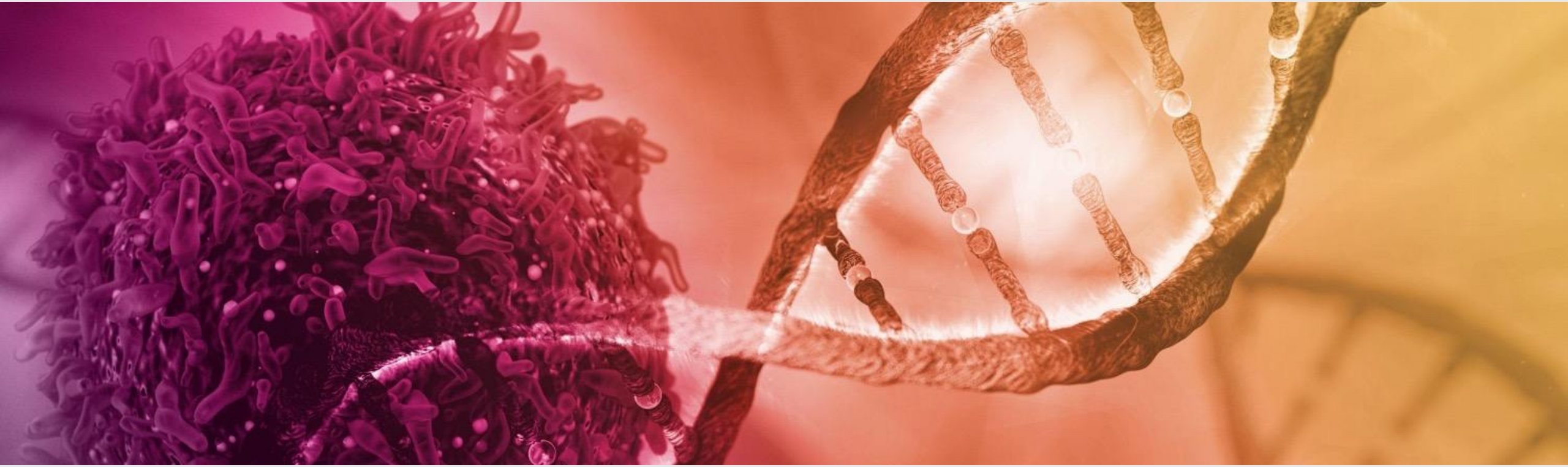


Achilles Therapeutics

Post-SITC Review and Corporate Update

November 12, 2021

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

Agenda and participants on today's call

Participants

Dr Samra Turajlic
THETIS Chief Investigator

The ROYAL MARSDEN

Iraj Ali
CEO & Board Member

Syncona McKinsey&Company

Sergio Quezada
CSO & Founder

UCL CANCER INSTITUTE UCL CANCER RESEARCH UK

Karl Peggs
CMO & Founder

UCL CANCER INSTITUTE UCL

Lee Stern
VP IR & External Comms

SOLEBURY TROUT trout CAPITAL

Agenda

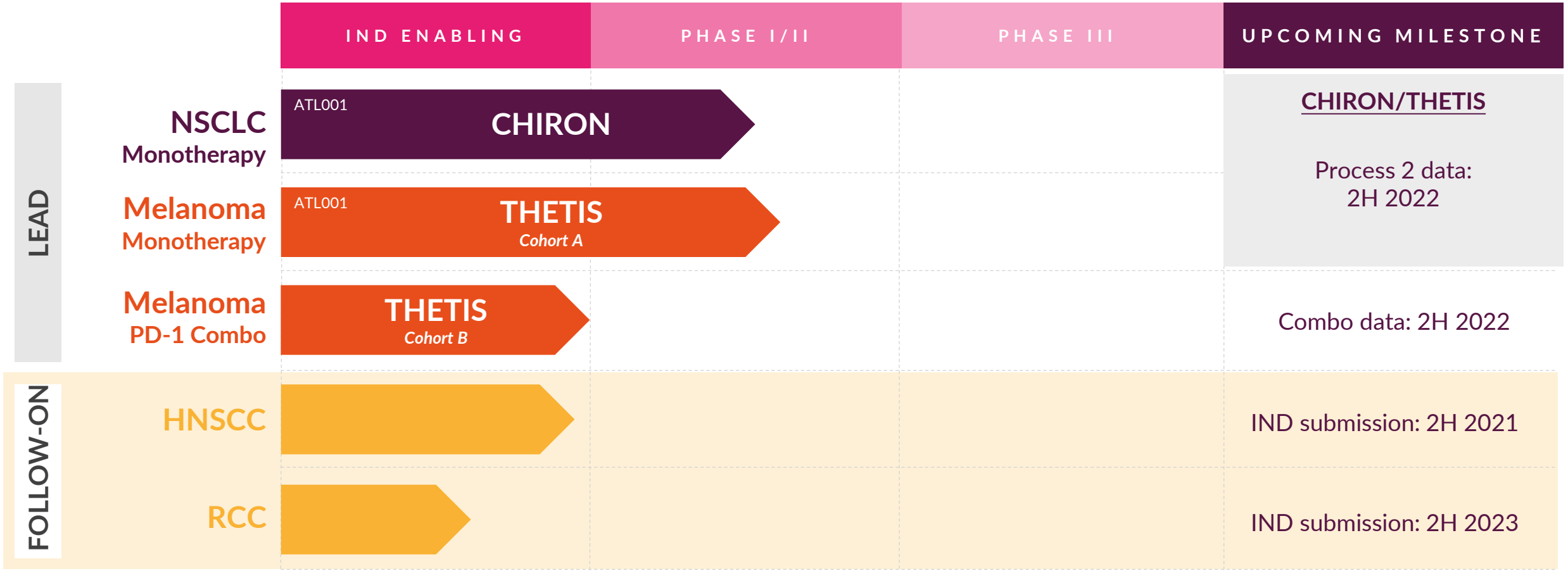
- Introduction to Achilles Therapeutics
- ESGCT Review
- THETIS/CHIRON PI/IIa update
- VELOS™ Manufacturing Process 2 update
- Q&A

A clinical stage company developing precision T cell therapies to treat solid tumors

NASDAQ: **ACHL**
Precision TIL therapy

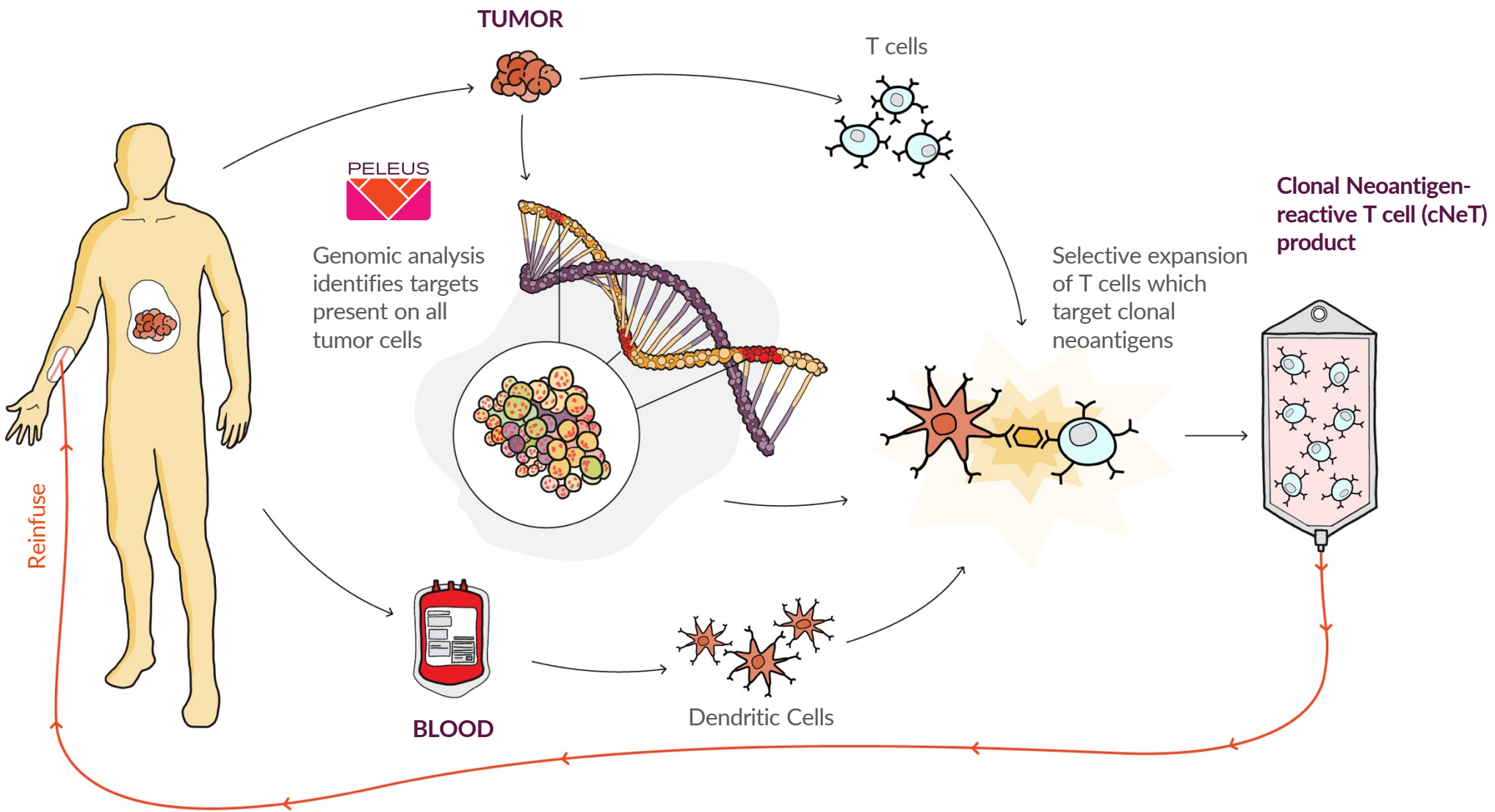
- Two open-label Phase I/IIa clinical trials ongoing in NSCLC and melanoma and next program to enter the clinic in 2022
- Interim analysis across NSCLC & melanoma (Process 1) highlights engraftment kinetics, product characterization, and ability to define tumor-reactive component; Open Process 2 high-dose cohort with patient data in 2H 2022
- Designing a closed, automated and scalable manufacturing process to deliver over 1,000 doses annually to supply late stage clinical trials and initial commercial products; GMP modular facility is a blueprint for global commercial supply
- Science based on pioneering research led by Profs. Charlie Swanton, Karl Peggs, Mark Lowdell and Sergio Quezada into tumor evolution, immune-regulation and the translation of precision T cell therapies
- Financed to complete ongoing phase I/IIa clinical trials, expand manufacturing capacity and bring additional programs into the clinic with September 30 cash of $282M

Our current pipeline

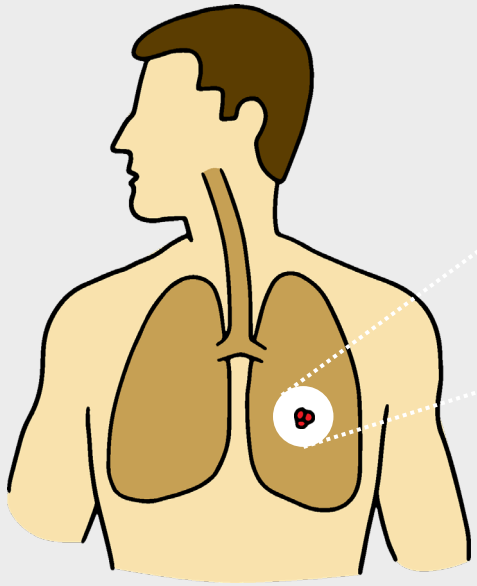


Precision TIL therapy targeting clonal neoantigens

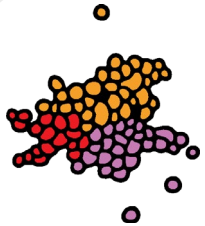
Using cutting edge personalized genomics to target all cells in a patient's tumor



