
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 6-K

**REPORT OF FOREIGN ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
OF THE SECURITIES EXCHANGE ACT OF 1934**

For the month of February 2023

(Commission File No. 001-40241)

LAVA Therapeutics N.V.

(Translation of registrant's name into English)

Yalelaan 60
3584 CM Utrecht, The Netherlands
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F.
Form 20-F Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (1):
Yes No

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (7):
Yes No

LAVA Therapeutics, N.V.

On February 16, 2023, LAVA Therapeutics, N.V. (Company) issued a press release announcing initial data from the ongoing Phase 1/2a Clinical Trial of LAVA-1207 in refractory metastatic castration-resistant prostate cancer (mCRPC) in a poster presentation at the American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium. A copy of this press release is filed herewith as Exhibit 99.1.

On February 16, 2023, the Company also updated its Investor Presentation on the Company's website. A copy of the investor presentation is filed herewith as Exhibit 99.2.

EXHIBIT LIST

Exhibit	Description
99.1	Press Release, dated February 16, 2023
99.2	LAVA Therapeutics, N.V. Investor Presentation

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereto duly authorized.

LAVA Therapeutics, N.V.
(Registrant)

Date: February 16, 2023

By: /s/ Fred Powell

Fred Powell
Chief Financial Officer

LAVA Therapeutics Announces Initial Data from the Ongoing Phase 1/2a Clinical Trial of LAVA-1207 in Therapy Refractory mCRPC at the 2023 ASCO GU Symposium

- ***Favorable safety profile to date, with no occurrence of high-grade (>2) cytokine release syndrome or dose-limiting toxicities***
- ***Preliminary signs of anti-tumor activity were observed, with iRECIST stable disease (iSD) in 8 out of 14 evaluable patients at week 8 and PSA levels stabilizing or decreasing in heavily pre-treated patients***
- ***Dose escalation is ongoing***

Utrecht, The Netherlands and Philadelphia, Pa., USA – February 16, 2023 – LAVA Therapeutics N.V. (Nasdaq: LVTX), a clinical stage immuno-oncology company focused on developing its proprietary Gammabody™ platform of bispecific gamma-delta T cell engagers to transform the treatment of cancer, today announced initial clinical data from its ongoing Phase 1/2a study of LAVA-1207 in patients with therapy refractory metastatic castration resistant prostate cancer (mCRPC). The data are presented in a poster presentation at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) taking place in San Francisco from February 16-18, 2023.

“These early data from the first five cohorts of our Phase 1/2a study indicate LAVA-1207 to have a favorable safety profile in patients with therapy refractory metastatic castration resistant prostate cancer. Importantly, preliminary signs of clinical activity were observed with disease stabilization and PSA reduction during dose escalation in these heavily pretreated patients,” said Niven Mehra, M.D., Ph.D., medical oncologist at the Radboud University Medical Center in Nijmegen, The Netherlands. “We are encouraged by the progress of this trial and will continue to enroll patients for additional cohorts.”

LAVA-1207 is an Fc-containing humanized bispecific antibody that directly engages prostate-specific membrane antigen (PSMA) and the Vδ2-T cell receptor chain of Vγ9Vδ2-T cells to mediate potent killing of PSMA-expressing prostate cancer cells. The objectives of the Phase 1/2a study (EudraCT 2021-001789-39; NCT05369000) are to investigate safety and tolerability, evaluate pharmacokinetic and pharmacodynamic effects, immunogenicity and preliminary antitumor activity of LAVA-1207. LAVA-1207 is administered via intravenous infusion every two weeks.

The data presented to date show that a total of 20 patients have been treated with doses ranging from 1.5 to 120 micrograms of LAVA-1207, with treatment duration ranging from 4 to 38 weeks. The safety profile is favorable to date, without occurrence of high grade (>2) cytokine release syndrome or dose-limiting toxicities. LAVA-1207 showed predictable and linear pharmacokinetics and on-mechanism pharmacodynamics including Vγ9Vδ2-T cell activation. Preliminary signs of anti-tumor activity were observed at week 8, with iRECIST stable disease (iSD) in 8 out of 14 evaluable patients and PSA levels stabilizing or decreasing. The largest overall decrease in PSA was 61% (46% vs baseline). The patient improved clinically with improvement in pain and fatigue. Dose escalation is continuing both in Europe and the U.S.



"We are encouraged by these initial data for LAVA-1207," said Stephen Hurly, president and chief executive officer of LAVA Therapeutics. "At LAVA Therapeutics, we are committed to transforming cancer therapy. I am thrilled to see our second clinical asset continuing to move forward, and an emerging safety profile with the potential for differentiation from prior generation PSMA directed bispecific T-cell engagers."

Details of the poster presentation are as follows:

Abstract #: 153

Abstract Title: *Early dose escalation of LAVA-1207, a novel bispecific gamma-delta T cell engager (Gammabody™), in metastatic castration-resistant prostate cancer (mCRPC) patients*

Session Title: Poster Session A: Prostate Cancer

Poster Board #: E13

Session Date: Thursday, February 16, 2023

Session Time: 11:30 AM-1:00 PM PT; 5:45 PM-6:45 PM PT

Presenter: Niven Mehra, MD, PhD, Department of Medical Oncology, Radboud University Medical Center, Nijmegen, The Netherlands

LAVA-1207

LAVA-1207 is a Gammabody™ that conditionally activates Vγ9Vδ2 (Vgamma9 Vdelta2) T cells upon crosslinking to prostate-specific membrane antigen (PSMA) to trigger the potent and preferential killing of PSMA-positive tumor cells, including metastatic castration-resistant prostate cancer (mCRPC).

About LAVA Therapeutics

LAVA Therapeutics N.V. is a clinical-stage immuno-oncology company utilizing its proprietary Gammabody™ platform to develop a portfolio of bispecific gamma-delta T cell engagers for the potential treatment of solid and hematologic malignancies. The Company utilizes bispecific antibodies engineered to selectively kill cancer cells by triggering Vγ9Vδ2 (Vgamma9 Vdelta2) T cell antitumor effector functions upon cross-linking to tumor-associated antigens. LAVA-051, the Company's lead candidate for the treatment of multiple myeloma, chronic lymphocytic leukemia, and acute myeloid leukemia, is enrolling patients in a Phase 1/2a clinical study (EudraCT 2020-004583-26; NCT04887259). A Phase 1/2a clinical study to evaluate LAVA-1207 in patients with metastatic castration-resistant prostate cancer (mCRPC) is also enrolling (EudraCT 2021-001789-39; NCT05369000). For more information, please visit www.lavatherapeutics.com, and follow us on LinkedIn, Twitter and YouTube.

LAVA's Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements, including in respect to the company's anticipated growth and clinical developments plans, and the timing and results of clinical trials. Words such as "anticipate," "believe," "could," "will," "may," "expect," "should," "plan," "intend," "estimate," "potential" and similar expressions (as well as other words or expressions referencing future events,



conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on LAVA's expectations and assumptions as of the date of this press release and are subject to various risks and uncertainties that may cause actual results to differ materially from these forward-looking statements. Forward-looking statements contained in this press release include, but are not limited to, statements about the preclinical & clinical data, clinical development and scope of clinical trials, and the potential use of our product candidates to treat various tumor targets. Many factors, risks and uncertainties may cause differences between current expectations and actual results including, among other things, the timing and results of our research and development programs and preclinical and clinical trials, our ability to obtain regulatory approval for and commercialize our product candidates, our ability to leverage our initial programs to develop additional product candidates using our Gammabody™ platform, and the failure of LAVA's collaborators to support or advance collaborations or our product candidates. The COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity. In addition, there may be adverse effects on our business condition and results 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 and hostilities between Russia and Ukraine. LAVA assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

CONTACTS

Argot Partners (IR/Media)
212-600-1902
lava@argotpartners.com



Gamma delta T cell engagers for the development of next-generation cancer therapeutics

Corporate Presentation
February 2023

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. 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 timing of our clinical trials for LAVA-1207, and the submission of INDs or CTAs for our other product candidates; our ability to develop and obtain regulatory approval for commercialize any of our product candidates; the failure of LAVA’s collaborators to support or advance collaborations or our product candidates; 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. 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 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. By attending this presentation, you acknowledge and agree that you are cautioned not to place undue reliance on any forward-looking statements, and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of the Company.

