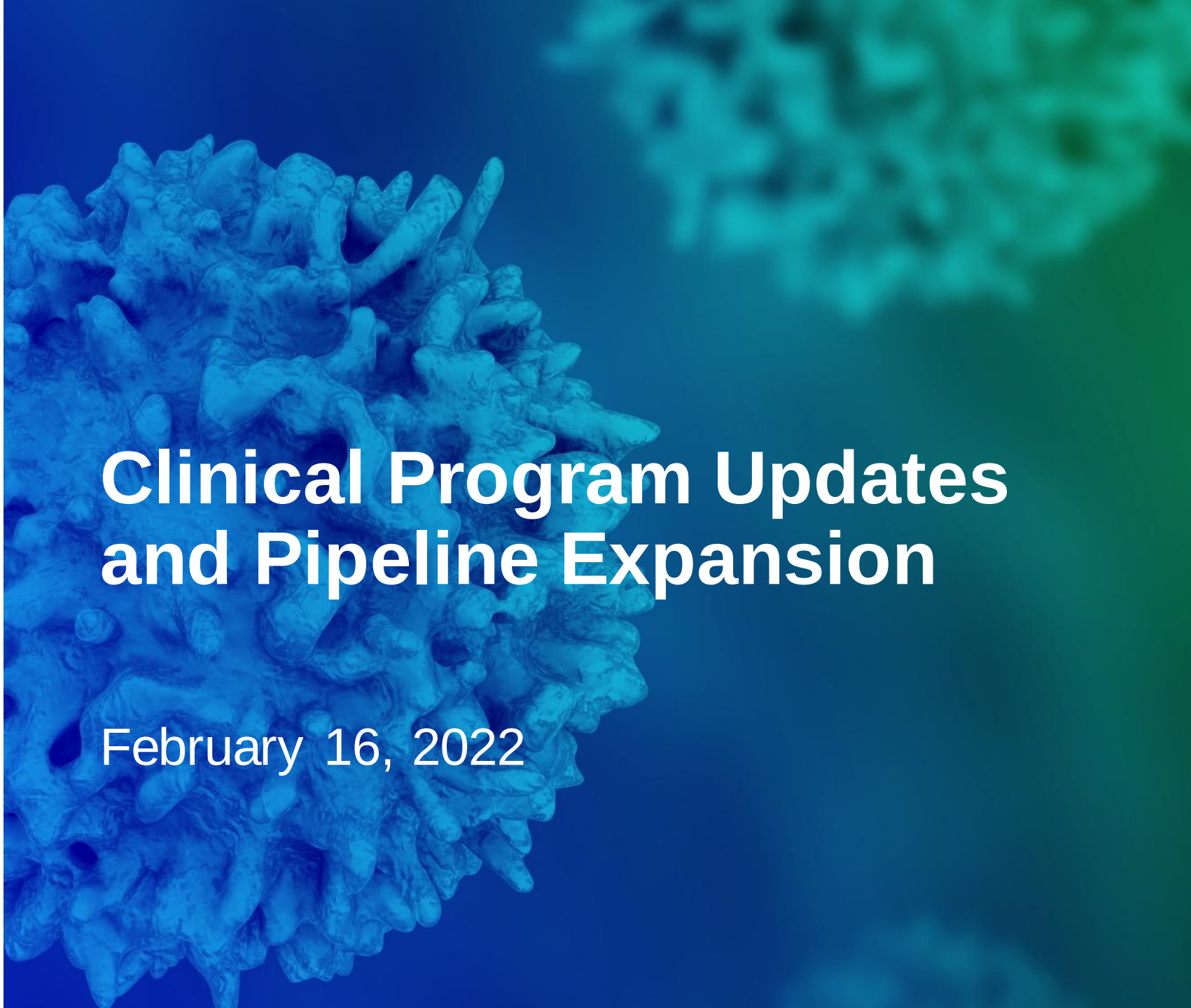
MARKER Therapeutics

Clinical Program Updates and Pipeline Expansion



February 16, 2022

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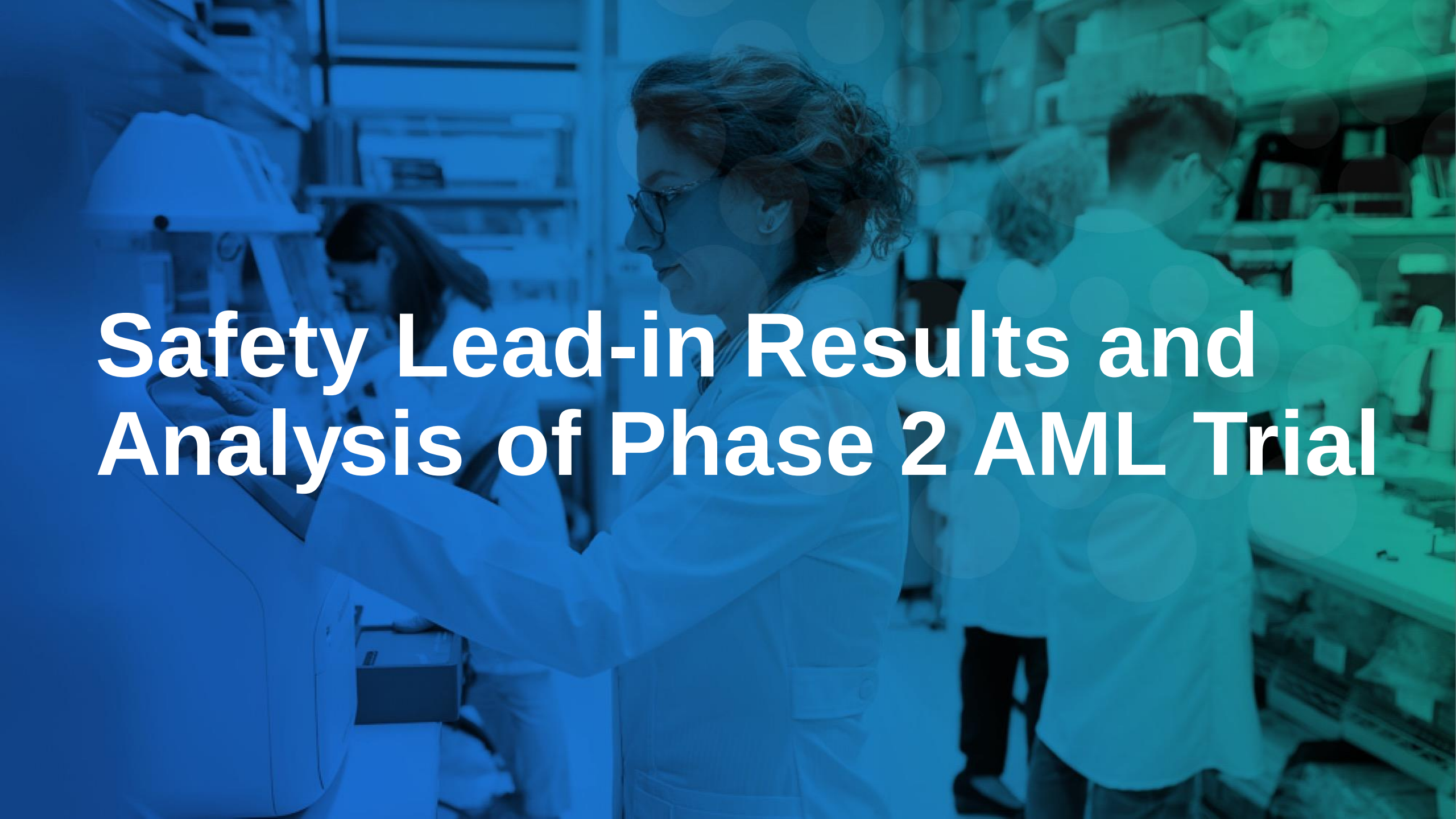
Agenda

- **Welcome and introduction**
- **Marker safety lead-in patient results and analysis of phase 2 AML trial**
- **Improvements to T cell manufacturing process**
- **Pipeline updates**

Executive Summary

- **MT-401 generated a clinical response in an MRD+ patient in the safety lead-in stage of Marker's phase 2 AML trial**
  - After receiving MT-401, an MRD+ patient converted to MRD-
  - Targeted antigen-specific T cells from MT-401 inversely correlate with MRD, suggestive of anti-tumor activity
  - Epitope spreading occurred in the patient with proliferation of non-targeted antigens, an indication of significant contribution of the endogenous immune system
- **Developed additional process manufacturing improvements that result in an improved MT-401 and other products to bolster tumor killing**
  - Increased antigen specificity and diversity
  - New manufacturing process produces a product that is 4x more potent which greatly improves tumor killing potential
  - Manufacturing time is further reduced to 9 days; previously reduced manufacturing time from 36 days (BCM ADSPAM trial) to 20 days (current Marker P2 trial)
    - Reduced manufacturing time provides opportunity to focus and treat MRD+ patients; MRD+ patients have a short window before becoming full relapse patients
- **Marker intends to initiate additional clinical trials in 2023**
  - Pancreas, lymphoma and an off-the-shelf ("OTS") AML/MDS trial
  - Plan to file INDs for pancreas and lymphoma trials in 2022
  - OTS AML/MDS trial approved under current AML IND. Potential 1st patient dosed in 2023
  - Undertaking pre-clinical studies for a 12-antigen product as well as combination therapies



Safety Lead-in Results and Analysis of Phase 2 AML Trial

Phase 2 AML Study Overview

180 Patient Phase 2 AML Trial

Group 1 (adjuvant):
120 Patients

Relapse-free survival (RFS)

Group 2 (active disease-frank relapse or MRD^{+}):
60 Patients

Complete remission (CR), Duration of CR (DOCR)

Safety Lead-In: 6 patients
Safety endpoint

Phase 2 AML Trial: Safety Lead-In Summary

Purpose of Safety Lead-In	Patient Population	Summary Results
• Tested safety of using a new vendor in the manufacturing process • 3 patients treated with product manufactured using legacy reagent and 3 additional patients treated with product manufactured using the new reagent	• Enrolled 6 patients total • 1 MRD+ patient • 5 frank relapse patients	• Although efficacy was not a primary endpoint, MRD+ patient converted to MRD- • No dose-limiting toxicities • No objective response from frank relapse patients • Safety lead-in satisfied safety requirements with FDA and main Phase 2 stage of the AML trial began enrolling July 2021

Clinical response in MRD+ AML patient

Safety Lead-In Cohort Characteristics

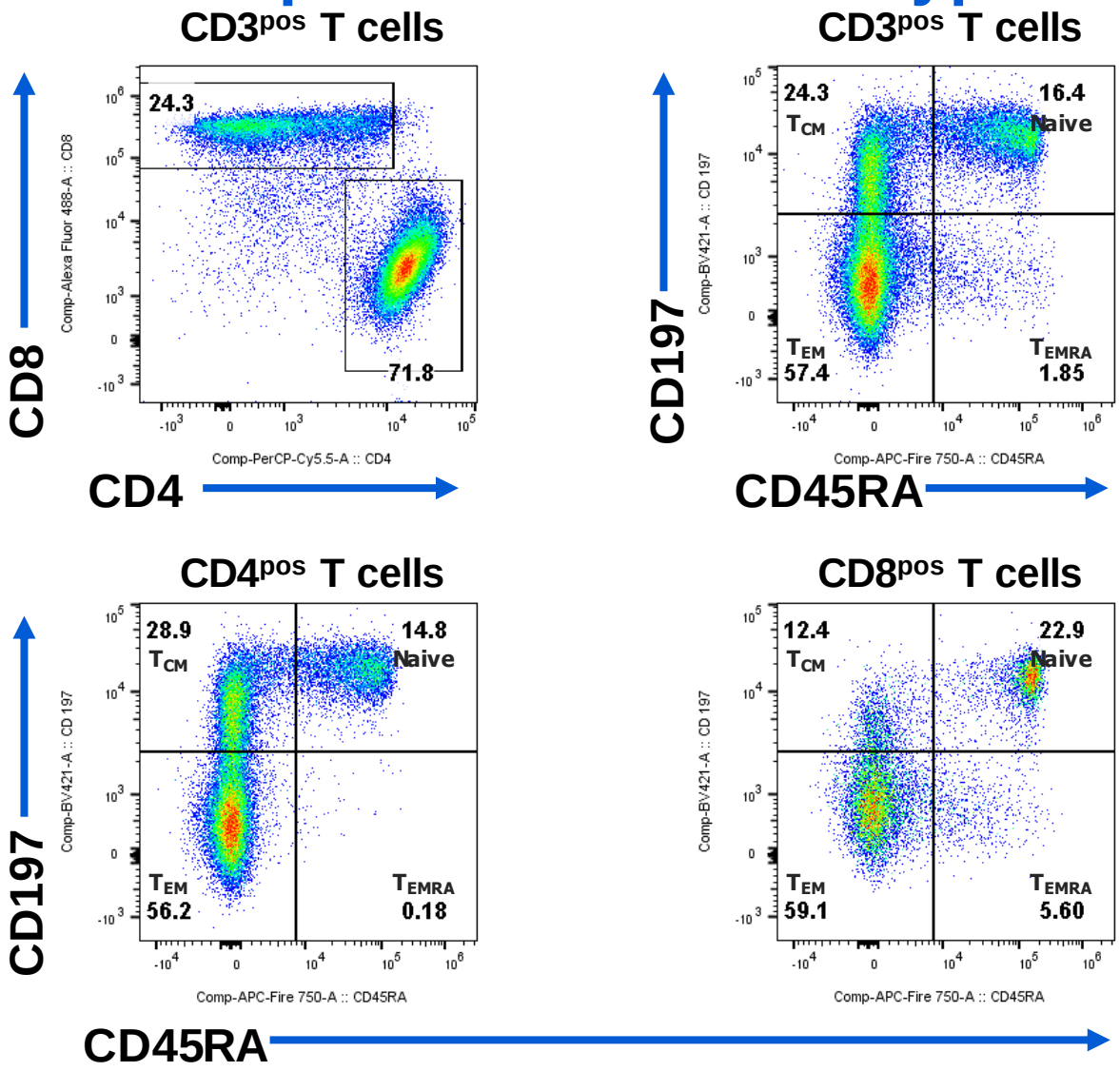
Patient Demographics	Total (N = 6)
Age	
Median (Min, Max)	52 (42, 66)
≥ 65	2
Male	2
Disease Status	
MRD+	1
Frank Relapse	5
Number of Prior Lines of Therapy (Prior to Transplant)	
1	1
2	2
3	1
4	0
≥ 5	2