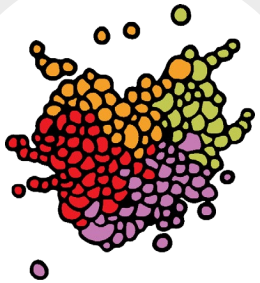
Achilles has developed proprietary technology to **target all tumor cells**



Tumors are **clonal in origin** and originate from a group of cells that are exactly the same



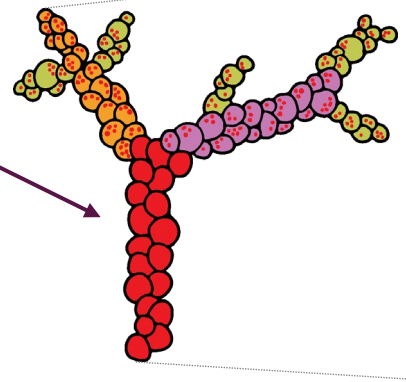
Tumors evolve, developing many new mutations resulting in **heterogeneity** that enables them to evade targeting[1]

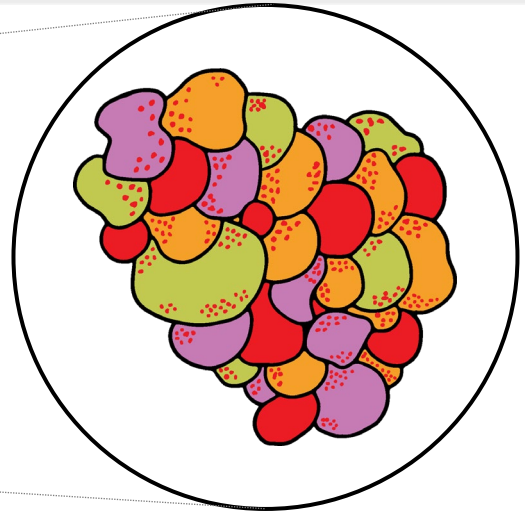


To kill all of the tumor cells we believe you need to target the **clonal neoantigens formed early in tumor evolution**

Achilles has developed proprietary technology to identify the original tumor mutations **present on all cancer cells**, **clonal neoantigens**

We are able to identify and **target multiple clonal neoantigens** with our Clonal Neoantigen-reactive T cell (cNeT) therapy





Clonal neoantigens are present on **primary tumors and all metastases**

1. Gerlinger et al., NEJM, 2012

Exclusive commercial access to the TRACERx database to develop our bioinformatics platform

TRACERx

A clinical study of tumor evolution

The TRACERx study comprises **multi-region, longitudinal, data from over 780 NSCLC patients** collected over a period of 5 years[1,2,3,4]

Over **3,000 tumor region samples,** comprising **one of the largest** bioinformatic data sets of its kind

The learnings from TRACERx **can be applied to other solid tumors**

PELEUS

PELEUS®

A proprietary platform to identify clonal neoantigens

We have developed the proprietary **PELEUS** platform, which can identify the patient's unique clonal neoantigens

The PELEUS platform has been built using the **extensive data from TRACERx** combined with our own **proprietary statistical models**

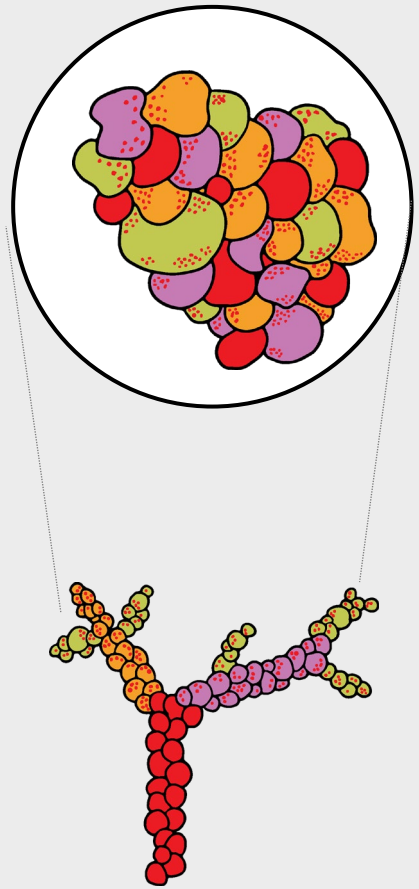
The PELEUS platform is **trained and improved** using new TRACERx data

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

Our precision TIL therapy specifically targets clonal neoantigens

Clonal neoantigens represent the ideal targets for solid tumor treatment

Unique proteins expressed on every cancer cell within a patient but not on healthy tissue



- **Achilles has a unique capability to target clonal neoantigens**
- **Our process can deliver tumor specificity and potency improvements over standard TIL**
- **Clonal neoantigens are better targets than tumor associated antigens, which are present on some tumor cells and on healthy tissue**
- **Clonal neoantigens are better targets than neoantigens, which are present on some, but not all, tumor cells**

Achilles is building a transformative oncology business

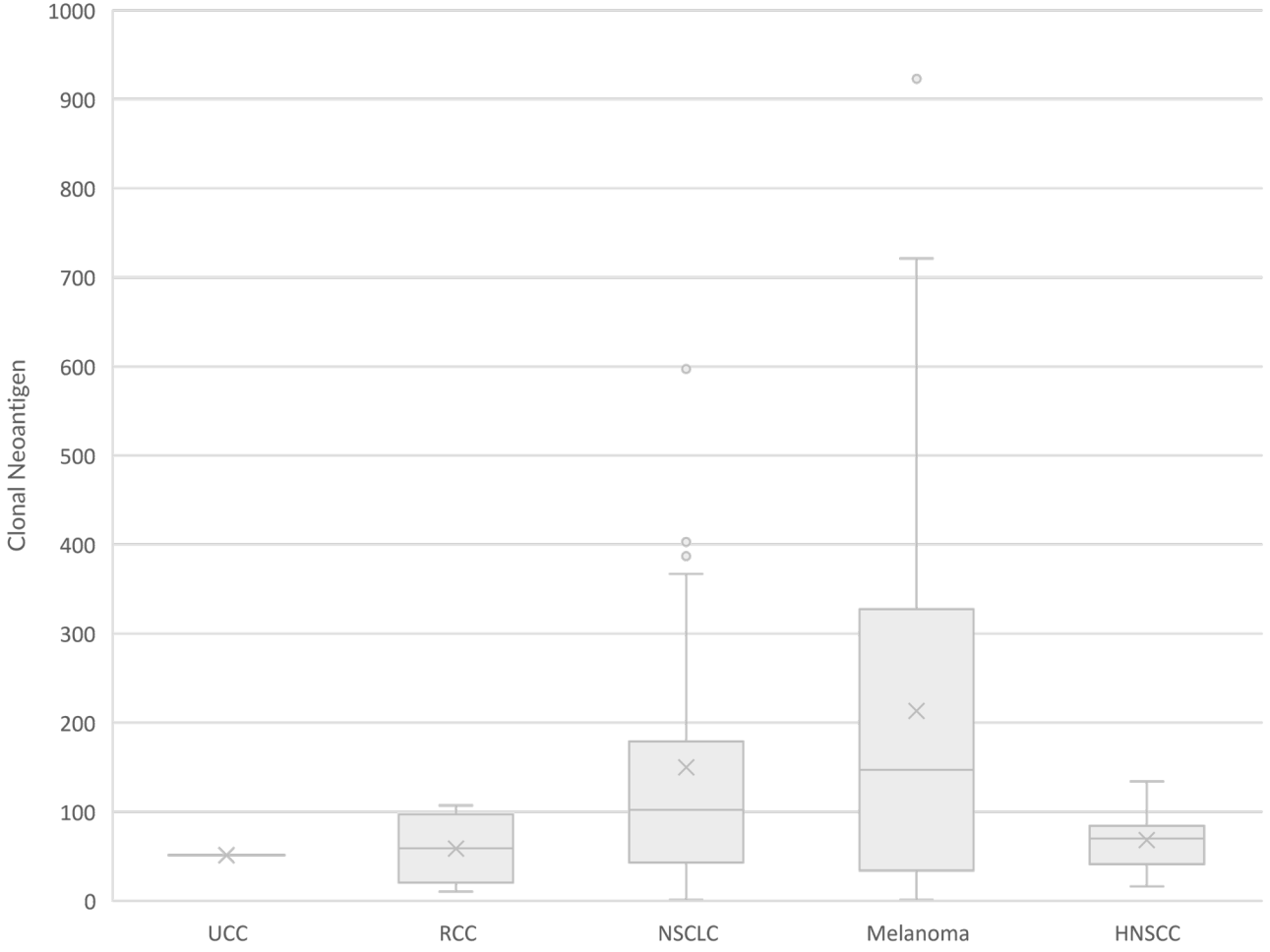
- Two ongoing clinical trials with near-term data readouts and plans to add new indications
- Exclusive access to TRACERx, which gives the unique capability to address clonal neoantigens
- cNeT platform can target multiple cancer antigens present in all tumor cells
- Technology allows us to develop a potency-based release assay
- Robust and commercially scalable manufacturing process designed to be fully closed and automated
- Cash to complete planned I/IIa clinical trials, expand manufacturing capacity, and broaden pipeline

Multicentre, prospective research protocol for development of a clonal neoantigen-reactive T cell therapy pipeline across multiple tumour types

ESCGT 2021

Highlights of presentation given on October 22, 2021
Full presentation at https://ir.achillestx.com/events-and-presentations

Results



- At time of data cut-off for submission, **n=90 samples** had undergone analysis with **PELEUS™**
- A median of **71 clonals** were identified in Head and Neck samples (n=16)
- This is consistent with what we observe in large **public data sets (TCGA) where the median is 68**
- This is a lower median than **NSCLC (107) and Melanoma (156)**
- Data for **renal (n=4) and bladder (n=1) still immature** at time of data cut-off

Results

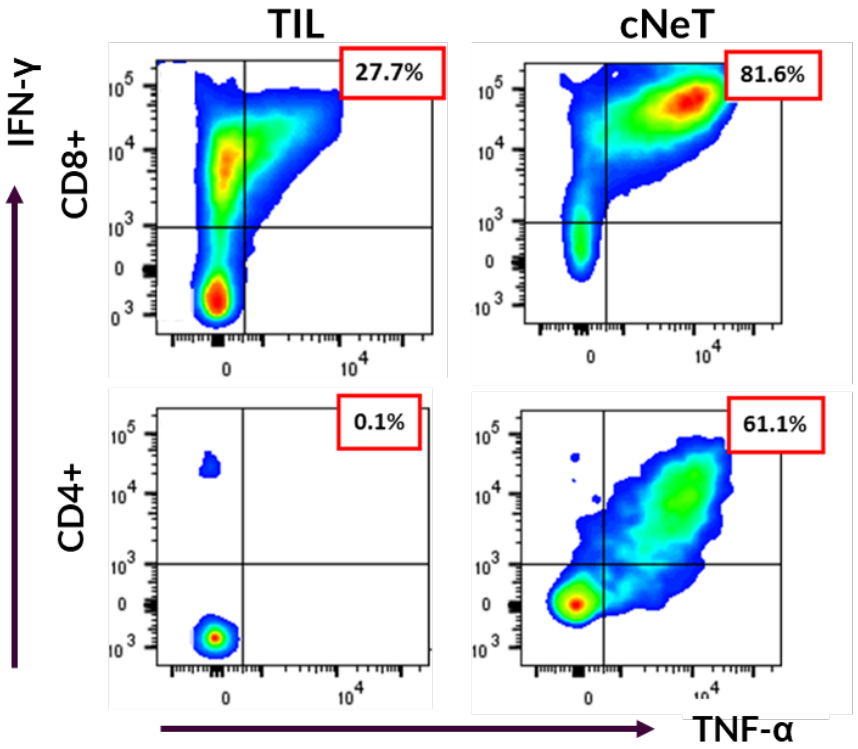
- **VELOS™ manufacturing process** expands **TILs** from tumour fragments whilst **monocyte-derived dendritic** cells are generated from whole blood

