Gamma-delta T cell engagers for next-generation cancer therapeutics

Investor Presentation

September 2024

Legal Disclosure: Forward-looking Statements

This presentation contains statements that constitute forward-looking statements. Many of the forward-looking statements contained in this presentation can be identified by the use of forward-looking words such as “anticipate,” “believe,” “could,” “expect,” “should,” “plan,” “intend,” “estimate” and “potential,” and similar terms and phrases. Forward-looking statements appear in a number of places in this presentation and include, but are not limited to, statements regarding our intent, belief or current expectations, including statements relating to the timing of the initiation of the clinical trials, including the expansion phase of the Phase 1 trial to evaluate LAVA 1207 in combination with KEYTRUDA®, the timing of regulatory submissions, including the Phase 1 trial of LAVA-1266 in AML and LAVA's cash runway and the sufficiency of resources to pursue development. Forward-looking statements are based on our management’s beliefs and assumptions and information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors. These risks and uncertainties include, among other things; the timing and results of our research and development programs, preclinical studies and clinical trials, including the availability of data therefrom, expectations regarding enrollment in clinical trials, the timing of our clinical trial for LAVA-1207, and the submission of INDs or CTAs for our other product candidates; the expected safety profile of LAVA’s product candidates; our ability to develop and obtain regulatory approval for and commercialize any of our product candidates; potential uses of LAVA’s product candidates to treat various tumor targets, including AML, MDS, mCRPC, CRC, NSCLC, and HNSCC, and improve patient outcomes, the ability of low-dose interleukin-2 to increase the number of Vγ9Vδ2 T cells available for engagement by LAVA’s product candidates; the relationship between Vδ2 T cells and antitumor activity; the potential synergies between LAVA’s product candidates and other immuno-oncology approaches; the potential market opportunity our product candidates seek to address; our intellectual property position; the ability of LAVA’s collaborators to support or advance collaborations or our product candidates; any payments to us under our license agreement with LAVA’s collaborators or our agreements with our collaborators and our cash runway; our ability to leverage our initial programs to develop additional product candidates using our Gammabody® platform; and the risk that positive results in a preclinical study or clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials. In addition, there may be adverse effects on our business condition and results of operations from general economic and market conditions and overall fluctuations in the United States and international equity markets, including deteriorating market conditions due to investor concerns regarding inflation, interest rates, the Russian invasion of Ukraine and the Israel-Hamas war. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in the filings we make with the Securities and Exchange Commission from time to time.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, the events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. We qualify all of our forward-looking statements by these cautionary statements.

Any forward-looking statements represent the Company’s views only as of the date of this presentation and do not represent its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements.

Investment Highlights

Proprietary Gammabody® Platform

- Potential first-in-class Platform maximizing the unique anticancer potential of Gamma-Delta T cells[1]
- Engineered to selectively activate Vδ2 T cells upon cross-linking with tumor-associated antigen
- Designed to drive larger therapeutic window with low incidence of high-grade CRS and limited on-target/ off-tumor toxicities while maintaining anticancer activity

Progressing mCRPC Study in Phase 1

- Lead program LAVA-1207 in mCRPC currently enrolling dose level 12 monotherapy cohort
- Enrollment in combination arm with KEYTRUDA® (pembrolizumab) initiated in Q2 2024[2]
- Next update planned for Q4 2024

Growing Pipeline

- Clinical trial enabling activities are underway, to support initiation of trials in Australia by YE 2024

Validating Strategic Partners

- Pfizer worldwide license agreement for PF-08046052[3] for EGFR+ tumors, in Phase 1
- Received $7 million Phase 1 enrollment milestone
- Johnson & Johnson Innovative Medicine collaboration has selected a lead candidate, in preclinical development

Strong Team, IP and Cash Position

- Experienced management team, with a diverse portfolio of product and platform IP and a cash balance of $86.8 million[4], with an expected runway into mid-2026

1. Gamma-delta T cells are abbreviated as Vγ9Vδ2 or Vδ2 in this deck. 2. LAVA announced a clinical collaboration with Merck & Co., on January 25, 2024. 3. Formerly LAVA-1223, 4. Based on cash, cash equivalents and investments as of June 30, 2024, mCRPC = Metastatic Castration-Resistant Prostate Cancer, CRS = Cytokine Release Syndrome, IL-2 = Interleukin-2.

Gammabody® Platform Pipeline: Potential in Hematologic Malignancies and Solid Tumor Indications

Pipeline			
Candidate	**Target**	**Indication(s)**	**Preclinical / Phase 1 / Phase 2**
LAVA-1207	PSMA	mCRPC Monotherapy	
		+ IL-2	
		+ Pembrolizumab[1]	
LAVA-1266	CD123	Hematologic Malignancies	
LAVA-1427		Undisclosed	
LAVA-1433		Undisclosed	
Strategic Partnerships			
PF-08046052	EGFR	Solid Tumors	Pfizer
Johnson & Johnson Innovative Medicine		Undisclosed	Johnson&Johnson Innovative Medicine

Solid Tumor Hematologic malignancy Undisclosed

1. LAVA announced a clinical collaboration with Merck & Co., on January 25, 2024 for LAVA-1207. PSMA: prostate-specific membrane antigen; EGFR: epidermal growth factor receptor; mCRPC: metastatic castration-resistant prostate cancer

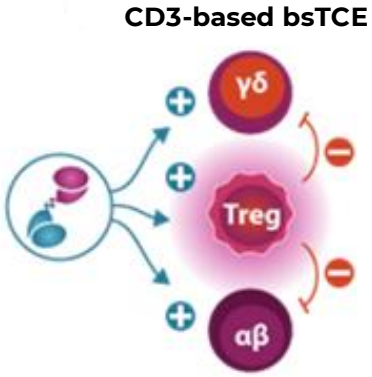
Gammabody® Platform

Overview

LAVA's Bispecific T Cell Engager Strategy is Focused on Recruiting Vδ2-T Cells

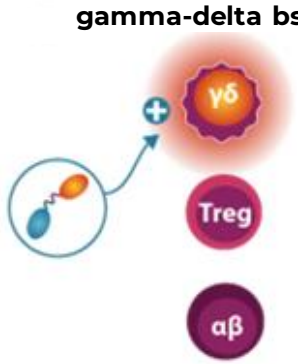
1st generation T cell engagers

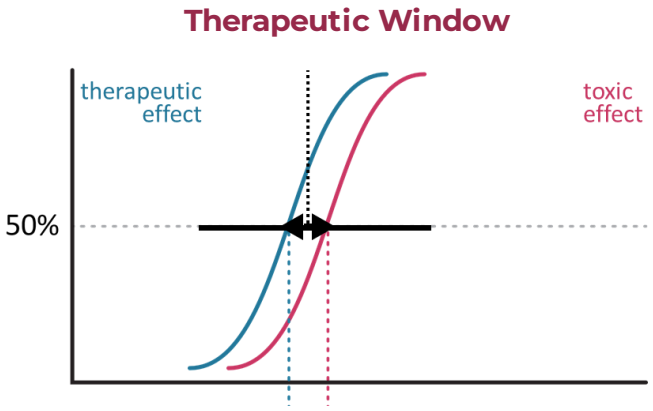
- CD3 (pan) T cell activators
- High grade cytokine release syndrome (CRS) toxicities
- On-target/off-tumor toxicities
- Co-activation of Tregs
- Sporadic efficacy in solid tumors

