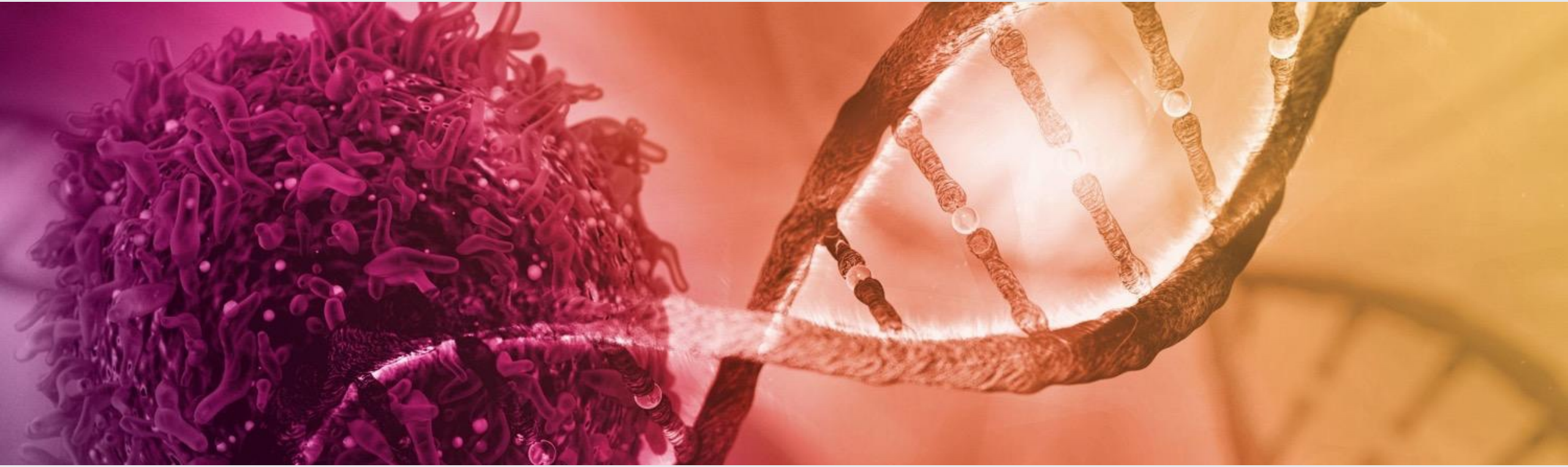

Achilles Therapeutics

Precision T cell therapies to treat solid tumors

September 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.

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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
- Q4 2021: Interim analysis on 8-10 patients across NSCLC & melanoma (Process 1), highlighting engraftment kinetics, product characterization, and ability to define tumor-reactive component; Open Process 2 high-dose cohort
- 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
- Team of ~200 employees (HQ in London); fully financed to complete ongoing phase I/IIa clinical trials, expand manufacturing capacity and bring additional programs into the clinic with June 30 cash of $299M

Our senior management team & board

Senior Leadership Team

Iraj Ali
CEO & Board Member

Syncona · McKinsey&Company

Sergio Quezada
CSO & Founder

UCL Cancer Institute · Cancer Research UK

Karl Peggs
CMO & Founder

UCL Cancer Institute

Robert Coutts
CFO

KPMG · Syncona

Daniel Hood
Chief Legal Officer

Intercept · Gilead

Beverley Carr
CBO

gsk · cAT (Cambridge Antibody Technology)

Ed Samuel
SVP Technical Operations

Orchard therapeutics · Cognate BioServices, Inc.

