A Multi-Modality Probody® Therapeutic Pipeline to Address Major Unmet Needs in Oncology

First Quarter Earnings Update
May 8, 2024

Forward-Looking Statements

This presentation may contain projections and other forward-looking statements regarding future events. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, technology platform, development strategy, prospective products, preclinical and clinical pipeline and milestones, regulatory objectives, expected payments from and outcomes of collaborations, and likelihood of success, are forward-looking statements. Such statements are predictions only and involve known and unknown risks, uncertainties and other important 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 the forward-looking statements. These risks and uncertainties include, among others, the costs, timing and results of preclinical studies and clinical trials and other development activities; uncertainties inherent in the initiation and enrollment of clinical trials; uncertainties on the availability and timing of data from clinical trials; the risk that initial clinical data may not reflect later clinical trial results; the unpredictability of the duration and results of regulatory review; the uncertainty of market acceptance for approved products and innovative therapeutic treatments; competition; the potential not to receive partnership milestone, profit sharing or royalty payments; the possible impairment of or inability to obtain intellectual property rights; possible safety or efficacy concerns with our drug candidates; and general business, financial and accounting risks and litigation. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. More information concerning us and such risks and uncertainties is available on our website and in our press releases and in our public filings with the U.S. Securities and Exchange Commission. We are providing this information as of its date and do not undertake any obligation to update or revise it, whether as a result of new information, future events or circumstances or otherwise. Additional information may be available in press releases or other public announcements and public filings made after the date of this presentation.

This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). No representation is made as to their safety or effectiveness for the purposes for which they are being investigated/

Today's Speakers

Dr. Sean McCarthy, *D.Phil*
Chairman and CEO

Dr. Wayne Chu, M.D.
Chief Medical Officer

Agenda

Q1 2024 Updates & T-Cell Engager Strategy
Dr. Sean McCarthy, *D.Phil.* – Chairman and CEO

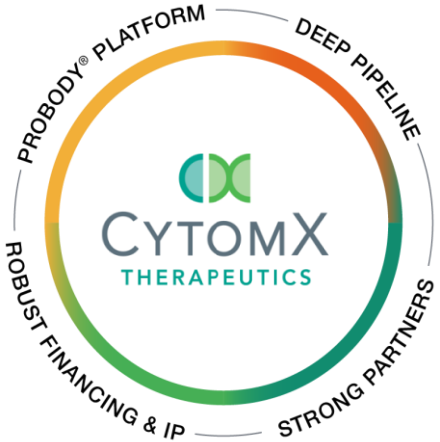
CX-904 Phase 1a study – Initial Dose Escalation Data
Dr. Wayne Chu, M.D. – Chief Medical Officer

Next Steps & Concluding Remarks
Dr. Sean McCarthy, *D.Phil.* – Chairman and CEO

Q&A Session

Company Snapshot

Addressing Major Unmet Need in Oncology



PROBODY® Platform: Unique antibody masking strategy for tumor localization and enhancement of therapeutic index

Pipeline: >15 Probody programs in multiple therapeutic modalities; 3 clinical-stage molecules with retained commercial rights

Lead Programs: CX-904 (EGFR-CD3), CX-2051 (EpCAM ADC), and CX-801 (IFN-α2b)

Partners: Bristol Myers Squibb, Amgen, Astellas, Regeneron, Moderna

Financials: ~$150M cash balance as of Q1 2024 with cash runway to the end of 2025, excluding any potential milestones or new business development

