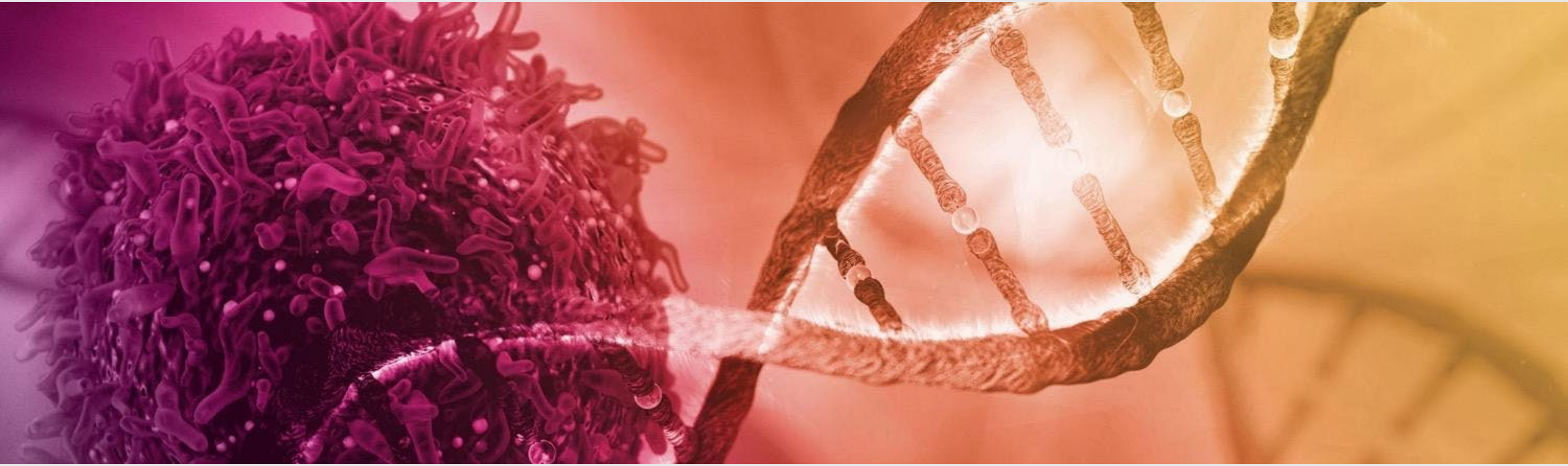

Achilles Therapeutics

AI-Powered Precision TIL Therapy

May 2022

Forward-Looking Statements

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

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

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

Precision targeting for solid tumors using clonal neoantigen-reactive T cells (cNeT)

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

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

Trackable precision T cell therapies

Able to target multiple tumor antigens with unprecedented precision and tracking in patients

Differentiated, scalable manufacturing

VELOS™ manufacturing process designed to be closed and automated for commercial scale

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Multiple near-term catalysts

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Our Management team

Iraj Ali
CEO

Syncona
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Karl Peggs
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Robert Coutts
CFO

KPMG
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Shree Patel
EVP Patient Supply Operations

Cell Medica

Ed Samuel
EVP Technical Operations

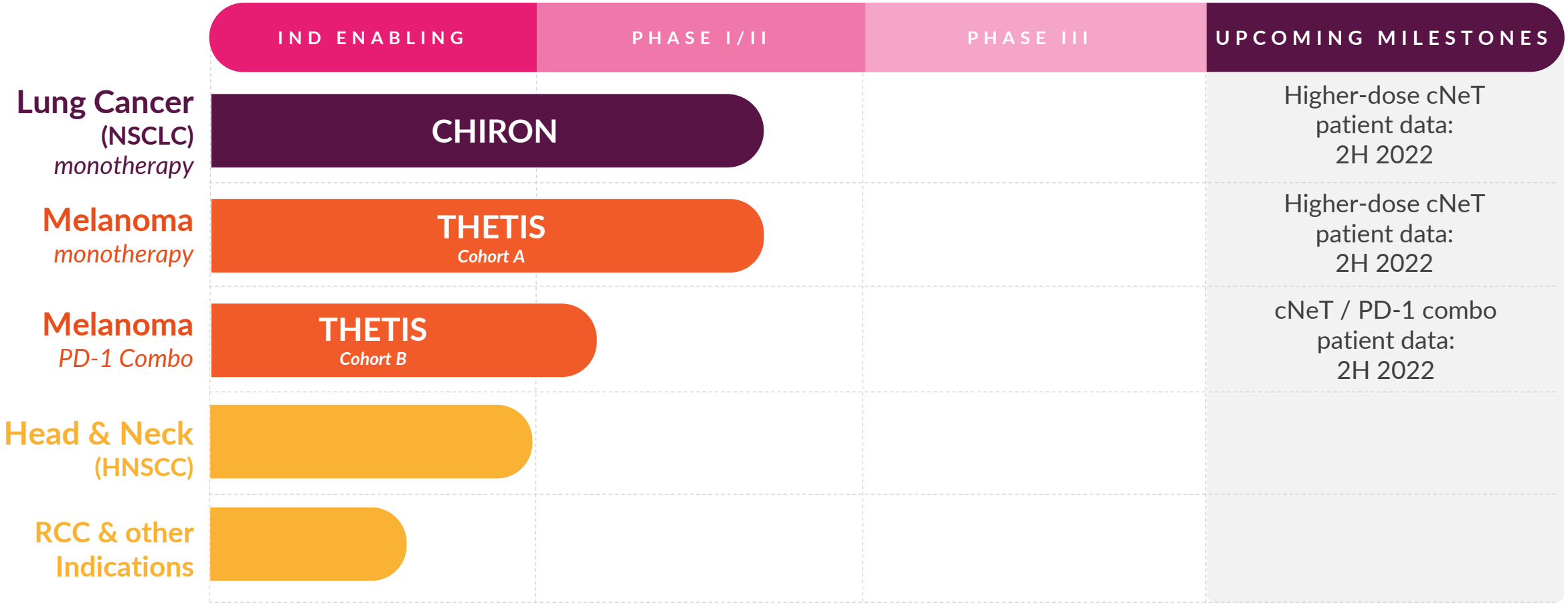
Orchard therapeutics
COGNATE BIOSERVICES

