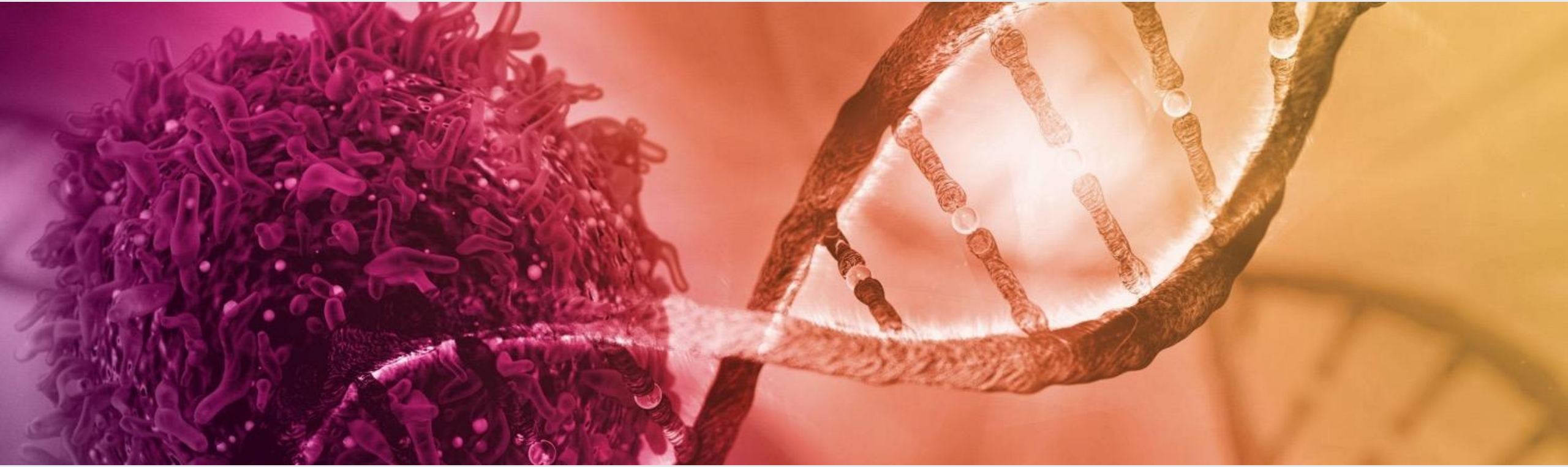


Achilles Therapeutics

Precision T cell therapies to treat solid tumors

May 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

A clinical stage immuno-oncology company developing precision T cell therapies to treat multiple types of solid tumors

NASDAQ: **ACHL**
Precision TIL therapy

- Two open-label Phase I/IIa clinical trials ongoing for NSCLC and melanoma; initial data warrant moving to higher clonal neoantigen T cell (cNeT) doses and opening PD-1 combination cohort in melanoma
- Evaluating a pipeline of pre-clinical targets, anticipating additional programs to enter the clinic by 2022 with at least one IND this year
- 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
- ~180 employees with headquarters in London
- Nasdaq IPO (March 31, 2021) raised ~$175 million; Company fully financed to complete ongoing P I/IIa clinical trials, expand manufacturing and expand clinical pipeline