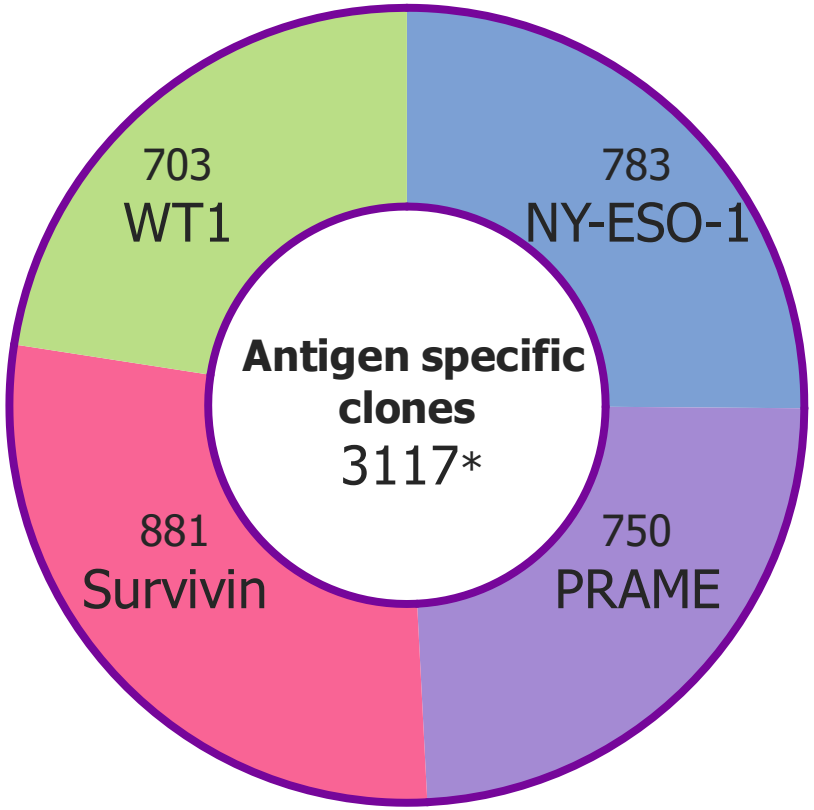
Patient #	Donor Type	Genetic Mutations	Genetic Abnormalities
1) **107-01-A**	Haplo	c-KIT	t(8;21)(q22;q22.1) [RUNX1-RUNX1T1]
2) **103-01-A**	MUD	NPM1, TET2	46XX
3) **114-01-B**	Haplo	NRAS, ETV6, RBM-15, MLLT10	46XY, wt NPM1 without or with FLT3-ITD
4) **108-01-B**	MRD	Monosomy 7, Inversion 3	46,XX, INV(3)(Q21Q26.2)[4]/45, IDEM, -7[2]/46,XX[14]
5) **101-01-A**	Haplo	NRAS, U2AFQ Mutation	Normal karyotype
6) **103-02-B**	Haplo	NRAS, TP53	ASXL1, SETBP1, SRSF2, APC

Patient 107-01-A Details

- 43yo Hispanic M w/ AML (recurrent genetic abnormalities)
- 5 prior lines of therapy (I+C, FLAG-IDA+ IC chemo, MEC +IC chemo, azacitidine, decitabine)
- Haploidentical donor
- Genetic mutations: c-KIT
- Genetic abnormalities: t(8;21)(q22;q22.1) [RUNX1-RUNX1T1]
- No dose-limiting toxicity (DLT)

T Cell Composition and Phenotype of Patient 107-01-A Product

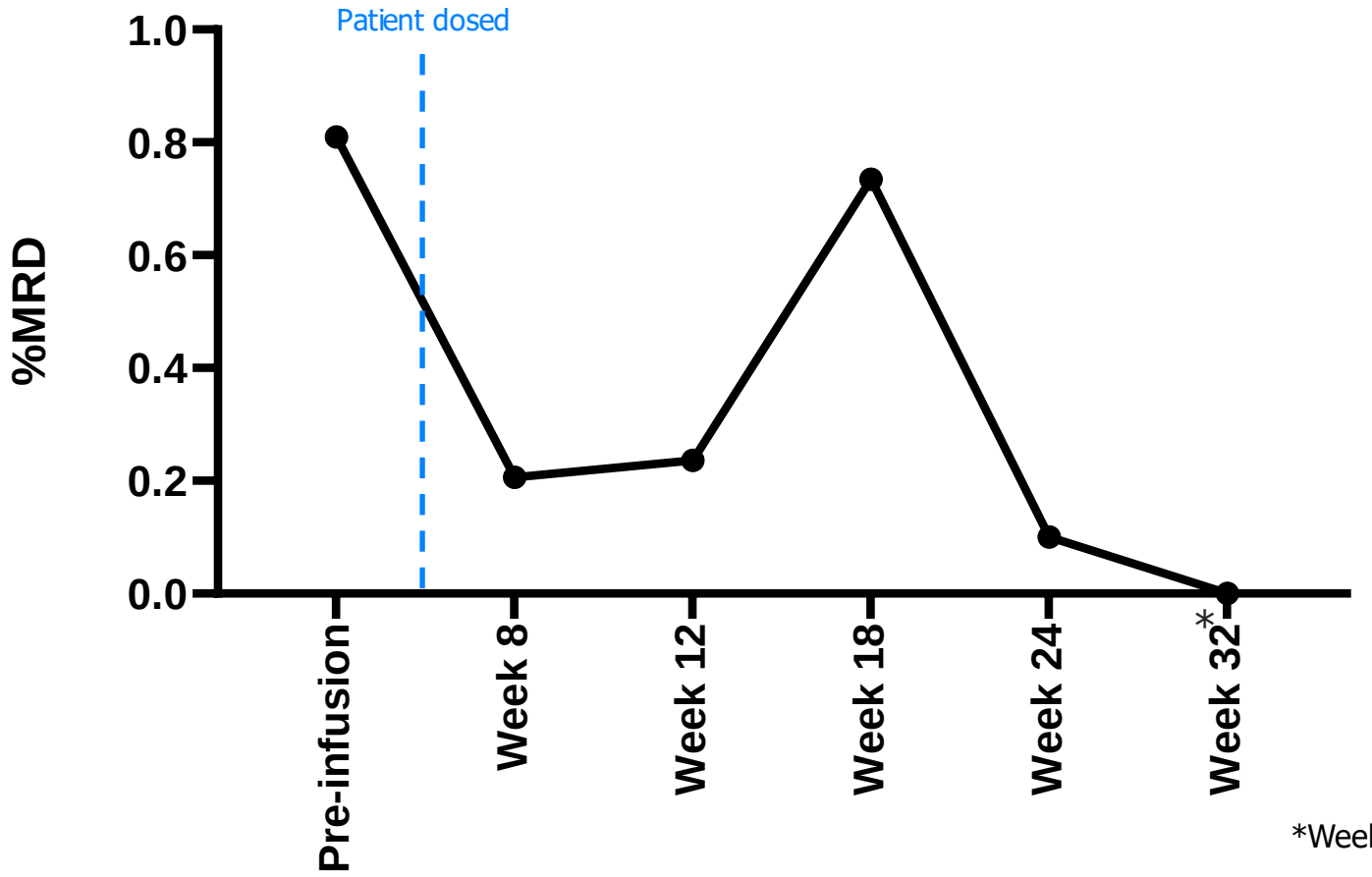




*Total number of individual clones in final product = 27,369

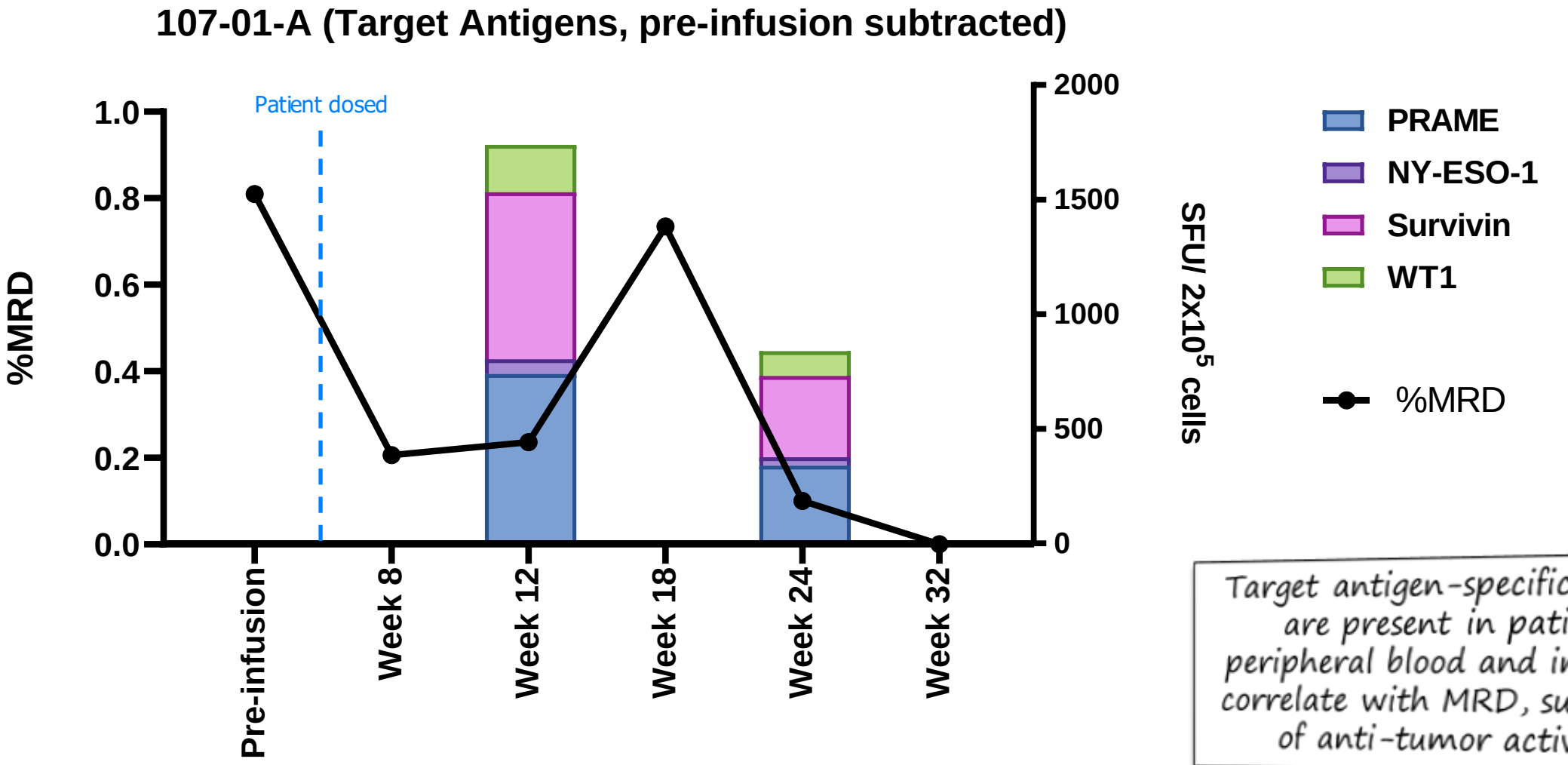
Patient product is a mixture of CD4 & CD8 T cells that are predominantly effector memory cells comprising of more than 3,000 TCRs– unlike a single TCR transgenic clone.

Disease Assessment (%MRD) of Patient 107-01-A



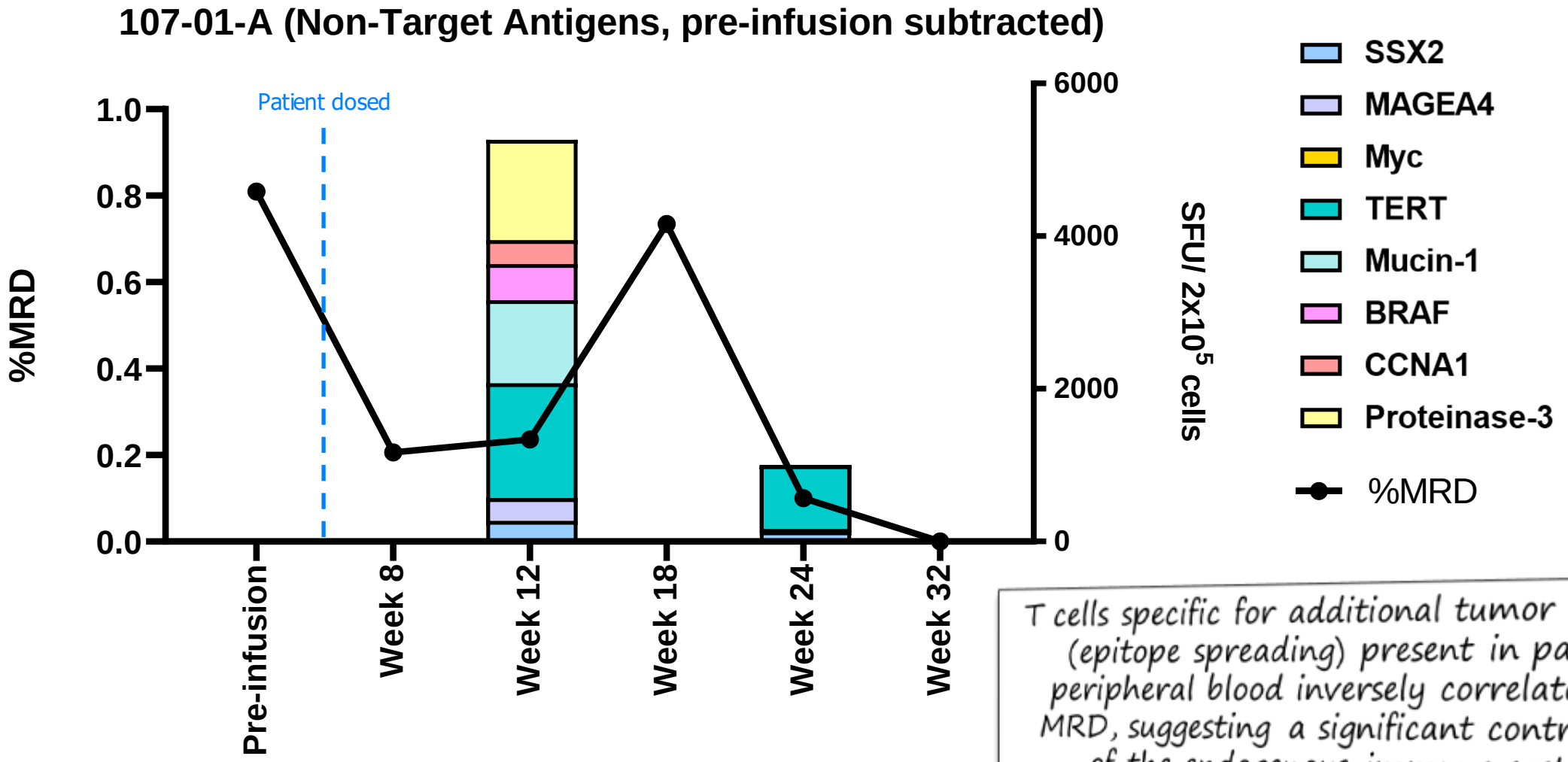
*Week 32 sample was peripheral blood instead of bone marrow.