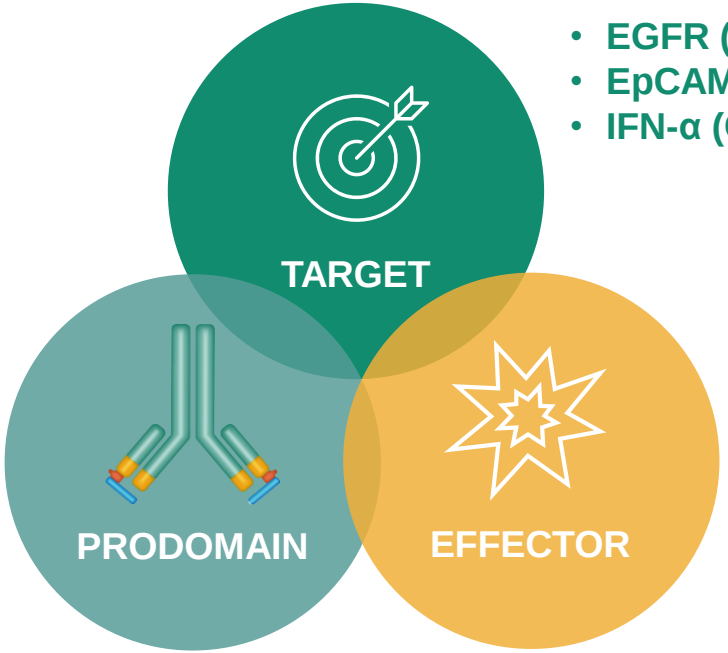
Organization: ~120 employees; seasoned executive team with ~200 years of collective biotech experience; integrated R&D capabilities to support wholly-owned and collaboration programs

CytomX Product Design Strategy Leverages the PROBODY® Platform

Optimized selection of target, prodomain and effector function

Targets with **validated efficacy and broad anti-tumor potential** that need localization to unlock potential

- **EGFR (CX-904)**
- **EpCAM (CX-2051)**
- **IFN-α (CX-801)**



Optimized tuning of masking to **maximize potential therapeutic index**

Matching "effector" to target to maximize anti-cancer activity

- **T-Cell Engager**
- **ADC**
- **Cytokine**

CytomX is Executing to Plan and Entering a Data-Rich Period

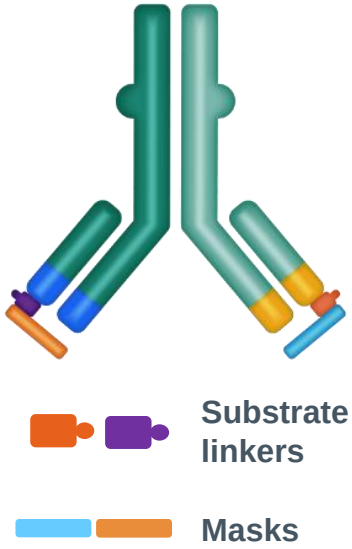
2024 & 2025 Potential Milestones

Program	Stage	2024	2025
CX-904 (EGFR TCE)	Phase 1 Dose Escalation	✓ Initial Phase 1a Dose Escalation data ❑ Additional Ph1a Update by end of 2024 ❑ Decision to Expand to Phase 1b in Conjunction with Amgen	❑ Phase 1b Initiation
CX-2051 (EpCAM ADC)	Phase 1 Dose Escalation	✓ Phase 1 Initiation in EpCAM+ tumors including CRC in 1H 2024 ✓ Cleared First Escalation Cohort	❑ Initial Phase 1 Data in 1H 2025
CX-801 (IFNα2b)	✓ IND Cleared (Jan '24)	❑ Phase 1 Initiation in Solid Tumors including Melanoma, RCC and HNSCC in 1H 2024	❑ Initial Phase 1 Data
Research Collaborations	Preclinical	✓ $10 million in Astellas milestones achieved in Q1 2024 • More than 10 ongoing preclinical programs with partners; majority are TCEs • Additional research milestones achievable in 2024 – 2025 and beyond	

PROBODY® T-Cell Engager Strategy

CytomX PROBODY® T-cell Engagers are Designed to Address Key Limitations of Conventional TCEs in Solid Tumors

PROBODY® T-Cell Engagers



- **Conventional T-Cell engagers** are highly potent, but their use in solid tumors is significantly limited by:
  - Systemic toxicities such as Cytokine Release Syndrome (CRS) and ICANS
  - On-target, off-tumor toxicity
- **Masked, Conditionally activated Probody® T-Cell engagers** are designed to retain potent anti-tumor activity while having less systemic toxicities
- CytomX has a **broad pipeline of internal and partnered PROBODY® TCE programs** with retained commercial rights on select programs, including CX-904 (EGFR-CD3)

