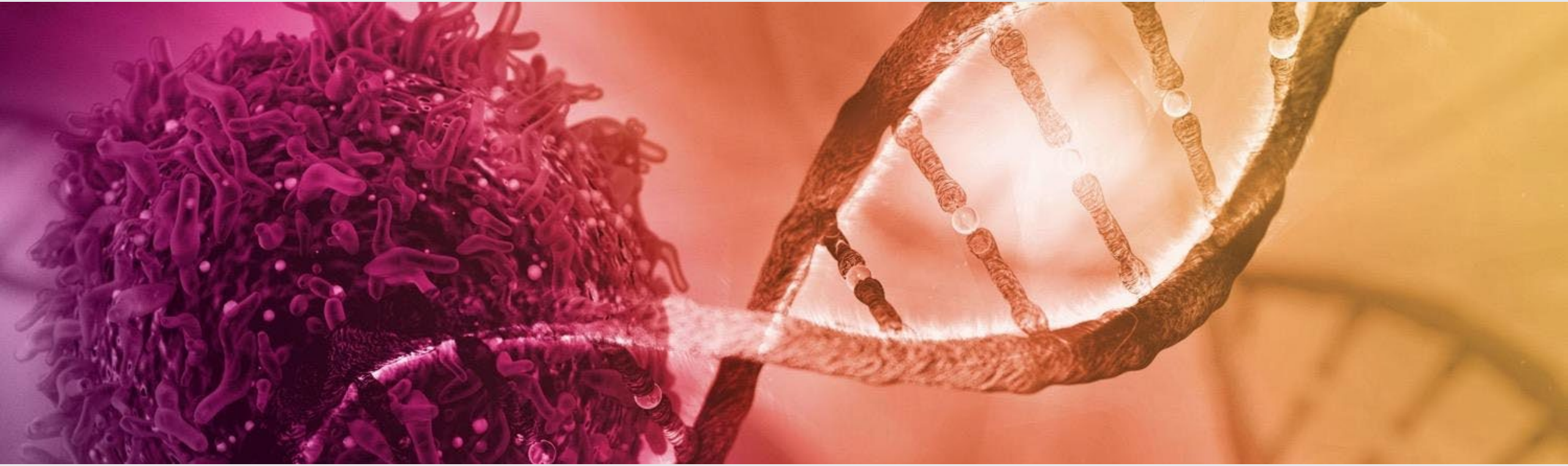

Achilles Therapeutics

Precision T cell therapies to treat solid tumors

January 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

Developing precision cell therapy for solid tumors: clonal neoantigen-reactive T cells (cNeT)

Targeting Personalized Clonal Neoantigens, Present on all Tumor Cells

Tumor eradicating potential designed to overcome limitations of current therapies

Industry-leading clonal neoantigen discovery using real world patient data (TRACERx) and a proprietary bioinformatics tool (PELEUS®) to enable precision T cell targeting

Targeted and Trackable Precision TIL Therapies

T cell therapy with unprecedented precision and tracking

Addressing multiple patient specific clonal neoantigen targets with T cell therapy tailored to each patient

Differentiated Manufacturing

Scalable commercial manufacturing process designed to be closed and automated

Natural dendritic cell step reduces need for high-dose IL-2, improves T cell fitness, and delivers CD4+/CD8+ T cells targeting multiple clonal neoantigens

Multiple Near-Term Catalysts

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cNeT / PD-1 inhibitor (nivolumab) combination data in melanoma - 2H 2022

Strong Cash Position

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Funds ongoing clinical trials, expanded manufacturing, and additional clinical programs

NASDAQ:
ACHL

Our Management team

Iraj Ali
CEO

Syncona
McKinsey&Company

Sergio Quezada
CSO

UCL
CANCER RESEARCH UK
Memorial Sloan Kettering Cancer Center

Karl Peggs
CMO

UCL NIHR National Institute for Health Research
Memorial Sloan Kettering Cancer Center

