

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



Corporate Presentation | August 2022

NASDAQ: CADL

Forward Looking Statements

This Presentation contains forward-looking statements and information. 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.

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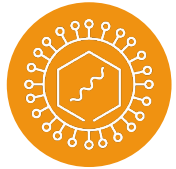
Candel overview: Oncolytic viral immunotherapies

- Two key investigational medicines



- CAN-2409

- Engineered, replication-defective adenoviral gene construct encoding HSV-thymidine kinase
- Ongoing clinical trials in NSCLC, high-grade glioma (HGG), pancreatic cancer, and prostate cancer
- Pipeline in a product
- Upcoming catalysts (Q4 2022): NSCLC and 1st line treatment of HGG



- CAN-3110

- Engineered, replication-competent herpes simplex virus with tumor-specificity
- Opportunity for expansion of indications outside the brain
- Upcoming catalyst (Q4 2022): Phase 1b clinical trial data in recurrent HGG

- enLIGHTEN™ Discovery Platform based on HSV technology

- Strong scientific support from external experts, including high-profile Research Advisory Board
- Significant unmet need and commercial opportunity for each selected indication
- IPO in July 2021 provided net proceeds of \$71.3M plus \$20.0M of long-term debt in Feb 2022
- Cash of \$94.3M as of March 31, 2022 – funds currently planned operations into Q1 2024

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



Paul-Peter Tak, M.D., Ph.D., FMedSci
President & Chief Executive Officer



Nathan Caffo
Chief Business Officer



Christopher Matheny, Pharm.D., Ph.D.
Vice President, Development Leader



Seshu Tyagarajan, Ph.D., RAC
Chief Technical and Development Officer



Francesca Barone, M.D., Ph.D.
Chief Scientific Officer



John Canepa
Chief Financial Officer



Susan Stewart, J.D.
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*



Roy Herbst, M.D., Ph.D.

*Chief of Medical Oncology
Yale Cancer Center*



Edward Benz, M.D.

*President and CEO Emeritus
Dana-Farber Cancer Institute*



Philip Kantoff, M.D.

*Former Chair, Department of Medicine
Memorial Sloan Kettering Cancer Center*



Henry Brem, M.D.

*Director, Department of Neurosurgery
Professor of Neurosurgery
Johns Hopkins University*

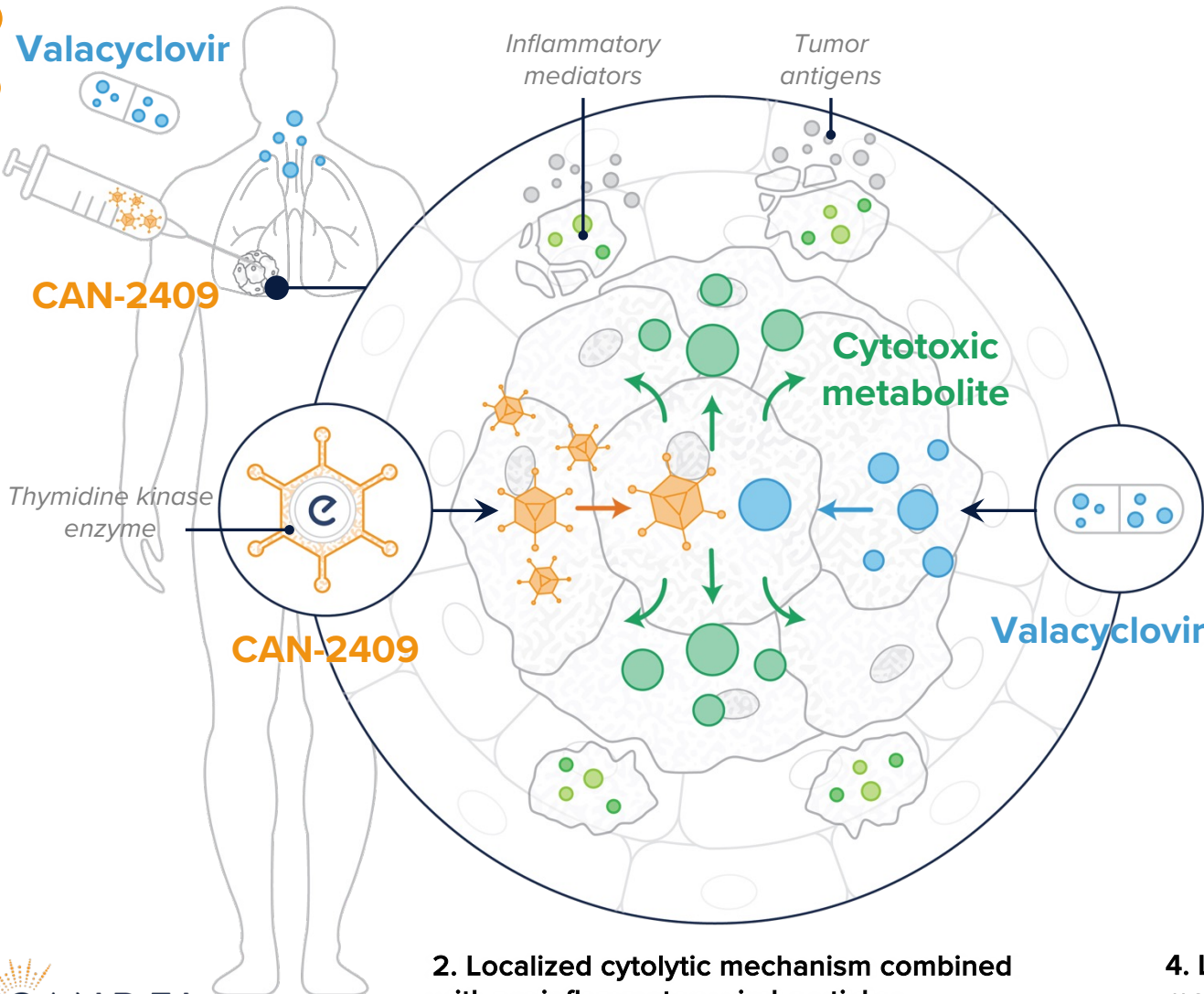


Padmanee Sharma, M.D., Ph.D.

*Professor of Genitourinary Medical Oncology and
Immunology
MD Anderson Cancer Center*