T Cell Specificity for Target Antigens: Patient 107-01-A



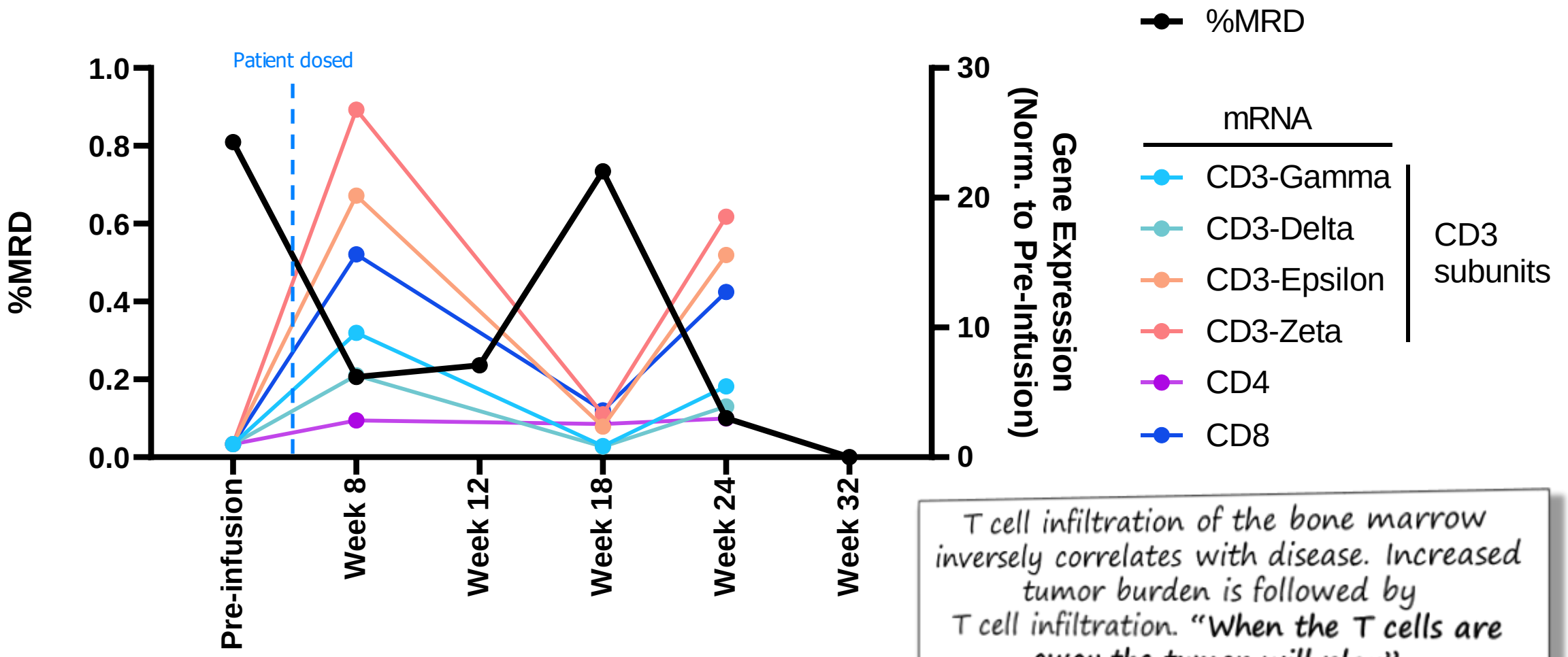
Target antigen-specific T cells are present in patient peripheral blood and inversely correlate with MRD, suggestive of anti-tumor activity.

T Cell Specificity for Non-Target Antigens: Epitope Spreading: Patient 107-01-A



T cells specific for additional tumor antigens (epitope spreading) present in patient peripheral blood inversely correlate with MRD, suggesting a significant contribution of the endogenous immune system.

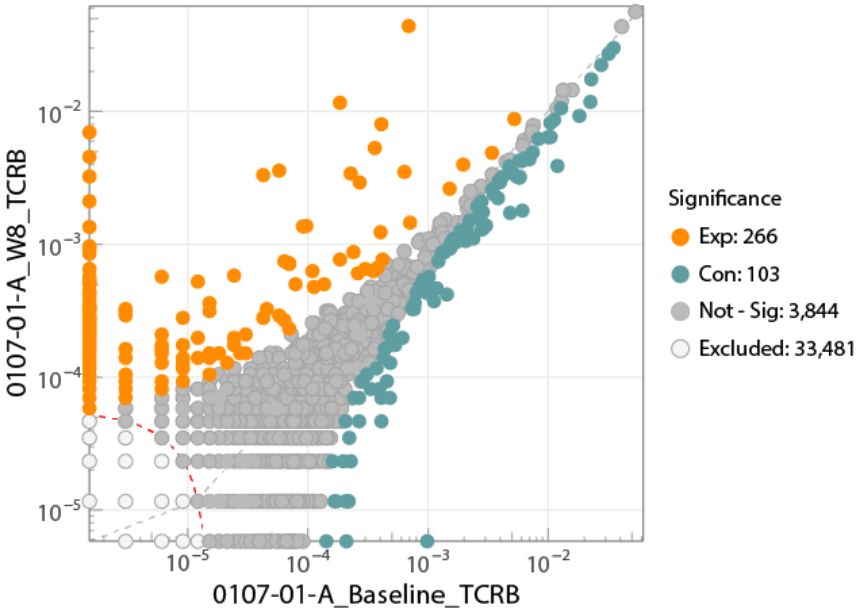
T Cell Gene Expression Within Patient 107-01-A Bone Marrow Detected by Next Generation Sequencing



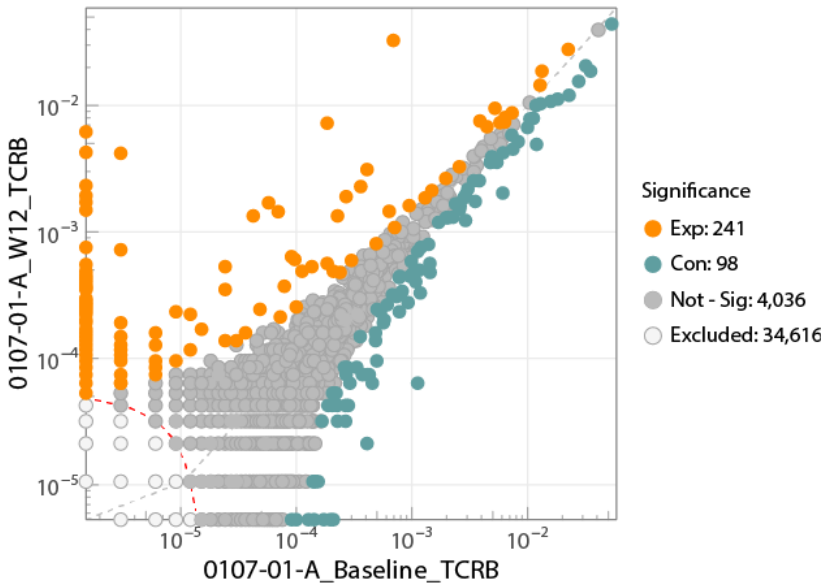
T cell infiltration of the bone marrow inversely correlates with disease. Increased tumor burden is followed by T cell infiltration. "**When the T cells are away the tumor will play**".

Expansion of Peripheral T Cell Clones in Patient 107-01-A Compared to Pre-infusion

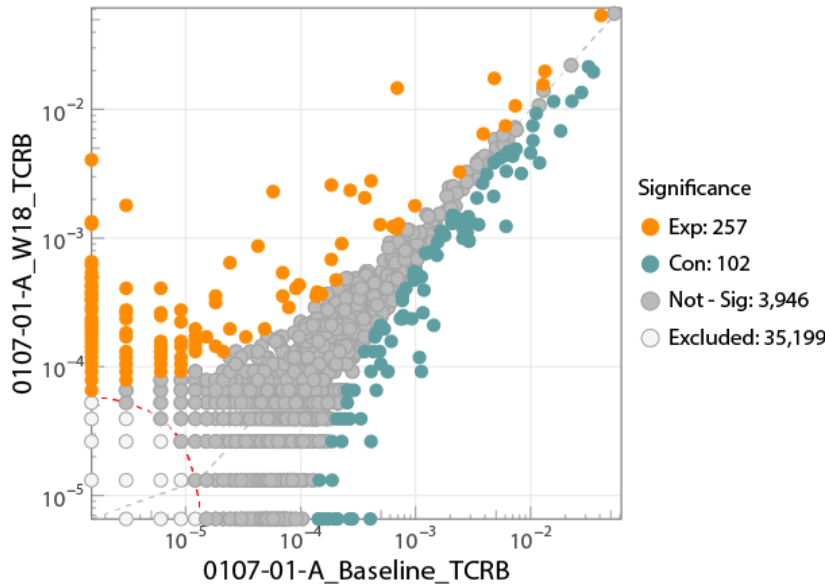
Week 8



Week 12



Week 18



- Expanded Clones
- Contracted Clones

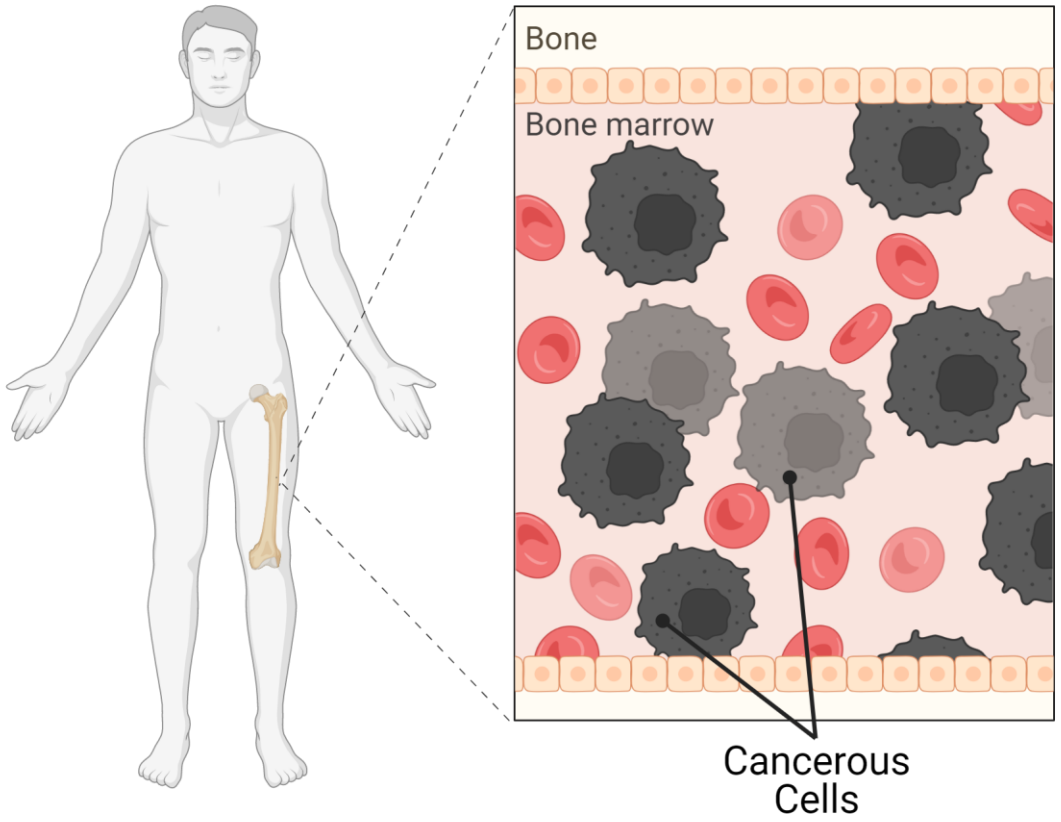
Clonal expansion/contraction of T cells can be observed throughout patient immune monitoring using TCR sequencing. A significant number of different T cell clones expand in the patient after product infusion.

