

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



Corporate Presentation | May 2024

NASDAQ: CADL

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; the therapeutic benefit of our programs, including the potential for our programs to extend patient survival; 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; our ability to continue as a going concern, 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; and developments and projections relating to our competitors or our industry. 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.

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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 May 14, 2024.

CAN-2409: Mechanism of action

Please visit <https://vimeo.com/822135123>

1. CAN-2409 locally administered combined with oral prodrug

Valacyclovir

CAN-2409

Thymidine kinase enzyme

CAN-2409

Inflammatory mediators

Tumor antigens

Cytotoxic metabolite

Valacyclovir

2. Localized cytolytic mechanism combined with proinflammatory viral particles

3. CAN-2409 induces CD8+ cytotoxic T cells

Macrophage

Dendritic cell

B-cell

Fibroblast

T-cell

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



CAN-2409: Replication-defective adenoviral gene construct engineered for in situ vaccination against pan-solid tumors

- Proof of concept in patients with prostate cancer, non-small cell lung cancer, pancreatic cancer, and other solid tumors
- > 1,000 patients dosed
- Fast Track Designation in prostate cancer, non-small cell lung cancer, and pancreatic cancer
- Special Protocol Assessment (SPA) in localized prostate cancer
- Monotherapy activity of CAN-2409 in NSCLC patient: Nearly 50% decrease in tumor volume in 3 weeks



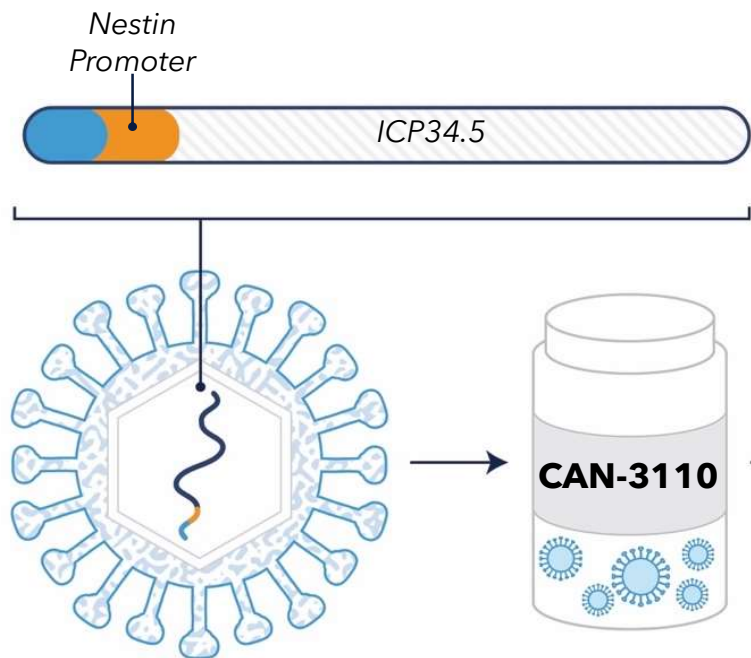
Day 0
Tumor Dimensions: 148 x 40 x 82 mm
(10^{12} vp dose)



Day 22
Tumor Dimensions: 100 x 34 x 75 mm

CAN-3110: Mechanism of action

Please visit <https://vimeo.com/822133681>



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

Virus expands in Nestin expressing tumor cells, causing oncolytic activity

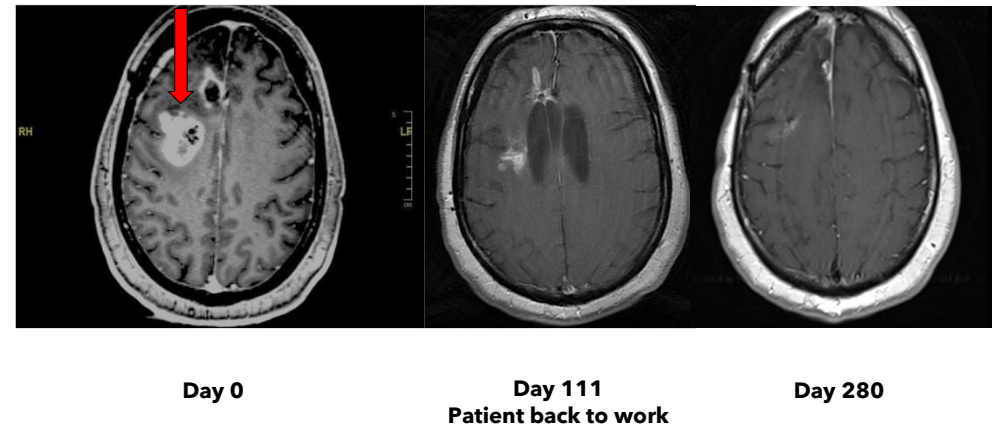


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CAN-3110 is an investigational product and its mechanism of action in humans has not been definitively established. This depiction of the CAN-3110 mechanism of action and the MoA video linked above are based on preclinical data and observations in clinical studies to date

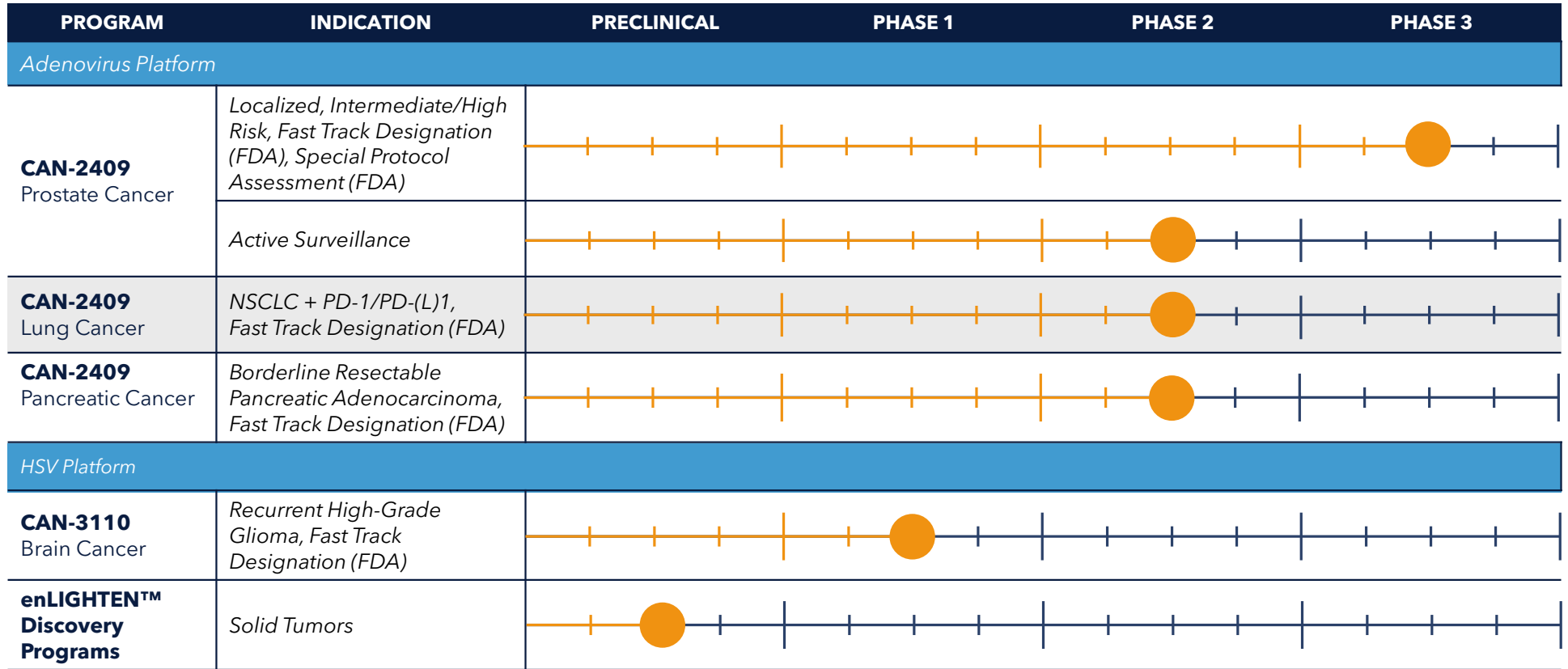
CAN-3110: Replication-competent HSV-1 engineered to enhance selective killing of cancer cells while sparing healthy neighboring cells

- Proof of concept in patients with recurrent high grade glioma (mostly glioblastoma)
- > 50 patients dosed
- Data published in Nature*
- Fast Track Designation in recurrent high-grade glioma
- First cohort of patients treated with multiple injections of CAN-3110
- IND-enabling work in a second indication characterized by Nestin expression being planned

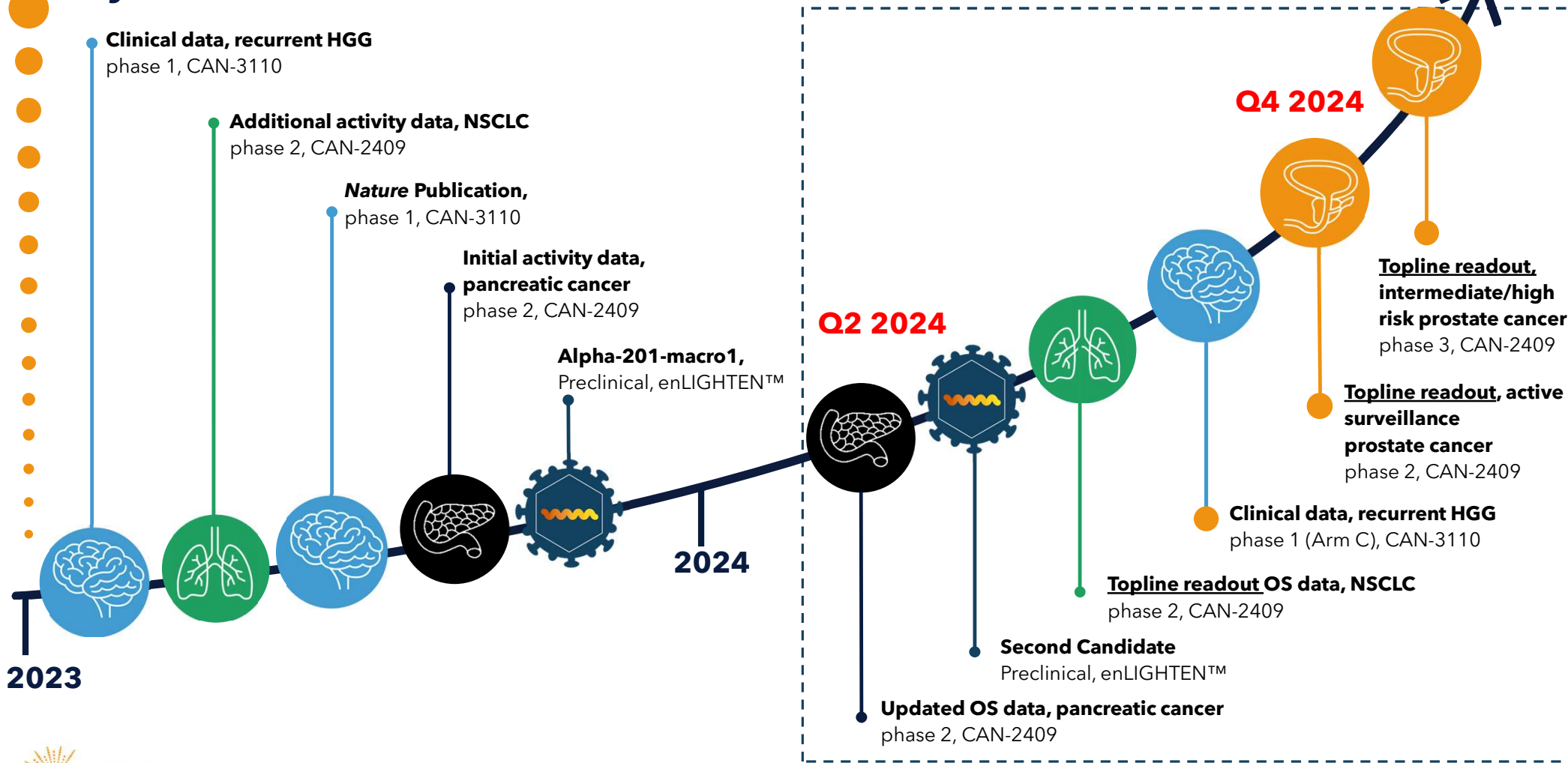
Monotherapy activity of CAN-3110 in recurrent high-grade glioma: Clinical effect on injected tumor and uninjected tumor



Pipeline focused on value creation



Key achievements and future milestones



Milestones for CAN-2409 this year (2024)

Study	Population	Potential success scenario
Phase 2 randomized clinical trial in borderline resectable pancreatic cancer	US + EU5: ~13,000 patients/year	mOS 28.8 months vs. 12.5 months in control group <i>Disclosed in April 2024</i> ACHIEVED ✓
Phase 2 clinical trial in NSCLC with inadequate response to ICI	US + EU5: ~74,000 patients/yr	mOS 20.6 months in progressive disease patients vs. ~12 months in historical controls ACHIEVED ✓
Phase 2b randomized clinical trial in localized low/intermediate risk prostate cancer (active surveillance population)	US + EU5: ~98,000 patients/yr	Significant improvement in progression-free survival (Q4 2024)
Phase 3 randomized clinical trial in localized intermediate/high risk prostate cancer	US + EU5: ~110,000 patients/yr	Significant improvement in disease-free survival (Q4 2024)