Pioneering Next-Generation Cancer Therapeutics

Proprietary Gammabody™ platform

- Bispecific antibody platform to engage Vγ9Vδ2 T cells for highly specific tumor cell killing
 - Leverage the unique quality of Vγ9Vδ2 T cells to selectively kill tumor cells while sparing normal cells
 - Fully modular approach amenable to the use of existing and newly generated antibodies from any platform
 - Gammabody™ combines potent tumor cell killing with no activation of suppressor T cells, low potential for on-target/off-tumor toxicity, and cytokine release syndrome

Clinical stage company

- 2 programs in Phase 1/2a trials
 - LAVA-051 (CD1d), initial data released ASCO and ASH 2022. Additional data expected to be released 2023
 - LAVA-1207 (PSMA), initial data presented at ASCO-GU (Q1 2023). Additional data expected to be released H2 2023

Robust pipeline

- LAVA-1266 (CD123) projected to enter the clinic in the next 2 years and LAVA-1223 (EGFR, licensed to Seagen)
- Multiple additional preclinical programs
 - Includes partnered discovery program with Janssen (J&J)

Solid financials and partnerships

- \$142.7M (Q3 2022) in cash and investments; >24 months cash runway
- Collaborations with Janssen (J&J) and Seagen

Gammabody™ Pipeline: Potential in Hematological and Solid Tumor Indication

Candidate	Target	Indication(s)	Discovery	Preclinical	Phase 1	Phase 2	Milestones	
LAVA-051	CD1d	MM CLL AML					<ul style="list-style-type: none"> Initial data released ASCO 2022 Additional data in 2023 	
LAVA-1207	PSMA	mCRPC					<ul style="list-style-type: none"> Initial data released ASCO GU 2023 Additional data 2H 2023 	
LAVA-1223	EGFR	Solid Tumors					<ul style="list-style-type: none"> Licensed to Seagen Sep 2022 	
LAVA-1266	CD123	Hematologic Malignancies					<ul style="list-style-type: none"> IND/CTA filing expected in 2024 	
LAVA-1278	CD40	Hematologic Malignancies						
Janssen Collaboration	undisclosed							

MM: multiple myeloma
 CLL: chronic lymphocytic leukemia
 AML: acute myeloid leukemia
 PSMA: prostate-specific membrane antigen
 EGFR: epidermal growth factor receptor
 mCRPC: metastatic castration-resistant prostate cancer

 Hematologic malignancy  Solid Tumor

Team Led by Experienced Leaders in the Biotech and Pharma Field



Steve Hurly, MSc, MBA
President & CEO

- 25+ years leadership experience in life sciences industry
- Seasoned drug developer and biotech strategist



Ton Adang, PhD
CDO

- Vast experience in drug development
- Extensive experience in product discovery and project management (e.g., KEYTRUDA)



Amy Garabedian, MSc, JD
General Counsel

- Extensive global, diversified legal and team building experience
- Almost 20 years practicing law, including over 15 years in the biotech and pharmaceutical industry



Charles Morris, MBChB, MRCP
CMO

- Medical oncologist, seasoned CMO with 25+ years of global oncology drug development
- Supported several approvals including including TREANDA® (bendamustine and Faslodex® (fulvestrant)



Paul Parren, PhD
EVP

- Industry leader in antibody science and drug development
- Vast experience inventing and developing therapeutic antibodies and technologies, including DARZALEX, RYBREVANT, TEPEZZA, TIVDAK & DuoBody



Fred Powell
CFO

- 20+ years of global CFO/leadership experience in biopharma
- Deep expertise across investor relations, finance, capital markets, operations and information technology



Hans van der Vliet, MD, PhD
CSO

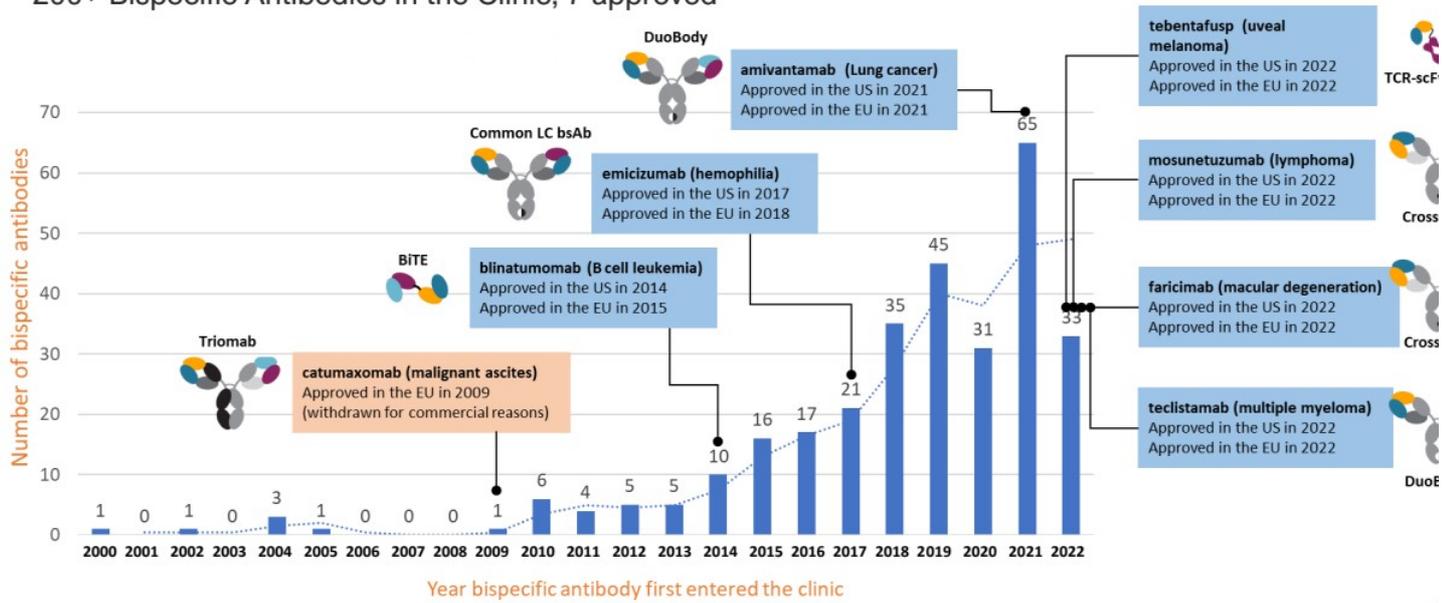
- Inventor of LAVA's gamma delta T cell engager platform
- Medical oncologist, extensive experience in pre-clinical and clinical research



LAVA's Proprietary Gammabody™ Platform
Bispecific Gamma Delta T Cell Engagers

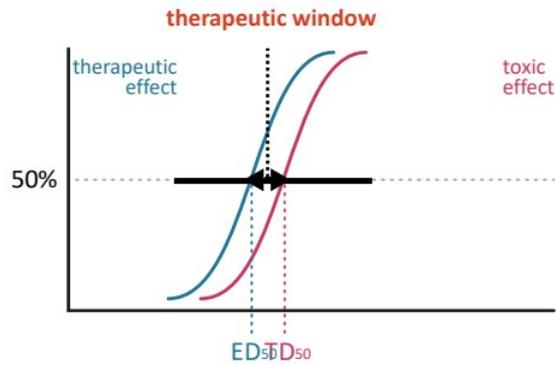
Enthusiasm for Bispecific T Cell Engagers

- High expectations for T cell bi-specific therapies driving significant development
- 200+ Bispecific Antibodies in the Clinic, 7 approved

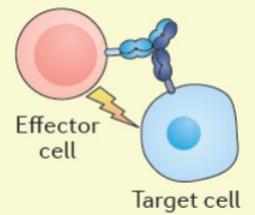


Enthusiasm for Bispecific T Cell Engagers

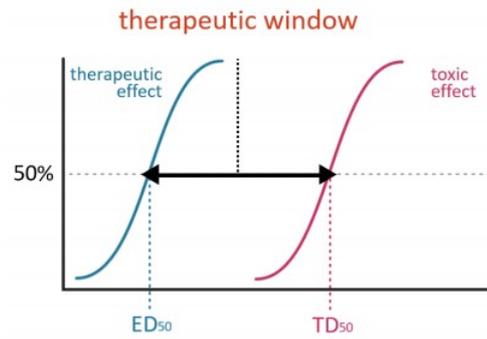
- High expectations for targeted T cell therapies in cancer, **but often:**
 - **Narrow therapeutic window:**
 - **Cytokine Release Syndrome**
 - **On-target/off-tumor-related toxicities**
 - Activates **immunosuppressive T cells**
 - **Sporadic efficacy in solid tumors**