Details of Patient Tumor Dynamics are Revealed Through Next Generation Sequencing

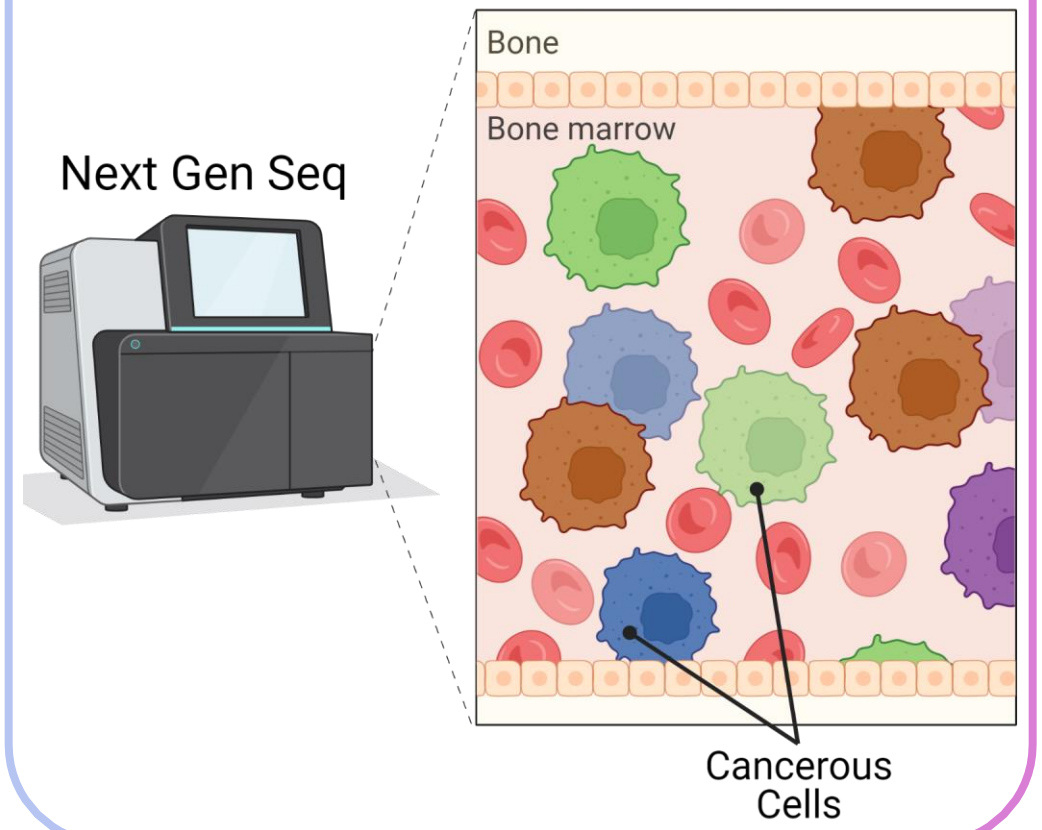
AML Patient

Bone Marrow Biopsy

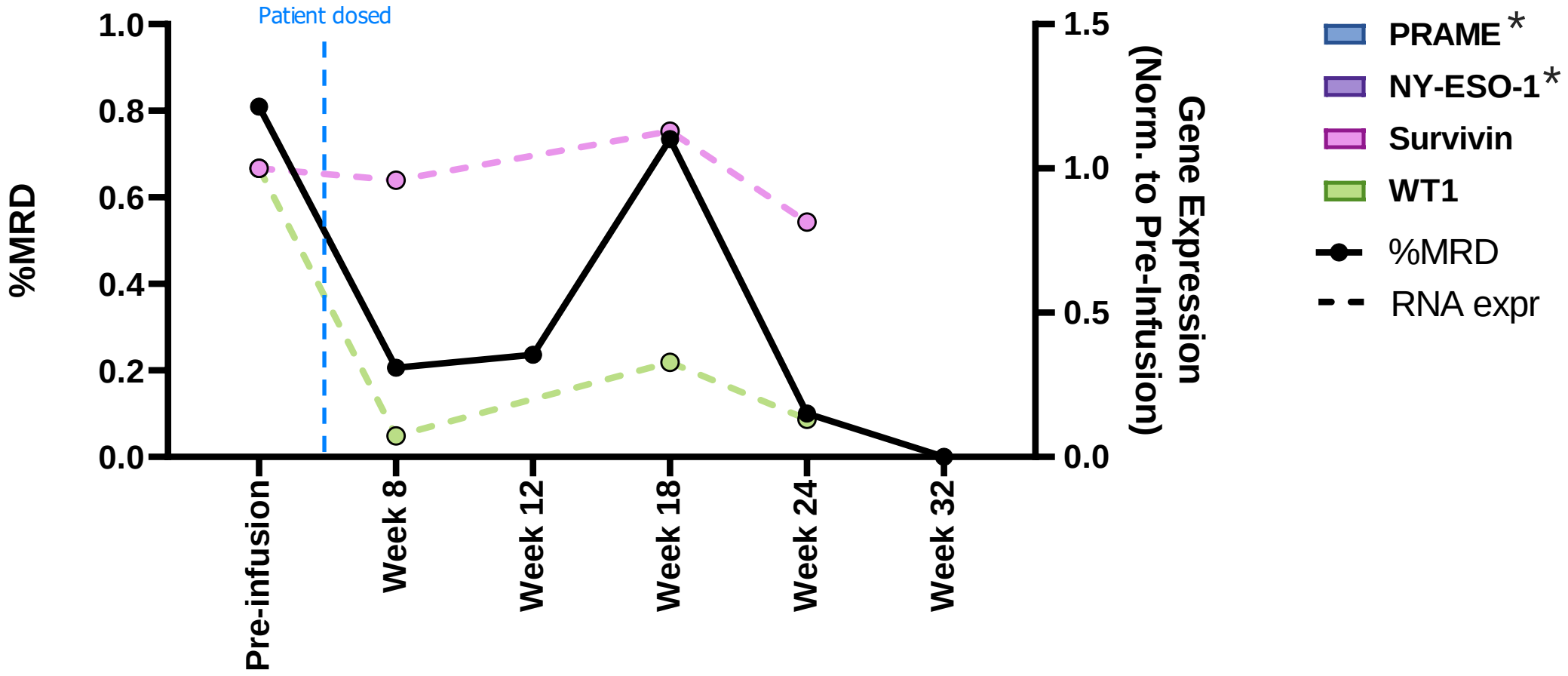
MRD testing provides "black and white" view of patient cancer



Next Generation Sequencing provides gene/antigen expression within tumors

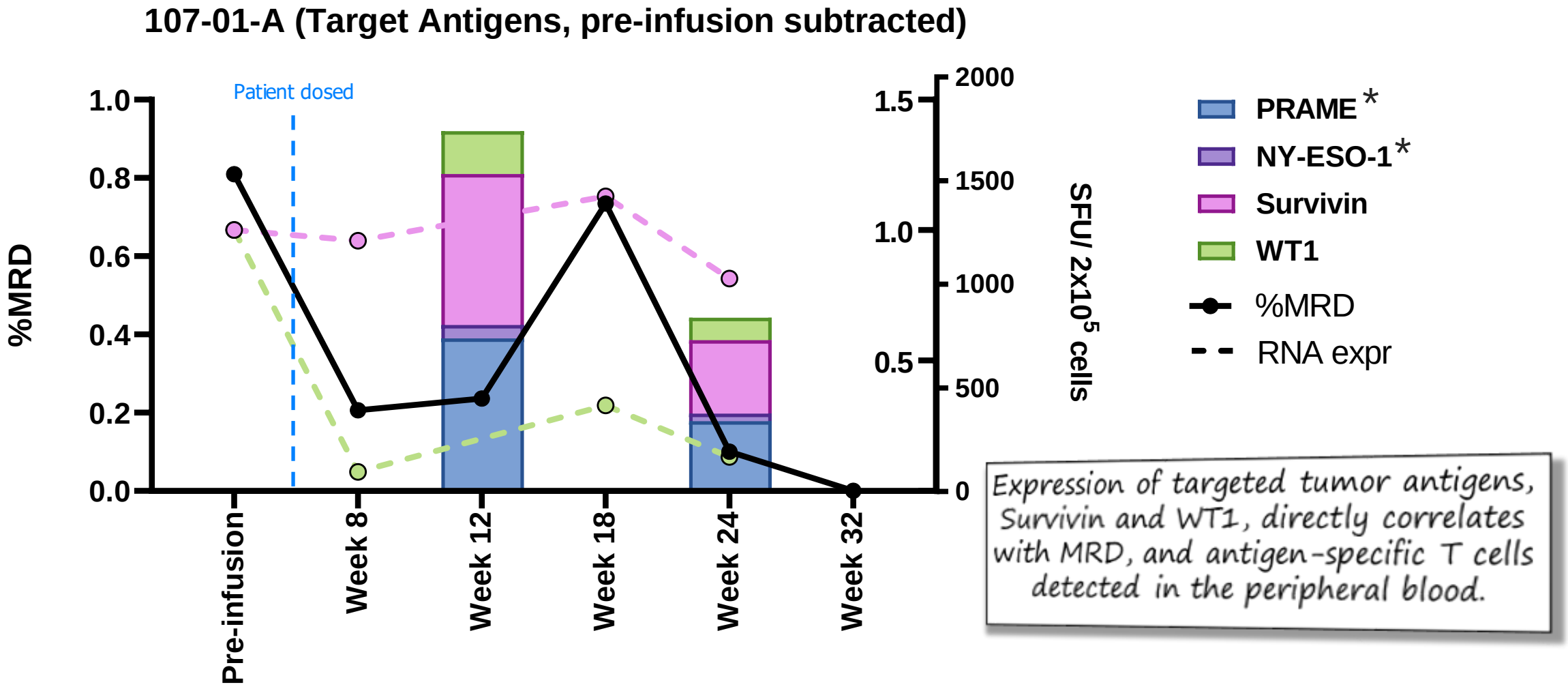


Antigen Expression in Bone Marrow of Patient 107-01-A



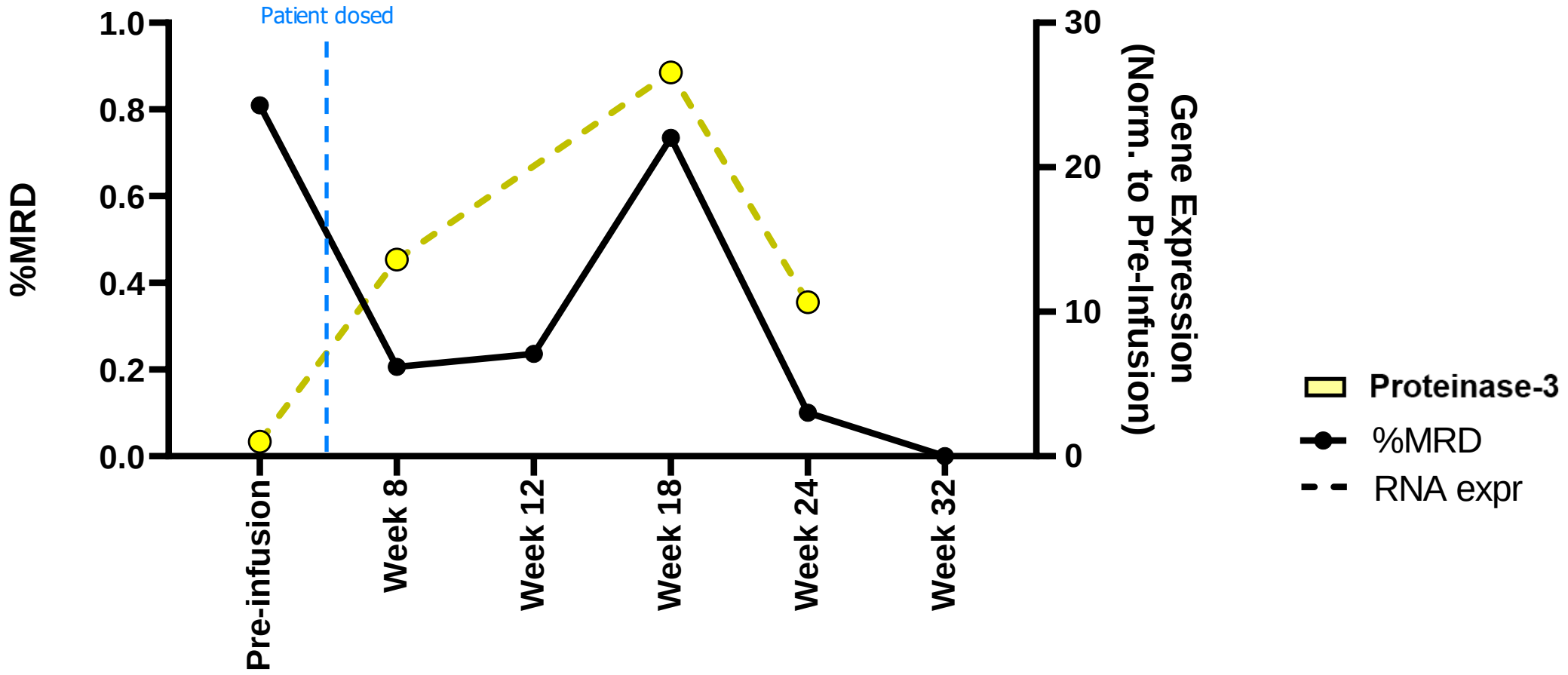
* PRAME & NY-ESO-1 transcripts not detected by mRNA-seq