CX-904 (EGFR-CD3) Builds on CytomX Scientific Leadership

Masking EGFR antibody therapeutics to widen therapeutic window

Science Translational Medicine, 2013

RESEARCH ARTICLE

CANCER

Tumor-Specific Activation of an EGFR-Targeting Probody Enhances Therapeutic Index

Luc R. Desnoyers,[1]* Olga Vasiljeva,[1]* Jennifer H. Richardson,[1] Annie Yang,[1] Elizabeth E. M. Menendez,[1] Tony W. Liang,[1] Chihunt Wong,[1] Paul H. Bessette,[1] Kathy Kamath,[1] Stephen J. Moore,[1] Jason G. Sagert,[1] Daniel R. Hostetter,[1] Fei Han,[1] Jason Gee,[1] Jeanne Flandez,[1] Kate Markham,[1] Margaret Nguyen,[1] Michael Krimm,[1] Kenneth R. Wong,[1] Shouchun Liu,[1] Patrick S. Daugherty,[2] James W. West,[1] Henry B. Lowman[1]†

Target-mediated toxicity constitutes a major limitation for the development of therapeutic antibodies. To redirect the activity of antibodies recognizing widely distributed targets to the site of disease, we have applied a prodrug strategy to create an epidermal growth factor receptor (EGFR)–directed Probody therapeutic—an antibody that remains masked against antigen binding until activated locally by proteases commonly active in the tumor microenvironment. In vitro, the masked Probody showed diminished antigen binding and cell-based activities, but when activated by appropriate proteases, it regained full activity compared to the parental anti-EGFR antibody cetuximab. In vivo, the Probody was largely inert in the systemic circulation of mice, but was activated within tumor tissue and showed antitumor efficacy that was similar to that of cetuximab. The Probody demonstrated markedly improved safety and increased half-life in nonhuman primates, enabling it to be dosed safely at much higher levels than cetuximab. In addition, we found that both Probody-responsive xenograft tumors and primary tumor samples from patients were capable of activating the Probody ex vivo. Probodies may therefore improve the safety profile of therapeutic antibodies without compromising efficacy of the parental antibody and may enable the wider use of empowered antibody formats such as antibody-drug conjugates and bispecifics.

Proof-of-concept that masking can reduce EFGR on-target toxicities

Cancer Research, 2022

CANCER RESEARCH | TRANSLATIONAL SCIENCE

A Probody T Cell–Engaging Bispecific Antibody Targeting EGFR and CD3 Inhibits Colon Cancer Growth with Limited Toxicity

Leila M. Boustany, Sherry L. LaPorte, Laurie Wong, Clayton White, Veena Vinod, Joel Shen, Wendy Yu, David Koditek, Michael B. Winter, Stephen J. Moore, Li Mei, Linnea Diep, Yuanhui Huang, Shouchun Liu, Olga Vasiljeva, Jim West, Jennifer Richardson, Bryan Irving, Marcia Belvin, and W. Michael Kavanaugh

ABSTRACT

T cell–engaging bispecific antibodies (TCB) are highly potent therapeutics that can recruit and activate cytotoxic T cells to stimulate an antitumor immune response. However, the development of TCBs against solid tumors has been limited by significant on-target toxicity to normal tissues. Probody therapeutics have been developed as a novel class of recombinant, protease-activated antibody prodrugs that are "masked" to reduce antigen binding in healthy tissues but can become conditionally unmasked by proteases that are preferentially active in the tumor microenvironment (TME). Here, we describe the preclinical efficacy and safety of CI107, a Probody TCB targeting EGFR and CD3. *In vitro*, the protease-activated, unmasked CI107 effectively bound EGFR and CD3 expressed on the surface of cells and induced T-cell activation, cytokine release, and cytotoxicity toward tumor cells. In contrast, dually masked CI107 displayed a >500-fold reduction in antigen binding and >15,000-fold reduction in cytotoxic activity. *In vivo*, CI107 potently induced dose-dependent tumor regression of established colon cancer xenografts in mice engrafted with human peripheral blood mononuclear cells. Furthermore, the MTD of CI107 in cynomolgus monkeys was more than 60-fold higher than that of the unmasked TCB, and much lower levels of toxicity were observed in animals receiving CI107. Therefore, by localizing activity to the TME and thus limiting toxicity to normal tissues, this Probody TCB demonstrates the potential to expand clinical opportunities for TCBs as effective anticancer therapies for solid tumor indications.