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

Board of Directors

Edwin Moses
Chairman

Ablynx, A Sanofi Company

Carsten Boess
Non-Executive Director

Synageva BioPharma · Alexion

Derek DiRocco
Non-Executive Director

RA Capital

Michael Giordano
Non-Executive Director

Bristol Myers Squibb

Julie O'Neill
Independent NED

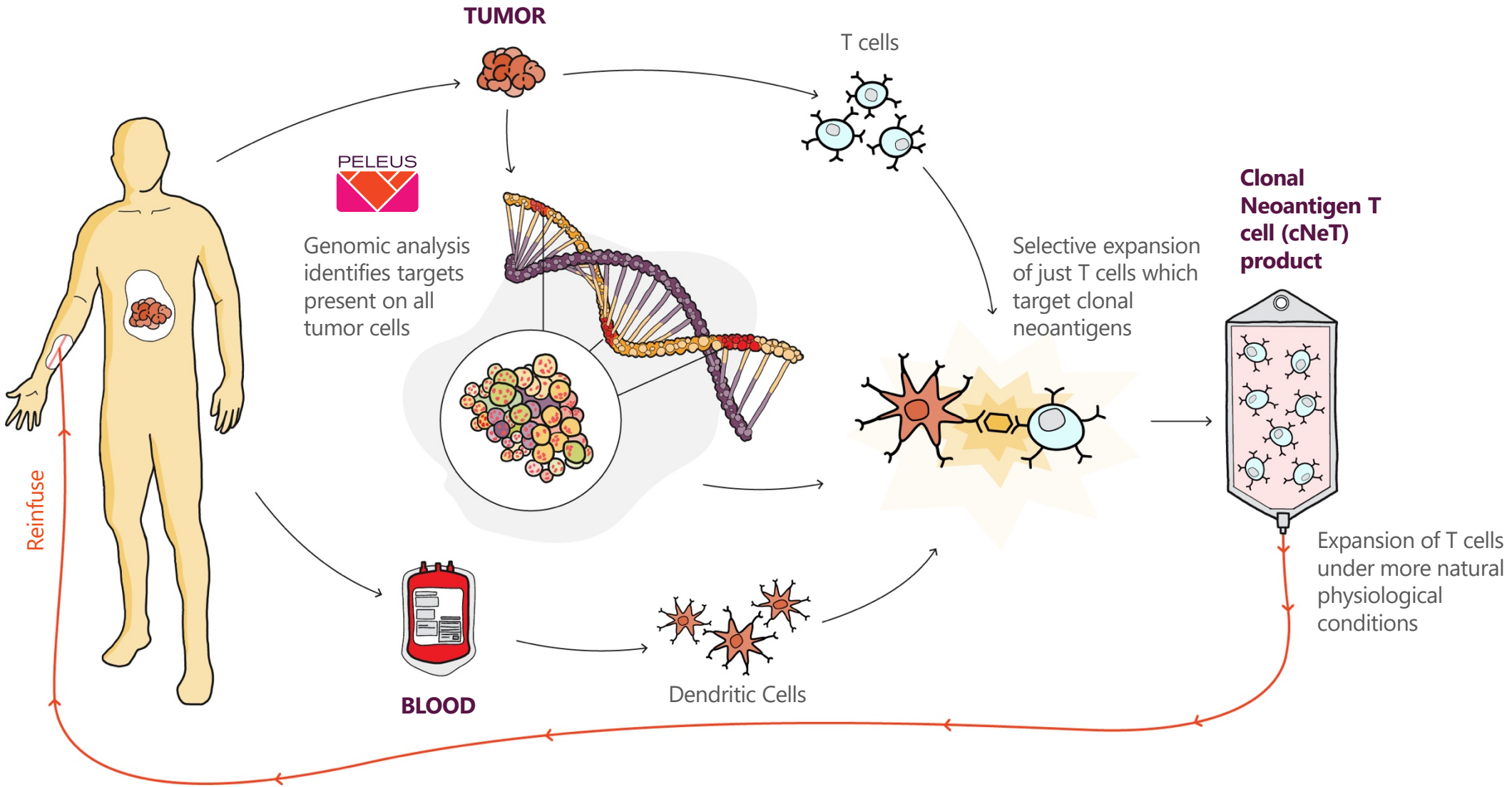
Alexion · Gilead

Rogier Rooswinkel
Non-Executive Director

Forbion

Precision TIL therapy targeting clonal neoantigens

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



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

We believe 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 **continuously trained and improved** with the 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 leads the next wave of immuno-oncology approaches

Uniquely positioned to target clonal neoantigens

Tumor associated antigens

TMUNITY

TCR² THERAPEUTICS

MARKER THERAPEUTICS

Fate THERAPEUTICS

Adaptimmune TRANSFORMING T CELL THERAPY

Neoantigens

IOVANCE BIOTHERAPEUTICS

InstilBio

BIONTECH

neogene THERAPEUTICS

PACT pharma

genocea

TAILORED THERAPEUTICS

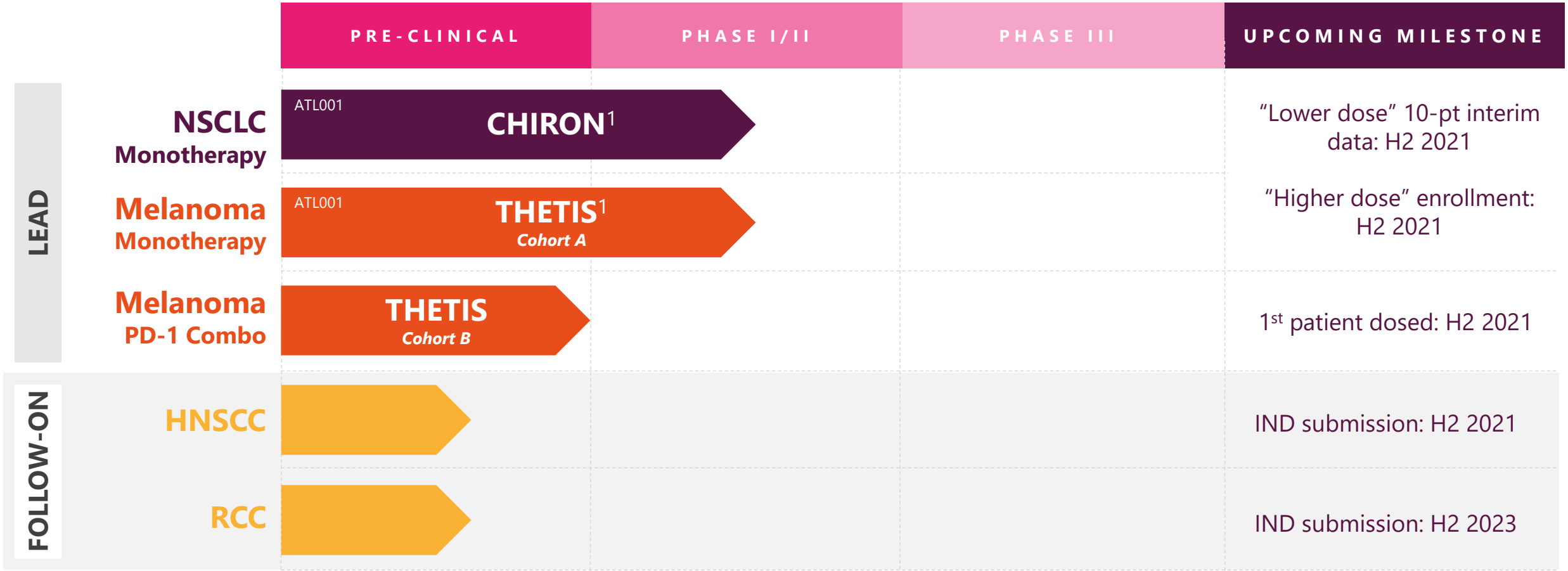
Clonal neoantigens

ACHILLES THERAPEUTICS
transformative T cell therapy

Achilles has a unique capability to target clonal neoantigens

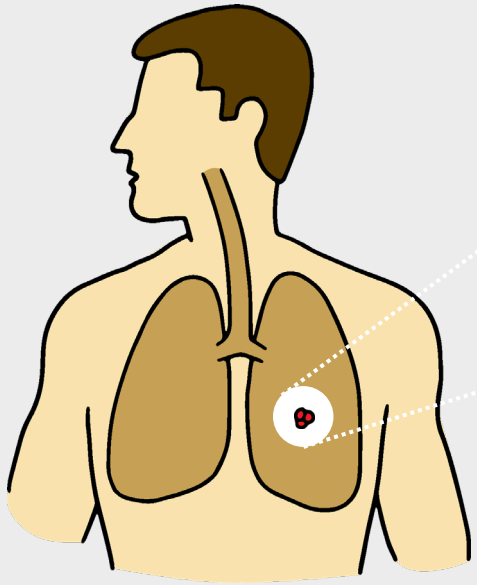
- Precision TIL-based approach
- Designed to target multiple clonal neoantigens
- Specific and functionally-fit CD4+ and CD8+ T cells

Our current pipeline



1. *Depending on the results of our Phase I/II monotherapy trials, we plan to engage with the FDA and EMA to discuss the addition of a Phase III registrational trail cohort in each study*

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



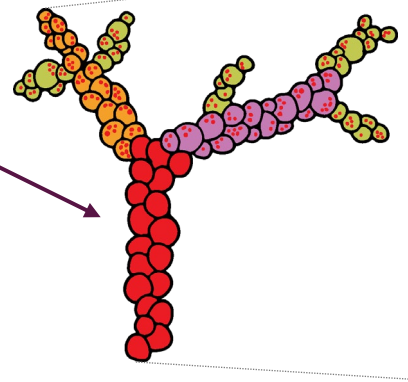
Tumors are **clonal in origin** and originate from a group of cells that are exactly the same