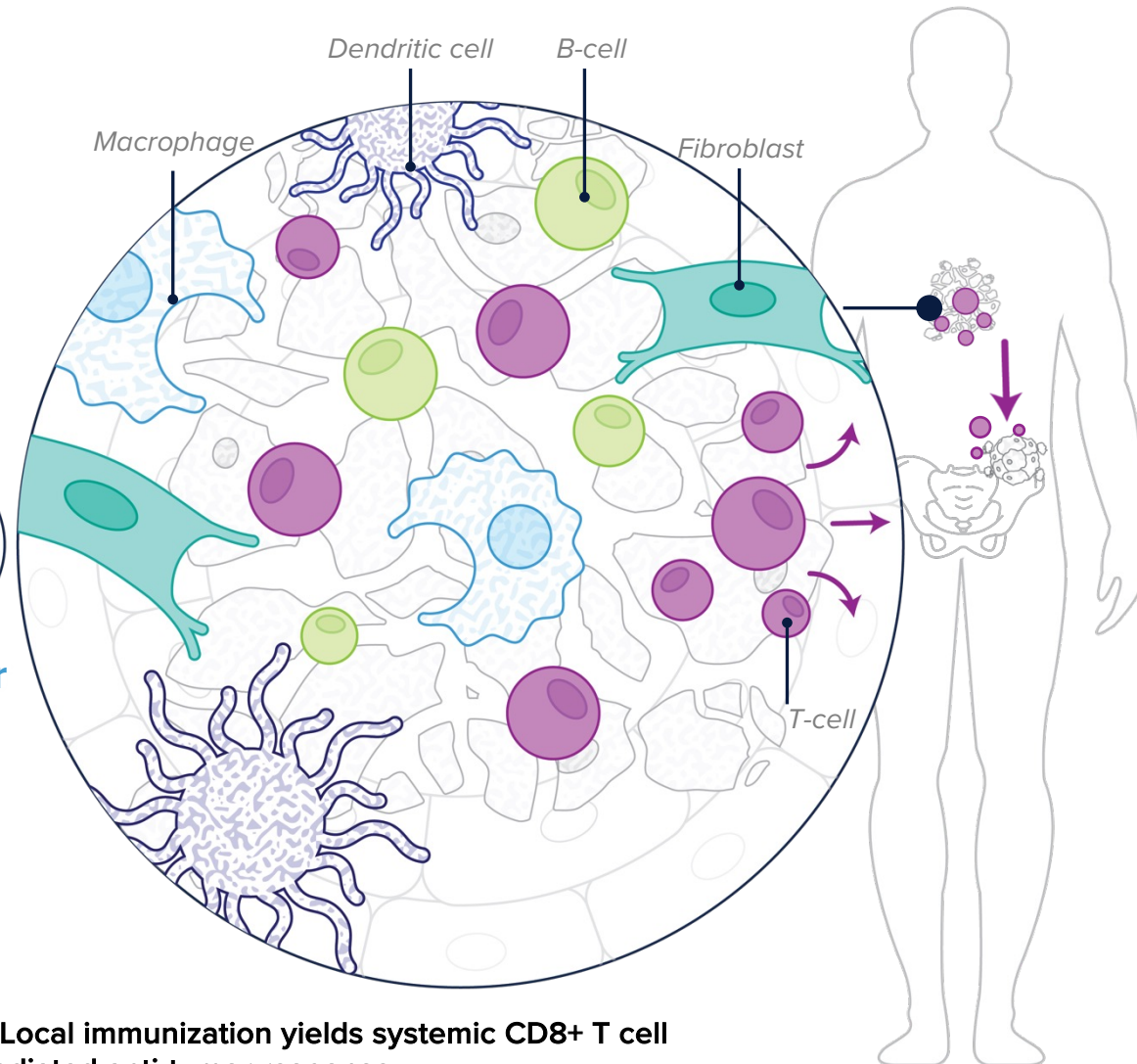
CAN-2409: Mechanism of action

1. CAN-2409 locally administered and oral prodrug



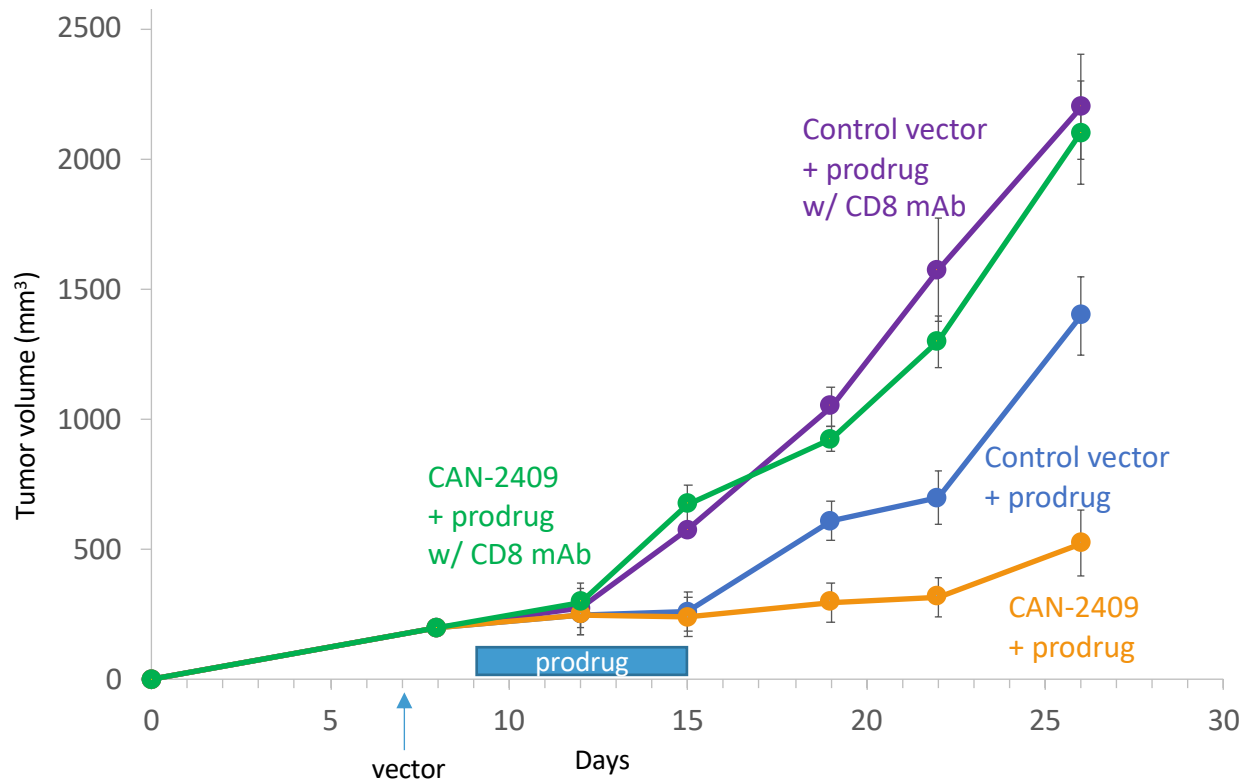
2. Localized cytolytic mechanism combined with proinflammatory viral particles

3. CAN-2409 induces CD8+ cytotoxic T cells



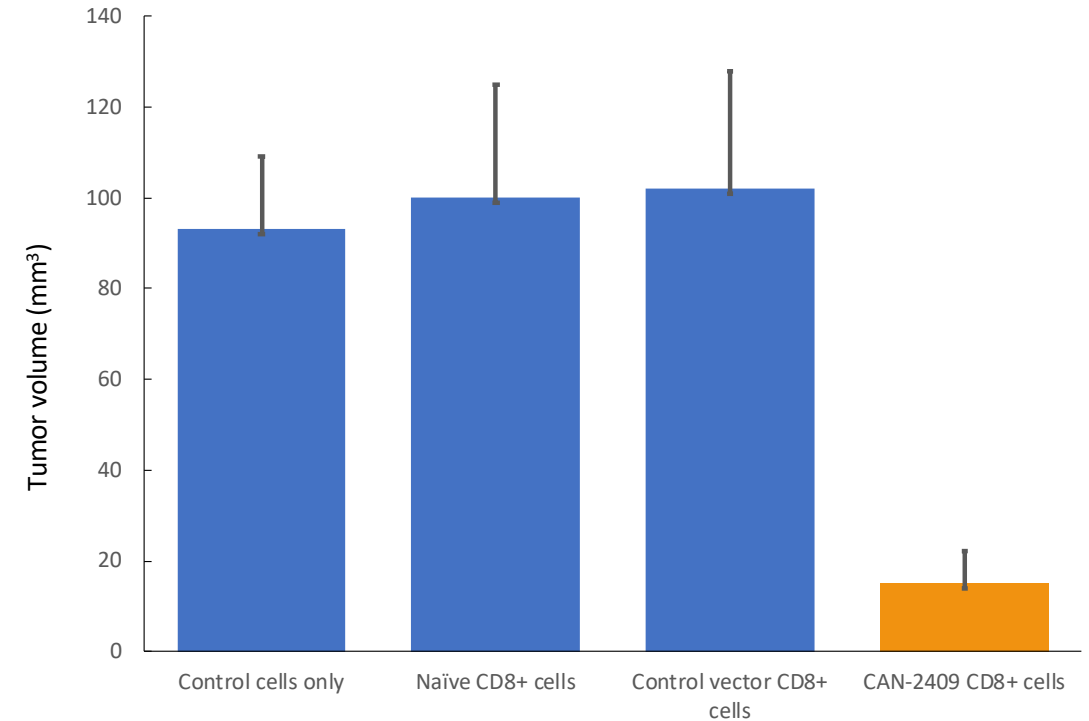
4. Local immunization yields systemic CD8+ T cell mediated anti-tumor response

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)



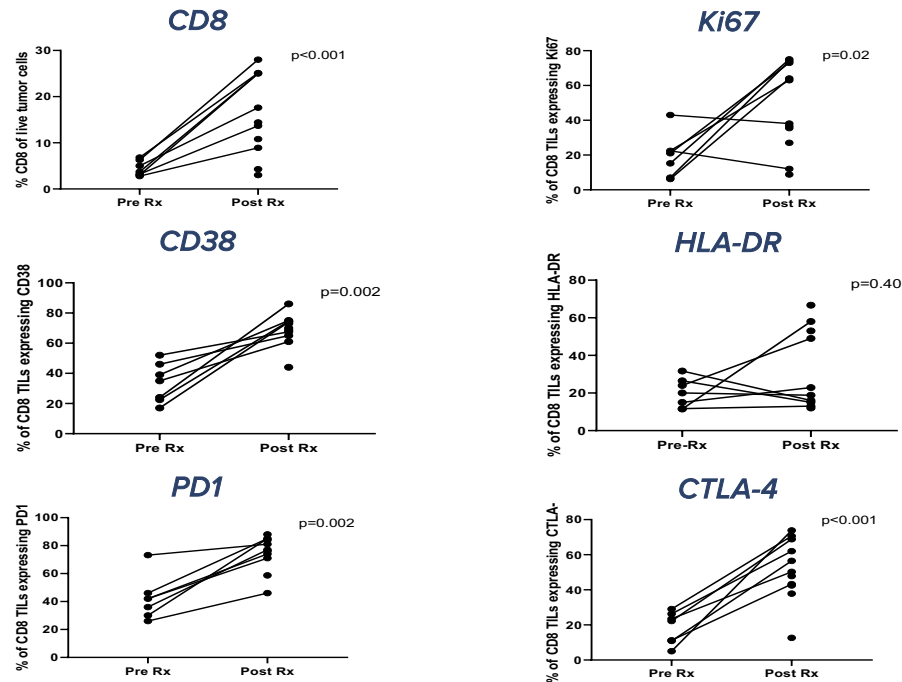
CD8+ cells from 'cured' mice protect naïve mice from tumor challenge