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



Paul Peter Tak, MD, PhD, FMedSci

President & Chief Executive Officer



Charles Schoch, MBA, MSA, CPA

Interim Chief Financial Officer



Francesca Barone, MD, PhD

Chief Scientific Officer



Garrett Nichols, MD, MS

Chief Medical Officer



Seshu Tyagarajan, PhD, RAC

Chief Technical and Development Officer



Susan Stewart, JD

Chief Regulatory Officer



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*

Candel at a glance



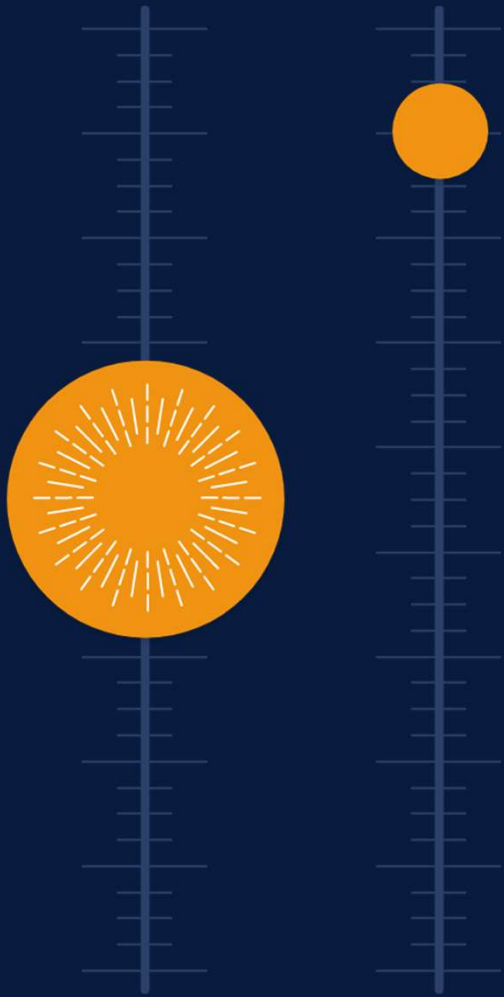
- CAN-2409: Off-the-shelf pan-solid tumor therapy, individualized anti-cancer immune response
 - Proof of concept in patients across multiple solid tumors
 - Fast Track Designation in NSCLC, pancreatic cancer, and prostate cancer
 - “Pipeline in a product” strategy advancing multiple programs in several large indications
 - Upcoming catalysts:
 - Topline phase 2b (Active Surveillance) prostate cancer clinical data (Q4 2024)
 - Topline phase 3 (Intermediate/High Risk) prostate cancer clinical data (Q4 2024)



- CAN-3110: Oncolytic HSV-1 designed for tumor-specific replication
 - Proof of concept in patients with recurrent high-grade glioma published in *Nature*
 - Fast Track Designation
 - Opportunity for creation of “pipeline in a product” by expansion into indications beyond brain cancers
 - Clinical and immunological biomarker data, evaluating repeat dosing regimen of CAN-3110 (H2 2024)



- Corporate Highlights
 - Very experienced Executive Team and strong scientific support from high-profile Research Advisory Board
 - Cash and cash equivalents of \$25.7 million as of March 31, 2024; expected runway into Q4 2024
 - IP protection: CAN-2409 (2034, method of use); CAN-3110 (2036, composition of matter); 12 years data exclusivity
 - Low-cost manufacturing



CAN-2409



Off-the-shelf therapy, individualized cancer response

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	<i>Localized Prostate Cancer Intermediate / High Risk</i>	<ul style="list-style-type: none"> Fast-track status 711 patients 2:1 Randomization Primary Endpoint: Disease-free survival 	→			Q4:2024
CAN-2409	<i>Localized Prostate Cancer Active Surveillance</i>	<ul style="list-style-type: none"> 187 patients 2:1 Randomization Primary Endpoint: Progression-free survival 	→			Q4:2024
CAN-2409 +PD-1/PD-(L)1	<i>Non-Small Cell Lung Cancer</i>	<ul style="list-style-type: none"> Fast-track status 80 patients Primary Endpoint: Response by RECIST criteria and disease control rate 	→			Q2:2024
CAN-2409	<i>Borderline Resectable Pancreatic Adenocarcinoma</i>	<ul style="list-style-type: none"> Fast-track status 13 patients 1:1 Randomization Primary Endpoint: Safety and survival rate at 24 mos 	→			Q2:2024

CAN-2409: Prostate cancer opportunity

Incidence of localized prostate cancer in the US by risk level



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**

- Prostate cancer is the second leading cause of cancer death among men in the US
- Global annual incidence projected to rise from 1.4 million in 2020 to 2.9 million by 2040 due to aging populations and increase screening[^]
- No new treatments approved for newly diagnosed, localized prostate cancer during the last > 30 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*

[^]Source: James ND et al. Lancet 2024 Apr 4:S0140-6736(24)00651-2

[#]Consistent with market research combined with interviews with 22 KOLs (12 US; 10 EU) and 16 US payors. May 2023

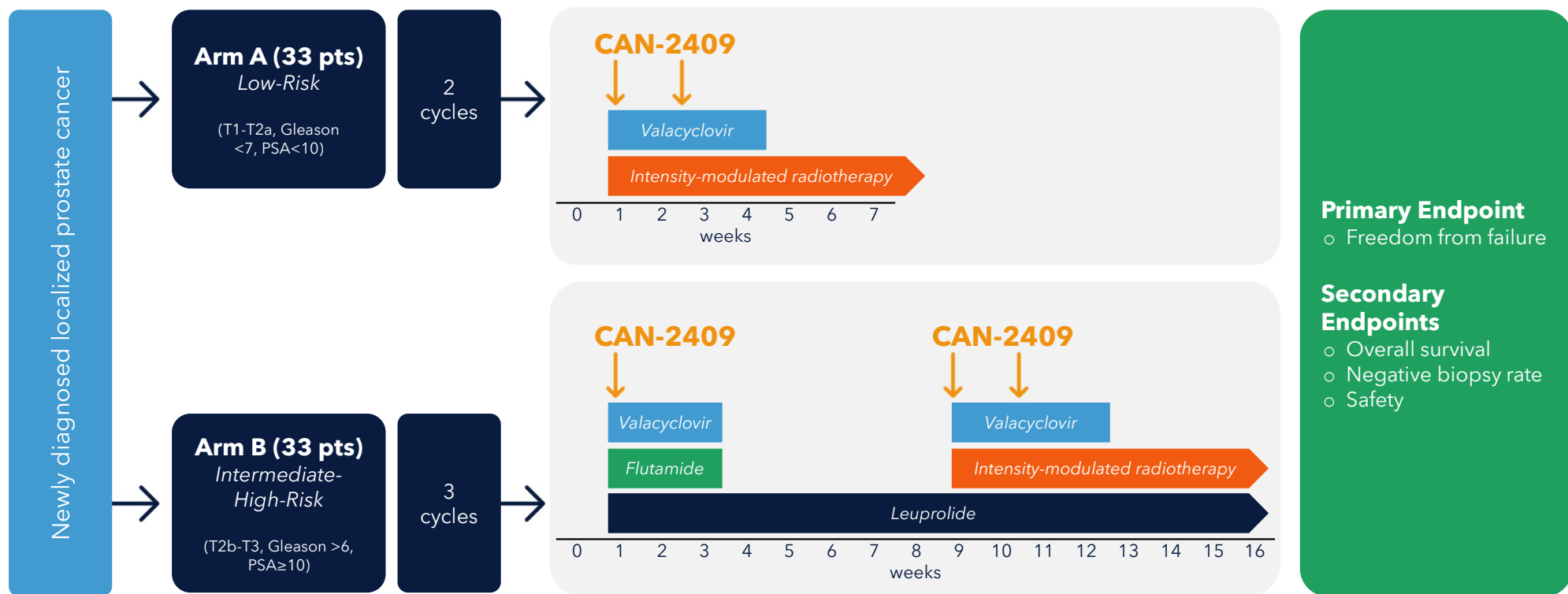
*Source: EvaluatePharma, accessed May 2023



CAN-2409: Prostate cancer opportunity in active surveillance population

- Active surveillance population (US) ~40,000 pts / year
- There is a ~30% risk of reporting cancer-specific anxiety in this population
- 30-50% of patients will still undergo radical therapy due to disease progression within 5 yrs
 - Patients will then face side effects and complications of radical therapy, including urinary incontinence and erectile dysfunction
 - Next, one third of these patients will still have recurrence after radical therapy
- Lifetime cost of active surveillance estimated at ~\$21,000 without providing therapeutic treatment
- **Opportunity for development of a well-tolerated therapy that stops progression of the disease**

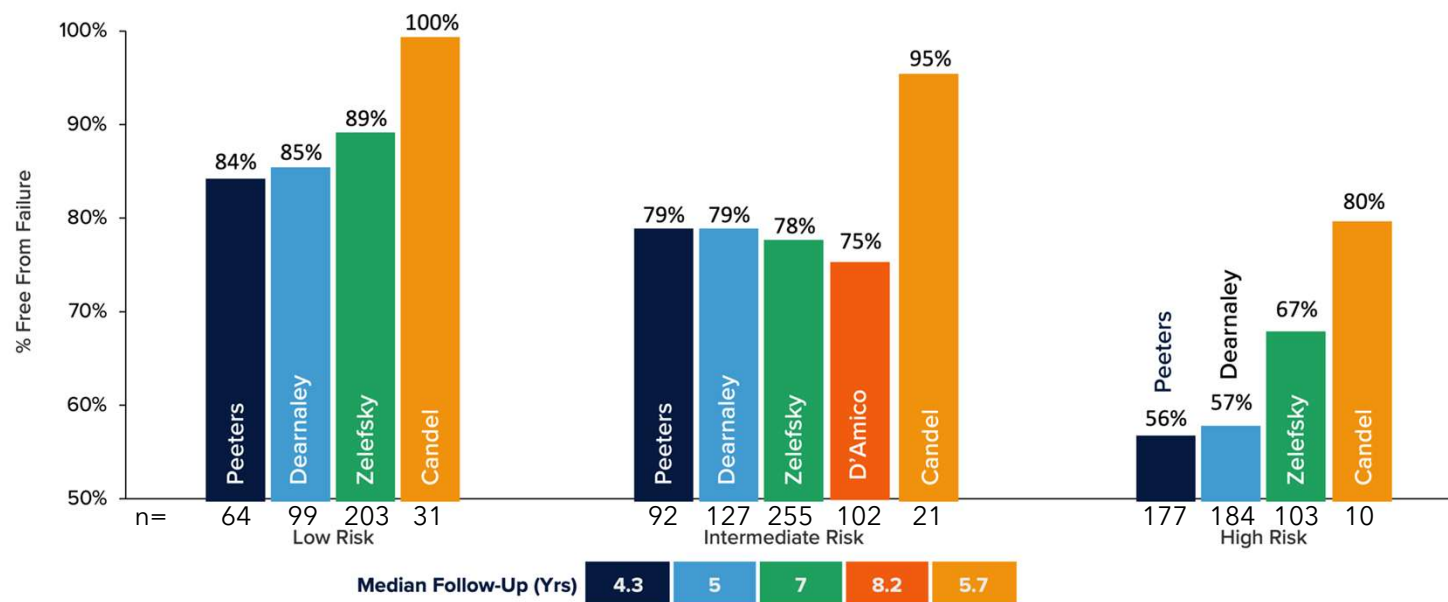
Completed phase 2a clinical trial of CAN-2409 combined with radiotherapy +/- androgen deprivation therapy



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)

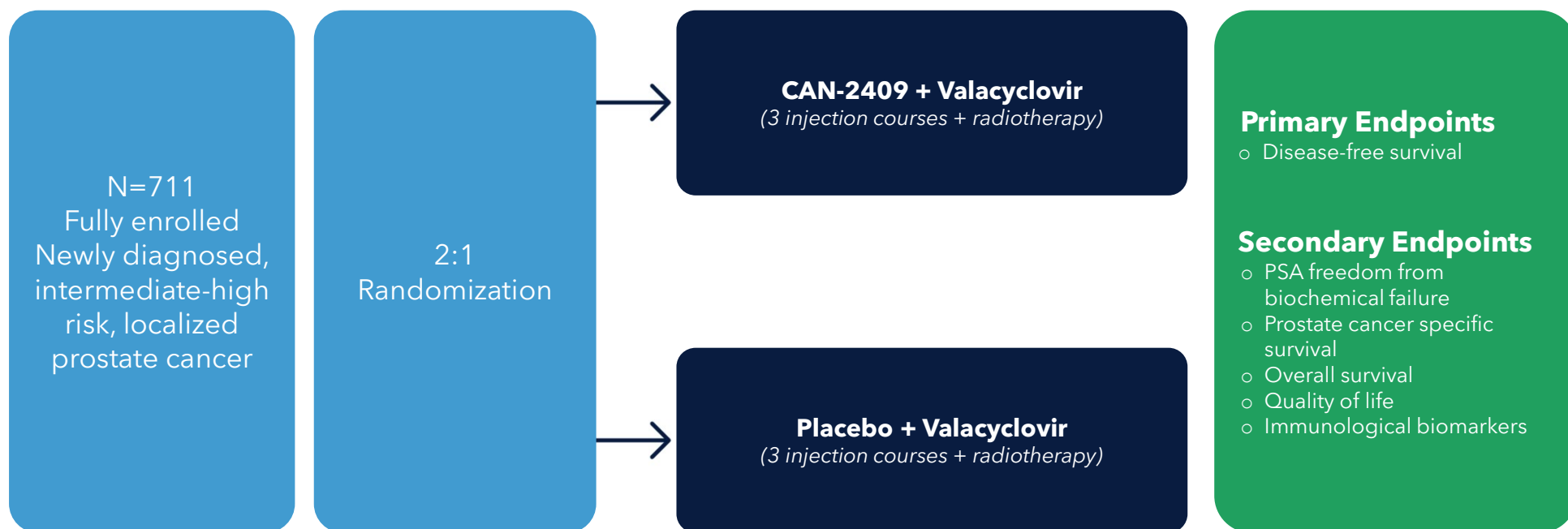
Clinical evidence supports ongoing phase 3 clinical trial of CAN-2409 in combination with SoC as first line treatment



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)