Daniel Hood
General Counsel

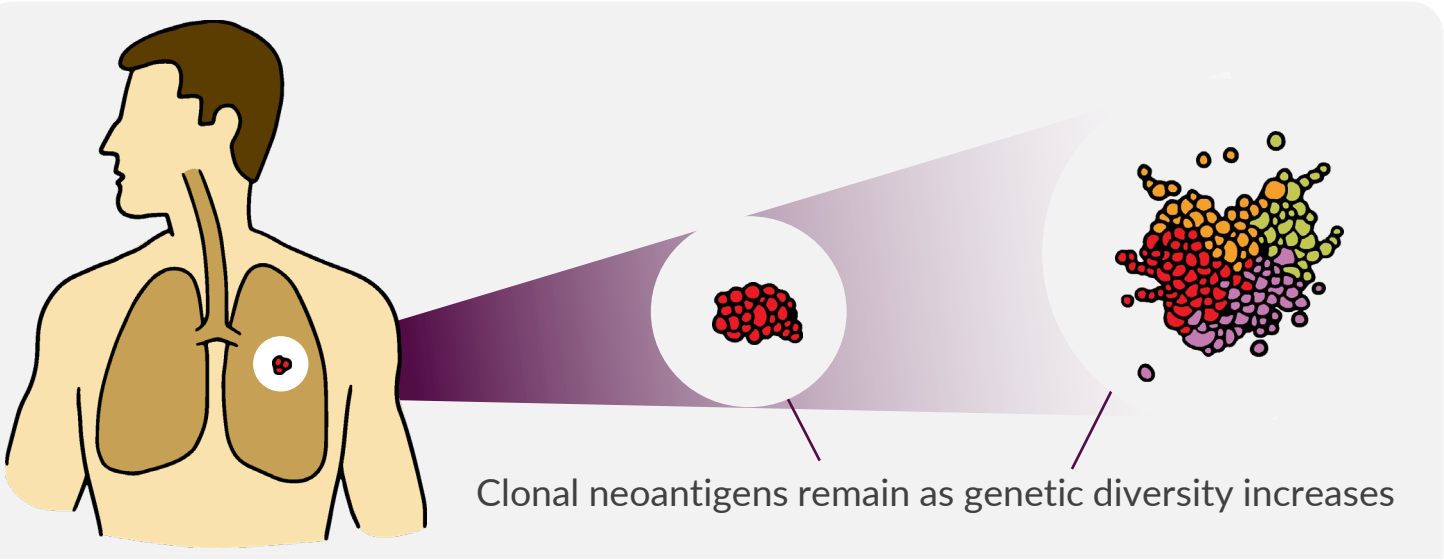
Intercept
GILEAD

Experienced leadership with decades in cell therapy drug development

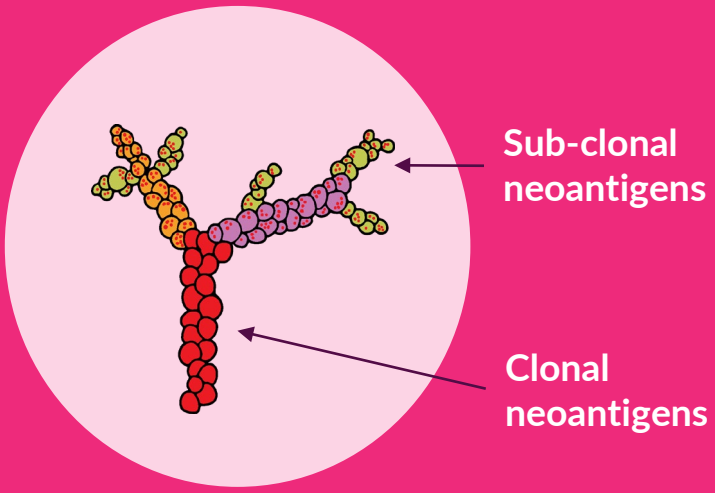
Differentiated pipeline of precision T cell therapies across multiple solid tumors



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



- Tumors are constantly evolving and acquiring new mutations
- Genetic diversity enables tumors to develop resistance to standard therapies (e.g., loss of a target) which leads to disease relapse
- Despite increased genetic diversity the original mutations (clonal neoantigens) always remain[1]
- Achilles' technology identifies the original (clonal) mutations and enables targeting of multiple antigens present only on tumor cells



Clonal neoantigens are

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

1. Gerlinger et al., NEJM, 2012

Clonality is key to the eradication of tumors

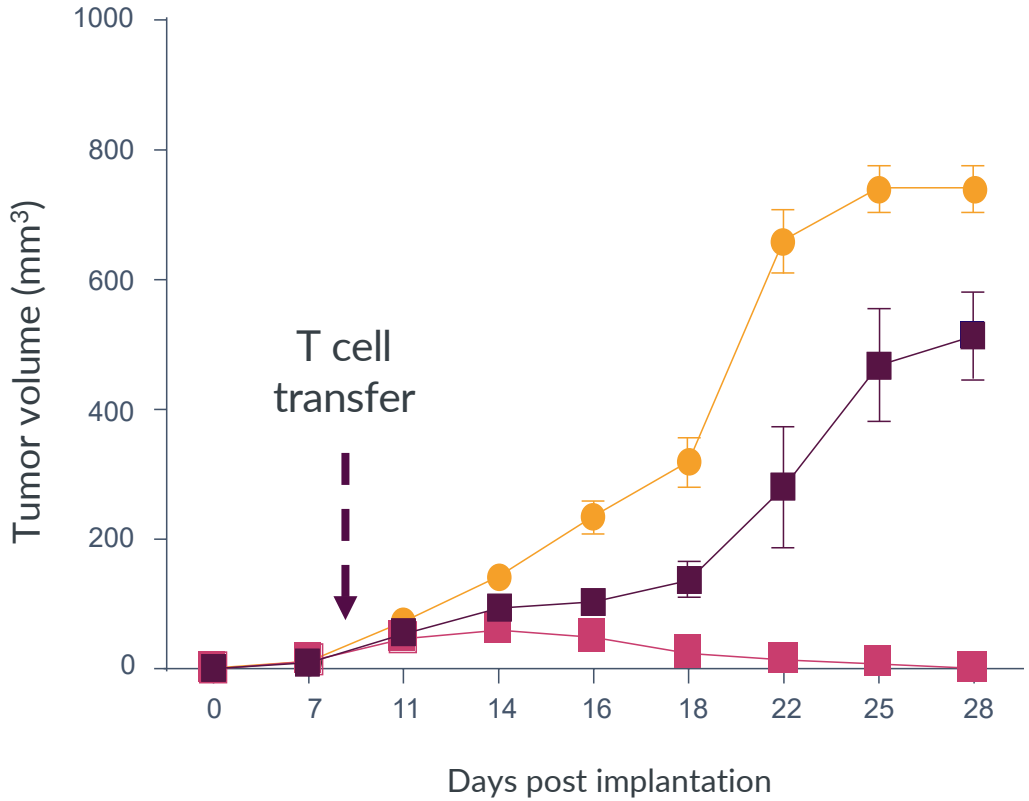
Mice implanted with tumor cells expressing sub-clonal (on a sub-set of cells) and clonal (on all cells) antigens