- These are then co-cultured after dendritic cells are **pulsed with neoantigen peptides** (determined by PELEUS™) to drive the expansion

- The process delivers both **CD4+ and CD8+ T cells**. There is a strong body of pre-clinical data which shows **CD4+ and CD8+** T cells can work in concert to deliver **robust and durable responses**[1-3]

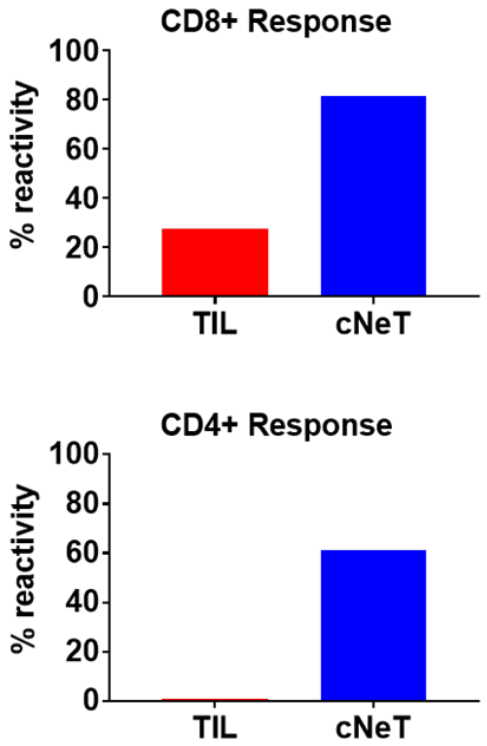
T cell specificity and potency[4]

Cytokine secretion measured through flow cytometric analysis, *n=1*



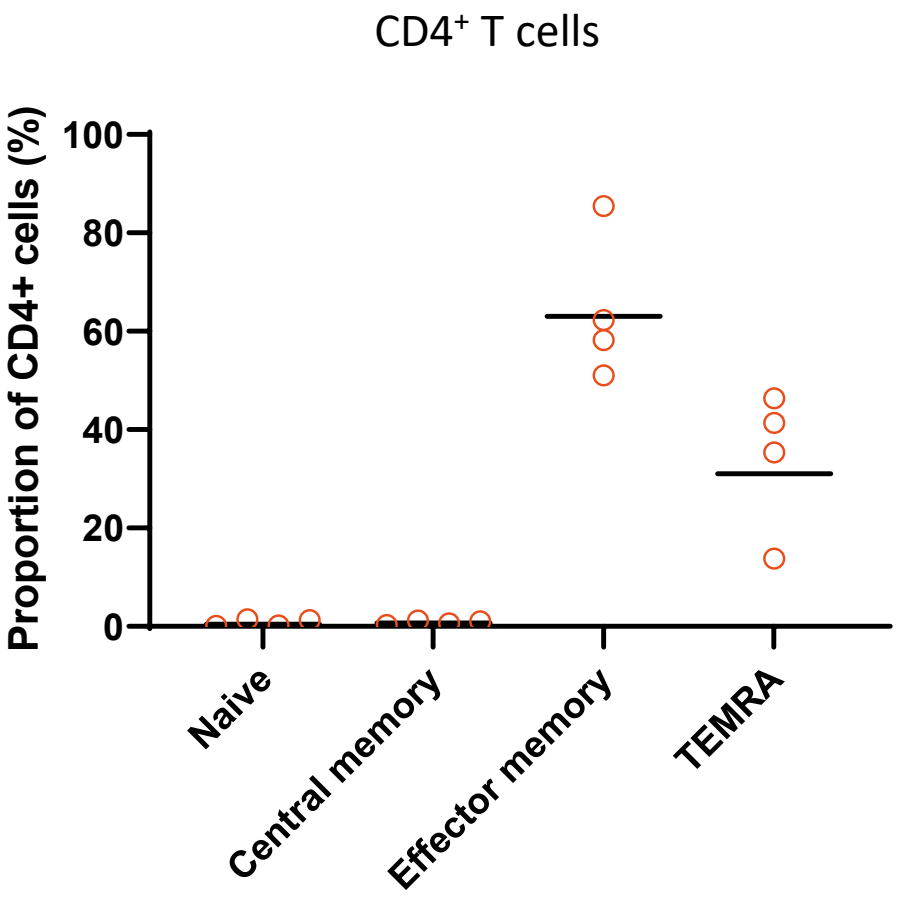
T cell specificity and potency[4]

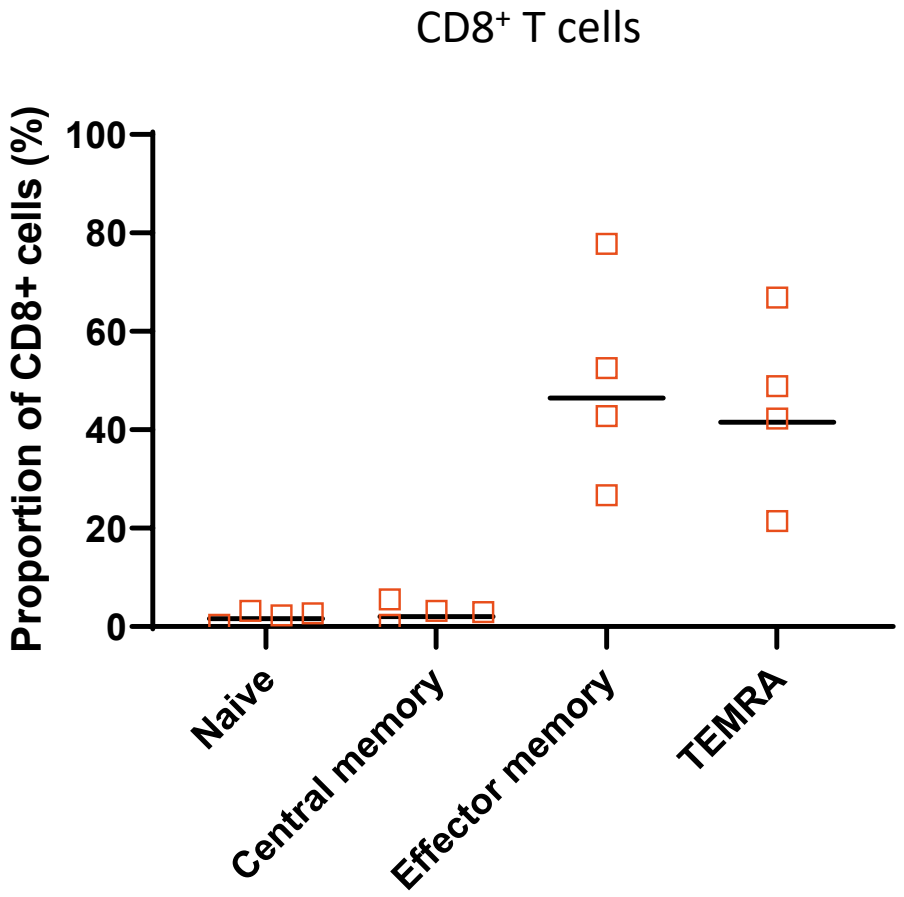
% reactivity, *n=1*



1. Hunder et al., NEJM, 2008;
2. Church et. al., Eur J Immunol, 2014;
3. Antony et al. J Immunol, 2005;
4. Achilles' data measuring the production of inflammatory cytokines in response to clonal neoantigens