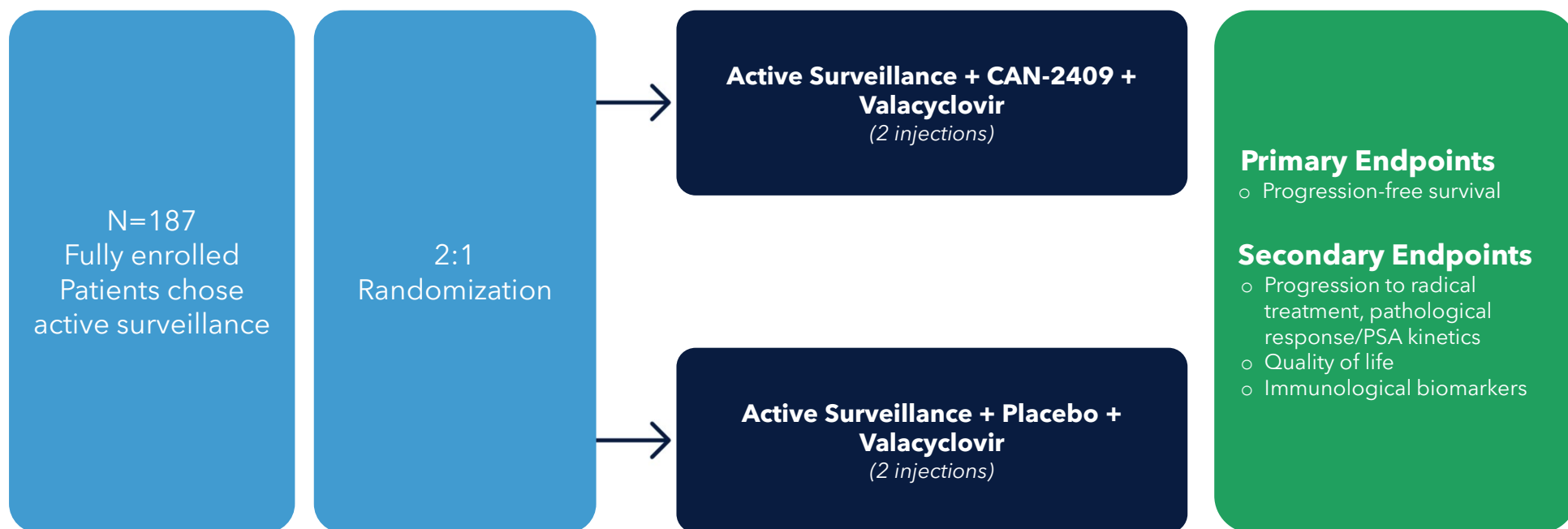


NCT01436968

Conducted under agreement with FDA under Special Protocol Assessment

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

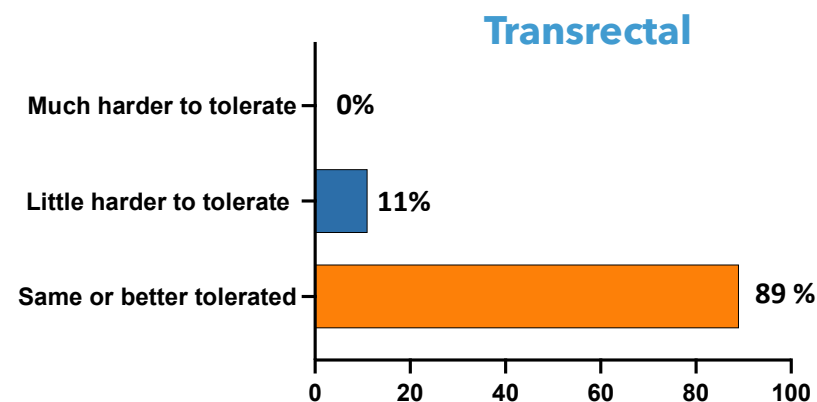
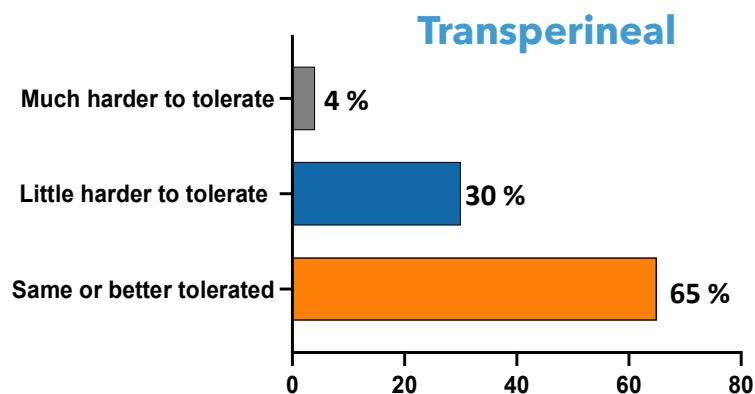
Study is still blinded
187 patients treated
362 injections performed

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)

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

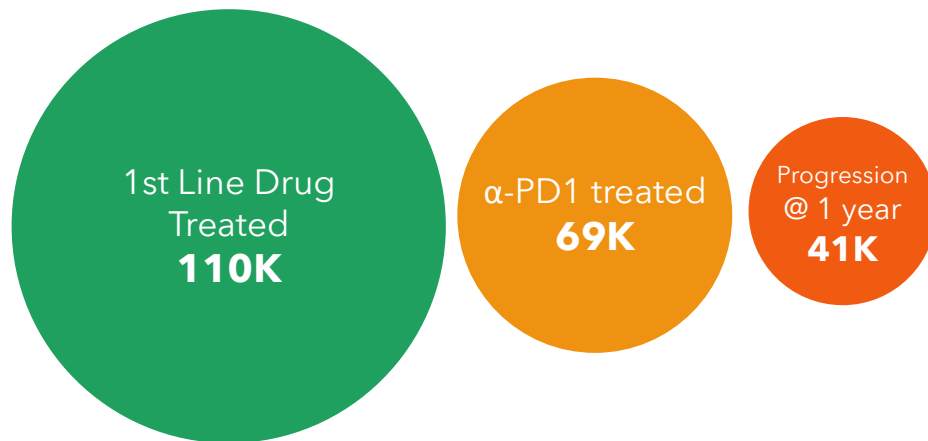
Patient questionnaire substudy n=32

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?"



CAN-2409: Non-small cell lung cancer opportunity

Incident advanced NSCLC in the US¹



- Lung cancer is the most commonly diagnosed cancer in the US with NSCLC representing over 80% of all lung cancer diagnoses²
- 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 anti-PD1 treated patients will have progressive disease³
 - In ICI inadequate responders with SoC docetaxel⁴
 - **Median overall survival (mOS) <12 months**
- Significant opportunity to improve response to ICIs by teaching the immune system how to recognize the cancer cells
- NSCLC cancer therapy global market was estimated at \$32B in 2023 and is expected to grow to \$52B by 2028⁵

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[#]

Upside to this target population as ~25% of patients treated in the 2L setting receive an anti-PD-1/L1

¹ SEER Cancer Statistics Factsheets, accessed Mar 2024

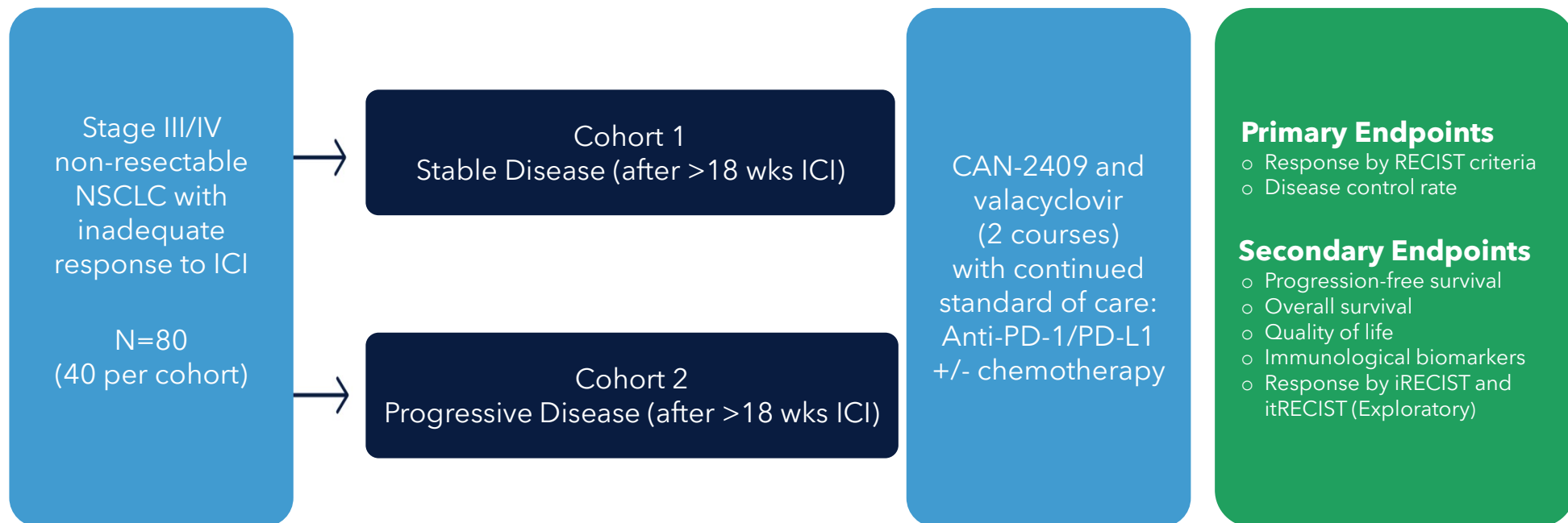
² American Cancer Society Website, accessed Mar 2024

³ Gandi L et al. NEJM 2018; 378:2078-92

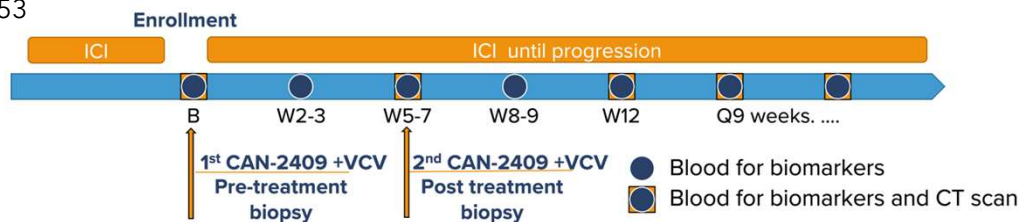
⁴ Reckamp K et al. J Clin Onc 2022;40:2295-2306

⁵ 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

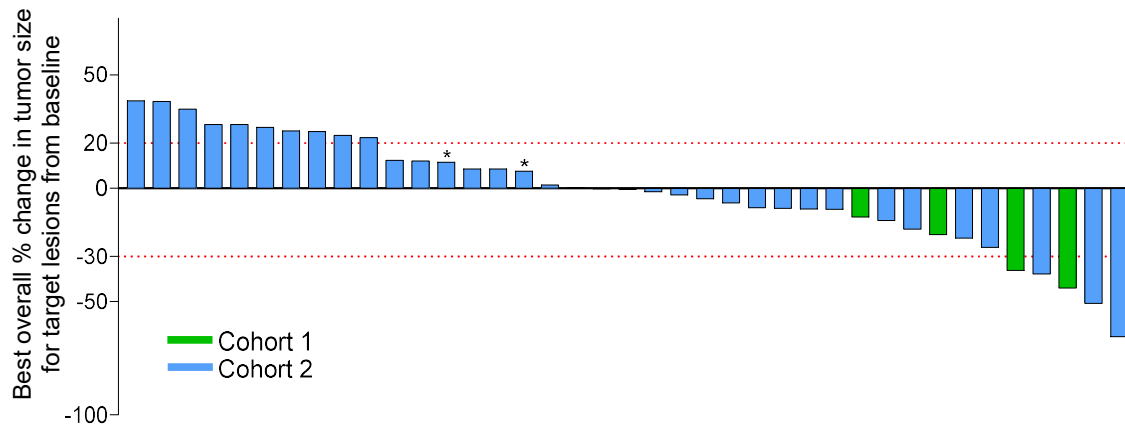


NCT04495153



Evidence that CAN-2409 can control 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

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

PA-003 (Cohort 1)

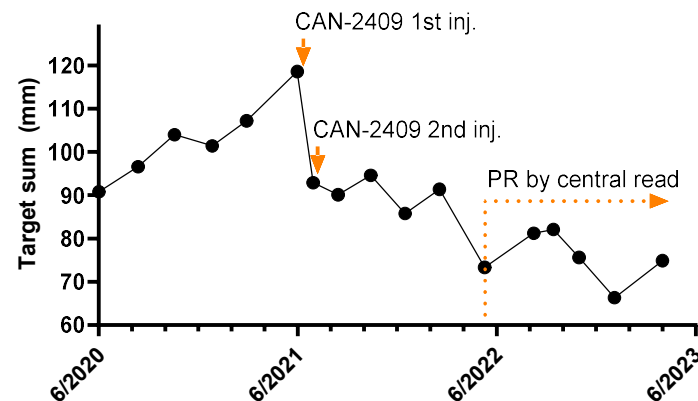
73M, Stage III non-squamous NSCLC diagnosed Jan'20
 PD-L1 < 1%
 Initial therapy: pembro + carbo + pemetrexed Feb'20
 Maintenance: pembro + pemetrexed from Jun'20 which continued on-trial
 OS 24 mo (ongoing as of LFV)

Legend

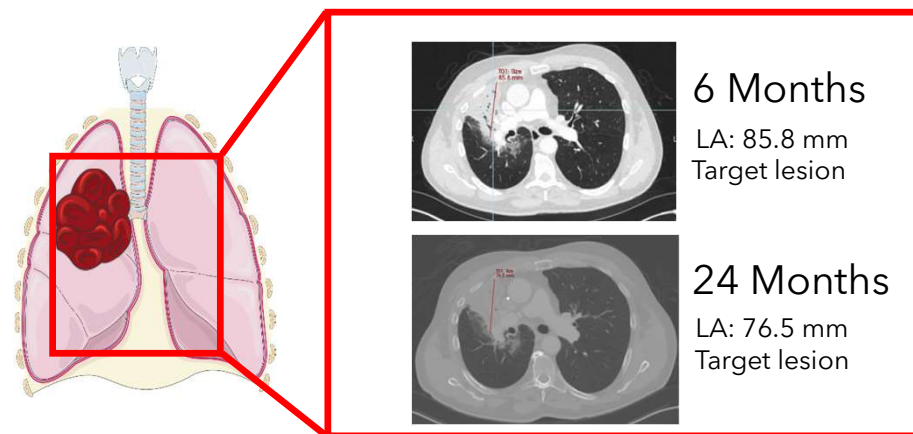
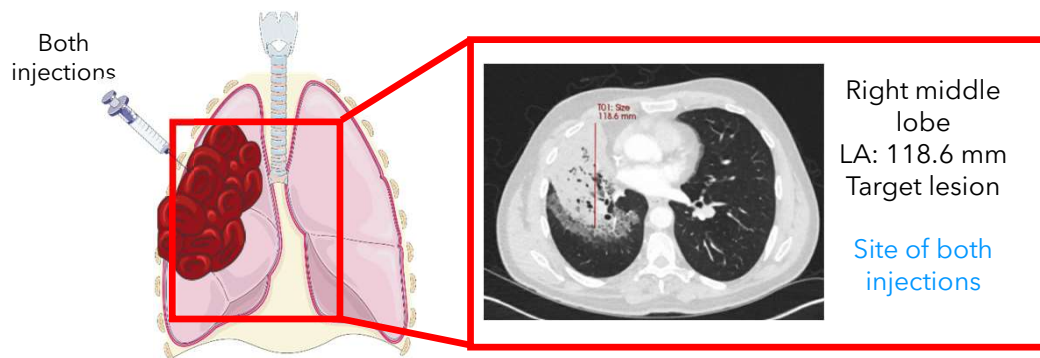
RECIST target lesions (red)