Robert Coutts
CFO

KPMG
Syncona

Daniel Hood
CLO

Intercept
GILEAD

Ed Samuel
SVP Technical Operations

Orchard therapeutics
COGNATE BIOSERVICES

Shree Patel
SVP Clinical Operations

Cell Medica

Experienced leadership with decades in cell therapy drug development

World-renowned directors and advisors

Board of Directors

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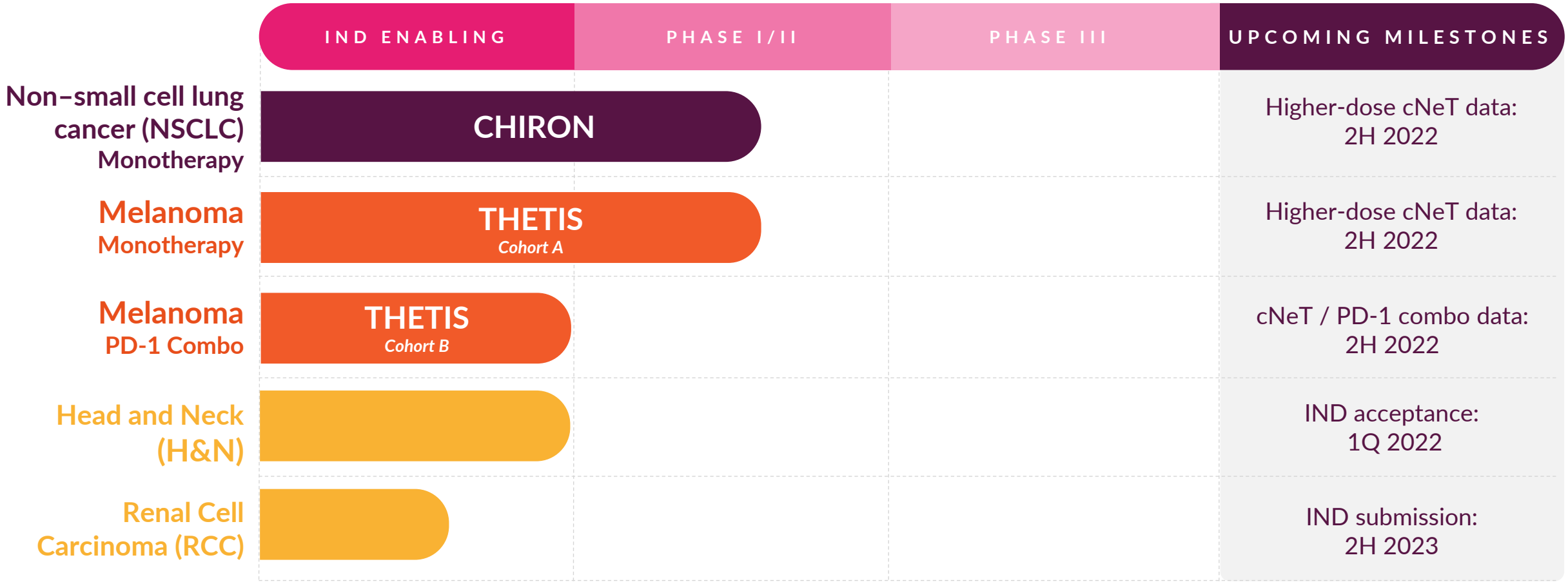
Memorial Sloan Kettering Cancer Center

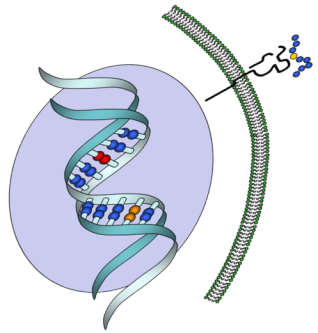
Mark Lowdell
Director, Centre for Cell, Gene & Tissue Therapeutics
NHS Royal Free

Markwin Velders
Former VP Operations and Managing Director EU
Kite Pharma

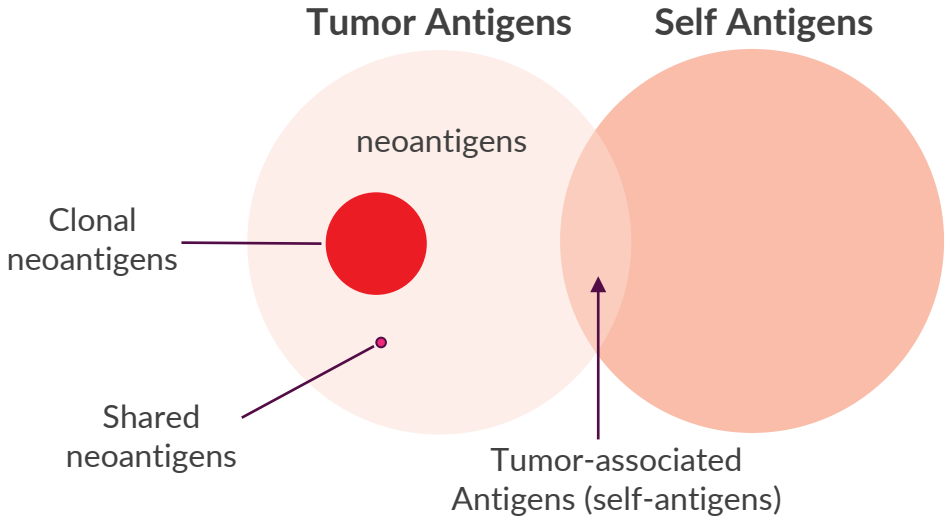
Differentiated and focused pipeline of precision T cell therapies across solid tumors

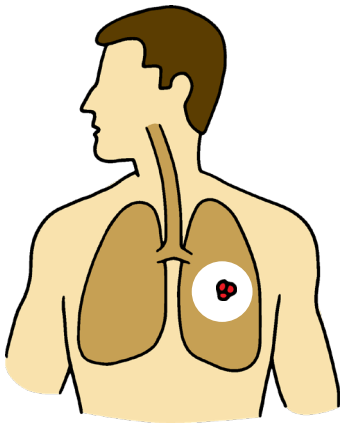


Clonal neoantigens are novel tumor-specific targets present on all tumor cells…
… but they have been challenging to identify



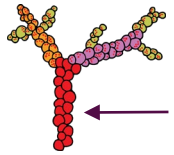
Mutated peptides or ***neoantigens*** are displayed on cell surface of cancer cells





Clonal neoantigens are the original mutations formed early and **present on all cancer cells**

Over time the development of **new mutations** (subclonal neoantigens) creates genetic heterogeneity[1] which confounds treatment with standard therapies



Achilles has developed proprietary technology to distinguish and identify each patient's **clonal neoantigens** present on their tumor cells

Clonal neoantigens are:

A subset of neoantigens formed early in tumor evolution

Expressed on all tumor cells including metastases[1]

Absent from healthy cells and tissues

The ability to identify clonal neoantigens has been challenging because of the lack of **multi-region, longitudinal, deep sequencing data** and bioinformatics **to confirm true clonality**

1. Gerlinger et al., NEJM, 2012

Unique and industry leading capability to identify clonal neoantigens
Using proprietary TRACERx patient study and PELEUS bioinformatics platform to define clonality

TRACERx Clinical study and database of tumor evolution

Longitudinal data across 5 yrs from over 780 NSCLC patients[1,2,3,4]