Results



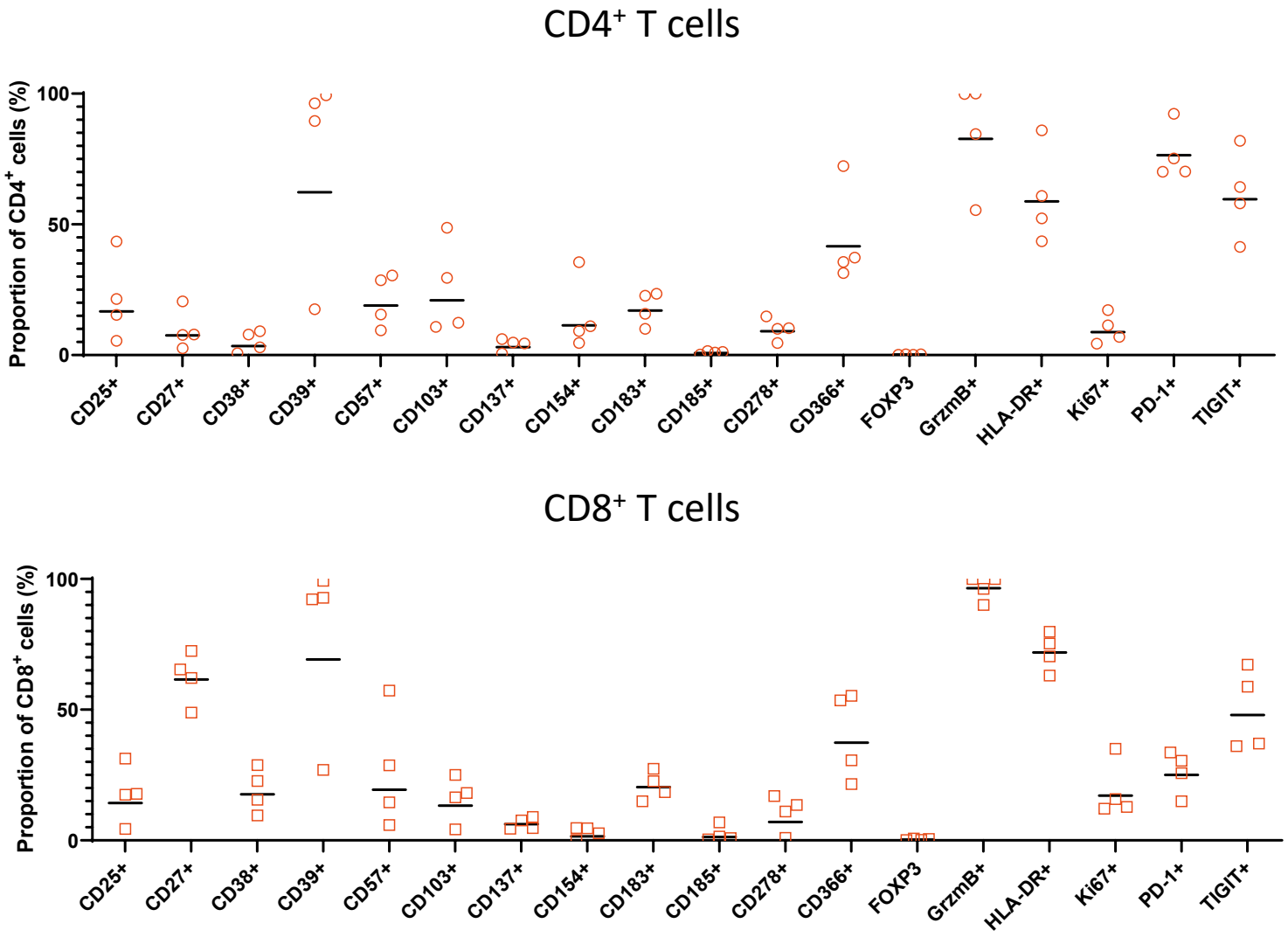


Memory phenotype is dominated by effector memory cells in the process

Full phenotyping of all CD4+ and CD8+ cells

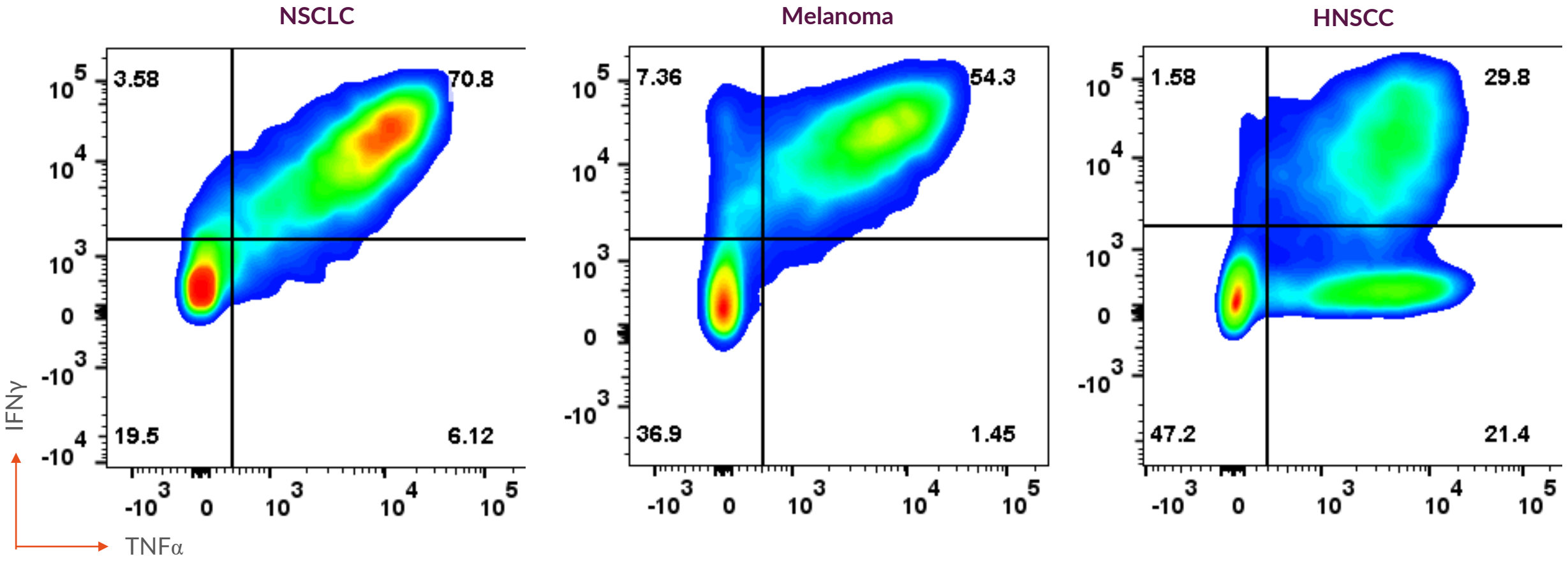
Favourable pattern of phenotypes within both cell types:

- **Conservation of CD25** expression
- **High levels of CD27** expression in CD8+ cells
- **Low expression of CD57**



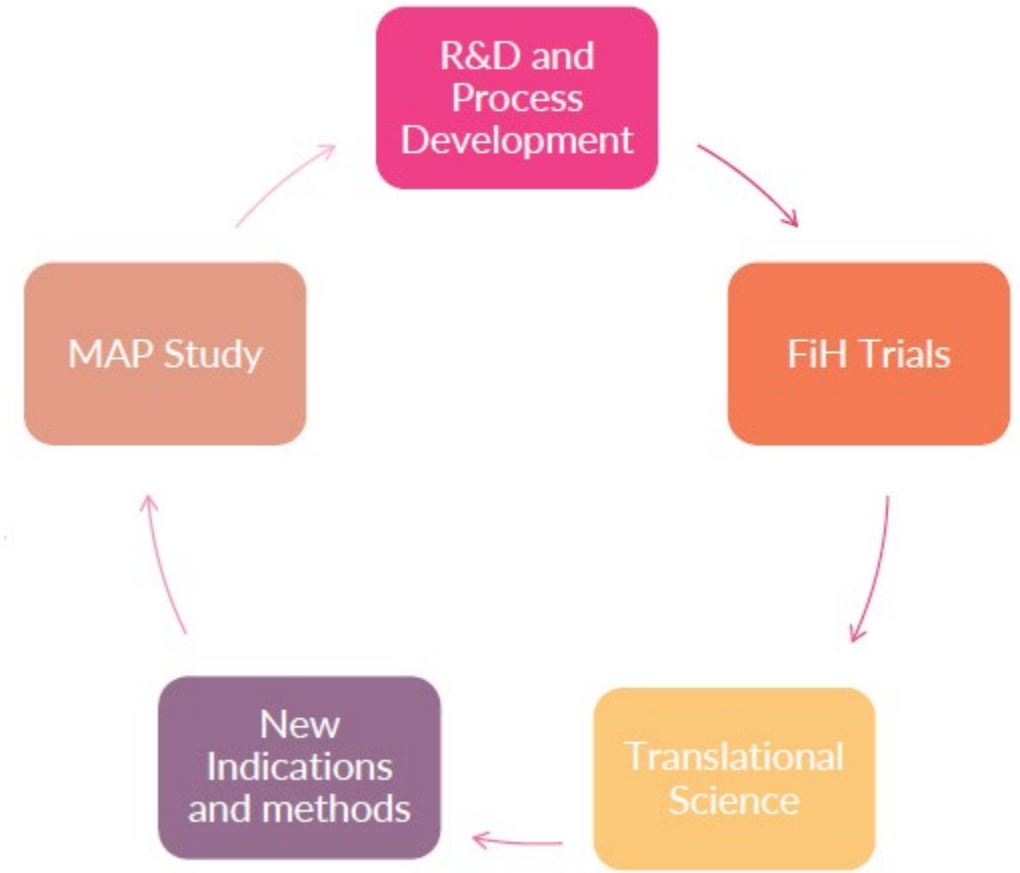
VELOS™ generates with highly potent cNeT cells

Gated CD3⁺-Overnight stimulation with neoantigen peptide pools



Conclusions

- The **Material Acquisition Platform (MAP)** study has been extremely successful in the accumulation of a broad set of tumour-related materials
- MAP continues to expand into new countries and indications
- Initial data suggests **TIL extraction and cNeT production is possible across a range of solid malignancies** and patient characteristics
- Elucidating this information will help to enable the **expansion of Achilles' interventional trials of cNeT** products in new indications
- Future participants will help establish the possibility **of blood-derived cNeT products**, without need for surgical procurement of tissue



Sensitive quantification and tracking of the active components of a clonal neoantigen T cell (cNeT) therapy: From manufacture to peripheral circulation

SITC 2021

November 12, 2021

Sensitive quantification and tracking of the active components of a clonal neoantigen T cell (cNeT) therapy: From manufacture to peripheral circulation

Samra Turajlic[1], Andrew Furness[1], Mariam Jamal-Hanjani[2], Ruth Plummer[3], Judith Cave[4], Fiona Thistlethwaite[5], Emma Leire[6], Jen Middleton[6], Eloise Williams[6], Amy Baker[6], Chloe Maine[6], Michael Epstein[6], Monica Sassi[6], Katy Newton[6], Michael Grant[6], Matilde Saggese[6], Sergio A. Quezada[6], Martin Forster[2]

1 Royal Marsden NHS Foundation Trust, London, UK, 2 UCL Cancer Institute / University College London Hospitals NHS Foundation, London, UK, 3 Newcastle Hospitals NHS Foundation Trust, Newcastle, UK, 4 University Hospital Southampton NHS Foundation Trust, Southampton, UK, 5 The Christie NHS Foundation Trust, Manchester, UK, 6 Achilles Therapeutics UK Ltd, London, UK

For further information on Achilles Therapeutics UK's clinical trials, please contact the Chief Medical Officer - Professor Karl Peggs - at K.Peggs@achillestx.com

Background

Ex-vivo expanded tumour infiltrating lymphocytes (TIL) show promise in delivering durable responses among several solid tumour indications.

However, characterising, quantifying and tracking the active component of TIL therapy remains challenging as the expansion process does not distinguish between tumour reactive and bystander T-cells. Achilles Therapeutics has developed ATL001, a patient-specific TIL-based product, manufactured using the VELOS™ process (Figure 1) that specifically targets clonal neoantigens present in all tumour cells within a patient.

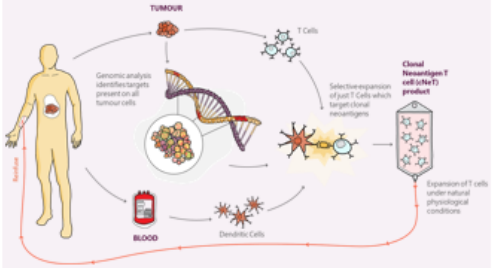


Figure 1. VELOS™ Process

Two Phase I/IIa clinical trials of ATL001 are ongoing in patients with advanced Non-Small Cell Lung Cancer, CHIRON (NCT04032847), and metastatic or recurrent melanoma, THETIS (NCT03997474).

Extensive product characterisation and immune-monitoring are performed through Achilles' manufacturing and translational science programme. This enables precise quantification and characterisation of the active component of this therapy – clonal neoantigen-reactive T cells (cNeT) during manufacture and following patient administration, offering unique insight into the mechanism of action of ATL001 and aiding the development of next generation processes.

