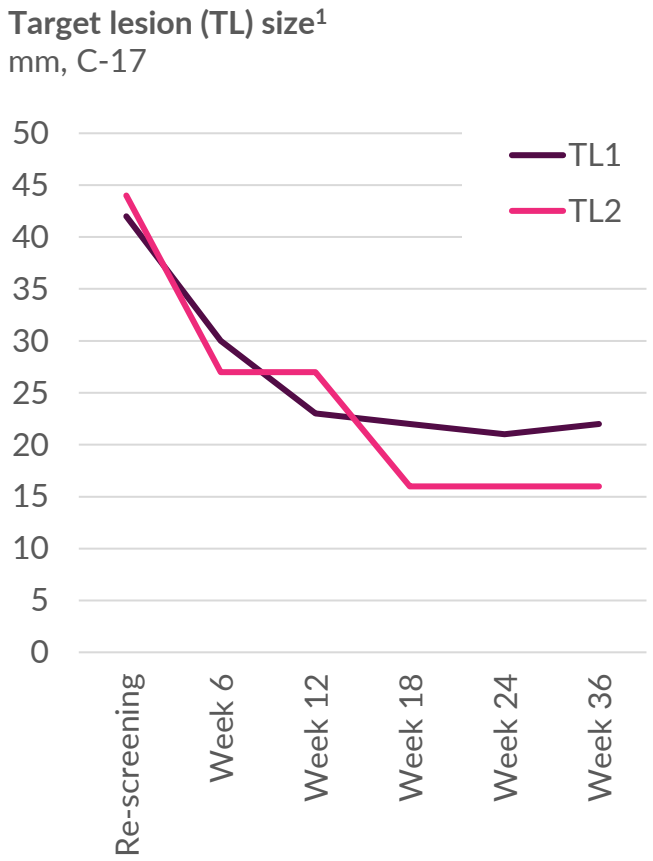


CD3+ T Cell Dose (M)	cNeT reactivity (%)	cNeT dose (M)	CD8 cNeT dose (M)
371	77	287	63
24	65	16	0.2
138	9	12	7
833	5	43	0
14	13	2	0.2
80	54	43	42

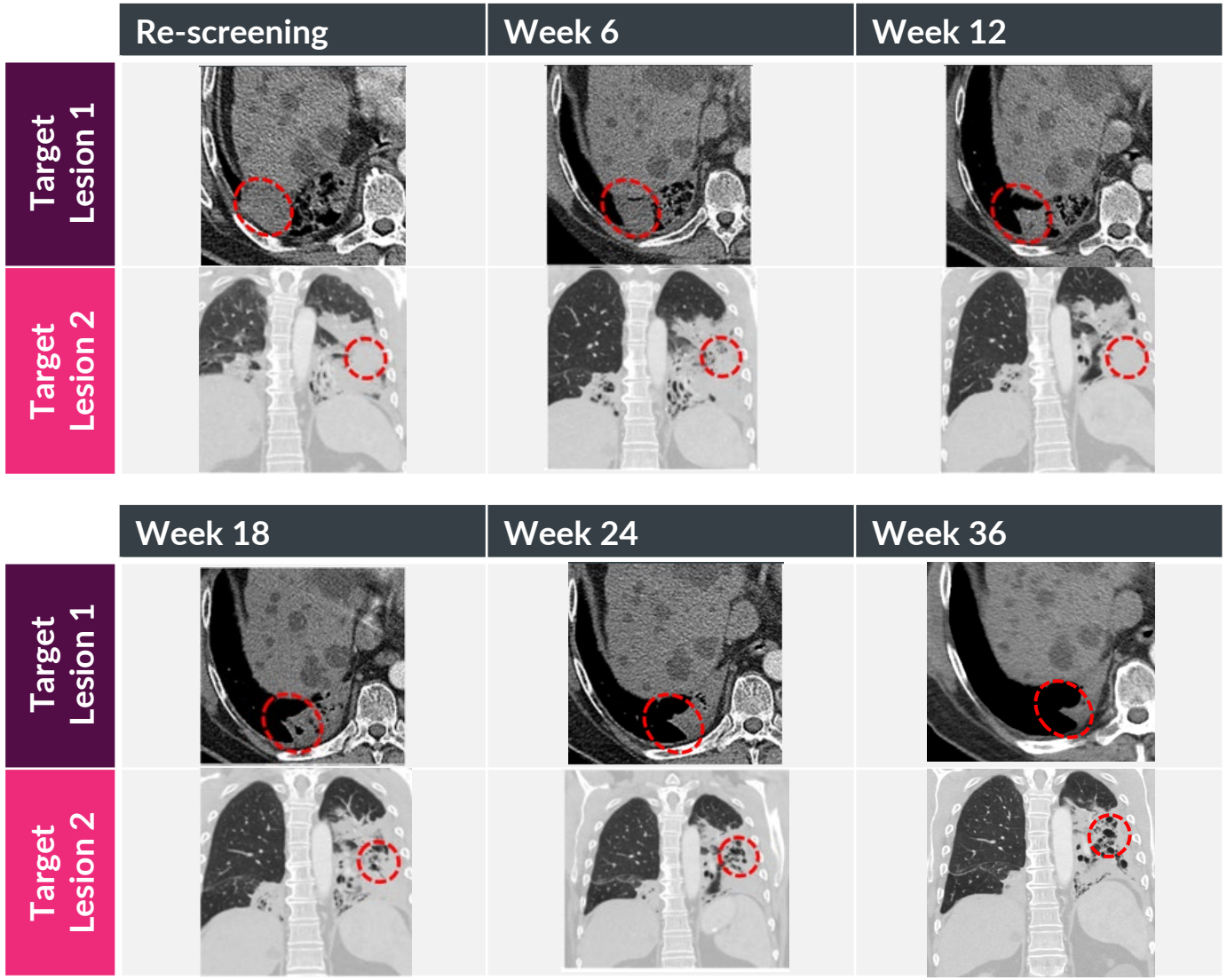
Best response to cNeT of the six patients dosed: three SD, three PD

