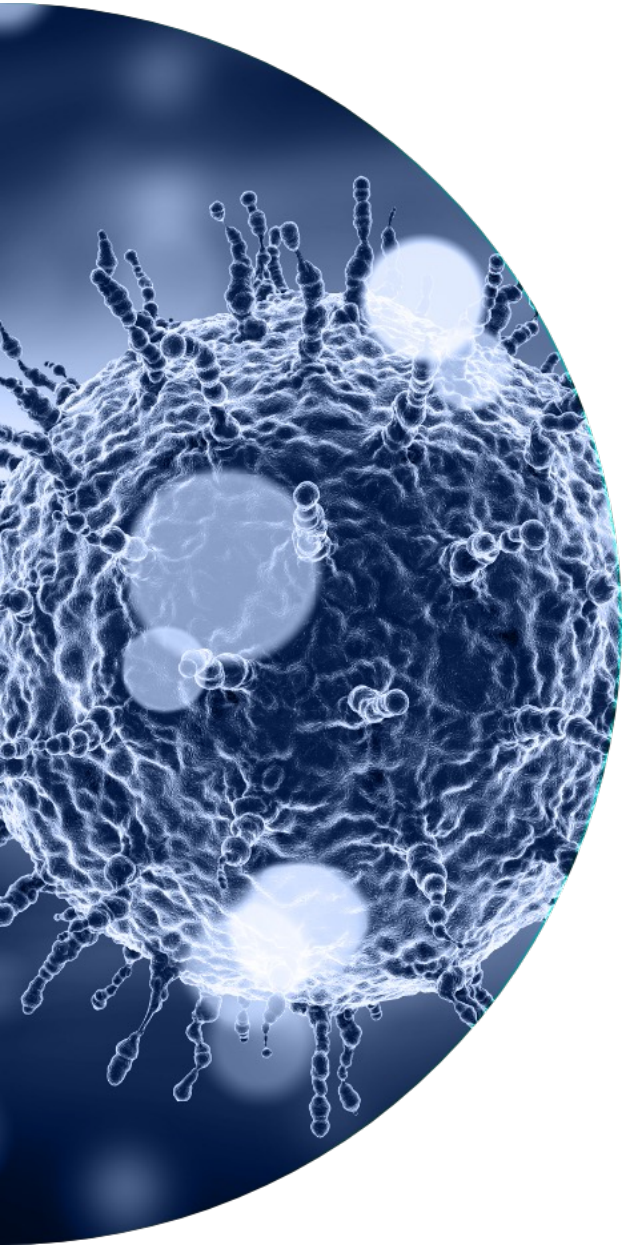

CANDEL THERAPEUTICS

# Tipping the balance in favor of the immune system to fight cancer

Corporate Presentation | November 2023

NASDAQ: CADL

10November2023 Update

# Forward Looking Statements

This Presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this Presentation, including express or implied statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market size, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "target," "seek," "predict," "potential," "continue" or the negative of these terms or other comparable terminology. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market size, 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. Forward-looking statements in this Presentation include, but are not limited to, statements about: the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs; our ability to efficiently discover and develop product candidates; our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project; our ability to obtain and maintain regulatory approval of our product candidates; our ability to compete with companies currently marketing or engaged in the development of treatments that our product candidates are designed to target; our reliance on third parties to conduct our clinical trials and to manufacture drug substance for use in our clinical trials; the size and growth potential of the markets for our product candidates and our ability to serve those markets; the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates; our ability to obtain and maintain adequate intellectual property rights; our estimates of our future expenses, revenue, capital requirements or our need for or ability to obtain additional financing; the potential benefits of strategic collaboration agreements, our ability to enter into additional strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise; our financial performance; developments and projections relating to our competitors or our industry; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to, our preclinical studies or current and future clinical trials. We caution the recipient not to place considerable reliance on the forward-looking statements contained in this Presentation. The forward-looking statements in this Presentation speak only as of the date of this document, and we undertake no obligation to update or revise any of these statements. Our business is subject to substantial risks and uncertainties, including those referenced above.

Certain information contained in this Presentation relates to or is based on estimates, projections and other information concerning the Company's industry, its business and the markets for its programs and product candidates and studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Presentation involves a number of assumptions; there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

These forward-looking statements are based on the beliefs of our management as well as assumptions made by and information currently available to us. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. If such assumptions do not fully materialize or prove incorrect, the events or circumstances referred to in the forward-looking statements may not occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as required by law. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. Additional risks and uncertainties that could affect our business are included under the caption "Risk Factors" in our most recent Form 10-Q filed with the Securities and Exchange Commission on August 10, 2023.

# Candel at a glance

## Industry leader in the development of viral immunotherapies for patients living with cancer

- CAN-2409: Off-the-Shelf Therapy, Individualized Cancer Response
  - Engineered, replication-defective adenoviral gene construct encoding herpes simplex virus (HSV)-thymidine kinase
  - "Pipeline in a product" strategy advancing multiple programs in several large indications
  - Established proof of mechanism in patients in each indication currently under evaluation
  - Numerous upcoming catalysts:
    - Topline phase 2 OS data in NSCLC (Q2 2024)
    - Topline phase 2b (Active Surveillance) and phase 3 (Intermediate/High Risk) Prostate Cancer clinical data (Q4 2024)

- CAN-3110: Oncolytic Virus with Tumor-Specificity
  - Engineered, replication-competent HSV designed for tumor-specificity
  - Encouraging survival data recently announced during May 2023 ASGCT conference from phase 1 Recurrent High-Grade Glioma clinical trial
  - Publication in *Nature*
  - Opportunity for creation of "pipeline in a product" by expansion into indications beyond brain cancers
  - Clinical and immunological biomarker data on Arm C, evaluating repeat dosing regimen of CAN-3110 (2H 2024)

- enLIGHTEN™ Discovery Platform Based on Advanced Analytics and HSV Technology
  - Validating partnership with UPenn Center for Cellular Immunotherapies focused on combination with CAR-Ts in solid tumors

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# Leadership team with decades of experience in oncology, immunology and drug development

## Paul Peter Tak, M.D., Ph.D., FMedSci

*President & Chief Executive Officer*

gsk · sitryx · Flagship Pioneering · Amsterdam UMC University Medical Centers

## Jason Amello

*Chief Financial Officer*

genzyme · Akebia Therapeutics · saniona · ALAUNOS THERAPEUTICS

## Francesca Barone, M.D., Ph.D.

*Chief Scientific Officer*

Kintai Therapeutics · University of Birmingham

## Garrett Nichols, M.D., M.S.

*Chief Medical Officer*

gsk · ViiV Healthcare · CHIMERIX · istari ONCOLOGY

## Seshu Tyagarajan, Ph.D., RAC

*Chief Technical and Development Officer*

NOVARTIS · Roche · Biogen · Lilly

## Susan Stewart, J.D.

*Chief Regulatory Officer*

Tokai Medical Products · genzyme · Abbott

# Research Advisory Board of premier thought leaders

**James Allison, Ph.D.**
*Chair of the Department of Immunology*
*MD Anderson Cancer Center*
*Director of the Parker Institute for Cancer Research*
*2018 Nobel Recipient*

**Edward Benz, M.D.**
*President and CEO Emeritus*
*Dana-Farber Cancer Institute*

**Henry Brem, M.D.**
*Director, Department of Neurosurgery*
*Professor of Neurosurgery*
*Johns Hopkins University*

**Roy Herbst, M.D., Ph.D.**
*Chief of Medical Oncology*
*Yale Cancer Center*

**Philip Kantoff, M.D.**
*Former Chair, Department of Medicine*
*Memorial Sloan Kettering Cancer Center*

**Gary Nabel, M.D., Ph.D.**
*Chief Innovation Officer of OPKO and*
*President/CEO of ModeX Therapeutics*
*Former CSO Sanofi*

**Padmanee Sharma, M.D., Ph.D.**
*Professor of Genitourinary Medical Oncology*
*and Immunology*
*MD Anderson Cancer Center*

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# Clinical pipeline focused on value creation

| PROGRAM | INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|
| *Adenovirus Platform* | | | | | |
| **CAN-2409** Prostate Cancer | *Localized, Intermediate/High Risk, under SPA* | | | | |
| | *Active Surveillance* | | | | |
| **CAN-2409** Lung Cancer | *NSCLC + PD-1/PD-(L)1* | | | | |
| **CAN-2409** Pancreatic Cancer* | *Borderline Resectable Pancreatic Adenocarcinoma* | | | | |
| *HSV Platform* | | | | | |
| **CAN-3110** Brain Cancer | *Recurrent High-Grade Glioma* | | | | |
| **enLIGHTEN™ Discovery Programs** | *Solid Tumors* | | | | |

SPA – special protocol assessment
* Enrollment paused, subject to additional funding

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# CAN-2409

Off-the-shelf therapy, individualized cancer response

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# CAN-2409: Development program

## "Pipeline in a Product" approach advancing multiple programs in several large indications

| Candidate | Indication | Description | Current Phase | | | Timing of Next Milestone |
|---|---|---|---|---|---|---|
| | | | Phase 1 | Phase 2 | Phase 3 | |
| **CAN-2409** | *Localized Prostate Cancer Intermediate / High Risk* | ○ 711 patients<br>○ 2:1 Randomization<br>○ Primary Endpoint: Disease-free survival | → | → | → | Q4:2024 |
| **CAN-2409** | *Localized Prostate Cancer Active Surveillance* | ○ 187 patients<br>○ 2:1 Randomization<br>○ Primary Endpoint: Progression-free survival | → | → | | Q4:2024 |
| **CAN-2409 +PD-1/PD-(L)1** | *Non-Small Cell Lung Cancer* | ○ Fast-track status<br>○ 80 patients<br>○ Primary Endpoint: Response by RECIST criteria and disease control rate | → | → | | Q2:2024 |
| **CAN-2409** | *Borderline Resectable Pancreatic Adenocarcinoma* | ○ ~36 patients<br>○ 2:1 Randomization<br>○ Primary Endpoint: Safety and survival rate at 24 mos | → | → * | | Q4:2023 |

* Enrollment currently on hold

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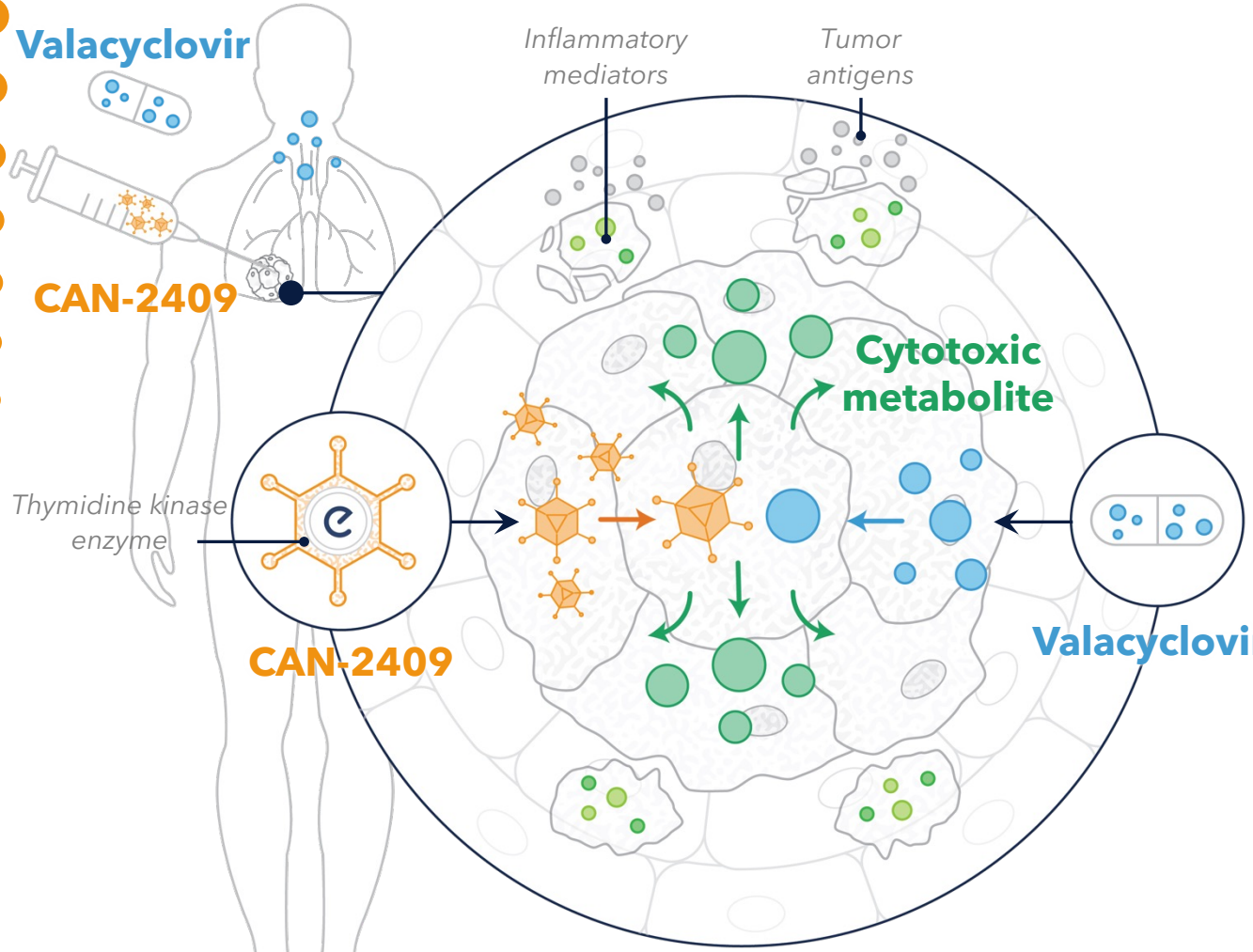
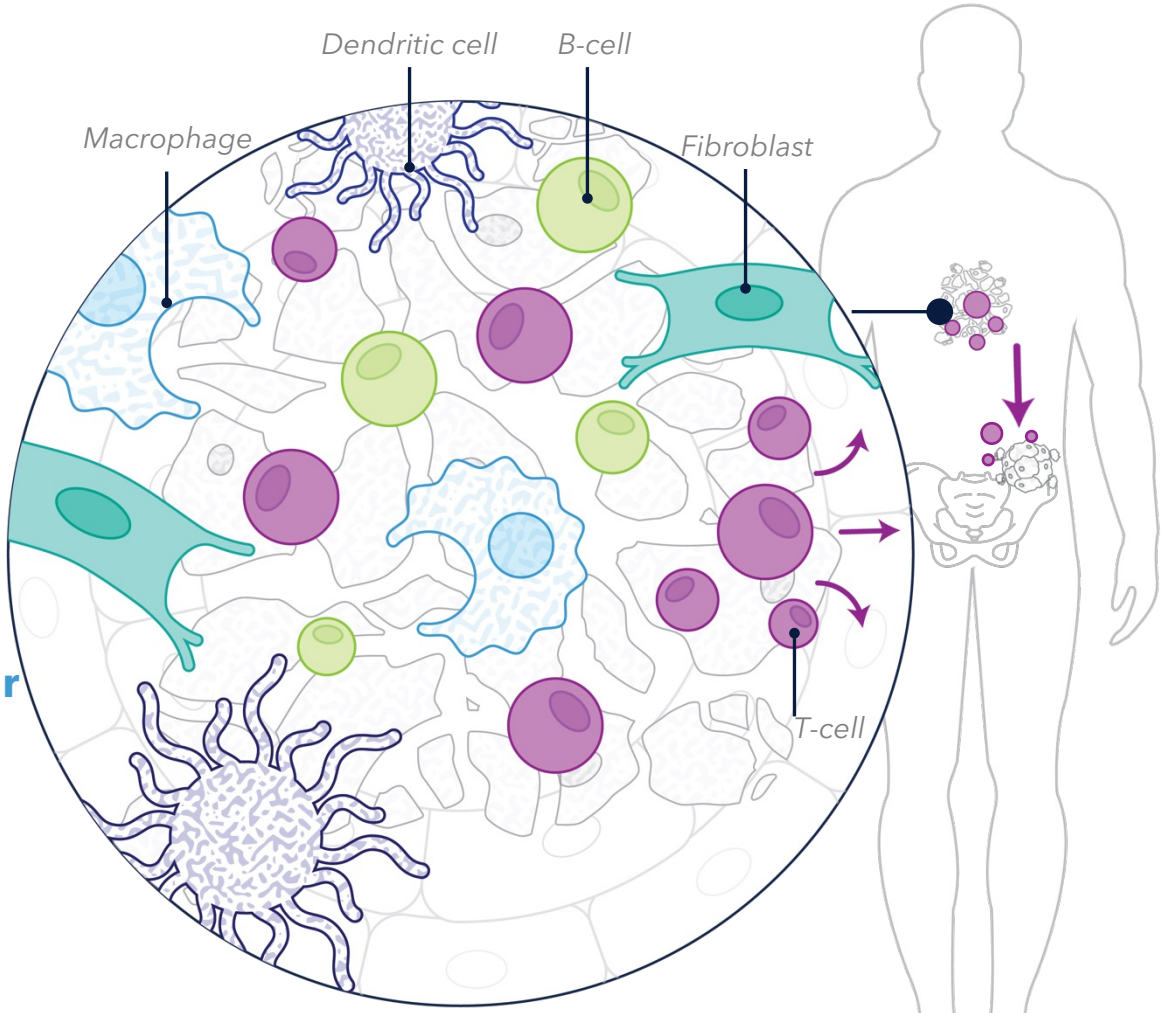
# CAN-2409: Systemic immunotherapy delivered intratumorally