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

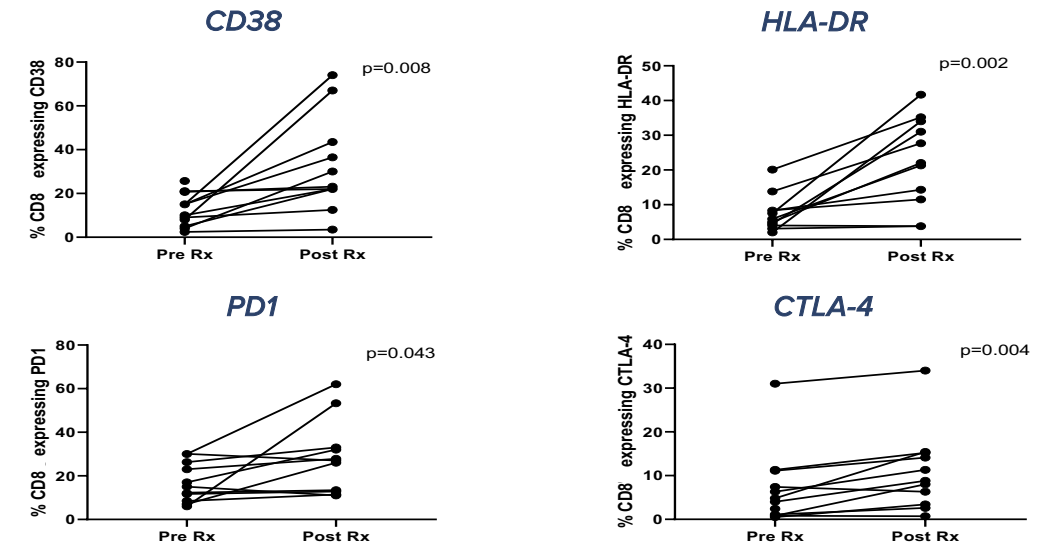
CAN-2409 treatment stimulates local and systemic CD8+ T-cell response in patients with cancer

Non-small cell lung cancer Ph 1 proof of mechanism clinical trial (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

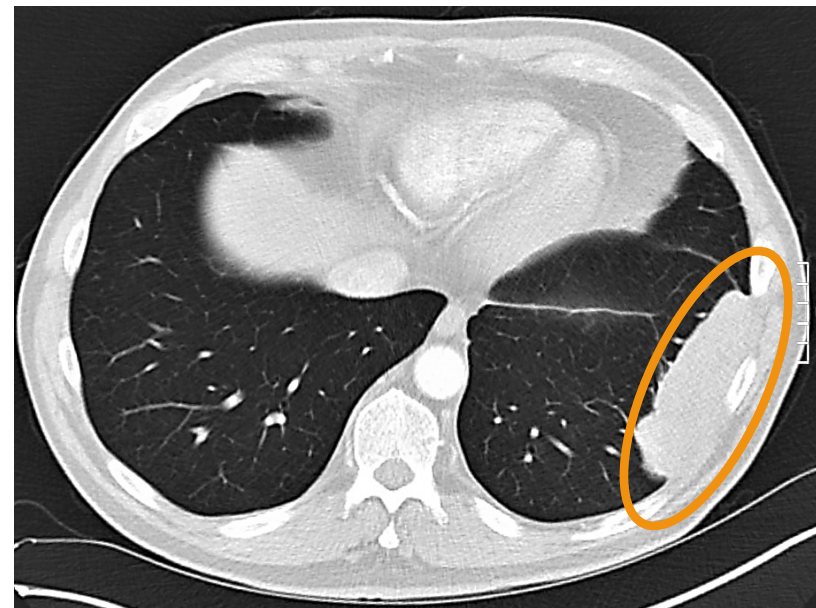
70 yr old male with a 14.8 cm stage IIIA sarcomatoid carcinoma



Day 0

Tumor Dimensions: 148 x 40 x 82 mm

1x10¹² vp dose

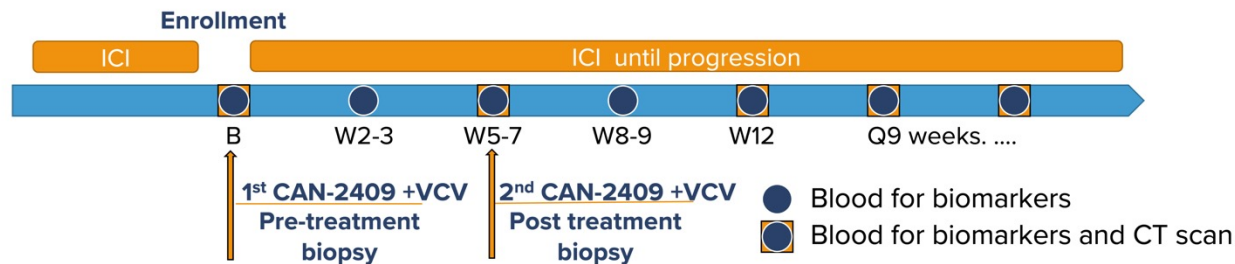
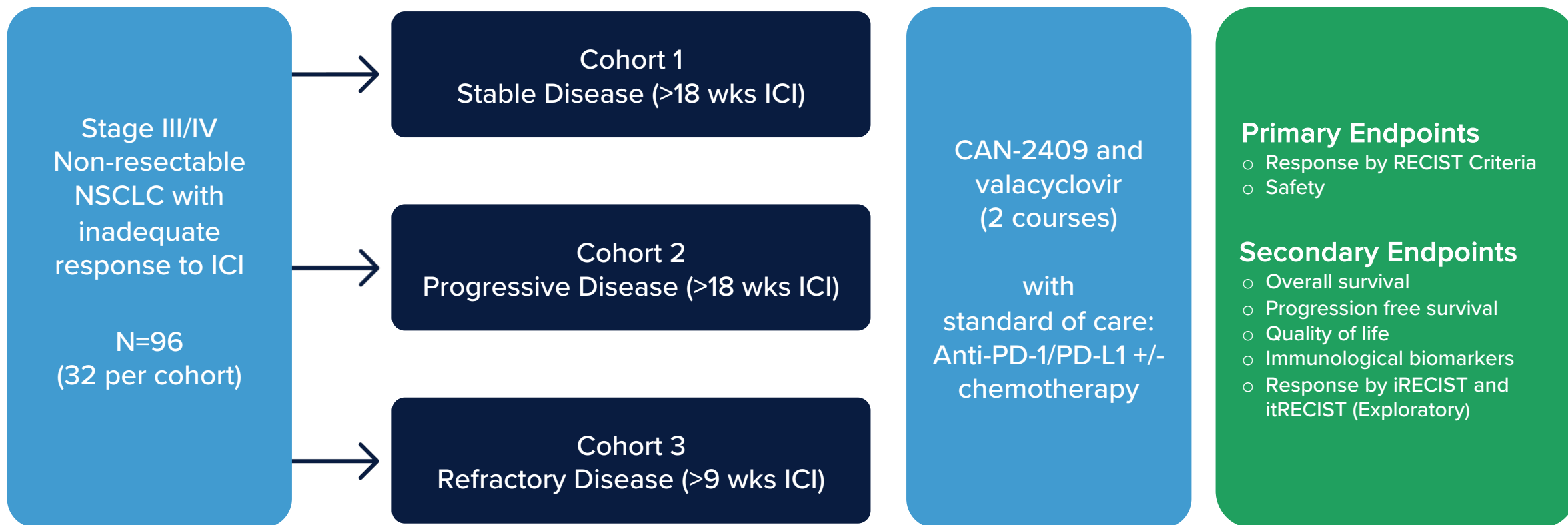