Results

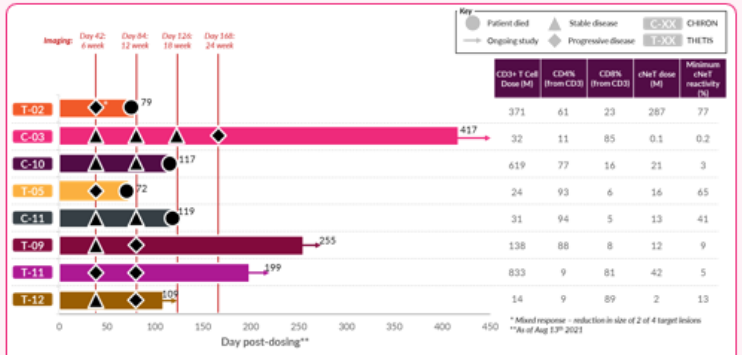


Figure 2. Dosed patients outcomes (based on RECIST v1.1) following ATL001 and characteristics

Immuno-monitoring shows heterogenous response to Short- and Long master peptide pools (SMP, LMP) at Re-Screening (RS) and subsequent to dosing (D0)

T-02
- Large detectable reactivity at RS for SMP
- Steroids at D11 may have dampened down reactivity D14 onwards
- W6 SMP increase

T-05
- Increased reactivity after infusion peaks at D10 (cNeT/ml), declines to baseline levels at W6
- No data D14 and D21 due to remote visits
- Cells expanding *in vivo*

C-11
- Reactivity of LMP at baseline
- Reactivity for LMP increases post dosing and peaks D7
- SMP Reactivity at D28

T-11
- Clear SMP reactivity pre-dosing, some reactivity observed D14 to W6 post-dosing
- Low LMP reactivity pre-dosing but increasing reactivity from D14 to W6 post-dosing

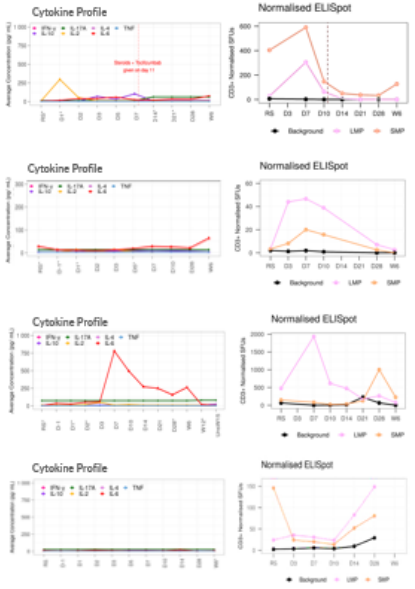


Figure 3. Normalised ELISpot results for dosed patients from baseline to 6 weeks post-dose

8 patients dosed to date

- 5 patients with melanoma (THETIS) and 3 patients with NSCLC (CHIRON) have received their ATL001 product
- The median age was 57 (range 30 – 71) and 6/8 patients were male
- The median number of previous lines of systemic anti-cancer treatment at ATL001 dosing was 2.5 (range 1 – 5)
- Median cNeT dose infused in this initial cohort was 14.2M (within a trial defined target range of 10-1000M)
- Unique single peptide reactivities were observed in 7 of 8 products (range 0 – 28, mean 8.6)
- cNeT were detected in 5/8 patients post dosing
- Best disease response was stable disease, with no objective radiological responses (RECIST v1.1) demonstrated to date from low doses of ATL001 generated using VELOS™ Process 1
- 4 patients remain in safety follow-up

Safety and tolerability

- In total, 34 ≥Grade 3 Adverse Events (AE) were recorded across the 8 dosed patients in THETIS and CHIRON
- 3 Adverse Events of Special Interest (AESI); three events of Cytokine Release Syndrome (CRS)
  - Two Grade 2 CRS events and one Grade 1
  - Events resolved in 3-8 days
- 2 neurological Suspected Unexpected Serious Adverse Reactions (SUSAR) were observed in two of the dosed patients:
  - Immune effector cell-associated neurotoxicity syndrome (ICANS) possibly related to ATL001
  - Encephalopathy – deemed unlikely related to ATL001 following IDSMC review

VELOS™ generates polyfunctional cNeT cells

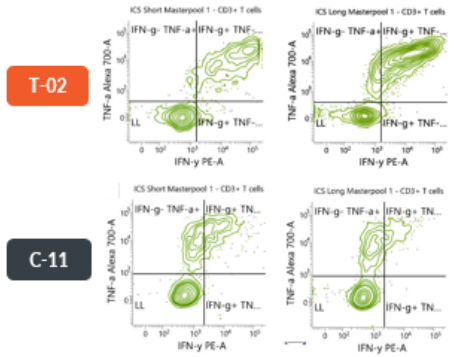


Figure 4. Gated CD3+–Overnight stimulation with neoantigen peptide pools

System Organ Class	Preferred Term	No. of AEs
Blood and lymphatic system disorders	Leukopenia	1
	Lymphopenia	2
	Neutropenia	4
	Anaemia	3
Gastrointestinal disorders	Diarrhoea	3
Infections and infestations	Cellulitis	1
	Infected seroma*	3
	Klebsiella sepsis	1
	Neutropenic sepsis	1
	Sepsis	1
	Urinary tract infection	1
Metabolism and nutrition disorders	Hypophosphataemia	2
Musculoskeletal and connective tissue disorders	Inguinal mass	1
	Musculoskeletal chest pain	1
Nervous system disorders	Neuralgia	1
	Neurotoxicity**	1
	Encephalopathy	1
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism	1
	Dyspnoea	2
	Hypoxia	1
	Pleural effusion	1
	Tachypnoea	1

Table 1. Adverse Events ≥Grade 3 (THETIS and CHIRON)
*The 3 events of infected seroma were all recorded within the same patient
**Neurotoxicity event attributed to Immune effector cell-associated neurotoxicity syndrome (ICANS)

Methods

ATL001 was manufactured using procured tumour and matched whole blood from 8 patients enrolled in the THETIS (n=5) and CHIRON (n=3) clinical trials.
Following administration of ATL001, peripheral blood samples were collected up to week 6.

- The active component of the product was detected via re-stimulation with clonal neoantigen peptide pools and evaluation of IFN-γ and/or TNF-α production.
- Deconvolution of individual reactivities was achieved via ELISPOT assays, normalised to T-cell component of PBMC.
- Immune reconstitution was evaluated by flow cytometry.
- cNeT expansion was evaluated by restimulation of isolated PBMCs with peptide pools and individual peptide reactivities (ELISPOT).

Future Directions

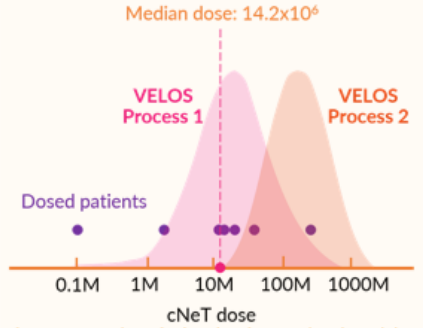


Figure 5. cNeT doses in dosed patients and projected dose range for VELOS™ Process 2

For more information of VELOS™ Process 2, please see SITC Poster Number: 193; presented by Joseph Robinson, PhD, Senior Scientist, Achilles Therapeutics

Conclusions

These data underscore our ability to sensitively detect, quantify and track the patient-specific cNeT component of ATL001 – during manufacture and post dosing. Our move to Process 2 allows dosing with higher cNeT numbers, up 1000M. As the dataset matures, these metrics of detection and expansion will be correlated with product, clinical and genomic characteristics to determine variables associated with peripheral cNeT dynamics and clinical response.

Results

8 patients dosed to date

- 5 patients with melanoma (THETIS) and 3 patients with NSCLC (CHIRON) have received their ATL001 product
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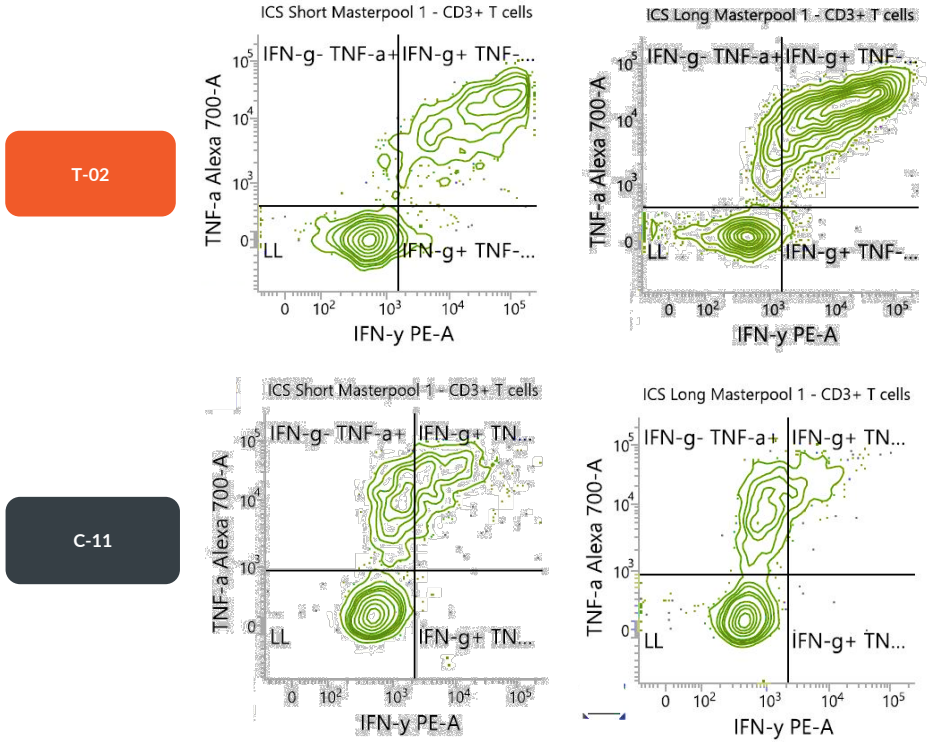
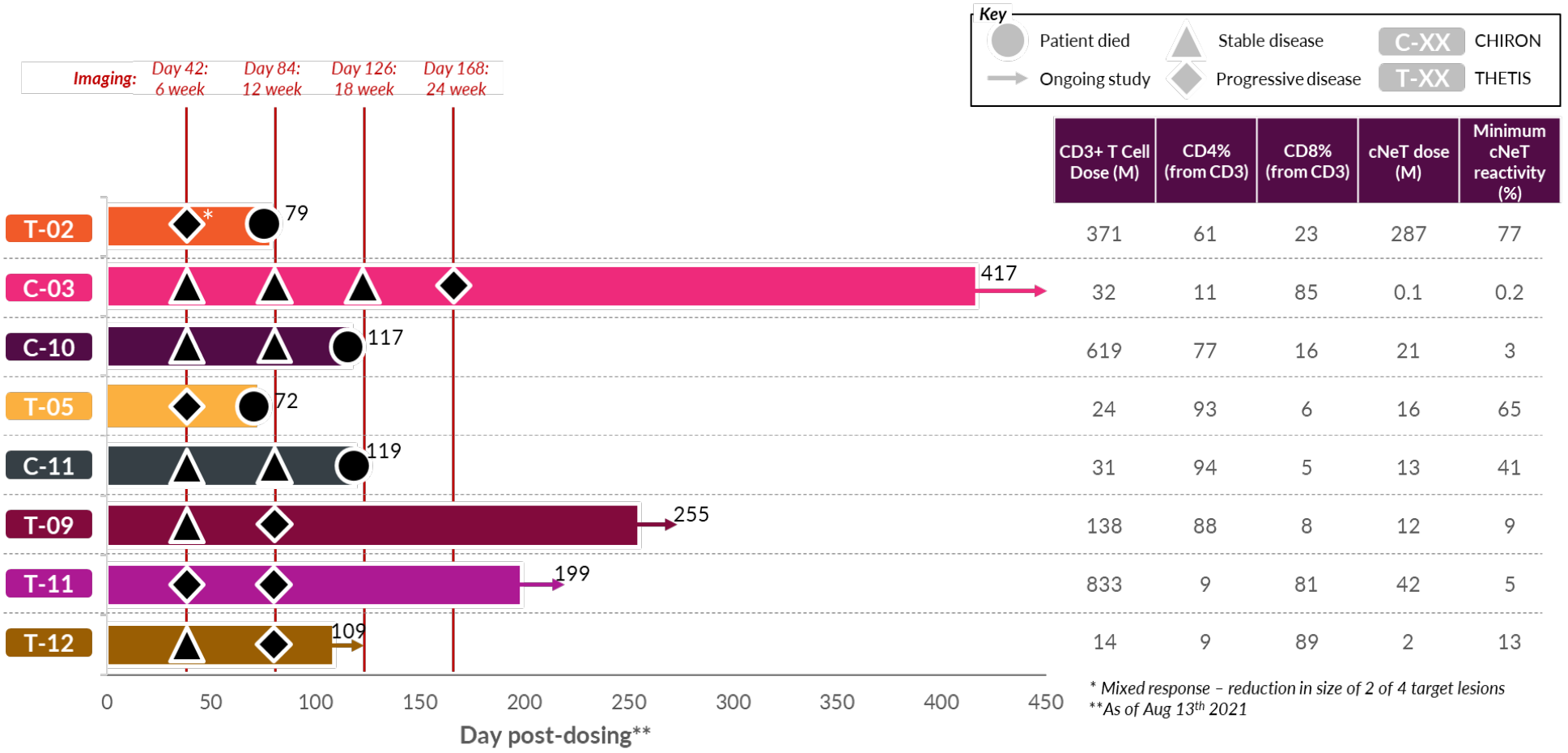