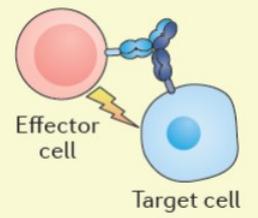
Bridging cells (in trans)



Strategies for Widening the Therapeutic Window



Bridging cells (in trans)

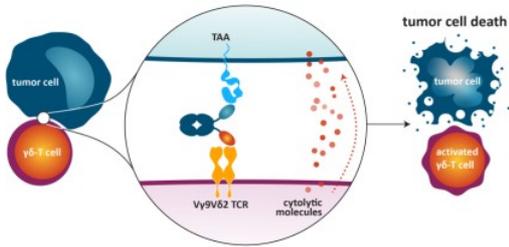


- Selecting 'tumor-specific' targets
 - Step-dosing / subcutaneous dosing
 - Decreasing affinity for T cells
 - Masking/site-specific activation
- **Recruiting alternative effector cells**
- Address only narrow target range, and/or
 - Cumbersome, and/or
 - Strongly decrease potency

Gammabody™ Platform: Bispecific $\gamma\delta$ T Cell Engagers

DIFFERENTIAL APPROACH

A versatile bispecific antibody platform for developing novel cancer therapeutics



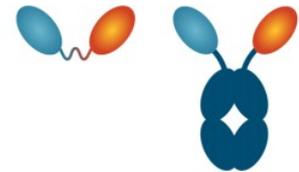
MECHANISM OF ACTION

LAVA's proprietary bispecific antibodies are designed to:

- Target V γ 9V δ 2 T cells to tumor antigens initiating selective tumor cell killing while sparing normal cells
- Carry a low potential for on-target/off-tumor toxicity and cytokine release syndrome (CRS)

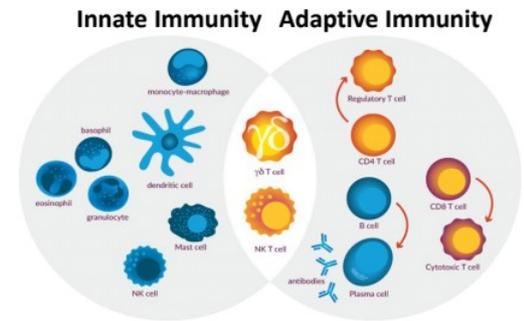
OFF-THE-SHELF THERAPEUTICS

- ✓ Fully modular platform
- ✓ High developability
- ✓ Small size favors tumor penetration
- ✓ Proven quality of antibody products
- ✓ 2 formats in the clinic : bsVHH and bsVHH-Fc



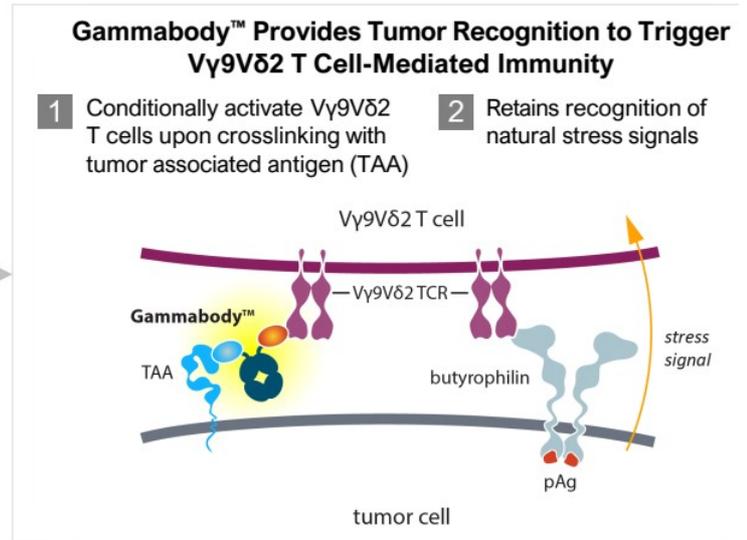
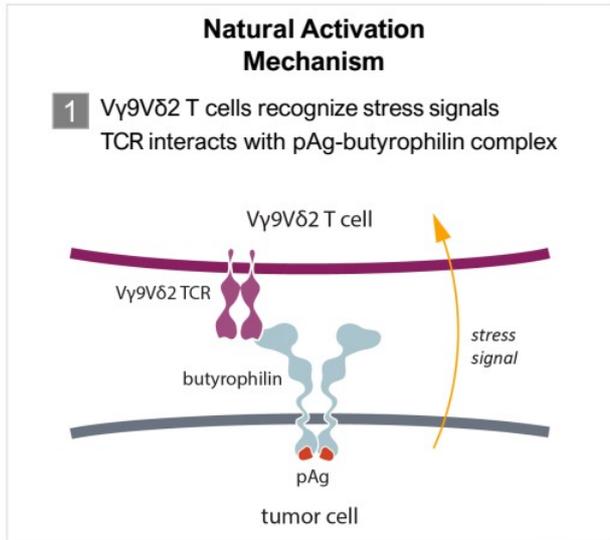
Bispecific $\gamma\delta$ T cell-engagers aim to harness innate & adaptive immunity

- Largest $\gamma\delta$ -T cell subset in blood: (~90-95% of total $\gamma\delta$ -T cells)
- Natural ability to recognize and kill tumor cells
- Highly cytotoxic
- Relatively abundant in tumor-infiltrating lymphocytes
- Presence of $\gamma\delta$ T cells associated with improved outcomes in cancer patients
- Recognize tumors through phosphoantigen-BTN2A1/3A1 complex
- Consistent proinflammatory cytotoxic effector T cell population
- Does not contain immune-dampening regulatory T cell subsets
- Ability to present antigen and orchestrate immune responses



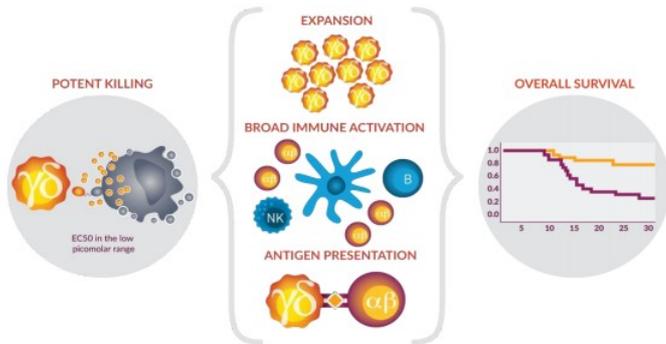
Adapted from Dranoff G., Nature Rev. Cancer 2004; 4: 11-22

Off-the-Shelf Gammabody™ Platform: Enhances Innate Tumor Recognition by Directing Vγ9Vδ2 T Cells to the Cancer Cells



LAVA's Gammabody™ directs Vγ9Vδ2 T cells to tumors with high affinity to induce direct tumor cell killing and orchestrate an immunological cascade of anti-cancer responses and while retaining tumor selectivity

Cascade of Anti-Cancer Responses – Potential Translation to Favorable Therapeutic Window



In addition to direct tumor cell killing, V γ 9V δ 2 T cells have the potential to orchestrate an immunological cascade response that includes activation of innate and adaptive immune cells in the tumor microenvironment

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

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Efficacy:

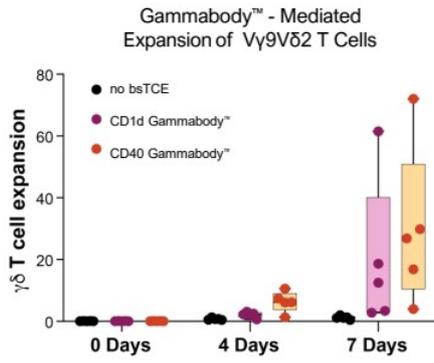
- Potent killing of cancer cells (EC₅₀s in the low picomolar range)
- No co-activation of immune-suppressive Tregs which dampen antitumor efficacy of cytotoxic T cells
- Orchestrate innate and adaptive immune responses, potentially resulting in potent and durable responses
- Activity against hematologic malignancies and solid tumors including immunologically “cold” tumors
- Potential for expansion of V γ 9V δ 2 T cells can result in an increased number of anti-tumor V γ 9V δ 2 T cells in the tumor

Safety:

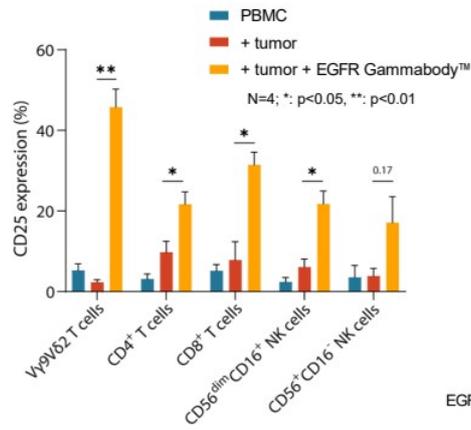
- Conditional activation with high accuracy
- Greatly reduced potential for cytokine release syndrome (CRS); No evidence of CRS in NHP studies

Expansion & Cascade Response Without Treg Activation in Preclinical Models

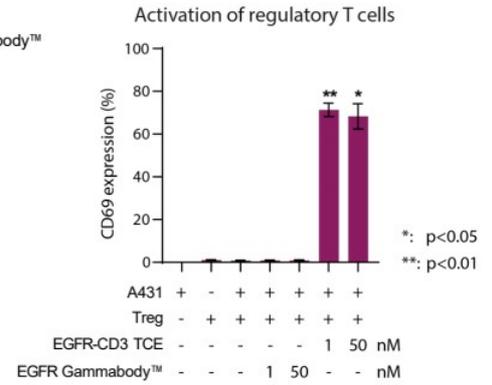
Expansion



Cascade Response



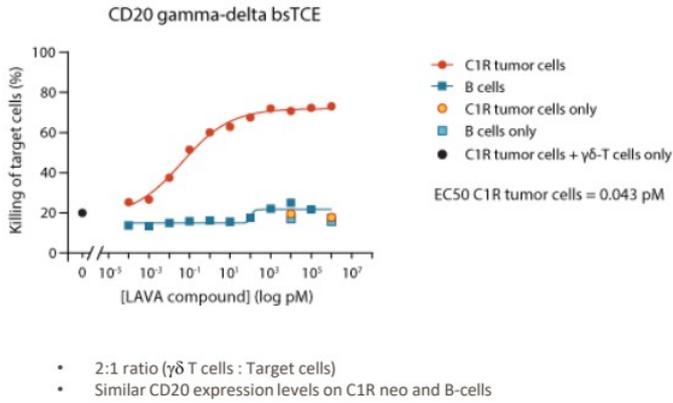
No Treg Activation



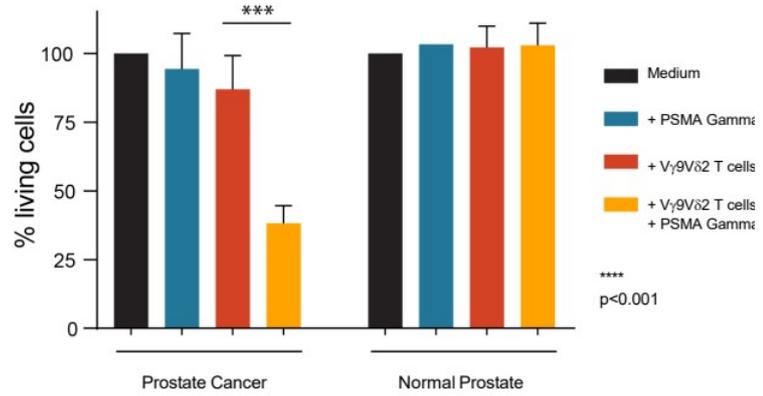
Gammabody™ can induce robust gamma delta T cell expansion and can amplify the anti-tumor immune response via downstream activation of other immune cells while avoiding co-activation of immunosuppressive T cells such as Tregs

Gammabody™ Can Selectively Kill Cancer Cells While Sparing Healthy Cells in Hematologic Malignancy and Solid Tumor models

CD20 Gammabody™ Mediated Killing



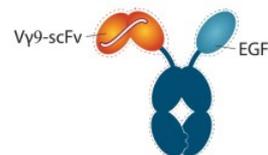
PSMA Gammabody™ Mediated Killing



Preferential killing of cancer versus healthy cells demonstrated *in vitro* and *ex vivo*;
 May prevent on-target/off-tumor mediated toxicity and allow for targeting of widely expressed tumor associated antigens

Non-Clinical Safety Data Indicate Good Tolerability

- Non-clinical safety studies using Gammabody™ molecules designed for cross-reactivity support the benign safety profile of the platform
- NHP studies completed with Gammabody™ molecules targeting CD1d, CD20 and EGFR
 - CD1d, CD20 targeting surrogate Gammabody™ (without Fc) were dosed up to 10 mg/kg (4 hr infusion, 4 doses, every 2 days) and biweekly at 1 mg/kg for 1 month
 - EGFR targeting surrogate Gammabody™ (without Fc) was dosed up to 10 mg/kg (4 hr infusion, 4 doses, every 2 days)
 - EGFR-targeting surrogate Gammabody™ (Fc-containing) was dosed up to 23 mg/kg (0.5 hr infusion, 4 weekly doses)
- **No signs of cytokine release syndrome, no changes in general health parameters, relevant clinical chemistry, hematology or histopathology observed**
- In contrast, EGFR-targeting is severely toxic for first generation bsTCEs
 - NHPs infused with a CD3xEGFR BiTE required euthanasia within 3 days at doses that were 200-fold lower (on a molar basis) compared to an EGFR Gammabody with cell death observed in all tissues expressing EGFR (Lutterbuese et al., PNAS 2010)



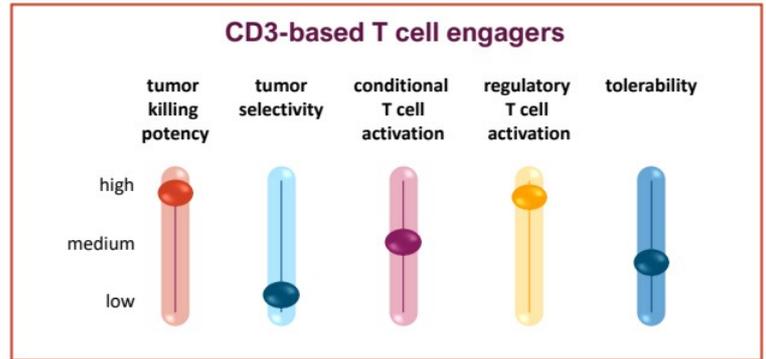
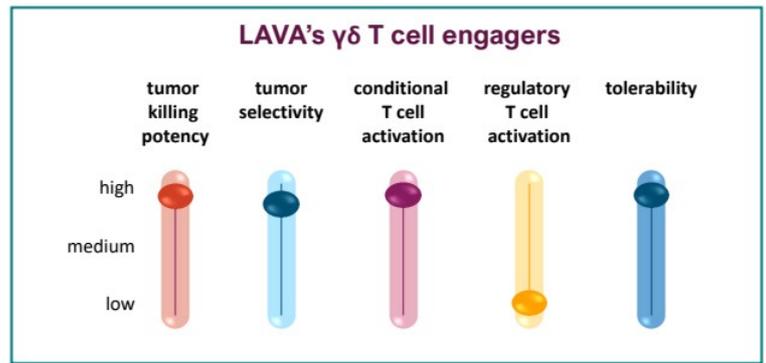
Gammabody™ Platform: A Novel T cell engager approach for cancer therapy

$\gamma\delta$ T cell engager platform

- Highly potent (kills at picomolar concentrations)
- Recruits additional immune effector cells by antigen presentation and cascade response
- No activation of regulatory T-cells

- Tumor-cell selective, relative sparing of healthy cells expressing the target
- Low risk for on-target / off tumor toxicity
- Low risk for CRS anticipated
- Potential for a wide therapeutic window

- Applicable to hematological and solid tumor indications (including 'cold' tumors)



Clinical-stage company

LAVA-051

*Targets CD1d to Activate $V\gamma 9V\delta 2$ T Cells and iNKT Cells
for the Potential Treatment of CLL, MM & AML*