Day 22

Tumor Dimensions: 100 x 34 x 75 mm

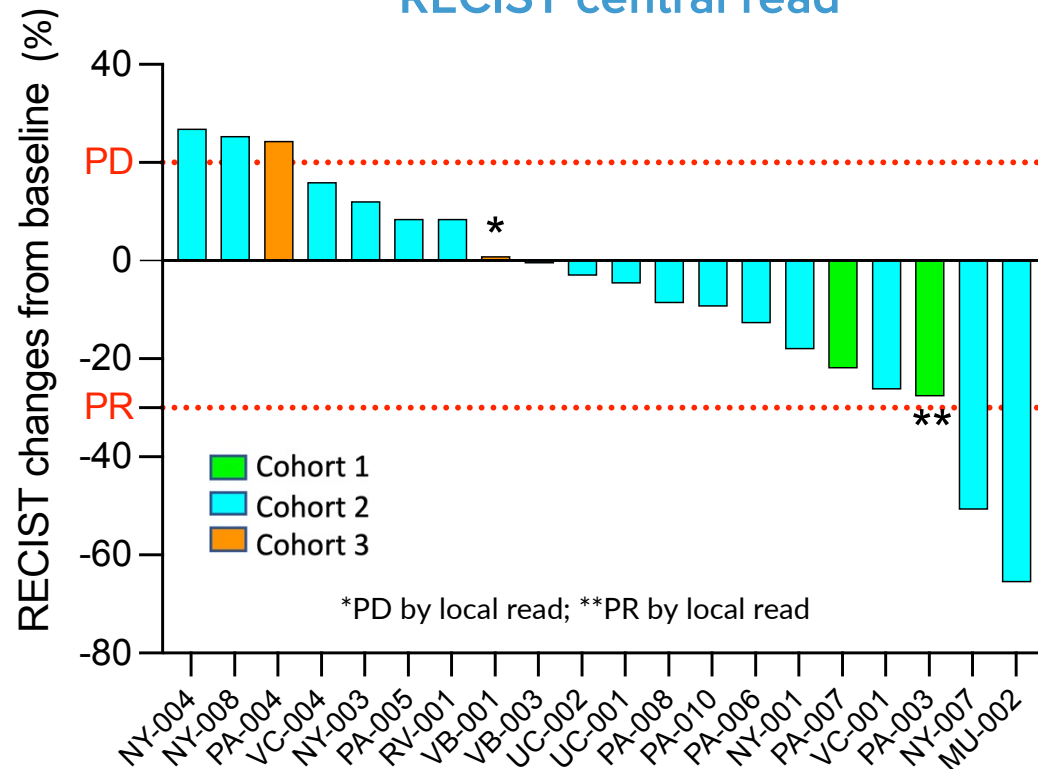
Nearly 50% decrease in tumor volume* in 3 weeks

Ongoing phase 2 clinical trial of CAN-2409 in combination with ICI in stage III/IV NSCLC



Clinical activity in first evaluable NSCLC patients after CAN-2409 treatment

Best responses
RECIST central read



Efficacy measures

Cohort	Completed 12-week treatment	PR	SD	PD	DCR	DoR for PR (w)	DoR for SD (w)
1	2	1**	1	0	50%	24.1+	26.9
2	16	2	12	2	87.5%	26.7-37.9+	5.4+ - 50.4+
3	2	0	0	2*	0%	n/a	n/a

PR= partial response; SD= stable disease; PD= progressive disease; DCR = disease control rate

DoR PR= weeks from PR to progression

DoR SD=weeks from SD to progression

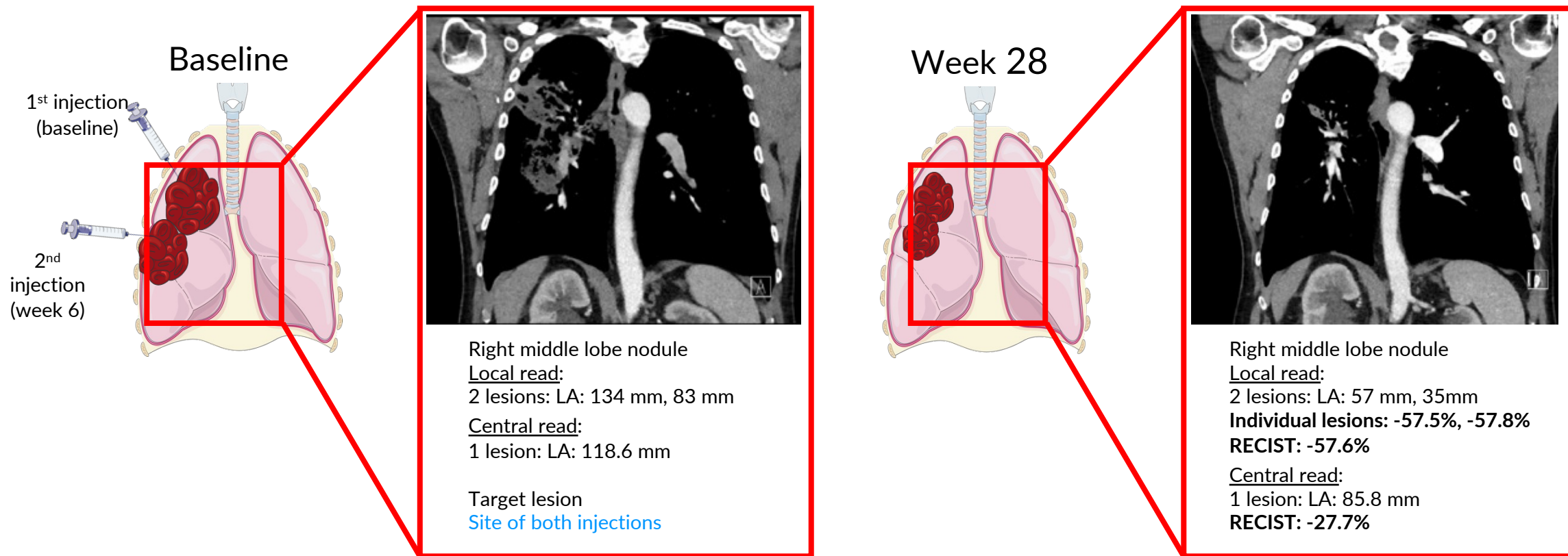
+ongoing response

*PD by local read; **PR by local read

Patients were considered evaluable if they completed both courses of CAN-2409 followed by valacyclovir and had > 12 weeks follow up

C Aggarwal et al. Abstract #9037 ASCO June 2022

Response in patient with previous stable disease >15mos



Legend

RECIST target lesions (red)

*Schematics to show general lesion injection orientation; not to scale
LA = long axis*

PA-003 (Cohort 1)

73M, Stage III Non-SQ, PD-L1<1%

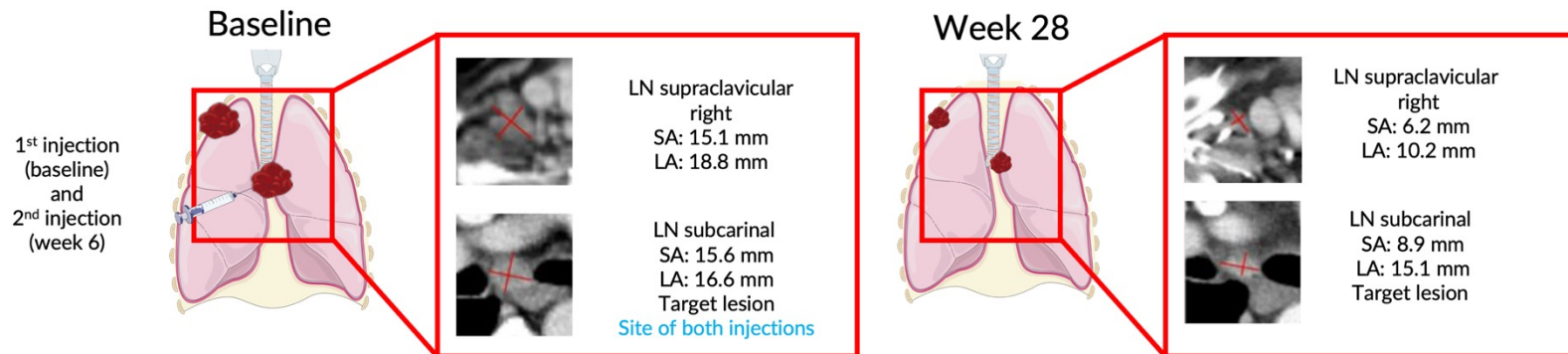
Diagnosed Jan'20, Started pembro + carbo + pemetrexed Feb'20, pembro + pemetrexed cont. from Jun'20 through trial