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

LFV: last follow up visit



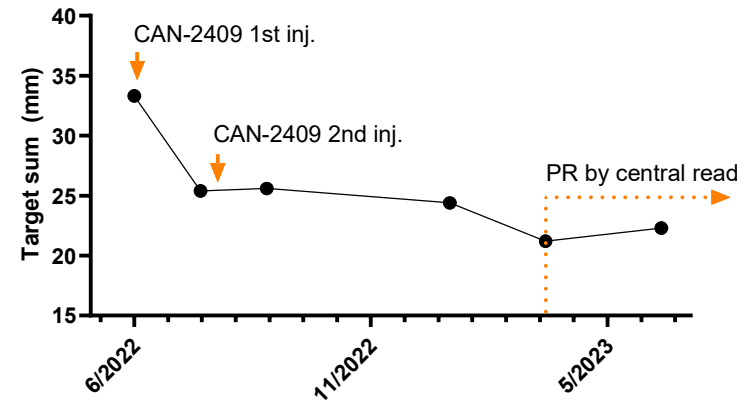
Baseline



Patient with continued tumor shrinkage after CAN-2409 treatment

VB-007 (Cohort 1)

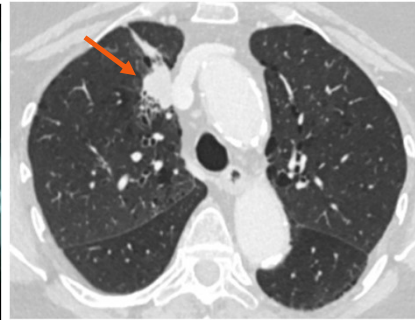
84F, Stage IV non-squamous NSCLC diagnosed Aug'21
 PD-L1 < 1%; SMARC4 alteration
 Initial therapy: platinum-based chemotherapy + pembro
 Maintenance: pembro which continued on-trial
 OS 12.1 mo (PR is ongoing as of LFV)



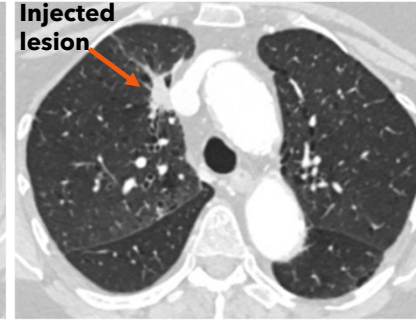
FDG-PET



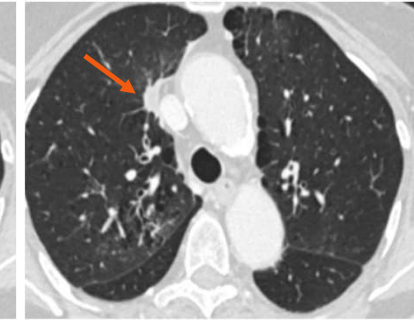
Treatment Naïve



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.



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

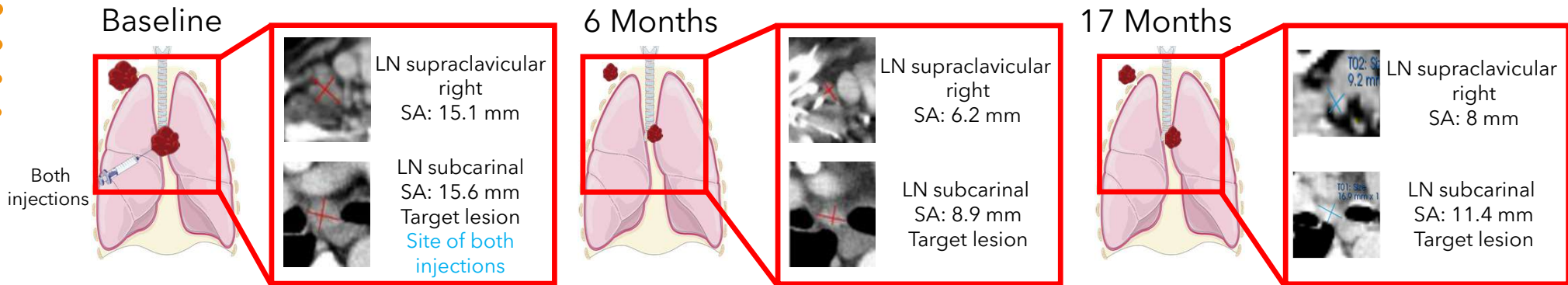
Maintenance: nivolumab from Sep'19, continued on-study

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

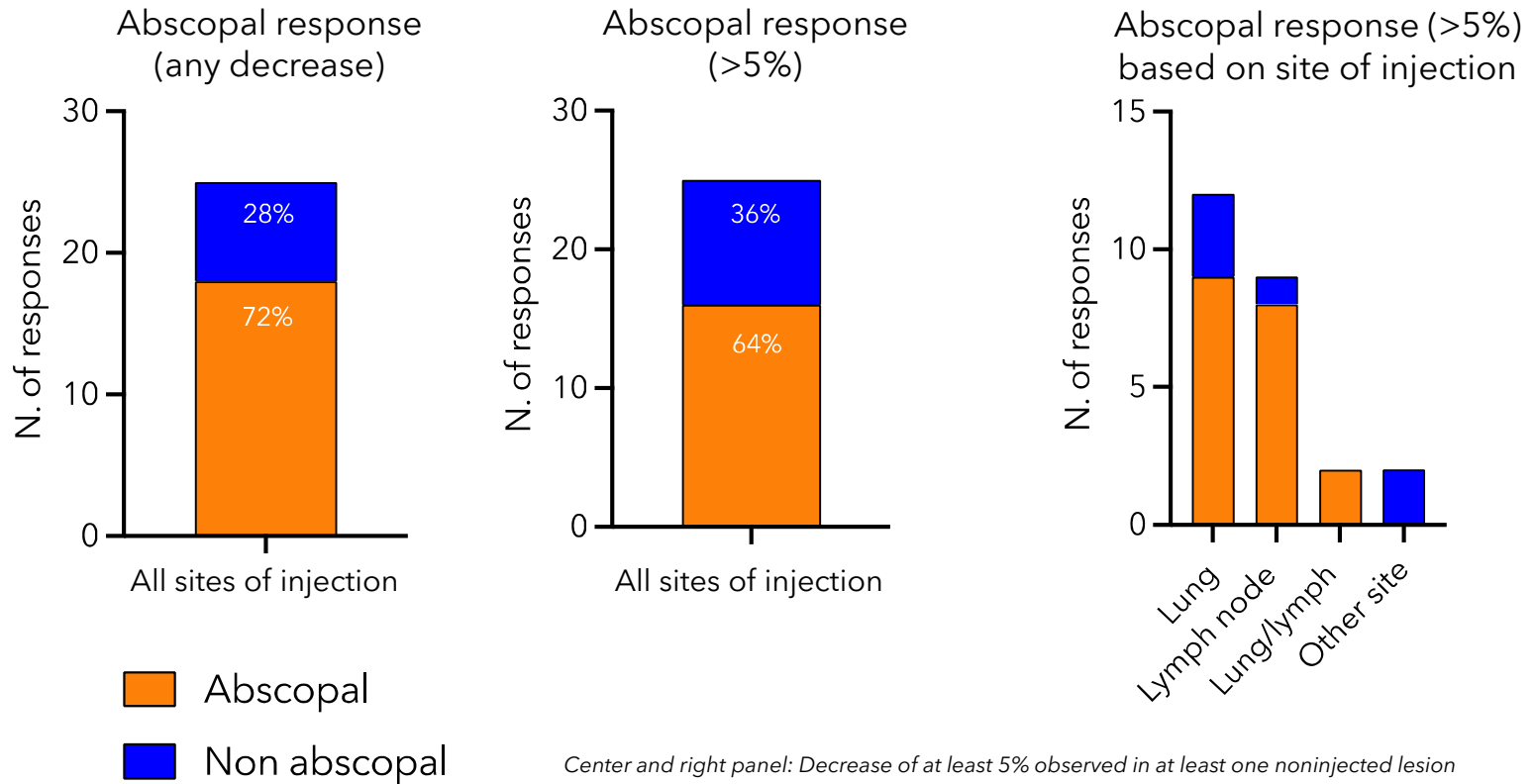
27

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

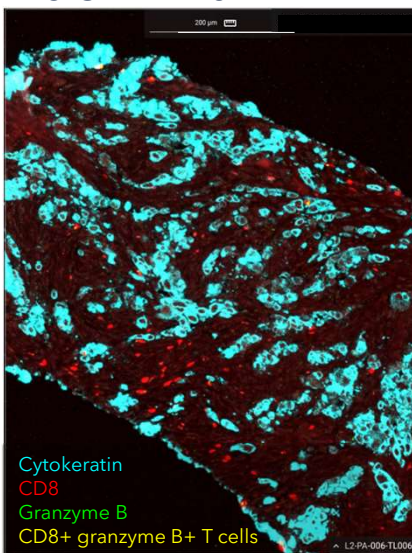


Center and right panel: Decrease of at least 5% observed in at least one noninjected lesion

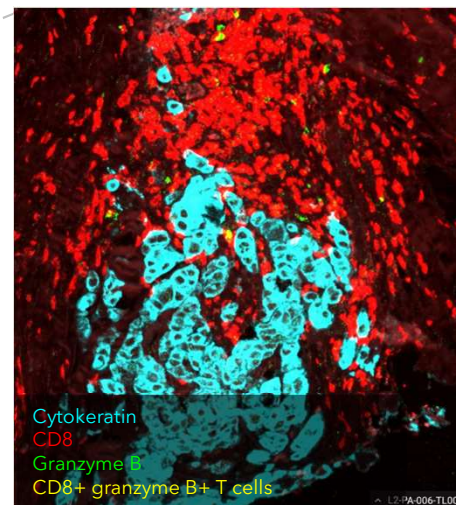
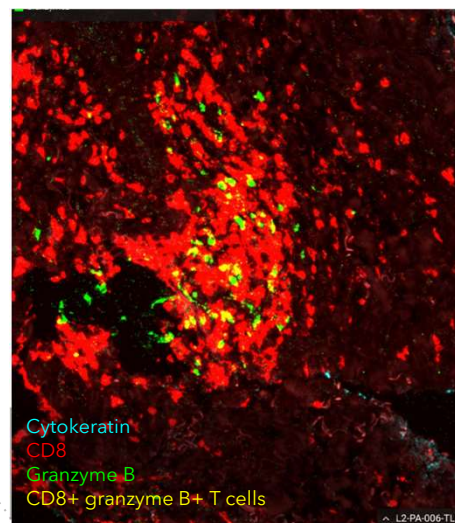
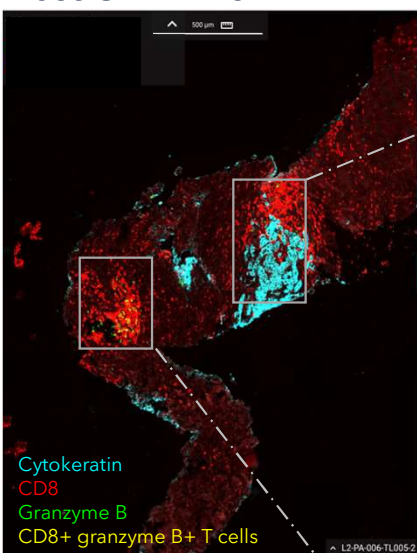
CAN-2409 induces expansion of CD8+ cytotoxic tumor infiltrating lymphocytes in the tumor microenvironment

PA006

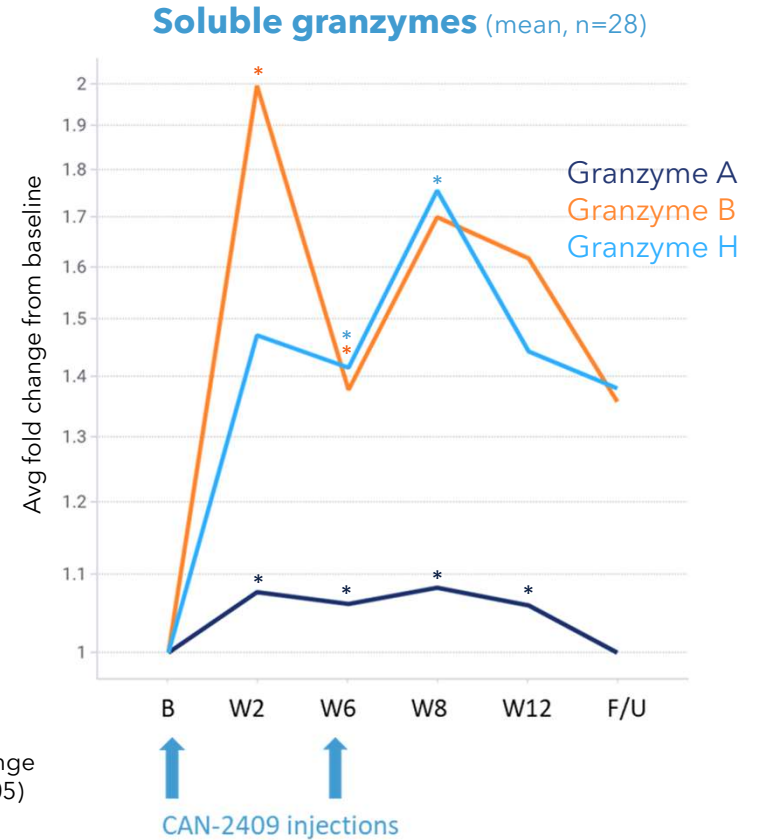
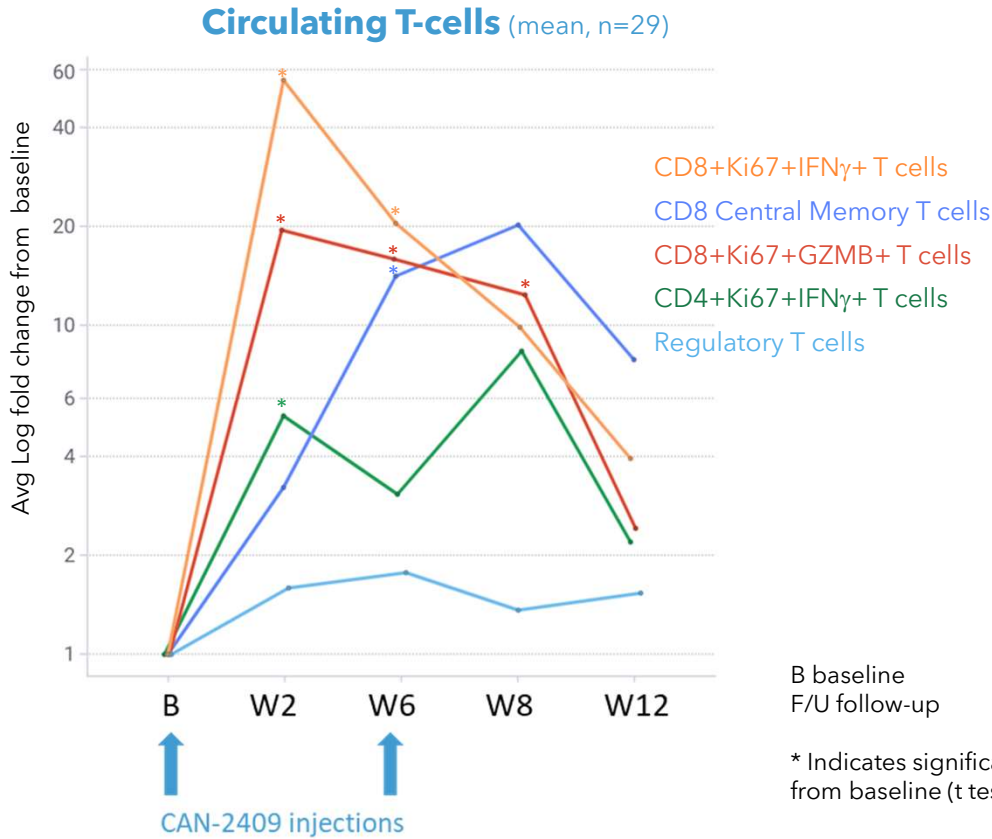
Pre CAN-2409