Shree Patel
SVP Clinical Operations

Cell Medica

Non-Executive Board of Directors

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Chairman

Ablynx, A Sanofi Company

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Non-Executive Director

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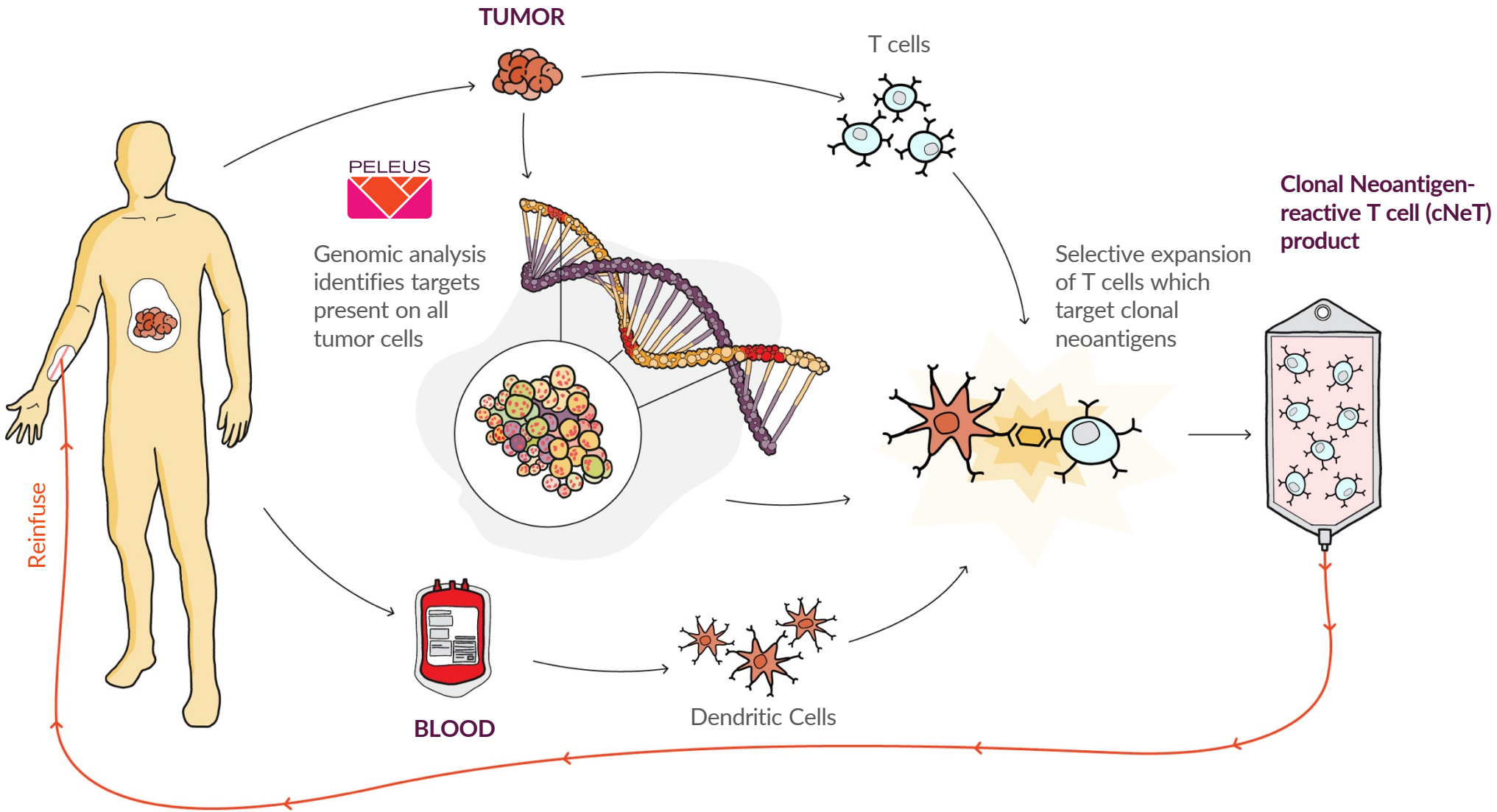
Non-Executive Director

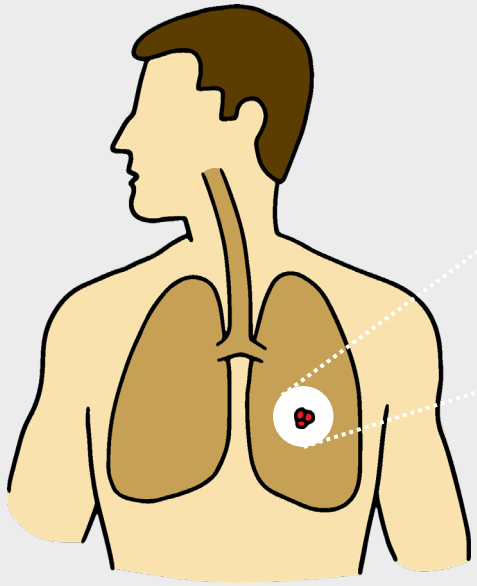
Alexion · Gilead

Precision TIL therapy targeting clonal neoantigens

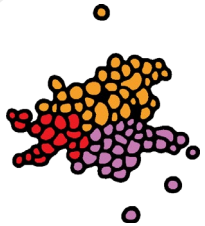
Using cutting edge personalized genomics to target all cells in a patient's tumor



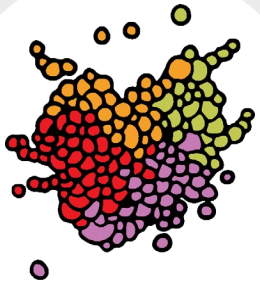
Achilles has developed proprietary technology to **target all tumor cells**



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



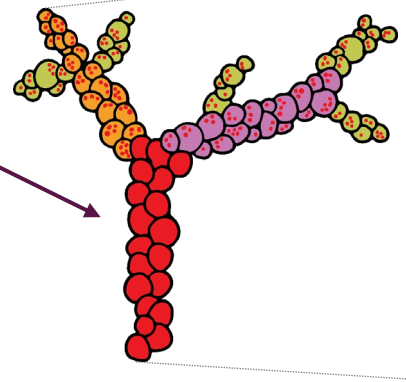
Tumors evolve, developing many new mutations resulting in **heterogeneity** that enables them to evade targeting[1]

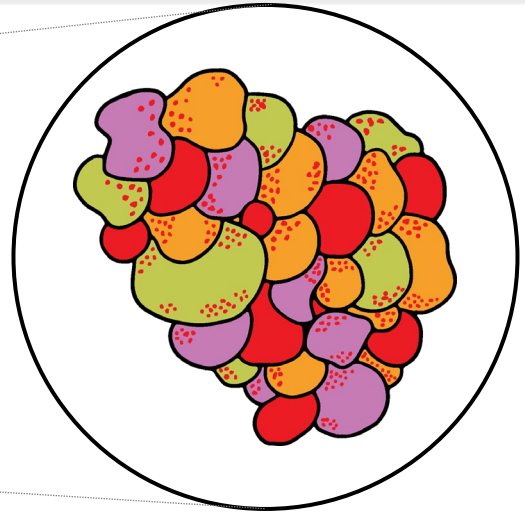


To kill all of the tumor cells we believe you need to target the **clonal neoantigens formed early in tumor evolution**