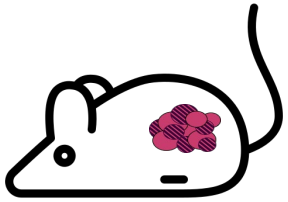
Mice were then treated with murine T cells reactive to sub-clonal (■) and clonal antigens (■)

Targeting clonal antigens expressed on every tumor cell leads to complete tumor regression in this model

Change in tumor size in a mouse model of cancer

Tumor volume, mm^3, (*n=6*)





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

PELEUS®: A validated platform for identification of clonal neoantigens powered by AI

Clonal neoantigen identification is computationally complex

- Solving the heterogenicity problem requires processing of very large DNA data sets
- The process requires multiple steps and has no universally accepted protocol
- 22 groups using the same DNA sequencing data showed <20% overlap of neoantigen identification[1]

PELEUS

Compares tumor DNA to healthy DNA to differentiate clonal and subclonal neoantigens

Achilles has developed an AI-powered solution

- Accurate neoantigen identification requires an advanced computational approach
- AI and machine learning have been developed to enable accurate and rapid processing of very large complex data sets
- Neoantigen predictions are then validated with real-world patient data

1. *Wells et al., 2020, Cell 183, 818-834*

Achilles AI-platform is validated with two types of real-world patient data

TRACERx

- Commercial rights to the largest longitudinal patient data set[1-4]
- 3,200 tumor regions collected from 795 NSCLC patients over 5 years
- Multi-region data from primary & metastatic sites to confirm clonal status
- Unparalleled network of 15 NHS sites

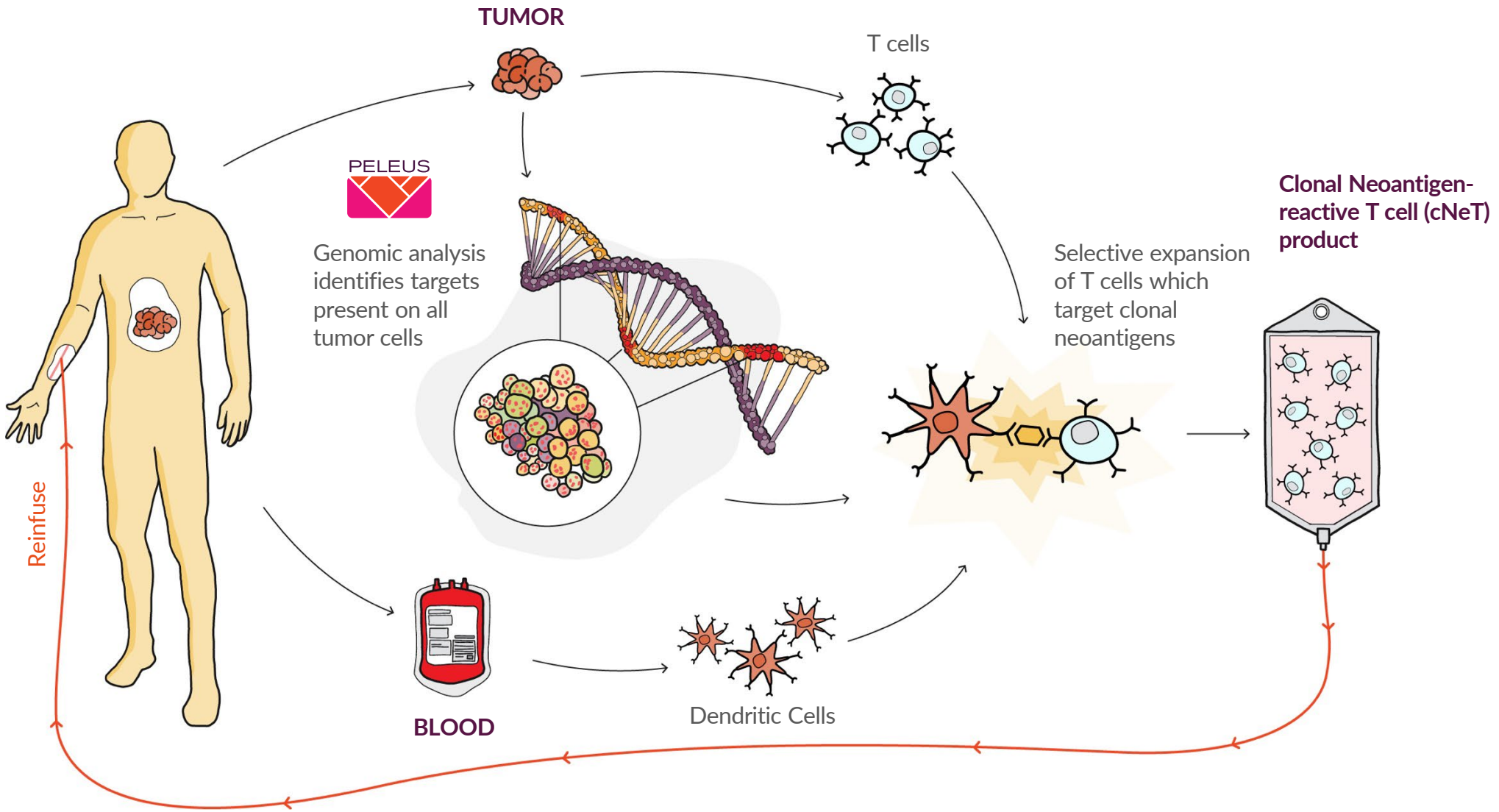
Reactive T cells are identified against clonal neoantigens