Post CAN-2409

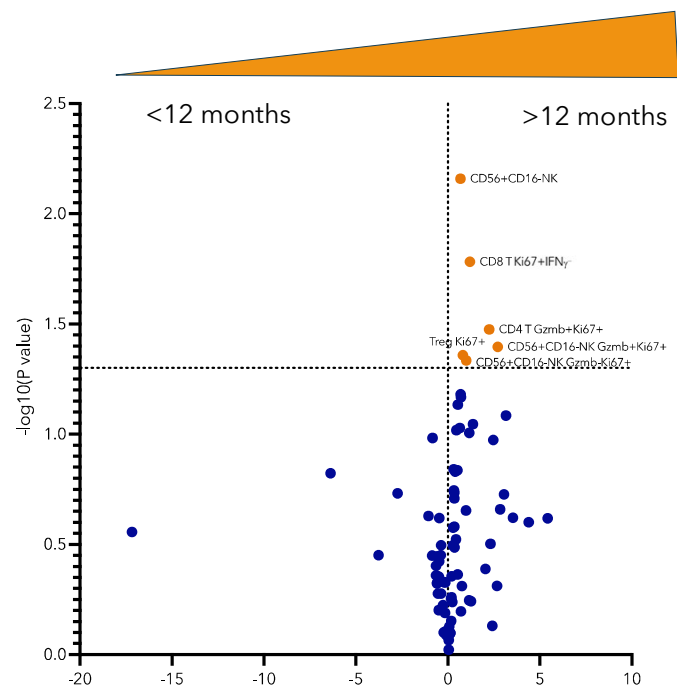


CAN-2409 significantly increases frequency of circulating cytotoxic T cells and serum levels of soluble granzymes



Changes in immune cells in peripheral blood after 2nd injection of CAN-2409 are associated with subsequent 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

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)

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 be implemented by clinicians
 - Stem cell transplantation, implant radiotherapy, interventional radiology, interventional cardiology

Encouraging safety data, clinical activity and immunological changes after CAN-2409 in NSCLC

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



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

CAN-2409: Pancreatic ductal adenocarcinoma opportunity

Incidence of pancreatic ductal adenocarcinoma in the US by risk level¹



- Limited available treatment options for patients suffering from pancreatic cancer beyond resection when possible and chemotherapy
- Borderline resectable disease: median overall survival <18 months (with neoadjuvant chemoradiation and resection)²
- Metastatic disease: median overall survival ~11 months (with FOLFIRINOX)³
- 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 2028⁴

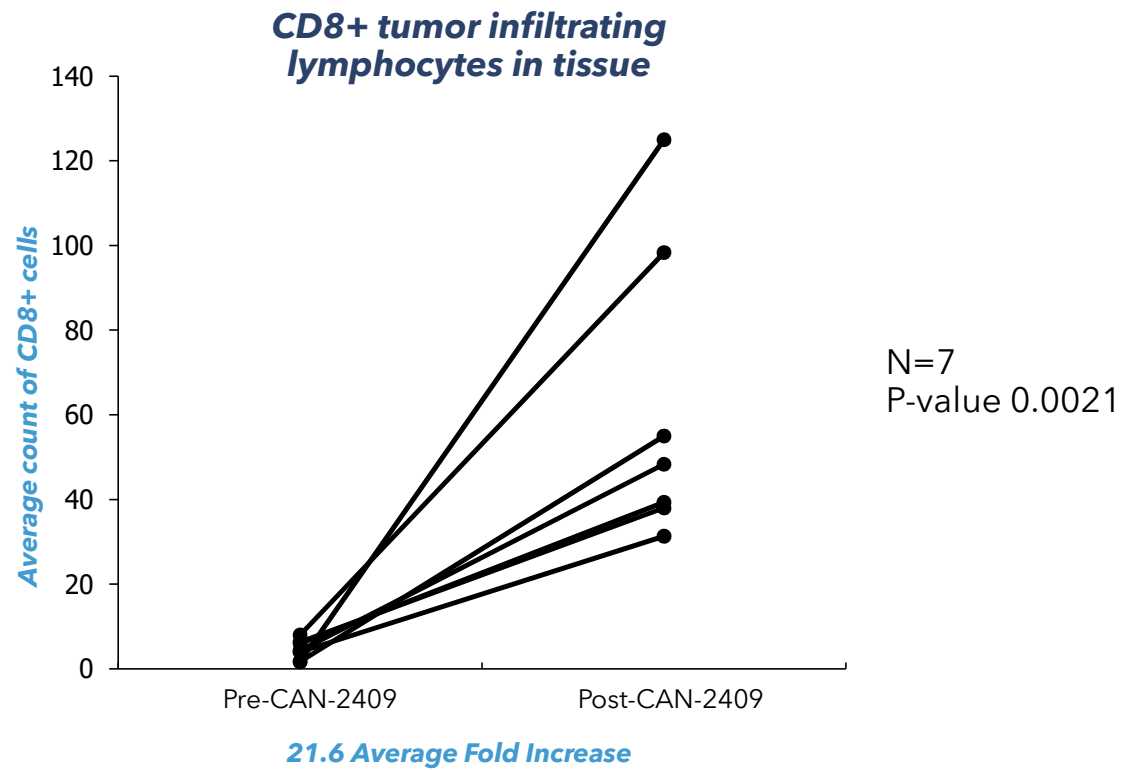
¹ Park W et al. JAMA 2021;326:851-862

² Versteijne E et al. J Clin Onc 2020; 38:1763-1773

³ Conroy T et al. NEJM 2011; 364:1817-1825

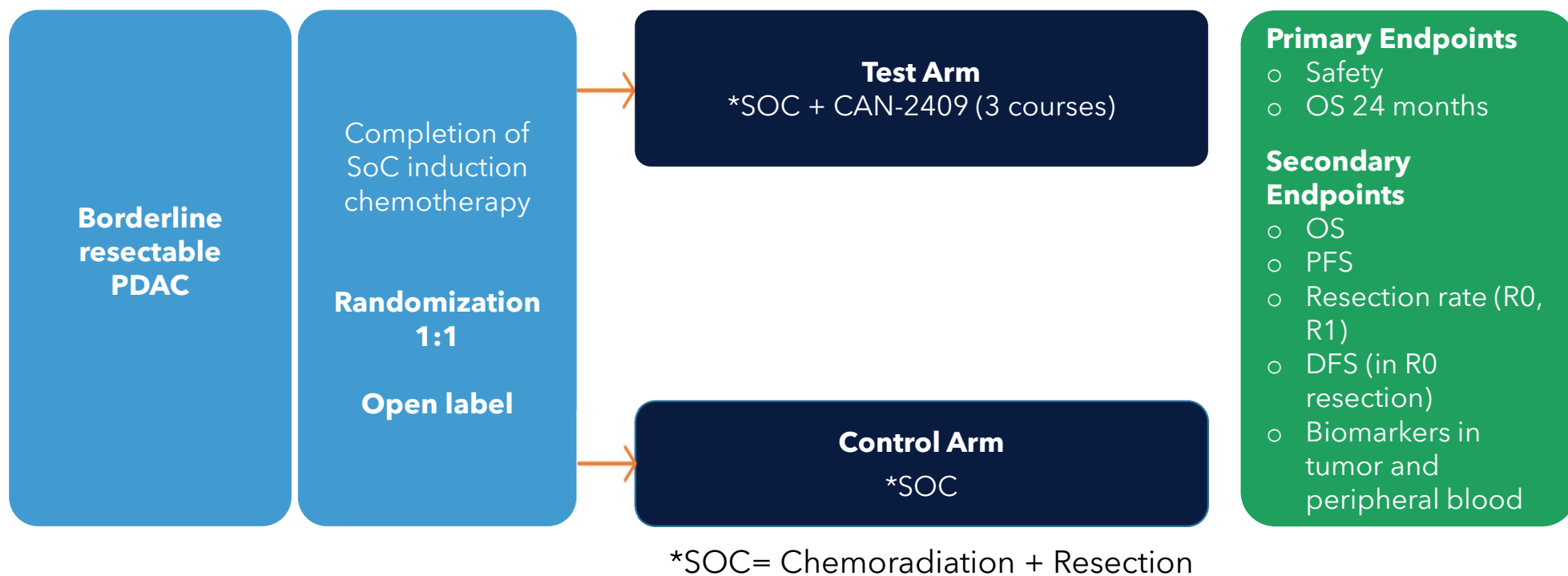
⁴ Source: EvaluatePharma, accessed May 2023

Completed phase 1 clinical trial of CAN-2409 in pancreatic ductal adenocarcinoma: Infiltration by CD8+ tumor infiltrating lymphocytes



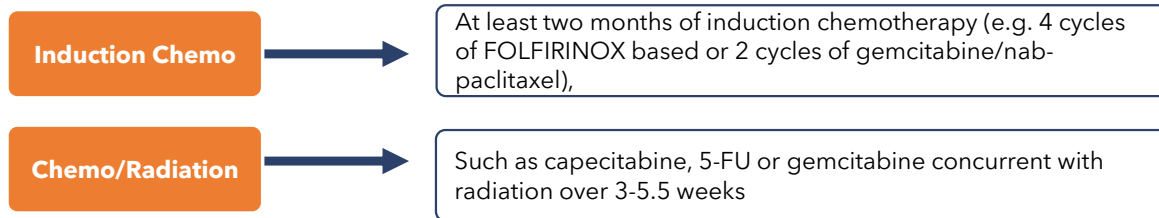
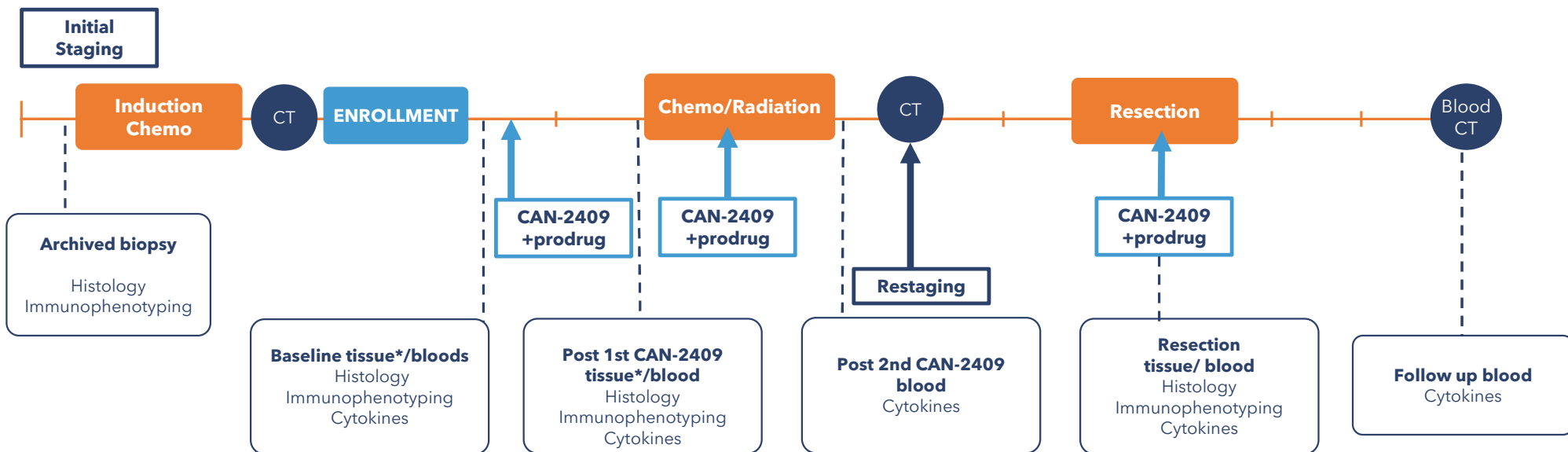
Randomized phase 2 clinical trial of CAN-2409 in borderline resectable pancreatic ductal adenocarcinoma (PDAC)

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



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

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

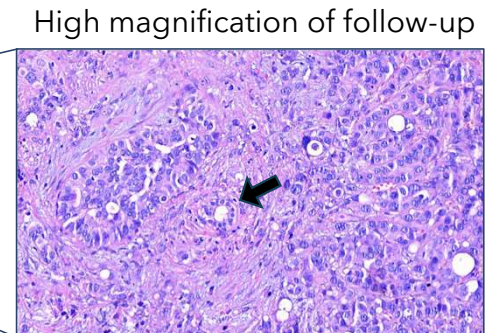
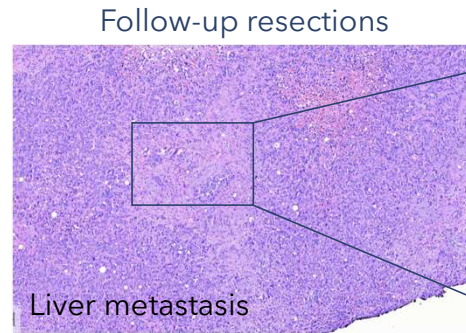
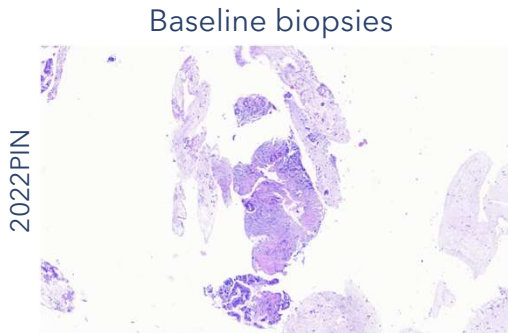