One of the largest deep sequencing, multi-region and multi-time point bioinformatic data sets with over 3,000 tumor samples

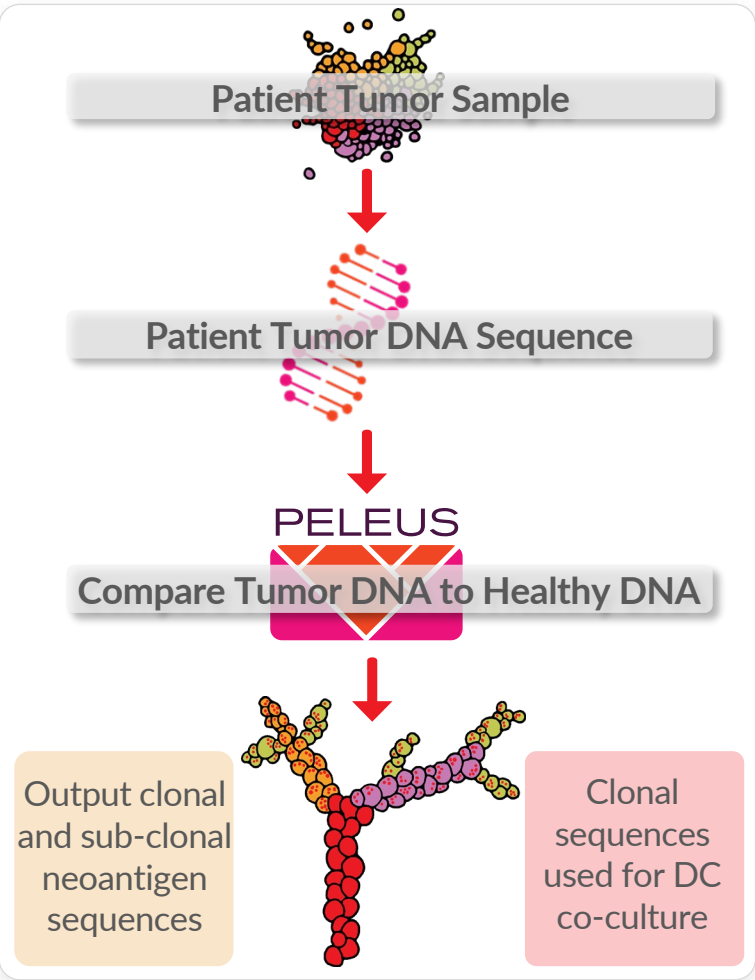
Applicable across solid tumor types

PELEUS Proprietary bioinformatics platform

Industrialized extensive data from TRACERx into proprietary algorithms

Designed and trained using TRACERx data

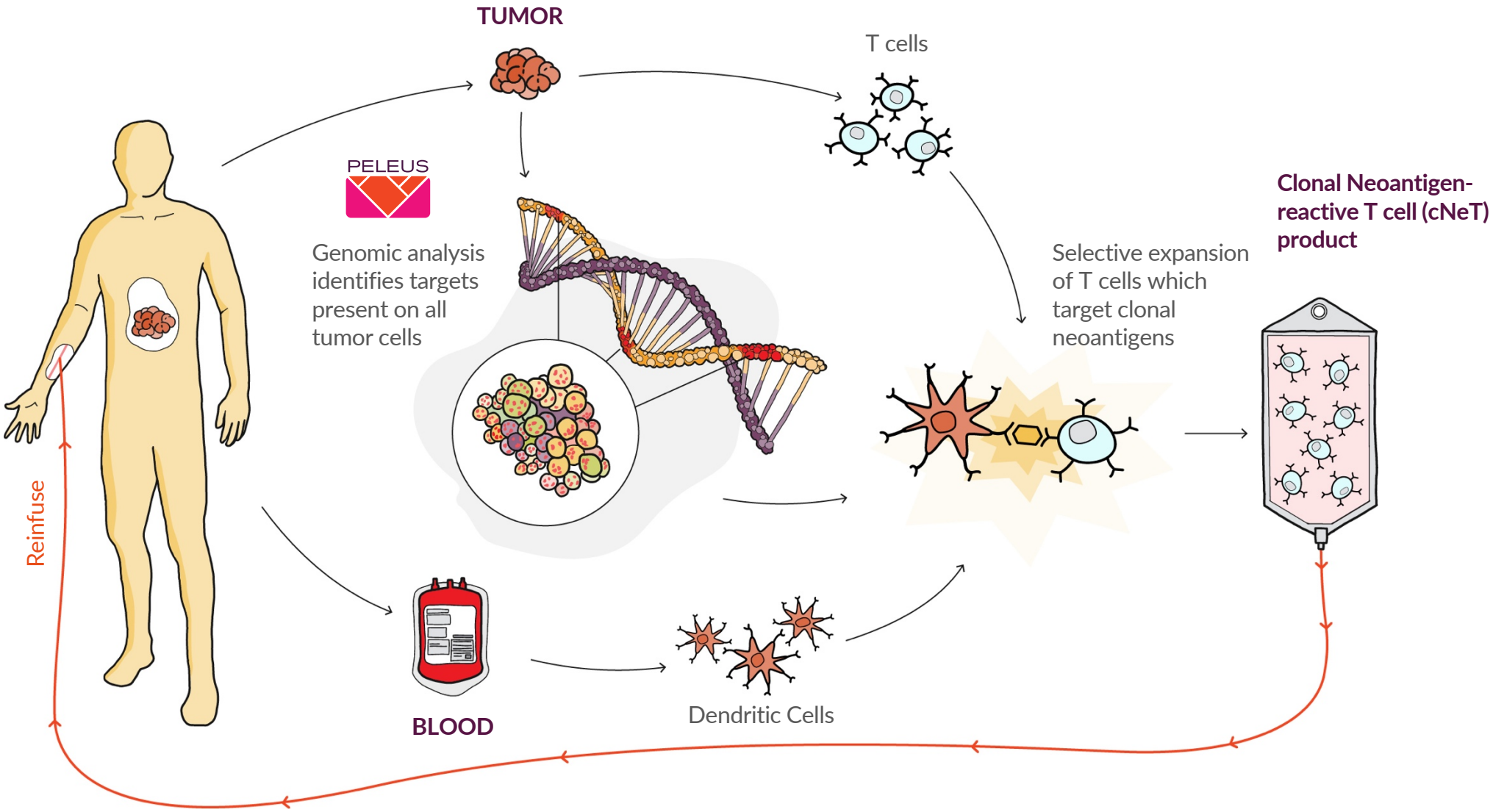
Sophisticated algorithms distinguish tumor DNA from non-tumor DNA and clonal from sub-clonal neoantigens for each patient