[1]*As of 15/11/2022*
**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



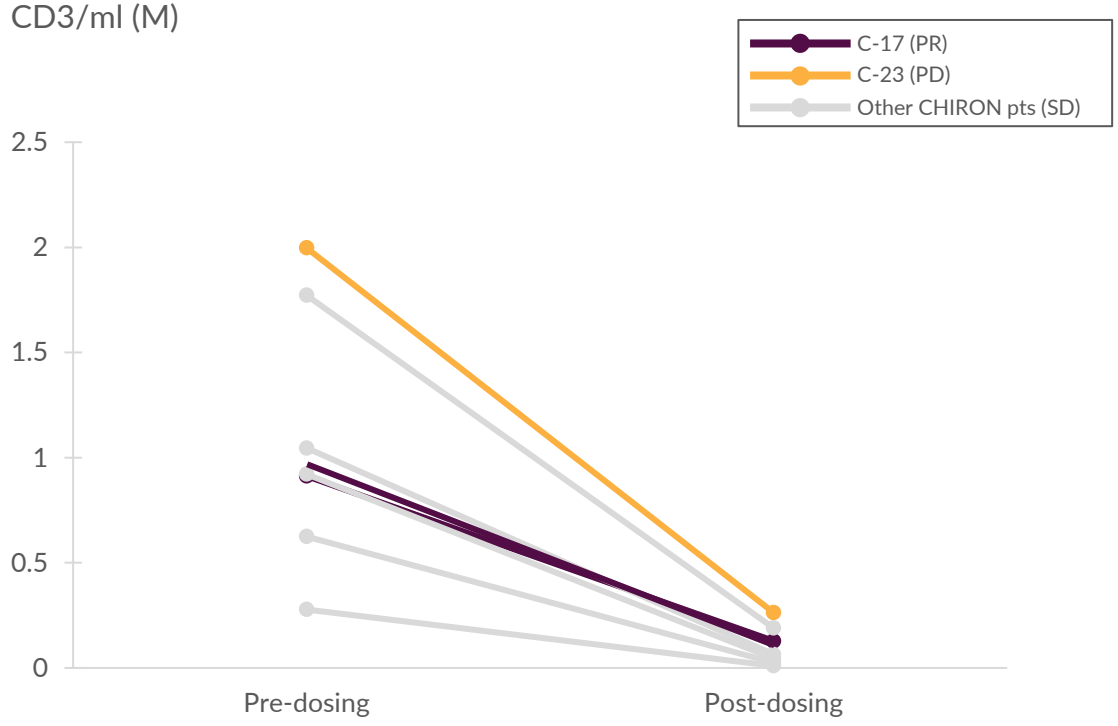
Total target lesion reduction of 56% at wk 36, with a 64% reduction in Target Lesion 2