- Identification of T cells reactive to predicted clonal neoantigens in patient samples validates the PELEUS® platform
- Over 120 patients prospectively analyzed to date across multiple cancer types
- Patient tumor samples validate and train PELEUS® AI predictions

1. Jamal-Hanjani et al., Plos Biol, 2014
2. Jamal-Hanjani et al. NEJM, 2017
3. Abbosh et al., Nature, 2017
4. Rosenthal et al., Nature, 2019

VELOS™ process delivers precision clonal neoantigen targeting TIL therapy

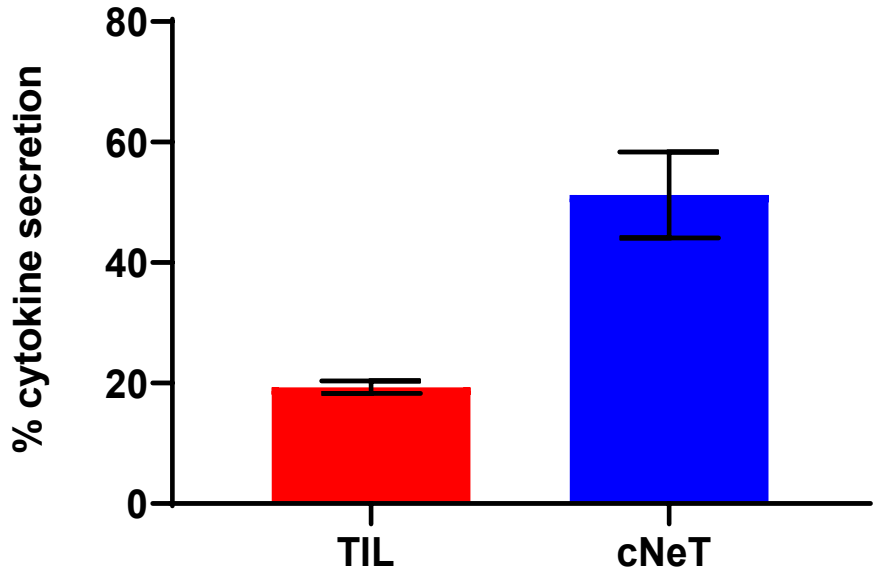
Cutting edge personalized genomics and machine learning enable targeting of all cancer cells



cNeT have improved specificity, function and fitness compared to standard TIL

T cell fitness[1]

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

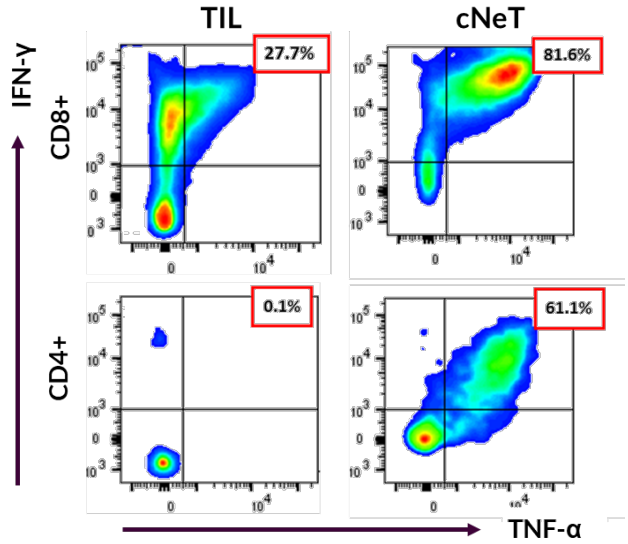


Natural dendritic cell-driven expansion improves **T cell fitness**

T cell specificity and function[2]

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

VELOS™ selectively expands tumor-derived clonal neoantigen reactive CD4+ and CD8+ T cells with improved **specificity and potency**



CD4+ and CD8+ T cells can work in concert to deliver **robust and durable responses**[3-5]

1. *Achilles data measuring the ability of T cells to produce inflammatory cytokines in response to the same polyclonal stimulation*