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

Tumor associated antigens

Present on some tumor cells and on healthy tissue

Fate THERAPEUTICS

TCR² THERAPEUTICS

MARKER THERAPEUTICS

TMUNITY

Adaptimmune TRANSFORMING T CELL THERAPY

Neoantigens

Present on some tumor cells

IOVANCE BIOTHERAPEUTICS

InstilBio

BIONTECH

neogene THERAPEUTICS

PACT pharma

genocea

TAILORED THERAPEUTICS

Clonal neoantigens

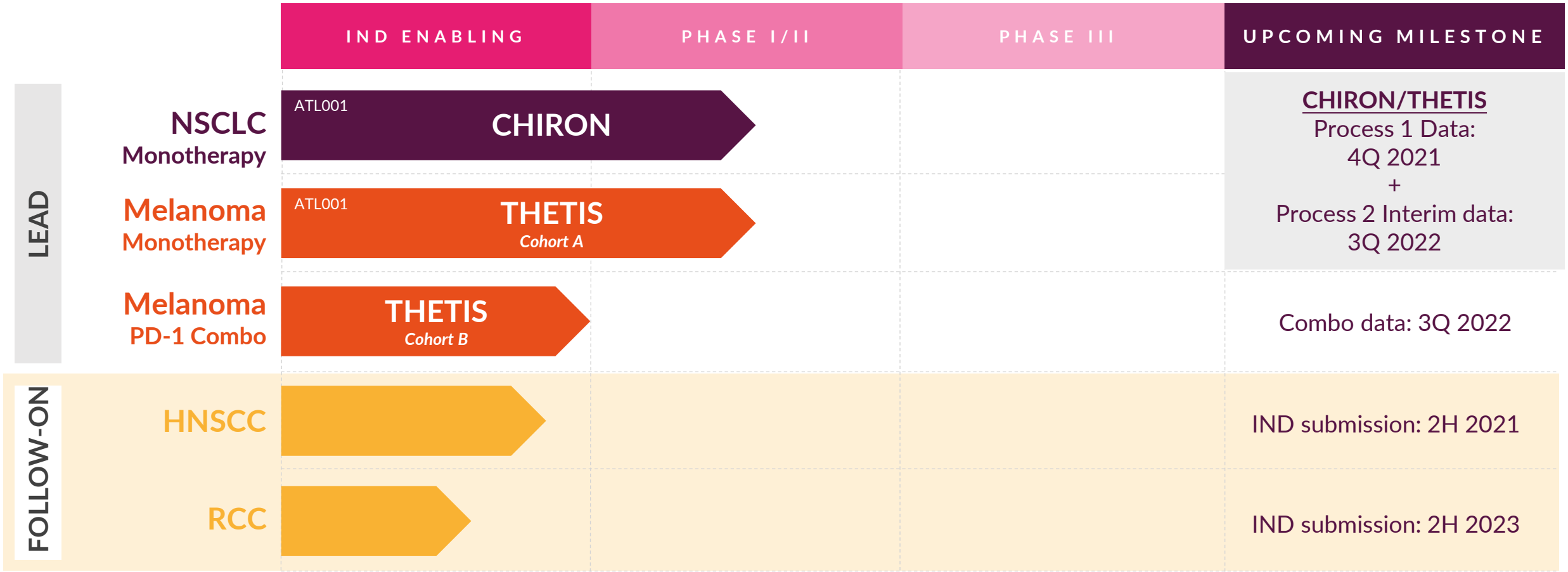
Present on all tumor cells, absent from healthy tissue

ACHILLES THERAPEUTICS
transformative T cell therapy

Achilles has a unique capability to target clonal neoantigens

Our process can deliver tumor specificity and potency improvements over standard TIL