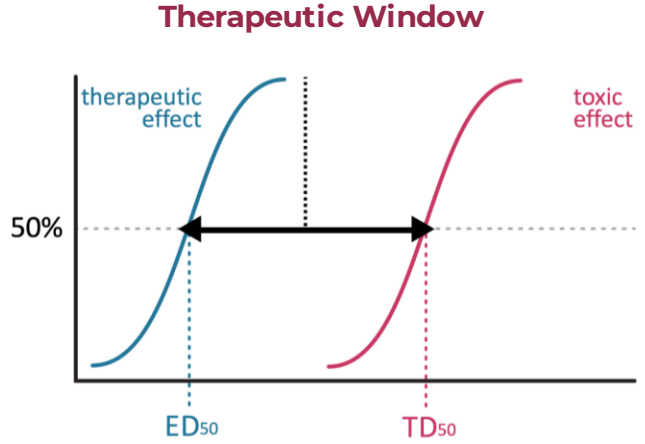


LAVA's next-generation approach

- Recruitment of Vδ2 T cells
- Homogeneous population of antitumor immune effector cells
- Avoids co-activation of Tregs
- Anticipated low incidence of high-grade CRS and on-target/off-tumor toxicity
- Unique antigen presenting function

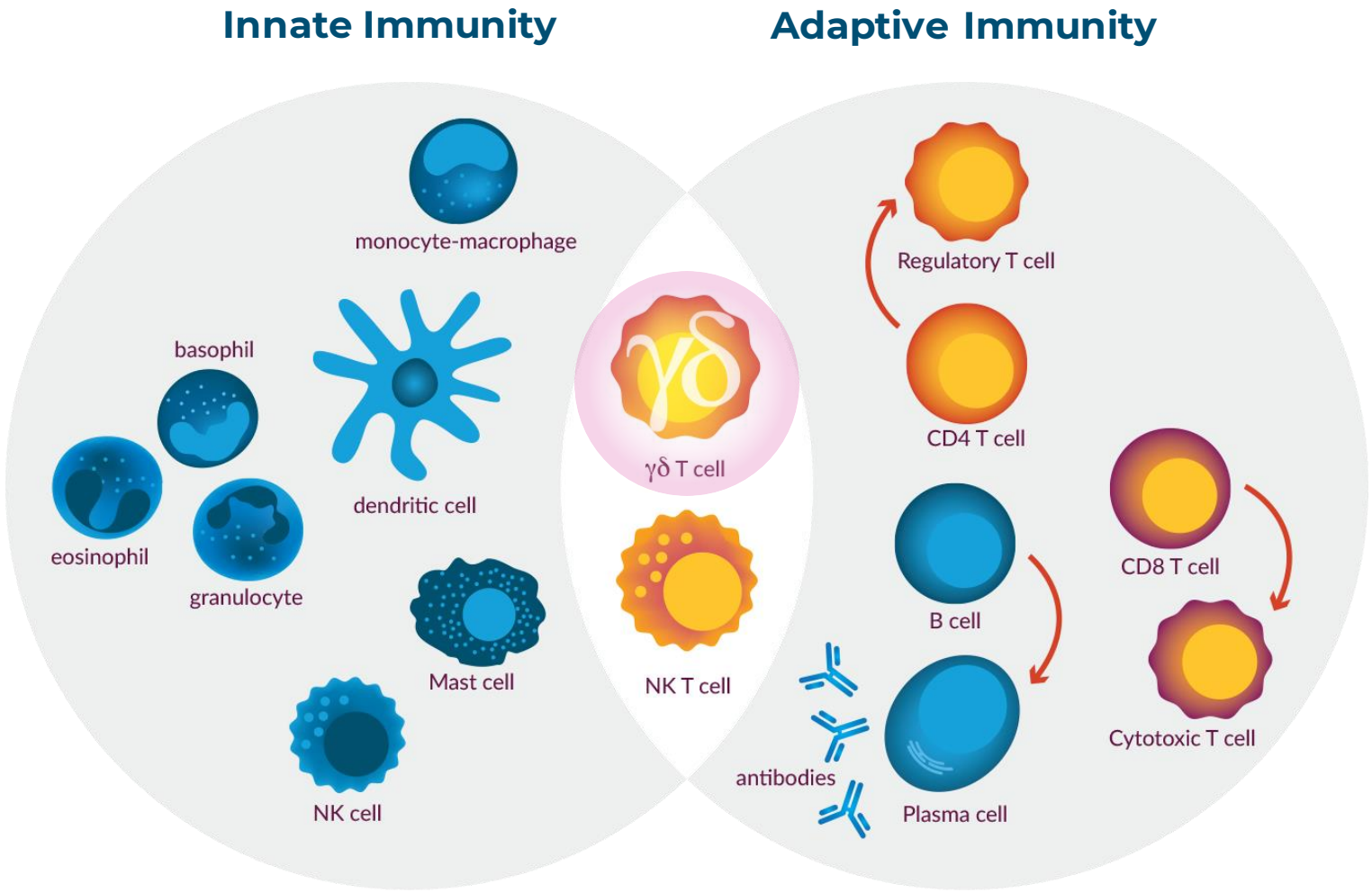






Vδ2 T Cells

Positioned at the interface between innate and adaptive immunity



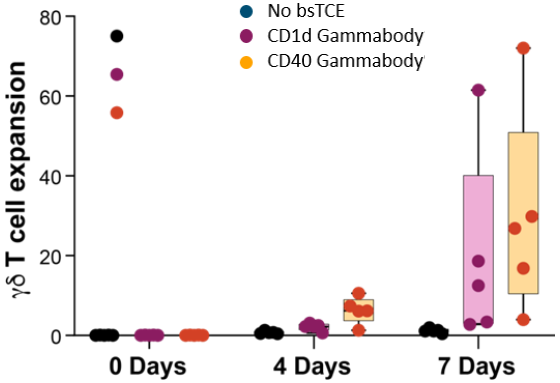
- Largest γδ T cell subset in blood: (~90-95% of total γδ T cells)
- Natural ability to recognize and kill tumor cells
- Presence of Vδ2 T cells associated with improved outcomes in cancer patients
- Recognize tumors through phosphoantigen-BTN2A1/3A1 complex
- Consistent pro-inflammatory cytotoxic effector T cell population

Adapted from Dranoff G, Nature Rev Cancer 2004; 4: 11-22 Kabelitz D et al., Cell Mol Immunol 2020; 17: 925–939

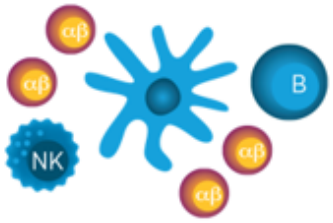
Selective Activation of Vδ2 T Cells has the Potential to Coordinate the Immune Response Against Tumors

EXPANSION

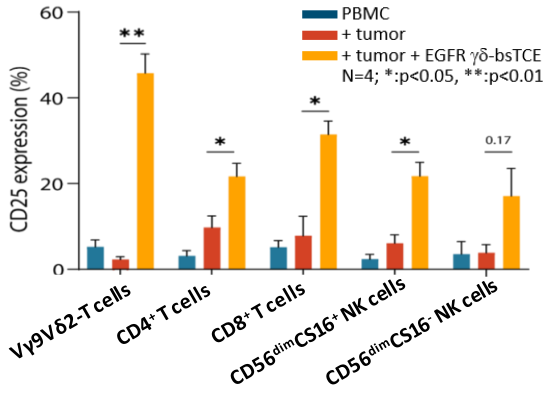
Vδ2 T cell expansion[1]