*** If feasible**

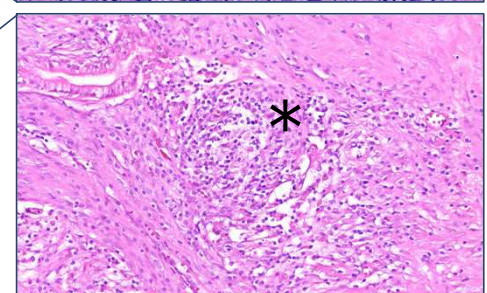
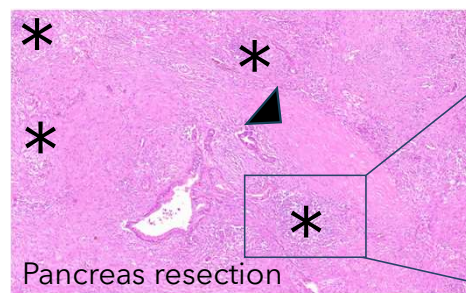
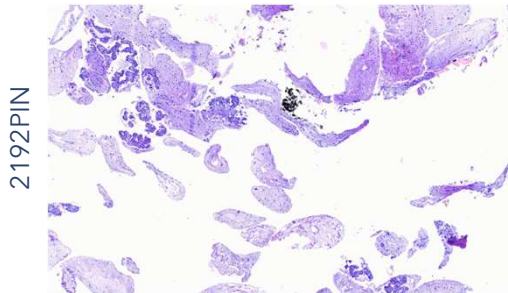
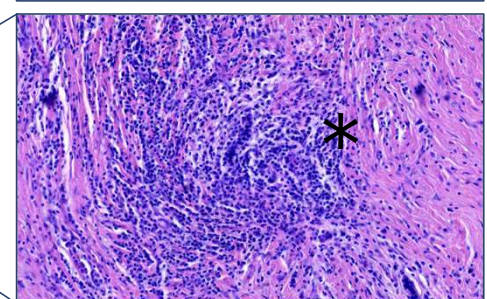
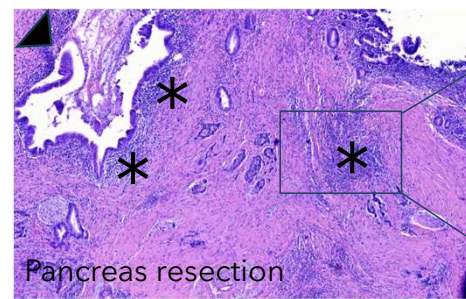
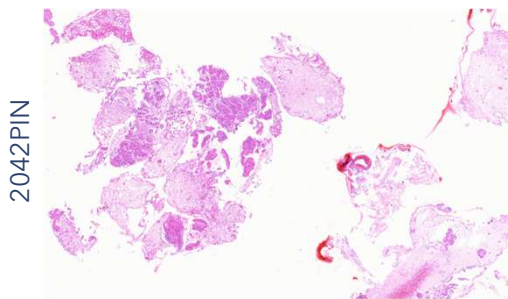
Prodrug = valacyclovir or IV acyclovir

CAN-2409 induces formation of dense lymphocyte aggregates, disruption of tumor structures, and necrosis in PDAC

Control



Test arm



Arrows: cancer cell. Arrowheads: disrupted tumor structures and tumor necrosis. Asterisk: immune cells

Overall survival in borderline resectable PDAC patients

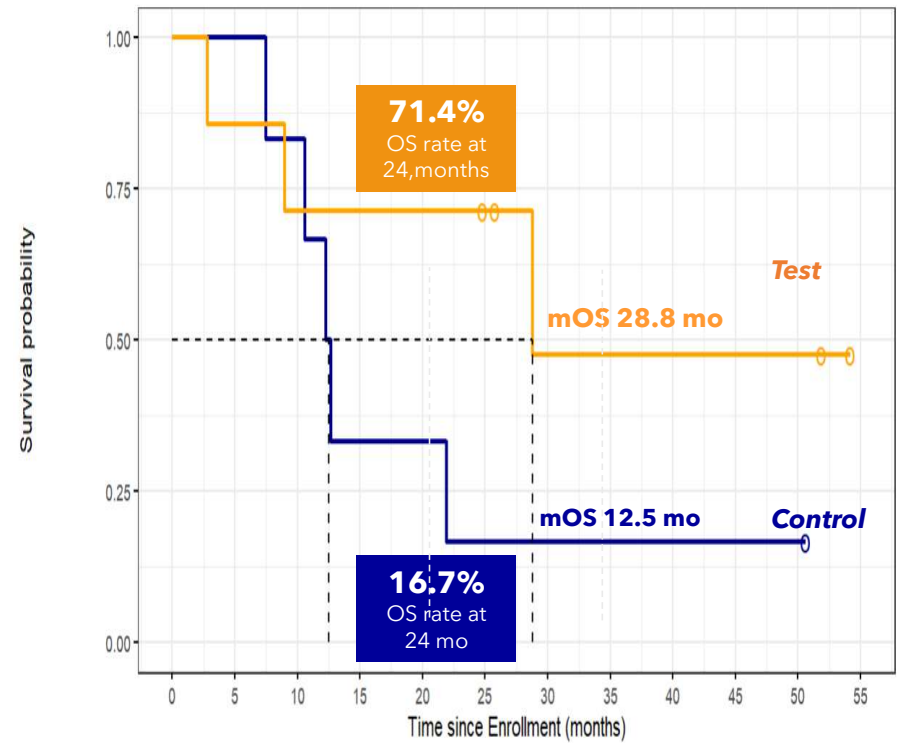
Data as of 3/29/2024

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*	3/28/2024	50.6+	54.8+	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	2/22/2024	54.2+	61.7+	A
2172PIN	T	Unresected	N/A*	1/14/2024	28.8	34.7	D
2082PLB	T	Resected	IA	2/26/2024	51.9+	57.0+	A
2182PLB	T	Resected	IB	3/04/2024	25.8+	32.3+	A
2192PIN	T	Resected	IA	3/20/2024	24.8+	30.3+	A

*Refer to slide with details on surgical status

pathologic tumor stage at resection

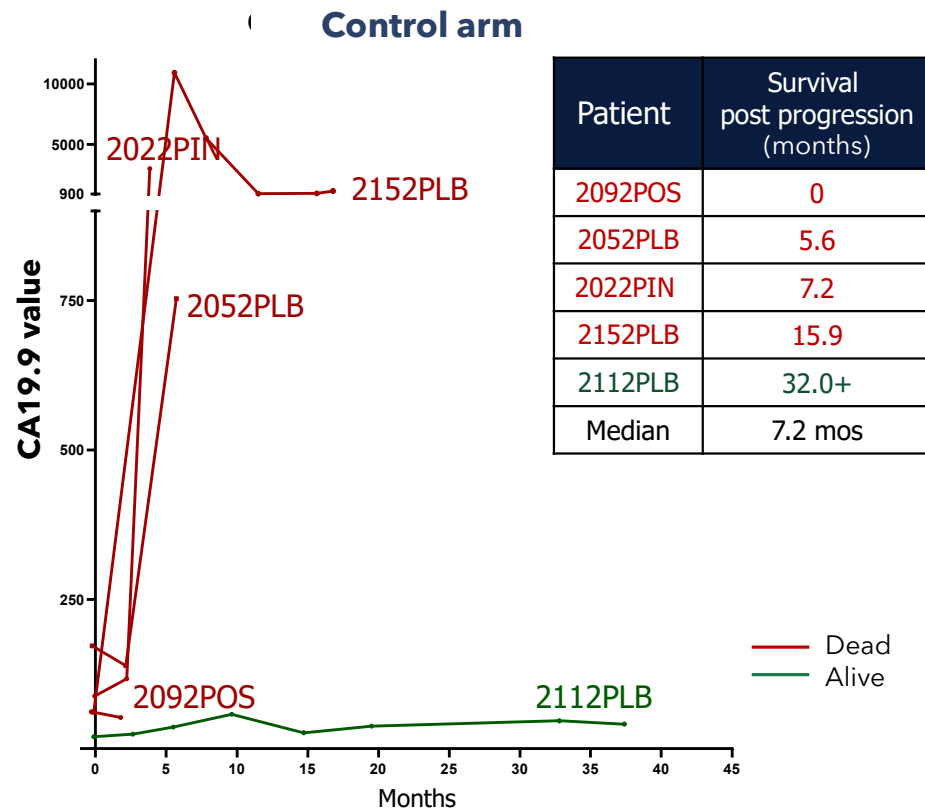
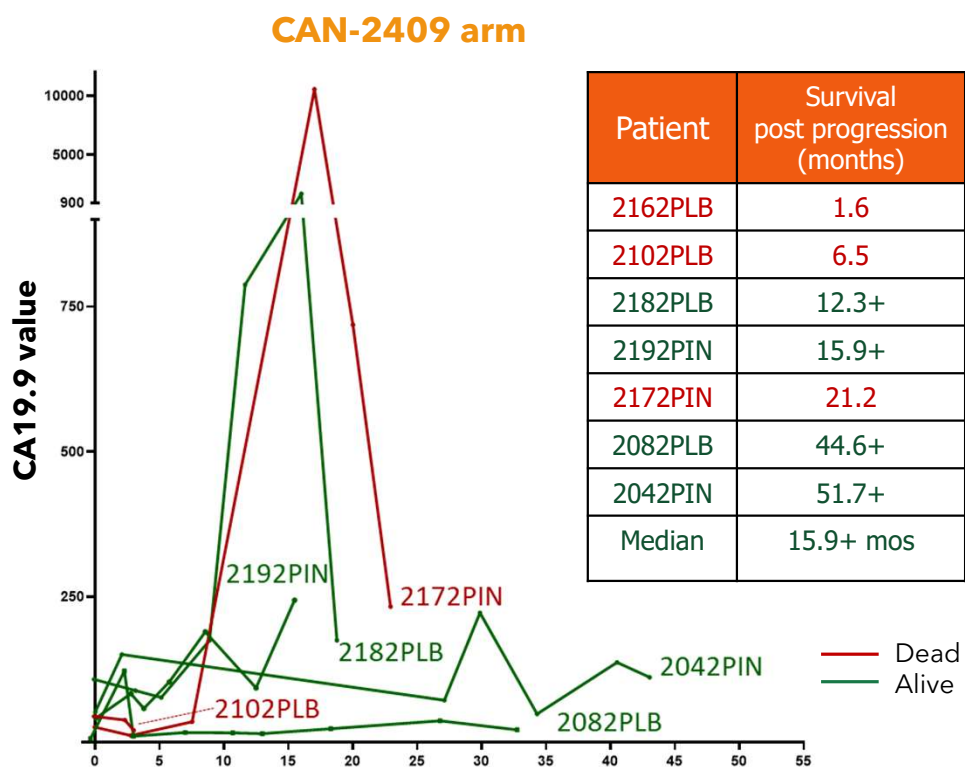
Time since enrollment



Censored = alive, still under follow-up

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

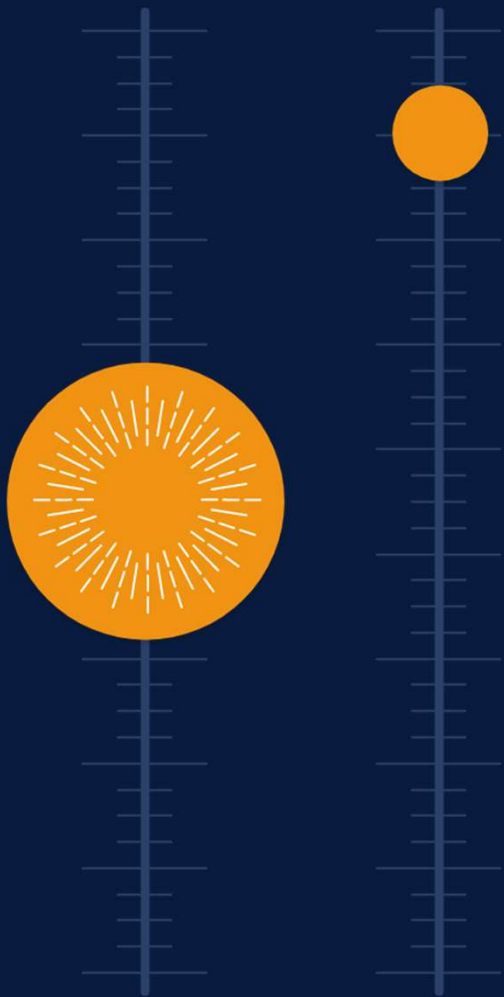
CA19-9 biomarker response associated with ongoing survival in CAN-2409 arm, but not in control arm, in patients with progressive disease



- CAN-2409 arm cases 2172, 2182 recurred, but CA19.9 (marker of tumor burden) responded to salvage chemo with ongoing survival
- Control arm cases 2022, 2152, 2052 recurred, but CA19.9 did not respond to salvage chemo and patients died

Encouraging safety data, clinical activity and immunological changes after CAN-2409 in pancreatic cancer

- Notable improvements in estimated median overall survival of 28.8 months after experimental treatment with CAN-2409 versus only 12.5 months in control group
- At 24 months, survival rate was 71.4% in CAN-2409 treated patients versus only 16.7% in the control group after chemoradiation. At 36 months, estimated survival was 47.6% in the CAN-2409 group versus 16.7% in the control group
- Multiple injections of CAN-2409 were generally well tolerated, with no dose-limiting toxicities and no cases of pancreatitis
- In patients with progressive disease, there was a CA19-9 and survival response to salvage chemotherapy in the CAN-2409 arm but not in control arm
- CAN-2409 activates the immune response in the pancreatic tumor and peripheral blood



CAN-3110



Oncolytic virus with tumor-specificity

CAN-3110: High-grade glioma opportunity

Prevalence of glioblastoma in the US¹



- 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 diagnosis²
- Median overall survival < 6-9 months in recurrent high-grade glioma³
- 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'