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

Precision TIL therapy targeting clonal neoantigens

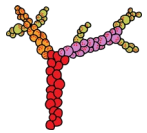
Using cutting edge personalized genomics to target all cancer cells in the patient



Achilles cNeT generated by VELOS™ manufacturing can overcome standard TIL limitations

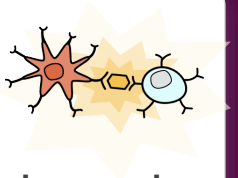
cNeT: Clonal neoantigen-reactive T cells generated by VELOS manufacturing offer precision & potency

Precision expansion of T cells targets patient-specific clonal neoantigens



Correlates with the efficacy of TIL[1] and checkpoint inhibitors[2]

DC-driven T cell expansion and low levels of IL-2 increase fitness and expand patient eligibility



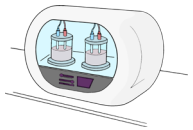
Drives CD4+ and CD8+ T cell anti-tumor immunity

Measurable and trackable

Antigen-specific potency
T cell engraftment and expansion capabilities

In vivo cNeT quantification and tracking post-dosing

Proprietary commercial-scale process



Designed to be a closed, automated manufacturing process, delivering competitive commercial COGS

Standard TIL: Despite impressive results, opportunities exist for improvement of standard TIL therapies

Non-specific expansion of all T cells

No control over which antigens are targeted

Expansion using high doses of IL-2

T cells with reduced fitness and anti-tumor activity[3]

Unknown potency and expansion

Product makeup unknown and cells cannot be tracked following administration

Manufacturing based on an academic process

Developed in the 1980s

1. Lauss et al., Nature Comm, 2017
2. Snyder et al., NEJM, 2014
3. Gattinoni et al. J Clin Invest, 2005

Achilles' cNeT therapy targets patient-specific clonal neoantigens expressed on all tumor cells

Tumor associated antigens

Present on some tumor cells and on healthy tissue

Fate THERAPEUTICS
Adaptimmune TRANSFORMING T CELL THERAPY
TMUNITY
TCR² THERAPEUTICS
MARKER THERAPEUTICS

Unselected Neoantigens

Present on some tumor cells

IOVANCE BIOTHERAPEUTICS
InstilBio
BIONTECH
OBSIDIAN THERAPEUTICS
Lyell
neogene THERAPEUTICS
genocea
PACT pharma

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

We believe our process can deliver tumor specificity and potency improvements over standard TIL

Strong evidence that neoantigens are attractive targets in oncology

Positive efficacy outcomes with checkpoint inhibitors correlated with mutational burden

Neoantigens are likely being targeted by T cells following checkpoint therapy

NEJM, 2014
Snyder et al

Clinical benefit in TIL therapy improves with increased neoantigens

Neoantigens are the likely targets for TIL therapy

Nature Comms, 2017
M Lauss et al

Frequency of neoantigen reactive T cells within TIL correlated with improved survival

Neoantigens are the likely targets for TIL therapy

J Clin Invest, 2021
N Kristensen et al

Adoptive transfer of TIL targeting a single neoantigen delivered tumor reduction and long-term disease control

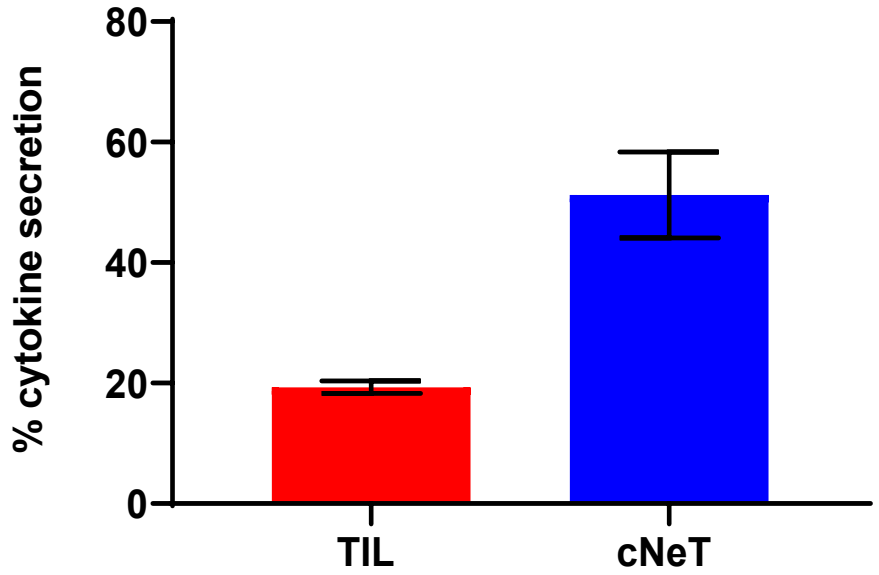
Neoantigens are the likely targets for TIL therapy and targeting a single neoantigen can deliver long term disease control