Our current pipeline



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

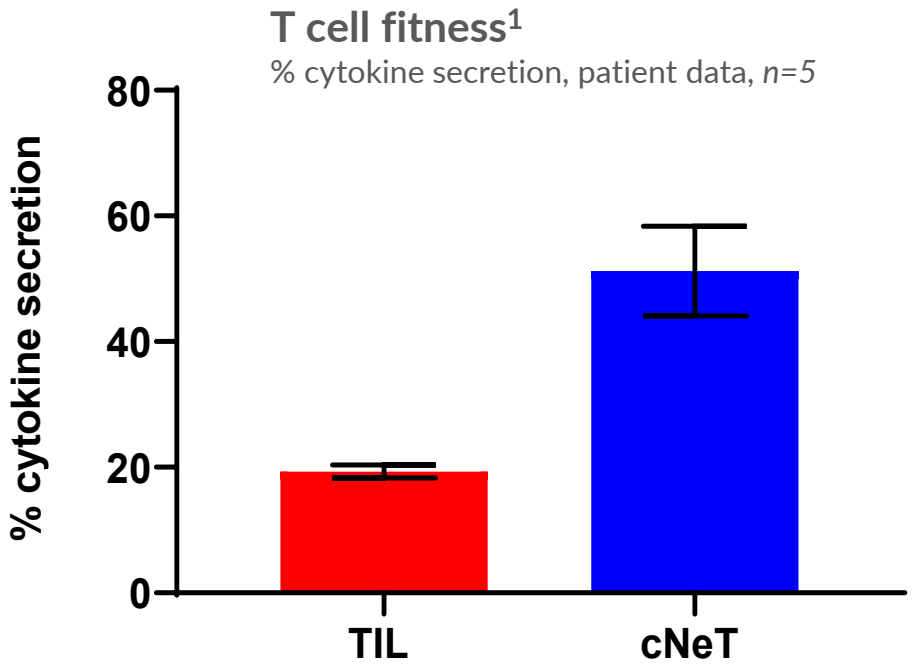
Potent polyclonal product

- 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*

cNeT have demonstrated improved T cell fitness compared to standard TIL

- Natural dendritic cell-driven expansion delivers **significant improvement in T cell fitness** for cNeT compared to standard TIL
- The fitness of all T cells can be assessed through the non-specific activation of the CD3+ T cell co-receptor



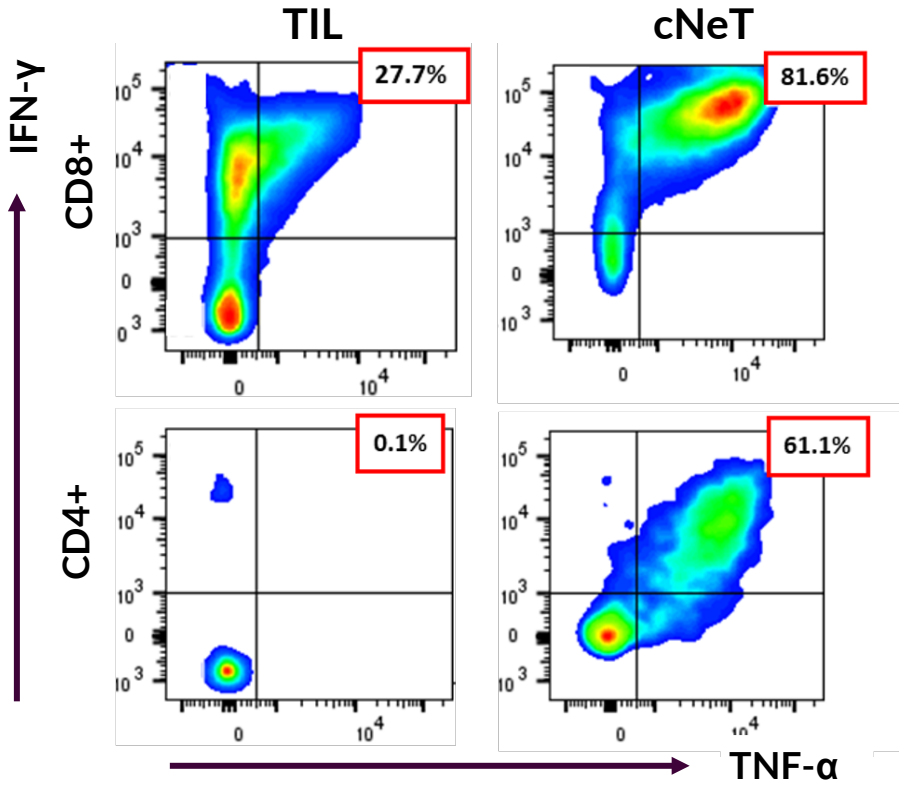
1. Achilles' data measuring the ability of T cells to produce inflammatory cytokines in response to the same polyclonal stimulation

cNeT have demonstrated improved specificity and potency compared to standard TIL

The cNeT process (VELOS™) selectively expands tumor reactive T cells that can deliver a product with improved **specificity and potency** as defined by their ability recognize tumor clonal neoantigens

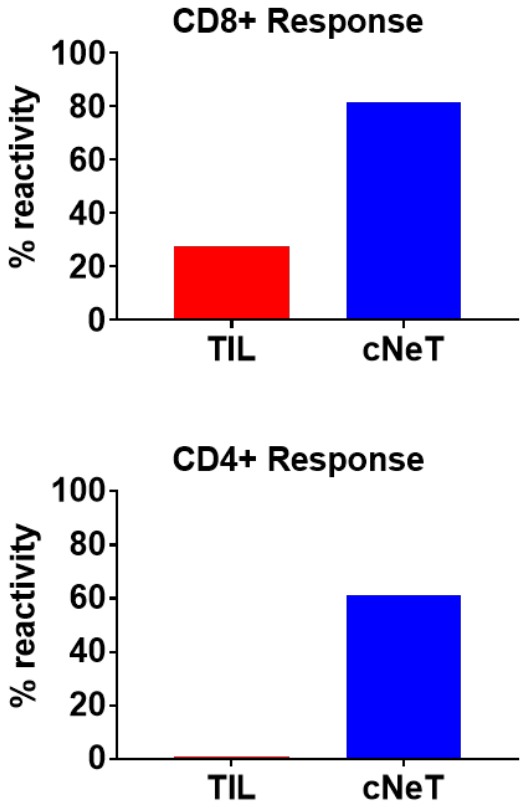
T cell specificity and potency[4]