**1. CAN-2409 locally administered combined with oral prodrug**




**2. Localized cytolytic mechanism combined with proinflammatory viral particles**

**3. CAN-2409 induces CD8+ cytotoxic T cells**




**4. Local immunization yields systemic CD8+ T cell mediated response against injected tumor and uninjected metastases**

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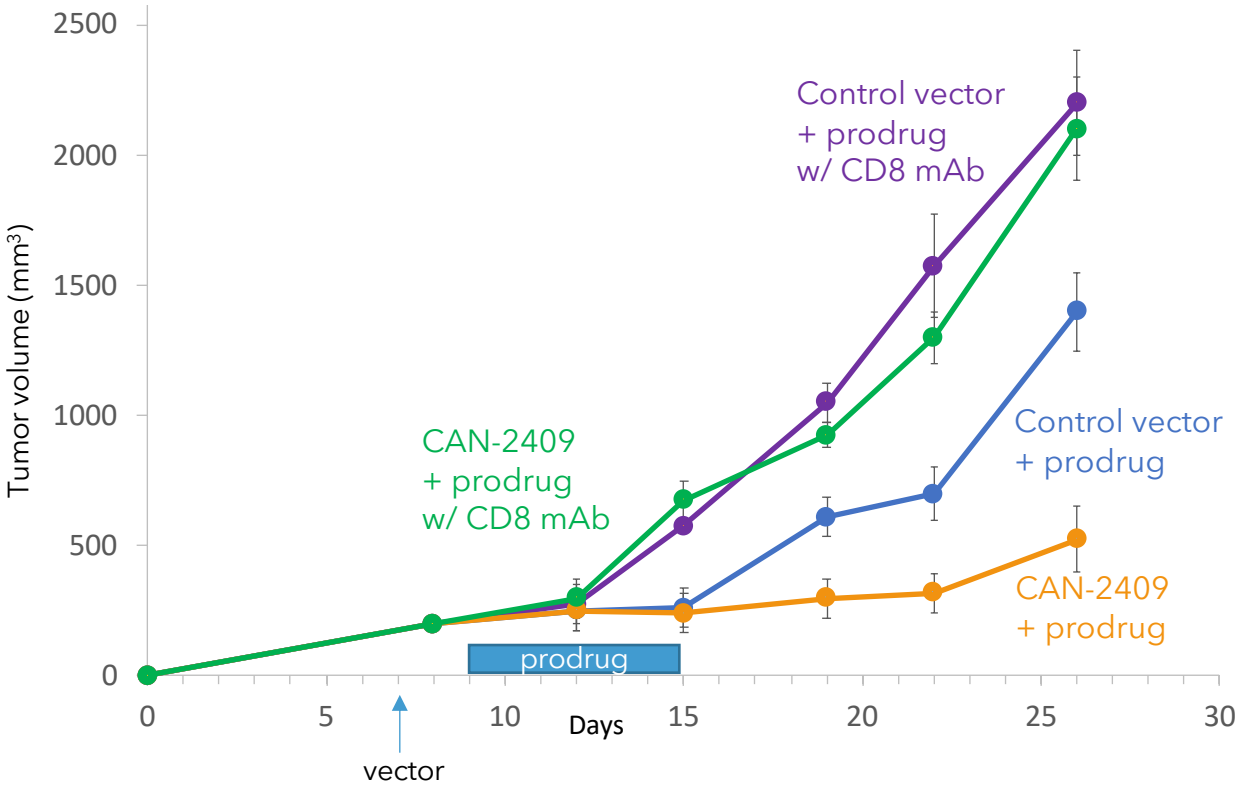
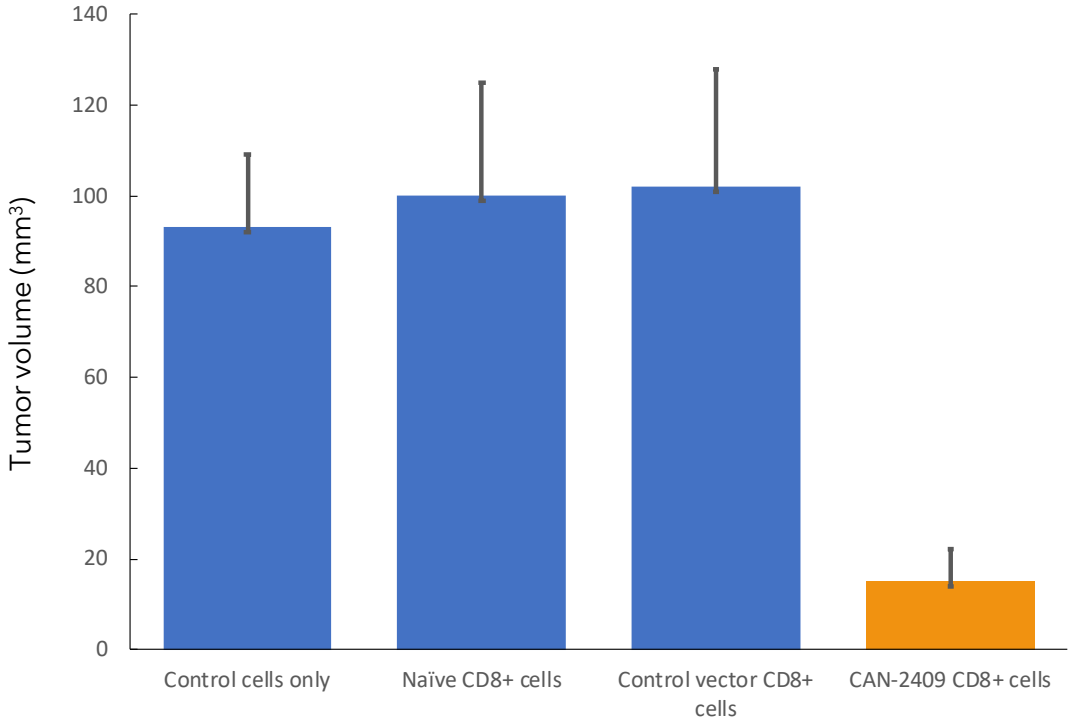
# Response to CAN-2409 treatment is dependent on CD8+ T cells and transferable in mouse models of cancer




## Depletion of CD8+ cells eliminates effect

***Esophageal cancer model (AKR) flank tumors in C57Bl/6 mice (n = 8 per group)***




## CD8+ cells from 'cured' mice protect naïve mice from tumor challenge

***Winn Assay: Lung cancer model (TC-1) flank tumors in C57Bl/6 mice (n = 5 per group)***

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# CAN-2409: Prostate cancer opportunity

## Incidence of localized prostate cancer in the US by risk level


- Prostate cancer is the second leading cause of cancer death among men in the US
- Many men diagnosed with early low/intermediate risk prostate cancer opt for active surveillance over available treatment options, which have a multitude of side effects and impair quality of life
- Within 10 years, 21-38% of these men develop intermediate/high risk cancers that require interventions where the standard of care is radical prostatectomy and radiotherapy combined with ADT/chemical castration
- No new treatments approved for newly diagnosed, localized prostate cancer during the last > 15 years
- Significant opportunity for new treatment for both the active surveillance and intermediate/high risk populations with a favorable tolerability profile and potential to reduce progression and/or recurrence
- Prostate cancer therapy market globally was estimated at $13B in 2022 and is expected to grow to $21B by 2028*

***Target label for CAN-2409#***

- ***Indicated in newly diagnosed localized prostate cancer in combination with radiotherapy +/- short-term ADT, in patients with intermediate- to high-risk disease***
- ***Indicated in newly diagnosed localized prostate cancer in patients with NCCN-defined low-risk disease, or patients with intermediate-risk disease undergoing active surveillance***

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*#Consistent with market research combined with interviews with 22 KOLs (12 US; 10 EU) and 16 US payors. May 2023*
**Source: EvaluatePharma, accessed May 2023*

# Completed phase 2a clinical trial of CAN-2409 combined with radiotherapy +/- androgen deprivation therapy

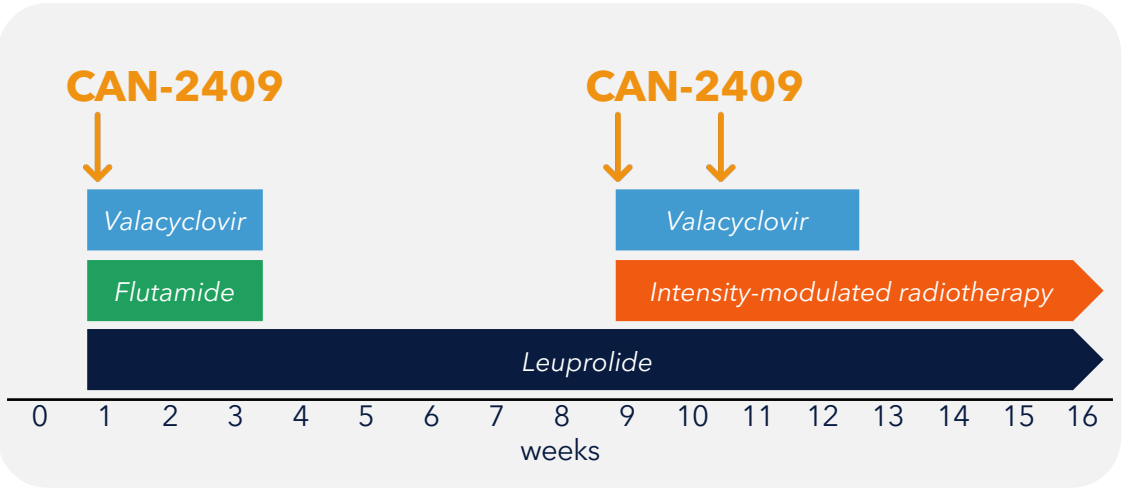
Newly diagnosed localized prostate cancer

**Arm A (33 pts)**
*Low-Risk*
(T1-T2a, Gleason <7, PSA<10)

2 cycles


**Arm B (33 pts)**
*Intermediate-High-Risk*
(T2b-T3, Gleason >6, PSA≥10)

3 cycles



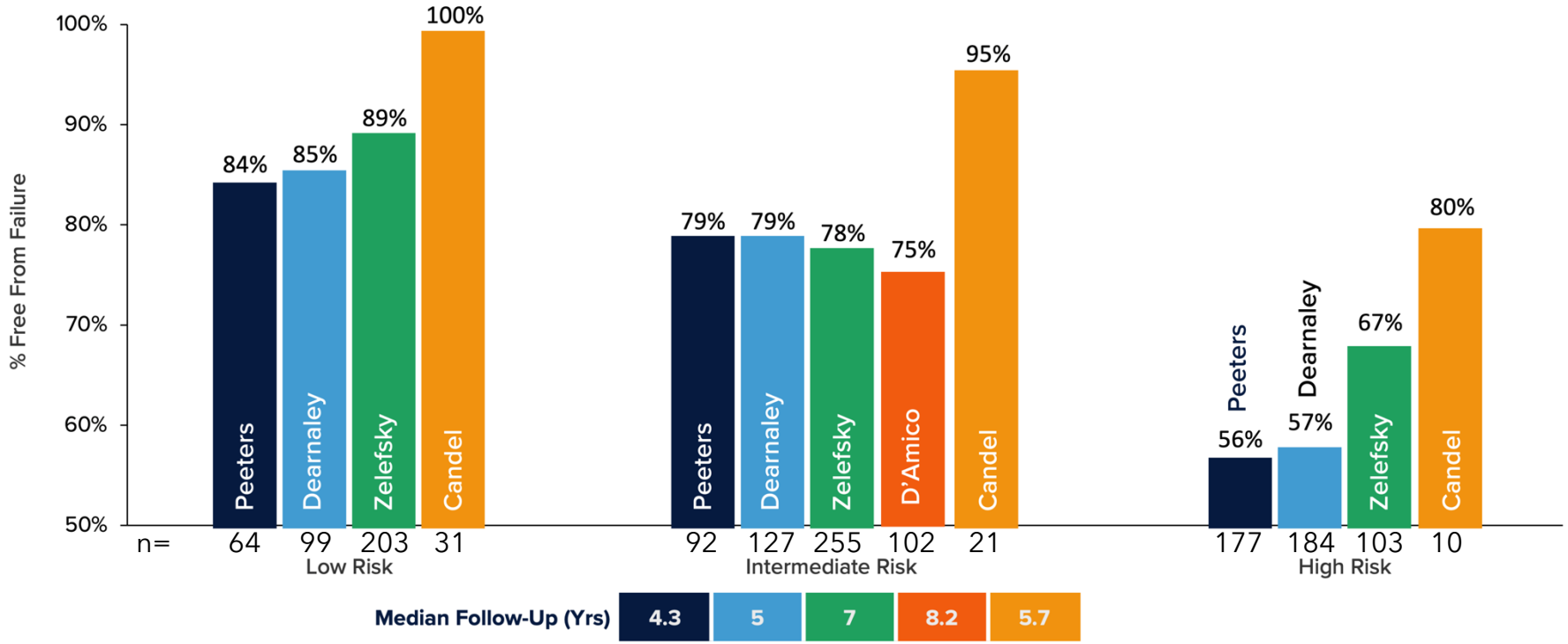

**Primary Endpoint**
- Freedom from failure

**Secondary Endpoints**
- Overall survival
- Negative biopsy rate
- Safety

# Completed phase 2a trial demonstrated consistently improved freedom from failure rates in newly diagnosed, localized prostate cancer

- Pathological complete response (pCR) observed in 93% of the biopsies available at 2yrs (37%-73% in control populations)
- Low risk patients achieved PSA < 2ng/ml in 77% of CAN-2409 treated patients versus 58% in control populations
- Significant increase in activated CD8+ T cells compared to baseline (p=0.0003)

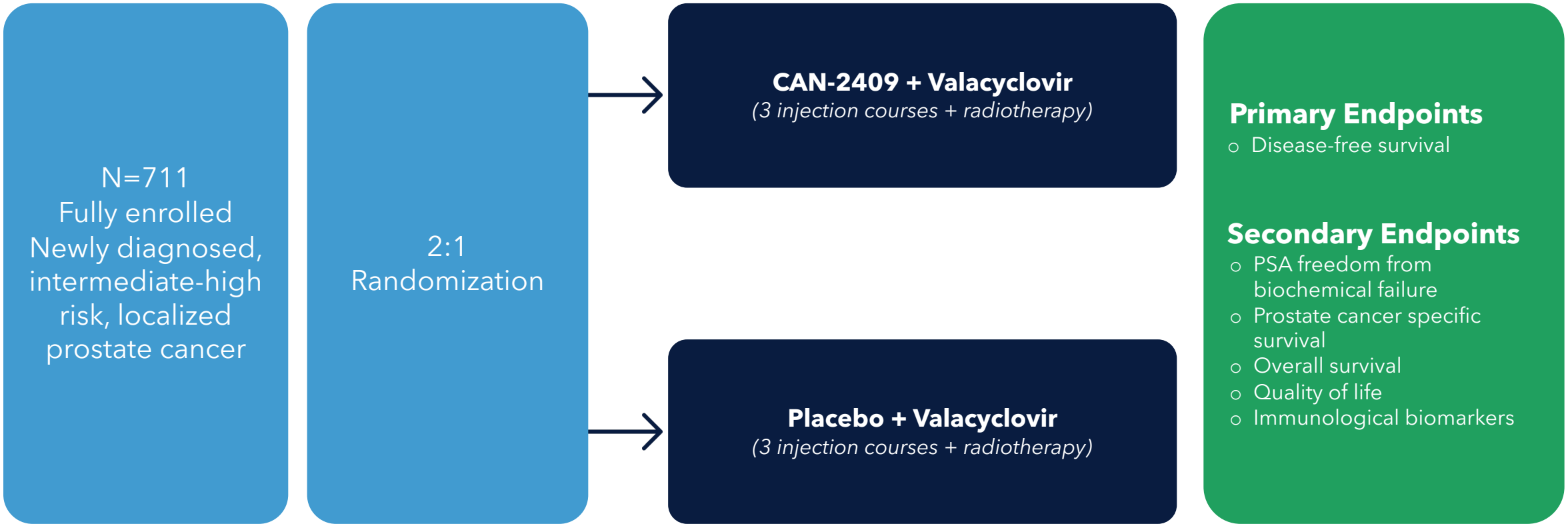
**Clinical evidence supports ongoing phase 3 clinical trial of CAN-2409 in combination with SoC as first line treatment**




*Failure was measured from the start date of treatment until the date of treatment failure defined as clinical failure or biochemical failure, whichever first, according to the Phoenix ASTRO consensus (Nadir +2)*

# Fully accrued phase 3 clinical trial of CAN-2409 in patients with prostate cancer – Newly diagnosed, intermediate/high risk population

***PIs: Dr. T. DeWeese (JHU) and Dr. P. Scardino (MSKCC)***




NCT01436968

**Conducted under agreement with FDA under Special Protocol Assessment**

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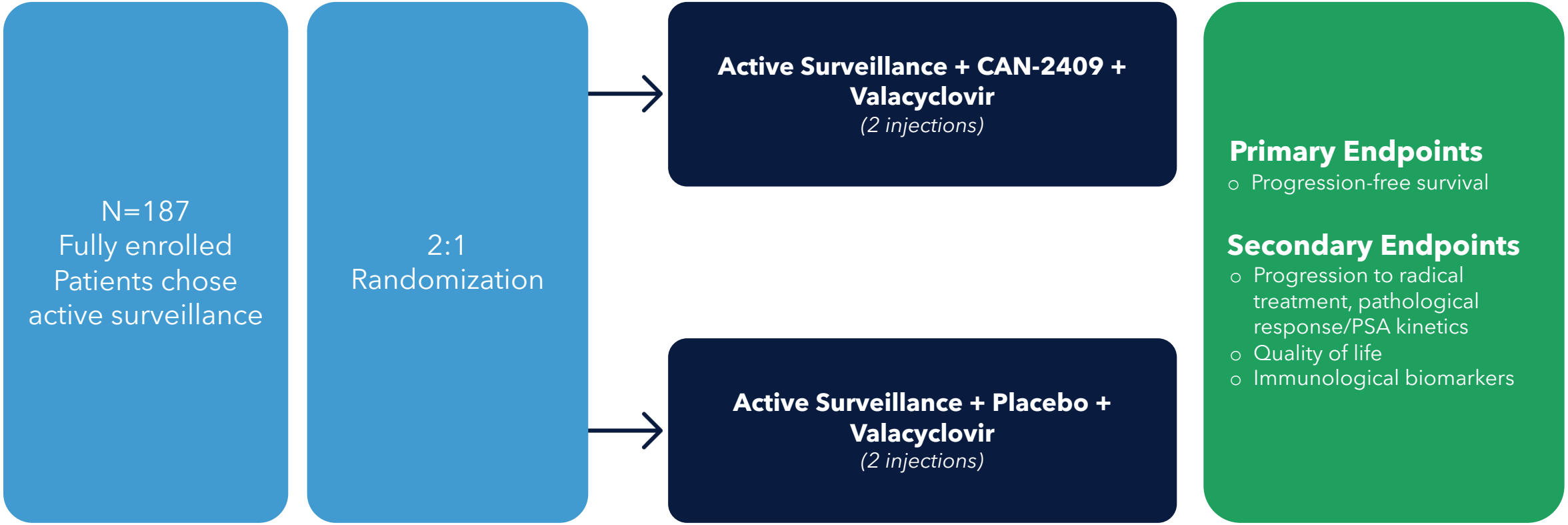
# Fully accrued phase 2b clinical trial of CAN-2409 in patients with prostate cancer – Active surveillance population

***PI: Dr. S. Eggener (UChicago)***



# Ongoing phase 2b clinical trial: CAN-2409 is generally well-tolerated
# Monotherapy – Active surveillance population

**~ 33% patients experienced flu-like symptoms**
**< 1% infections requiring hospitalization**

Study is still blinded
187 patients treated
362 injections performed

| Most common PT (>=5%) | CTC grade | | | | n=187 |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | Total (%) |
| Flu-like symptoms | 40 (21) | 20 (11) | 1 (1) | 0 | 61 (33) |
| Chills | 39 (21) | 13 (7) | 1 (1) | 0 | 53 (28) |
| Fever | 39 (21) | 9 (5) | 1 (1) | 0 | 49 (26) |
| Fatigue | 27 (14) | 10 (5) | 1 (1) | 0 | 38 (20) |
| Elevated AST/ALT | 28 (15) | 3 (2) | 1 (1) | 0 | 32 (17) |
| Elevated Creatinine | 23 (12) | 5 (3) | 1 (1) | 2 (1) | 31 (17) |
| Headache | 20 (11) | 5 (3) | 0 | 0 | 25 (13) |
| Urinary tract infection | 1 (1) | 15 (8) | 2 (1) | 0 | 18 (10) |
| Nausea | 12 (6) | 4 (2) | 0 | 0 | 16 (9) |
| Low Hemoglobin | 15 (8) | 0 | 0 | 0 | 15 (8) |
| Diarrhea | 10 (5) | 3 (2) | 0 | 0 | 13 (7) |
| Malaise | 10 (5) | 2 (1) | 0 | 0 | 12 (6) |
| Hematuria | 12 (6) | 0 | 0 | 0 | 12 (6) |
| Urinary frequency | 9 (5) | 2 (1) | 0 | 0 | 11 (6) |
| Urinary tract pain | 6 (3) | 3 (2) | 0 | 0 | 9 (5) |
| Urinary urgency | 7 (4) | 2 (1) | 0 | 0 | 9 (5) |
| Elevated Alkaline Phosphatase | 8 (4) | 1 (1) | 0 | 0 | 9 (5) |
| Elevated Bilirubin | 7 (4) | 3 (2) | 0 | 0 | 10 (5) |