Figure 4. Gated CD3+-Overnight stimulation with neoantigen peptide pools

Figure 2. Dosed patients outcomes (based on RECIST v1.1) following ATL001 and characteristics



	CD3+ T Cell Dose (M)	CD4% (from CD3)	CD8% (from CD3)	cNeT dose (M)	Minimum cNeT reactivity (%)
T-02	371	61	23	287	77
C-03	32	11	85	0.1	0.2
C-10	619	77	16	21	3
T-05	24	93	6	16	65
C-11	31	94	5	13	41
T-09	138	88	8	12	9
T-11	833	9	81	42	5
T-12	14	9	89	2	13

* *Mixed response – reduction in size of 2 of 4 target lesions*
***As of Aug 13th 2021*

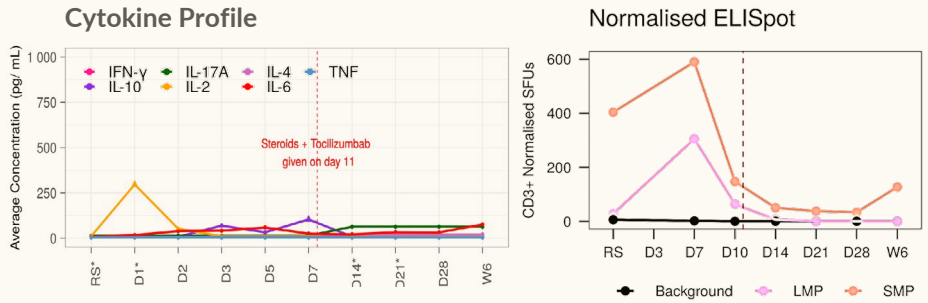
Results

Figure 3. Normalised ELISpot results for dosed patients from baseline to 6 weeks post-dose

Immuno-monitoring shows heterogenous response to Short- and Long master peptide pools (SMP, LMP) at Re-Screening (RS) and subsequent to dosing (D0)

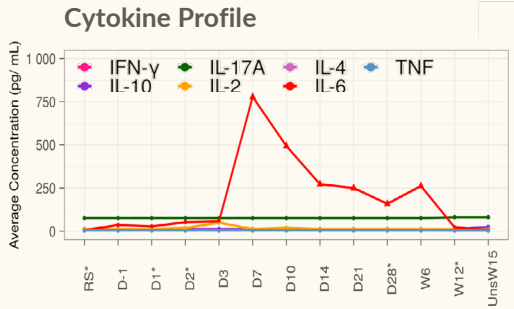
T-02

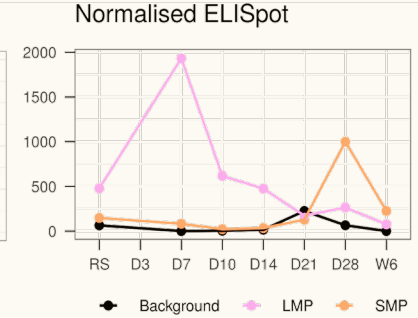
- Large detectable reactivity at RS for SMP
- Steroids at D11 may have dampened down reactivity D14 onwards
- W6 SMP increase



C-11

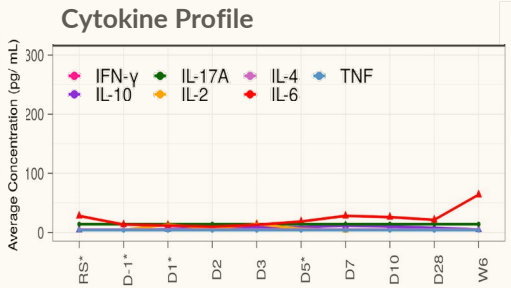
- Reactivity of LMP at baseline
- Reactivity for LMP increases post dosing and peaks D7
- SMP Reactivity at D28

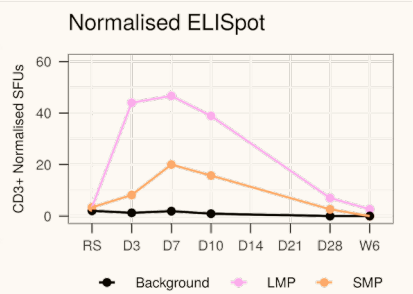




T-05

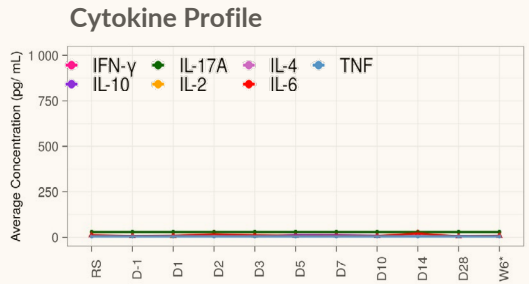
- Increased reactivity after infusion peaks at D10 (cNeT/ml), declines to baseline levels at W6
- No data D14 and D21 due to remote visits
- Cells expanding in vivo

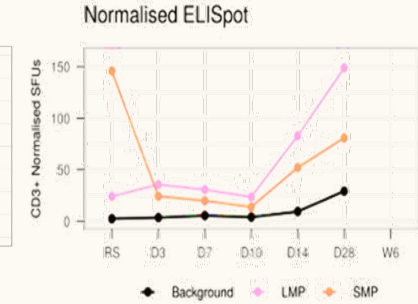




T-11

- Clear SMP reactivity pre-dosing, some reactivity observed D14 to W6 post-dosing
- Low LMP reactivity pre-dosing but increasing reactivity from D14 to W6 post-dosing





Results

Safety and tolerability

- In total, 34 ≥Grade 3 Adverse Events (AE) were recorded across the 8 dosed patients in THETIS and CHIRON
- 3 Adverse Events of Special Interest (AESI); three events of Cytokine Release Syndrome (CRS)
  - Two Grade 2 CRS events and one Grade 1
  - Events resolved in 3-8 days
- 2 neurological Suspected Unexpected Serious Adverse Reactions (SUSAR) were observed in two of the dosed patients:
  - Immune effector cell-associated neurotoxicity syndrome (ICANS) possibly related to ATL001
  - Encephalopathy – deemed unlikely related to ATL001 following IDSMC review

Table 1. Adverse Events ≥Grade 3 (THETIS and CHIRON)

System Organ Class	Preferred Term	No. of AEs
Blood and lymphatic system disorders	Leukopenia	1
	Lymphopenia	2
	Neutropenia	4
	Anaemia	3
Gastrointestinal disorders	Diarrhoea	3
Infections and infestations	Cellulitis	1
	Infected seroma*	3
	Klebsiella sepsis	1
	Neutropenic sepsis	1
	Sepsis	1
	Urinary tract infection	1
Metabolism and nutrition disorders	Hypophosphataemia	2
Musculoskeletal and connective tissue disorders	Inguinal mass	1
	Musculoskeletal chest pain	1
Nervous system disorders	Neuralgia	1
	Neurotoxicity**	1
	Encephalopathy	1
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism	1
	Dyspnoea	2
	Hypoxia	1
	Pleural effusion	1
	Tachypnoea	1

*The 3 events of infected seroma were all recorded within the same patient
**Neurotoxicity event attributed to Immune effector cell-associated neurotoxicity syndrome (ICANS)

The Achilles VELOS™ Process 2 boosts the dose of highly functional clonal neoantigen-reactive T cells for precision personalized cell therapies

SITC 2021

November 12, 2021

The Achilles VELOS™ Process 2 boosts the dose of highly functional clonal neoantigen-reactive T cells for precision personalized cell therapies

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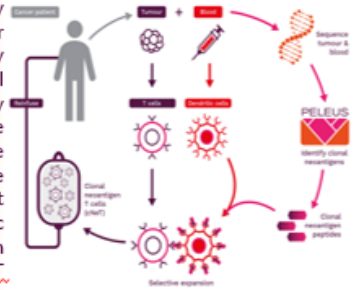
1) Achilles Therapeutics UK Limited, London, United Kingdom; 2) Royal Marsden NHS Foundation Trust, London, United Kingdom; 3) University College London Cancer Institute, London, United Kingdom; 4) UCLH and Barts NHS Trusts, London, United Kingdom; 5) Corresponding author – for further information please email: s.quezada@achillestx.com

Introduction

Adoptive transfer of ex-vivo expanded Tumour-Infiltrating Lymphocytes (TIL) has shown promise in the clinic. However, the non-specific expansion of TILs and the lack of understanding of the active component of TIL has resulted in poor correlation between clinical response and dose as well as poor understanding of response and resistance mechanisms. The VELOS™ manufacturing process generates a precision and personalised treatment modality by targeting clonal neoantigens with the incorporation of an antigen-specific expansion step to enrich the product for these specificities. Achilles has developed a second VELOS™ process to boost the neoantigen-reactive cell dose while maintaining key qualitative features associated with function. Here we report the in-depth characterisation of clonal neoantigen-reactive T cells (cNeT) products expanded using the two VELOS™ processes.

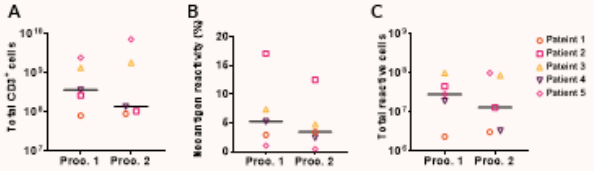
Methods

- Matched tumours and peripheral blood from patients undergoing routine surgery were obtained from patients with primary NSCLC (n=3) or metastatic melanoma (n=2) (NCT03517917).
- TIL were expanded from tumour fragments in the presence of IL-2.
- Peptide pools, corresponding to the clonal mutations identified using the PELEUS™ bioinformatics platform, were generated.
- cNeT were expanded by co-culture of TIL with peptide-pulsed autologous dendritic cells.
- For VELOS™ Process 2 additional media supplementation was added throughout the process. Cell expansion was boosted at the end of the co-culture with an optimized stimulation cocktail.
- Neoantigen reactivity was assessed using our proprietary potency assay with peptide pool rechallenge followed by intracellular cytokine staining. Single peptide reactivities were identified using ELISpot and flow cytometric analysis for in-depth phenotyping of cNeT was performed.



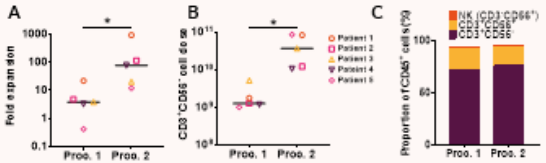
Results

Figure 1: Clonal neoantigen specific TIL can be identified following the culture of tumour fragments in VELOS™ Process 2



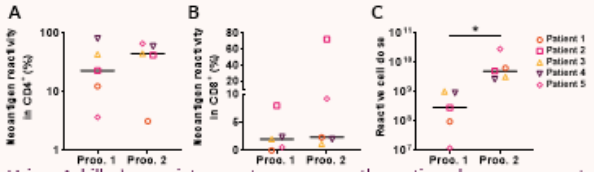
Following culture of tumour fragments with IL2, processes 1 and 2 yielded similar numbers of TIL (A; values scaled to tumour mass). Achilles' proprietary potency assay was used to identify the proportion of clonal neoantigen reactive cells within the TIL (B). The total number of clonal neoantigen reactive TIL was similar in Processes 1 and 2 (C). Lines at median; n=5.