Antigen Expression in Bone Marrow of Patient 107-01-A vs T Cell Specificity

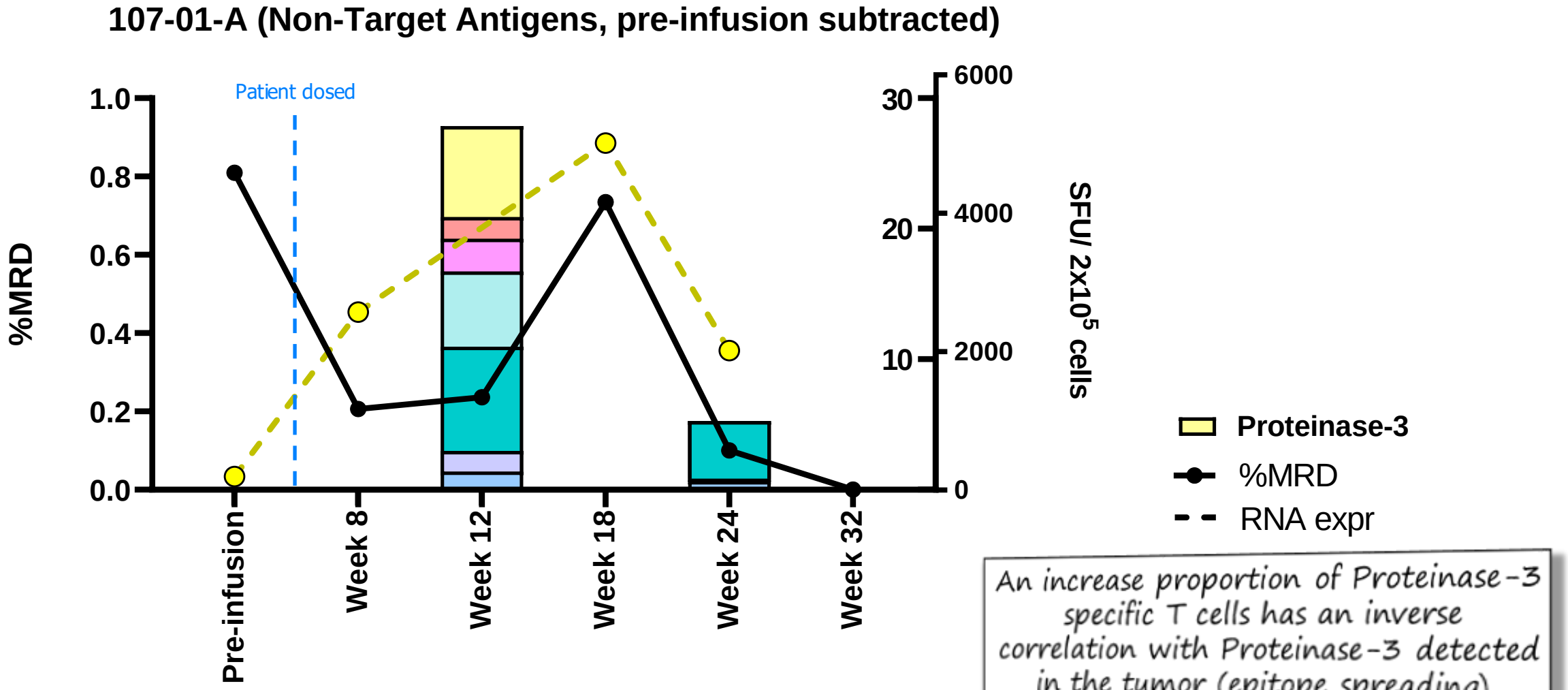


* PRAME & NY-ESO-1 transcripts not detected by mRNA-seq

Antigen Expression in Bone Marrow of Patient 107-01-A: Non-target Antigens

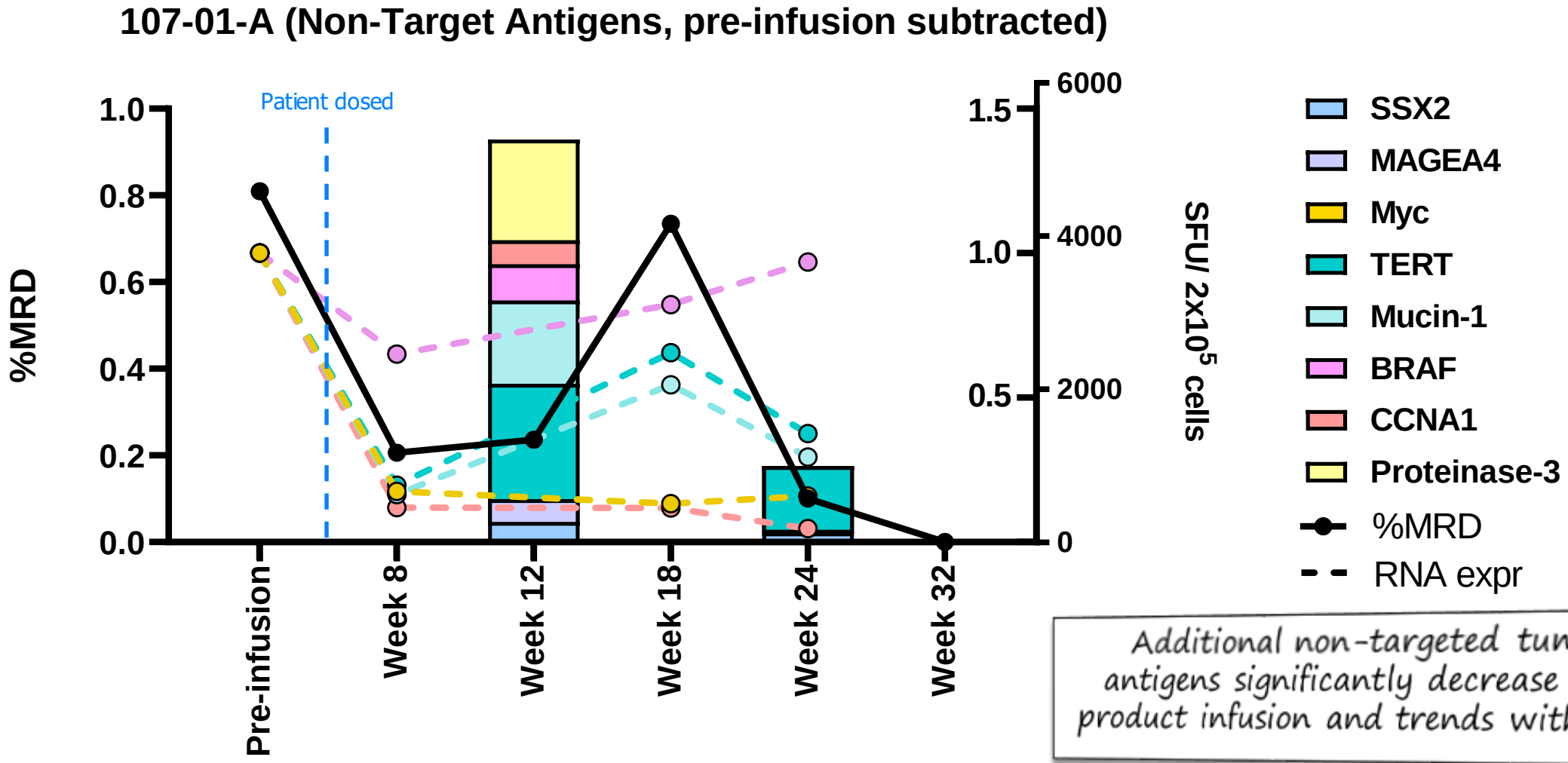


Antigen Expression in Bone Marrow of Patient 107-01-A vs T Cell Specificity – Non-target Antigens



An increase proportion of Proteinase-3 specific T cells has an inverse correlation with Proteinase-3 detected in the tumor (epitope spreading).

Antigen Expression in Bone Marrow of Patient 107-01-A vs T Cell Specificity – Non-target Antigens



Additional non-targeted tumor antigens significantly decrease after product infusion and trends with MRD.

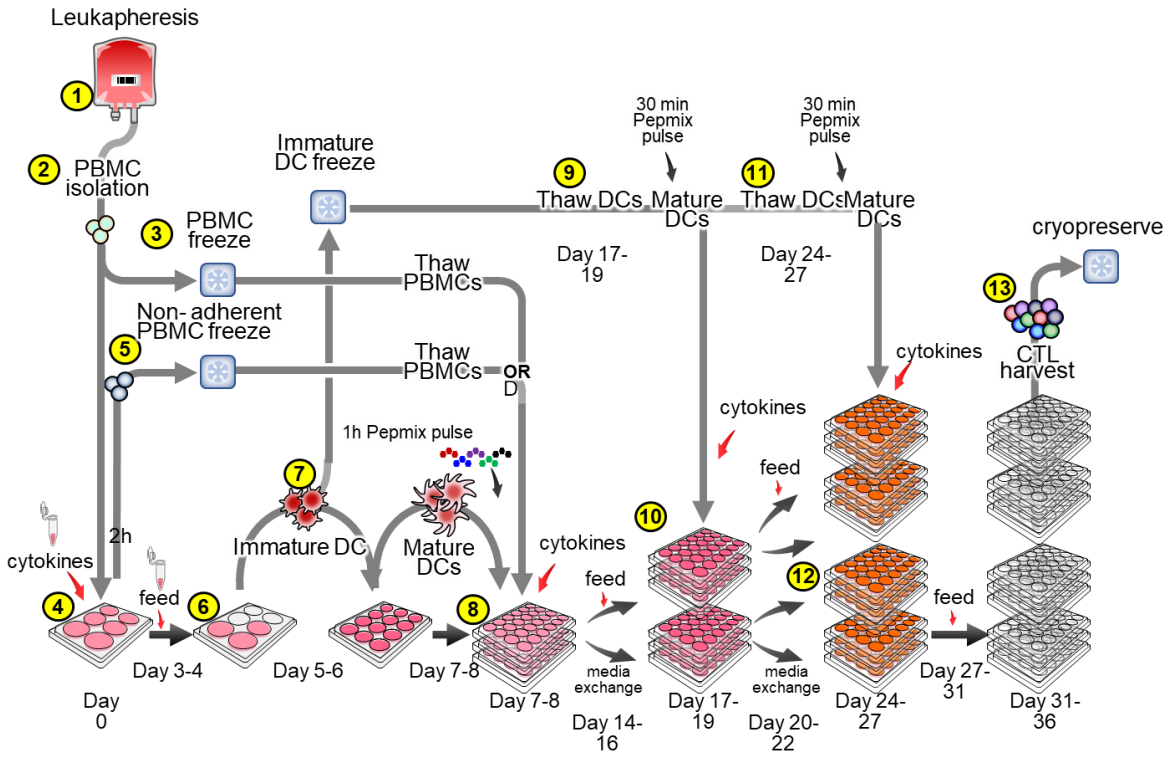
Takeaways from the Safety Lead-In of Phase 2 AML Trial

- **Encouraging overall safety**
  - No CRS or neurotoxicity
  - Safety data confirms the results from Phase 1 / 2 trials at BCM across over 150 patients
- **The immuno-monitoring data indicates the evidence of epitope spreading after infusion of MT-401**
- **These results support the study of MT-401 in AML patients particularly those that are MRD+**

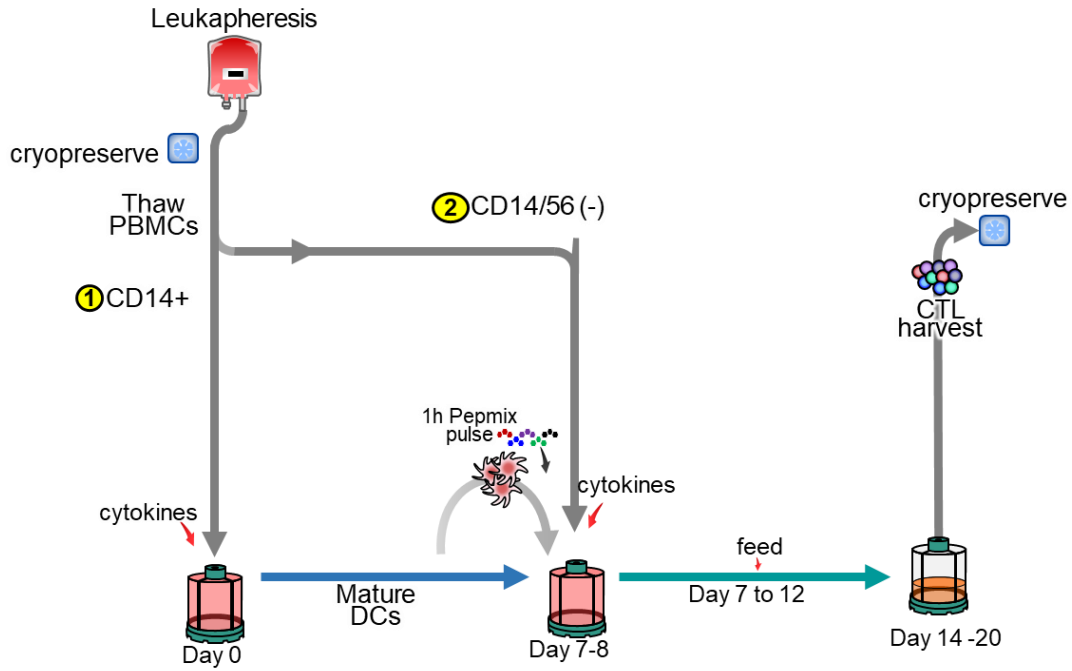
T Cell Manufacturing Process Improvements

Current Marker Process is Improved Over Initial BCM Process

BCM Process
36 days



Current Marker Process
20 days



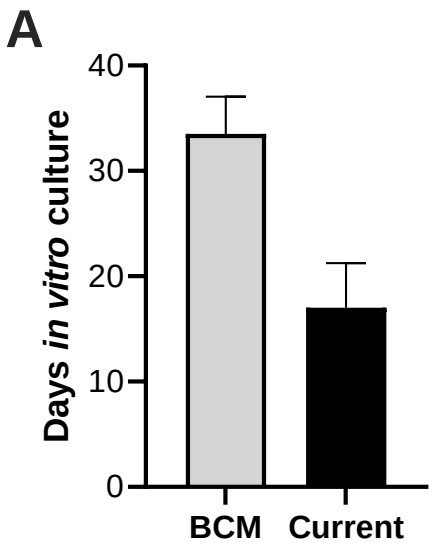
Current Marker Process is Improved over Initial BCM Process