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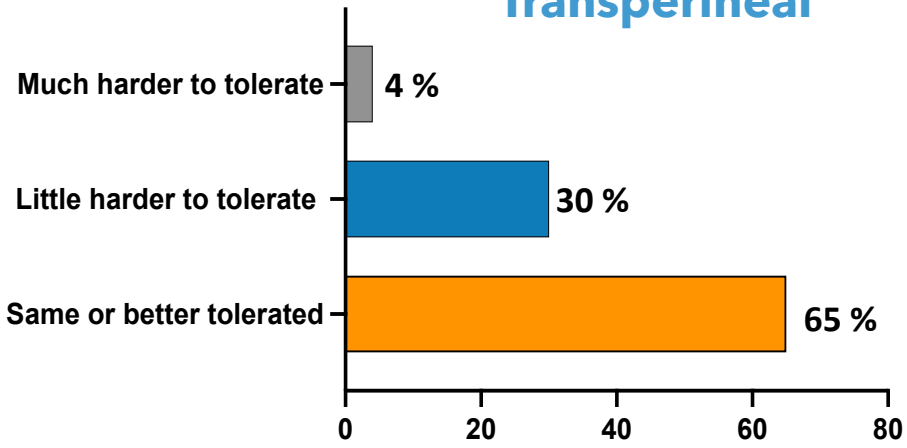
*Eggener S. AdMeTech Foundation's Fifth Global Summit on Precision Diagnosis and Treatment of Prostate Cancer, September 2021*

# Ongoing phase 3 clinical trial: Most patients tolerate intraprostatic injection same or better than prostate biopsy

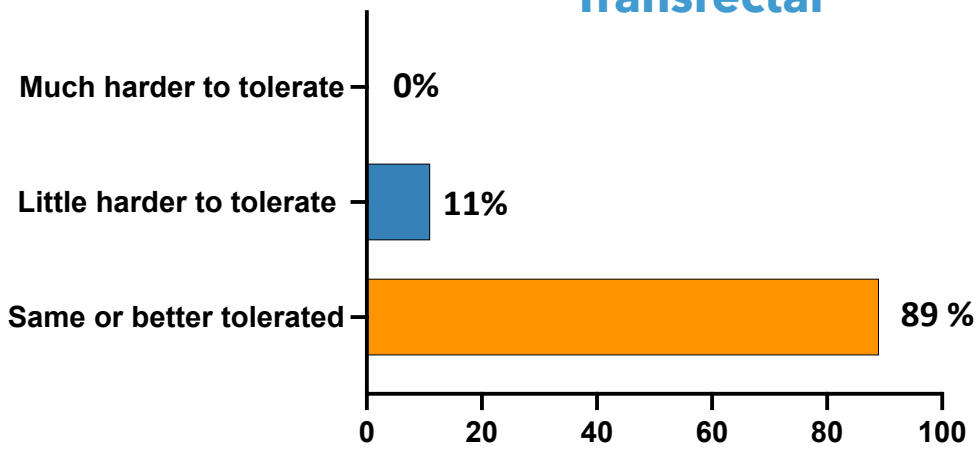
## Patient questionnaire substudy n=32

**In total > 2000 intraprostatic injections**
**(40% transperineal; 56% transrectal; 4% not reported)**
***"How did you tolerate the study procedure as compared to a prostate biopsy?"***

### Transperineal




### Transrectal

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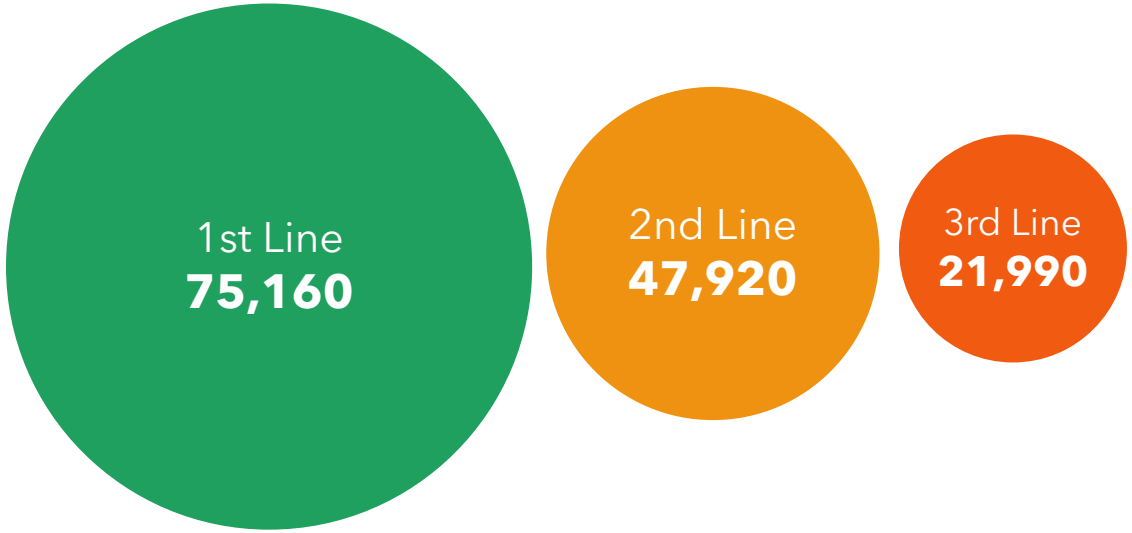
*Aguilar L. 28th Annual Prostate Cancer Foundation Scientific Retreat, October 2021*

# CAN-2409: Non-small cell lung cancer opportunity

## Prevalence of NSCLC in the US




- Lung cancer is the most commonly diagnosed cancer in the US with NSCLC representing over 80% of all lung cancer diagnoses
- Majority of NSCLC patients without actionable mutations are treated with immune checkpoint inhibitors (ICI) as 1st line treatment
- After one year of ICI treatment, 60% of patients will have progressive disease*
  - In ICI inadequate responders:
  - Median progression-free survival 4-6 months
    - Median overall survival 10-13 months
- Significant opportunity to improve response to ICIs by teaching the immune system to recognize the cancer cells
- NSCLC cancer therapy global market was estimated at $27B in 2022 and is expected to grow to $55B by 2028**

***Target label for CAN-2409: Indicated as adjunct to standard-of-care immune checkpoint inhibitor treatment (+/- chemotherapy) in stage III / IV NSCLC patients not responding to first-line or later ICI treatment#***



*#Market research and interviews with 13 KOLs (8 US and 5EU) Dec. 2020*
**Reckamp K et al. J Clin Onc 2022;40:2295-2306*
***Source: EvaluatePharma, accessed May 2023*

# Ongoing phase 2 clinical trial of CAN-2409 + continued ICI in stage III/IV NSCLC patients with an inadequate response to ICI

Stage III/IV non-resectable NSCLC with inadequate response to ICI

N=80
(40 per cohort)

Cohort 1
Stable Disease (after >18 wks ICI)

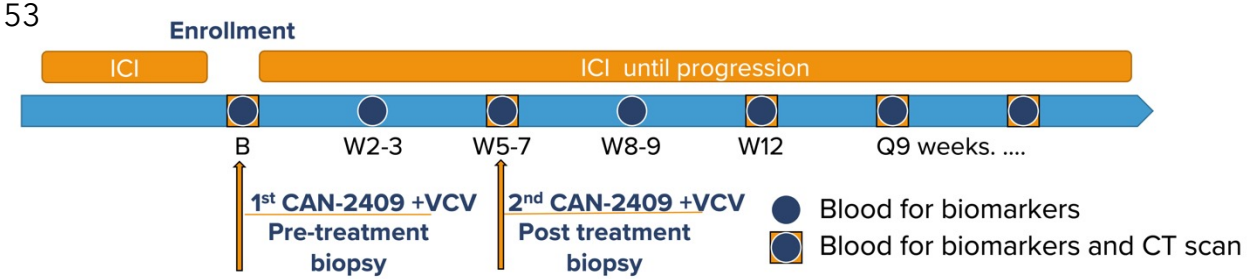
Cohort 2
Progressive Disease (after >18 wks ICI)

CAN-2409 and valacyclovir (2 courses) with continued standard of care: Anti-PD-1/PD-L1 +/- chemotherapy

**Primary Endpoints**
- Response by RECIST criteria
- Disease control rate

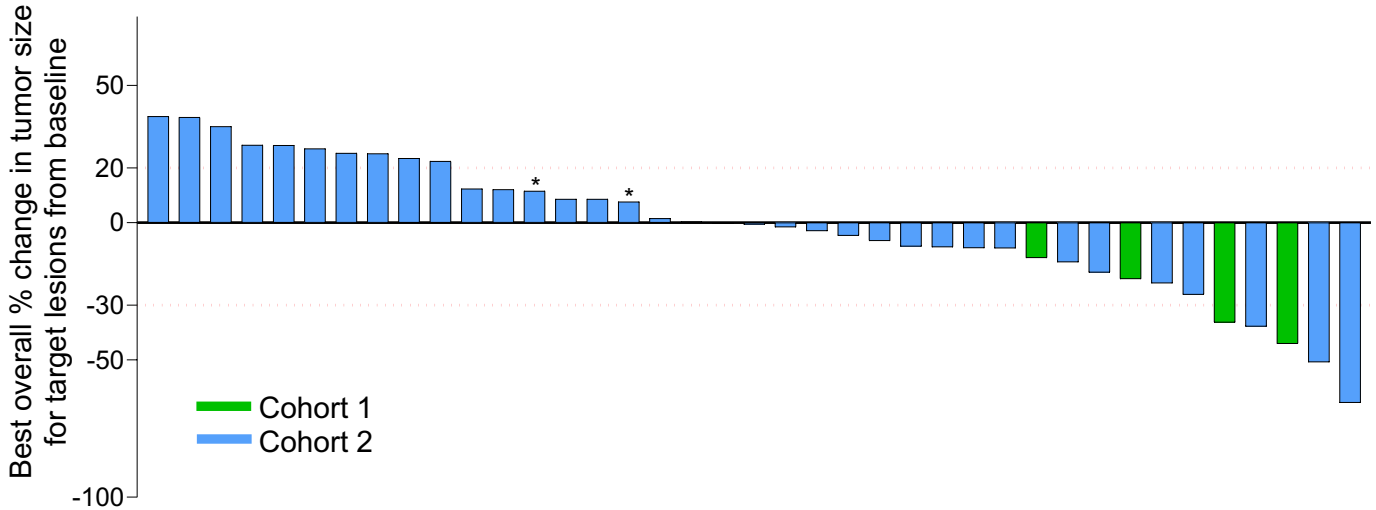
**Secondary Endpoints**
- Progression-free survival
- Overall survival
- Quality of life
- Immunological biomarkers
- Response by iRECIST and itRECIST (Exploratory)

NCT04495153



# Evidence that CAN-2409 controls disease

## Most patients entering clinical trial with progressive disease despite immune checkpoint inhibitor treatment achieved disease control after administration of CAN-2409




| Coh | N | PR | SD | PD | ORR | DCR | DoR for PR[2] | SD duration[2] |
|---|---|---|---|---|---|---|---|---|
| 1 | 4[1] | 2 | 2 | 0 | 50% | N/A | 7.7 mo. (2.7+ to 12.8+) | 4.9 mo (3.6+ to 6.2) |
| 2 | 35 | 3 | 20 | 12 | 9% | 66% | 6.1 mo (2.8+ to 16.3) | 3.9 mo (1.4+ to 14.5) |
| Total | 39 | 5 | 22 | 12 | 13% | N/A | | |

[1] An additional evaluable patient in Cohort 1 had a pending central read at time of data cutoff
[2] Median (range) for DoR and SD duration
+ indicates response was ongoing at date of last follow up

Data shown based on blinded independent central review (BICR) of radiographic data per RECIST 1.1 in evaluable patients

Evaluable patients are those who received 2 courses of CAN-2409 + prodrug (valacyclovir) and completed the 12-week treatment window

*Disease progression due to a new lesion

PR: partial response, SD: stable disease, PD: progressive disease, ORR: objective response rate, DCR: disease control rate, DoR: duration of response

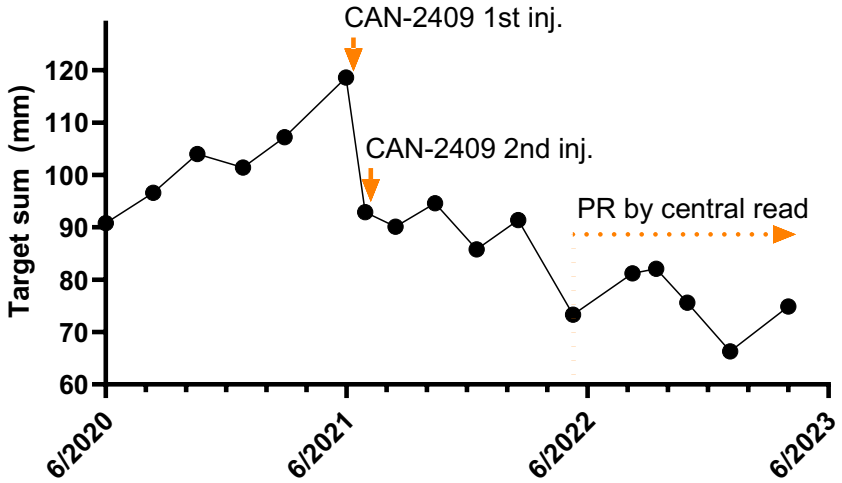


*Data on file, September 2023*

# Partial response in extended lung mass with durable post-treatment tumor regression after CAN-2409 treatment (> 2 years, ongoing)

## PA-003 (Cohort 1)

73M, Stage III non-squamous NSCLC diagnosed Jan'20
PD-L1<1%
Initial therapy: pembro + carbo + pemetrexed Feb'20
Maintenance: pembro + pemetrexed from Jun'20 which continued on-trial
OS 24 mo (ongoing as of LFV)



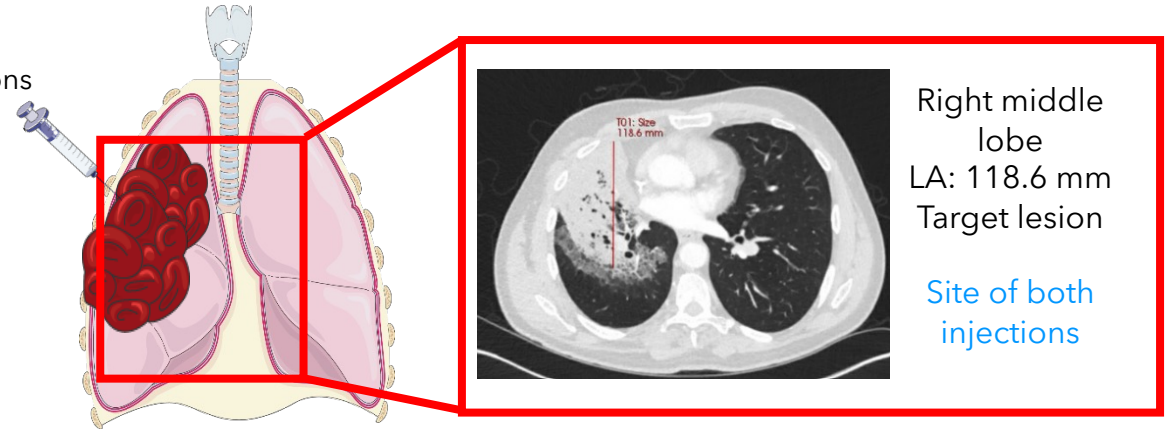

**Legend** LFV: last follow up visit

**RECIST target lesions (red)**

*LN = lymph node; LA = long axis; SA = short axis*

Baseline

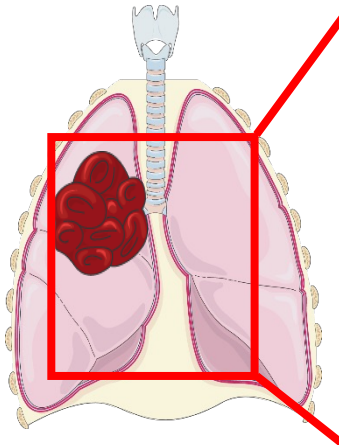
Both injections

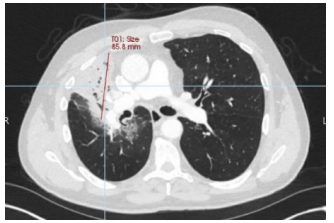




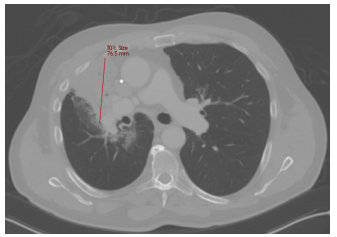
Right middle lobe
LA: 118.6 mm
Target lesion

Site of both injections





6 Months
LA: 85.8 mm
Target lesion



24 Months
LA: 76.5 mm
Target lesion

*Schematics to show general lesion injection orientation; not to scale*

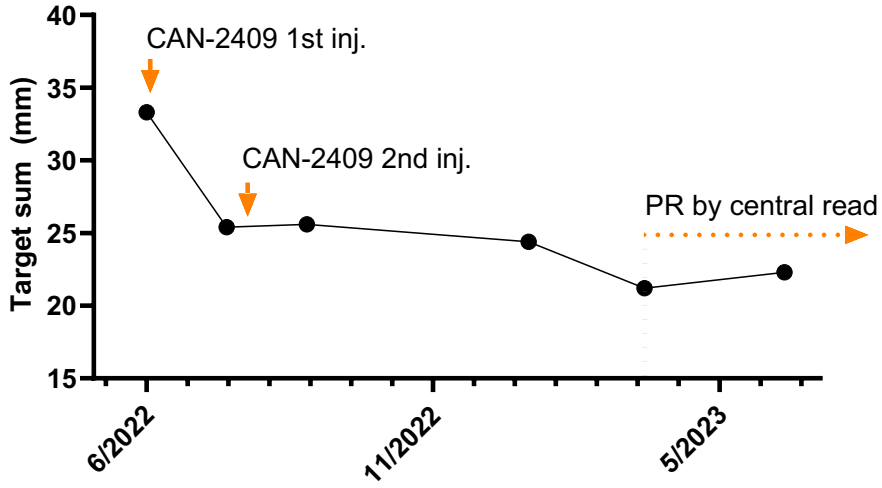
*Data on file, September 2023*

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*

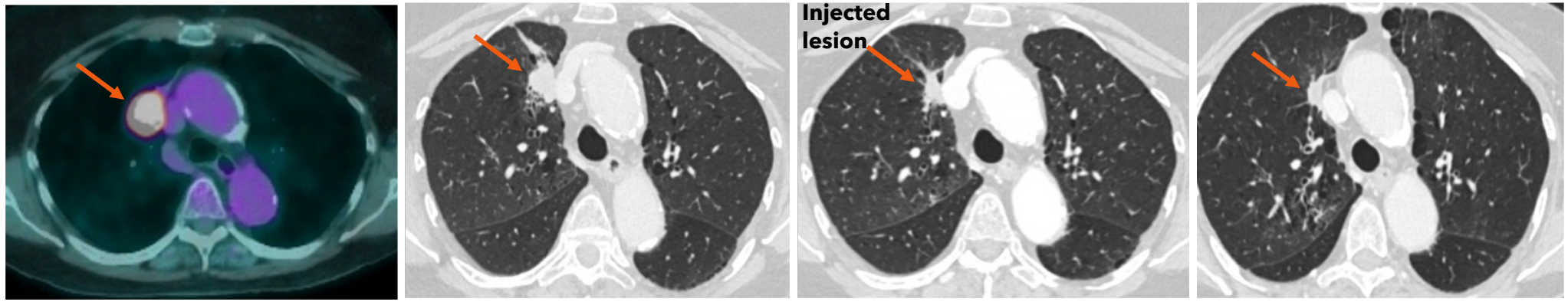
# Patient with continued tumor shrinkage after CAN-2409 treatment