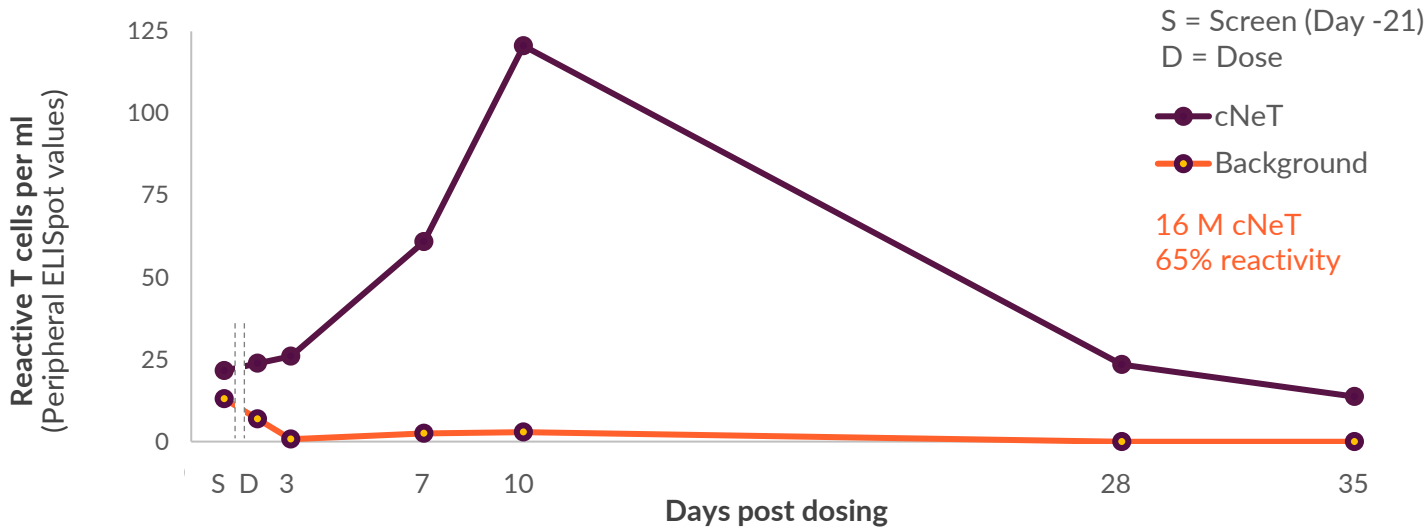
2. *Achilles' data measuring the production of inflammatory cytokines in response to clonal neoantigens*
3. *Hunder et al., NEJM, 2008*
4. *Church et. al., Eur J Immunol, 2014*
5. *Antony et al. J Immunol, 2005*

Achilles can leverage established regulatory principles to develop a potency assay

The Achilles cNeT platform allows:

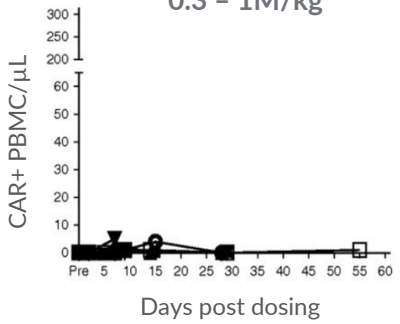
- Quantification of tumor reactivity and cNeT dose for each product (not possible with TIL therapy)
- Determination if increasing cNeT dose improves cNeT persistence and activity as seen in CAR-T therapy
- Correlation of cNeT dose and persistence with anti-tumor effect
- Product release on cNeT dose and basis for potency assays

Melanoma Patient Case Study[1]: Expansion and detection of cNeT post-dosing

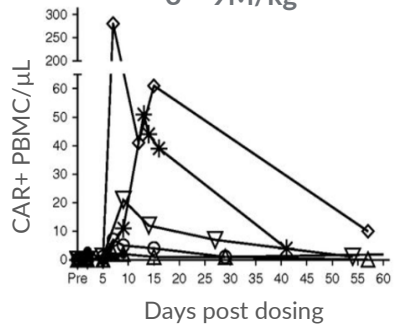


cNeT have similar patterns of expansion as seen in CAR-T

Low-dose CAR-T[2]
0.3 – 1M/kg



High-dose CAR-T[2]
3 – 9M/kg



1. AACR 2021, SITC 2021
2. Blood 20016, Ali SA

Aim to deliver clinical doses of >100M cNeT from our VELOS™ manufacturing process

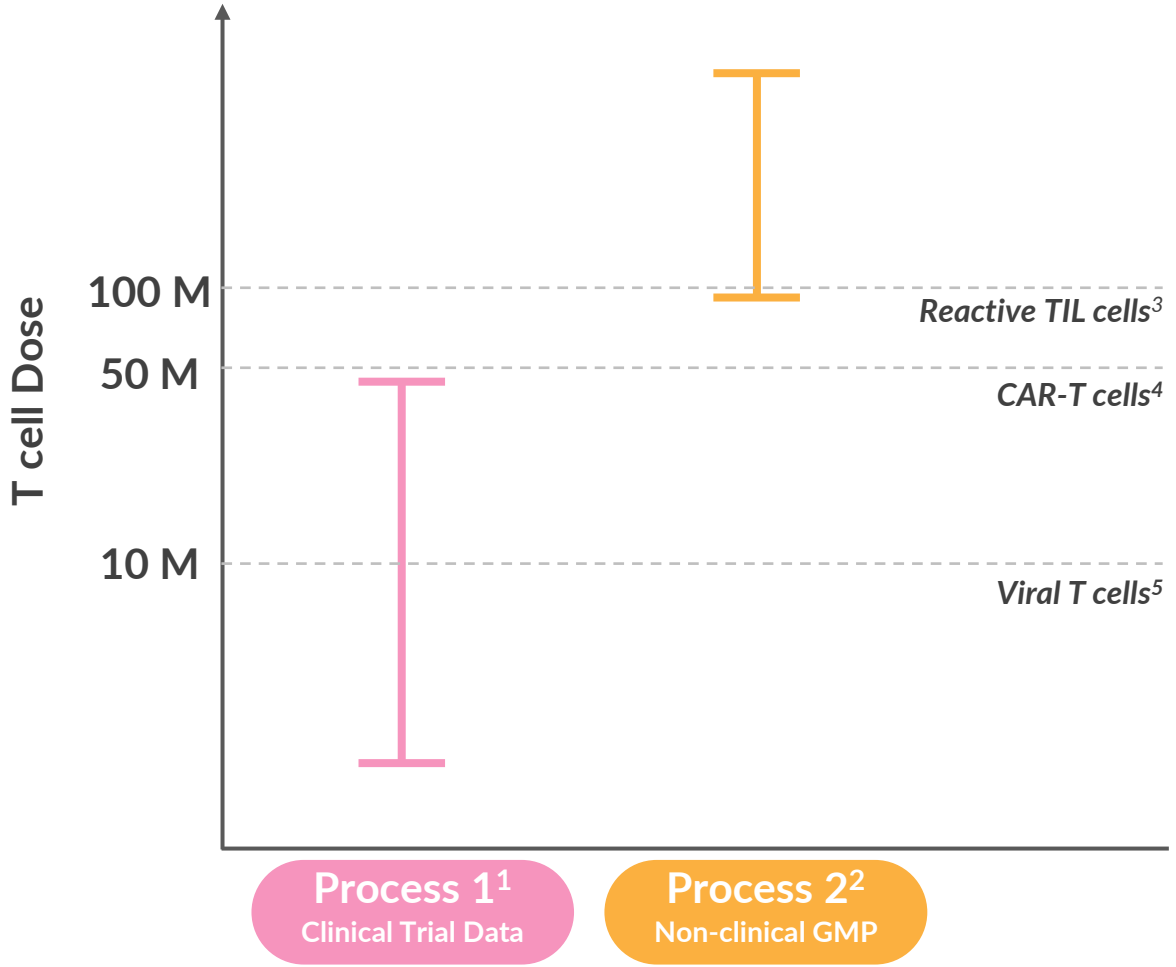
	Process 1	Process 2
Pre-Expansion	T cells are harvested from the tumor	Cytokines boost tumor-reactive cell harvest
Expansion	Dendritic cells loaded with clonal peptides activate and drive cNeT expansion	Optimized DC-driven co-culture followed by short T cell boost increases final cNeT dose