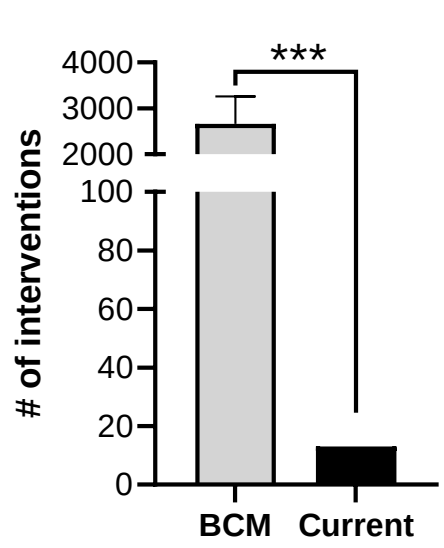
A – Reduced *in vitro* T cell culture time

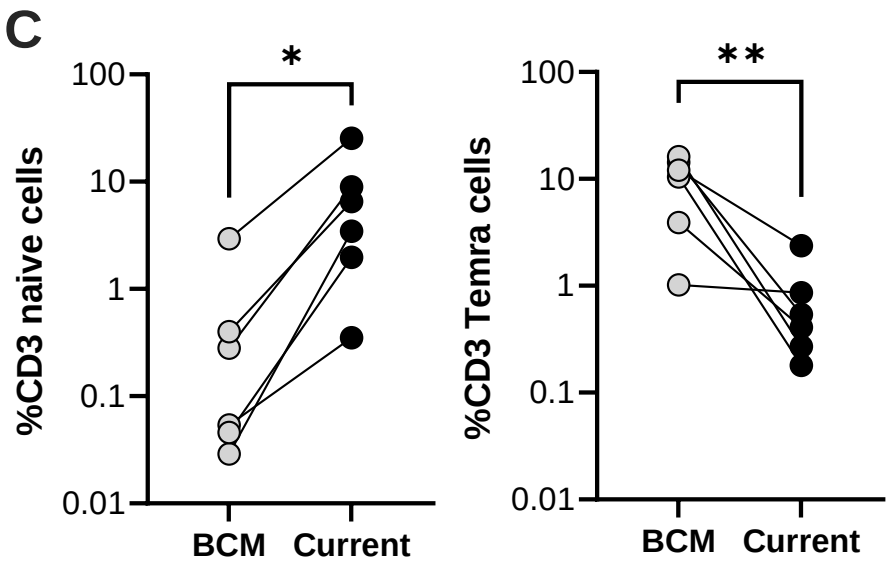
B – Decreased # of interventions

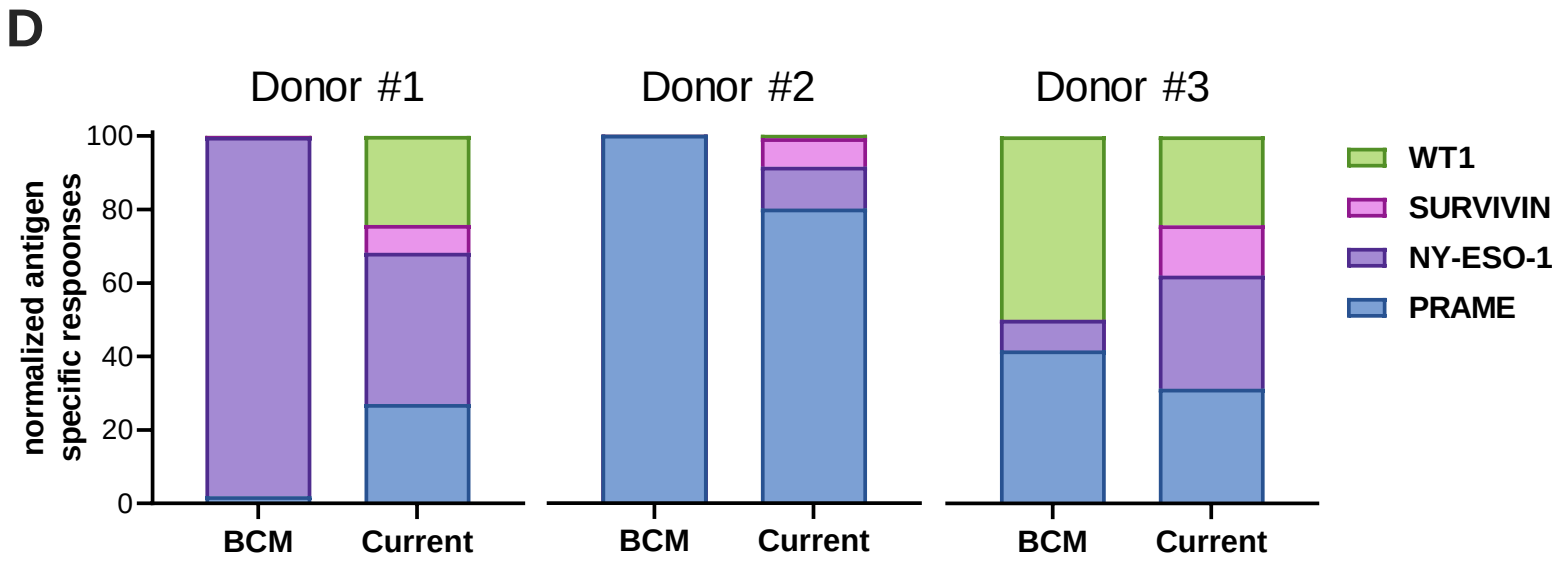
C – Increased T cell phenotype

D – Increased antigen diversity







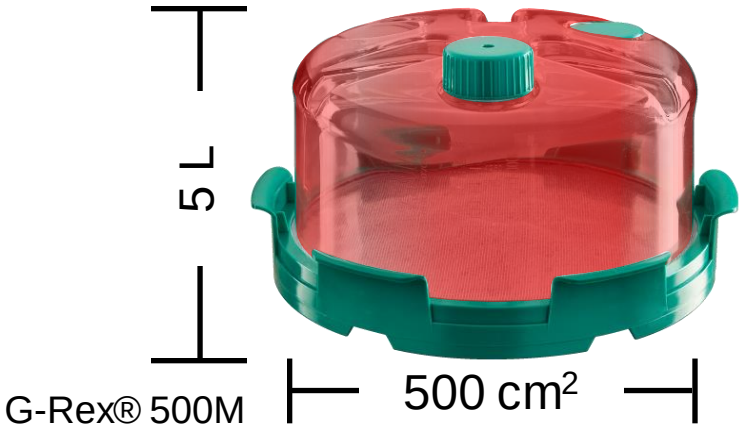


Streamlining the Manufacturing Process for Larger-Scale Production

Culture Initiation

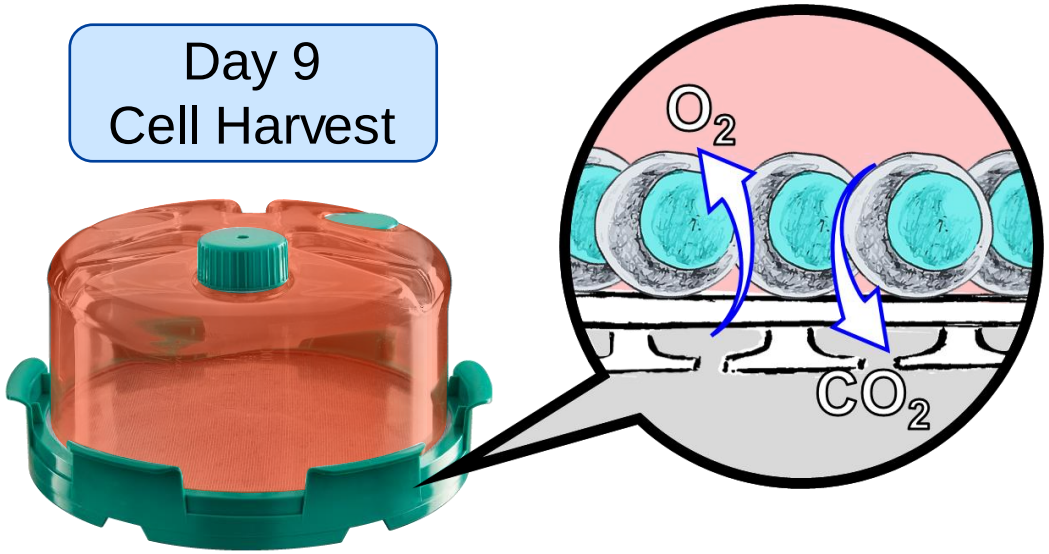
Expansion of mTAA-specific T Cells

Day 9 Cell Harvest



Incubation

No Interventions

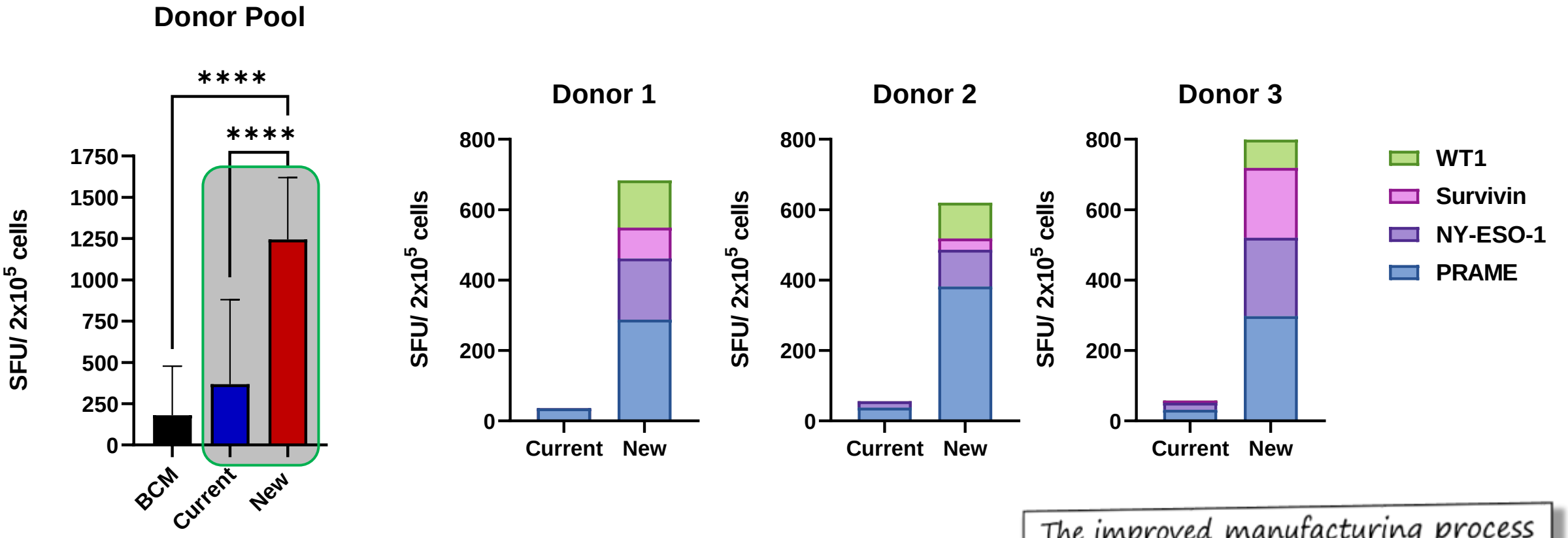


- PBMCs & APCs
- 5 L of media
- Cytokines
- mTAA peptides

MT-401

2×10^{10} cells

The Streamlined Manufacturing Process Further Increases T Cell Specificity: Six-fold Increase in Magnitude

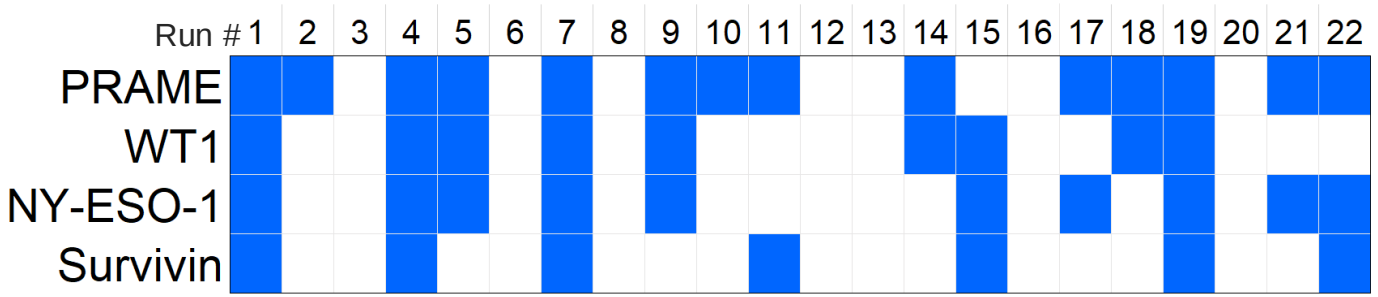


The improved manufacturing process developed by Marker has significantly increased antigen specificity and diversity over the current processes.