BROAD IMMUNE ACTIVATION

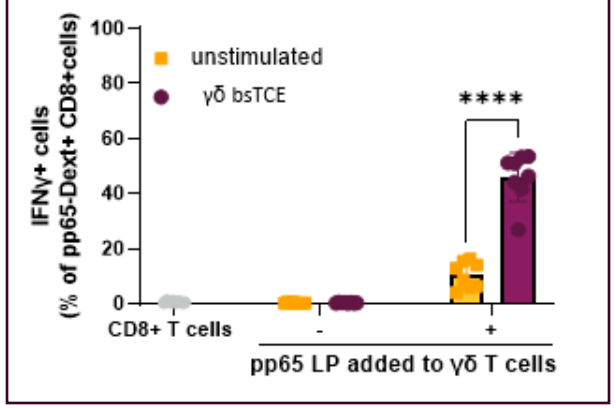


Downstream T and NK cell activation



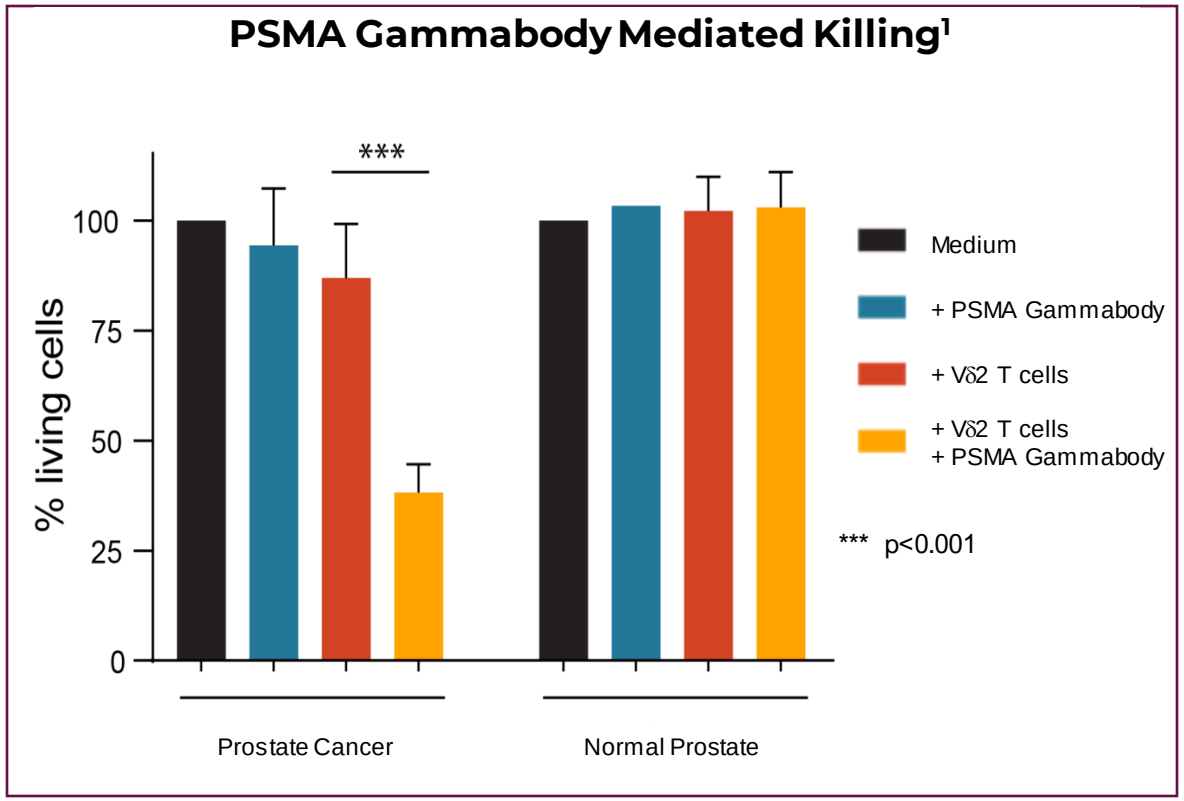
ANTIGEN PRESENTATION

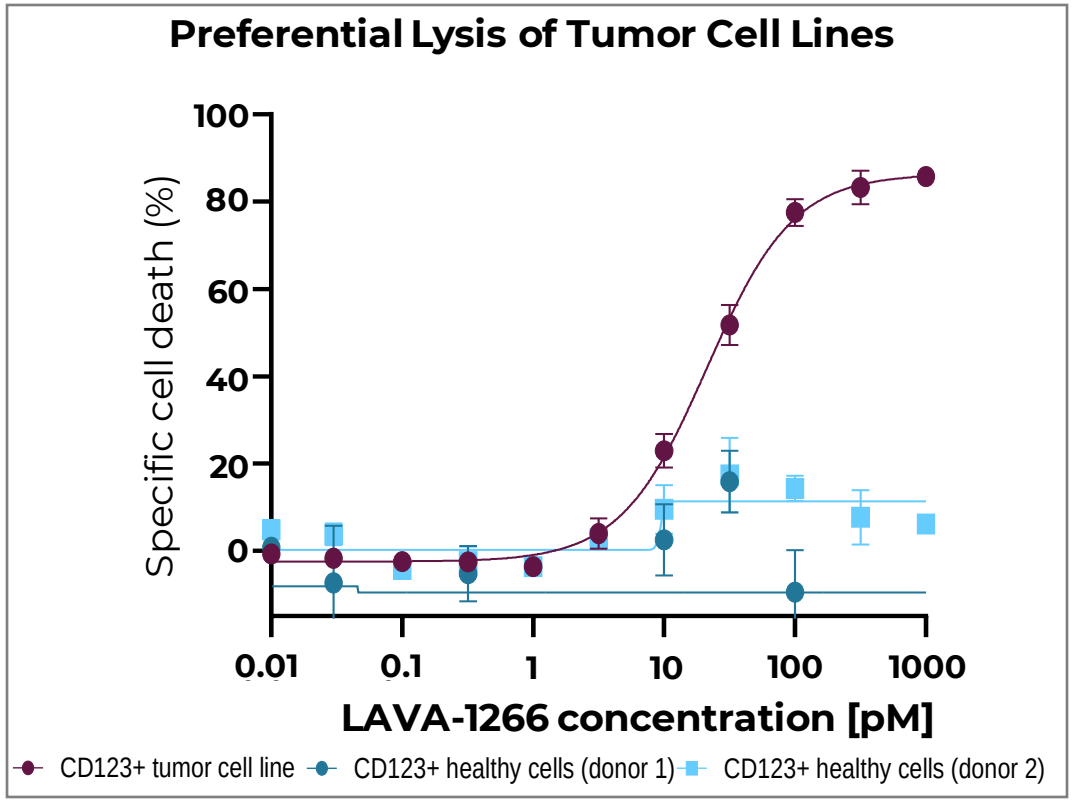
CD8+ T cell IFN-γ production[3]



1 Lameris R et al. Cell Reports Med 2023, Data on file, 2 King L, et al, Cancer Immunol Res 2023; 11:1237-1252, 3 King L, et al. in preparation

Sparing of Normal Tissue is a Key Differentiator of the Gammabody® Platform[1]