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



T cell specificity and potency[4]

% reactivity, *n=1*



VELOS manufacturing process has been shown to produce both **CD4+ and CD8+ T cell** populations. 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]

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

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

Achilles has two ongoing Phase I/IIa clinical trials

CHIRON — Advanced non-small cell lung cancer (Stage III-Stage IV)
Open-label

- Up to 40 patients with advanced unresectable or metastatic NSCLC
- Never-smokers and EGFR/ALK/Ros-1 mutations excluded
- cNeT monotherapy with option for PD-1 inhibitor combination cohort
- Evaluating safety, tolerability and activity (RECIST), biomarkers of clinical activity and bespoke ctDNA assay
- Ongoing in UK, EU and US

THETIS Cohort A — Recurrent or metastatic malignant melanoma; monotherapy
Open-label

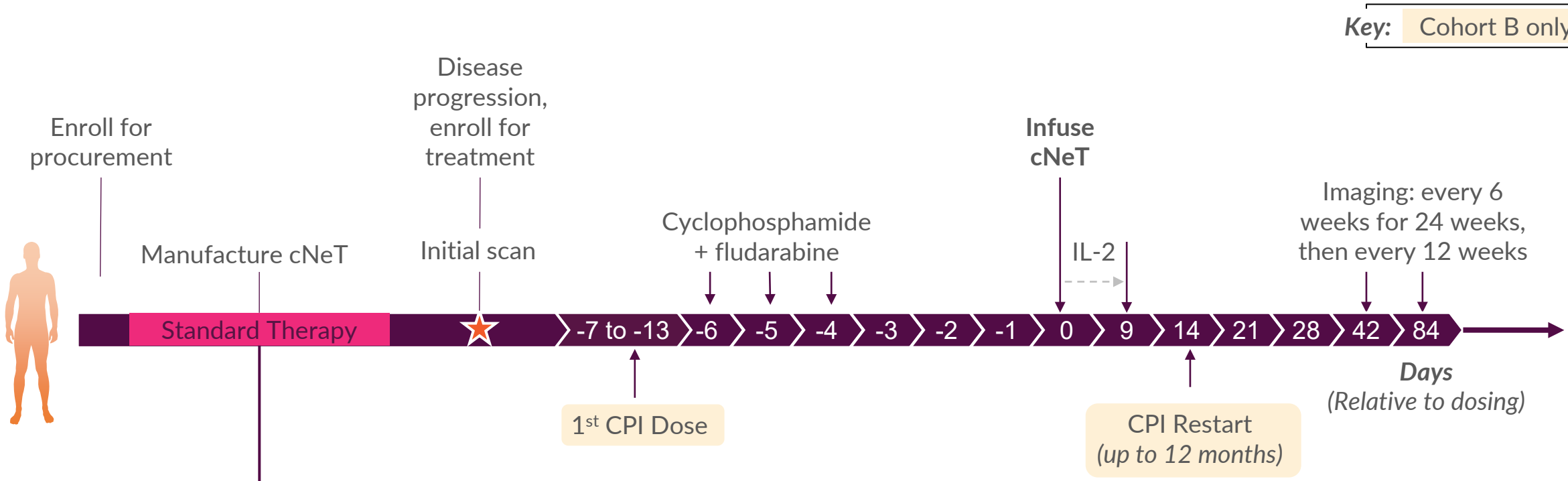
- Up to 40 patients with metastatic or recurrent melanoma (monotherapy)
- Acral, uveal and mucosal melanoma excluded
- Evaluating safety, tolerability and activity (RECIST)
- Ongoing in UK, EU and expanding to US

THETIS Cohort B — Combination with checkpoint inhibitor
Open-label

- Up to 20 checkpoint refractory patients in combination with PD-1 inhibitor (nivolumab)
- Checkpoint dosed prior to cNeT dosing (~7-13 days) and restarted at day 14 post-dosing

CHIRON and THETIS trial design

cNeT therapies can be readily delivered within standard treatment pathways



- **Option to procure tissue before, after and during systemic therapy**
- cNeT can be manufactured during checkpoint therapy

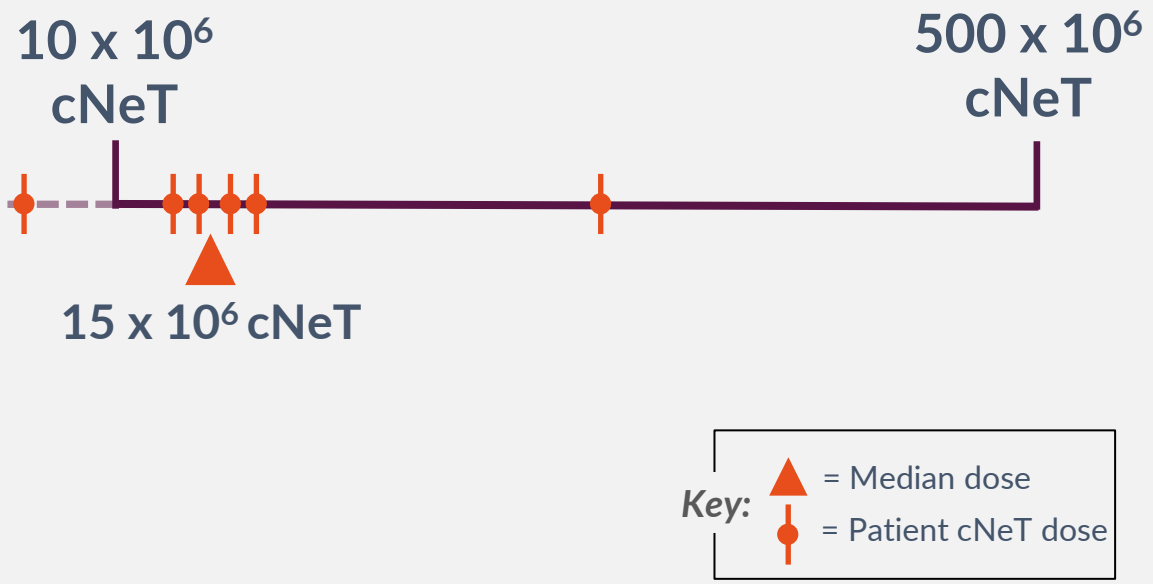
- **Well-tolerated pre-conditioning and IL-2 regimens** (vs. existing TIL therapy)
- Lower cyclophosphamide and IL-2 dose delivered over a longer period