*PR by local read

Evidence of abscopal effect in NSCLC

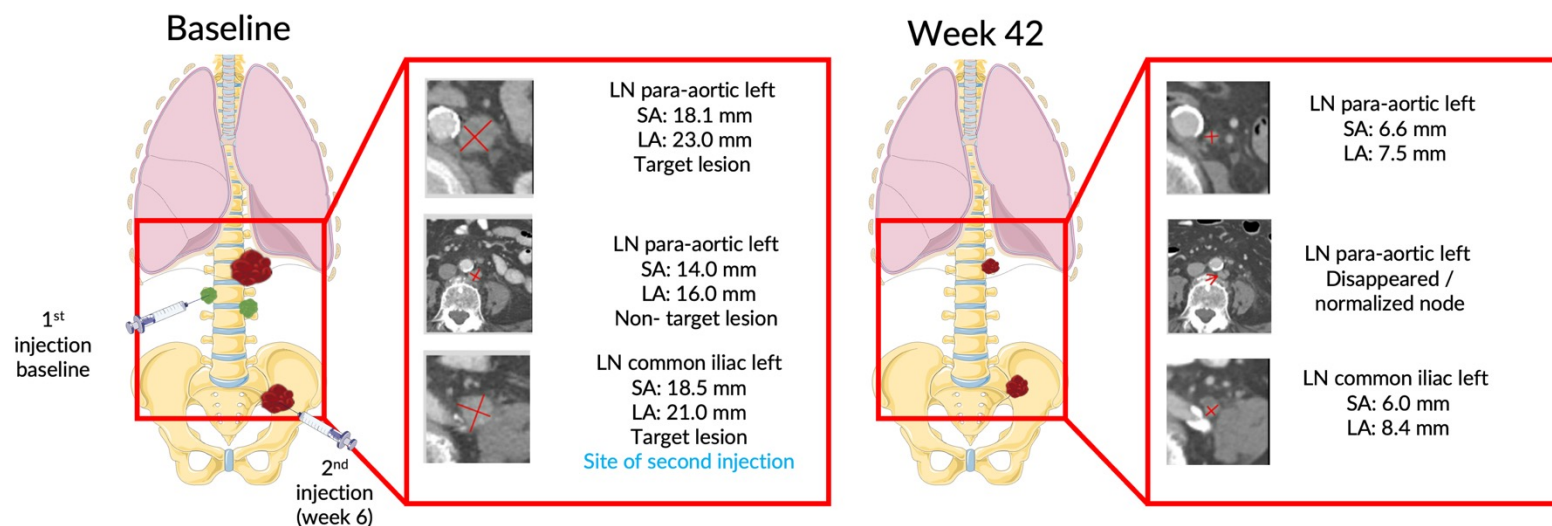
NY-007: Patient with partial response and evidence of abscopal effect

NY-007 (Cohort 2)
74M, Stage IV Non-SQ
PD-L1 <1%
Diagnosed Feb'19
cisplatin/etoposide Feb'19 to Jul'19,
nivolumab monotherapy from Sep'19
thru trial
PR by local and central read



MU-002: Patient with partial response and evidence of abscopal effect

MU-002 (Cohort 2)
69F, Stage III 2013, Stage IV 2019
Non-SQ
PD-L1 unknown
Started pembro monotherapy Jan'20
thru trial
PR by local and central read



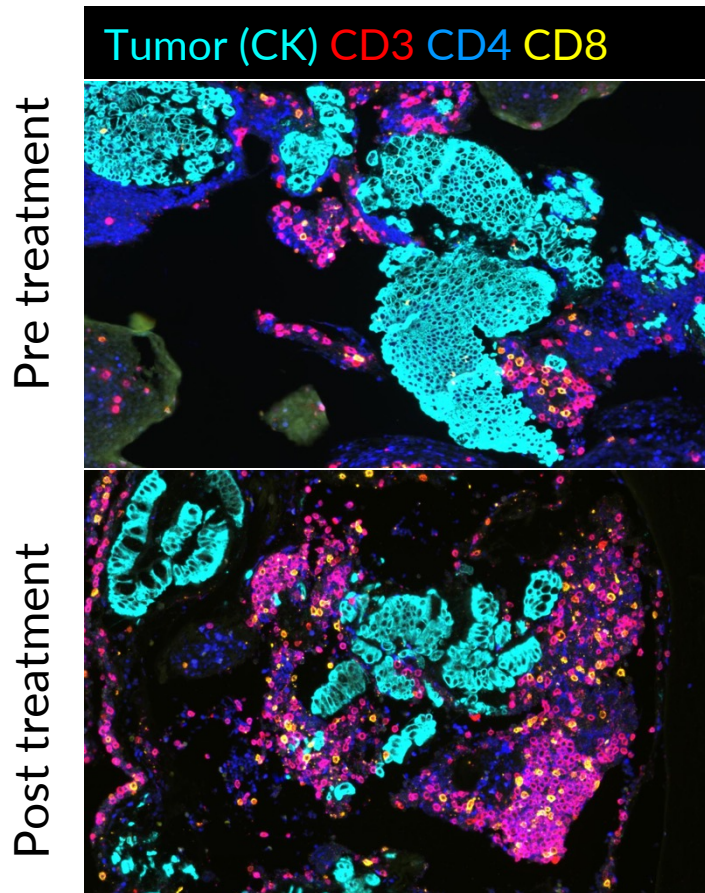
Legend

RECIST target lesions (red)

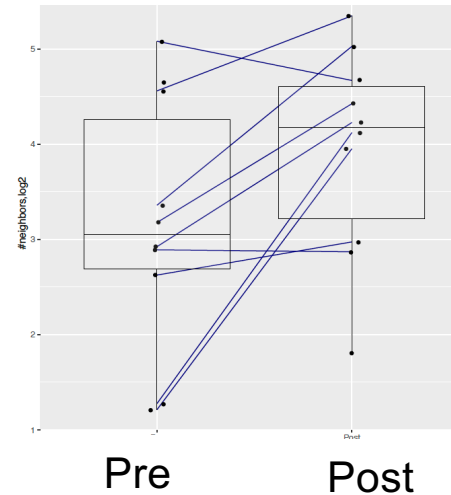
RECIST Non-target lesions (green)

Schematics to show general lesion injection orientation; not to scale
LN = lymph node; LA = long axis; SA = short axis

CAN-2409 increases local and systemic frequency of cytotoxic T cells after CAN-2409 treatment in NSCLC