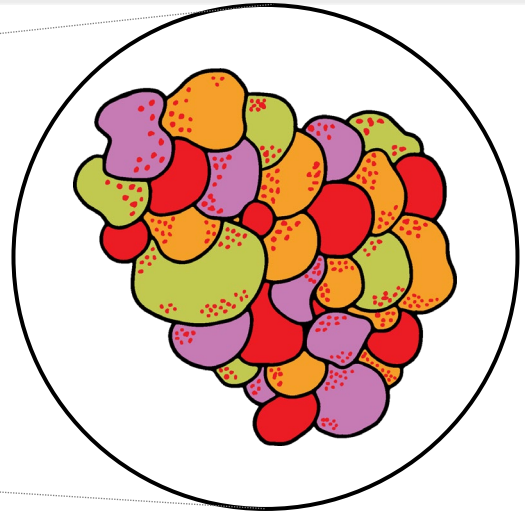
Tumors evolve, developing many new mutations resulting in **heterogeneity** that enables them to evade targeting[1]

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 (using TRACERx) to identity 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 Targeting T cell therapy, or cNeT





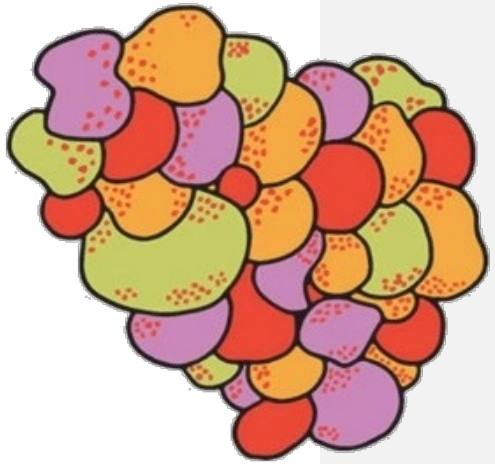
Clonal neoantigens are present on **primary tumors and all metastases**

1. Gerlinger et al., NEJM, 2012

Clonal neoantigens have the potential to unlock consistently effective, precision TIL therapy

TIL

- TIL has delivered **long-term durable disease control** in multiple solid tumor settings[1-4]
- T cell expansion is **non-specific** with no control over which antigens are targeted and the approach results in subclonal targeting, reducing chances of complete disease control
- Requires **very high (non-physiological) levels of IL-2** that result in T cell exhaustion and reduced anti-tumor activity[5]



Red: clonal neoantigens

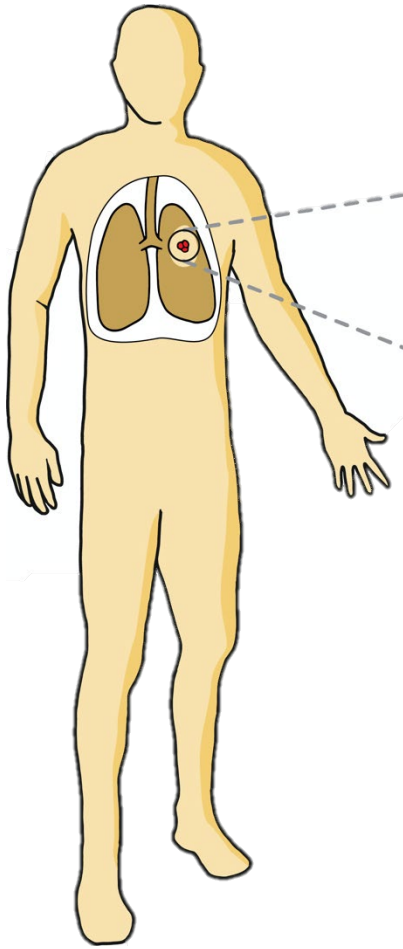
Purple, green and orange: subclonal neoantigens

cNeT

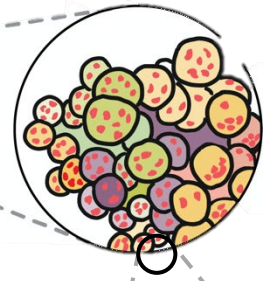
- Ability to **measure** antigen-specific potency and **monitor** antigen-specific T cell engraftment and expansion
- Provides **precision targeting of clonal neoantigens** shown to correlate with the anti-tumor activity of TIL[6] and checkpoint inhibitors[7]
- Clonal neoantigen targeting provides a means to target **all the tumor cells**
- **Using dendritic cells** to drive T cell expansion reduces the need for IL-2 expansion, **producing a fitter T cell**

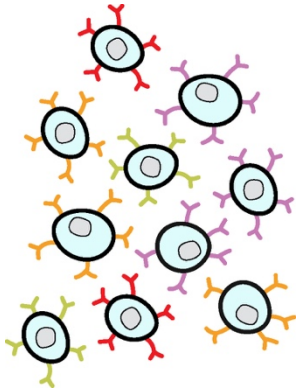
1. Besser et al., Clin. Can. Res., 2010
2. Forget et al., Clin. Can. Res. 2018
3. Rosenberg et al., Clin. Can. Res. 2015
4. Moffitt Investigator Sponsored Study update at AACR April 2020
5. Gattinoni et al. J Clin Invest, 2005
6. Lauss et al., Nature Comm, 2017
7. Snyder et al., NEJM, 2014

cNeT therapy is mechanistically differentiated from standard TIL through dendritic cell selection of clonal reactive T cells



T cells harvested from tumor are a mix of bystander, sub-clonal and clonal targeting T cells

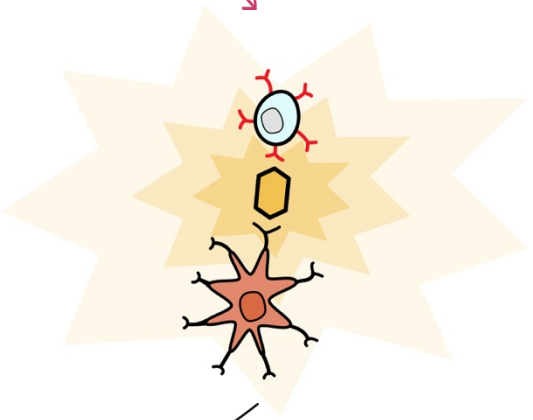




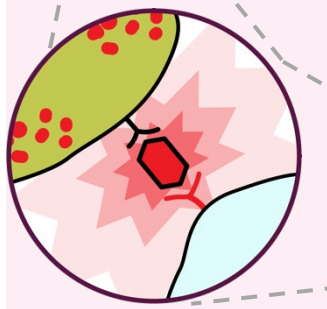
Tumor derived T cells have been imprinted to traffic to tumor