Initial CHIRON & THETIS patient summary

Patient summary

- Data from first six dosed patients following scan 6 weeks post-cNeT infusion
  - 3 in CHIRON, 3 in THETIS
- Median 2.5 lines of prior therapy
- All had progressive disease at time of lymphodepletion
- Median dose at the low end of prospectively targeted therapeutic range
- cNeT doses manufactured using VELOS Process 1
  - Generated doses of 0.1M to 287M cNeT with high specificity and fitness

Prospectively Targeted Therapeutic cNeT range (VELOS Process 1)



cNeT tolerability and activity in the first six patients treated from CHIRON & THETIS

Tolerability

- **IDSMC** recommended that both clinical trials **continue as planned** with no modification
- **Tolerability similar to standard TIL** products not enriched for cNeT reactivities
  - Most higher-grade AEs from lymphodepletion regimen
- **No grade 3 or 4 IL-2 related toxicities**
- **Two SAEs observed**
  - One deemed unlikely related to cNeT
  - One deemed possibly related to cNeT

Activity

- **Stable disease** at 6 weeks post-dosing in 4 of 6 patients and progressive disease in 2 of 6[1]
- **Tumor reduction** in 2 of 4 lesions of approx. 55% and 90% in patient that received the highest cell dose
- **Evidence of engraftment** in 3 of 6 patients, with highest dose associated with highest engraftment
- **Ability to characterize** infused cells at level of individual cNeT reactivities, in contrast to standard TIL

Key Next Steps

Explore higher cNeT monotherapy doses and combination with PD-1 inhibitor

Incorporate additional cytokines to boost TILs extracted & cNeT generated (VELOS Process 2)