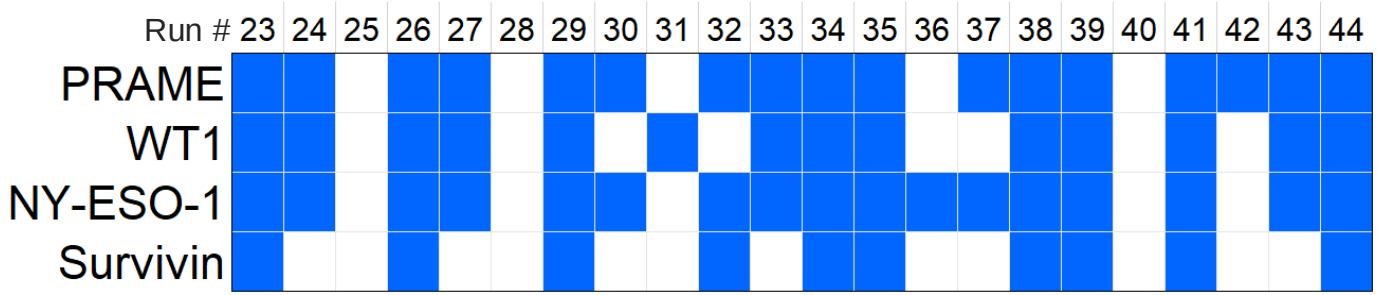
Process Evolution Yields Increased Diversity of T Cell Specificity Against All 4 Tumor Targets

Product positive for antigen

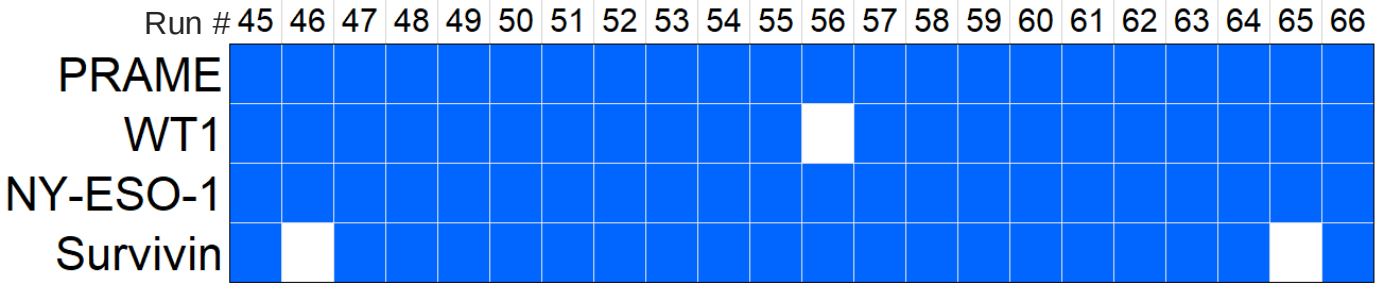
Product negative for antigen



BCM process



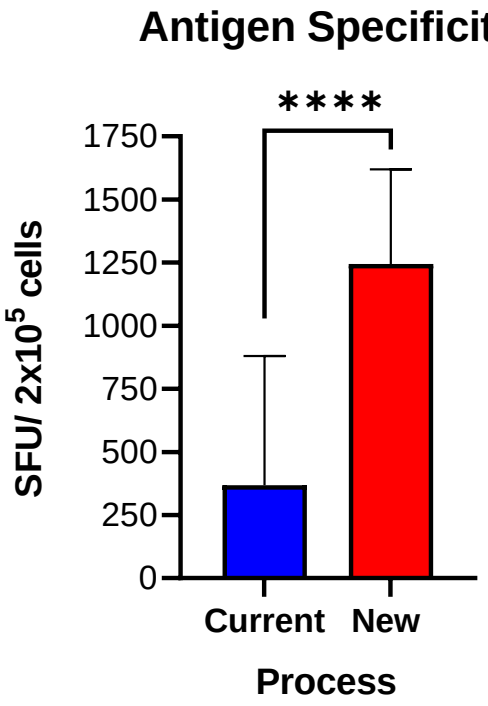
Current process

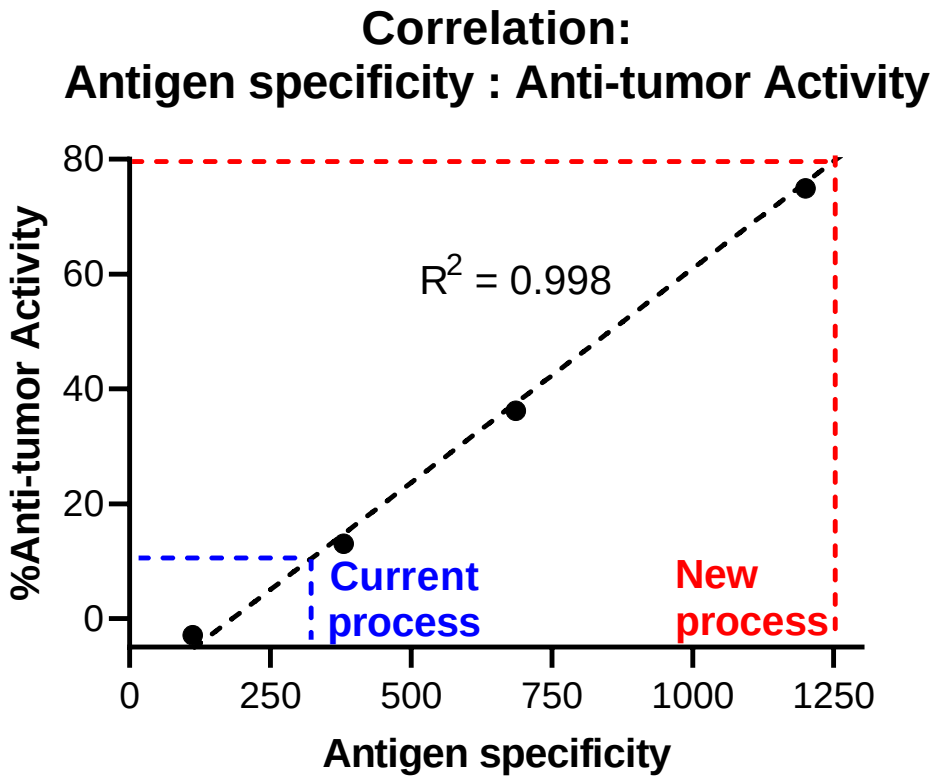


New (9D) process

Process improvements by Marker have resulted in an increased number of products with specificity for multiple tumor antigens.

Increased Antigen Specificity of mTAA-specific T Cells Correlates with Increased Anti-tumor Activity



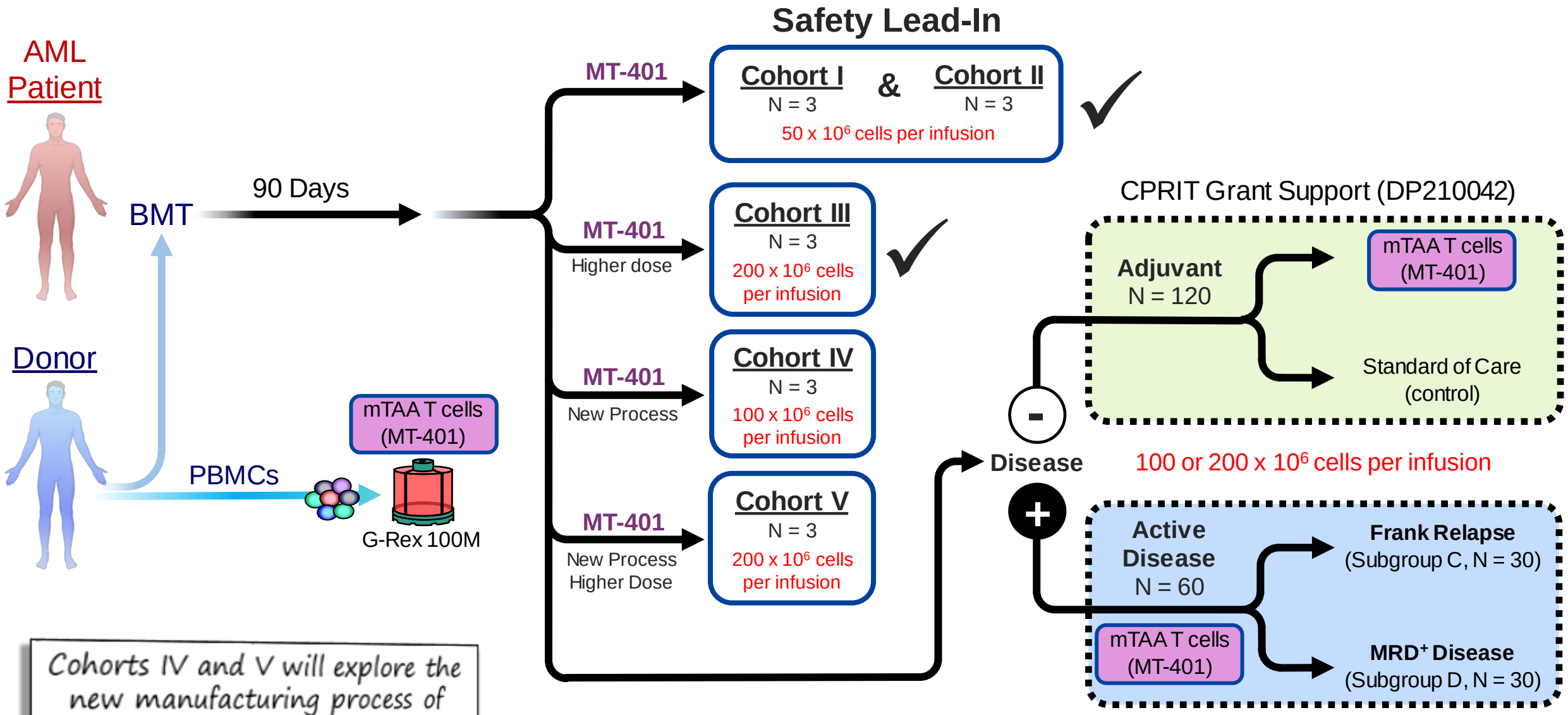


In vitro coculture experiments have demonstrated a linear correlation between anti-tumor activity and antigen specificity of mtAA T cells. Products manufactured with the new process are 4X more potent.

Takeaways from Development of New T Cell Manufacturing Process

- **New manufacturing process has the potential to improve patient outcomes**
  - Increased target antigen specificity and diversity results in a more potent product
  - Increases tumor killing potential of our products
- **Manufacturing time shortened to 9 days while greatly improving the product quality**
  - Demonstrated from prior clinical trials that patient outcomes are improved the sooner the patient receives the therapy
  - Addresses ability to target time-sensitive MRD+ patients

Phase 2 AML Study Schema



Cohorts IV and V will explore the new manufacturing process of MT-401 in patients with AML.

Pipeline Updates

MARKER Therapeutics

Scalable Production for an Off-The-Shelf Product

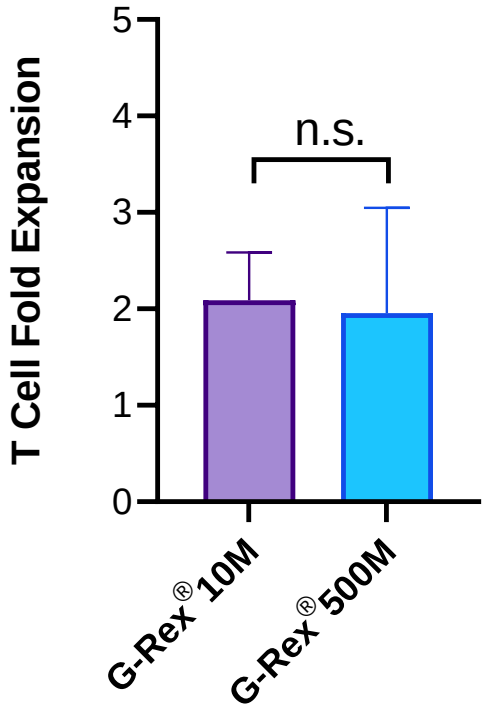


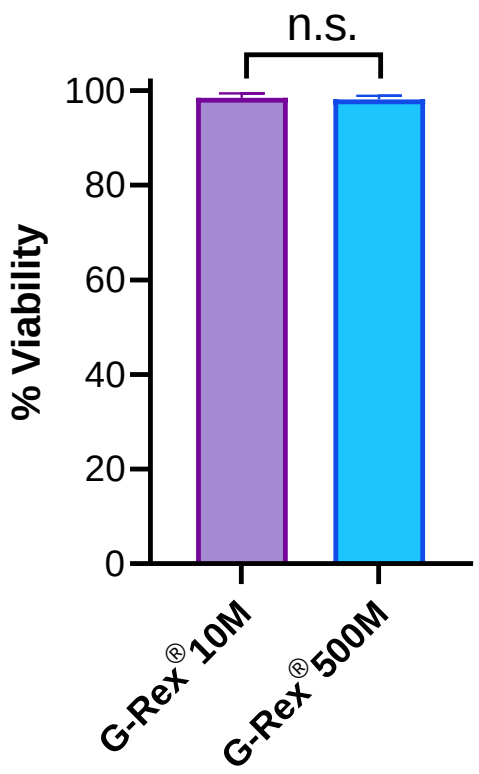


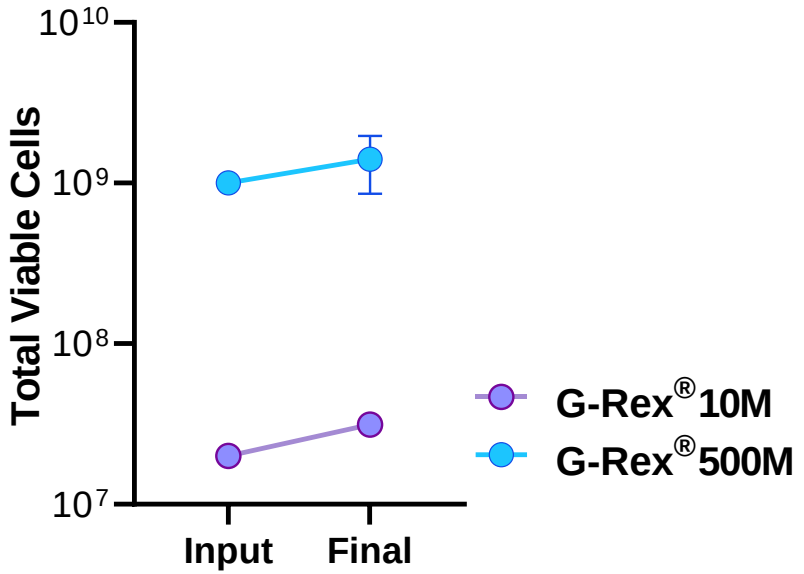
Manufacturing Scale-up for Large Scale Production Using G-Rex® 500