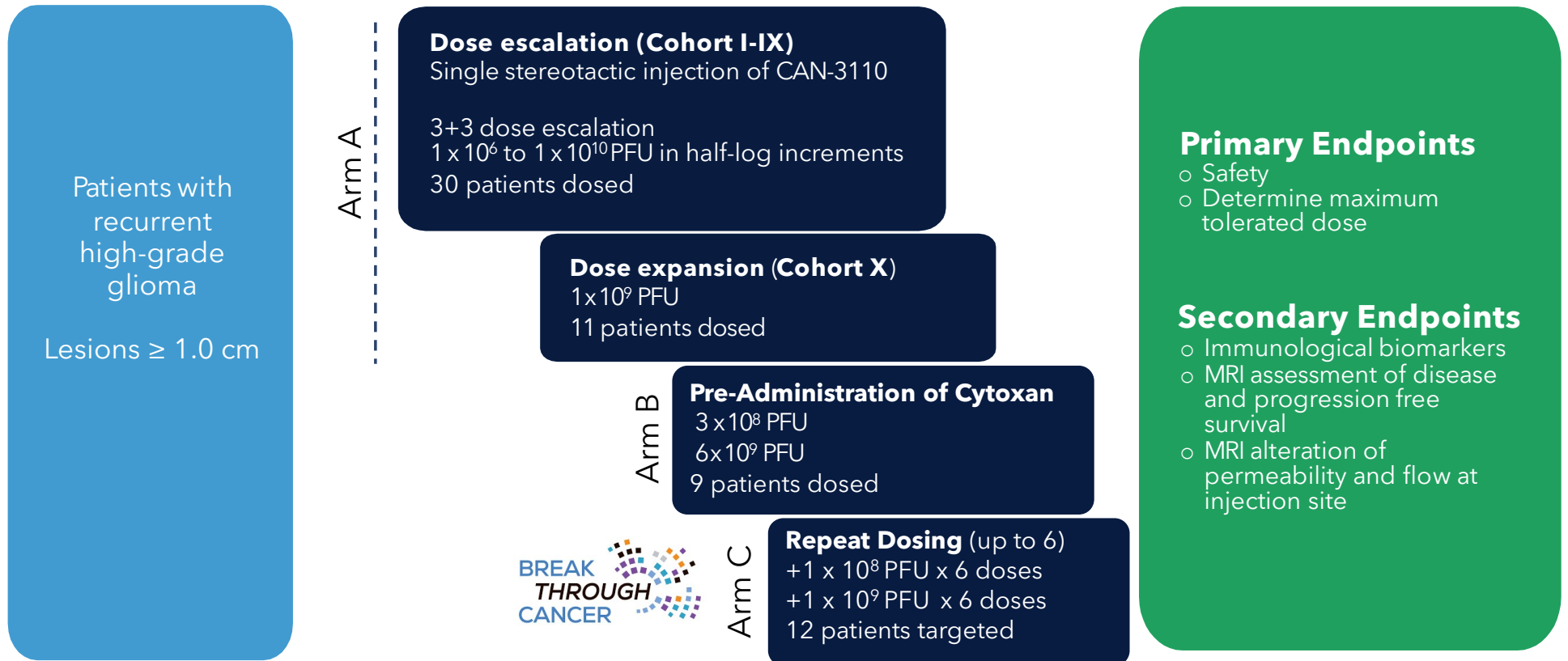
¹ Miller KD et al. *CA Cancer J Clin* 2021;71:381-406

² Stupp R et al. *Lancet Oncol.* 2009;10:459-466

³ vanLinde MC et al. *J Neuro Onc* 2017;135:183-192

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

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

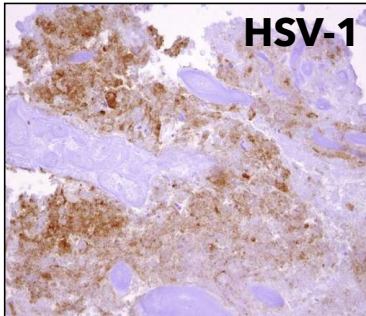


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CAN-3110 treatment in patients with recurrent high-grade glioma

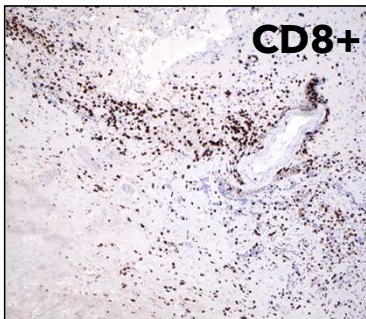
Persistent HSV antigen expression in injected tumors as well as uninjected tumors associated with CD8+ T cell infiltration after single CAN-3110 injection

injected lesion



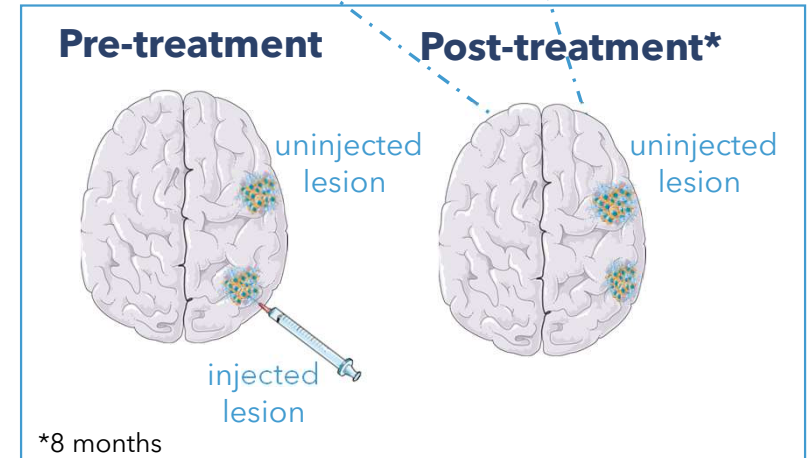
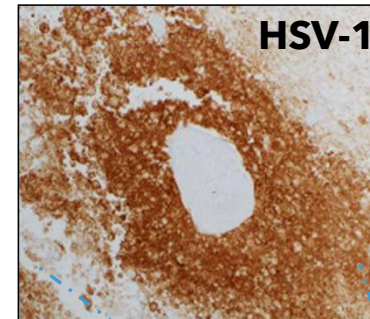
HSV1 antigen 6 weeks after injection of 1×10^6 pfu
 1.79×10^6 copies of viral DNA/mg
 2.97×10^5 copies of viral RNA transcript (ICP22)/mg

CD8+



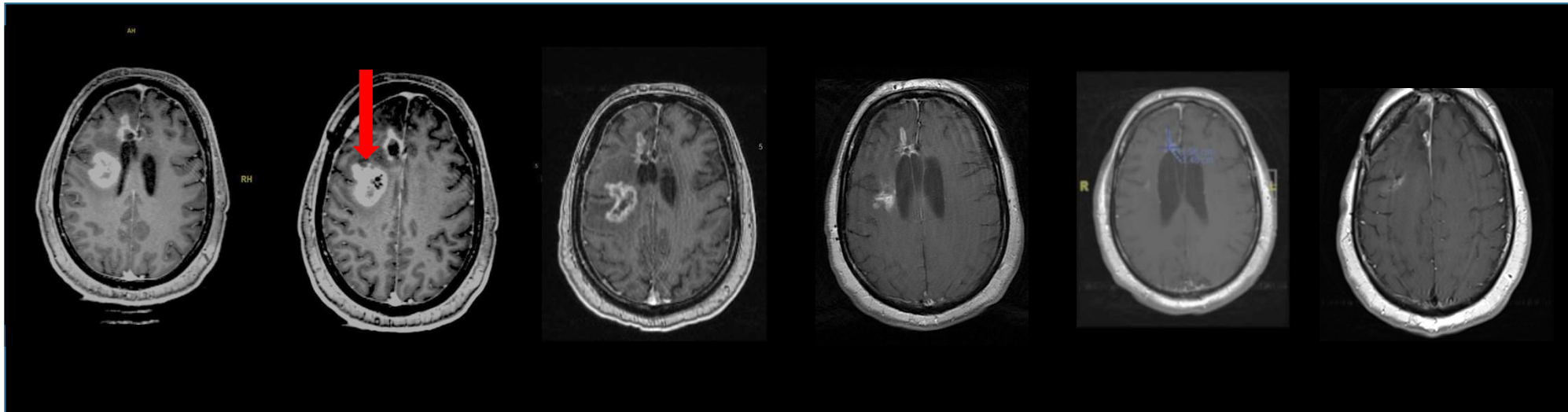
Infiltration by CD8+ cytotoxic T cells
(tumor infiltrating lymphocytes)

uninjected lesion



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

Clinical effect on injected tumor and uninjected tumor



Baseline

Day 0
Black hole within tumor
image is injection site
10⁶ PFU dose

Day 56
Reduction in contrast area
with no additional treatment

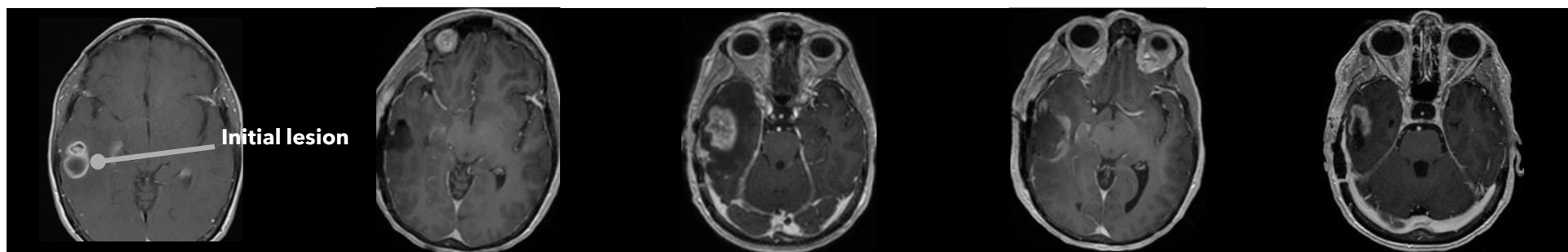
Day 111
Patient back to work

Day 168

Day 280

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

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



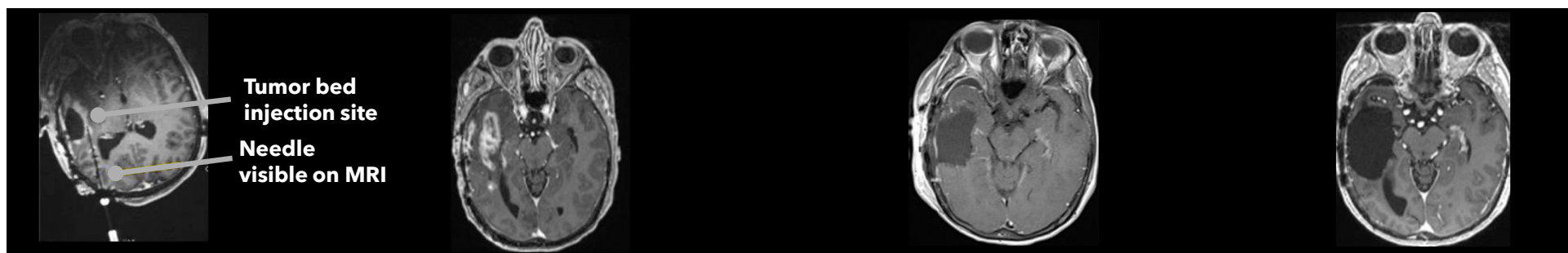
Day -262
Initial presentation

Day -259
Initial resection

Day -47
Tumor recurrence

Day -30
2nd subtotal resection

Day -14
Rapid progression



Day 0
CAN-3110 Injection

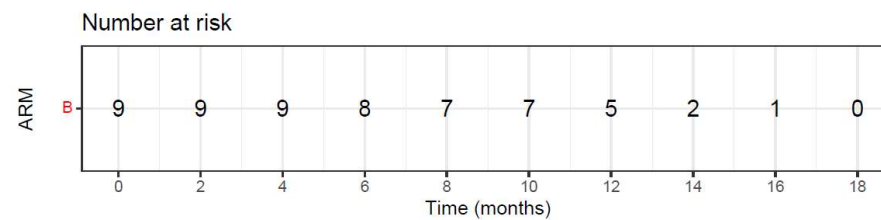
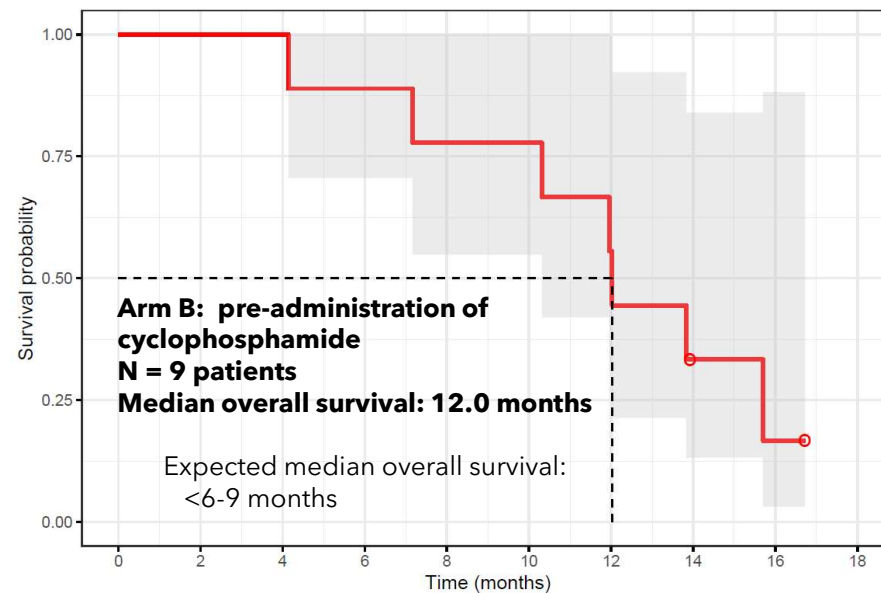
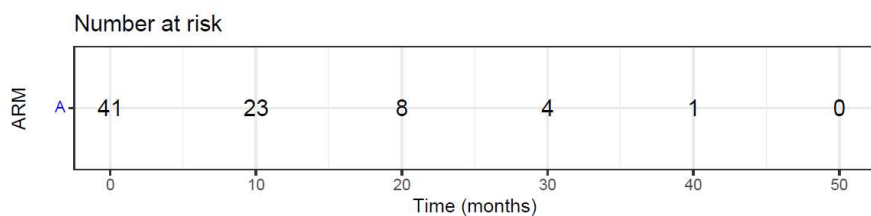
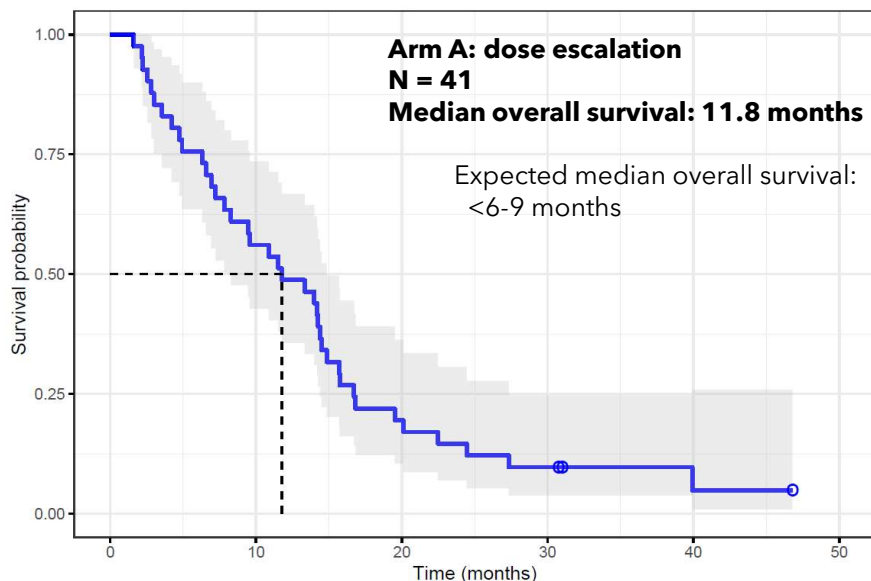
Day 91
Tumor recurrence with TIL

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.