Data reported February 5, 2021
1. Investigator reported

Precision T cell therapy
We can define and track our product in each patient

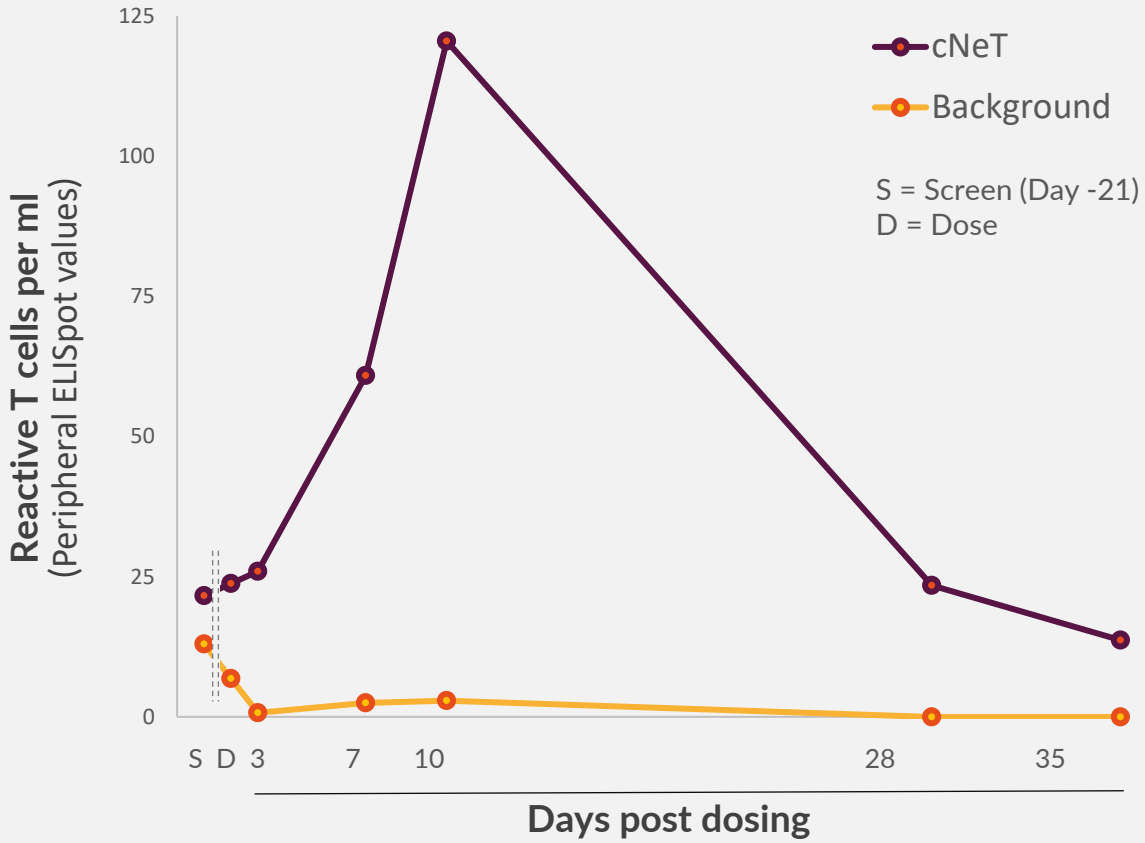
Detection of cNeT engraftment

- We specifically expand T cells (cNeT) that will **target patient specific clonal neoantigens**
- cNeT can be detected in the patient's blood post-dosing revealing **cNeT expansion kinetics**
- In contrast, it is not possible in **standard TIL** to readily characterize the tumor-reactive component, nor track engraftment and persistence post-infusion - there is **no demonstrated correlation** between T cell dose and response[1]
- We believe that **increasing dose will lead to improved T cell persistence and efficacy**, as seen in other T cell modalities e.g., CAR-T[2,3]

Patient Case Study[4]

Expansion and detection of cNeT post-dosing THETIS patient

16M cNeT dosed (65% reactivity)



1. Larkin et al, ASCO Presentation, 2021
2. Porter et al, Sci Transl Med, 2015
3. Stefanksi et al, Transplantion & Cellular Therapy Meeting, 2021
4. AACR 2021

VELOS Process 2 is expected to yield higher cNeT doses

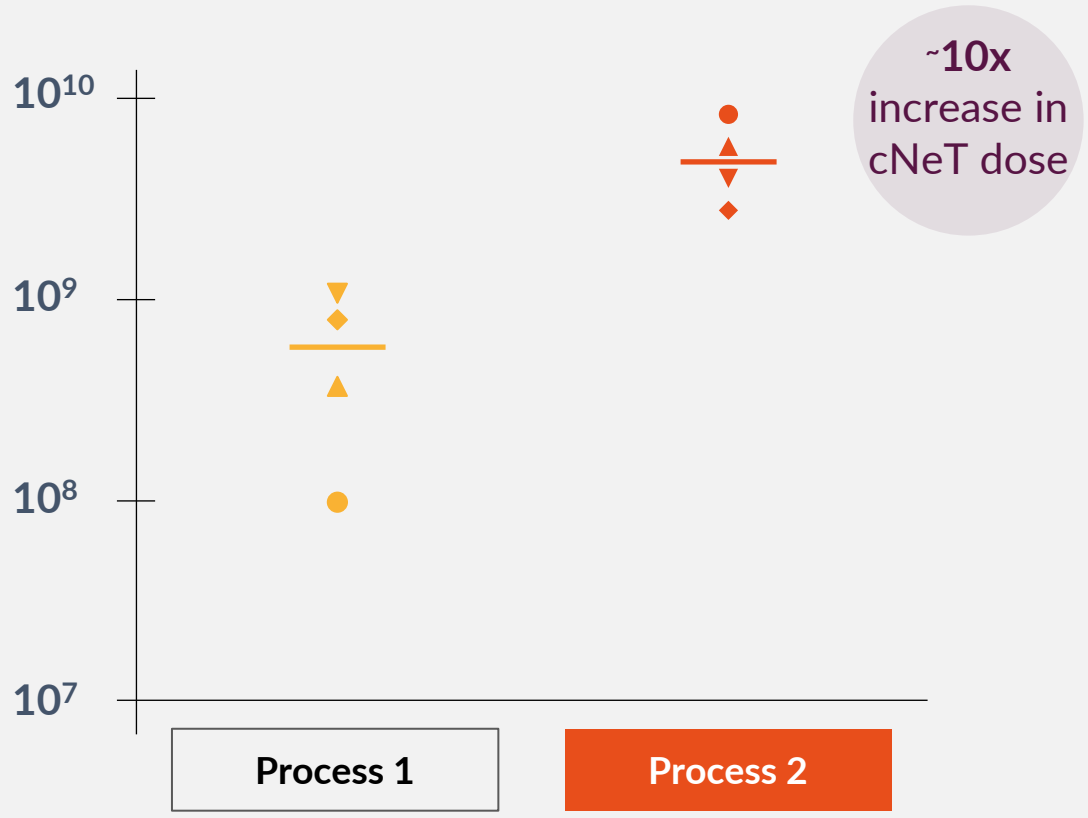
Targeting pre-expansion and expansion steps provides a consistent boost in TIL and cNeT

	Pre-Expansion	Expansion
Process 1	T cells are harvested from the tumor	Dendritic cells loaded with clonal peptides activate and drive cNeT expansion
Process 2	Additional cytokines boost the harvest of tumor reactive cells	Optimized DC-driven co-culture followed by short T cell boost increases final cNeT dose

Timelines for both processes are identical

cNeT dose by process*

cNeT reactivity as measured by our potency assay (IFNγ/TNFα positive cells)



*Data reported are in process development experiments which are indicative but not identical to full scale clinical GMP production