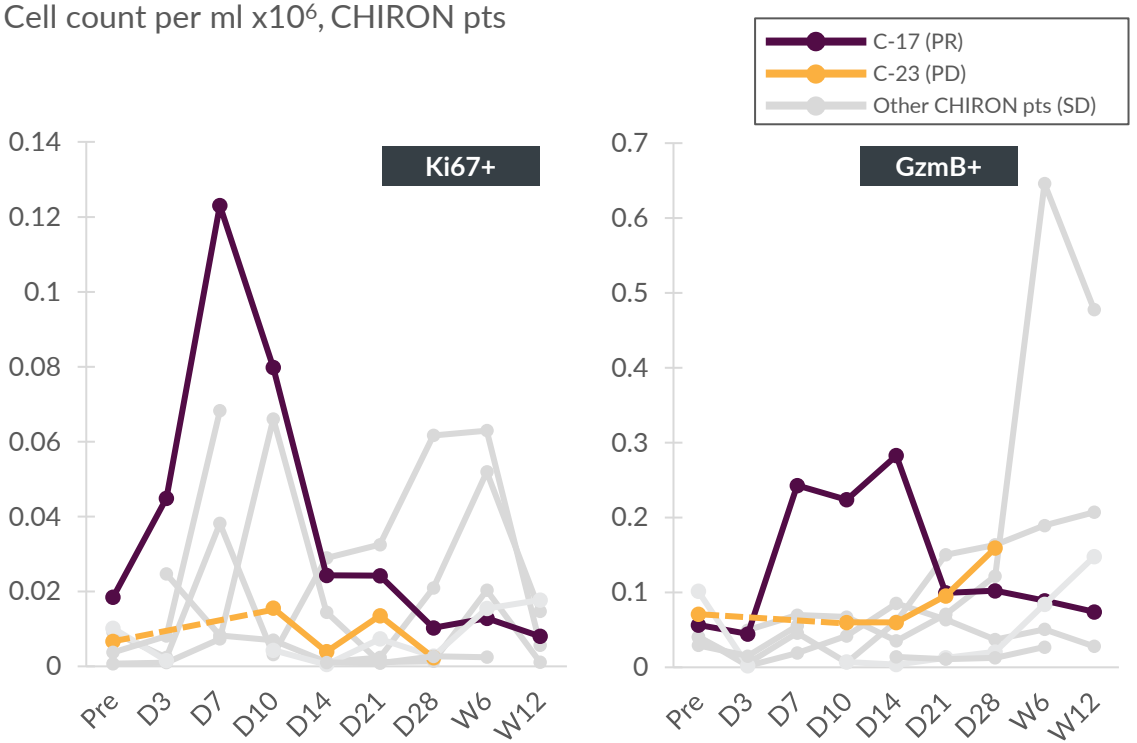
[1]*Site-reported lesion size*
NB C-17 known to have polycystic liver disease

Patient C-17: Efficient lymphodepletion and early reconstitution with functionally active T cells

Lymphodepletion
CD3/ml (M)



CD8+Ki67+ and CD8+GranzymeB+ cell populations
Cell count per ml x10^6, CHIRON pts