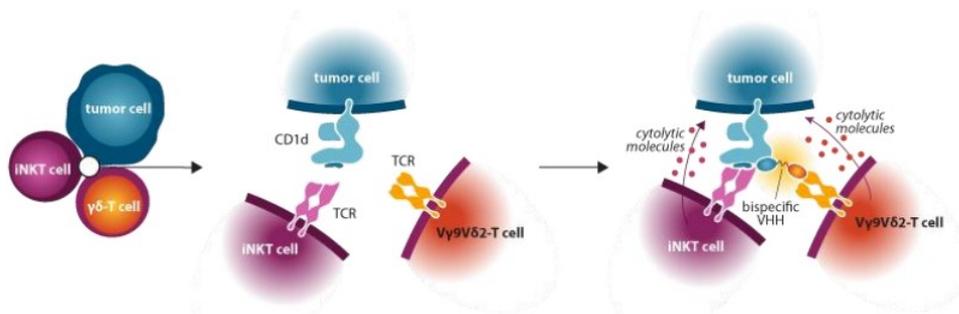
LAVA-051: First-in-Class Gammabody™ Targeting CD1d

Format

- Humanized bispecific single domain antibody (bsVHH) of 27kDa
 - Short plasma half-life, prolonged functional half-life through high affinity TCR binding

Mechanism of Action

- Engages V γ 9V δ 2 T cells to mediate potent killing of CD1d-expressing tumor cells
 - Activates iNKT cells to mediate killing of CD1d-expressing tumor cells as a secondary mechanism of action
 - CD1d is expressed on tumor cells in CLL, MM and AML
 - Pre-clinical data support mechanism of action, anti-cancer activity, effector cell expansion and tumor selectivity

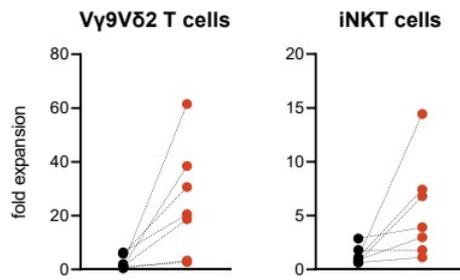


Status

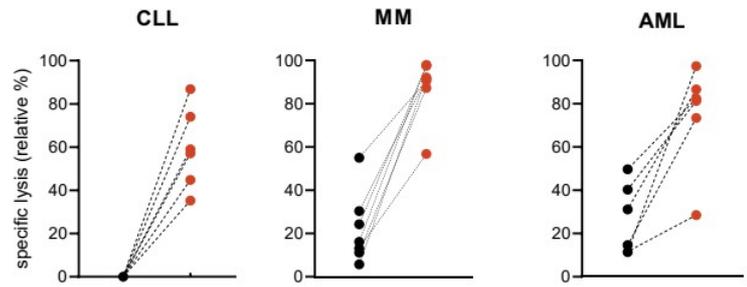
- Phase 1/2a clinical trial ongoing in MM, CLL and AML

LAVA-051: Pre-Clinical Data Support Mechanism of Action and Function

Expansion of V γ 9V δ 2 T and iNKT cells



Lysis of patient tumor cells

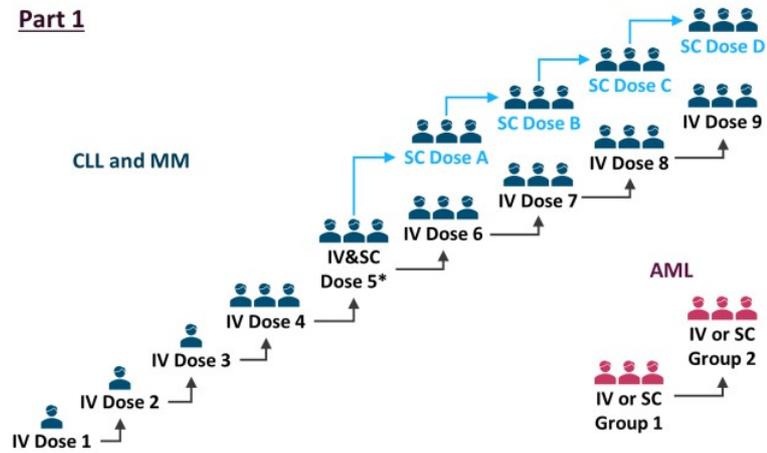


● negative control
● LAVA-051

- LAVA-051 triggers expansion of V γ 9V δ 2 T and iNKT cells in the presence of CD1d-positive tumor cells
- LAVA-051 mediates V γ 9V δ 2 T and iNKT cell-mediated cytotoxicity of patient CLL, MM and AML cells

LAVA-051 Phase 1/2a in Hematological Malignancies

- Primary objectives: investigate safety and tolerability of LAVA-051 and determine the recommended Phase 2 dose
- Secondary objectives: include evaluation of PK, PD, immunogenicity and preliminary antitumor activity
- LAVA-051 administered as 2-hour infusion (IV), or subcutaneous injection (SC) (day 1, 8 and twice a week thereafter)



* Cohort 5 only: 2nd dose administered SC, remaining doses IV
[Clinicaltrials.gov NCT04887259](https://clinicaltrials.gov/NCT04887259)
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LAVA-051 – Initial Phase 1 Data - Safety

- LAVA-051 has reached a dose of 200 µg (~400x the starting dose) in MM and CLL patients
- Most observed AEs have not been suspected to be related
- Frequency and severity of AEs have not correlated with increasing dose levels
- No CRS and no ICANS (ASTCT) and no clinically relevant increase in the CRS-related cytokine IL-6

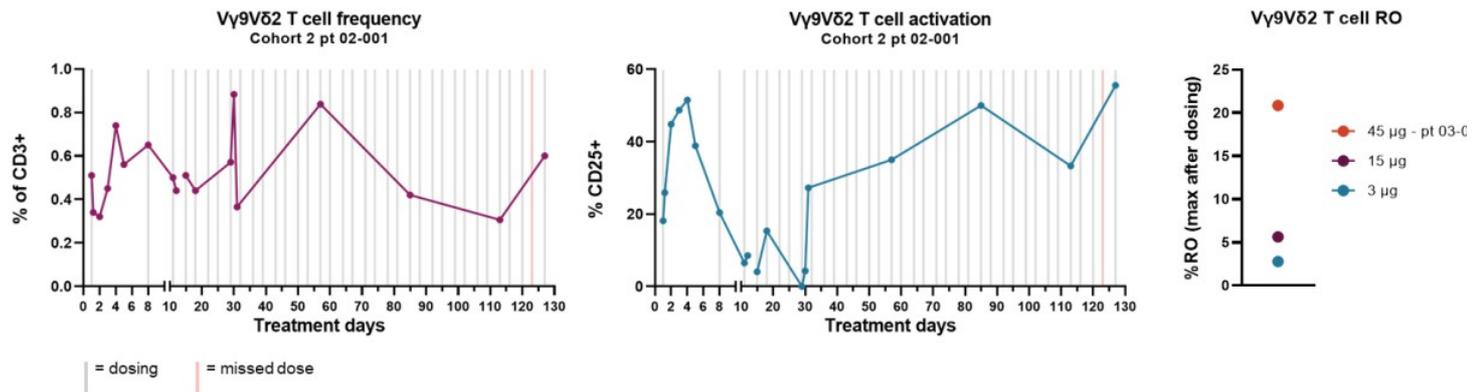
(Data cut-off date: 11 Nov 2022)

[ASH 2022 abstract #2014](#)

ICANS = Immune Effector Cell Associated Neurotoxicity Syndrome;
DLT = Dose Limiting Toxicity; ASTCT = American Society for Transplantation and Cellular Therapy
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LAVA-051 – Initial Phase 1 Data – Pharmacodynamics



- Pharmacodynamic parameters reflect changes expected for the LAVA-051 mechanism of action
 - Vγ9Vδ2-T cell activation markers (CD25 and CD69) upregulated following dosing
 - Maximum Vγ9Vδ2 T cell receptor occupancy (RO) increased with dose

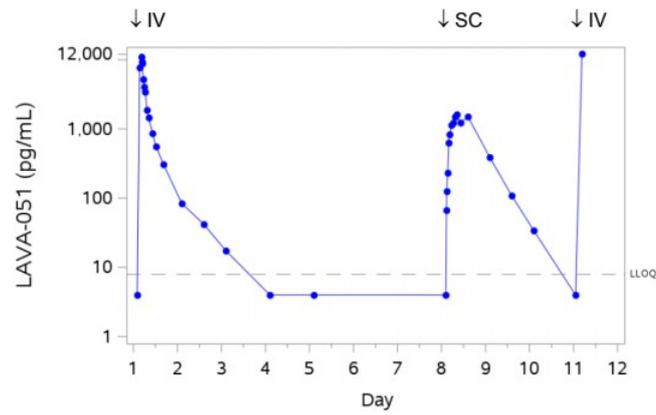
[ASCO 2022 abstract 2577](#); [ASH 2022 abstract #2014](#)