Scale-up of GMP manufacturing for late stage clinical trials and commercial launch

Royal Free Hospital

GMP facility operated by Achilles staff to support FiH studies

Cell & Gene Therapy Catapult

Supports both open and fully closed manufacturing process

Hayes

- GMP modular facility utilizing PODs
- Support multiple indications for late stage clinical studies and commercial supply
- Includes in-house peptide manufacturing

Online	2019	2021	2023
Peak Dose Capacity	50	200	1,000

Our process is designed from the ground up for commercial scale

Plan to incorporate closed processing into clinical supply in 2022

End-to-end closed process enables operation in simplified (lower cost) GMP facility

Tumor collection device

Tumor is collected in our bespoke device to **close the process from procurement**

Closed tumor processing

Closed processing at our GMP facilities reduces COGs, **eliminates human operator steps and drives scale-up**

Targeting a 6 - 8 week process at commercial stage (collection to dosing)

We continue to advance product and competitive improvements

Alternative starting materials (e.g. blood)

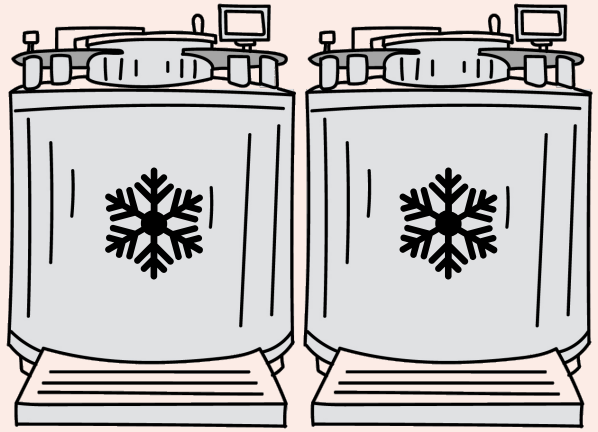
Manufacture of cNeT from blood and other sources

Gene-edited products

Targeted gene knock-down in cNeT

Early tumor sample archiving

Banking of tumor from earlier stage patients



Key anticipated 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
- [ ] Process 2 GMP data update
- [ ] Cell Therapy Catapult manufacturing online
- [ ] File IND in HNSCC
- [ ] Monotherapy data with Process 1 cNeT

2022

1 H

- [ ] 1st patient dosed with Process 2 cNeT
- [ ] Initiate tumor archiving program
- [ ] Establish US R&D facility
- [ ] Additional Process 1 monotherapy data

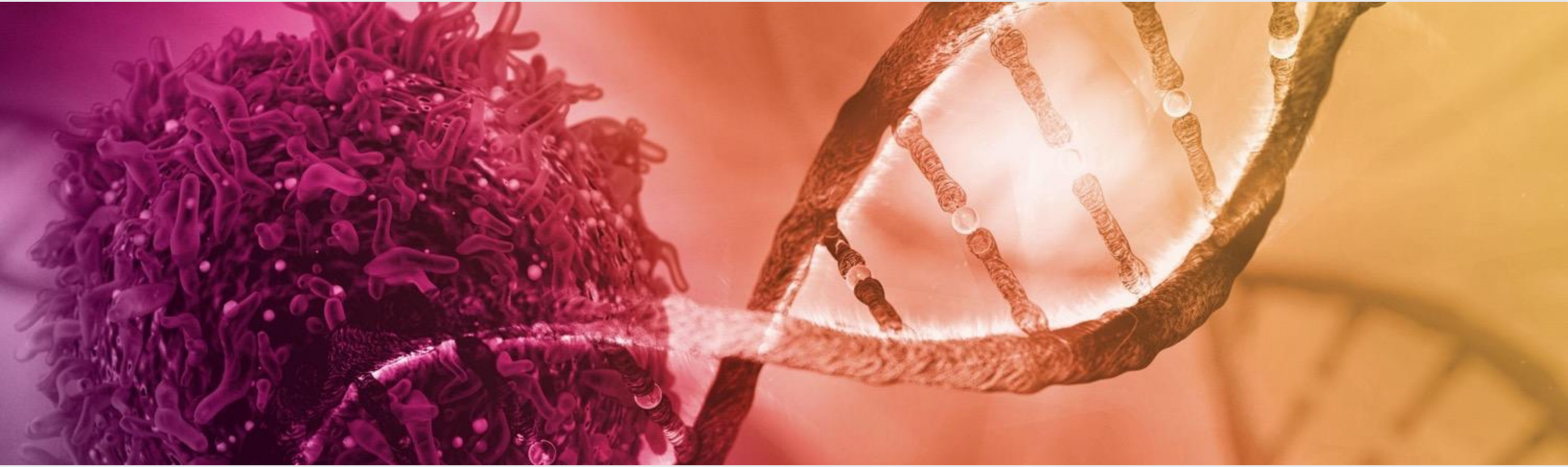
2 H

- [ ] Interim data from PD-1 / cNeT combo
- [ ] Interim data from Process 2 cNeT monotherapy
- [ ] Incorporate closed automation technology
- [ ] Open clinical study in follow-on indication
- [ ] Monotherapy data with Process 2 cNeT

Business is financed to complete phase I/IIa CHIRON and THETIS studies (2H 2023)

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



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