## VB-007 (Cohort 1)

84F, Stage IV non-squamous NSCLC diagnosed Aug'21
PD-L1 < 1%; SMARC4 alteration
Initial therapy: platinum-based chemotherapy + pembro
Maintenance: pembro which continued on-trial
OS 12.1 mo (PR is ongoing as of LFV)




**FDG-PET**




**Treatment Naïve** | **Prior to 1st injection** | **Post 2nd injection** | **1 year after 1st injection**

Scans kindly provided by Wade Iams, MD

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*



*Data on file, September 2023*

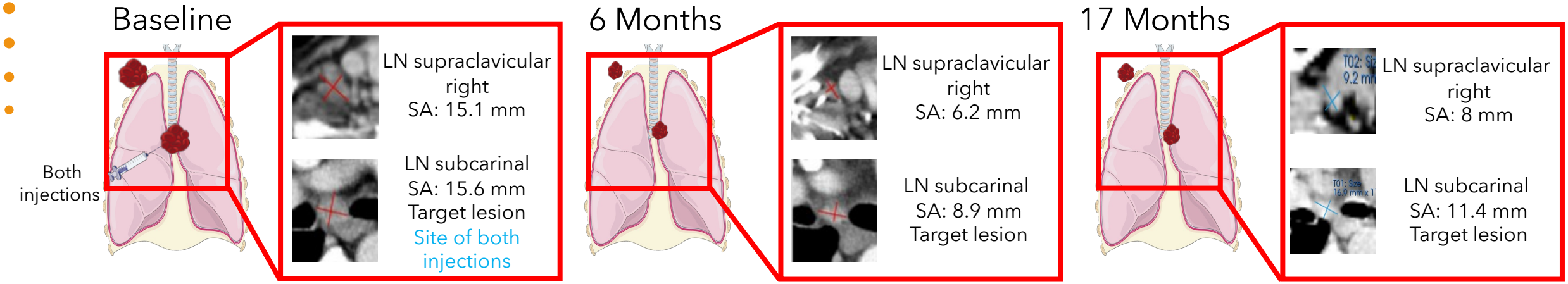
# Local injection induces systemic anti-tumor activity

## Evidence of abscopal effect, survival > 27 months (ongoing) after CAN-2409 treatment

### NY-007 (Cohort 2)

74M, Stage IV non-squamous NSCLC diagnosed Feb'19
PD-L1 <1%
Initial therapy: cisplatin/etoposide Feb-Jul'19
Maintenance: nivolumab from Sep'19, continued on-study
OS 27.9 mo (ongoing as of LFV)

**Legend**
**RECIST target lesions (red)**
*LN = lymph node; LA = long axis; SA = short axis*




*Schematics to show general lesion injection orientation; not to scale*

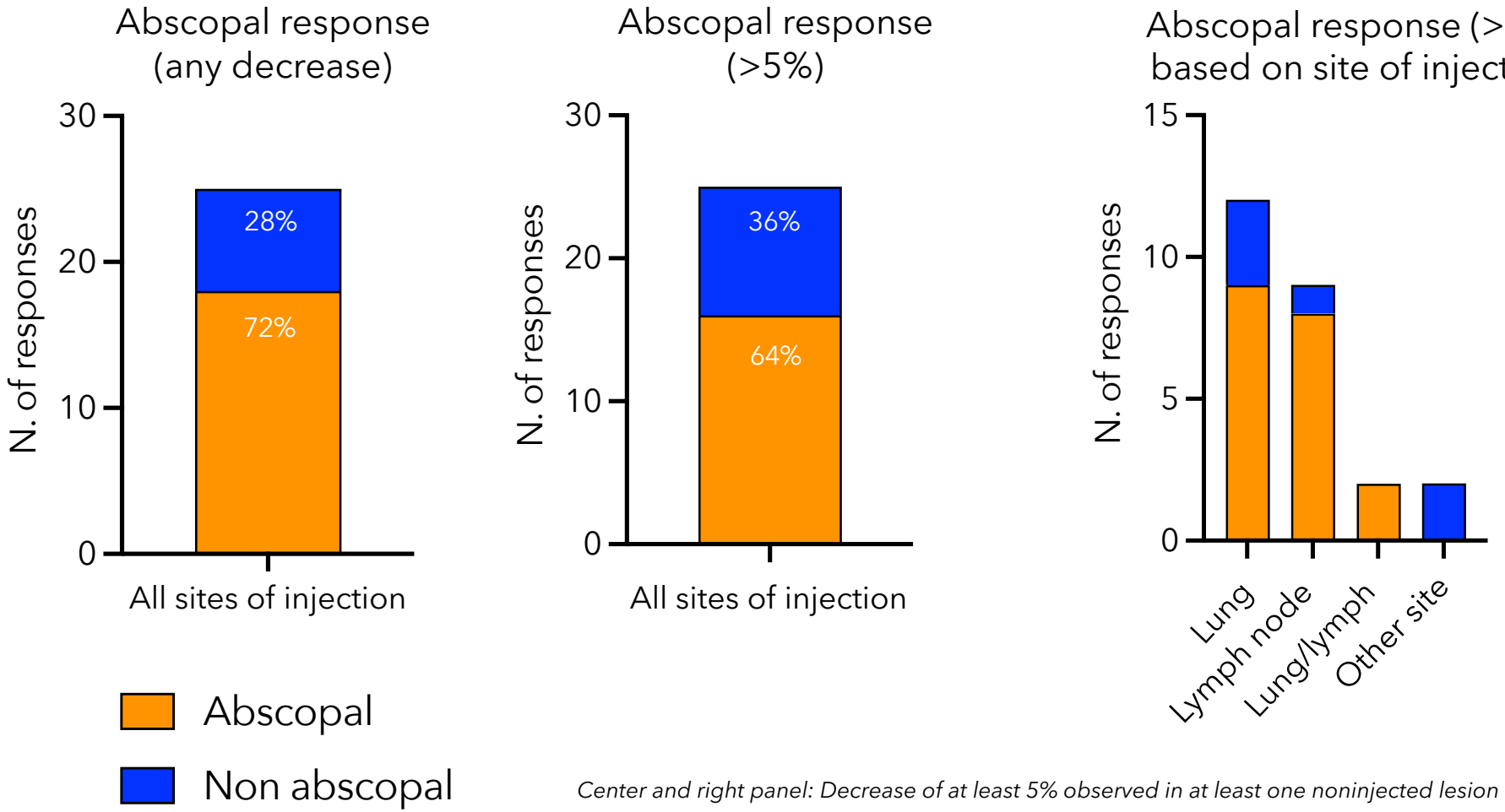
*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*



*Data on file, September 2023*

# Local injection induces systemic anti-tumor activity

## Regression of uninjected lesions in about two-thirds of evaluable patients presenting with multiple lesions




*Center and right panel: Decrease of at least 5% observed in at least one noninjected lesion*

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*

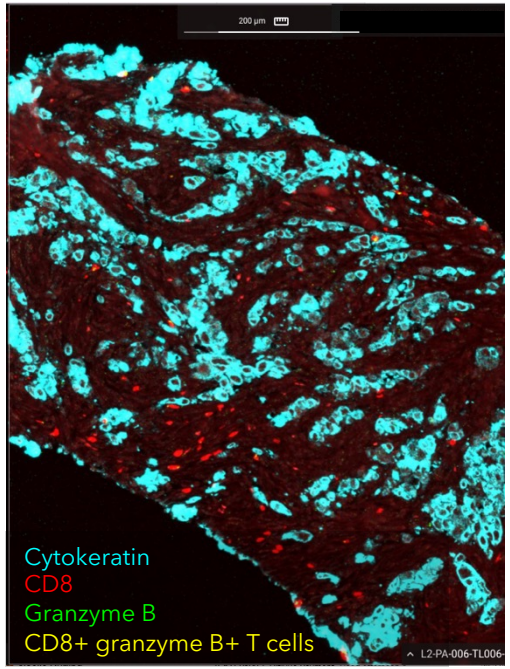


*Data on file, September 2023*

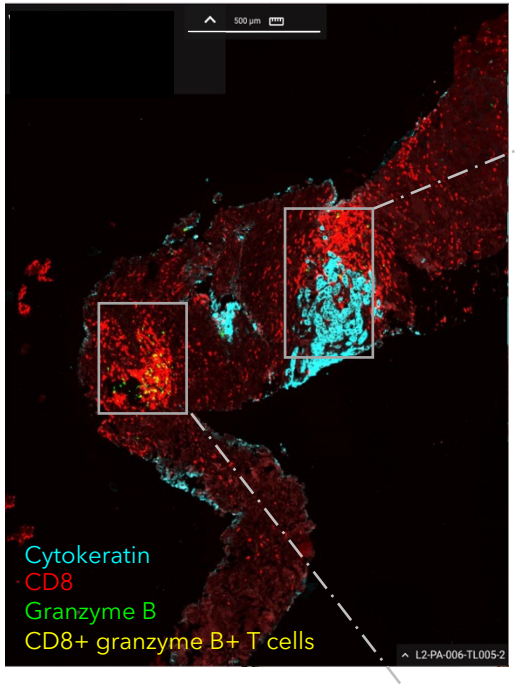
# CAN-2409 induces expansion of CD8+ granzyme B+ T cells in the tumor microenvironment

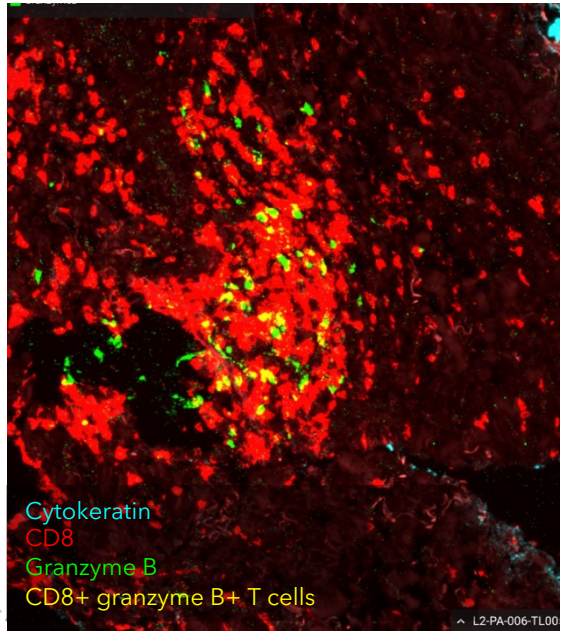
## PA006

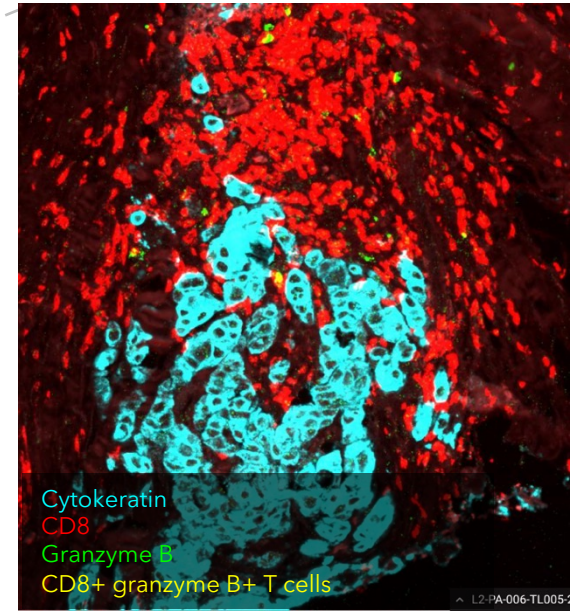
### Pre CAN-2409




### Post CAN-2409



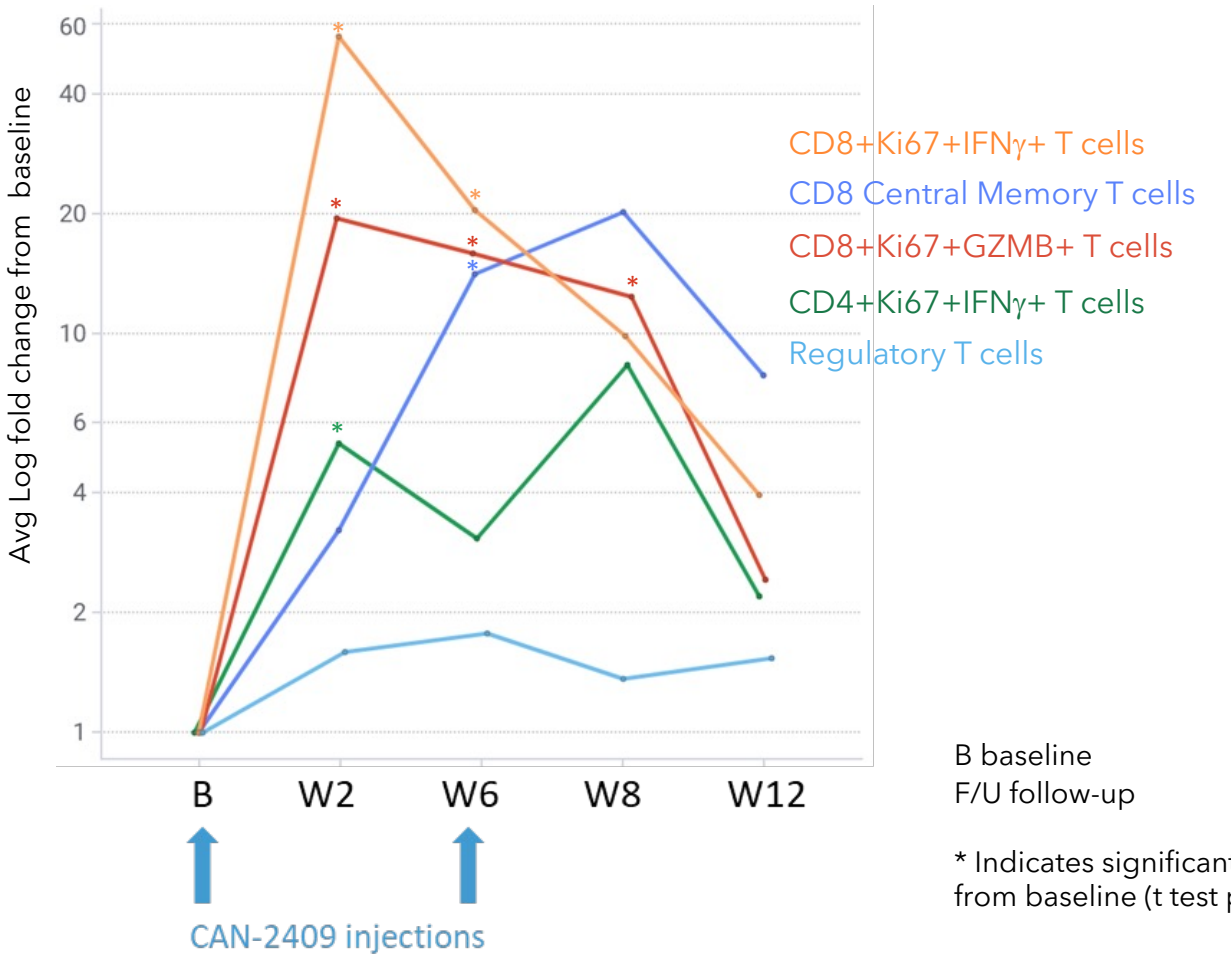

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 21 Oct 2022.*



*Aggarwal C et al. Virtual R&D Day, December 2022*

# CAN-2409 significantly increases frequency of circulating cytotoxic T cells and serum levels of soluble granzymes

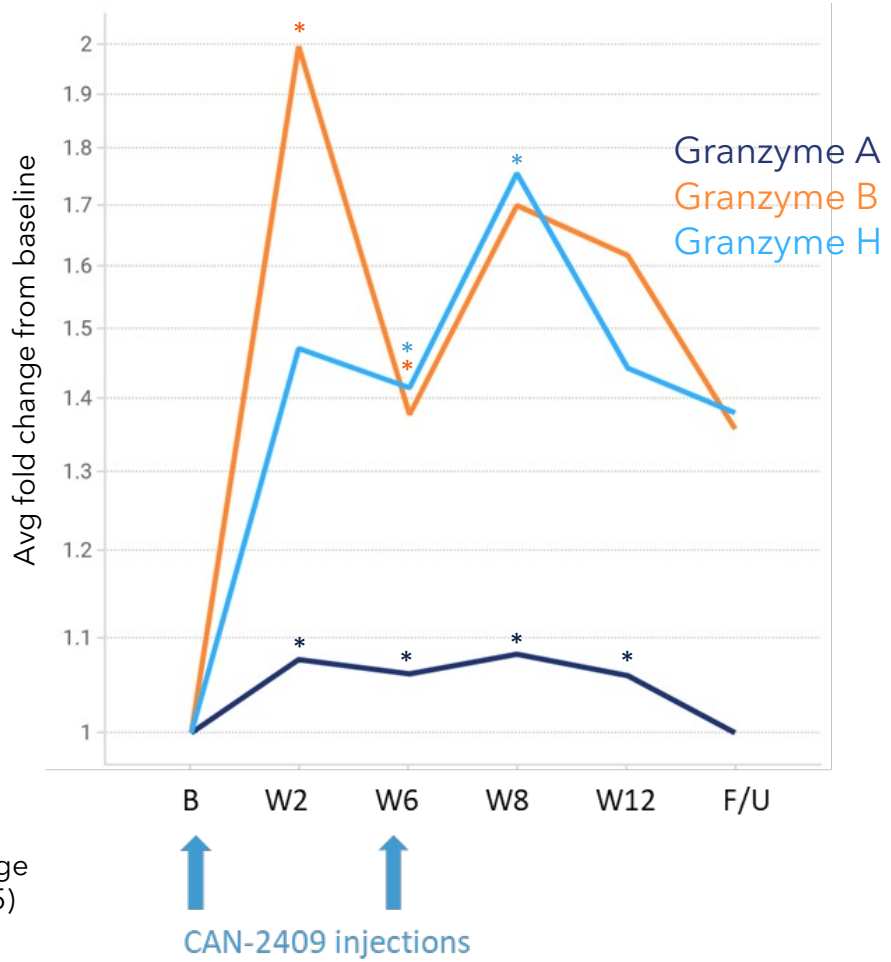
## Circulating T-cells (mean, n=29)