Process 2

- **Identical manufacturing timeline** to Process 1
- Maintains **high functional cell fitness** and **effector memory phenotype**
- **Approved** in UK, France, Germany & Spain

VELOS Manufactured Cell Doses

Compared to estimated lowest clinically active doses of other T cell therapies



1. SITC 2021 Poster 543
2. ESMO IO 2021 Poster 58P
3. J Clin Invest 2021, Kristensen
4. Blood 2017, Mueller
5. Lancet 2003, Peggs

Achilles has two ongoing Phase I/IIa clinical trials

CHIRON
Advanced NSCLC

Monotherapy

- Advanced unresectable or metastatic Stage III-Stage IV NSCLC
- Never-smokers and EGFR/ALK/Ros-1 mut excluded
- Open-label
- n = up to 40
- Option to open Cohort B in combination with a PD-1 inhibitor

Evaluating safety, tolerability and activity (RECIST), biomarkers of clinical activity and bespoke ctDNA assay

Ongoing in UK, EU and US

THETIS
Melanoma

Cohort A – Monotherapy

- Recurrent or metastatic malignant melanoma (n = up to 40); Open-label
- Acral, uveal and mucosal melanoma excluded

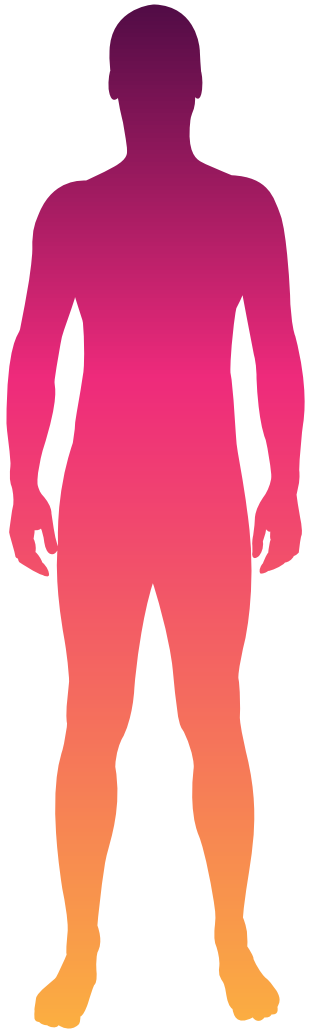
Cohort B – Combination with PD-1 inhibitor (nivolumab)

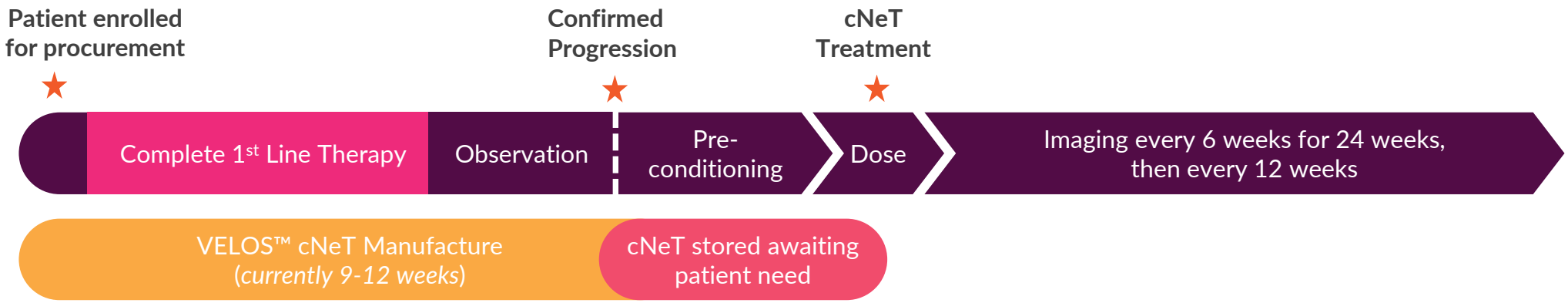
- n = up to 20 checkpoint refractory patients; Open-label
- CPI dosed 7-13 days prior to cNeT and restarted day 14 post-cNeT

Evaluating safety, tolerability and activity (RECIST)

Ongoing in UK, expanding to EU & US

cNeT therapies can be readily delivered within standard treatment pathways





Manufacturing

Manufactured and cryopreserved for infusion after patient progression

Tolerable pre-conditioning

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

Low IL-2

Lower dose IL-2 vs existing TIL therapy

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

Heavily pretreated patients with advanced cancer

- 2.5 median lines of prior therapy
- 14.2m median cNeT dose[1] in monotherapy
- All had progressive disease at time of lymphodepletion
- Five recurrent or metastatic malignant melanoma patients (THETIS)
- Three advanced unresectable or metastatic NSCLC patients (CHIRON)

cNeT tolerability profile

- Tolerability similar to standard TIL products not enriched for cNeT reactivities
- No higher-grade adverse events more commonly associated with the use of higher doses of IL-2
- Three SAEs deemed unlikely related and one ICANS event deemed to be possibly related to cNeT treatment