TIL manufacture

Achilles cNeT manufacture

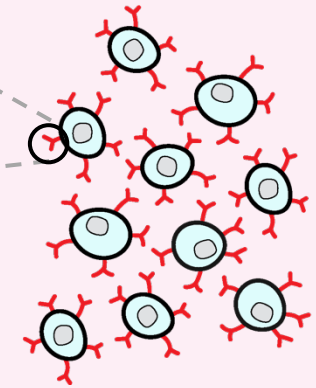


Dendritic cells (with clonal peptides) are able to select and activate a sub-set of the T cells from the tumor

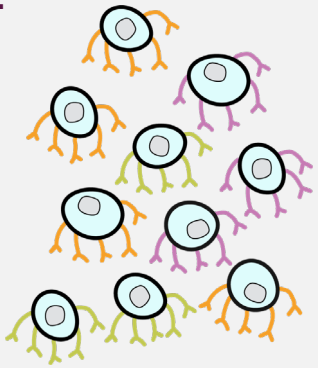


cNeT is able to target the clonal neoantigens (red) present on all tumor cells

cNeT



TIL



Standard TIL manufacture using very high (non-physiological) IL-2 results in T cell exhaustion and risk of sub-clonal or bystander cells dominating the product reducing the chance of seeing a complete response

Key

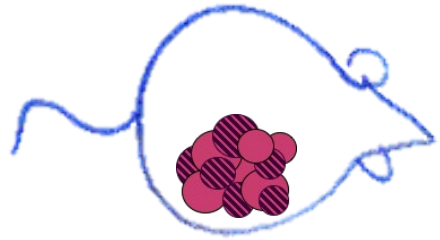
Clonal T cell

Sub-clonal T cell (green, purple, orange)

Clonality is key to the eradication of tumors

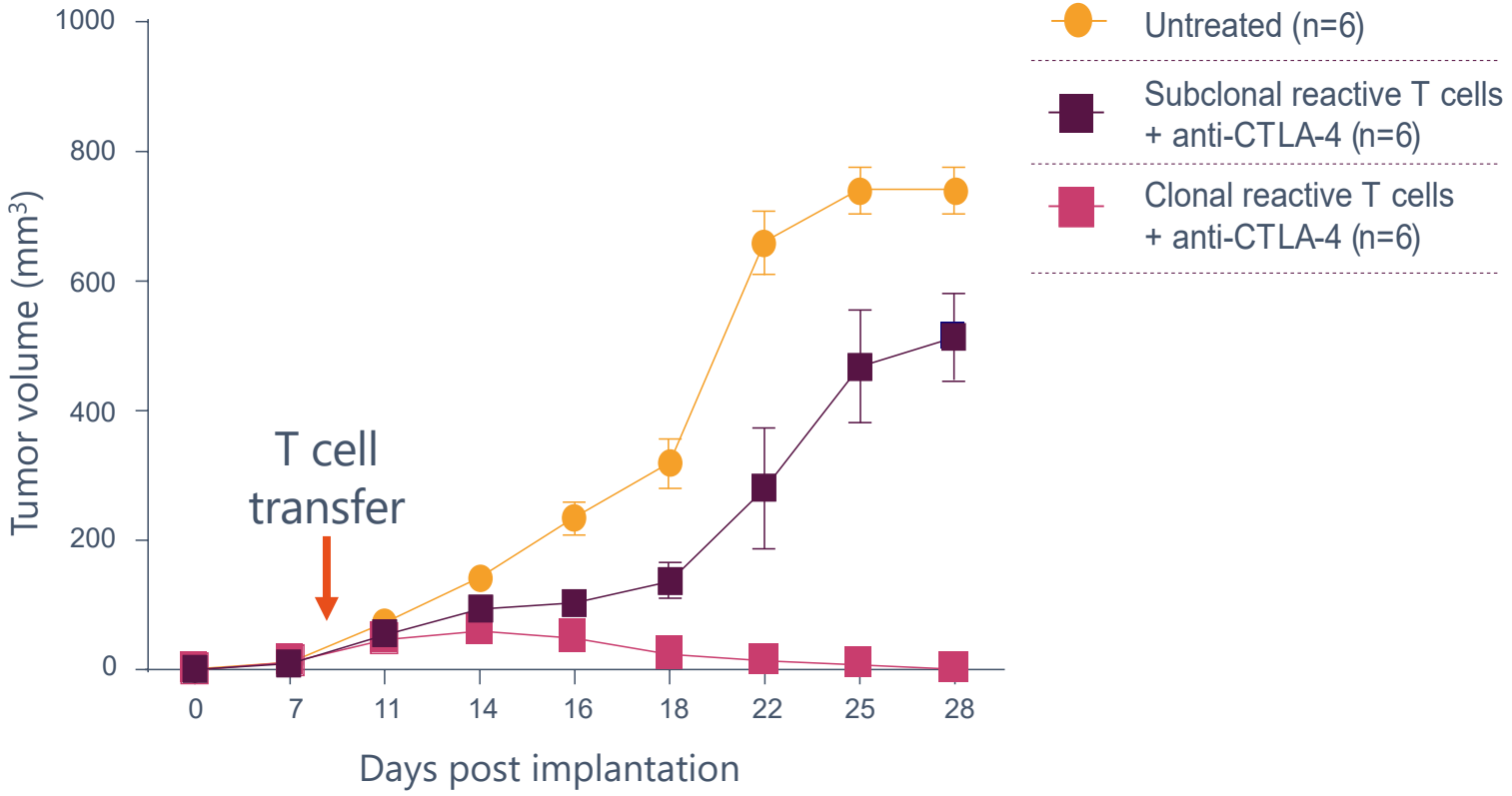
- Immune-competent mice were implanted with murine tumor cells expressing sub-clonal (on a sub-set of cells) and clonal (on all cells) antigens
- Mice were lymphodepleted and treated with murine T cells reactive to sub-clonal (■) and clonal antigens (■)

Targeting clonal antigens expressed in every tumor cell leads to complete tumor regression in an animal model