B baseline
F/U follow-up

* Indicates significant change from baseline (t test $p<0.05$)

## Soluble granzymes (mean, n=28)



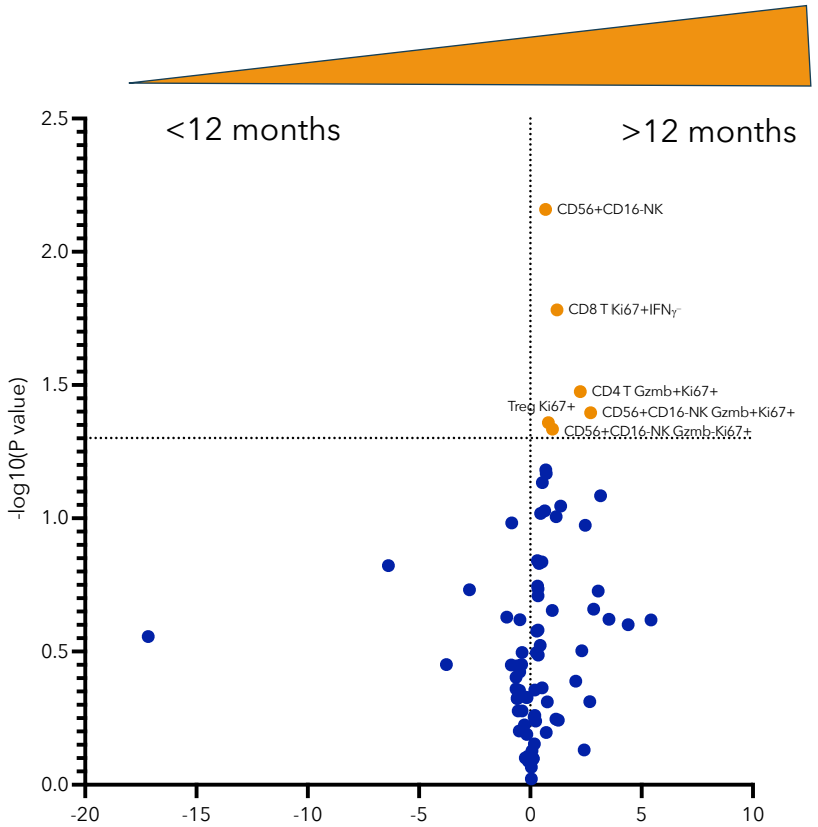

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*



*Data on file, September 2023*

# Early changes in immune cells in peripheral blood after CAN-2409 treatment are associated with prolonged survival

## Changes in circulating cells post 2nd injection




Multiparameter flow cytometry
Fold changes between 1st and 2nd injection in short (< 12months; n=6) and long (> 12 months; n=11) survivors

*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*



*Data on file, September 2023*

# Bronchoscopic delivery of CAN-2409 is a simple extension of existing care for NSCLC patients and is well-tolerated

## Majority of lung and thoracic lymph node lesions are accessible for outpatient bronchoscopic injection


- Therapeutic delivery tool based on extensive experience with bronchoscopic biopsy, a routine outpatient procedure (15 min, outpatient setting)
- Transbronchial needle injection (TBNI) presents similar complication rate as biopsy (extremely rare)
- Latest generation of TBNI includes ultrasound-guided transbronchial injection of lymph nodes and robotic bronchoscopy (already in use in LuTK02)



*DeMaio A, Sterman D. Eur Respir Rev 2020; 29: 200028*

# Systemic immunotherapy delivered intratumorally

- Intra-tissue injection is a proven strategy for in situ vaccination
- Optimal benefit/risk by minimizing systemic toxicity
- Systemic immune response: not all metastases need to be injected
- Durable responses after only 2-3 administrations
- Procedure is well tolerated by patients:
  - Administration to prostate takes 15-20 min in outpatient setting, often better tolerated than prostate biopsy, which is a routine procedure in urology
  - Administration to lung tumor takes 15-20 min in outpatient setting via bronchoscopy, which is a routine procedure in pulmonary medicine
  - For future indications, any location can be reached using image-guided injection, robotic delivery etc.
- Procedures with proven benefit/risk, patient tolerability, and cost-effectiveness will always be implemented by clinicians
  - Stem cell transplantation, implant radiotherapy, interventional radiology, interventional cardiology

# Encouraging safety, clinical activity and immunological changes after CAN-2409

## Initial data suggests 12-month survival is consistent with an increased tail on the maturing survival curve

- Encouraging number of long survivors suggests CAN-2409 may induce a new state of functional immunosurveillance and durable disease control in a subset of patients
- Of the 40 evaluable patients, 15 patients have lived ≥ 12 months; of these, 10 have lived > 18 months, of whom 70% (7/10) were alive as of last follow up. All 4 patients (100%) with OS > 24 months were alive at last follow up, with the longest reaching 31.7 months (data cutoff Aug 1, 2023)
- An additional 18 (out of the 40 evaluable) patients are also alive but have not yet reached 12 months of follow up

## Negative or low PD-L1 status appears to be associated with long survival in CAN-2409 treated patients

- Many patients treated with CAN-2409 have had long survival (≥ 12 months) despite having disease features generally associated with advanced disease and reduced likelihood to benefit from immune checkpoint inhibitor therapy, such as low or negative PD-L1 expression

## Biomarker data suggests association between immune cell activation and survival

- Scope of antitumoral immune response broadened through demonstration by CAN-2409 to engage the humoral arm of the immune system
- Increase observed in effector/cytotoxic T cells and NK cells in peripheral blood after the second CAN-2409 administration

## Topline overall survival data for Cohort 2 expected in Q2 2024

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*Note: From ongoing phase 2 NSCLC trial as of cutoff date, 1 Aug 2023.*



*Data on file, September 2023*

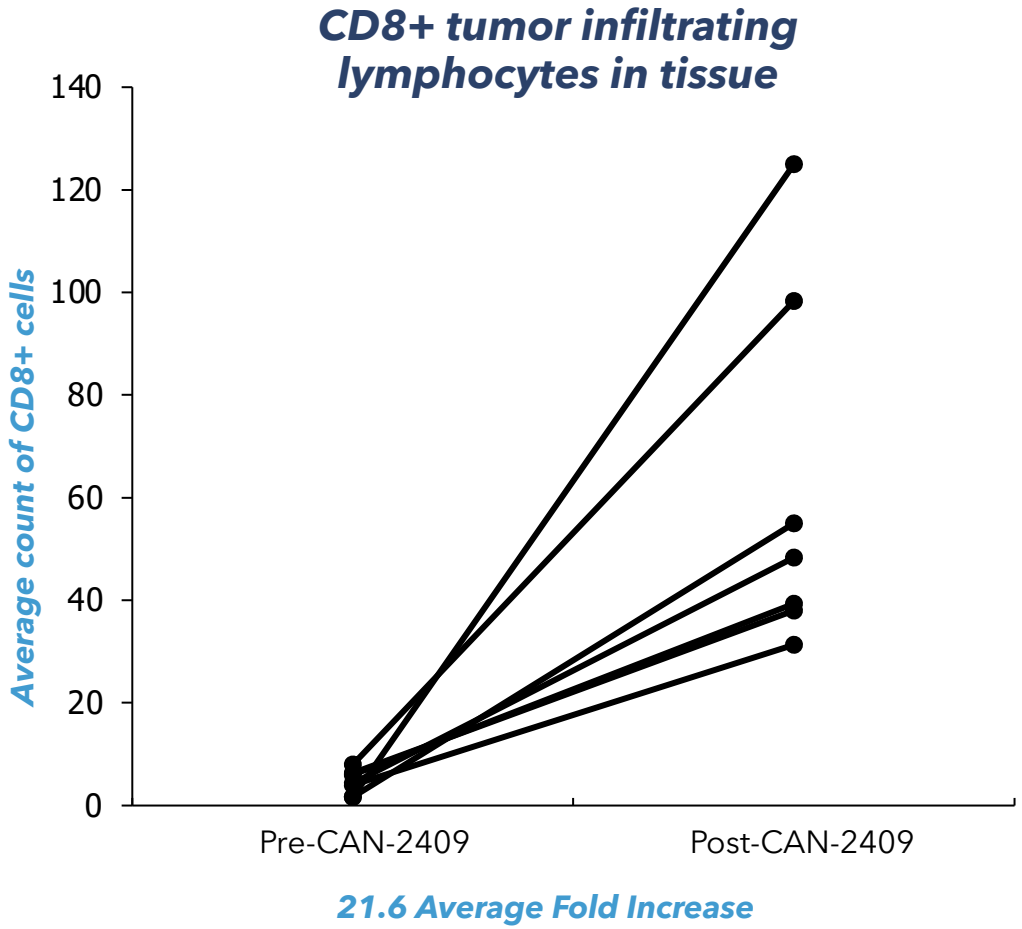
# CAN-2409: Pancreatic ductal adenocarcinoma opportunity

## Incidence of pancreatic ductal adenocarcinoma in the US by risk level


- Limited available treatment options for patients suffering from pancreatic cancer beyond resection when possible and chemotherapy
- Borderline resectable disease: median overall survival ~21-35 months (with neoadjuvant chemo and resection, lower with gem-abraxane or 5FU)
- Locally advanced disease: median overall survival 15-25 months (with neoadjuvant chemo; most cannot be resected)
- Metastatic disease: median overall survival ~11 months (with FOLFIRINOX)
- Significant opportunity to improve response rates by teaching the immune system how to recognize cancer cells
- Pancreatic cancer therapy global market was estimated at $800 M in 2022 and is expected to grow to $3.5 B by 2028[#]

*[#]Source: EvaluatePharma, accessed May 2023*

# Completed phase 1 clinical trial of CAN-2409 in pancreatic ductal adenocarcinoma: Infiltration by CD8+ T cells




N=7
P-value 0.0021

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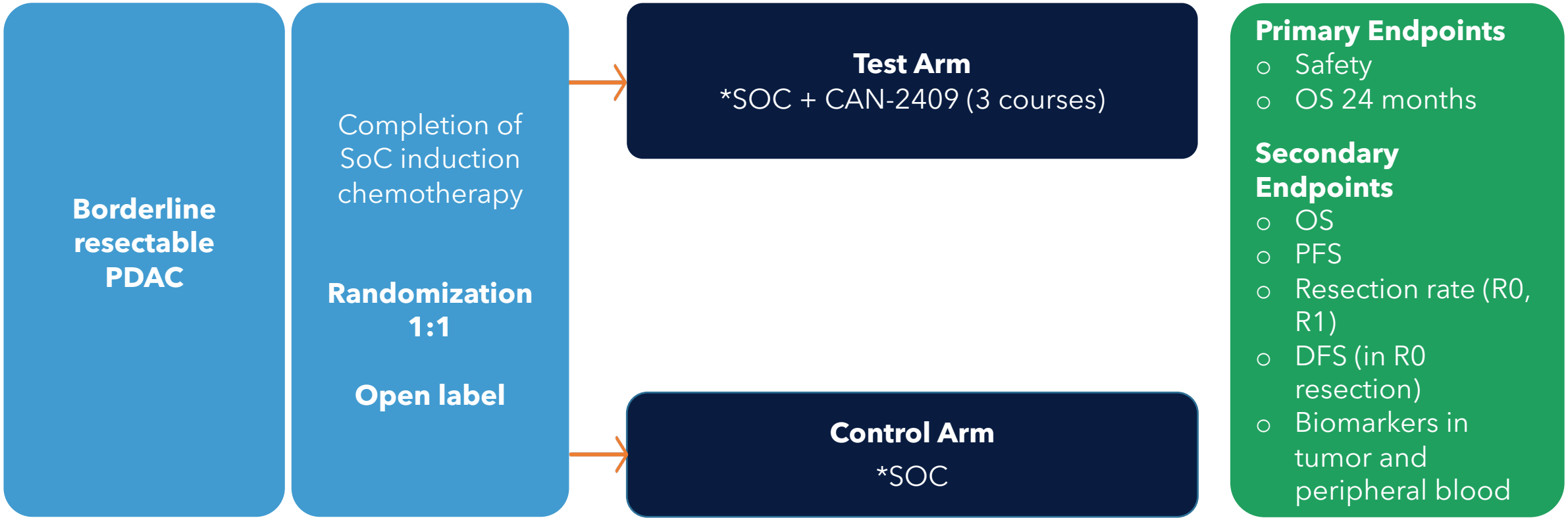
# PaTK02: Randomized phase 2 clinical trial of CAN-2409 in borderline resectable pancreatic ductal adenocarcinoma (PDAC)

## Reflecting v5/v6 of protocol (data collected to date reflects this design)




*SOC= Chemoradiation + Resection

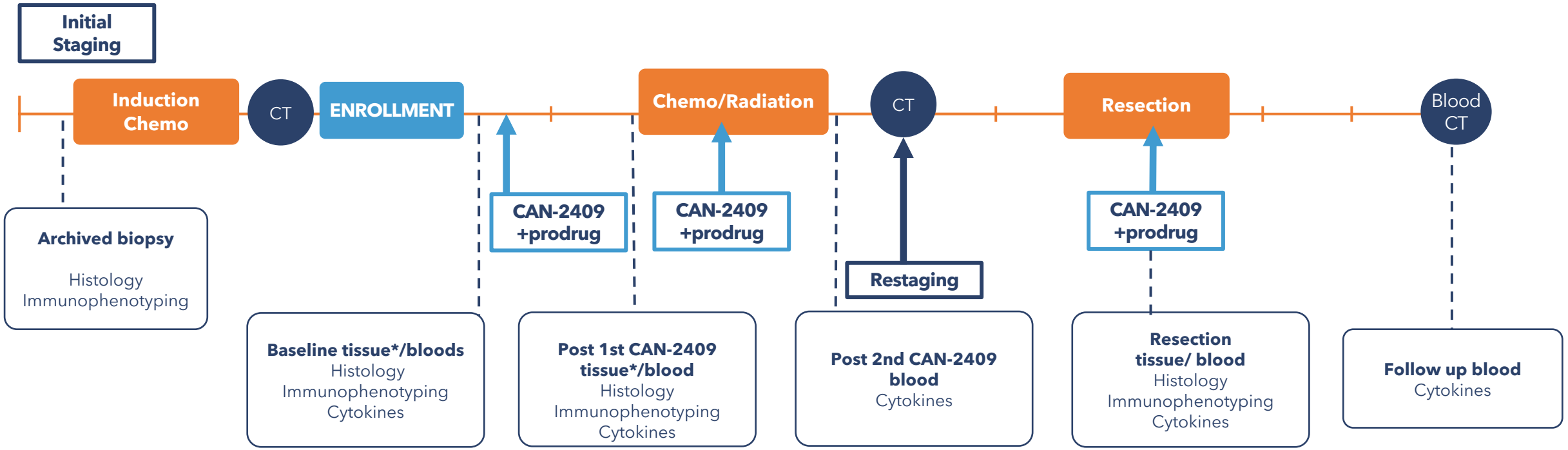
Funded in part by NIH Grant R44 CA203336



*Nichols G et al. SITC 2023 Abstract 653*

# SOC treatment timeline in non-metastatic PDAC and timing of CAN-2409 injections

## Through v5/v6 of protocol (data collected to date reflects this design)




**Induction Chemo** → At least two months of induction chemotherapy (e.g. 4 cycles of FOLFIRINOX based or 2 cycles of gemcitabine/nab-paclitaxel),

**Chemo/Radiation** → Such as capecitabine, 5-FU or gemcitabine concurrent with radiation over 3-5.5 weeks

*** If feasible**

Prodrug = valacyclovir or IV acyclovir

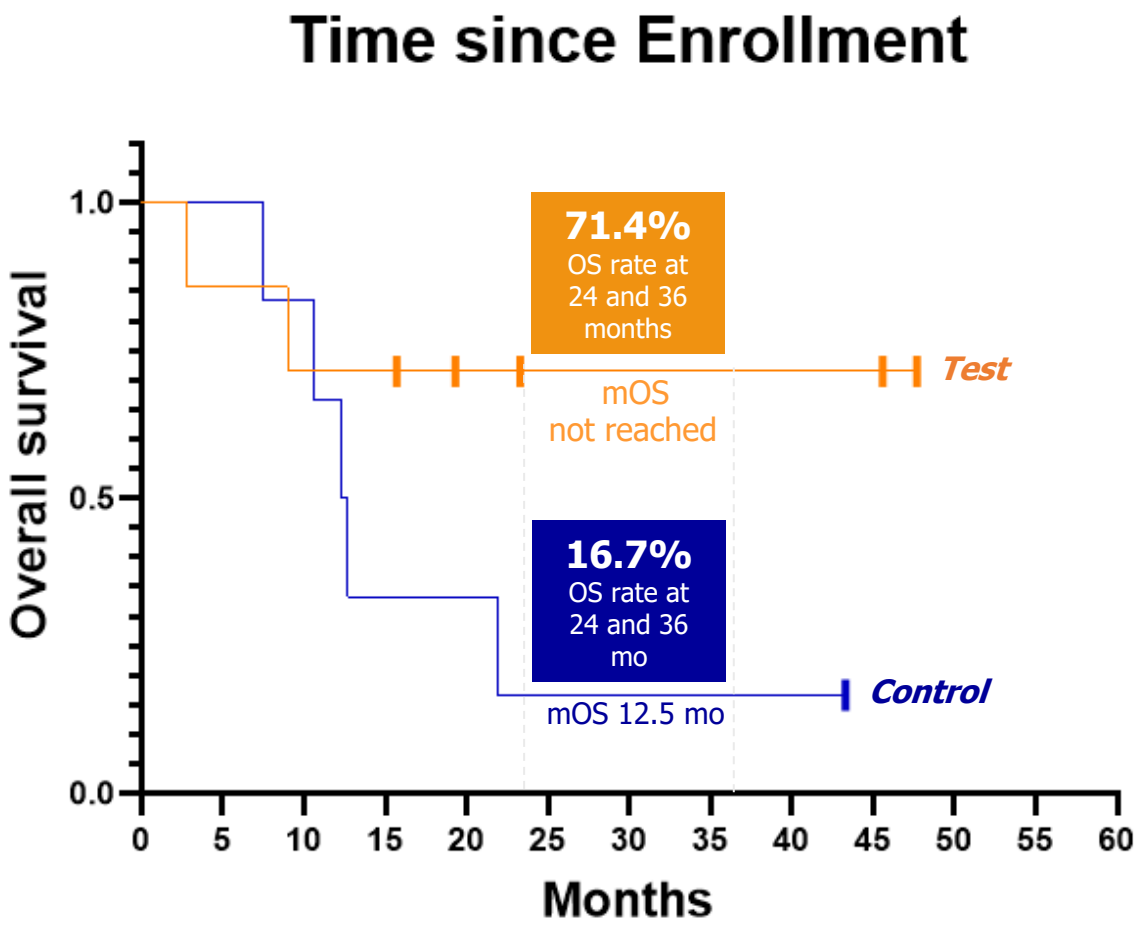
*Nichols G et al. SITC 2023 Abstract 653*