Data reported SITC Nov 12, 2021
1. First 8 patients in CHIRON/THETIS, SITC 2021

Initial cNeT doses showed stable disease in advanced patients in CHIRON & THETIS

Activity 6-weeks post treatment

- **Stable disease** in 5 of 8 patients[1]
- **Tumor reduction** in 2 of 4 lesions (55% and 90%) in patient with highest cell dose
- **Engraftment** in 5 of 7 patients, with dose associated response
- **2 to 28 reactivities observed** in 7 of 8 cNeT
- Median dose of 14.2 M

Patient	cNeT Dose (M)	Reactivity	Engrafted[2]	Best Response
C-03	0.1	0.20%	--	**SD**
T-12	2	13%	**Y**	**SD**
T-09	12	9%	N	**SD**
C-11	13	41%	**Y**	**SD**
T-05	16	65%	**Y**	PD
C-10	21	3%	N	**SD**
T-11	42	5%	**Y**	PD
T-02[3]	287	77%	**Y**	PD

Median 2.5 lines of prior therapy

Next steps: Explore higher-dose cNeT monotherapy and combination with PD-1 inhibitor

Data reported SITC Nov 12, 2021

1. *Investigator reported*
2. *cNeT detected post infusion*
3. *T-02 treated with steroids on day 11 to treat infection*

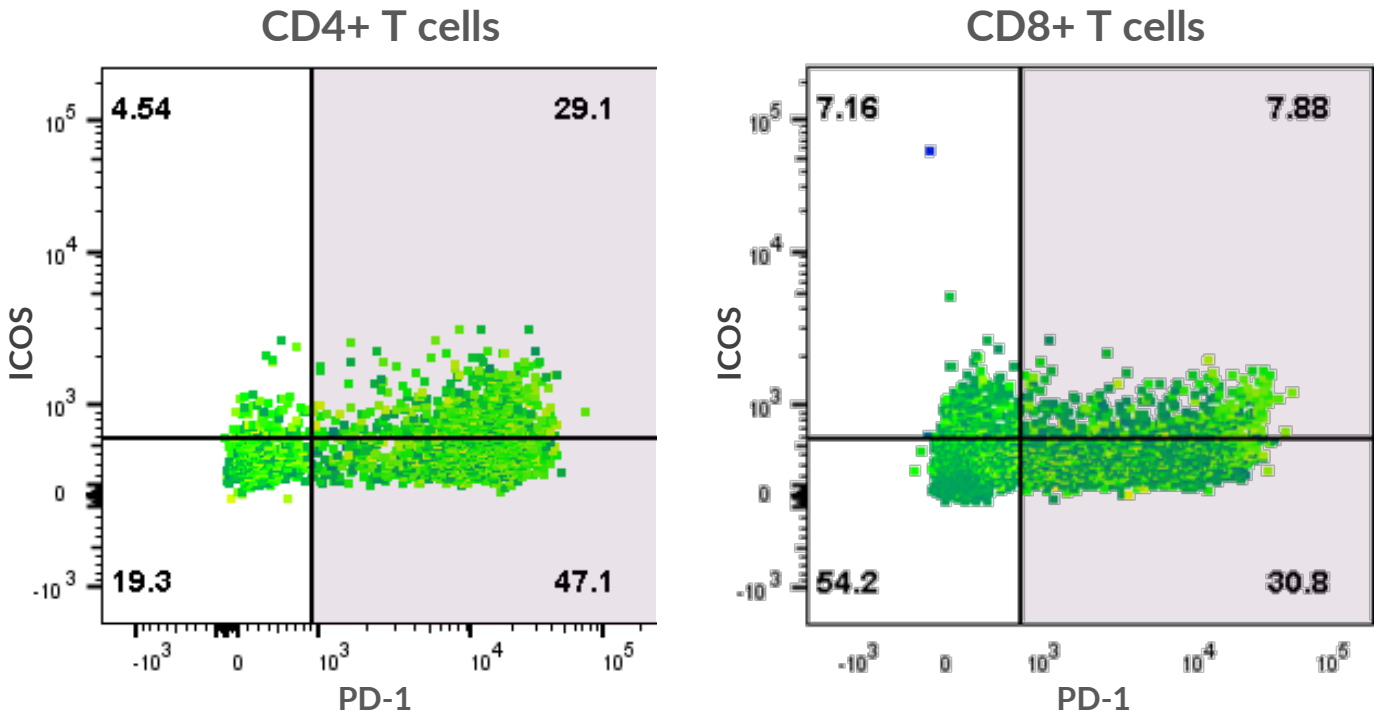
Potential for cNeT/PD-1 inhibitor combination in Melanoma (THETIS Cohort B)

Checkpoint molecules in immune regulation

- Normal immune regulation uses immune checkpoints to inhibit T cells from attacking healthy tissue
- Our data show PD-1 checkpoint is upregulated on a fraction of cNeT which could partially reduce anti-tumor activity[1]
- Targeting PD-1 with checkpoint inhibition could further increase cNeT activity

TIL-derived cNeT express elevated levels of PD-1 upon antigen encounter[1]

Cell surface marker flow cytometric analysis (*n=1*)



[1]*Achilles data*

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

	Royal Free Hospital	Cell & Gene Therapy Catapult	Center for Breakthrough Medicine	Hayes
				
	GMP facility supporting FiH studies	GMP facility supporting open and closed manufacturing process to support clinical and commercial supply	GMP facility in partnership with CBM, a CDMO in Greater Philadelphia	GMP modular facility to support multiple indications for late stage clinical and commercial supply
Online	**2019**	**2022**	**2023**	**2024**
Peak Capacity	**50** annual doses	**200** annual doses	**150-400*** annual doses	**1,000+** annual doses

*Initial plan of 150-200 doses with potential for expansion

Financial and company highlights

$237M

CURRENT CASH BALANCE[1]