Science, 2014
E Tran et al

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

T cell fitness[1]

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

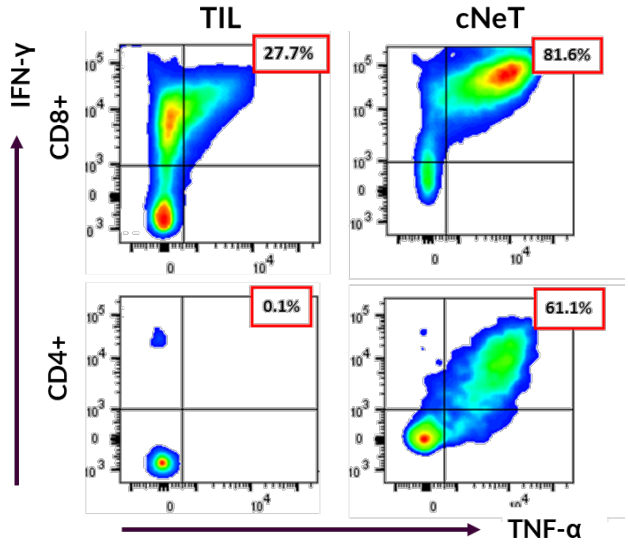


Natural dendritic cell-driven expansion improves **T cell fitness**

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*

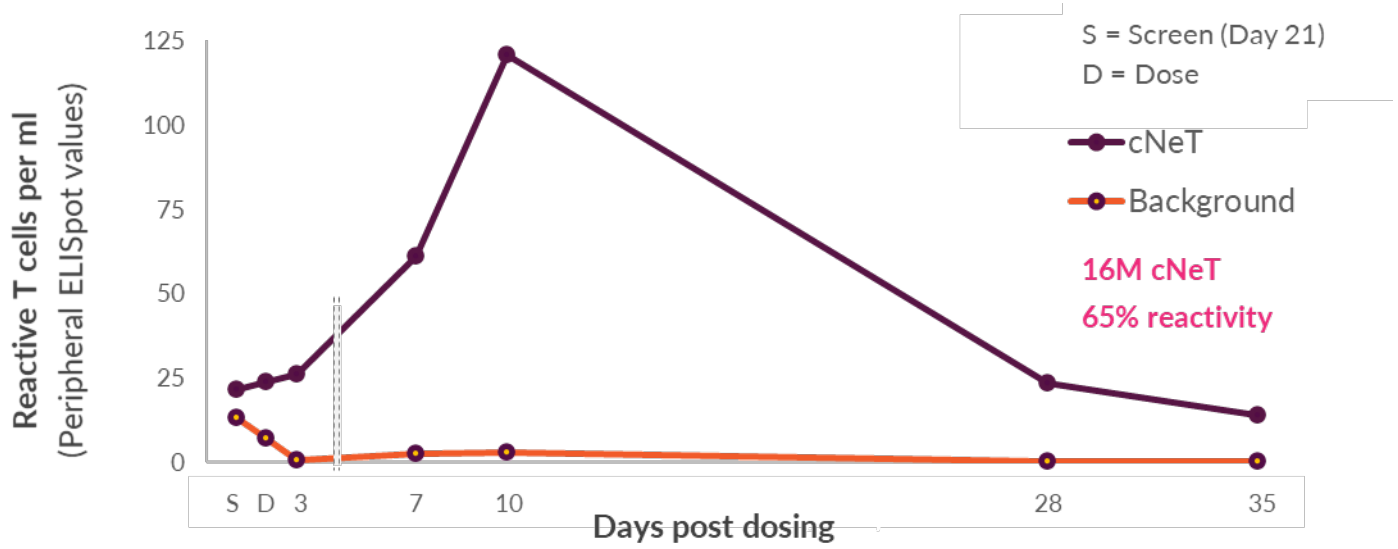
2. *Achilles' data measuring the production of inflammatory cytokines in response to clonal neoantigens*
3. *Hunder et al., NEJM, 2008*
4. *Church et. al., Eur J Immunol, 2014*
5. *Antony et al. J Immunol, 2005*

Achilles can leverage established regulatory principles to develop a potency assay

The Achilles Platform allows:

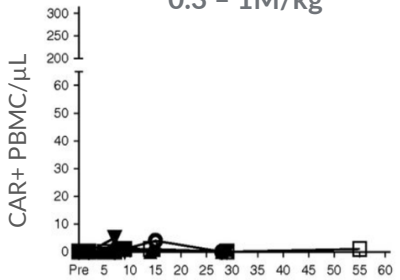
- Quantification of cNeT reactivity
- Calculation of the cNeT dose of each product
- Use of cNeT reactivity as both a release criterion and potency measure
- Correlation of infused cNeT dose with anti-tumor effect
- Determination if increasing cNeT dose will improve cNeT persistence (area under the curve & peak) as seen in CAR-T therapy
- Determination if increasing AUC correlates with positive clinical outcomes as seen with CAR-T therapy

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

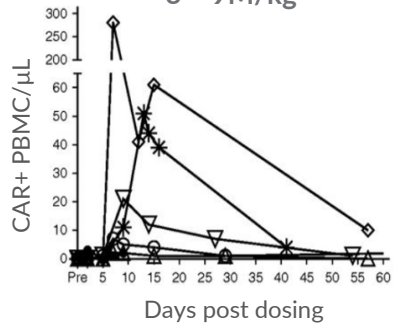


cNeT have similar patterns of expansion as seen in CAR-T

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

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)