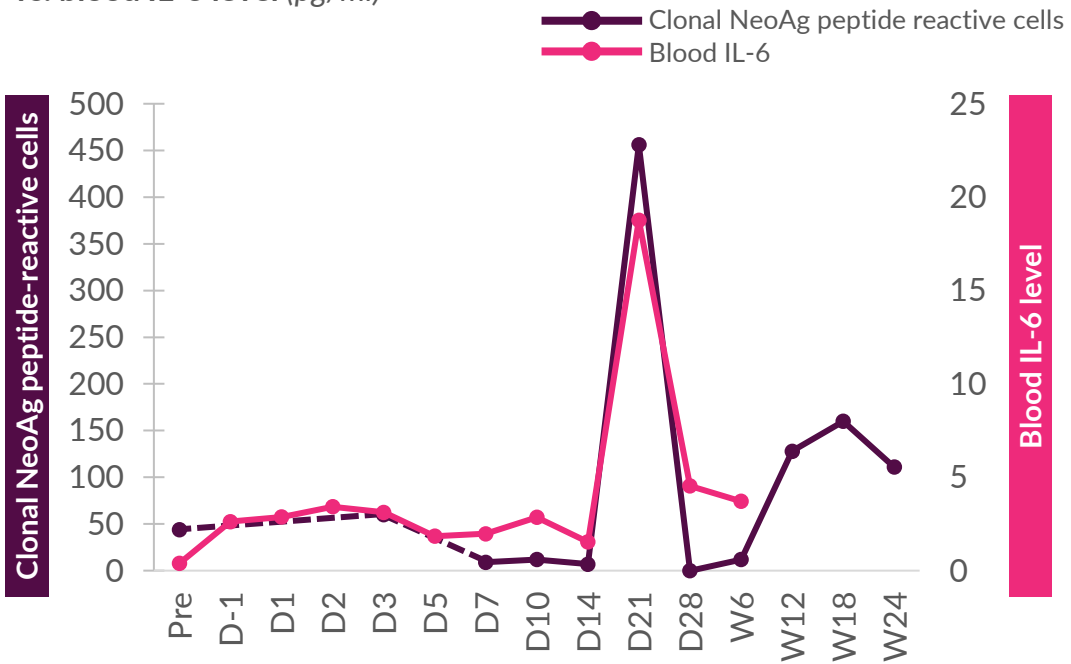
Low intensity conditioning regime is capable of producing effective lymphodepletion of patients' immune cells

- Phenotypic markers can be analysed to link response with changes in cellular characteristics in blood
- Proliferative and cytolytic cells are detected post-dosing in C-17 and such cells have been previously associated with responses to CPI[1]

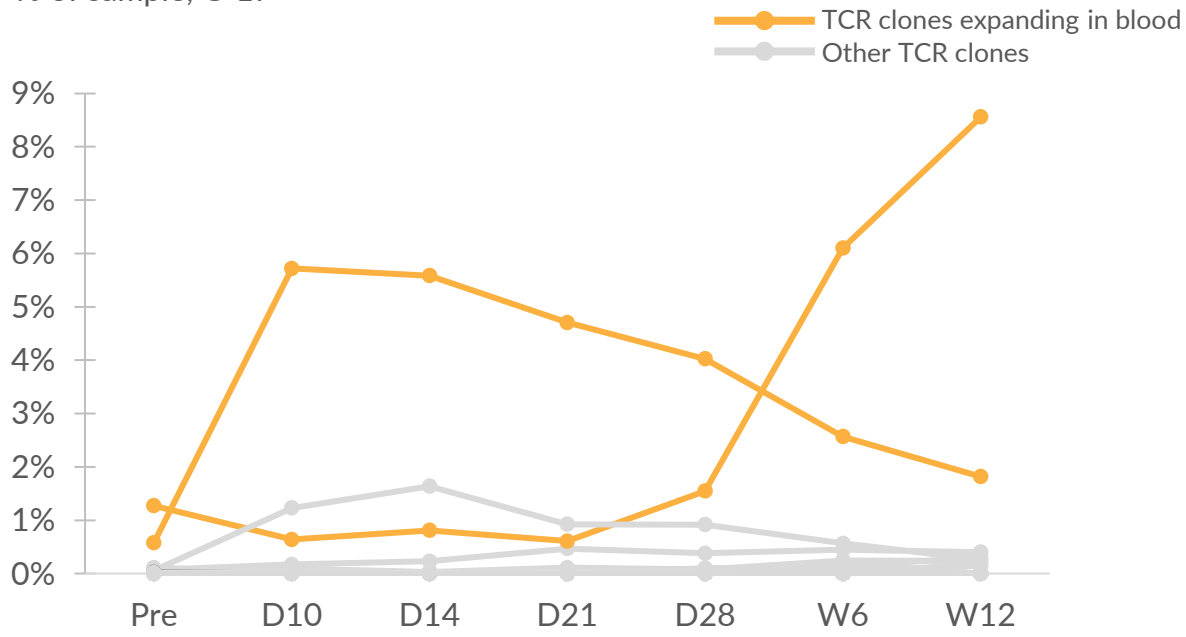
[1]*Machiraju et al, Oncoimmunology 2021*