# OS in borderline resectable PDAC patients

*Data as of 8/21/2023*

| PCN | Arm | Surgical result | pStage # | Date of last follow-up | OS mo (enrollment) | OS mo (diagnosis) | Alive (A) / Dead (D) |
|---|---|---|---|---|---|---|---|
| 2022PIN | C | Unresected | IV | 6/16/2020 | 10.6 | 17.2 | D |
| 2072PIN | C | Unresected | N/A* | 11/13/2020 | 12.7 | 52.4 | D |
| 2092POS | C | Unresected | N/A* | 7/23/2020 | 7.5 | 10.3 | D |
| 2052PLB | C | Resected | IIA | 10/3/2020 | 12.3 | 16.9 | D |
| 2152PLB | C | Resected | IIB | 9/25/2022 | 21.9 | 26.8 | D |
| 2112PLB | C | Resected | N/A* | 8/21/2023 | 43.3+ | 47.5+ | A |
| 2102PLB | T | Unresected | IV | 9/7/2020 | 9.0 | 13.7 | D |
| 2162PLB | T | Unresected | N/A* | 6/9/2021 | 2.8 | 8.3 | D |
| 2042PIN | T | Unresected | IV | 8/11/2023 | 47.7+ | 55.2+ | A |
| 2172PIN | T | Unresected | N/A* | 8/02/2023 | 23.3+ | 29.2+ | A |
| 2082PLB | T | Resected | IA | 8/21/2023 | 45.6+ | 50.7+ | A |
| 2182PLB | T | Resected | IB | 8/21/2023 | 19.4+ | 25.9+ | A |
| 2192PIN | T | Resected | IA | 6/21/2023 | 15.7+ | 21.2+ | A |

*Refer to slide with details on surgical status
# pathologic tumor stage at resection




**Censored = alive, still under follow-up**

Arm: **C** = Control; **T** = Test (CAN-2409+prodrug)

*Nichols G et al. SITC 2023 Abstract 653*

# CAN-3110

Oncolytic virus with tumor-specificity

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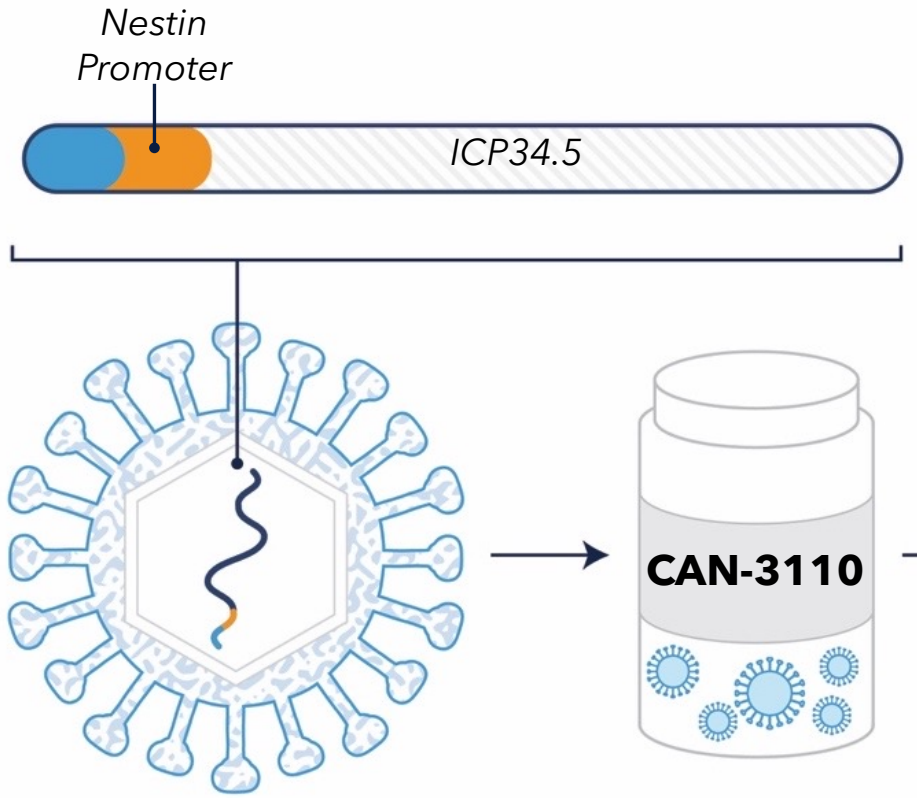
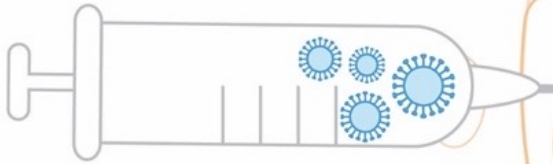
# CAN-3110: Replication-competent HSV with tumor-specificity











Nestin expression in tumor cells induces ICP34.5 expression, resulting in tumor-specific replication

Virus expands in Nestin expressing tumor cells, causing oncolytic activity

# CAN-3110: High-grade glioma opportunity

## Prevalence of glioblastoma in the US


- Glioblastoma, the most common form of high-grade glioma, is a rare and often deadly cancer
- Fewer than 10% of patients survive > 5 years past initial diagnosis
- Median overall survival < 6-9 months in recurrent high-grade glioma
- Current standard of care includes surgical resection with few available therapeutic options
- Significant opportunity to improve survival by teaching the immune system how to recognize the cancer cells and turn 'cold tumors' into 'hot tumors'

# Phase 1b clinical trial of CAN-3110 in recurrent high-grade glioma

## PI: Dr. E. Antonio Chiocca (Brigham & Women's)

Patients with recurrent high-grade glioma

Lesions ≥ 1.0 cm

NCT03152318

Arm A

**Dose escalation (Cohort I-IX)**
Single stereotactic injection of CAN-3110

3+3 dose escalation
$1 \times 10^6$ to $1 \times 10^{10}$ PFU in half-log increments
30 patients dosed

**Dose expansion (Cohort X)**
$1 \times 10^9$ PFU
11 patients dosed

Arm B

**Pre-Administration of Cytoxan**
$3 \times 10^8$ PFU
$6 \times 10^9$ PFU
9 patients dosed

BREAK THROUGH CANCER

Arm C

**Repeat Dosing** (up to 6)
+1 x $10^8$ PFU x 6 doses
+1 x $10^9$ PFU x 6 doses
12 patients targeted

## Primary Endpoints

- Safety
- Determine maximum tolerated dose

## Secondary Endpoints

- Immunological biomarkers
- MRI assessment of disease and progression free survival
- MRI alteration of permeability and flow at injection site

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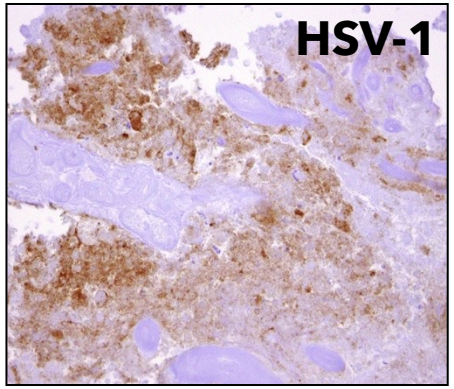
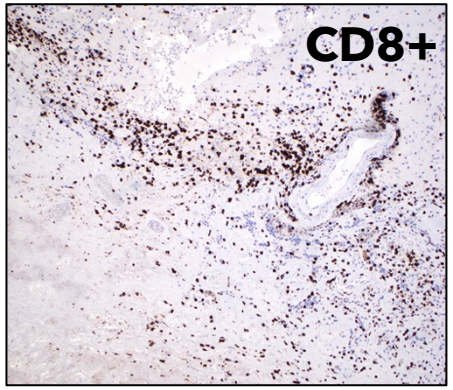
# CAN-3110 treatment in patients with recurrent high-grade glioma

## Persistent HSV antigen expression in injected tumors as well as uninjected tumors associated with CD8+ T cell infiltration after single CAN-3110 injection

injected lesion

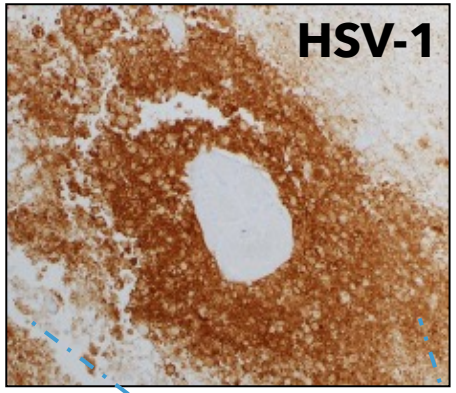


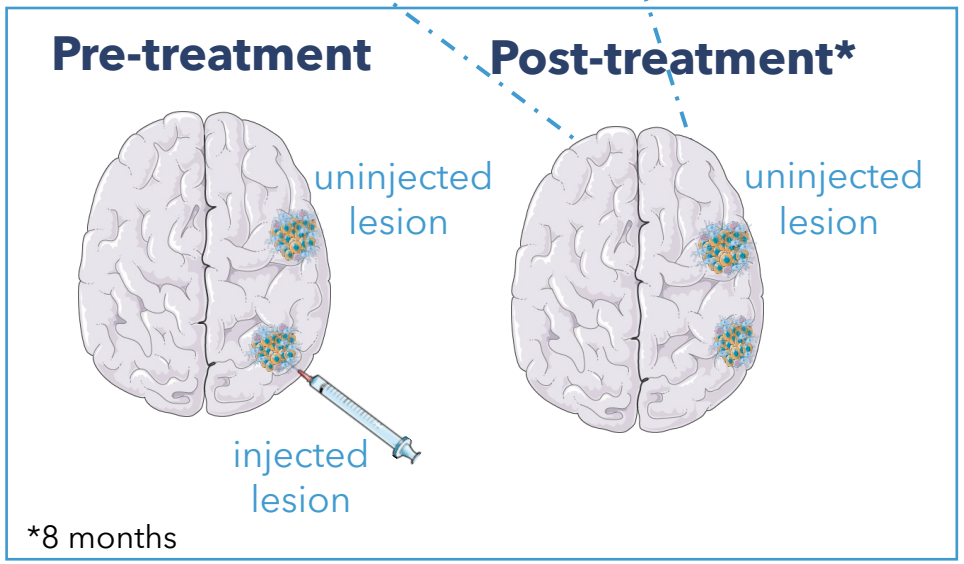

HSV1 antigen 6 weeks after injection of $1x10^6$ pfu
$1.79 \times 10^6$ copies of viral DNA/mg
$2.97 \times 10^5$ copies of viral RNA transcript (ICP22)/mg




Infiltration by CD8+ cytotoxic T cells
(tumor infiltrating lymphocytes)

uninjected lesion



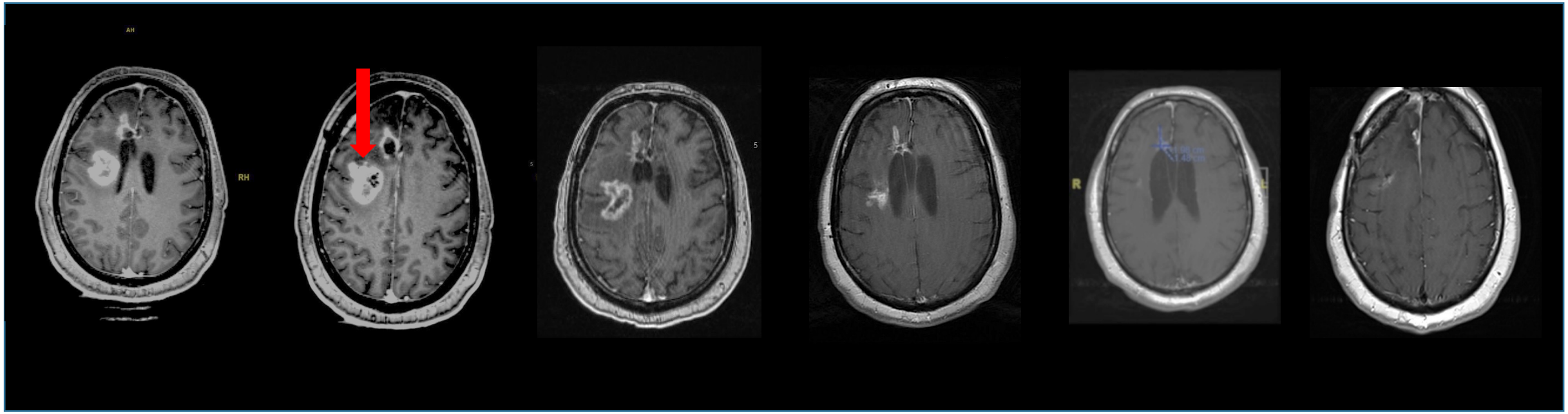






*Ling AL et al. Nature 2023;623:157-166*

# Monotherapy activity of CAN-3110 in recurrent high-grade glioma (arm A)

## Clinical effect on injected tumor and uninjected tumor



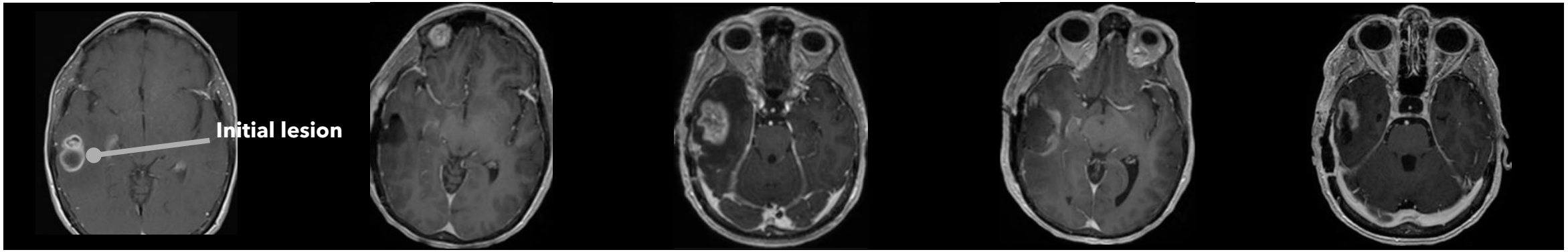
| Baseline | Day 0 | Day 56 | Day 111 | Day 168 | Day 280 |
|---|---|---|---|---|---|
| | Black hole within tumor image is injection site $10^6$ PFU dose | Reduction in contrast area with no additional treatment | Patient back to work | | |

56 YOM, IDH wild-type, MGMT partially methylated, right frontal mesial lesion initially treated with GTR, chemoradiation. Recurrences at two sites.