Change in tumor size in a mouse model of cancer

Tumor volume, mm^3



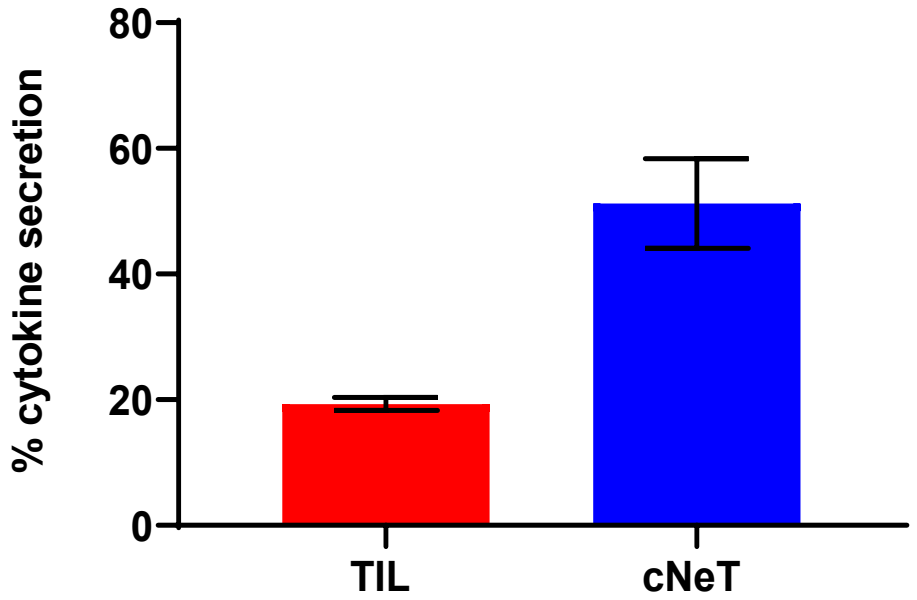
Quezada Lab, 2016 (Data published in patent application no. WO 2016/174085)

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
- Comparison of matched patient samples reveals a **significant improvement in T cell function** for cNeT compared to standard TIL

T cell fitness[1]

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



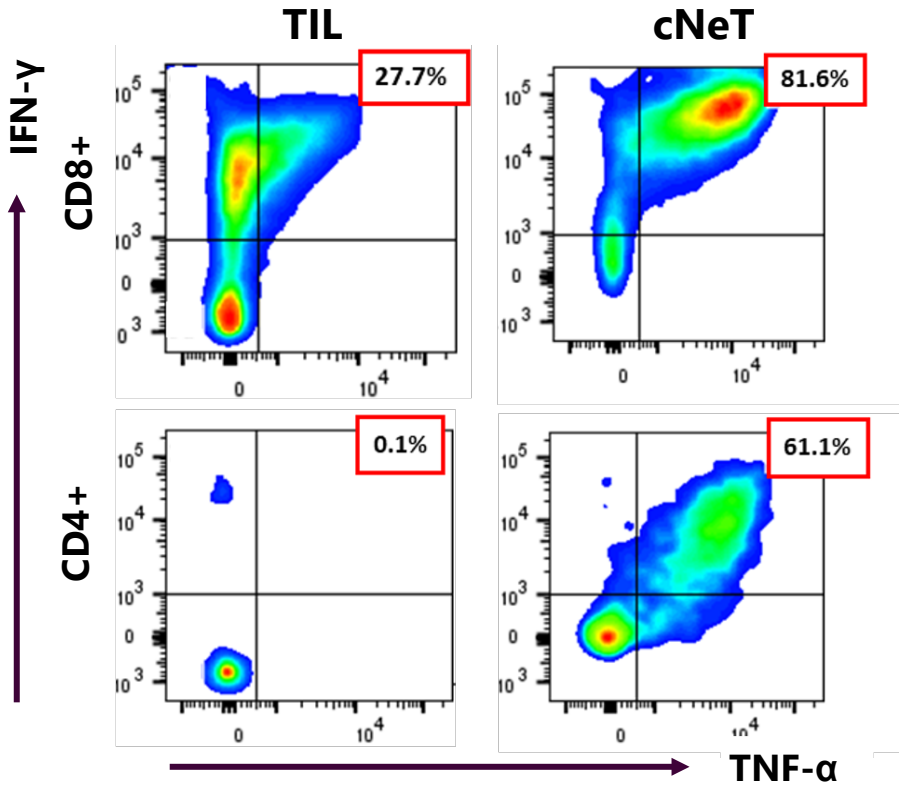
1. Achilles' data measuring the ability of T cells to produce inflammatory cytokines in response to the same polyclonal stimulation

cNeT have demonstrated improved activity compared to standard TIL

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]

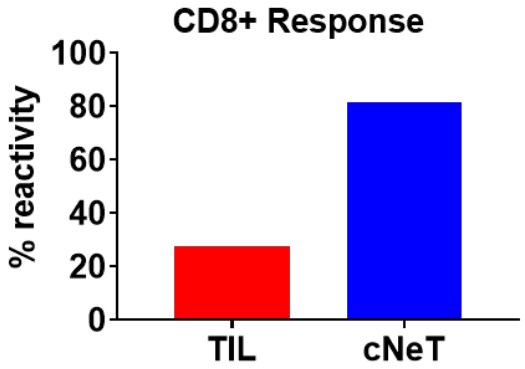
T cell specificity and potency[4]

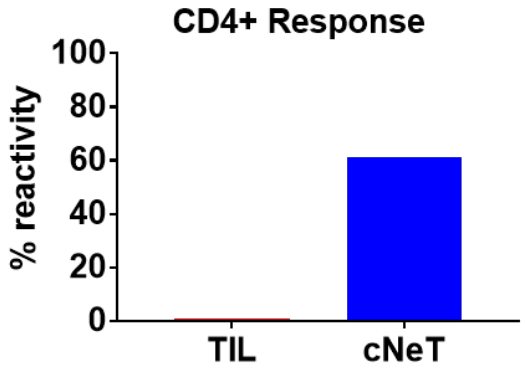
Cytokine secretion measured through flow cytometric analysis, *n=1*



T cell specificity and potency[4]