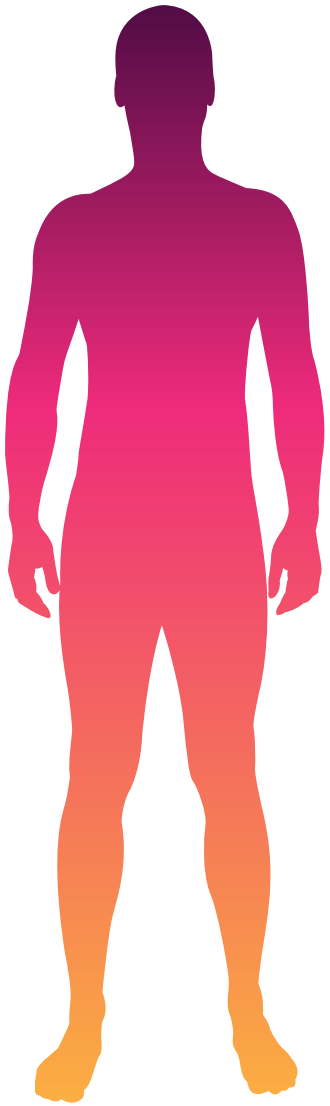
- n = up to 20 checkpoint refractory patients; Open-label
- Checkpoint dosed 7-13 days prior to cNeT and restarted day 14 post-cNeT

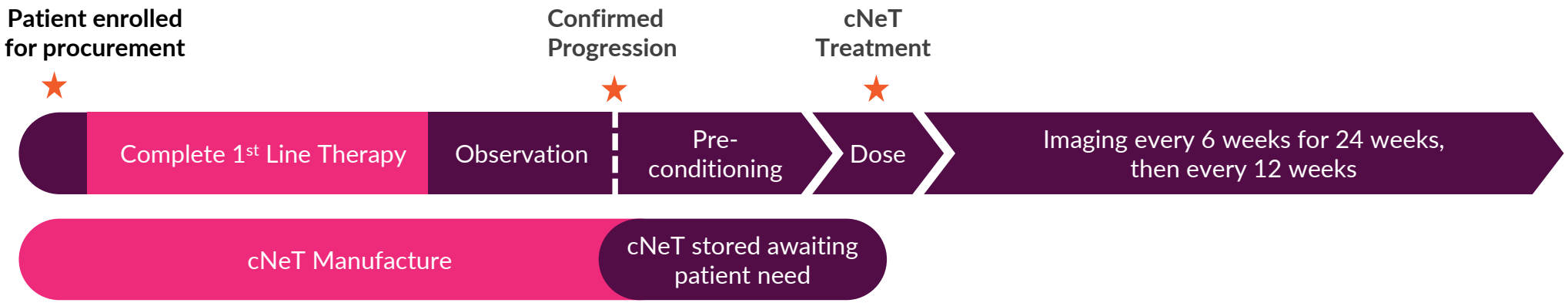
Evaluating safety, tolerability and activity (RECIST)

Ongoing in UK, expanding to EU & US

CHIRON and THETIS trial design

cNeT therapies can be readily delivered within standard treatment pathways





cNeT can be manufactured during checkpoint therapy

cNeT are manufactured then cryopreserved to await infusion after patient progression

cNeT can be delivered within standard treatment pathway

Pre-conditioning uses lower, CAR-T like, cyclophosphamide + fludarabine regimen that is well tolerated

Low-dose IL-2 regimen less toxic than used in existing TIL therapy

THETIS (melanoma) has active CPI combo arm (Cohort B)

1st CPI dose given 7 to 13 days before cNeT

CPI restarts 14 days after cNeT

Ongoing Phase I/IIa clinical trials CHIRON (NSCLC) & THETIS (Melanoma)