Figure 2: VELOS™ Process 2 generates a 29 fold greater number of T cells



During the selective expansion phase of the VELOS™ process, Process 2 gave a greater fold expansion of T cells (A; lines at median) and an increase in total T cells generated (B; values scaled to tumour mass; lines at median). The majority of cells generated by both processes were CD3+CD56- (C; bars show means). * p<0.05 one tailed Wilcoxon test, n=5.

Figure 3: VELOS™ Process 2 generates a 18 fold greater number of cNeT



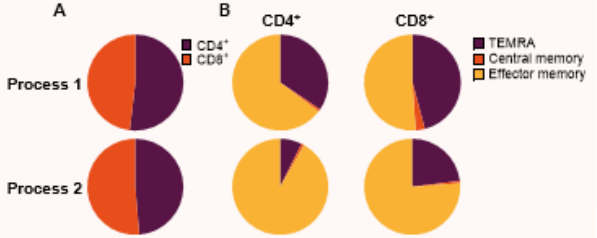
Using Achilles' proprietary potency assay, the active drug component (cNeT) was quantified for both CD4+ (A) and CD8+ (B) cells. No difference in the proportion of cNeT was observed between Process 1 and Process 2. The overall number of cNeT generated by Process 2 was significantly higher than was generated by Process 1. Lines at medians; * p<0.05 one tailed Wilcoxon test; n=5.

Figure 4: VELOS™ Process 2 generates a product with multiple clonal neoantigen reactivities

	Single peptide reactivities		
Patient	Process 1	Process 2	Difference
1	1	4	+3
2	1	3	+2
3	2	5	+3
4	2	17	+15
5	No data	18	N/A

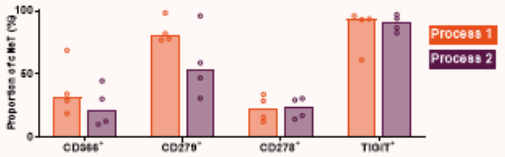
The number of individual clonal neoantigen reactivities was determined by ELISpot. VELOS™ Process 2 generated a product with reactivities to multiple clonal neoantigens without loss of reactivities compared to Process 1. For patient 5, insufficient cells were generated by Process 1 to carry out ELISpot.

Figure 5: VELOS™ Process 2 generates a product made up of mainly CD4+ and CD8+ effector memory cells



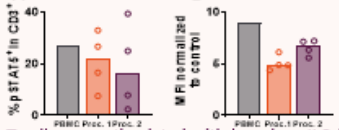
Phenotyping was carried out by flow cytometry at the end of the co-culture period. The VELOS™ processes generated products made up of both CD4+ and CD8+ cells (A; n=5). Products were primarily effector memory cells (CD45RA-CD197-) with some TEMRA cells (CD45RA+CD197-) and few central memory cells (CD45RA-CD197+). The products of Process 2 had a lower proportion TEMRA cells compared to Process 1 (B; n=4). Pie charts show mean frequencies.

Figure 6: cNeT from VELOS™ Process 2 express similar levels of immune checkpoint molecules



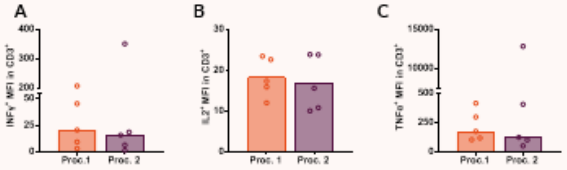
Restimulation with clonal neoantigen pareptide pools and staining for cytokine secreting cells enables phenotyping of the active drug component of the product of the VELOS™ process. cNeT from Process 2 showed no increase in immune checkpoint molecules compared to cNeT from Process 1. Bars at median; n=4.

Figure 7: T cells from VELOS™ Process 2 retain sensitivity to IL2



T cells were stimulated with low dose IL2 (100IU/ml) and phosphorylation of STAT5 was measured by flow cytometry. Phosphorylation occurred in similar proportions of CD3+ cells in both processes (A). Geometric mean fluorescence intensity (MFI) of pSTAT5 staining was also similar (B). Bars at median; n=4.

Figure 8: T cells from VELOS™ Process 2 retain capacity to secrete cytokines



T cells were stimulated with a poly clonal stimulus (Staphylococcal Enterotoxin B) and cytokine production was measured using Achilles proprietary potency assay. CD3+ cells from Process 1 and Process 2 generated similar amounts of INFγ (A), IL2 (B) and TNFα (C). Graphs show geometric mean fluorescence intensity (MFI) normalized to control; bars at median; n=5.

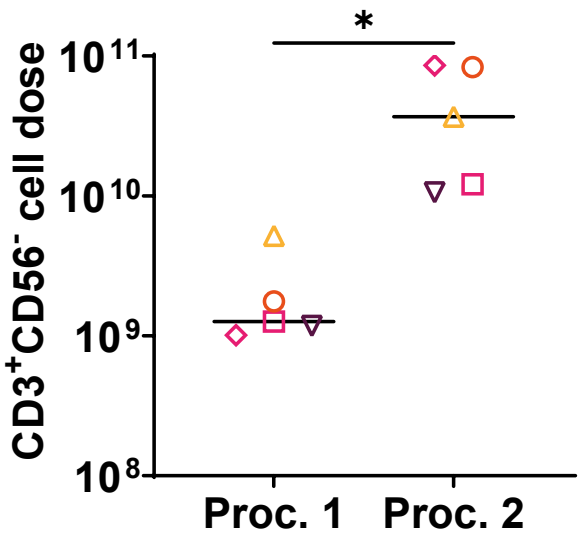
Conclusions

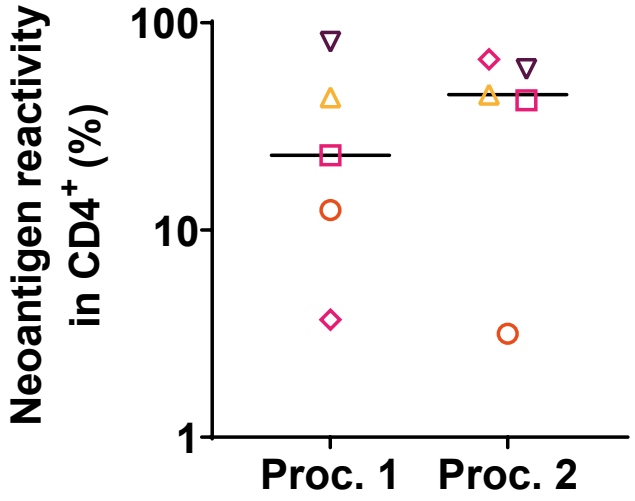
- Achilles proprietary potency assay quantifies cNeT dose facilitating optimization of the VELOS™ process.
- VELOS™ Process 2 generates an increased cNeT dose compared to Process 1
- cNeT generated using VELOS™ Process 2 maintain key phenotypic features associated with function
- This proof of concept data supports the transfer of VELOS™ Process 2 to clinical manufacture for two first in human studies for treatment of solid cancer.

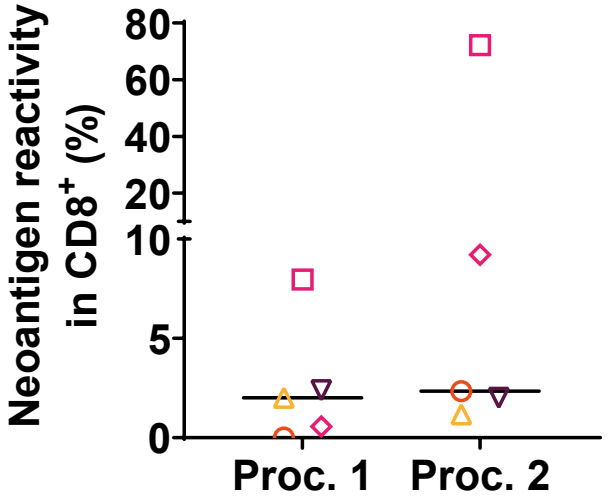
References
1: McGranahan N., et al. Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade. Science. 6280: 1463-1469 (2016)
2: Robertson J., et al. Adoptive cell therapy with tumour-infiltrating lymphocytes: the emerging importance of clonal neoantigen targets for next-generation products in non-small cell lung cancer. Immuno-oncology Technology. 3:1-7 (2019)

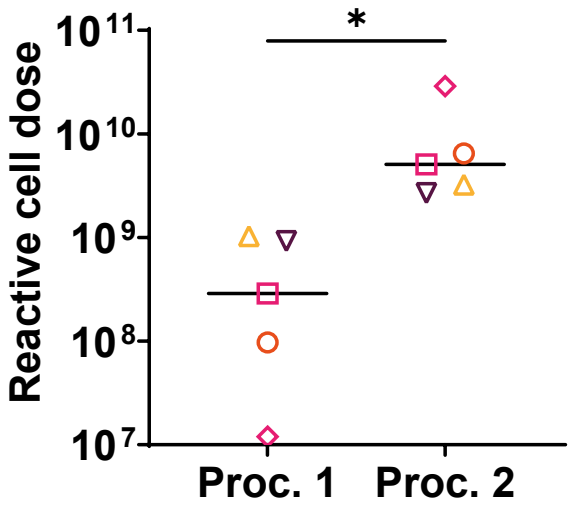
Acknowledgements
The authors would like to thank the participating patients and their families for donation of material used in this study.
Disclosures
This study was funded by Achilles Therapeutics UK Limited.

VELOS™ Process 2 generates a 18 fold greater number of cNeT









- Median T cell dose was 29 fold higher in process 2 compared process 1
- The proportion of cNeT in CD4+ cells was similar between processes
- The proportion of cNeT in CD8+ cells was similar between processes
- Median cNeT was 18 fold higher in process 2 compared to process 1

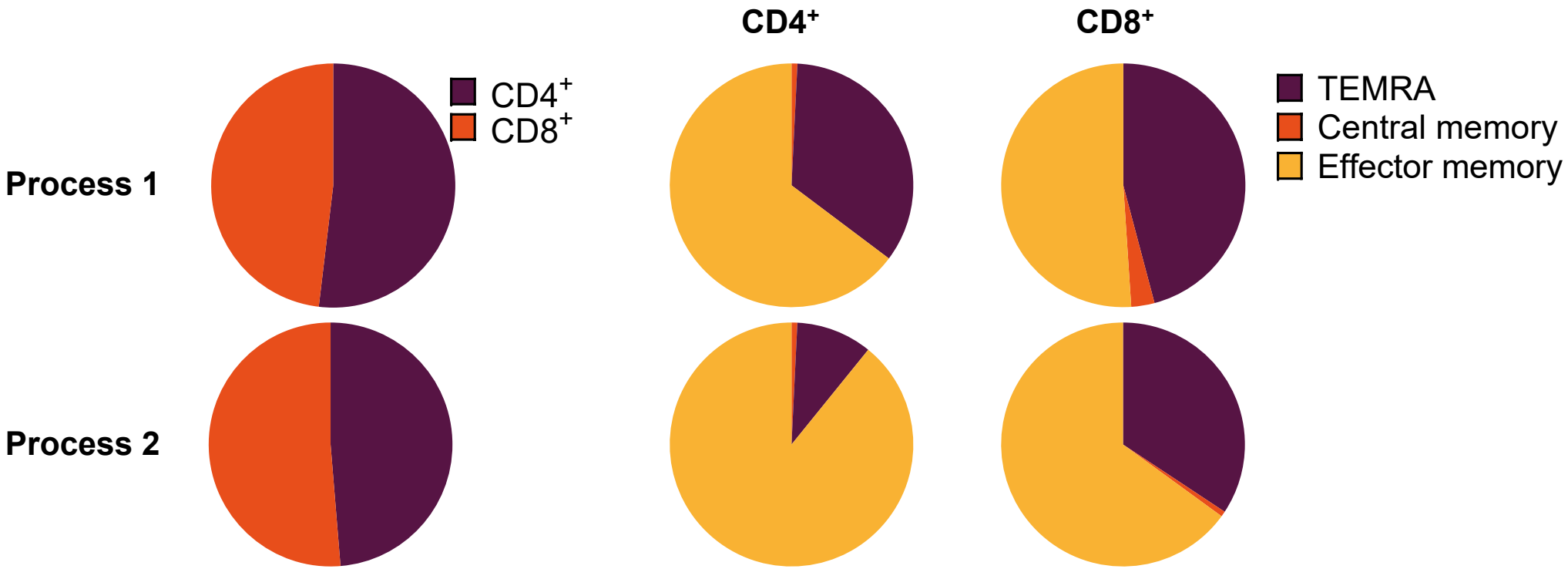
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5