*Ling AL et al. Nature 2023;623:157-166*

# Durable response for 2 years after CAN-3110 in recurrent high-grade glioma (arm A)



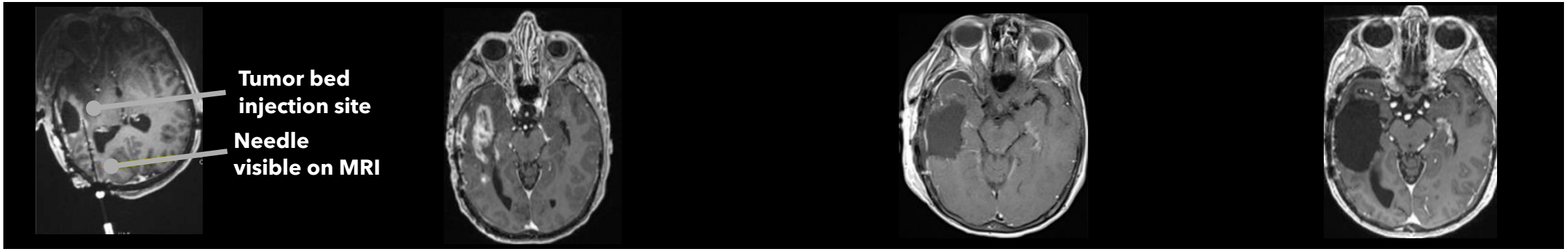

Day -262
Initial presentation

Day -259
Initial resection

Day -47
Tumor recurrence

Day -30
2nd subtotal resection

Day -14
Rapid progression




Day 0
**CAN-3110 Injection**

Day 91
Tumor recurrence with TIL

Day 96
After resection, histology shows TILs

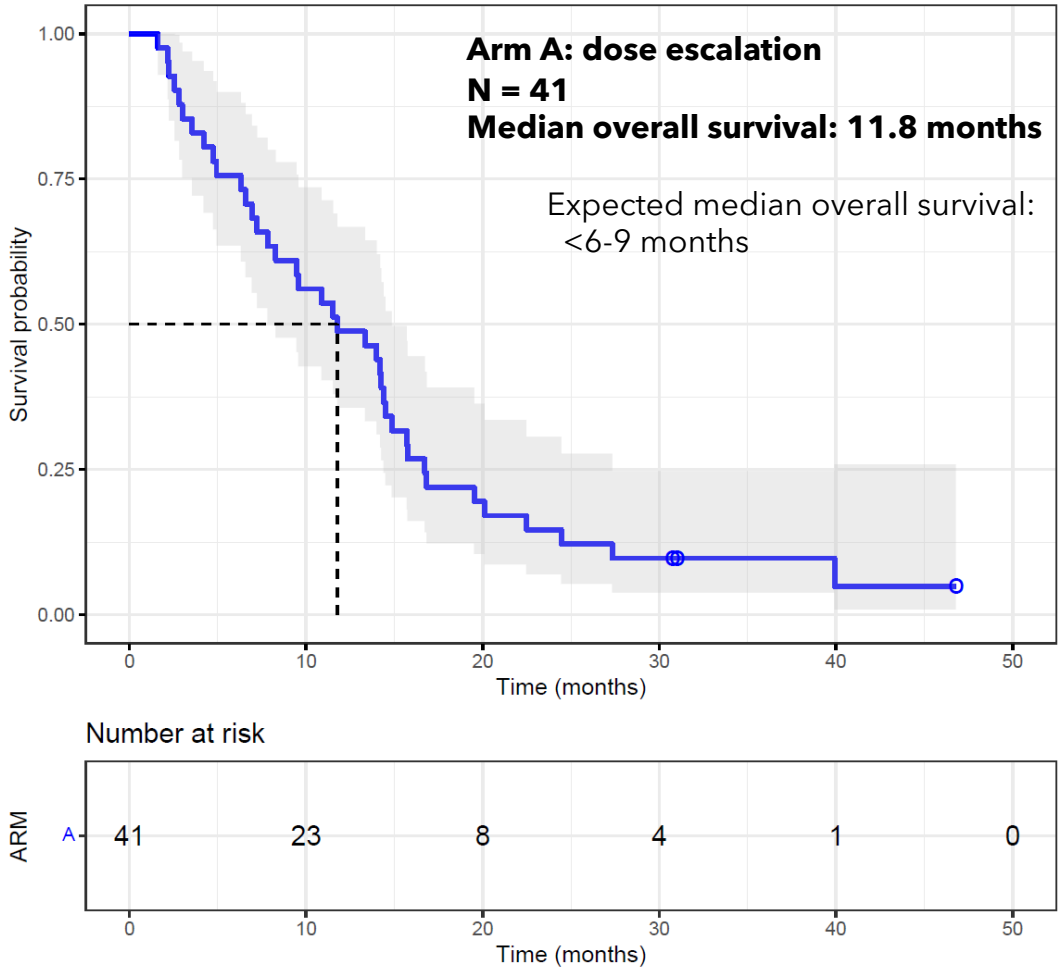
Day 630
No visible tumor

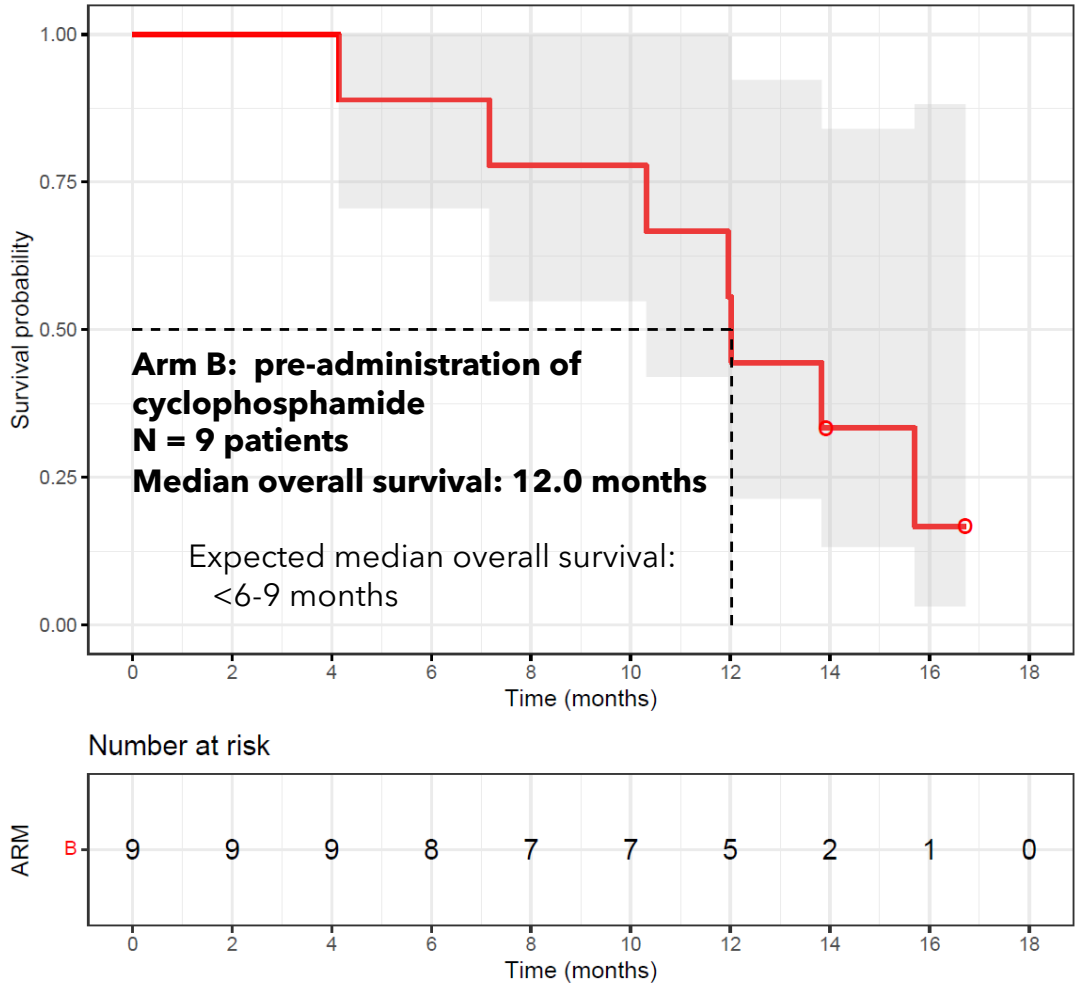
61 YOF, IDH wild-type, MGMT methylated glioblastoma, right temporal lesion initially treated with surgery, chemoradiation and temozolomide
CAN-3110 dose: $10^8$ PFUs. Patient passed away as passenger in a motor vehicle accident on day 717.



*Ling AL et al. Nature 2023;623:157-166*

# Encouraging overall survival in recurrent high-grade glioma after single injection of CAN-3110



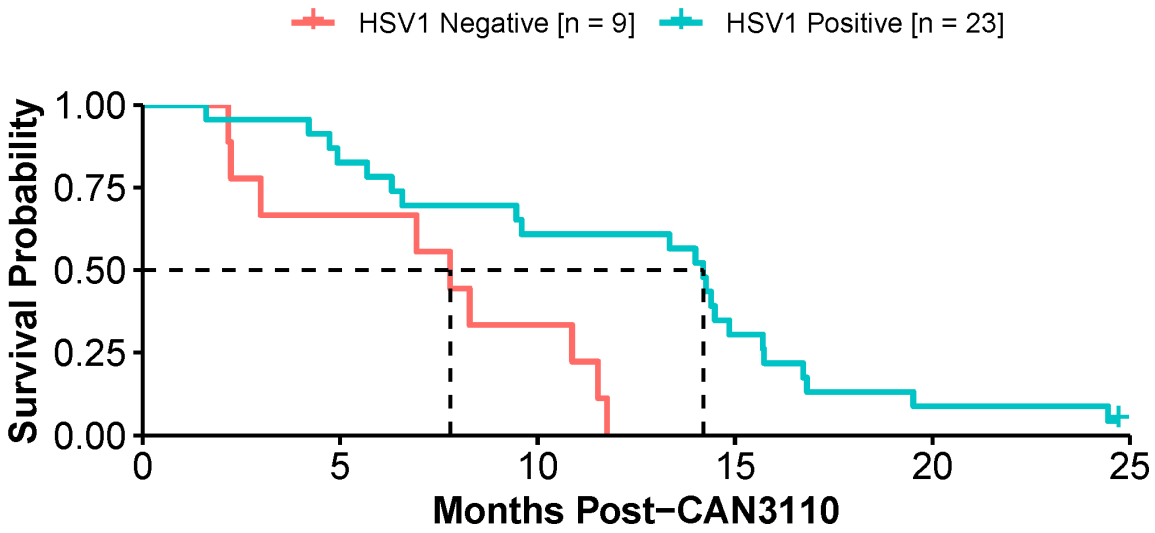

- 41 unique patients were dosed; one patient was treated twice, in cohort IX and X
- A total of 50 unique patients

*Note: As of cutoff date, 20 Apr 2023.*



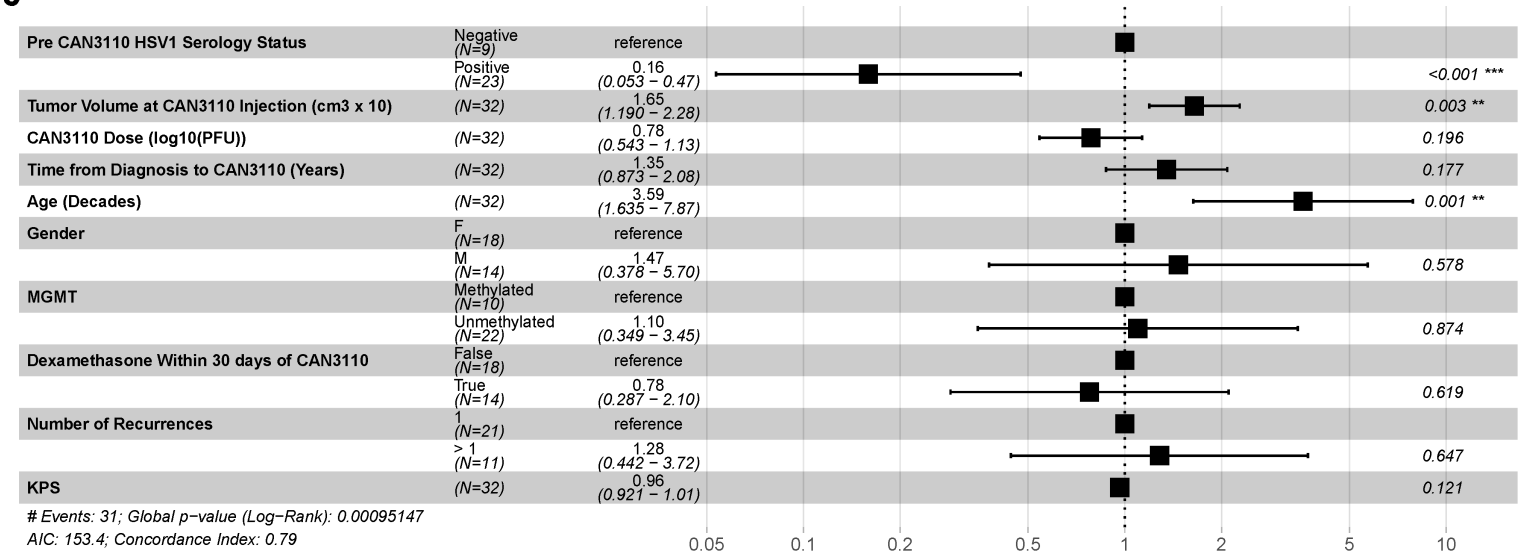
*Barone F et al. Oral Presentation. ASGCT May 2023*

# Prolonged survival after CAN-3110 treatment is associated with HSV1 seropositivity




HSV2 serology status is not associated with survival

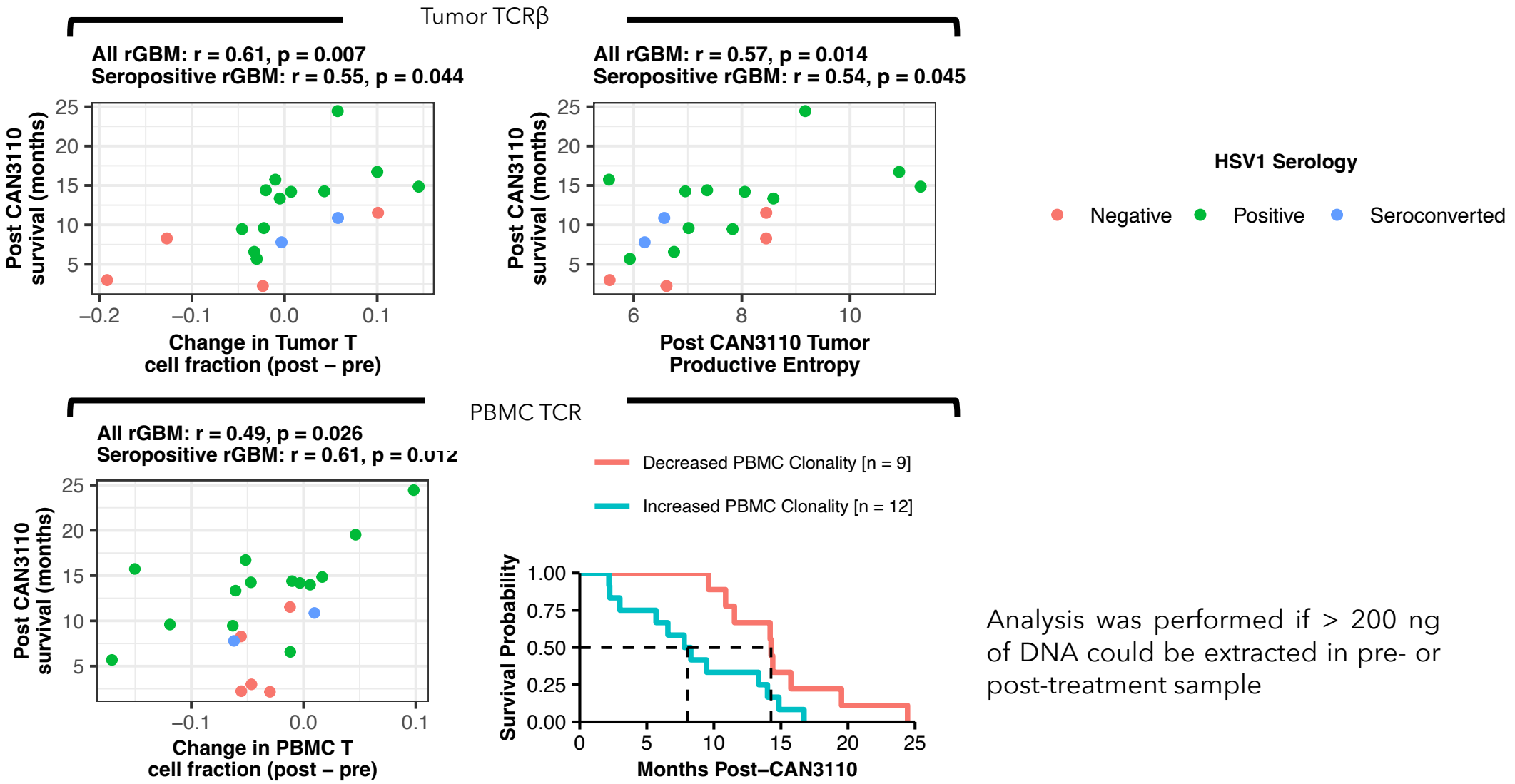
COxPH Hazard Ratios






*Ling AL et al. Nature 2023;623:157-166*

# Changes in T cell fractions and TCRβ diversity correlate with survival after CAN-3110 treatment




Analysis was performed if > 200 ng of DNA could be extracted in pre- or post-treatment sample



*Ling AL et al. Nature 2023;623:157-166*

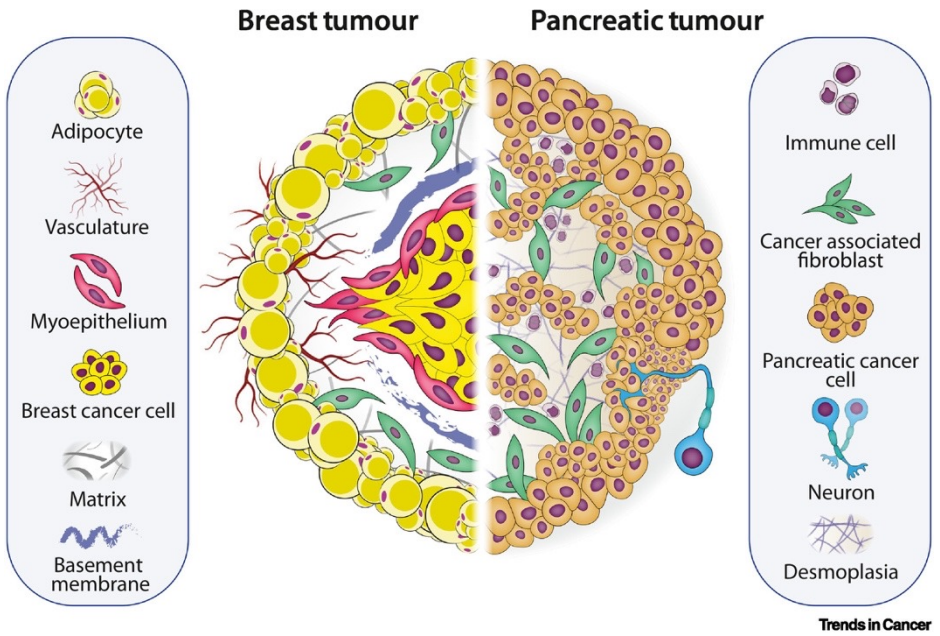
# enLIGHTEN™ Discovery Platform

A systematic, iterative HSV-based discovery platform leveraging human biology and advanced analytics

CANDEL THERAPEUTICS

# Breaking down the barriers to cancer immunotherapy

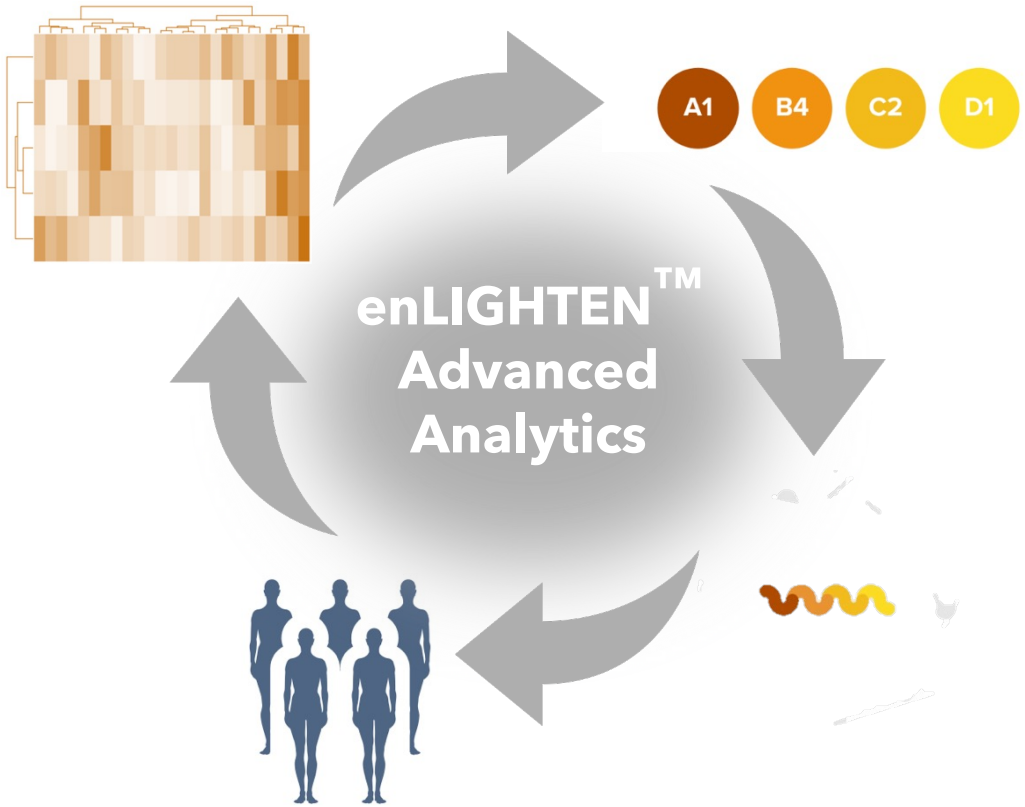
Immunotherapy treatment failure arises from heterogeneous mechanisms present in diverse tumor microenvironments (TME) that are inadequately addressed by single-target therapies




Candel's multimodal approach: viral immunotherapies designed to target the heterogeneous mechanisms in the TME and overcome immunotherapy resistance

*Carter E et al. Trends in Cancer 2021; 11:1033-1046*

# enLIGHTEN™: Viral immunotherapy by design




- Strong focus on human biology to increase probability of success
- Data-driven approach using advanced analytics to de-risk multimodal payload design
- Suite of proprietary, engineered HSV-1 vectors to enable fast translation to clinic
- Rapid and iterative approach
- Flexibility to design assets for monotherapy or combination therapy