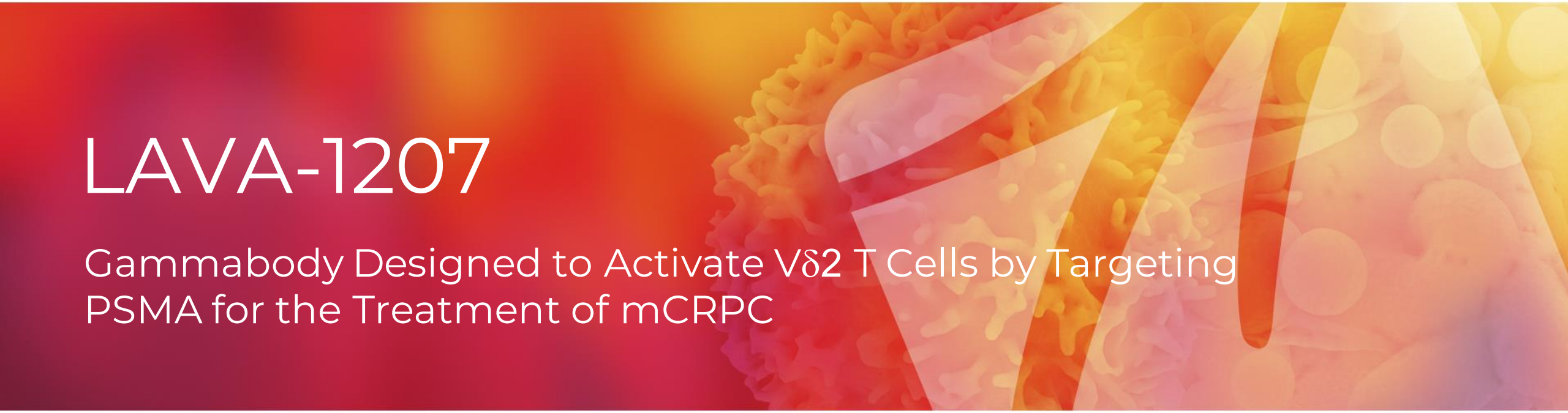


- **Potential for larger therapeutic window**
- **Preferential killing of cancer versus healthy cells demonstrated *in vitro* and *ex vivo***
- **Allows for targeting of widely expressed tumor-associated antigens**

1. In preclinical models, LAVA Therapeutics, data on file

LAVA-1207

Gammabody Designed to Activate Vδ2 T Cells by Targeting PSMA for the Treatment of mCRPC



LAVA-1207 Targets PSMA: Enrolling in Phase 1 Global Study

Update expected Q4 2024

PSMA is a clinically validated target

Highly-expressed in >90% prostate cancers[1]. Higher levels negatively correlated with survival[2]

FDA approval of Pluvicto, a PSMA-targeted radiopharmaceutical, provides clinical validation

High unmet need

While early-stage outcomes are good, mCRPC prevalence is 50,000 in the U.S.[3]

With ~35,000 prostate-cancer related deaths annually in the U.S.[4], 5-year survival for mCRPC is ~30%[5]

Strong scientific rationale

Reported relative abundance of Vδ2 T cells correlates with improved patient prognosis and makes mCRPC an attractive indication for Gammabody® Platform[6]

Phase 1 enrollment

Enrollment is ongoing in the U.S. and Europe (NCT05369000) for dose level 10 monotherapy

Clinical collaboration with Merck & Co., Inc.[7] adding a combination cohort with KEYTRUDA® (pembrolizumab)

Study update

Preliminary signs of clinical activity observed with disease stabilization and PSA reduction during early Phase 1 dose escalation

To minimize the risk of CRS events >grade 2 we have introduced premedication and step-dosing

Next update is planned for Q4 2024, targeting a medical conference

Sources: Items 1-5: based on information from Cancer.Net® and FMI (Future Market Insights); 6. Tosolini M et al. Oncoimmunology 2017, vol 6, e128472; 7. LAVA announced a clinical collaboration with Merck & Co., on January 25, 2024.

LAVA-1207 Phase 1 mCRPC

Dose Escalation

Therapy refractory mCRPC

Dosing: every 2 weeks

Optional adjustments
- Dose level
- Dosing frequency
- # cohorts

RP2D and schedule

Dose Expansion

Therapy refractory mCRPC

GOAL

Determine recommended dose and schedule based on optimal biological dose and/or maximum tolerated dose

GOAL

Confirm safety and determine preliminary anti-tumor activity

Patient Population

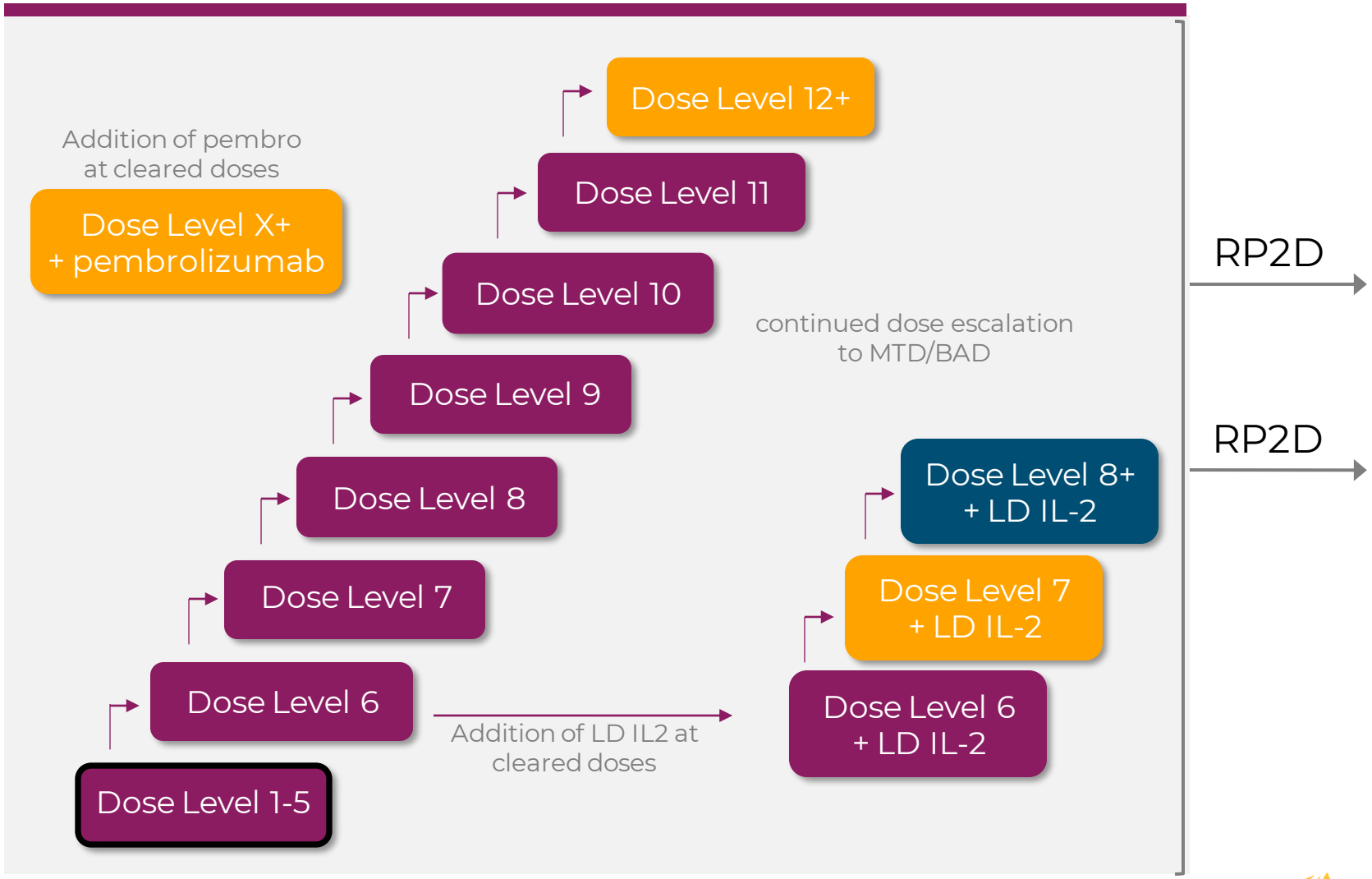
- Adult males with mCRPC
- At least 1 prior taxane
- At least 1 AR targeted therapy
- ECOG 0-1

Study Design =3+3, AR = Androgen receptor

LAVA-1207 Study Schema – Phase 1

Current Step Dosing Schedule

- Priming Dose 1 on Day 1: 120ug (outpatient visit)
- Priming Dose 2 on Day 8: 360ug (outpatient visit)
- Target Dose on Day 15 and q2w thereafter (only first target dose has mandatory hospitalization of 24h; flexibility to extend beyond 24h based on investigator discretion)