VELOS™ Process 2 generates a product with multiple clonal neoantigen reactivities

	Single peptide reactivities		
Patient	**Process 1**	**Process 2**	**Difference**
1	1	4	+3
2	1	3	+2
3	2	5	+3
4	2	17	+15
5	No data*	18	N/A

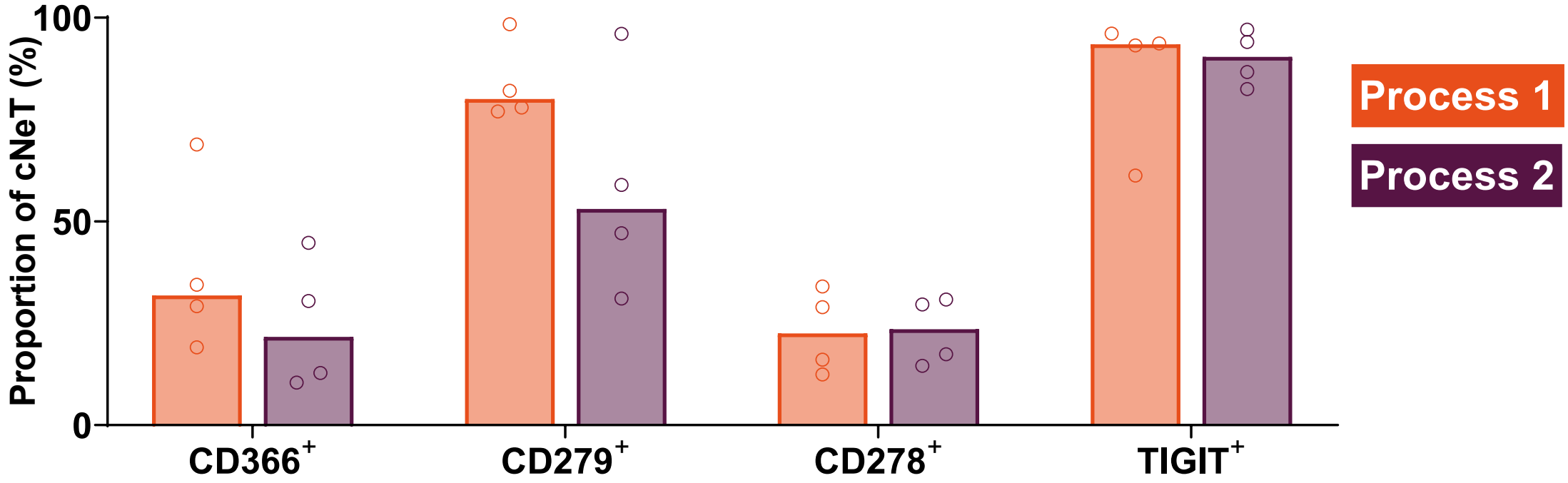
* ELISpot not carried out due to insufficient cells

The VELOS™ Process 2 product is mainly CD4+ and CD8+ effector memory cells

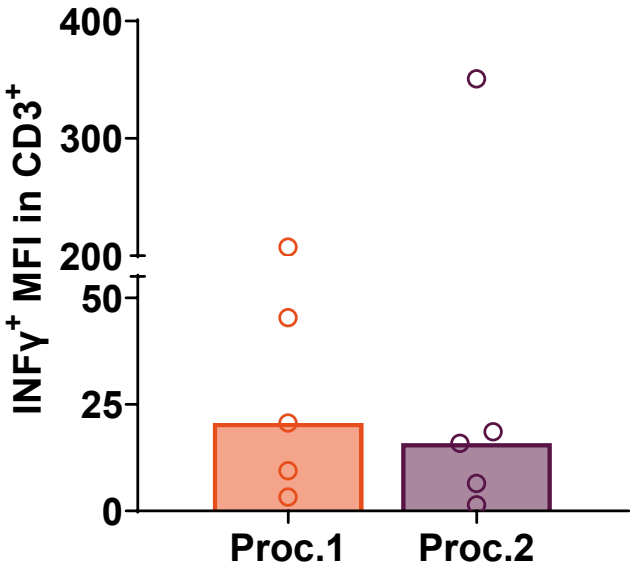


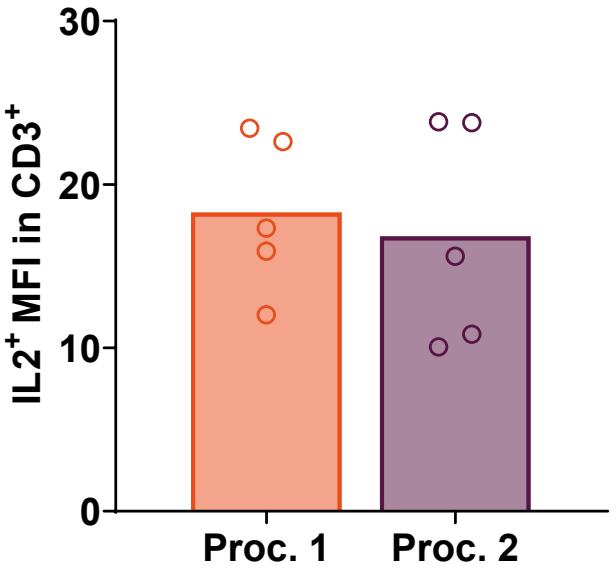
- The proportion of CD4+ and CD8+ cells was similar between processes
- The majority of CD4+ and CD8+ had effector memory phenotype (CD45RA-CD197-)
- The products of Process 2 appear to have a lower proportion of TEMRA (CD45RA+CD197-) compared to Process 1

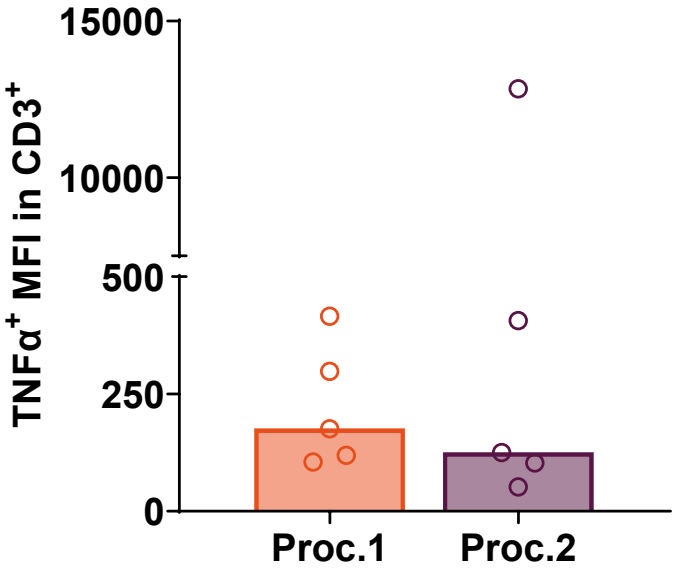
cNeT from VELOS™ Process 2 express similar levels of immune checkpoint molecules



T cells from VELOS™ Process 2 retain capacity to secrete cytokines







- The ability to produce cytokines is a key marker of T cell functionality
- T cells from both processes produced similar amount of cytokines in response to polyclonal stimulus

Conclusions

- Achilles proprietary potency assay quantifies cNeT dose facilitating optimization of the VELOS™ process.
- VELOS™ Process 2 generates an increased cNeT dose compared to Process 1
- cNeT generated using VELOS™ Process 2 maintain key phenotypic features associated with function
- This proof of concept data supports the transfer of VELOS™ Process 2 to clinical manufacture for two first in human studies for treatment of solid cancer

Parameter	Change from VELOS™ Process 1 to 2
T cell dose	29 fold increase
cNeT dose	18 fold increase
Phenotype	Similar
Cytokine production	Similar

Summary & Milestones

Our proprietary VELOS™ manufacturing process builds on standard TIL therapy but leverages clonal neoantigen targeting to deliver a more precise and potent product

VELOS
Manufacturing process

Precision platform

Selective expansion of tumor targeting T cells

- **Prospectively target patient-specific clonal neoantigens** shown to correlate with anti-tumor activity[1,2]
- Able to quantify the **active component (cNeT)** in each product and **track post-dosing** in blood or tissue
- **Enable a mechanistic understanding of cNeT therapy** (e.g., dose response) and a path to a **robust potency assay**

Potent product

Potent polyclonal product

- VELOS process delivers a **polyclonal product** able to target **multiple cancer antigens** present **on all tumor cells**
- Products contain both **T helper (CD4+)** and **cytotoxic T cells (CD8+)** subtypes
- Natural dendritic cell process **reduces the need for IL-2** in the VELOS process and post-dosing

1. *Lauss et al., Nature Comm, 2017*
2. *Snyder et al., NEJM, 2014*

Achilles can leverage established regulatory principles to develop a potency assay

Potency Assay

- Regulatory authorities require demonstration that the product contains an active component **of a specific identity and potency**
- Potency can be defined as the specific ability of the product to **effect a given result** that should take effect through the product's **mechanism of action**
- Timeline for interaction with regulatory authorities established and **will have an agreed upon plan prior to registrational studies**

Achilles cNeT

- With our platform **we can quantify the cNeT** component as a percentage of the total T cells (cNeT reactivity) and **calculate the cNeT dose** of each product
- cNeT reactivity can be used as both a **release criterion and potency measure**
- We believe that cNeT is the active component of TIL and will **correlate with anti-tumor effect**
- Further **phenotypic and functional characteristics** of cNeT can be measured to develop potency assays

Key anticipated clinical milestones

2021

- [x] Reported 6-pt FiH data in cNeT monotherapy
- [x] Open clinical sites in US and EU
- [x] Enroll first patient in the US
- [x] Monotherapy data with Process 1 cNeT
- [ ] Process 2 GMP data update
- [ ] File IND in HNSCC

2022

1H

- [ ] 1st patient dosed with Process 2 cNeT
- [ ] Initiate tumor archiving program

2H

- [ ] Interim data from Process 2 cNeT monotherapy
- [ ] Additional Process 1 monotherapy data
- [ ] Interim data from PD-1 / cNeT combo
- [ ] Monotherapy data with Process 2 cNeT

Achilles is building a transformative oncology business

- Two ongoing clinical trials with near-term data readouts and plans to add new indications
- Exclusive access to TRACERx, which gives the unique capability to address clonal neoantigens
- cNeT platform can target multiple cancer antigens present in all tumor cells
- Technology allows us to develop a potency-based release assay
- Robust and commercially scalable manufacturing process designed to be fully closed and automated
- Cash to complete planned I/IIa clinical trials, expand manufacturing capacity, and broaden pipeline