% reactivity, *n=1*

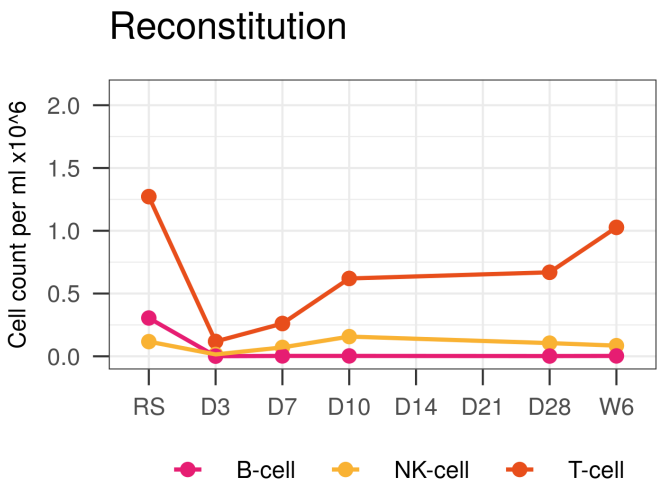


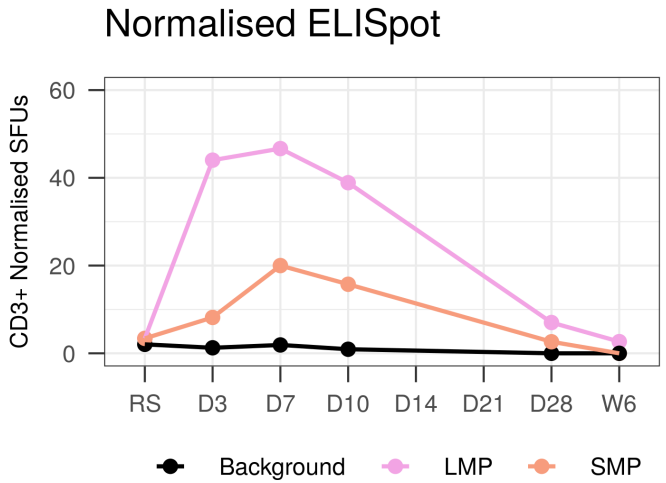


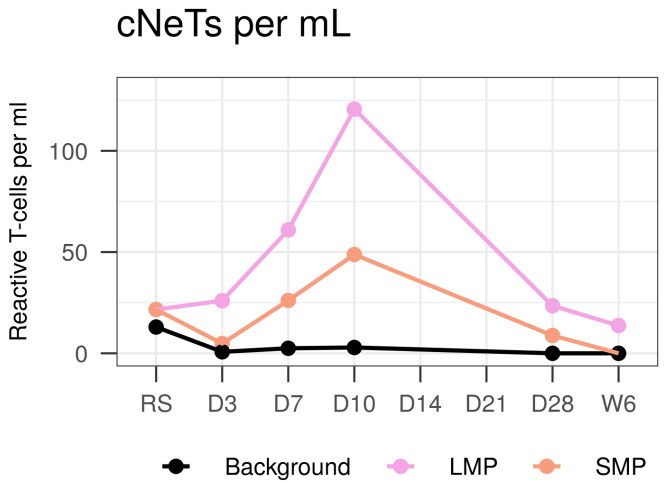
1. Hunder et al., NEJM, 2008;
2. Church et. al., Eur J Immunol, 2014;
3. Antony et al. J Immunol, 2005;
4. Achilles' data measuring the production of inflammatory cytokines in response to clonal neoantigens

AACR 2021 poster highlights strength of the Achilles translational research program

Patient T-05 case study illustrates the potential to develop a potency-based release assay (Poster 1508)





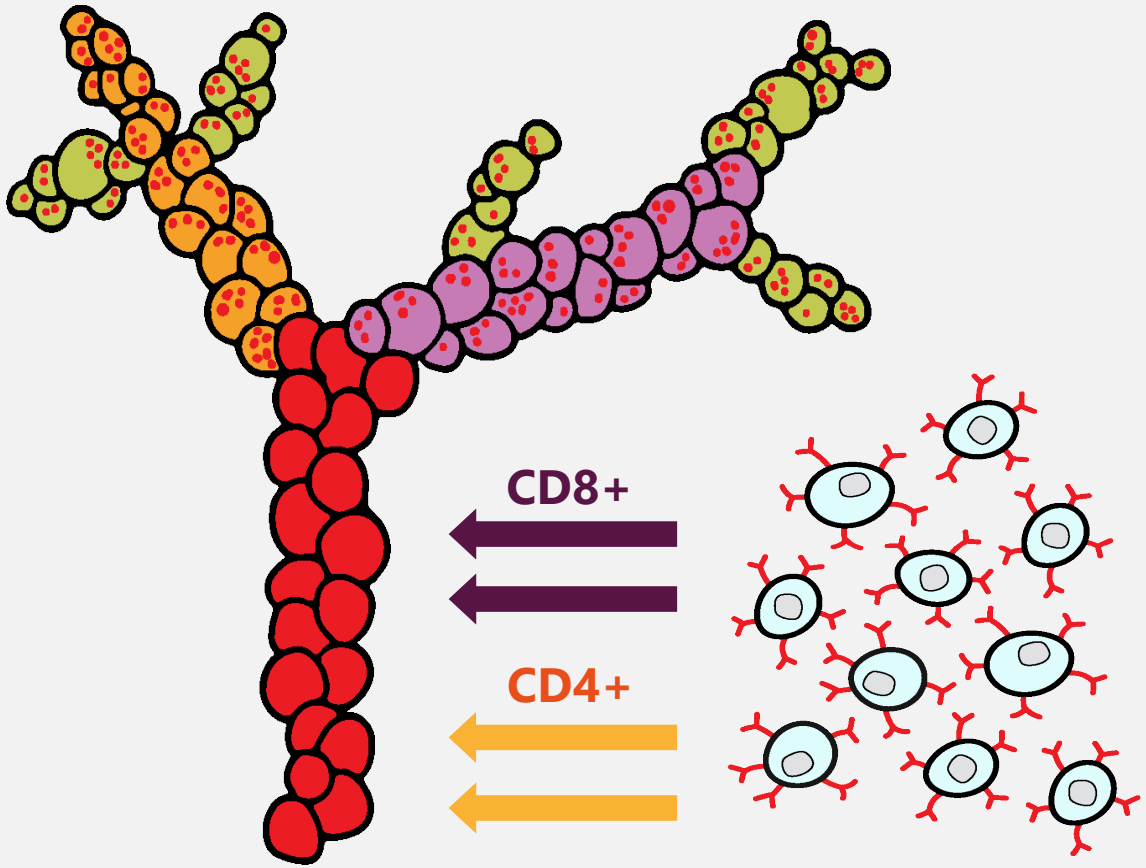


- cNeT were tracked pre- and post-dosing
- Shows expansion and detection of cNeT post dosing and an estimate of the quantity of reactive T cells in circulation
- Can generate equivalent data for each unique reactivity detected
- Data show increasing absolute levels of cNeT in the blood over first 10 days following infusion

- **Enables us to develop and potentially deliver a reliable manufacturing potency assay**
- **Offers insight into the *in-vivo* dynamics of cNeT and correlation with patient outcomes**