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LAVA-051 – Pharmacodynamics

Pharmacokinetics 1st dose IV, 2nd dose SC patient 32-001 cohort #5



- Linear LAVA-051 pharmacokinetics
- SC bioavailability 74% compared to IV (based on data from Pt 32-001)

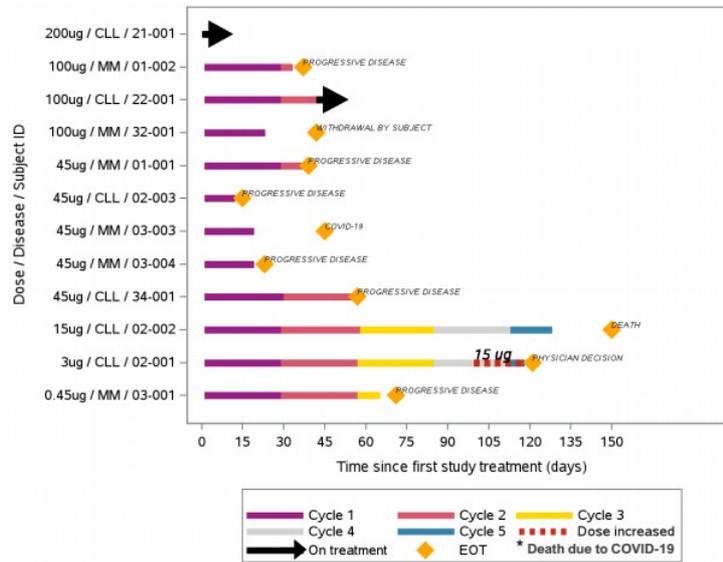
[ASH 2022 abstract #2014](#)

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LAVA-051 – Initial Phase 1 Data - Patient Characteristics and Time on Treatment

MM/CLL	6/6
Male/Female	8/4
Median age (range)	69 (59-76)
Prior therapies, median (range) – MM/CLL	4 (3-5) / 5.5 (4-13)

Data cut-off: 11 NOV 2022

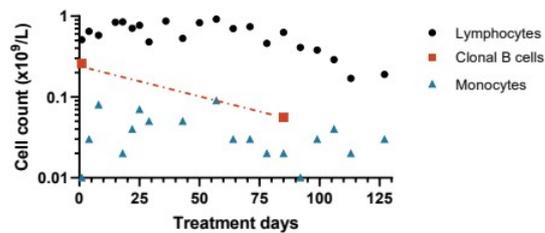


ASH 2022 abstract #2014, corrected
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LAVA-051 – Initial Phase 1 Data - Potential Signs of Activity

CLL

- Patient with R/R CLL (15 µg)
- Temporary enlargement and tenderness of several involved lymph nodes accompanied by grade 2 fever during Cycle 1
 - Resembled a tumor-flare reaction, as reported in CLL with lenalidomide
- **Patient assessed as having stable disease**
- **Percent of clonal B cells in peripheral blood decreased**
- **Numbers of CD1d expressing monocytes remained similar**



MM

- High-risk MM patient (45 µg)
- 4 prior lines of therapy within 6 years of diagnosis
- Refractory to last 3 lines of treatment
- **23% reduction in M-protein**

- Both patients ceased treatment due to CO

[EHA 2002 abstract #1463](#)

R/R = Relapsed/Refractory

Permission for photo obtained

Data on file: LAVA Therapeutics N.V

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LAVA-051: Summary of Initial Phase 1 Data Presented

- LAVA-051 is a next-generation bispecific $\gamma\delta$ T cell engager designed for a broad therapeutic window
- LAVA-051 has reached a dose of 200 μg (400x the starting dose) in MM and CLL patients
 - Most observed Adverse Events (AEs) have not been suspected to be related to LAVA-051 treatment
 - Frequency and severity of AEs have not correlated with increasing dose levels
 - No Cytokine Release Syndrome (CRS) and no ICANS (ASTCT - criteria)
 - No significant increase in the CRS-related cytokine IL-6
- Linear pharmacokinetics and satisfactory SC bioavailability
- PD parameters reflect changes as expected per Mechanism of Action
- Potential signs of clinical activity
- Trial continuing, including US sites (IND cleared) and evaluation of SC dosing



LAVA-1207

Gammabody™ that Activates $V\gamma 9V\delta 2$ T Cells by Targeting PSMA for the Treatment of mCRPC

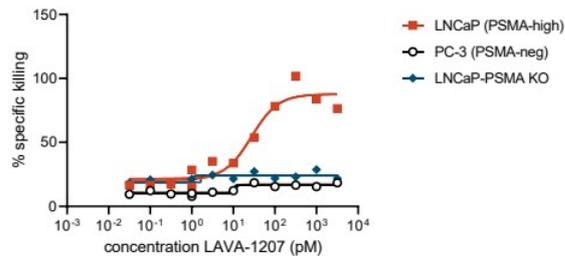
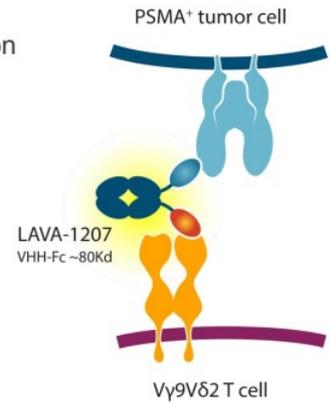
LAVA-1207: PSMA-targeting Gammabody™ for Prostate Cancer

Format

- Contains a Fc domain for extended plasma half-life; silenced to avoid off-target T cell activation
- Small size (compared to regular IgG antibodies) to facilitate tumor penetration

Mechanism of Action

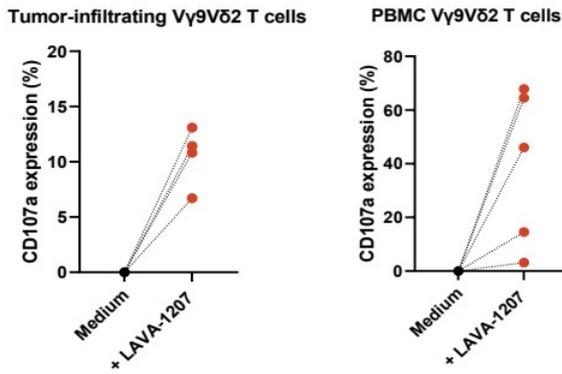
- Specifically directs V γ 9V δ 2 T cells to PSMA-expressing tumor cells
 - PSMA is a well-validated tumor target
- Mediates potent killing of PSMA-positive tumor cells
- Pre-clinical data support mechanism of action, anti-cancer activity & selectivity



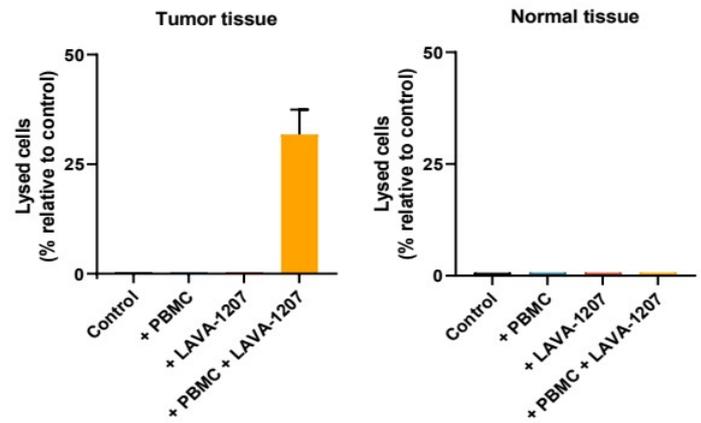
Status

- Phase 1/2a trial in mCRPC; patient recruitment ongoing (NCT05369000)

V γ 9V δ 2 T cell degranulation



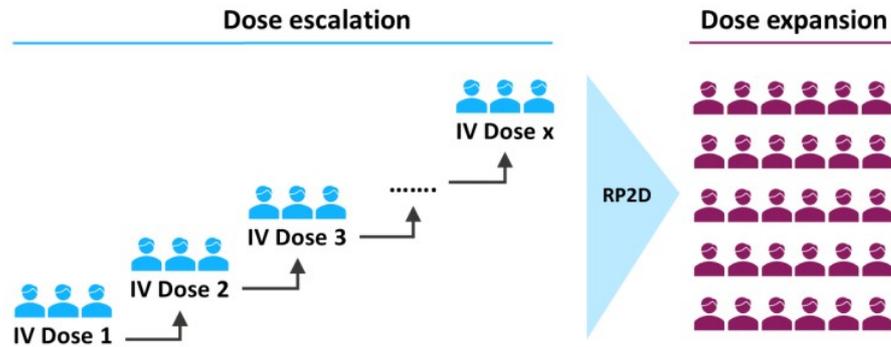
Preferential lysis of prostate tumor cells