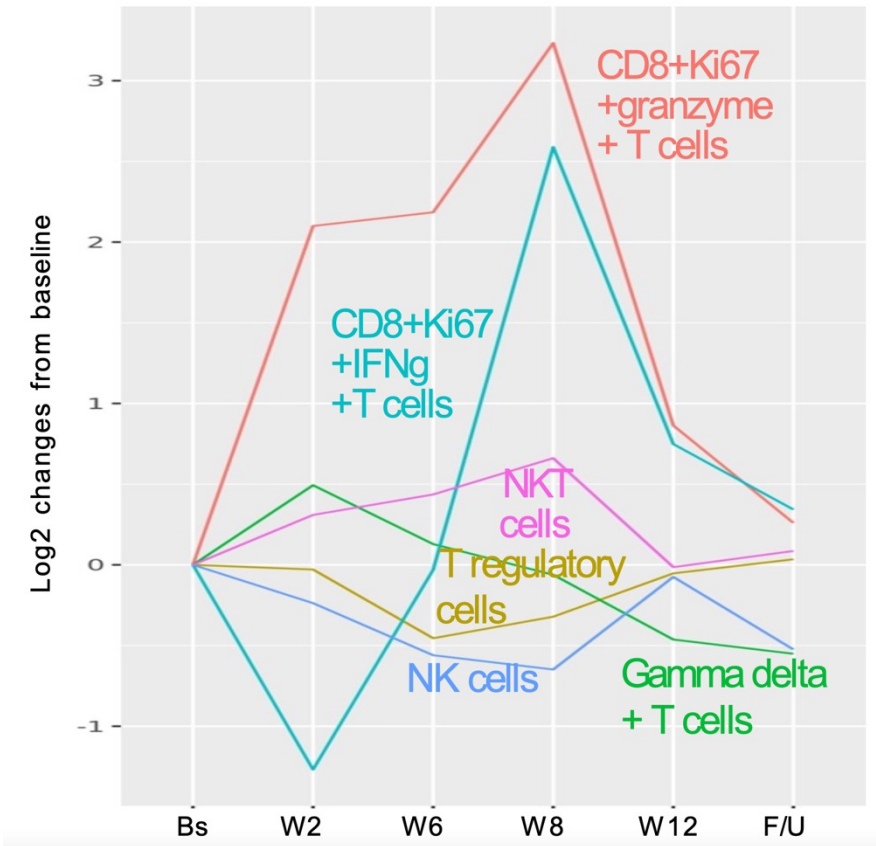


Proximity analysis CD8+ T cells in tissue



Frequency of T cells in 100µm radius distance from cancer cells

Frequency of cytotoxic cells subpopulations in peripheral blood

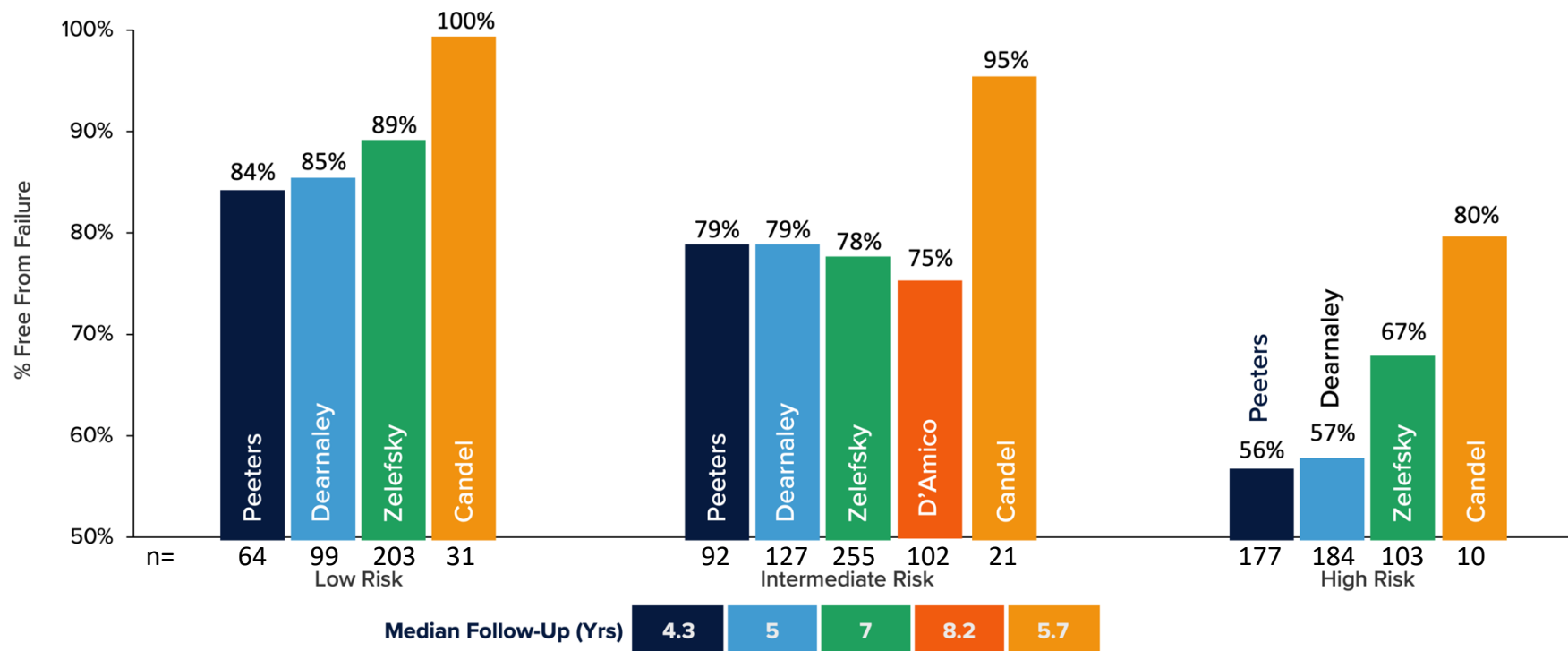


C Aggarwal et al. Abstract #9037 ASCO June 2022

Summary of phase 2 clinical trial of CAN-2409 in combination with ICI in NSCLC

- Disease control rate of 87.5% in patients who were all progressing on anti-PD-1 therapy at entry
- Partial response in 15% of the patients
- Evidence of tumor regression in both injected and uninjected lesions
- Induction of local and systemic cytotoxic T cell response
 - Post treatment tumor biopsies:
 - Increased infiltration of cytotoxic T cells
 - Increased T cell aggregation in proximity to tumor cells
 - Post treatment peripheral blood samples:
 - Increased actively proliferating, granzyme B positive T cells
 - Increased levels of soluble granzymes A, B, and H

Completed phase 2 clinical trial shows consistently improved freedom from failure rates in newly diagnosed, localized prostate cancer



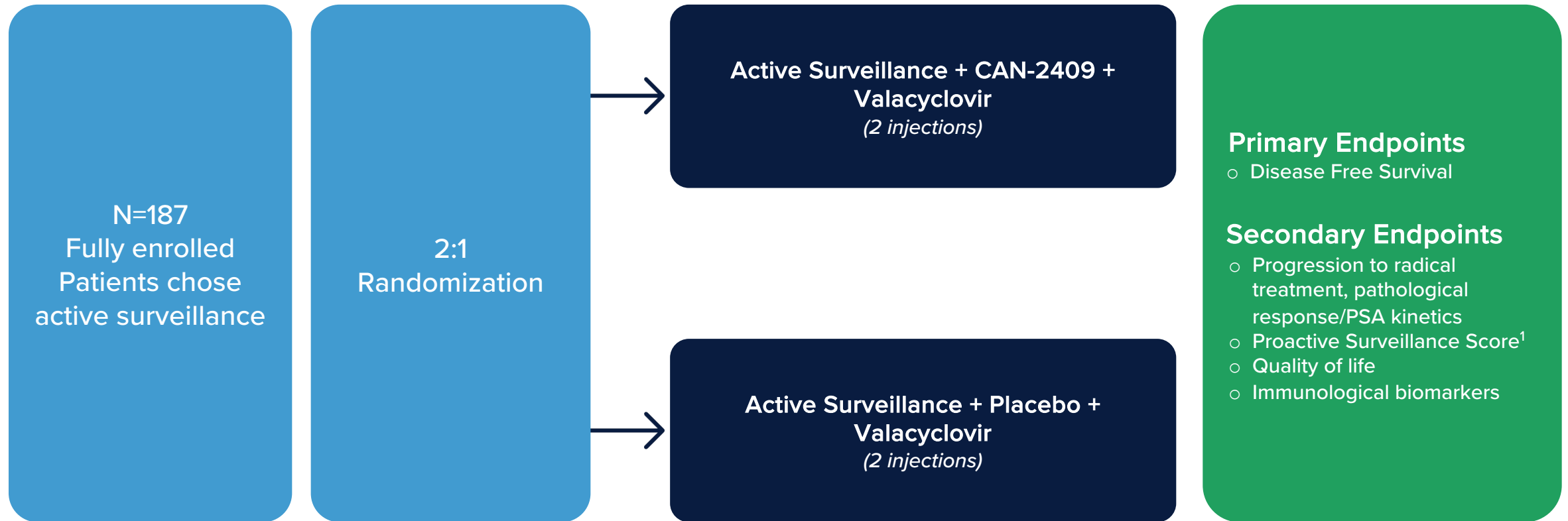
- Pathological complete response (pCR) observed in 93% of the biopsies available at 2yrs (37%-73% in control populations)
- Low risk patients achieved PSA < 2ng/ml in 77% of CAN-2409 treated patients versus 58% in control populations
- Significant increase in activated CD8+ T cells compared to baseline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

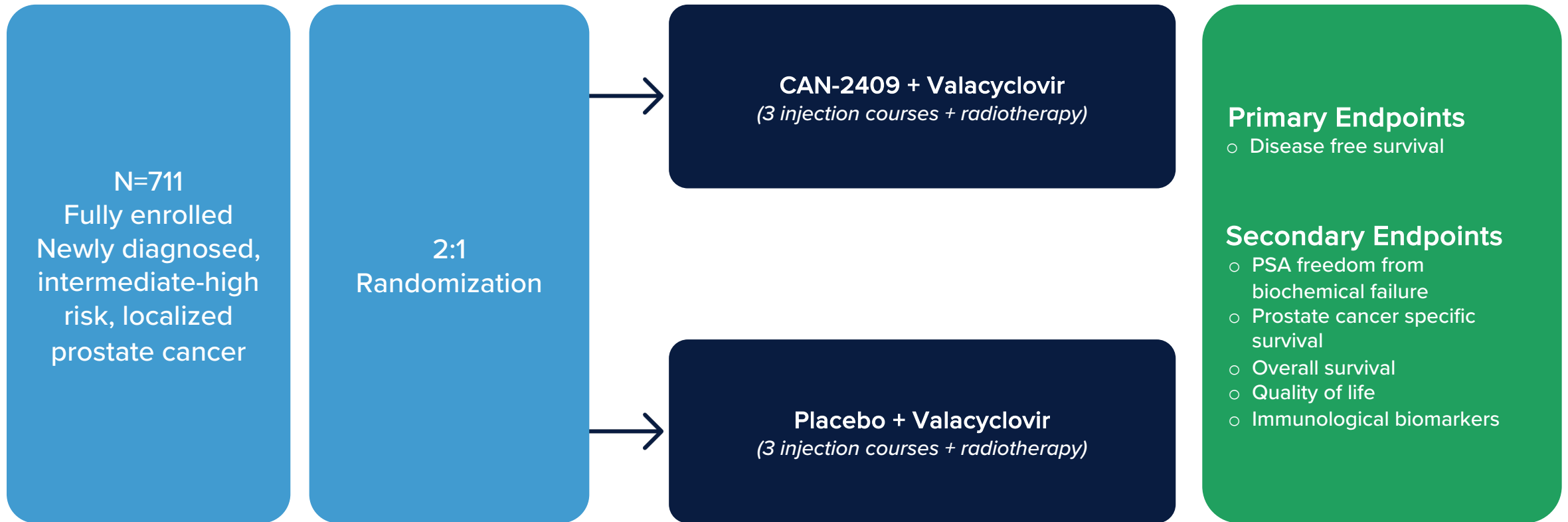
Fully accrued phase 2 clinical trial of CAN-2409 in patients with prostate cancer (active surveillance)

PI: Dr S Eggner (UChicago)



Fully accrued phase 3 clinical trial of CAN-2409 in patients with prostate cancer (newly diagnosed, intermediate/high risk)