2H 2024

CURRENT CASH RUNWAY

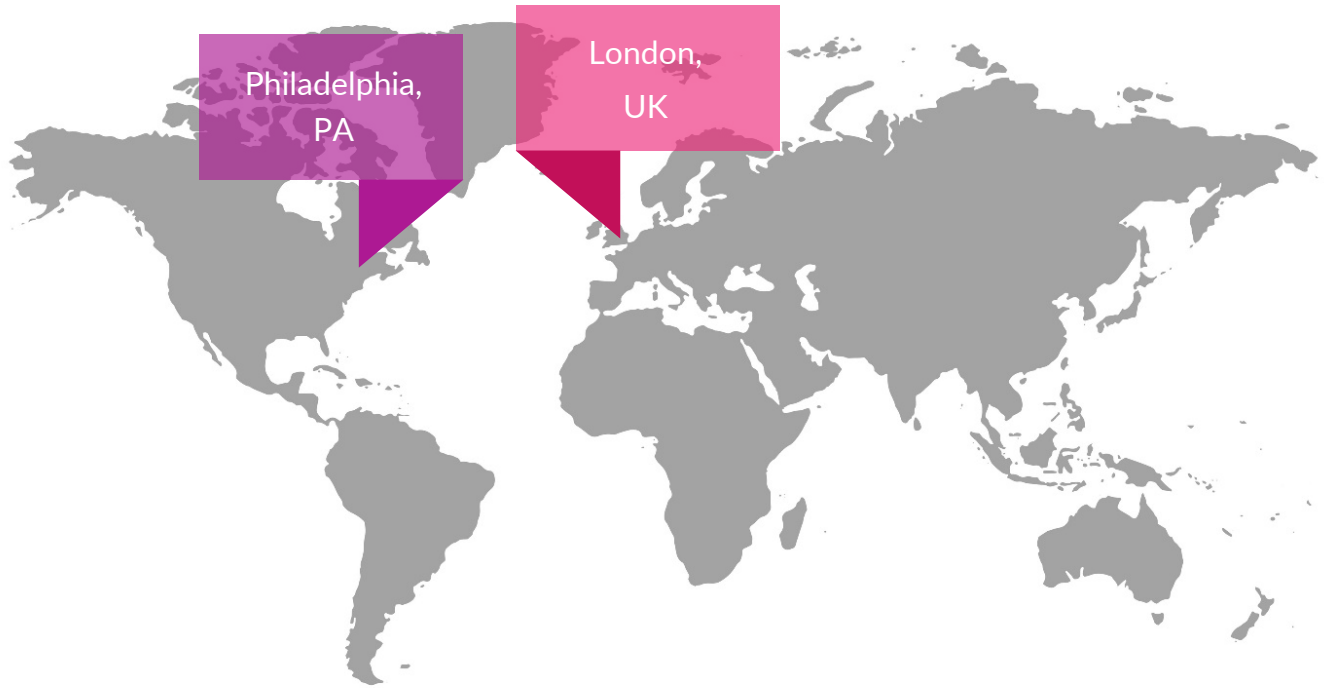
Global Operations

U.S. Headquarters

Philadelphia, PA

Global Headquarters

London, UK



1. *As of March 31, 2022*

Key anticipated 2022 milestones and updates

	2022			
	Q1	Q2	Q3	Q4
Higher-dose cNeT (Process 2)		First Patient Dose (Process 2)	Initial Process 2 monotherapy patient data	Initial Process 2 monotherapy patient data
PD-1 + cNeT combo (Process 1 & 2)	Open CPI combo cohort (melanoma)		First Patient Dose (combo)	Initial combo patient data
Facilities and Manufacturing	Establish US HQ and R&D	Catapult GMP License & US CDMO Partnership		
Tumor Archiving Program (TAP)		Initiate TAP program		

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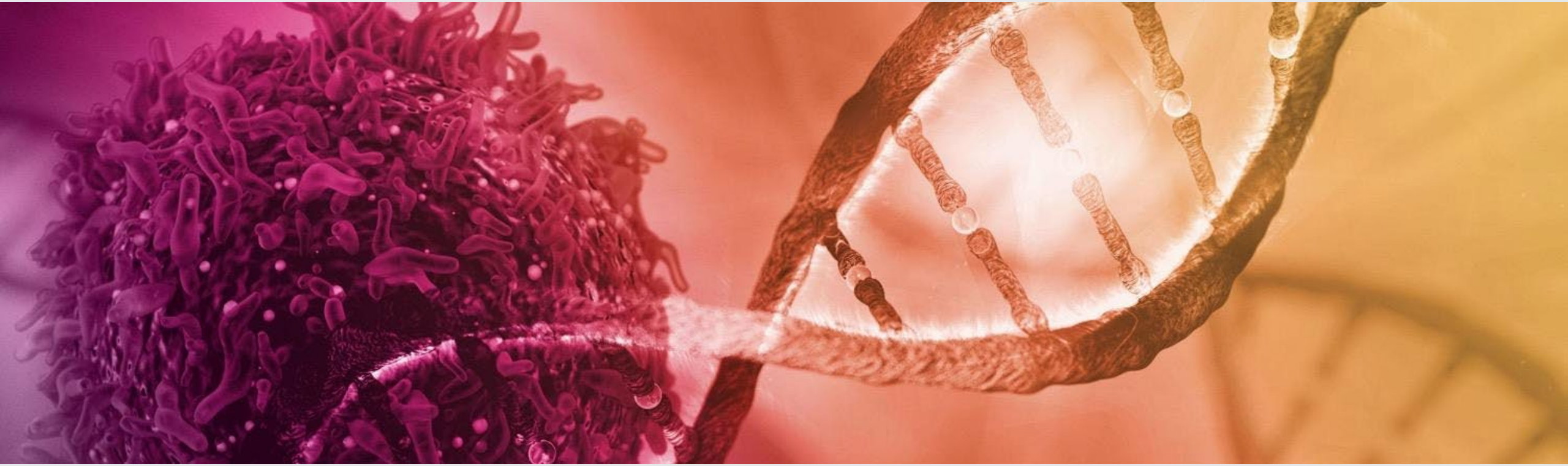

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