- LAVA-1207 triggers activation of autologous V γ 9V δ 2 T cells in the presence of patient-derived tumor cells
- LAVA-1207 induces selective tumor cell lysis

LAVA-1207 – Phase1/2a Study Design

- Dose escalation in patients with mCRPC (EudraCT 2021-001789-39; NCT05369000)
- Primary objectives: investigate safety and tolerability of LAVA-1207
- Secondary objectives: evaluate PK, PD, immunogenicity and preliminary signs of antitumor activity
- LAVA-1207 administered via IV infusion every 2 weeks

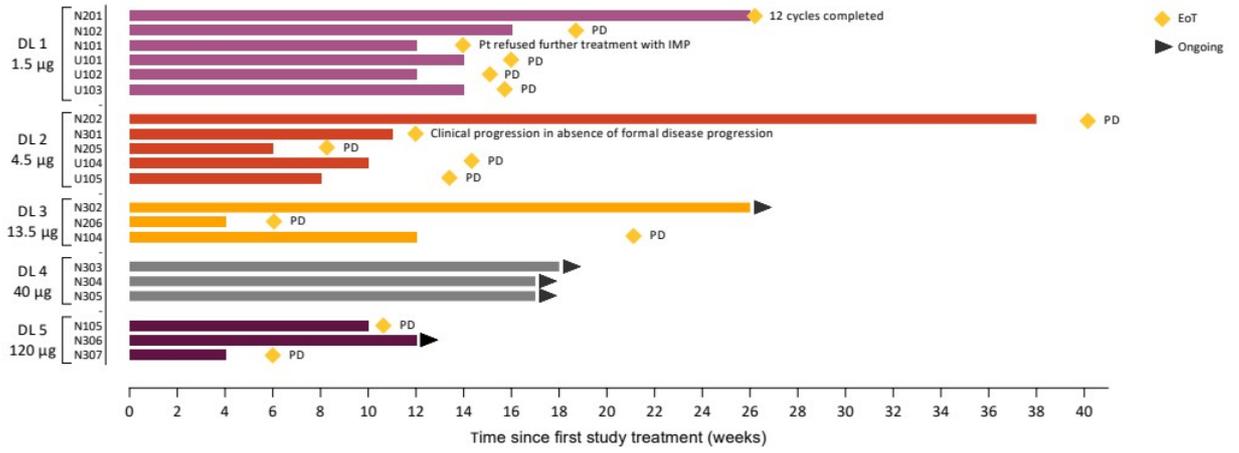


LAVA-1207 – Patient Baseline Characteristics

Age, median (range)	68 (51-76)
Years since diagnosis, median (range)	9 (3-21)
Prior systemic therapies, median (range)	4 (3-10)
Location of metastases	
Bone	19
Lymph node	14
Lung	2
Liver	5
Other visceral	2
Type of progression	
PSA	17
Bone	12
Nodal	12
Visceral	10

N=20

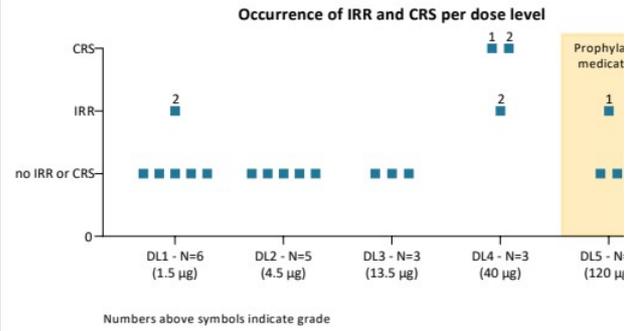
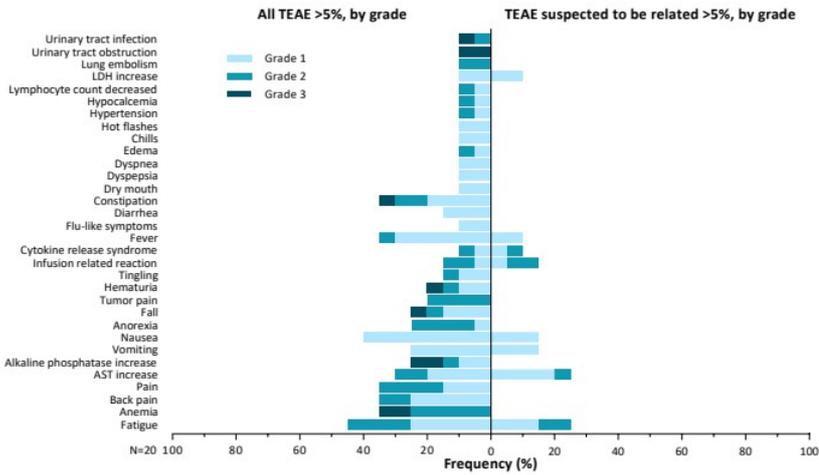
LAVA-1207 – Time on Treatment



Data cut-off date: 8 Dec 2022

- A dose level (DL) of 120 µg (starting dose, 1.5 µg, MABEL approach) completed
 - DL 1 included 6 pts, 3 from EU, 3 from US; DL 2 included 5 pts, 3 from EU, 2 from US
- A total of 20 patients have been treated with LAVA-1207 with treatment duration ranging from 4 to 38 weeks
- Next dose level: 360 µg

LAVA-1207 – Initial Phase 1 Data - Safety



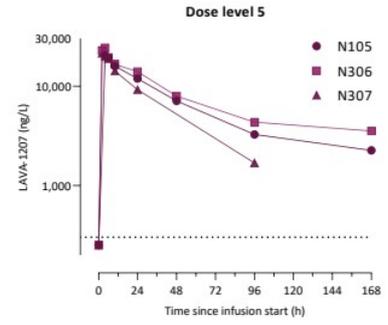
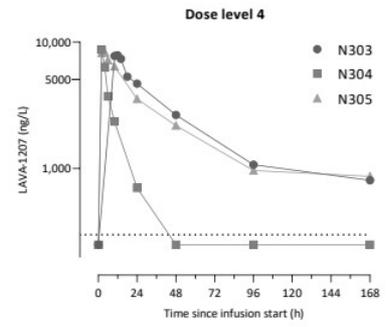
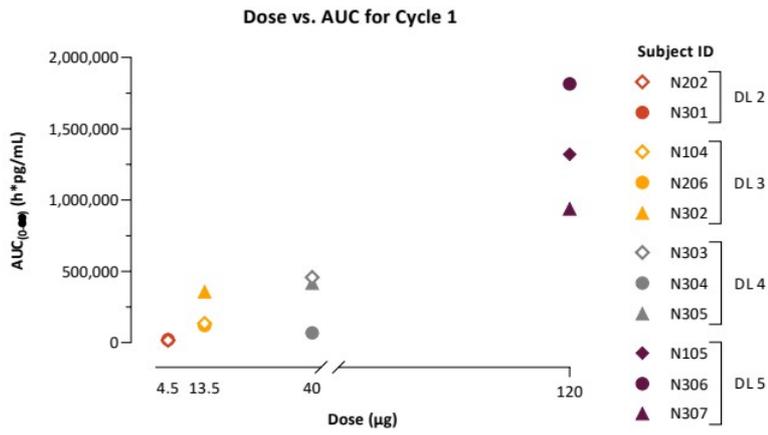
As of 20 Oct 2022, prophylaxis with antipyretic and antihistaminic treatment to mitigate potential fever, IRR or CRS was implemented.