Dose Level Cleared – ASCO GU 2023 Update
Dose Level Cleared
Ongoing
Additional dose levels Phase 1

LD IL2 = Low Dose Interleukin-2

Why explore the combination of LAVA-1207 and PD-1 mAb

- PD-1 can be expressed by Vδ2-T cells (in patient Tumor-Infiltrating Lymphocyte (TIL), PBMC) and is upregulated after exposure to bispecific γδ-TCE
  - This has the potential to dampen the antitumor effect of LAVA-1207 (and could be released by anti-PD1 mAb)
- bsTCE induced Vγ9Vδ2-T cell activation triggers downstream activation of NK and T cells via proinflammatory cytokine secretion and can induce naive CD4 and CD8 T cell responses through their unique Ag presenting ability
  - This may broaden the immune response that could be promoted by anti-PD1 mAb
- Anti-PD1 mAb therapy may therefore facilitate/potentiate the antitumor effect of LAVA-1207

Phase 1 Snapshot from ASCO GU 2023

Dose Levels 1-5
20 patients

- Median patient was 68 years old, had received 4 rounds of prior therapy and was median 9 years from diagnosis
- Metastases were primarily located in bone, lymph nodes and visceral tissues

Encouraging safety profile

- No occurrence of high-grade CRS (>2)
- No increase in severity/frequency of TEAEs (grade 1 and 2) with increasing doses, or treatment discontinuations due to adverse events
- One grade 4 AE occurred (spinal cord compression, DL5) which was non-related

Established data on pharmacokinetics

- Observed linear pharmacokinetics (PK)

Attractive early data on pharmacodynamics

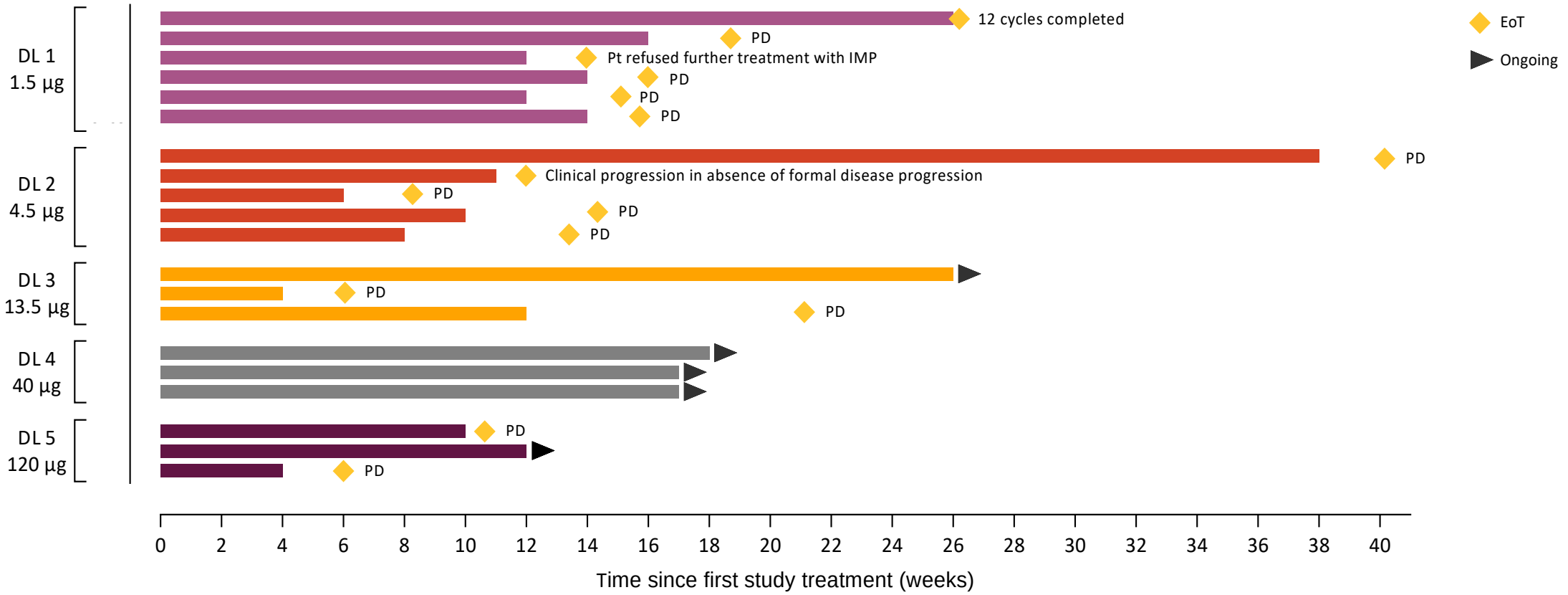
- Pharmacodynamics (PD) reflect changes expected per MOA
- Vδ2 T cell receptor occupancy increased with escalating dose

Activity and treatment duration

- PSA reductions observed
- Stable disease observed in 8 of 14 evaluable patients, as of ASCO GU 2023
- Data cutoff: 12/8/2022

1. All data on this slide are based on the ASCO GU 2023; Data cutoff: December 8, 2022, data on file, TEAE = treatment-emergent adverse events;

ASCO GU 2023: Time on Treatment

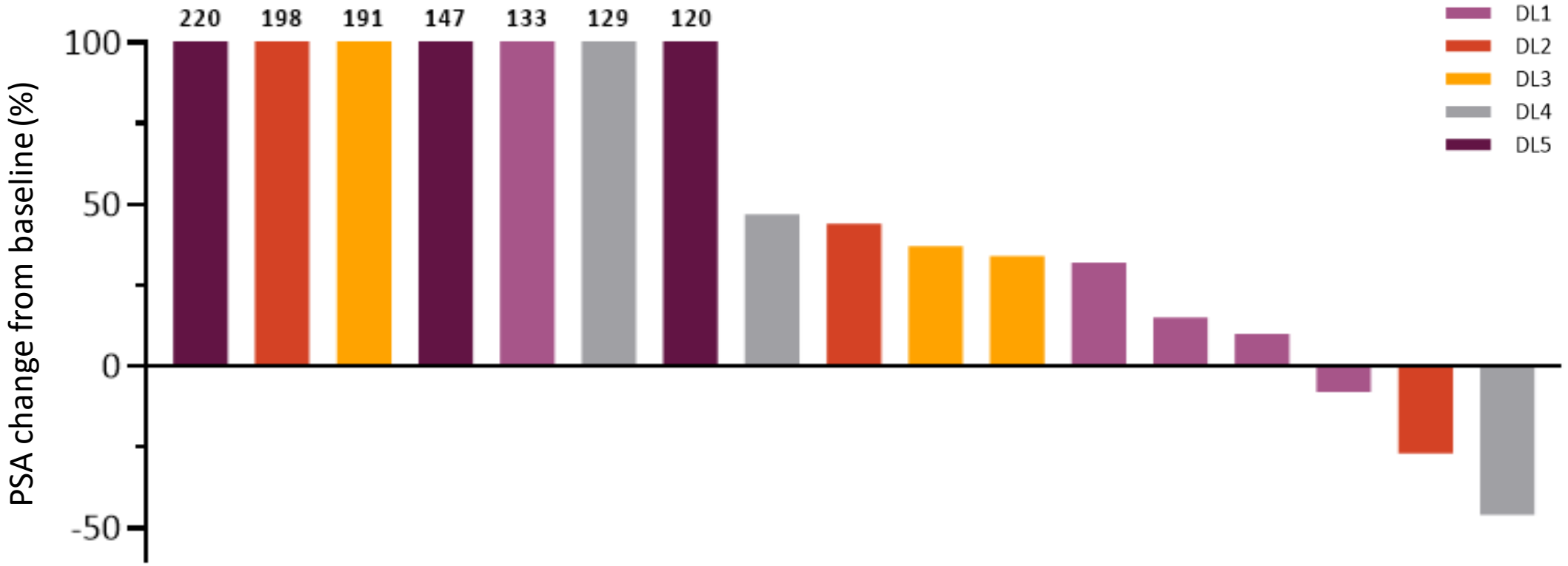


Subsequent to ASCO GU:

- Currently enrolling dose level 12 for monotherapy

Data cutoff: December 8, 2022, ASCO GU 2023

ASCO GU 2023: Best PSA Response



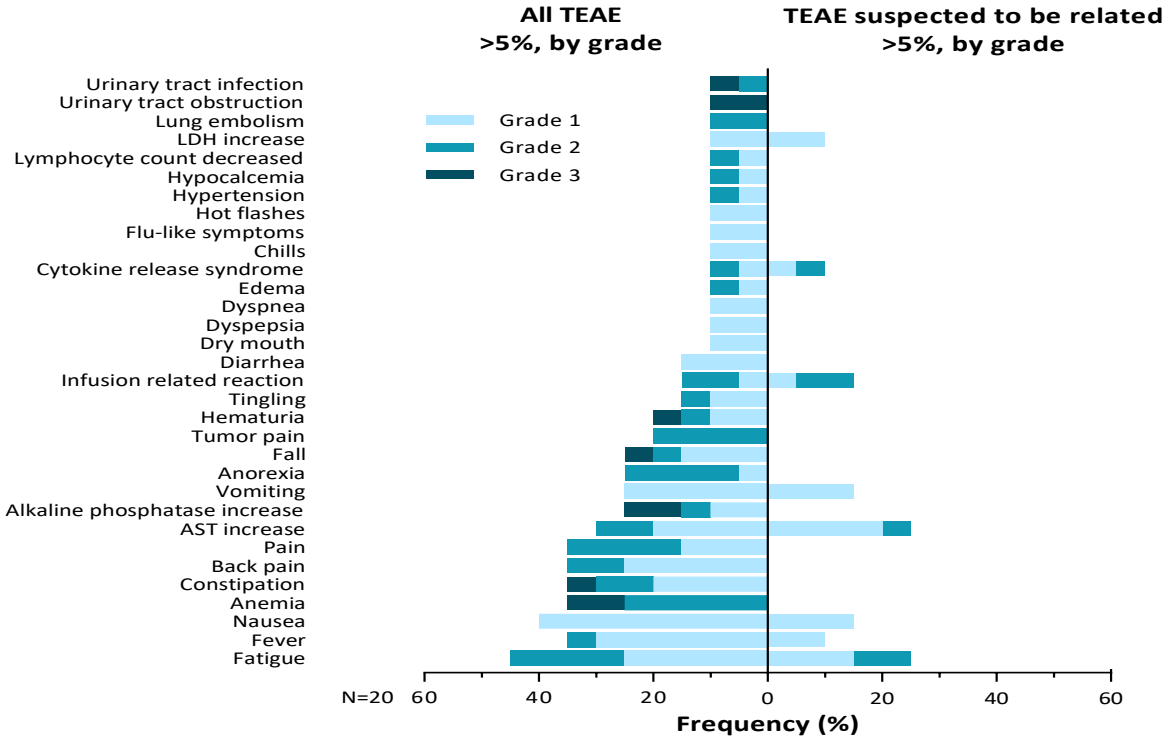
Subsequent to ASCO GU:

- Continue to see PSA reductions and other signs of potential antitumor activity

Data cutoff: December 8, 2022, ASCO GU 2023

ASCO GU 2023: Initial Phase 1 Safety Data

- Favorable safety profile with no occurrence of high-grade (>2) CRS
- TEAEs that were suspected to be related were grade 1 or 2
- No increase in severity or frequency of TEAEs with increasing doses
- One grade 4 AE occurred (spinal cord compression, DL 5), which was non-related



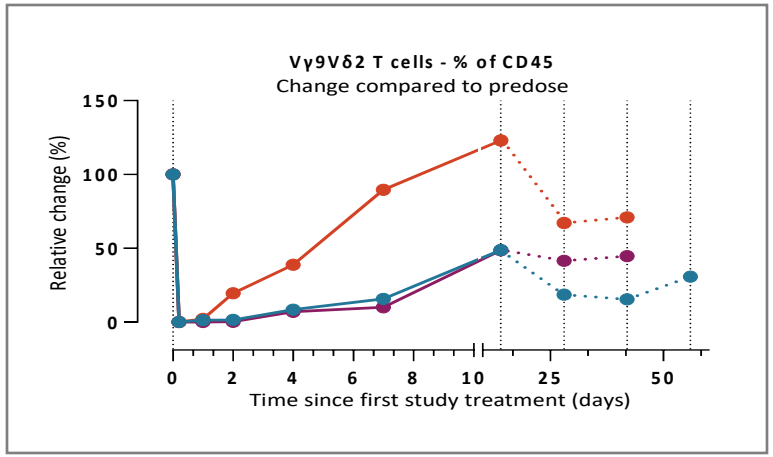
Subsequent to ASCO GU:

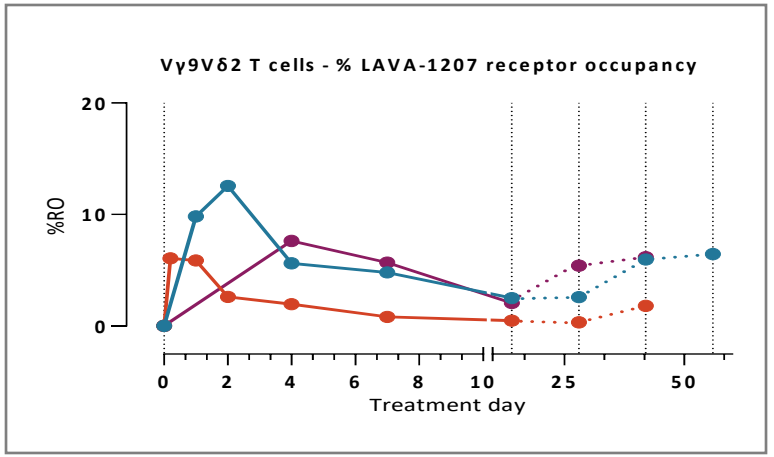
- Single dose-limiting toxicity (DLT) in cohort 6 noted in the monotherapy arm
- Three dose-limiting toxicities (DLTs) were observed in patients receiving IL-2 in addition to LAVA-1207 in a cohort with multiple doses of IL-2 per cycle
- Step-dosing introduced to minimize risk of high-grade CRS
- No grade >2 CRS observed before or since introduction of step-dosing

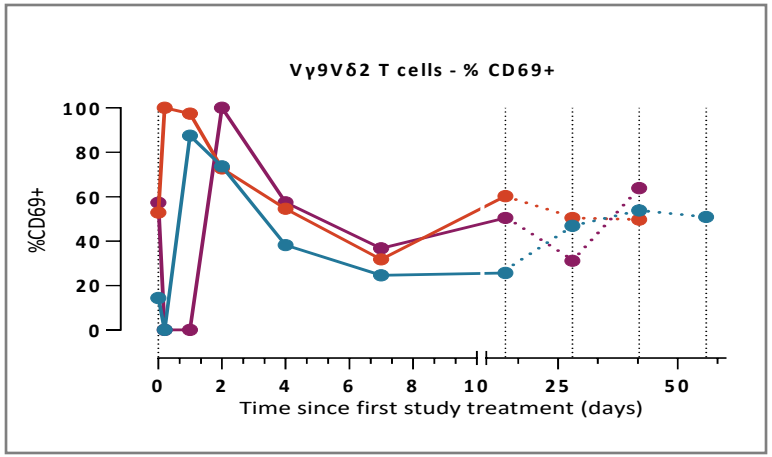
Data cutoff: December 8, 2022, ASCO GU 2023