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

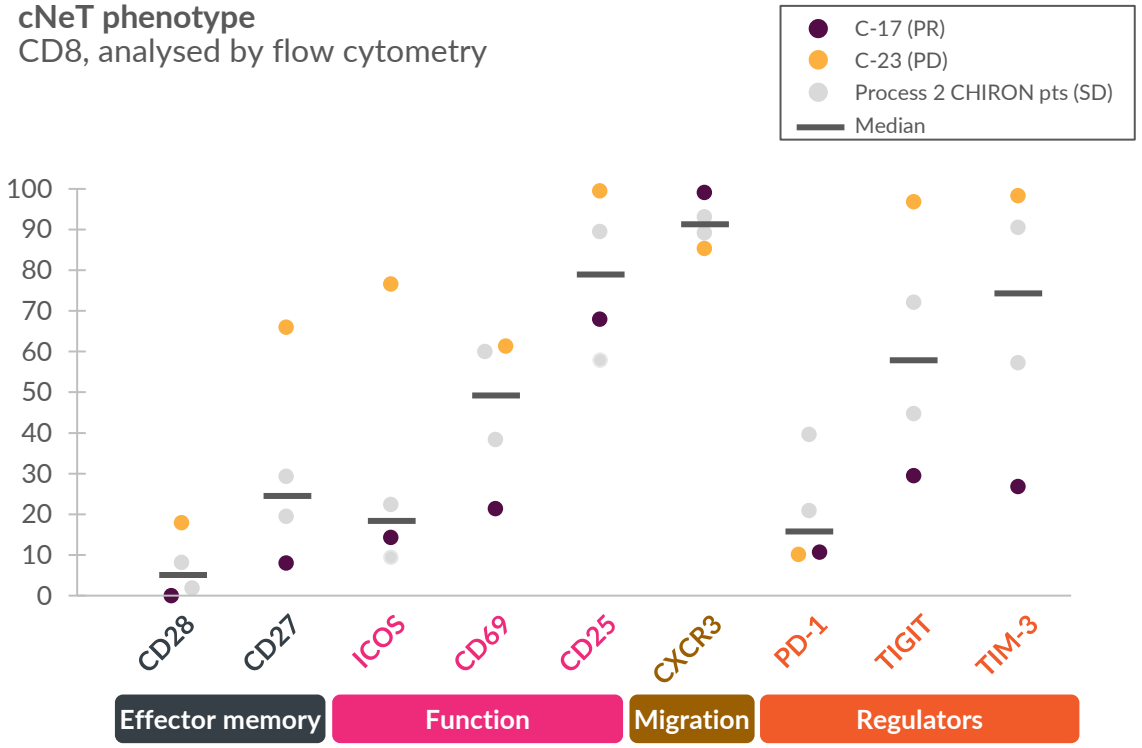


Cytokine-secreting clonal NeoAg reactive cells detected in blood-post dosing, with peak at Day 21 – coincident with peak in serum cytokine associated with T cell activity (IL-6)

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

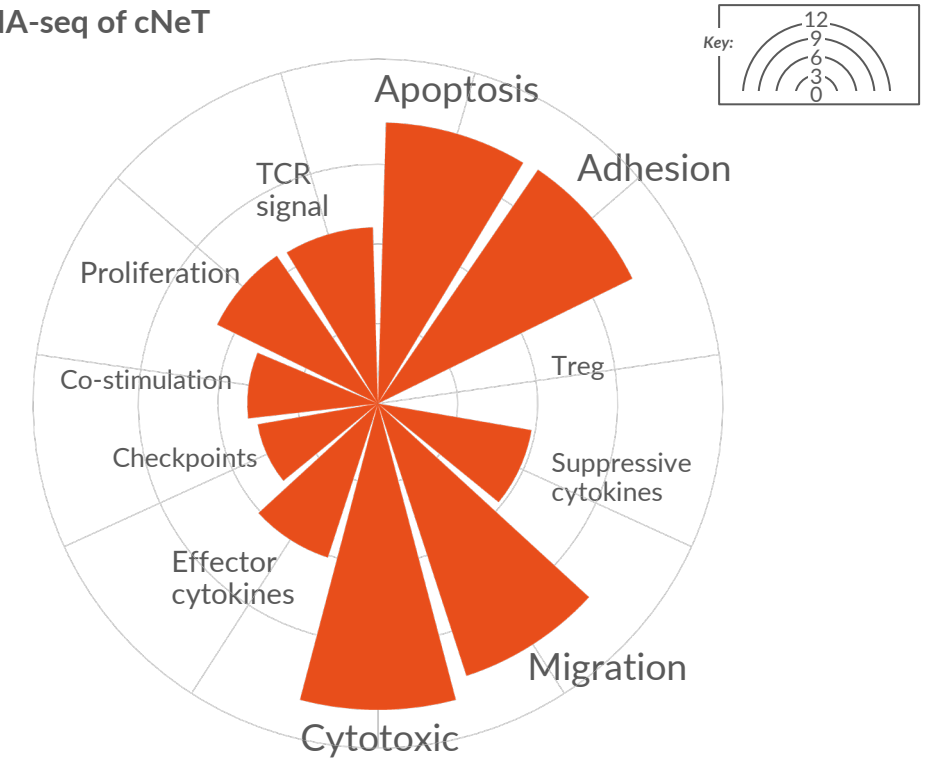
Patient C-17: dosed product shows IL-2 sensitivity, migratory receptors and a polyfunctional transcriptional programme including cytotoxicity, proliferation and effector function