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

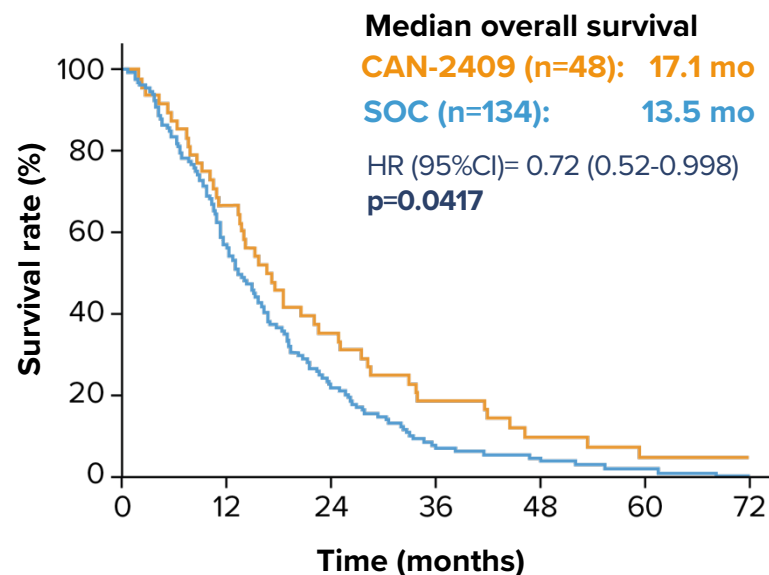


Conducted under agreement with FDA under Special Protocol Assessment

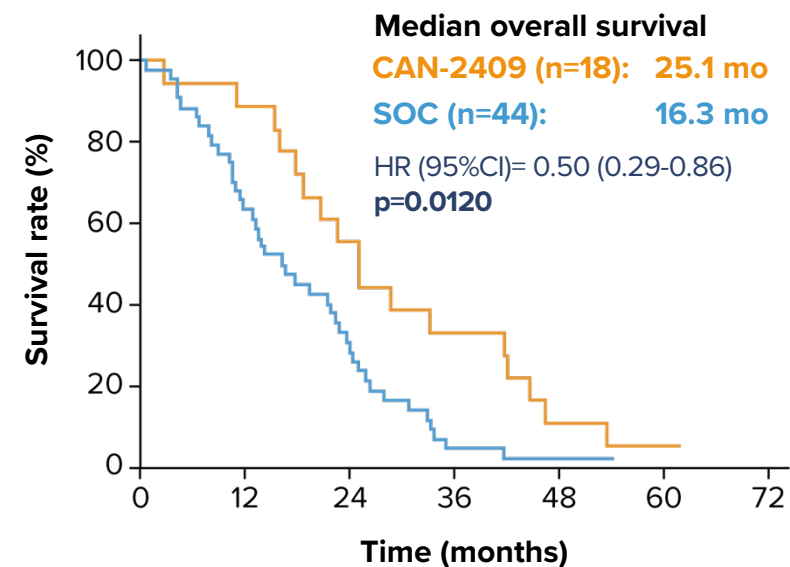
Significant survival benefit after CAN-2409 treatment in HGG

Compared to contemporary controls fulfilling the same inclusion and exclusion criteria

All patients:
All high-grade glioma,
All resection extent



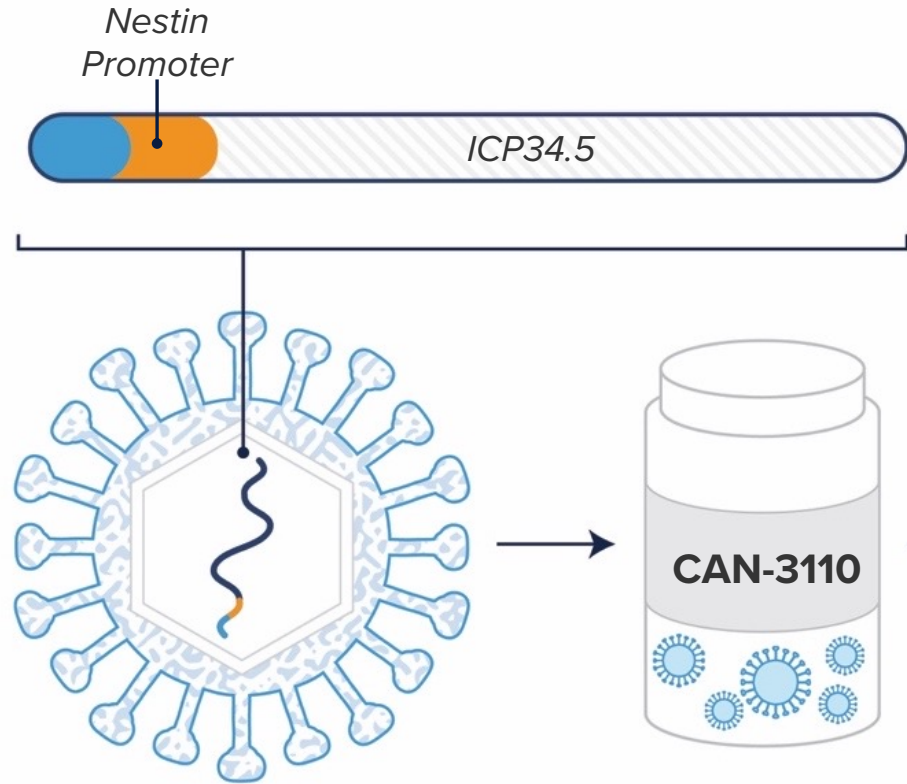
Prespecified subgroup:
glioblastoma with gross total resection



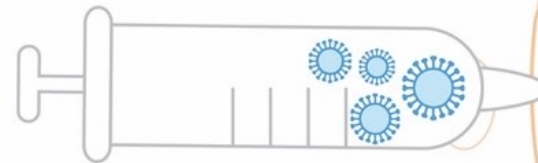
54% Relative improvement
(8.8 mo median survival benefit)

Clinical evidence supports adaptive phase 3 clinical trial of CAN-2409 in high-grade glioma patients undergoing Gross Total Resection and standard of care chemoradiation (reviewed with FDA)

CAN-3110: HSV “Nestin 34.5” construct



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



Virus expands in Nestin expressing tumor cells, causing oncolytic activity

Ongoing phase 1 clinical trial of CAN-3110 in patients with recurrent high-grade glioma

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

Patients with
recurrent
high-grade glioma



Dose escalation

*Single stereotactic injection of CAN-3110
3+3 dose escalation
 1×10^6 to 1×10^{10} PFU in half-log increments*

*Completed:
30 patients dosed
No dose-limiting toxicity observed
Maximum administered dose: 1×10^{10} PFU*