ASCO GU 2023: Pharmacokinetics and Pharmacodynamics

Continuing to see Vδ2 T cell receptor occupancy with increasing doses







Sbj 3 – Cohort 4
Sbj 4 – Cohort 4
Sbj 5 – Cohort 4

PK, PD Data in Keeping with MOA

- PK appears to be linear
- Pronounced drop in circulating Vδ2 T cell frequency 2 hr after dosing, suggesting Vδ2 T cell re-distribution, with subsequent recovery
- Vδ2 T cell activation markers (CD25 and CD69) upregulated following dosing
- Receptor occupancy detectable up to day 14 after EOI, with peak levels ranging from 6.1% to 12.6%

Data cutoff: December 8, 2022, ASCO GU 2023; EOI = end of infusion; Sbj = subject

LAVA-1266

Gammabody Designed to Activate Vδ2 T Cells by Targeting CD123 for the Treatment of Hematologic Malignancies

LAVA-1266 Targets CD123 for AML & MDS

Strong scientific rationale

Relative abundance of Vδ2 T cells in AML suggests this disease could be an attractive target for Gammabody therapies

High unmet need

Estimated new diagnoses in US in 2024: 62,770[1]

Estimated Deaths in US in 2024: 23,670[1]

Multiple levels of de-risking

Vδ2 T cell engaging arm partially derisked by LAVA-1207

CD123 clinically validated as a cancer target

Over-expressed in a wide range of hematologic malignancies

Promising preclinical data

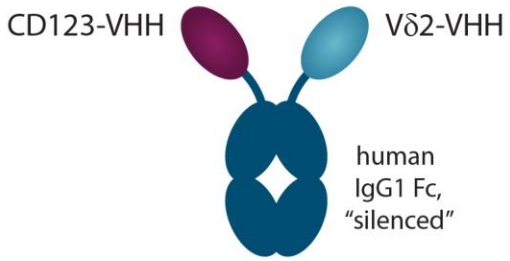
LAVA-1266 induced preferential lysis of CD123-expressing tumor cells while relatively sparing CD123-expressing normal cells

Program status

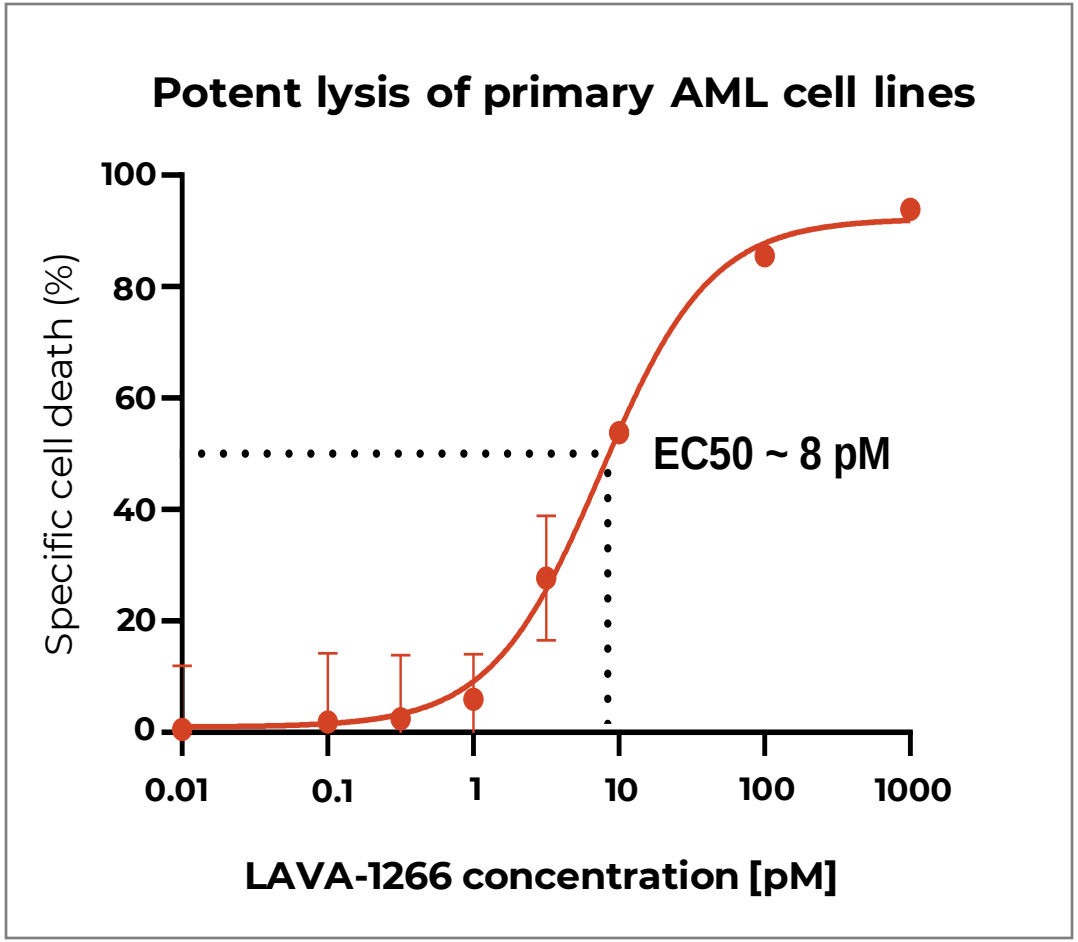
Clinical trial enabling activities are underway to support the initiation of a Phase 1 trial in AML and MDS in Australia by YE 2024

1. Source: https://seer.cancer.gov/statfacts/html/leuks.html; AML = acute myeloid leukemia, MDS = myelodysplastic syndromes

LAVA-1266: CD123-Targeting Bispecific Vδ2 T Cell Engager



- pM potency and activity at low effector to target cell ratios
- Increased survival in AML xenograft model
- No co-activation of immunosuppressive regulatory T cells
- Does not interfere with IL-3 induced proliferation (relevant for HPSC)
- Results in very limited *in vitro* cytokine release (incl. IL-6, TNF, IFN-γ)
- Preferentially targets CD123⁺ tumor cells to reduce the potential for on-target off-tumor toxicity



Strategic Partnerships

PF-08046052 for Solid Tumors: Phase 1 Underway[1]

Mechanism of action

Designed to induce preferential lysis of EGFR-expressing tumor cells while relatively sparing EGFR-expressing normal cells

Strategic partner

Pfizer

Agreement

Exclusive worldwide license agreement with Pfizer entered into Q3 2022
Pfizer to develop and commercialize PF-08046052
Potential for milestones of up to approximately $650 million and royalties