G-Rex® 10M

G-Rex® 500M

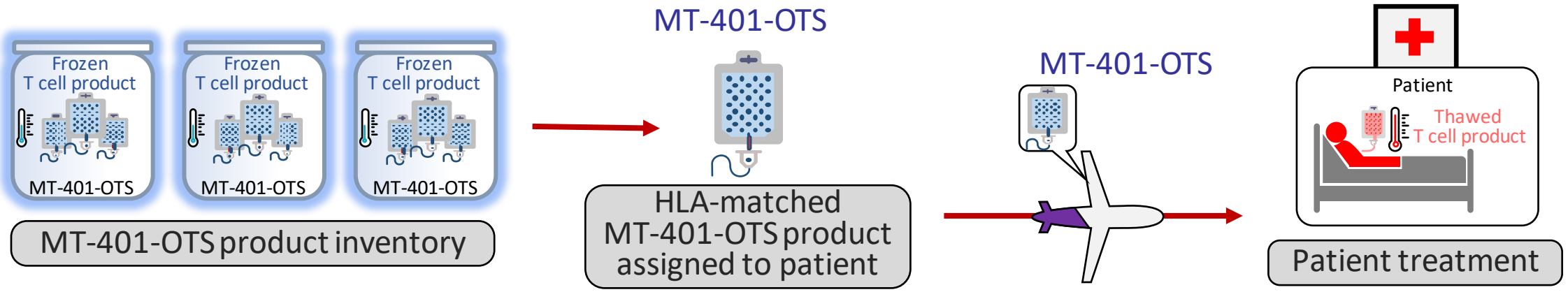






The new manufacture process is robust allowing for product scale up

A Scalable Manufacturing Process Allows the Generation of an On-Demand, Off-the-Shelf MT-401 Product



Benefits of OTS Program

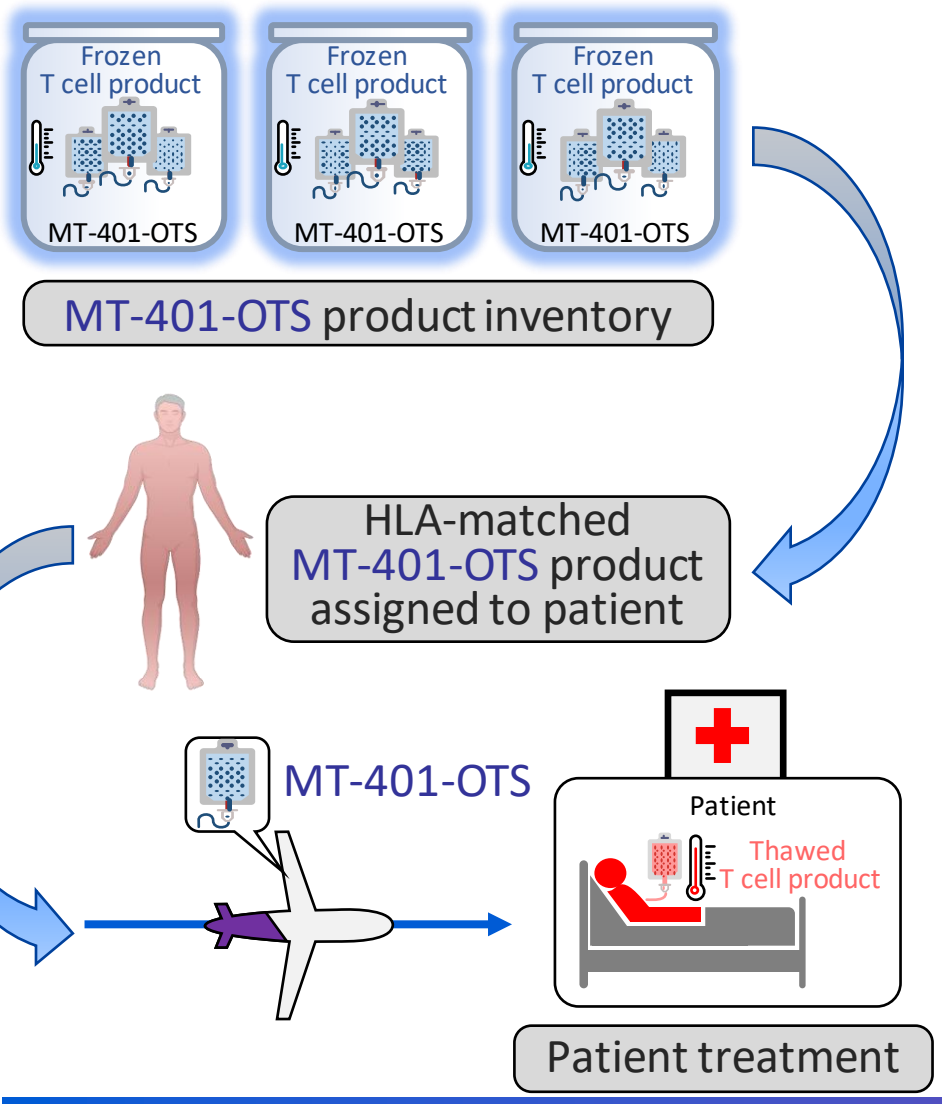
Rapid patient treatment (72h)

Cost benefit - product scalability

Ability to extend to other clinical indications

Clinically proven strategy in virus-specific T cells

Relapsed AML/MDS Off-the-Shelf Study Schema: Dose Escalation



Cohort I
N = 3 – 6
50 x 10^6 cells
single dose

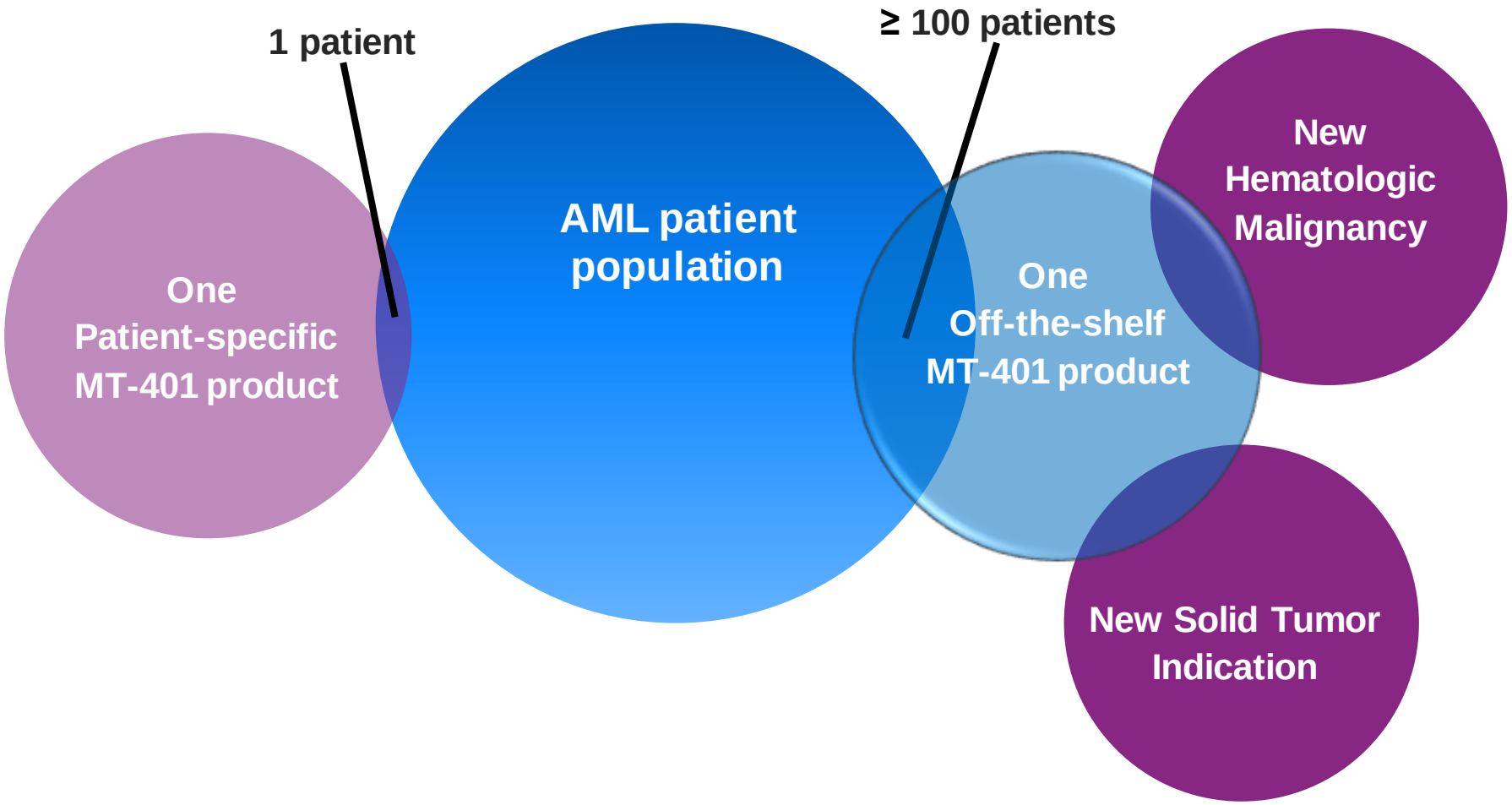
Cohort II
N = 3 – 6
100 x 10^6 cells
single dose

Cohort III
N = 3 – 6
100 x 10^6 cells
Once every 2 weeks
for 2 doses

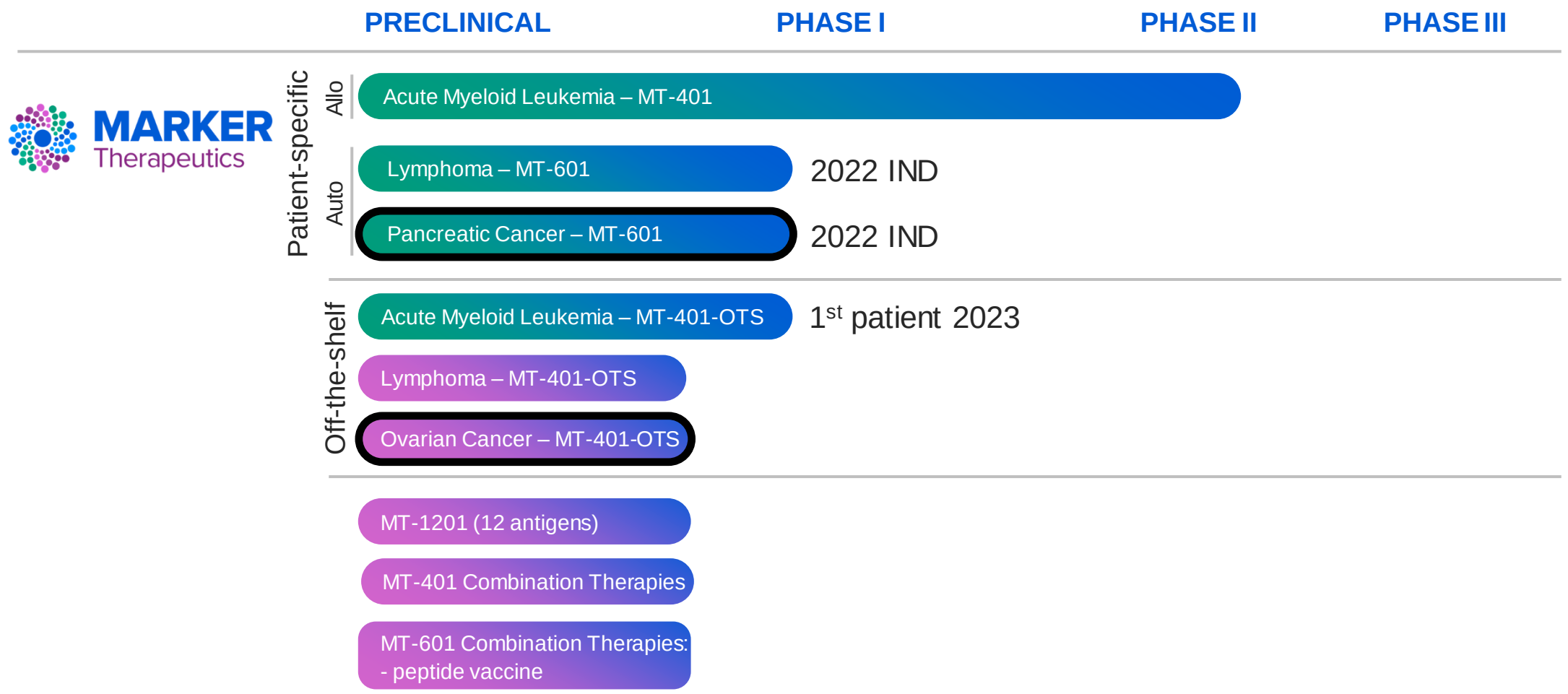
Cohort IV
N = 3 – 6
100 x 10^6 cells
Once every 2 weeks
for 4 doses

A dose escalation study begins the Off-the-Shelf MT-401 Study in AML/MDS.

An Off-the-Shelf Program Expands Treatment Capabilities



MultiTAA-Specific T Cell Platform Leading with AML



Key Milestones

Event	Expected Timing
• Begin implementing new manufacturing process into Phase 2 AML trial	Q1 2022
• Complete dose escalation for cohorts IV and V in Phase 2 AML trial under new manufacturing process	Q3 2022
• Preliminary topline readout of Group 2 patients in Phase 2 AML under prior manufacturing process	Q1 / Q2 2022
• Open main Phase 2 of AML trial under new manufacturing process	Q3 2022
• Enroll 10 patients in Phase 2 AML trial under new manufacturing process	Q4 2022
• Complete cell inventory for OTS program	Q4 2022
• Submit IND for pancreas trial	Q4 2022
• Submit IND for lymphoma trial	Q4 2022