cNeT phenotype
CD8, analysed by flow cytometry



- Product can be restimulated with specific clonal neoantigens and analysed by flow cytometry
- CD8 cNeT are fit, sensitive to IL-2, express receptors for tumour migration, and lower levels of inhibitory checkpoints than other products

Single cell RNA-seq of cNeT
#cells (log2)



- Single cell RNA-seq of cNeT identify functional modules of cytotoxicity, migration, proliferation and effector function
- Gene signatures that are identified in response to clonal neoantigen peptide show the active component is polyfunctional

Our translational science platform provides multiple parameters to deconvolute mechanism

CHIRON patients dosed to date

Range:	Upper
	Middle
	Lower

Dosed Product	cNeT dose	cNeT Reactivity	#CD8 reactive cNeTs	Tumour migration markers on cNeTs	Exhaustion markers on cNeTs	Patient immune reconstitution	Engraftment	Tumour escape	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

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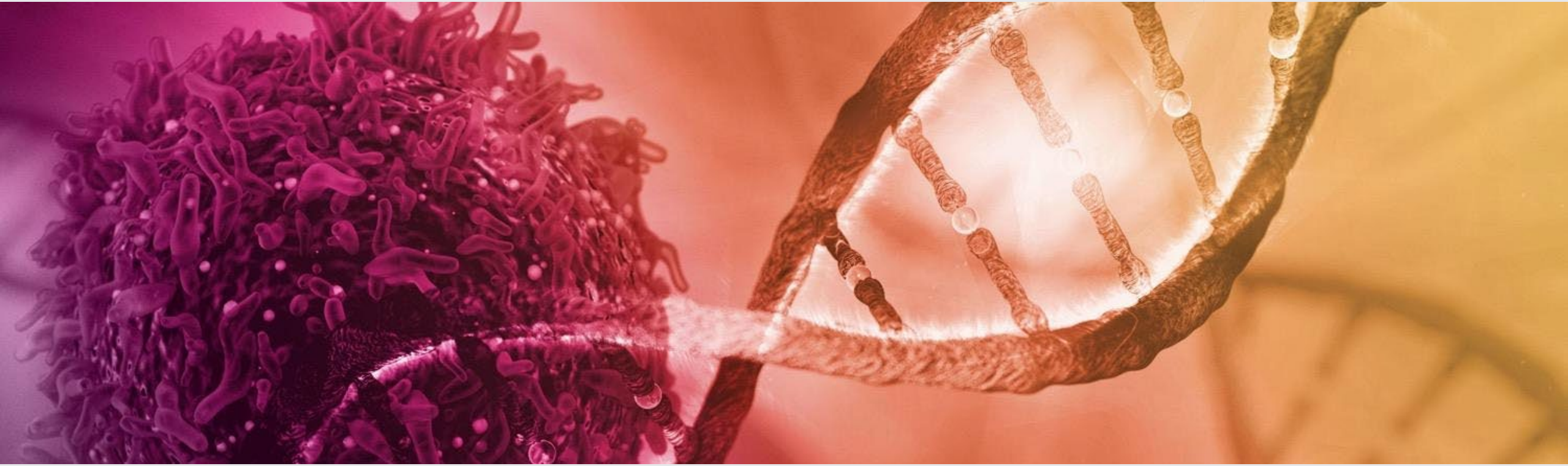

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