Patient summary

Data from first 8 patients following scan 6 weeks post-cNeT infusion

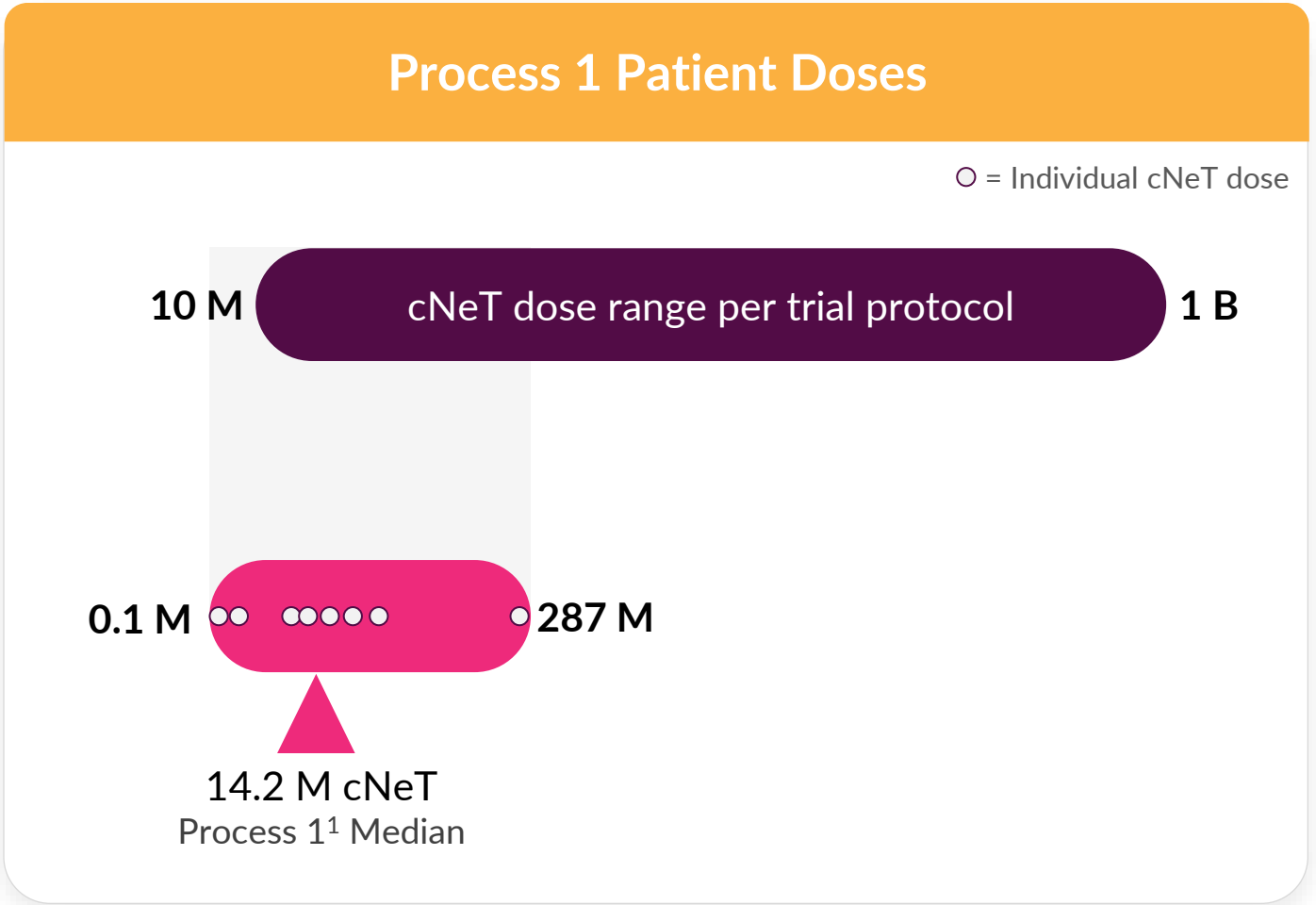
- 3 in CHIRON, 5 in THETIS

Median 2.5 lines of prior therapy

Median dose of 14.2m cNeT

- Low end of prospectively targeted therapeutic range

All had progressive disease at time of lymphodepletion



1. *First 8 patients in CHIRON/THETIS, SITC 2021*

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

Tolerability

- **Tolerability similar to standard TIL** products not enriched for cNeT reactivities, most higher-grade AEs from lymphodepletion regimen
- **No higher-grade adverse** events more commonly associated with the use of higher doses of IL-2
- **Three CRS** events and **one ICANS** event deemed to be possibly related to cNeT treatment
- Previously disclosed case of encephalopathy subsequently deemed **unlikely related to cNeT**

Activity (Process 1)

Patient	cNeT Dose (M)	Reactivity	Engrafted[1]	Best Response
T-02	287	77%	**Y**	PD
C-03	0.1	0.2%	--	**SD**
C-10	21	3%	N	**SD**
T-05	16	65%	**Y**	PD
C-11	13	41%	**Y**	**SD**
T-09	12	9%	N	**SD**
T-11	42	5%	**Y**	PD
T-12	2	13%	**Y**	**SD**

- **Stable disease** at 6 weeks post-dosing in 5 of 8 patients[2]
- **Tumor reduction** in 2 of 4 lesions of approx. 55% and 90% in patient that received the highest cell dose
- Range of **2 to 28 reactivities observed** in 7 of 8 products
- **Evidence of engraftment** in 5 of 7 patients, with highest dose associated with highest engraftment