Dose expansion

*1×10^9 PFU
12 patients dosed as of 30 April 2021*

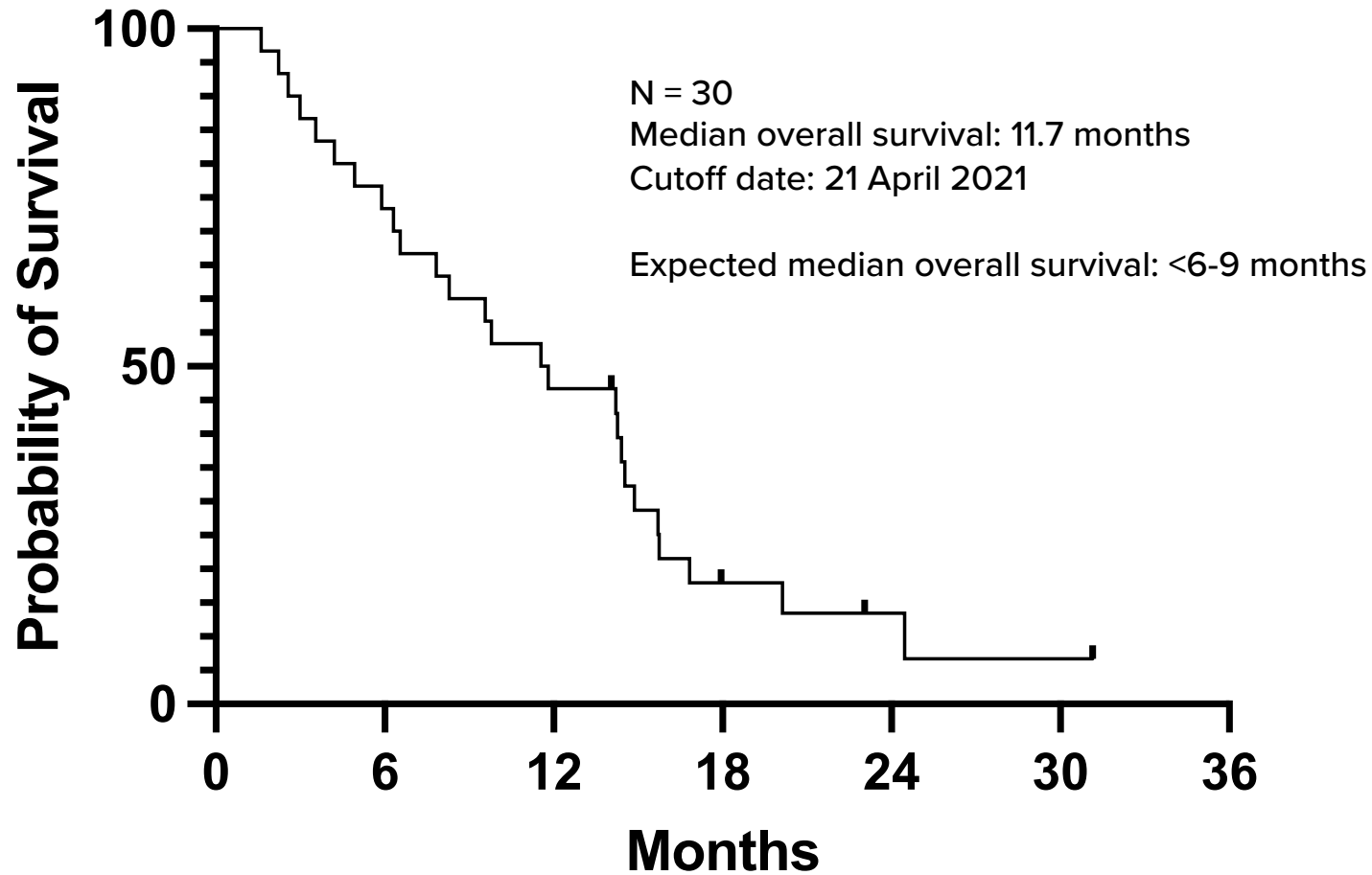
Primary Endpoints

- Safety
- Determine maximum tolerated dose

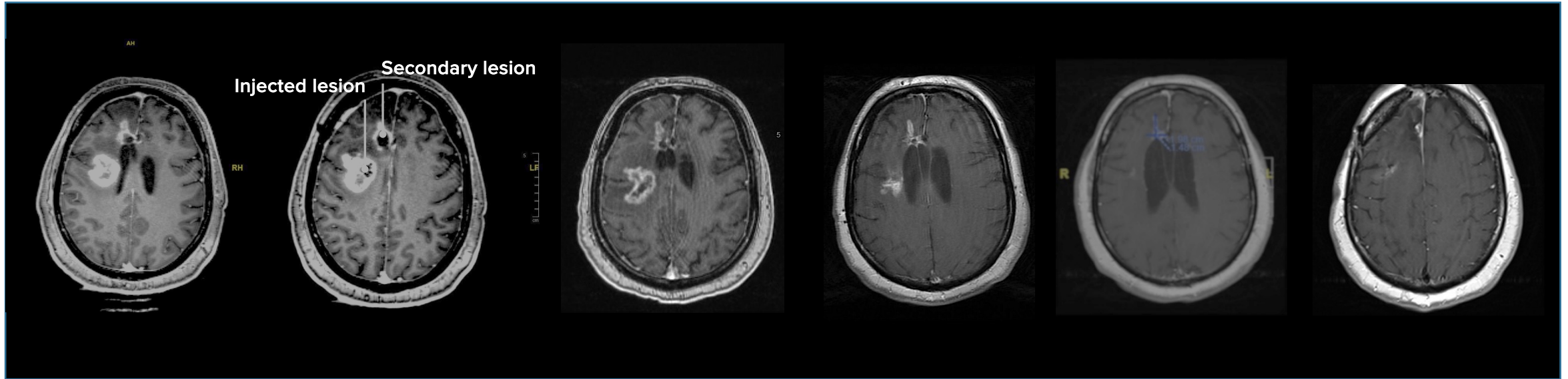
Secondary Endpoints

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

Survival in ongoing phase 1 clinical trial after single dose of CAN-3110 in recurrent high-grade glioma



Single agent activity of CAN-3110 in recurrent HGG patient with abscopal effect



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

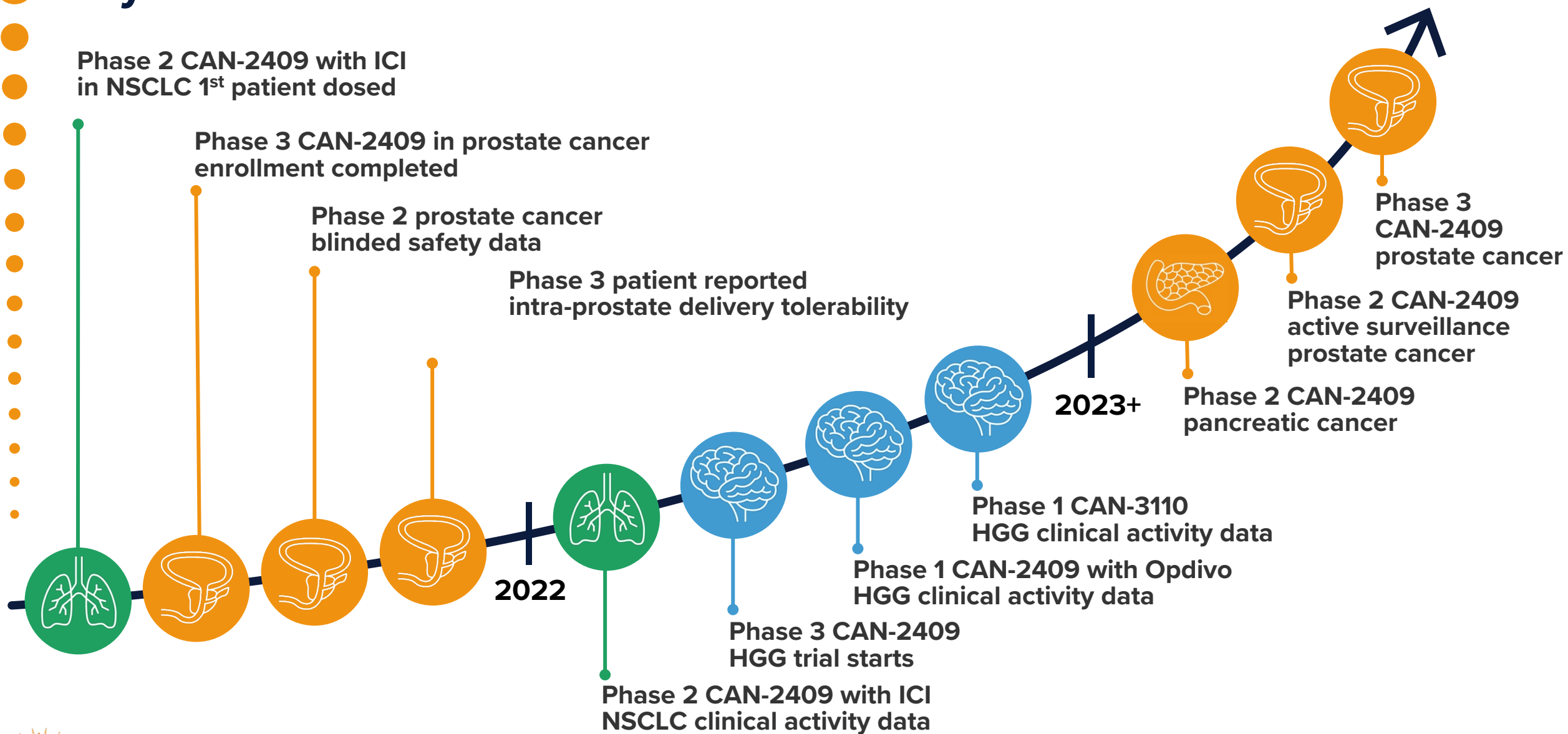
Day 168

Day 280

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

**Clinical effect on injected tumor
and uninjected tumor**

Key achievements and future milestones



Candel overview: Oncolytic viral immunotherapies

- Largely de-risked assets with near- and mid-term inflection points
 - CAN-2409
 - Phase 2 NSCLC; updated clinical data (Q4 2022)
 - Phase 3 HGG; commencing (mid-2022)
 - Phase 1 HGG; combination with Opdivo clinical activity data (Q4 2022)
 - Phase 2 localized, low-to-intermediate-risk prostate cancer (active surveillance) (Q4 2023)
 - Phase 3 localized, intermediate-to-high-risk prostate cancer (Q4 2024)
 - CAN-3110
 - Phase 1 recurrent HGG; updated clinical and biomarker data (Q4 2022)
 - enLIGHTEN™ Discovery Platform based on HSV technology
- Blockbuster potential for each selected indication
- Management team with proven success in immunology, oncology, and development
- Recent IPO provided net proceeds of \$71.3M plus \$20.0M of long-term debt in Feb 2022
- Cash of \$94.3M as of March 31, 2022 - funds currently planned operations into Q1 2024