Payments to date

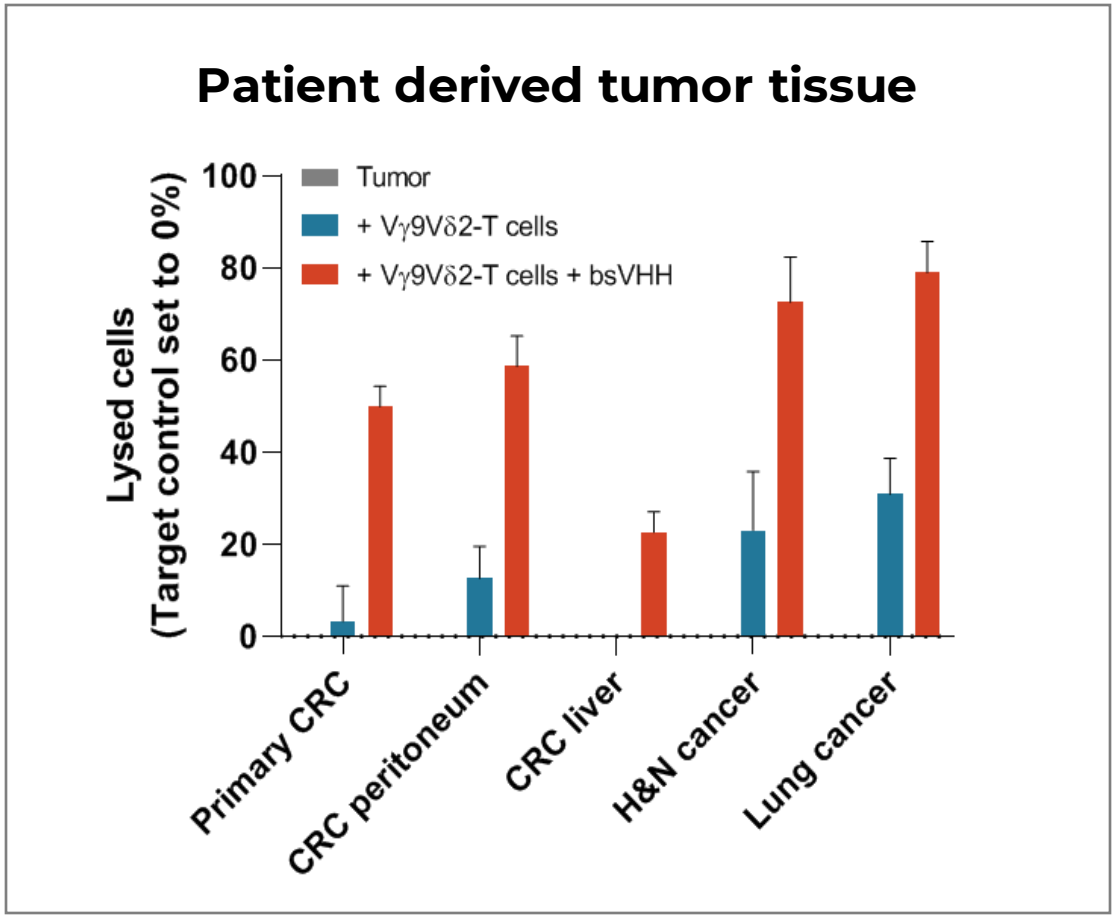
$50 million upfront received with the signing, Sept 2022
Received $7 million Phase 1 enrollment milestone, March 2024

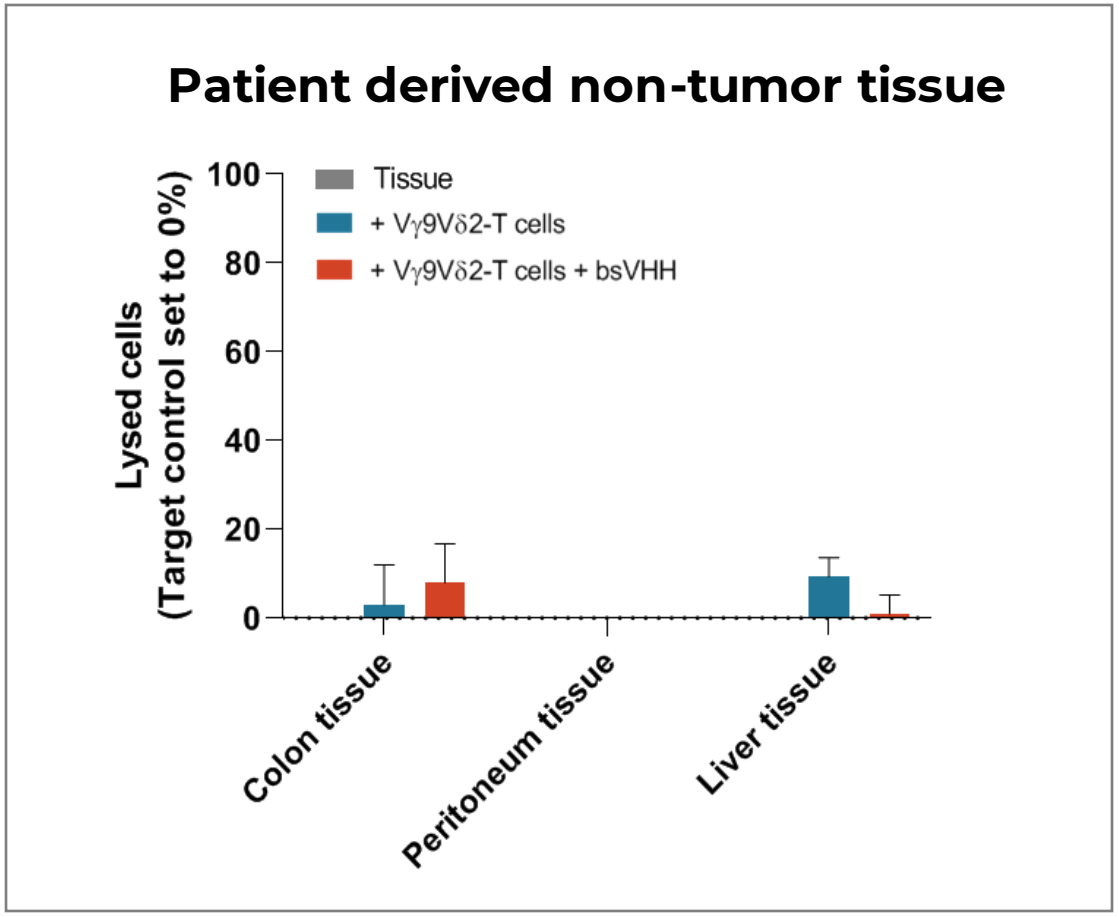
Program status

Phase 1 Clinical Trial (NCT05983133) initiated in Q4 2023
Program highlighted during Pfizer Oncology Innovation Day[1]

1. Link: Pfizer Oncology Innovation Day

PF-08046052 – EGFR-Targeting Gammabody





King L, et al. Cancer Immunol Res 2023 LAVA Therapeutics, data on file

Johnson & Johnson Innovative Medicine Collaboration: Lead Candidate Selected

Mechanism of action

Undisclosed tumor associated antigen

Strategic partner

Johnson&Johnson Innovative Medicine

Agreement

LAVA entered into a research collaboration and license agreement with J&J Innovative Medicine (May 2020) for the discovery and development of a novel bispecific gamma-delta T cell engager for the treatment of cancer

J&J Innovative Medicine is responsible for the future clinical development, manufacture, and commercialization of the candidate at J&J Innovative Medicine's sole cost and expense

Payments

Upfront payment received in July 2023

LAVA is eligible to receive development, regulatory and commercialization milestone payments and royalties

Program status

Product candidate onboarded June 2023

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Proprietary Gammabody® Platform

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- Engineered to selectively activate Vδ2 T cells upon cross-linking with tumor-associated antigen
- Designed to drive larger therapeutic window with low incidence of high-grade CRS and limited on-target/off-tumor toxicities while maintaining anticancer activity

Progressing mCRPC Study in Phase 1

- Lead program LAVA-1207 in mCRPC currently enrolling dose level 12 monotherapy cohort
- Enrollment in combination arm with KEYTRUDA® (pembrolizumab) initiated in Q2 2024[2]
- Next update planned for Q4 2024

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- Clinical trial enabling activities are underway, to support initiation of trials in Australia by YE 2024

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- Received $7 million Phase 1 enrollment milestone
- Johnson & Johnson Innovative Medicine collaboration has selected a lead candidate, in preclinical development

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LAVA THERAPEUTICS

Gamma-delta T cell engagers for next-generation cancer therapeutics

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