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

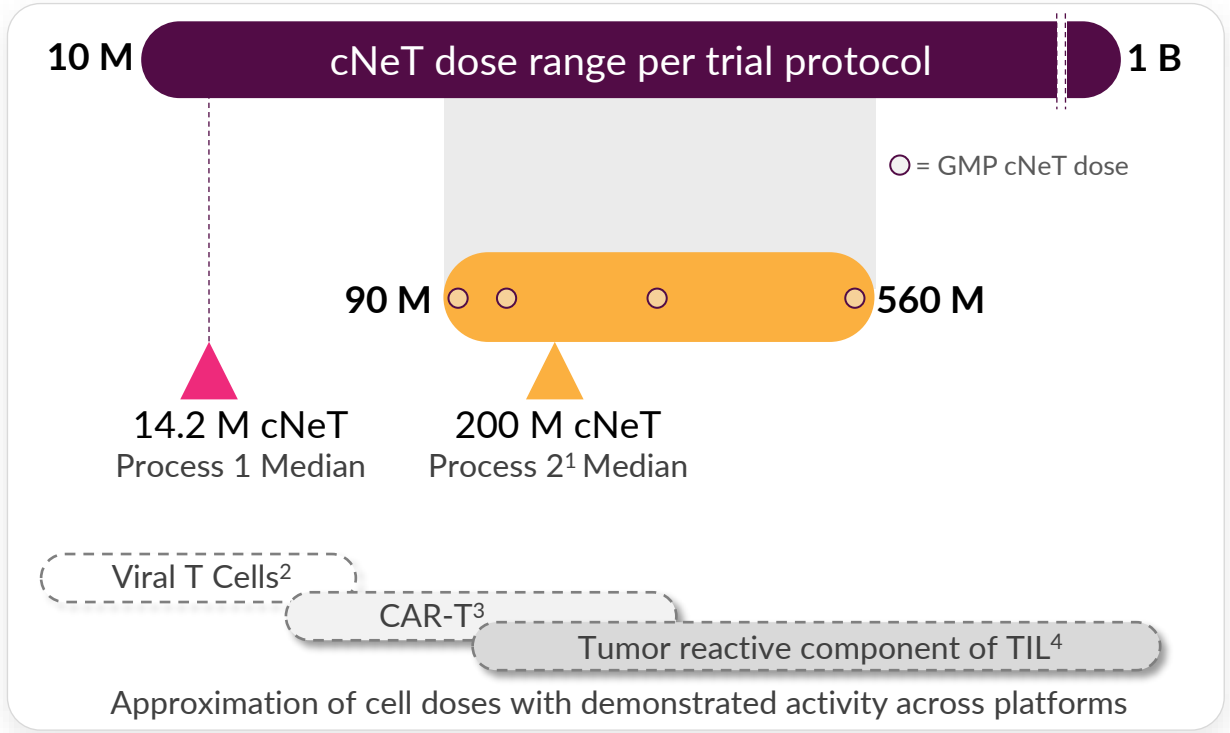
Data reported SITC Nov 12, 2021

1. *cNeT detected post infusion*
2. *Investigator reported*

VELOS Process 2 yielded >10-fold higher median cNeT doses in GMP validation runs

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

	Process 1	Process 2
Pre-Expansion	T cells are harvested from the tumor	Additional cytokines boost the harvest of tumor reactive cells
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



Approximation of cell doses with demonstrated activity across platforms

VELOS Process 2

- **Identical manufacturing timeline** to Process 1
- Cells maintain a **high functional fitness and effector memory phenotype**
- Expect Process 2 to **produce a significantly higher median cNeT dose (>10 fold)**

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

Our process has been designed from the ground up for commercial scale

Closed processing to be incorporated 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 commercial process from tumor sample collection to product release

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

	Royal Free Hospital (UK)	Cell & Gene Therapy Catapult (UK)	Hayes (UK)
			
	GMP facility supporting FiH studies	Supports both open and fully closed manufacturing process	GMP modular facility Supports multiple indications for late stage clinical studies and commercial supply Includes in-house peptide manufacturing
Online	**2019**	**2022**	**2024**
Peak Dose Capacity	**50**	**200**	**1,000+**

Initiated tech transfer to a US manufacturing facility expected to be online in 2H 2023

Financial highlights

$282M

CURRENT CASH BALANCE[1]

~$23M

EST AVG 2022 QTLY SPEND

1Q 2024

CURRENT CASH RUNWAY

Analyst Coverage

Tazeen Ahmad	Mark Breidenbach	Joe Catanzaro
BofA SECURITIES	OPPENHEIMER	PIPER SANDLER

Ingrid Gafanhao	Eric Joseph	Geulah Livshits
Kempen	J.P.Morgan	CHARDAN CAPITAL MARKETS

1. As of September 30, 2021

Key anticipated milestones

2021

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

2022

1 H

- [ ] Dose 1st patient with higher-dose cNeT (Process 2)
- [ ] Establish US R&D facility
- [ ] License Cell & Gene Therapy Catapult facility
- [ ] Initiate tumor archiving program (TAP)

2 H

- [ ] Dose 1st US patient
- [ ] Additional low-dose (Process 1) monotherapy data
- [ ] Monotherapy data from higher-dose cNeT (Process 2)
- [ ] Combination data from PD-1 / cNeT

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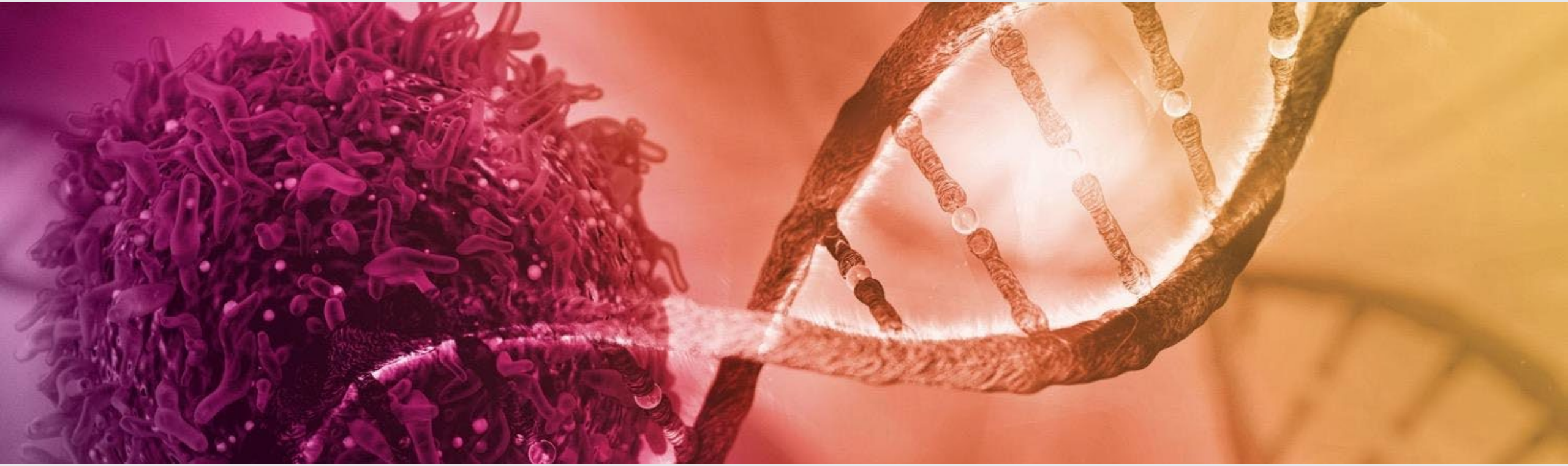
NASDAQ:
ACHL



Achilles Therapeutics

Precision T cell therapies to treat solid tumors

January 2022