Data cut-off date: 8 Dec 2022

- Most observed AEs not suspected to be related and no DLT
- Treatment emergent AEs (TEAEs) that were suspected to be related were grade 1 or 2
- No increase in severity or frequency of TEAEs with increasing doses and no patient discontinued treatment due to AE
- One grade 4 AE occurred (spinal cord compression, DL 5), which was non-related

[ASCO GU 2023 abstract #153](#)
Data on file: LAVA Therapeutics N.V.
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LAVA-1207 – Pharmacokinetics



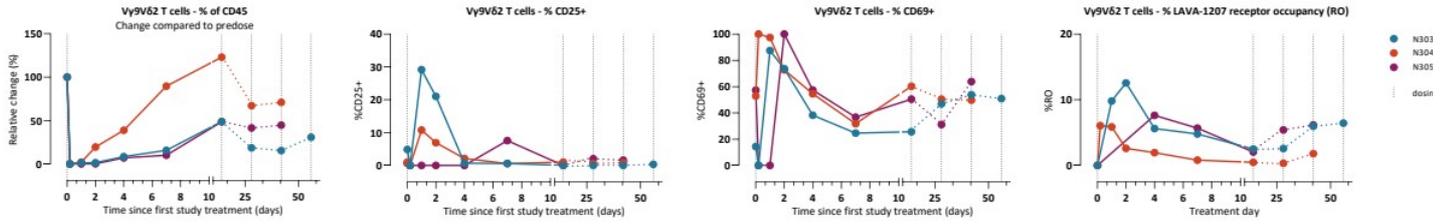
Data cut-off date: 8 Dec 2022

- Pharmacokinetics of LAVA-1207 appears linear

[ASCO GU 2023 abstract #153](#)
 Data on file: LAVA Therapeutics N.V.
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LAVA-1207 – Pharmacodynamics

Dose level 4 – 40 µg

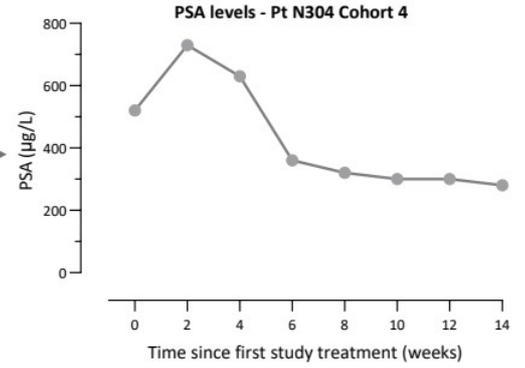
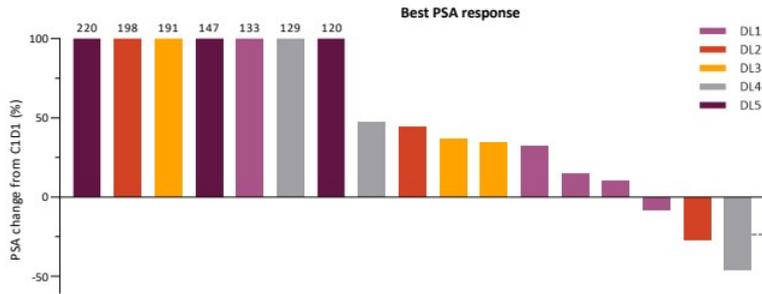


Data cut-off date: 8 Dec 2022

- Pharmacodynamics reflect changes expected as per MoA
 - Pronounced drop in Vγ9Vδ2-T cell frequency 2 hr after dosing, suggesting Vγ9Vδ2-T cell re-distribution, with subsequent recovery
 - Vγ9Vδ2-T cell activation markers (CD25 and CD69) upregulated following dosing
 - Receptor occupancy (RO) was detectable up to day 14 after EoI, with peak levels ranging from 6.1% to 12.6%

LAVA-1207 – Preliminary Signs of Antitumor Activity

- Out of 14 iRECIST evaluable patients, 8 had iSD at week 8.



Data cut-off date: 8 Dec 2022

Patient N304 – 40 µg

- Largest overall decrease in PSA was 61% (46% vs baseline)
- Per treating physician, the patient improve clinically with improvement in pain and fati
- Ongoing in the study

Summary of Initial Phase 1 Data Presented

- LAVA-1207 is a PSMA targeting bispecific antibody belonging to a novel class of $\gamma\delta$ T cell engagers (Gammabody™)
- LAVA-1207 has reached a dose of 120 μg (starting dose 1.5 μg) without the occurrence of high-grade (>2) CRS or DLTs in therapy refractory mCRPC patients
 - Frequency and severity of AEs do not appear to be dose-dependent
 - Most observed AEs were not suspected to be related
 - Next dose level (360 μg) is ongoing
- Preliminary signs of clinical activity observed with disease stabilization and PSA reduction during dose escalation
- Pharmacodynamics reflect changes as expected per MoA
- Dose escalation continues in both the EU and the US

LAVA-1223 – Licensed to Seagen

Gammabody™ for the treatment of EGFR-expressing solid tumors

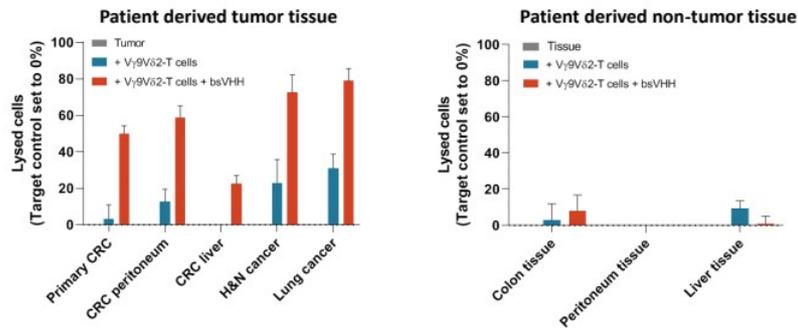
LAVA-1223: EGFR-Targeting Gammabody™

Format

- Gammabody™ format containing a silenced Fc domain

Mechanism of Action

- Induces preferential lysis of EGFR-expressing tumor cells while relatively sparing EGFR-expressing normal cells



Status

- Exclusive worldwide license agreement with Seagen Inc.
- Seagen to develop and commercialize LAVA-1223, potential for milestones of up to approximately \$650 million and royalty

LAVA-1266

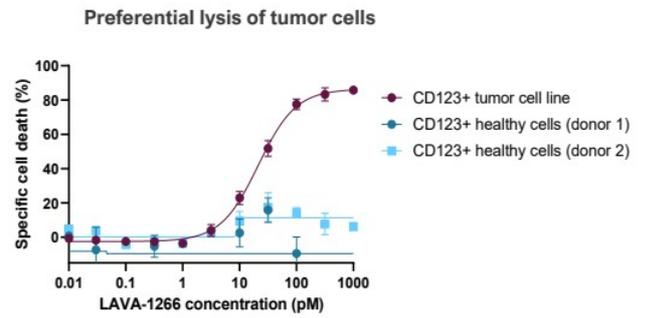
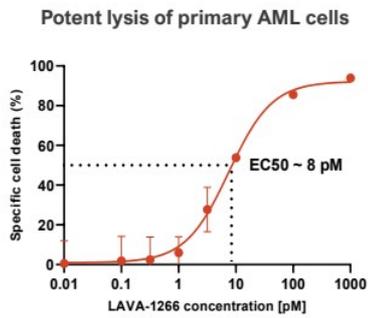
*CD123 Targeting Gammabody™ for the Treatment
of Hematologic Malignancies*

LAVA-1266: CD123-Targeting Gammabody™

In Development for Treating Hematological Malignancies

Mechanism of Action

- Induces preferential lysis of CD123-expressing tumor cells while relatively sparing CD123-expressing normal cells
 - CD123 is overexpressed in a wide range of hematological malignancies



Status

- CTA/IND enabling studies ongoing; filing anticipated in 2024



Milestones

Gammabody™ Pipeline: Potential in Hematological and Solid Tumor Indication

Candidate	Target	Indication(s)	Discovery	Preclinical	Phase 1	Phase 2	Milestones	
LAVA-051	CD1d	MM CLL AML					<ul style="list-style-type: none"> Initial data released ASCO 2022 Additional data in 2023 	
LAVA-1207	PSMA	mCRPC					<ul style="list-style-type: none"> Initial data released ASCO GU 2023 Additional data 2H 2023 	
LAVA-1223	EGFR	Solid Tumors					<ul style="list-style-type: none"> Licensed to Seagen Sep 2022 	
LAVA-1266	CD123	Hematologic Malignancies					<ul style="list-style-type: none"> IND/CTA filing expected in 2024 	
LAVA-1278	CD40	Hematologic Malignancies						
Janssen Collaboration	undisclosed							

MM: multiple myeloma
 CLL: chronic lymphocytic leukemia
 AML: acute myeloid leukemia
 PSMA: prostate-specific membrane antigen
 EGFR: epidermal growth factor receptor
 mCRPC: metastatic castration-resistant prostate cancer

 Hematologic malignancy  Solid Tumor



Gamma delta T cell engagers for the development of next-generation cancer therapeutics

Corporate Presentation
February 2023