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

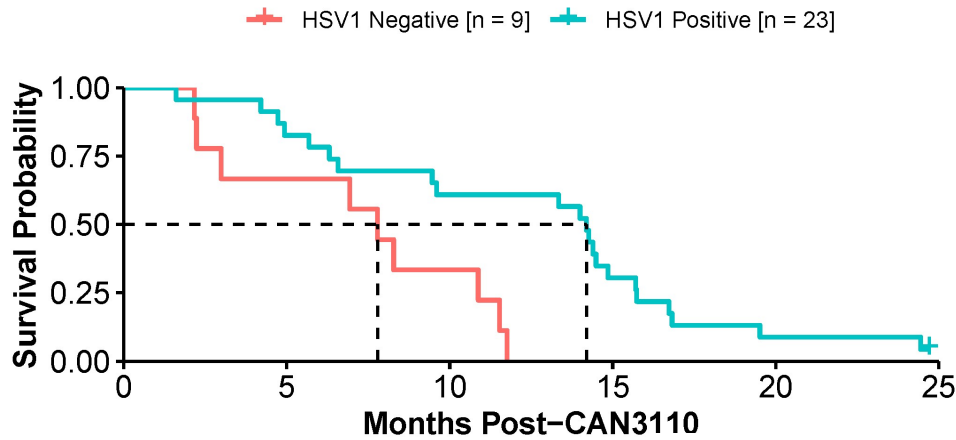


- 41 unique patients were dosed; one patient was treated twice, in cohort IX and X
- A total of 50 unique patients



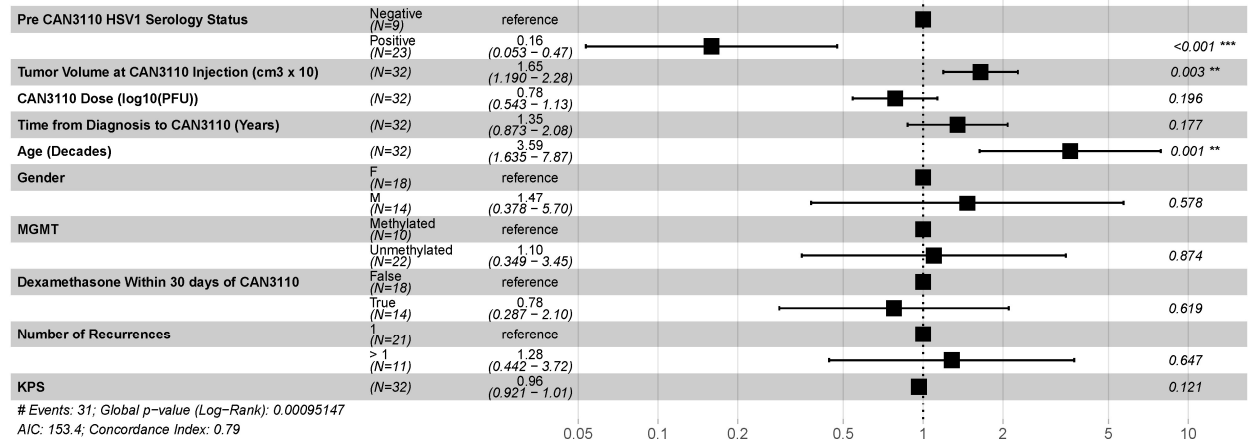
Note: As of cutoff date, 20 Apr 2023.

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

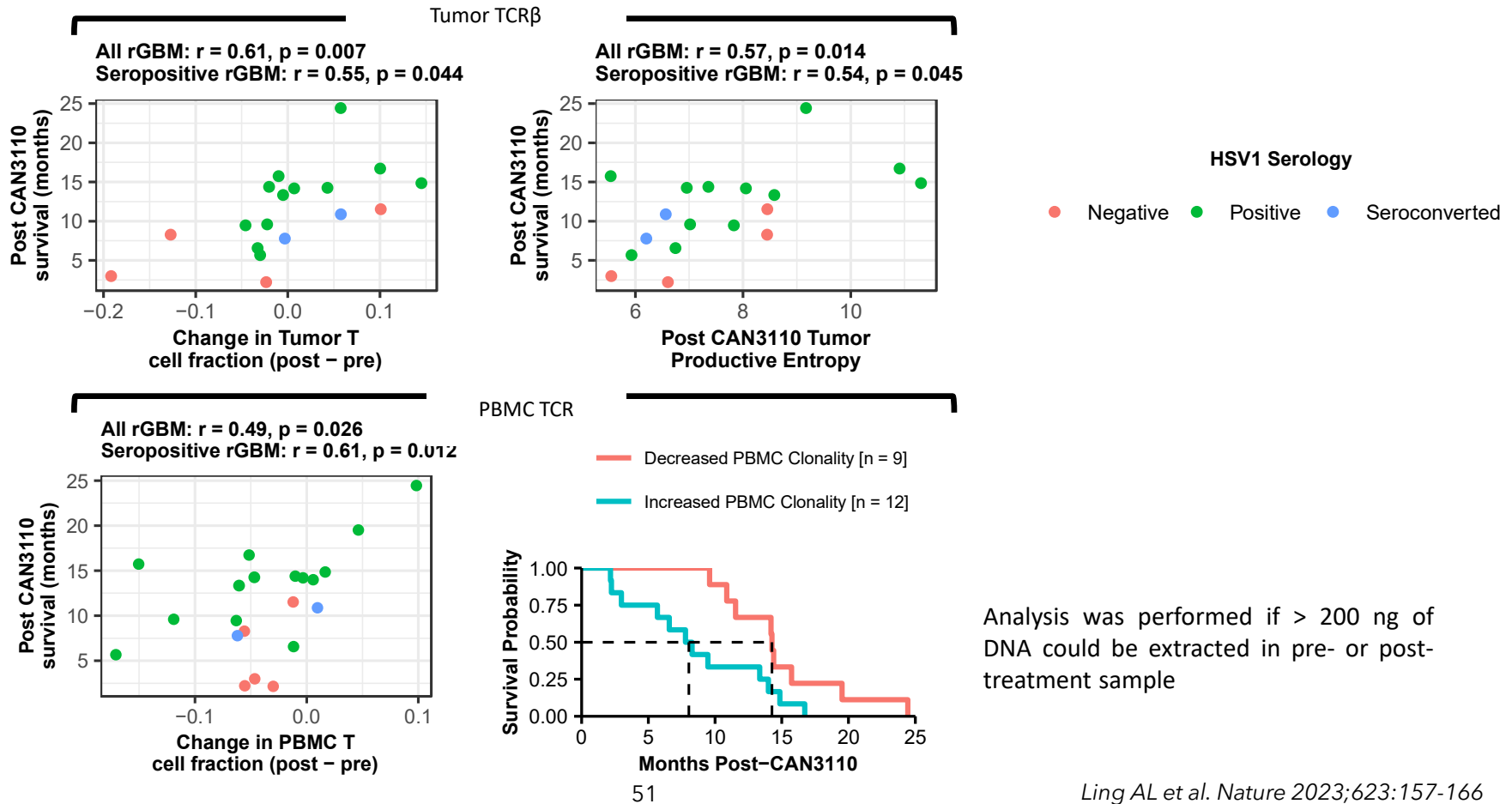


HSV2 serology status is not associated with survival

COxPH Hazard Ratios



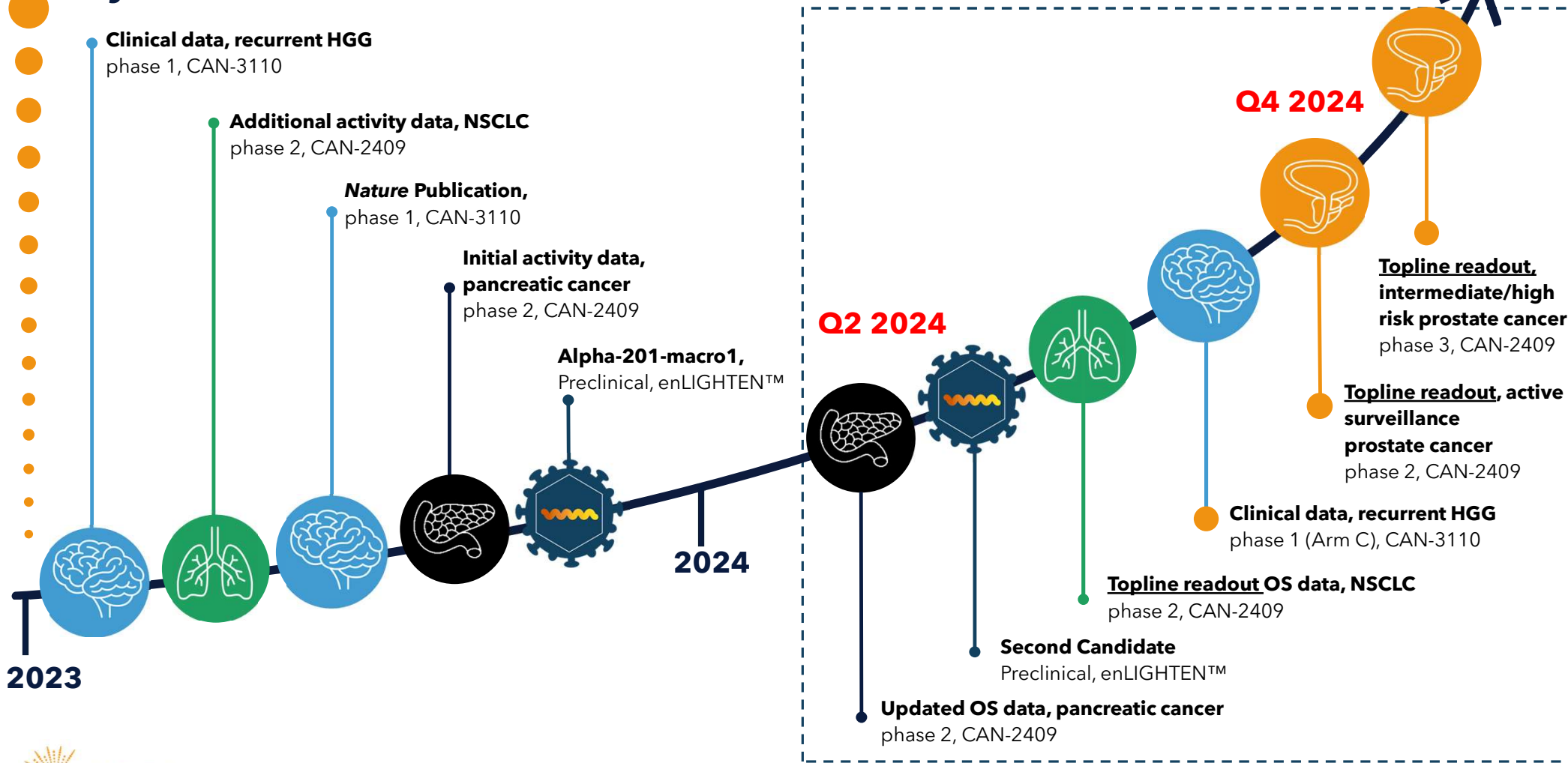
Changes in T cell fractions and TCR β diversity correlate with survival after CAN-3110 treatment



Encouraging safety data, clinical activity and immunological changes after CAN-3110 in recurrent high-grade glioma (glioblastoma)

- Monotherapy treatment with CAN-3110 in rHGG is well tolerated and associated with doubling of expected median overall survival
- Immunological changes in the tumor microenvironment are associated with improved survival and HSV1 seropositivity
- First six patients have been dosed in cohort C (fully funded by the Break Through Cancer foundation)
- Repeated injections of CAN-3110 (up to six) are safe and well tolerated
- Significant decrease in tumor cells and increased immune cell infiltration after CAN-3110 administration

Key achievements and future milestones



Candel at a glance



- CAN-2409: Off-the-shelf pan-solid tumor therapy, individualized anti-cancer immune response
 - Proof of concept in patients across multiple solid tumors
 - Fast Track Designation in NSCLC, pancreatic cancer, and prostate cancer
 - “Pipeline in a product” strategy advancing multiple programs in several large indications
 - Upcoming catalysts:
 - Topline phase 2b (Active Surveillance) prostate cancer clinical data (Q4 2024)
 - Topline phase 3 (Intermediate/High Risk) prostate cancer clinical data (Q4 2024)



- CAN-3110: Oncolytic HSV-1 designed for tumor-specific replication
 - Proof of concept in patients with recurrent high-grade glioma published in *Nature*
 - Fast Track Designation
 - Opportunity for creation of “pipeline in a product” by expansion into indications beyond brain cancers
 - Clinical and immunological biomarker data, evaluating repeat dosing regimen of CAN-3110 (H2 2024)



- Corporate Highlights
 - Very experienced Executive Team and strong scientific support from high-profile Research Advisory Board
 - Cash and cash equivalents of \$25.7 million as of March 31, 2024; expected runway into Q4 2024
 - IP protection: CAN-2409 (2034, method of use); CAN-3110 (2036, composition of matter); 12 years data exclusivity
 - Low-cost manufacturing