We are able to manufacture cNeT with a polyclonal CD4+ and CD8+ response

- Delivered **successful end-to-end manufacturing** in complex late-stage metastatic patients
- Demonstrated **CD4+ and CD8+ polyclonal product** targeting up to 28 clonal neoantigens
- Achieved **high T cell specificity and fitness**



Achilles has two ongoing Phase I/IIa clinical trials

CHIRON

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

- 40 patients with advanced unresectable or metastatic NSCLC
- Never-smokers and EGFR/ALK/Ros-1 mutations excluded
- cNeT monotherapy
- Evaluating safety, tolerability and activity (RECIST)
- Ongoing at 6 UK sites and recently expanded to first EU and US sites (up to an additional 4 US and 7 EU sites in 2021)

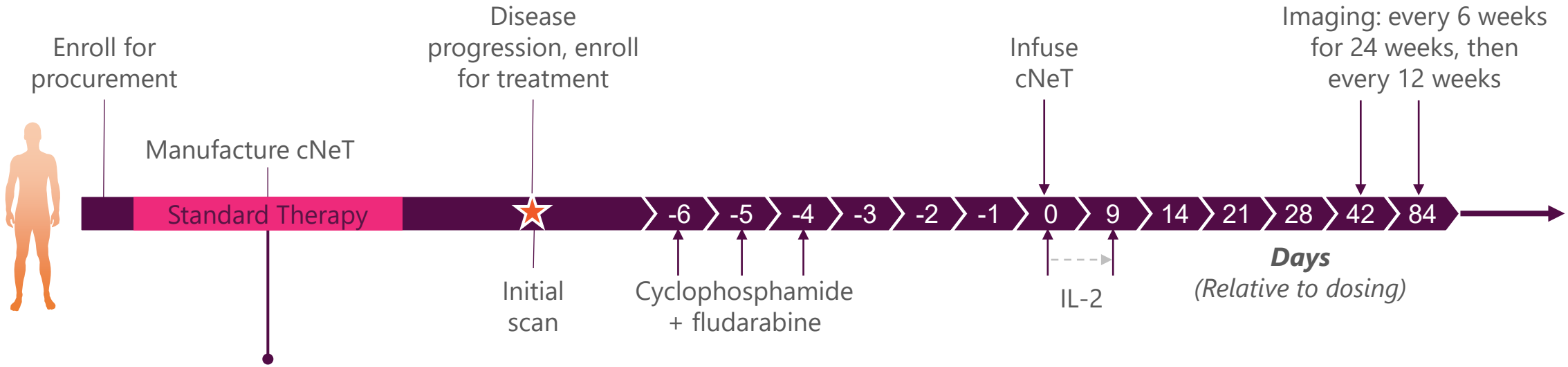
THETIS

Recurrent or metastatic malignant melanoma
Open-label

- 50 patients with metastatic or recurrent melanoma (including CPI combo cohort)
- Acral, uveal and mucosal melanoma excluded
- cNeT monotherapy and combination with PD-1
- Evaluating safety, tolerability and activity (RECIST)
- Ongoing at 3 UK sites, trial applications in the EU planned for 2021
- IND submitted in 2020 to enable expansion to US sites in 2022

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

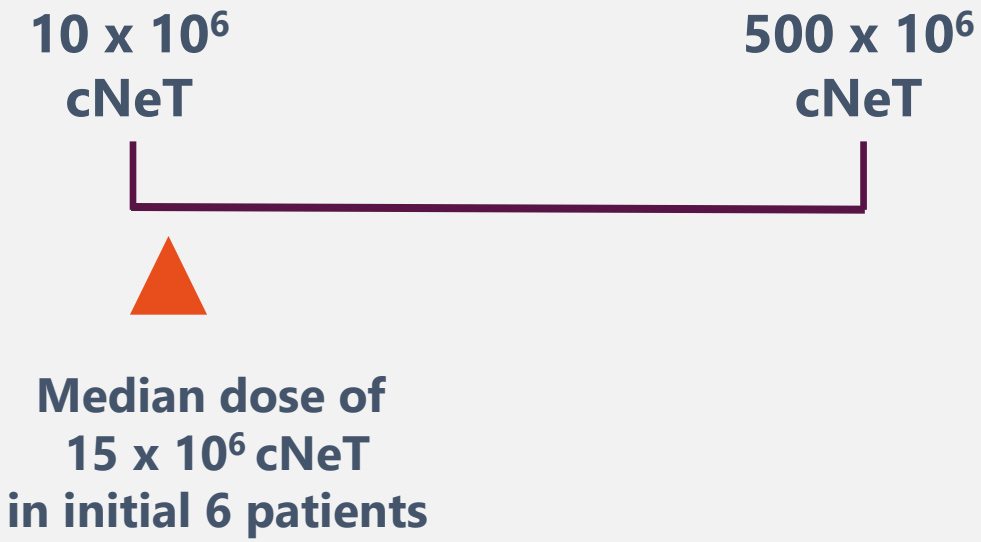
- **Well-tolerated pre-conditioning and IL-2 regimens** (vs. existing TIL therapy)
- Lower cyclophosphamide and IL-2 dose delivered over a longer period

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

Prospectively Targeted Therapeutic cNeT range



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
  - **Basis for potency assay**
  - **Documented polyclonality** of infused products and engrafted cells (up to 28 reactivities)

Key Next Steps

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

Incorporate additional cytokines to boosts TILs extracted & cNeT generated in DC expansion

Data reported February 5, 2021
1. Investigator reported

We believe a fully closed and automated end-to-end process will be critical to delivering personalized cell therapies at scale