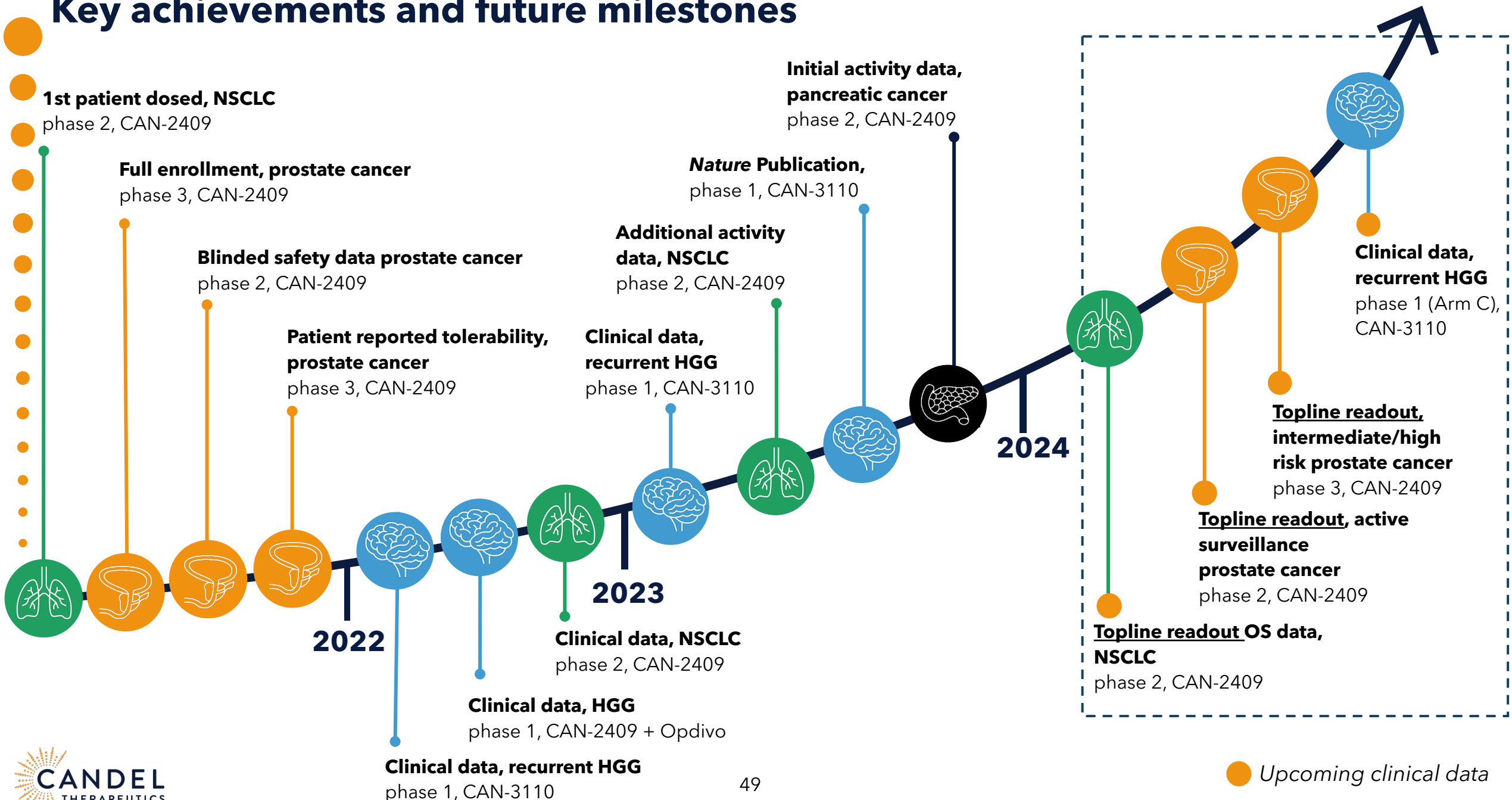
# Example of enLIGHTEN™ Discovery Platform use: Partnership with UPenn to enhance efficacy of CAR-T cells in solid tumors

Evaluation of combination immunotherapy using tailored HSV-1 based viruses to deliver payloads that could enhance the activity of CAR-T cells

| Features of Successful Drug Development* | Challenge for CAR-T Cells in Solid Tumors | Solution via HSV-1-Based OV |
|---|---|---|
| Exposure at the site of action | Insufficient CAR-T ingress | Features of the vector itself plus encoded factors turn cold tumors hot |
| Target binding / engagement | Antigenic heterogeneity | Expose TAAs via oncolysis |
| | | Encode factors to engage CAR-T cells |
| Expression of pharmacological activity | Suppressive TME | Encode cytokines to stimulate and activate CAR-T cells |
| | | Encode inhibitors of key suppressive factors |

*Morgan P et al. Drug Discovery Today 2012;17: 419-424*

# Key achievements and future milestones




CANDEL THERAPEUTICS



*Upcoming clinical data*

# Candel at a glance

## Industry leader in the development of viral immunotherapies for patients living with cancer

- CAN-2409: Off-the-Shelf Therapy, Individualized Cancer Response
  - Engineered, replication-defective adenoviral gene construct encoding herpes simplex virus (HSV)-thymidine kinase
  - "Pipeline in a product" strategy advancing multiple programs in several large indications
  - Established proof of mechanism in patients in each indication currently under evaluation
  - Numerous upcoming catalysts: topline phase 2 OS data in NSCLC (Q2 2024); topline phase 2b (Active Surveillance) and phase 3 (Intermediate/High Risk) Prostate Cancer clinical data (Q4 2024)

- CAN-3110: Oncolytic Virus with Tumor-Specificity
  - Engineered, replication-competent HSV designed for tumor-specificity
  - Encouraging survival data recently announced during May 2023 ASGCT conference from phase 1 Recurrent High-Grade Glioma clinical trial
  - Publication in *Nature*
  - Opportunity for creation of "pipeline in a product" by expansion into indications beyond brain cancers
  - Clinical and immunological biomarker data on Arm C, evaluating repeat dosing regimen of CAN-3110 (2H 2024)

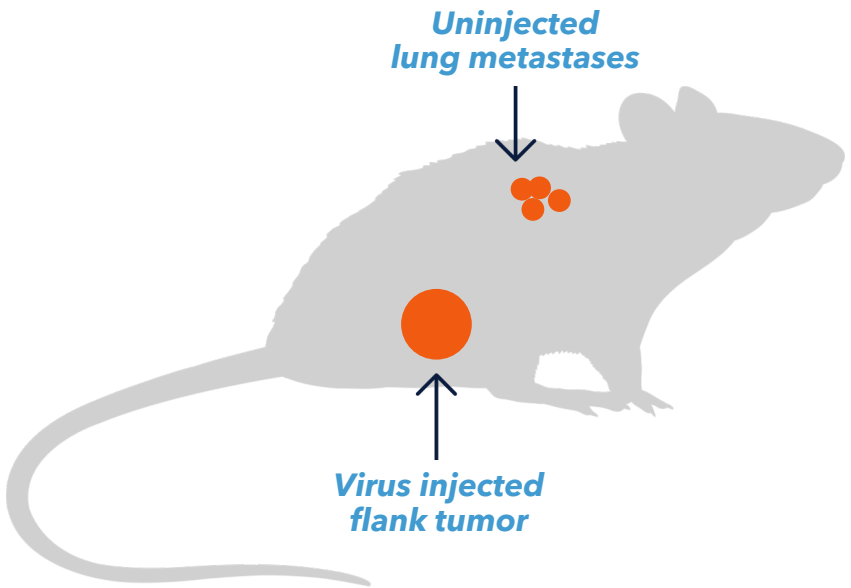
- enLIGHTEN™ Discovery Platform Based on Advanced Analytics and HSV Technology
  - Validating partnership with UPenn Center for Cellular Immunotherapies focused on combination with CAR-Ts in solid tumors

- Corporate Highlights
  - Very experienced Executive Team and strong scientific support from high-profile Research Advisory Board
  - Cash and cash equivalents of $51.9M as of June 30, 2023; expected runway into Q2 2024
  - IP protection: CAN-2409 (2034, method of use); CAN-3110 (2036, composition of matter); 12 years data exclusivity
  - Low-cost manufacturing

CANDEL THERAPEUTICS

# Additional slides

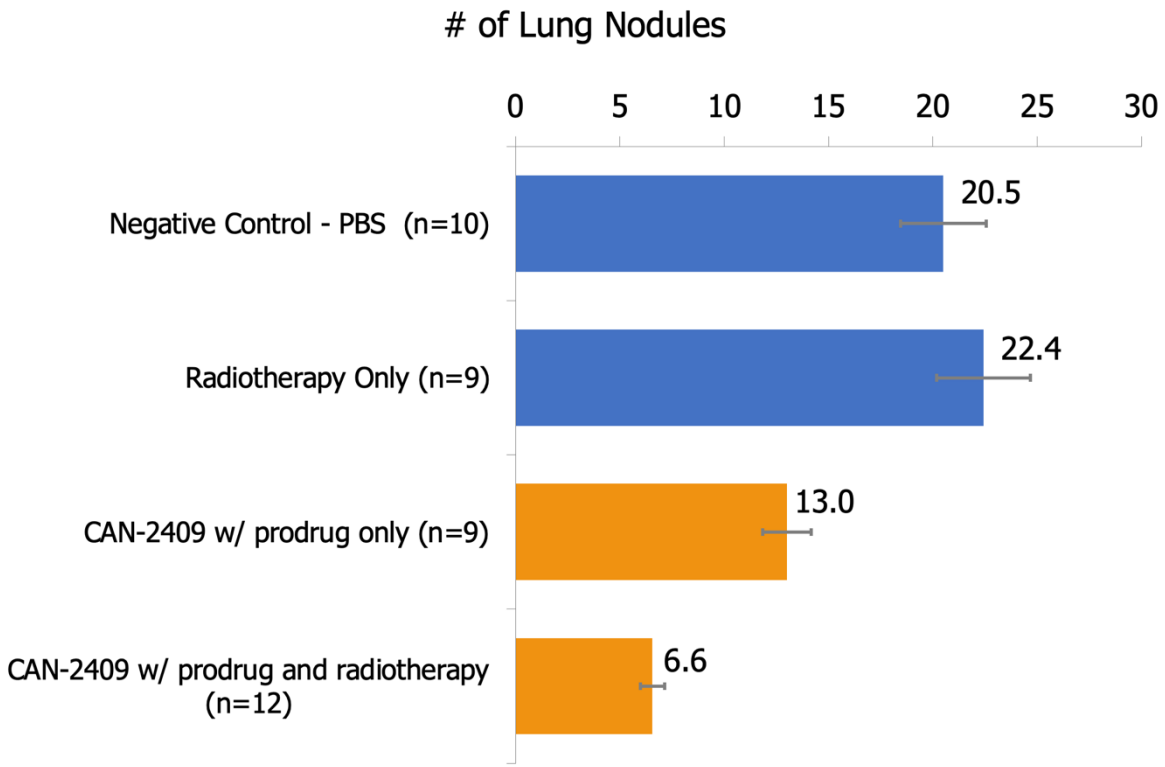
# CAN-2409 treatment teaches the immune system how to fight cancer in injected tumor and uninjected metastases




## Mice receive one of four treatment regimens

1. PBS
2. Radiotherapy
3. CAN-2409 with prodrug
4. CAN-2409 with prodrug plus radiotherapy

## Decrease in uninjected lung metastases



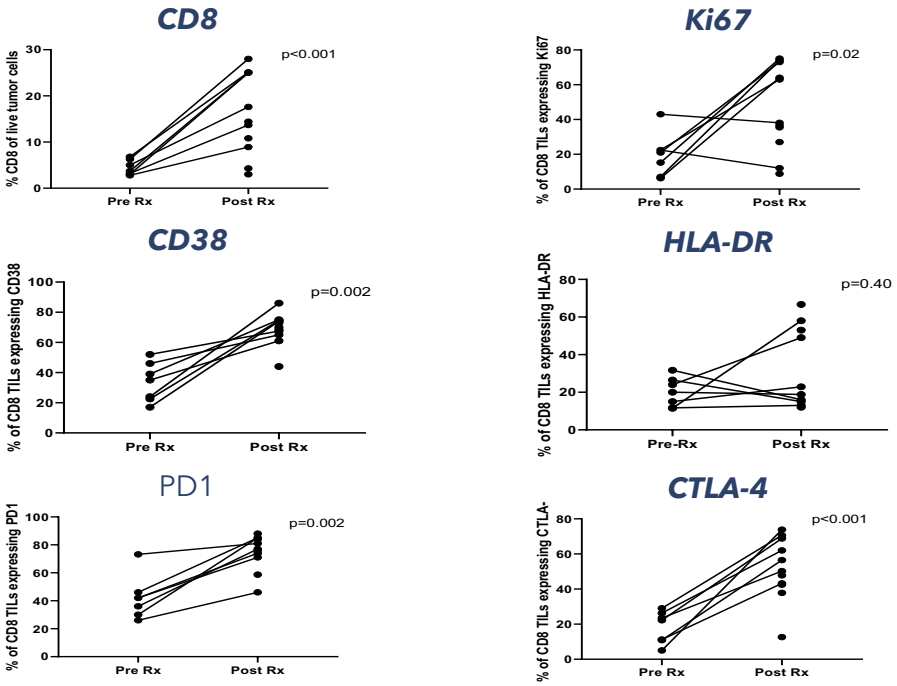

***Model of prostate cancer: RM-1 cells in C57BL/6 mice***

CANDEL THERAPEUTICS

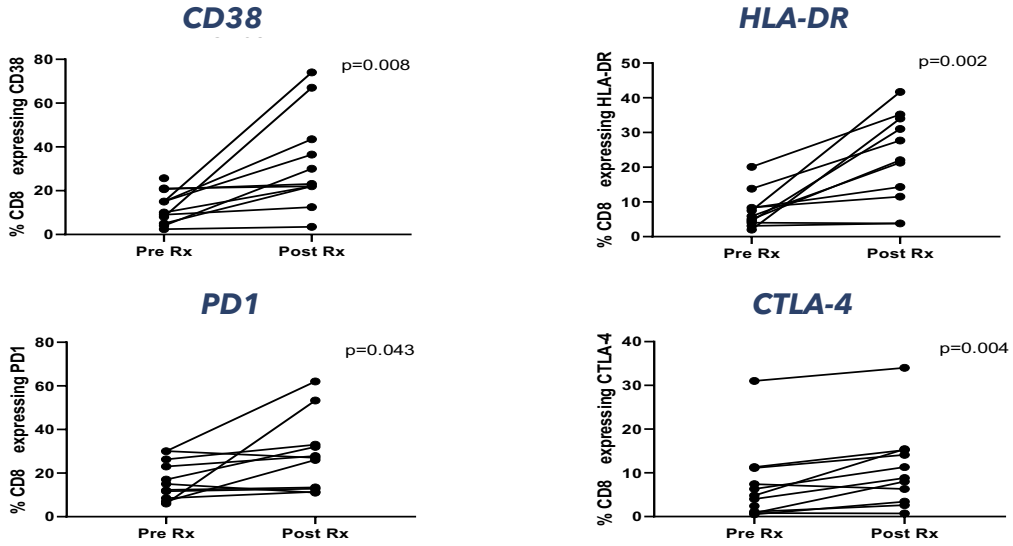
# CAN-2409 Treatment stimulates local and systemic CD8+ T-cell response in patients with cancer

## Non-small cell lung cancer phase 1 clinical trial proof of mechanism (n=12)

### TISSUE



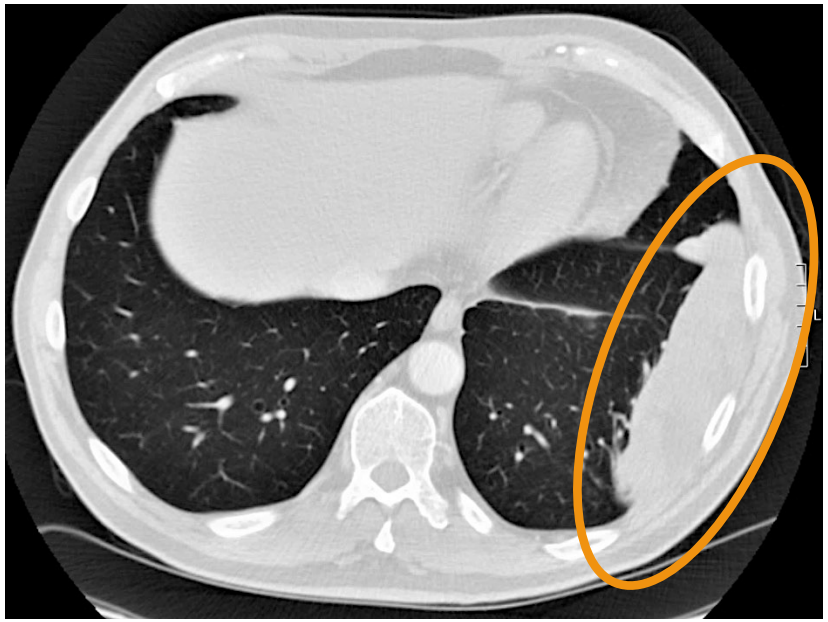

### PERIPHERAL BLOOD




**Clinical evidence supports ongoing phase 2 clinical trial of CAN-2409 in NSCLC**

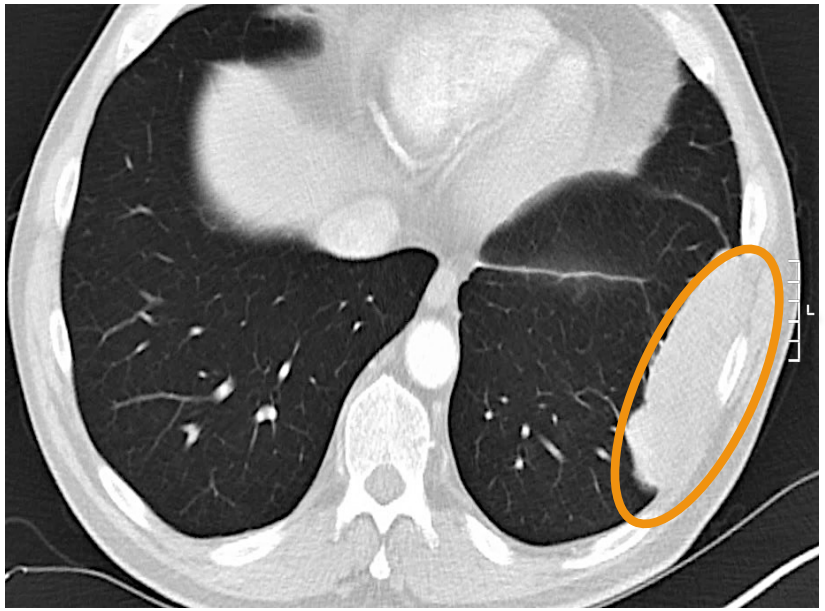
# Monotherapy activity of CAN-2409 in NSCLC

## 70 yr old male with a 14.8 cm stage IIIA sarcomatoid carcinoma



**Day 0**

**Tumor Dimensions: 148 x 40 x 82 mm**



**Day 22**

**Tumor Dimensions: 100 x 34 x 75 mm**

$1x10^{12}$ vp dose

**Nearly 50% decrease in tumor volume* in 3 weeks**

* p/6 x L x W x H