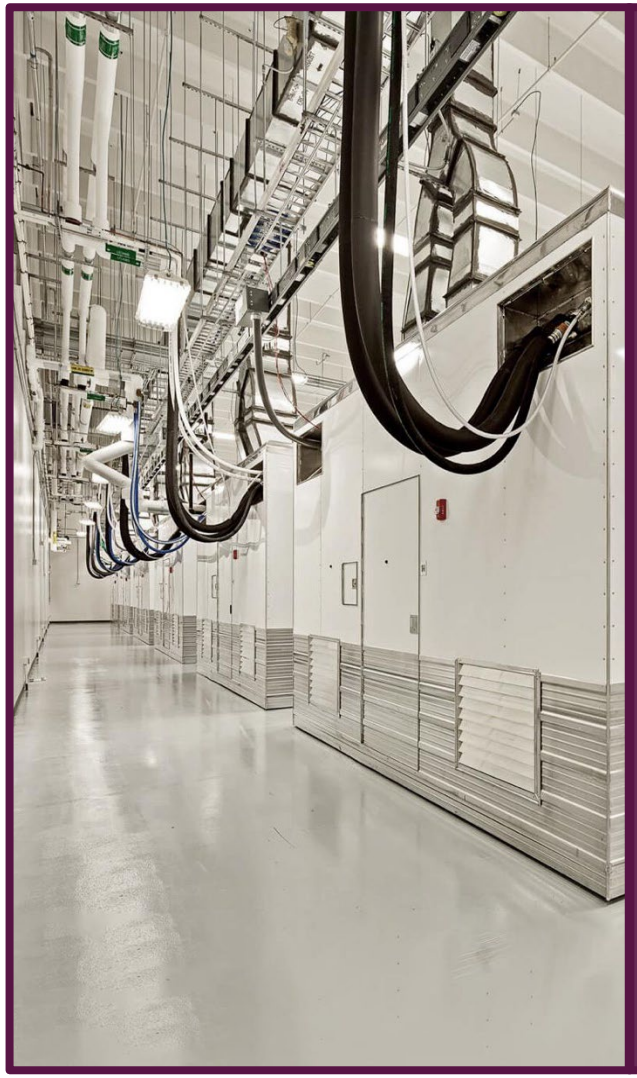
Collection Pot

Base station

Manufacturing process developed in the industrial setting targeting a **6-8 weeks process** at commercial stage

Developed technology in-house to support a fully **closed end-to-end process**

Closed setting facilitates **elimination of human operator steps**



GMP manufacturing capacity at Royal Free Hospital and Cell & Gene Therapy Catapult support our clinical trials

Plans to further expand manufacturing capacity in 2021 with Cell Therapy Catapult facility

Aim is to supply thousands of doses of commercial product annually

We continue to explore product and competitive improvements

Alternative starting materials (e.g. blood)

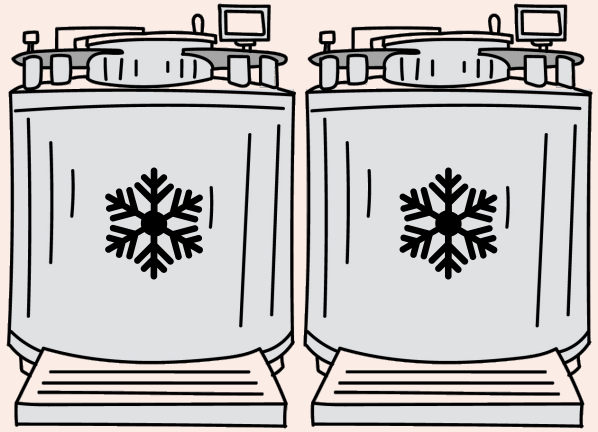
Manufacture of cNeT from blood and other sources

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
- [ ] 10-pt interim data in cNeT monotherapy
- [ ] 1st patient dosed in PD-1 / cNeT combo
- [x] Open clinical sites in US and EU
- [ ] Enroll first patient in the US
- [ ] File IND in HNSCC
- [ ] Cell Therapy Catapult manufacturing on-line

2022

1 H

- [ ] 1st patient dosed with higher dose cNeT
- [ ] 6-pt interim data from PD-1 / cNeT combo
- [ ] Initiate tumor archiving program
- [ ] Establish US R&D facility

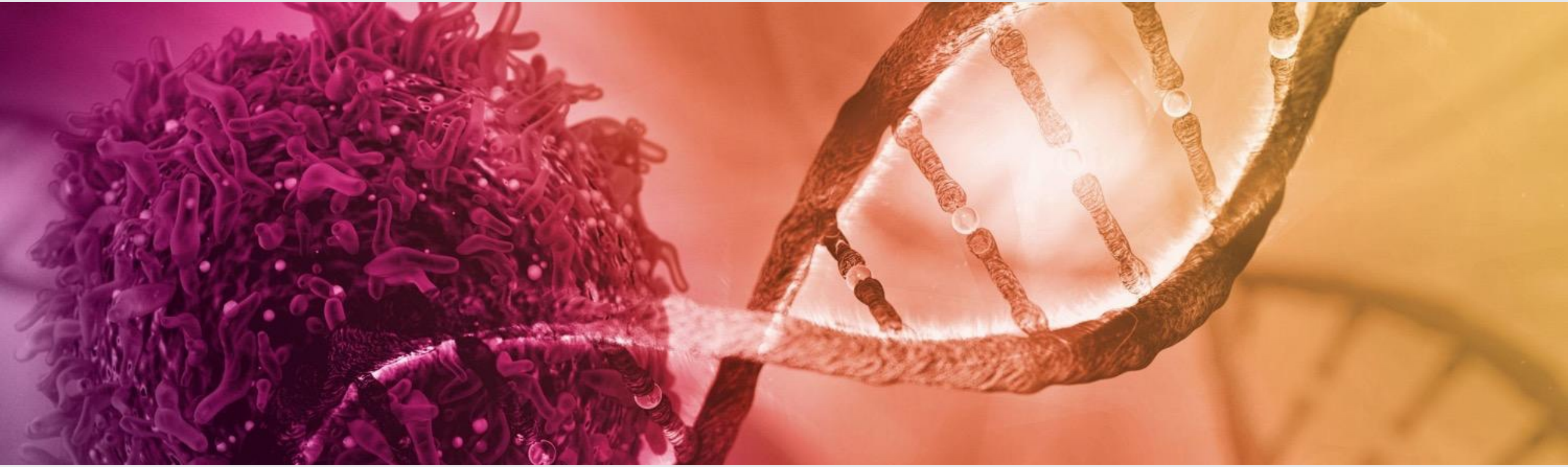
2 H

- [ ] 10-pt interim data with higher dose cNeT
- [ ] Incorporate closed automation technology
- [ ] Open clinical study in follow-on indication

YE 2020 cash of $178M + IPO proceeds of ~$175M fully finance P I/IIa CHIRON & THETIS and milestones

Achilles is building a transformative oncology business

- **Precision TIL therapy** using cutting edge neoantigen identification capability built from an extensive dataset **(780 patient TRACERx study)**
- cNeT approach enables targeting **multiple cancer antigens present in all tumor cells (clonal neoantigens)**
- Robust and **scalable manufacturing** process
- **Two ongoing clinical trials generating important data** with further near-term data readouts and plans to expand the platform into **new indications and alternative product formats**
- Nasdaq IPO (March 31, 2021); **Company fully financed** to complete ongoing P I/IIa clinical trials, expand manufacturing, expand clinical pipeline and **to deliver milestones**



Achilles Therapeutics

Precision T cell therapies to treat solid tumors

May 2021