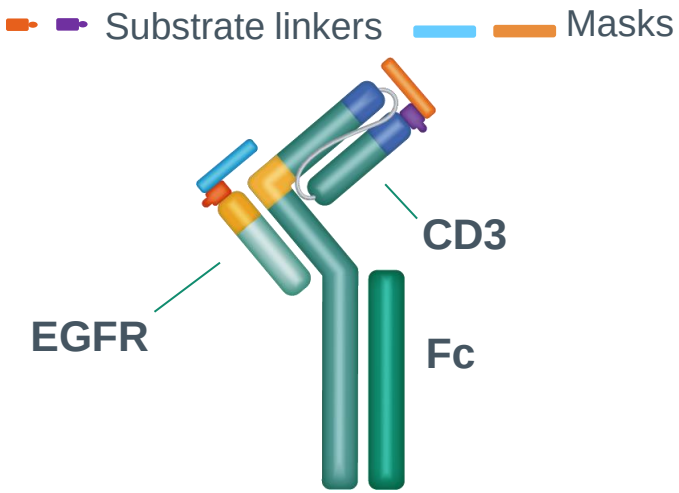
Significance: A conditionally active EGFR-CD3 T cell–engaging Probody therapeutic expands the safety window of bispecific antibodies while maintaining efficacy in preclinical solid tumor settings.

Proof-of-concept for efficacy and therapeutic window for masked EGFRxCD3

CX-904: Masked PROBODY® T-Cell Engager Targeting EGFR and CD3

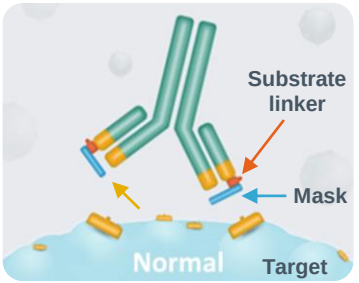
Format and therapeutic concept

CX-904

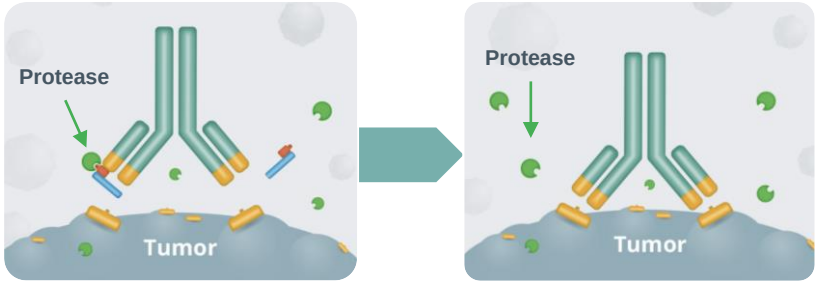


- Finely tuned masks and protease substrates
- Distinct “Prodomains” on EGFR and CD3 to optimize therapeutic window
- Fc domain for antibody-like PK/PD

“Masking” limits PROBODY therapeutic binding to healthy tissues



Tumor proteases “unmask” PROBODY therapeutics, allowing binding to tumor cells



CytomX Therapeutics

Key Goals of CX-904 Phase 1a Study

Data to date are supportive of PROBODY® TCE mechanism of action

- **Safety – Mitigate CRS and open a therapeutic window for EGFR T-Cell engager**
  - Maintained masking in circulation
  - No CRS or ICANS with step-dose schedules
  - Manageable EGFR-related toxicities
- **Assess efficacy and pharmacodynamic activity**
  - Confirmed RECIST 1.1 partial responses in metastatic pancreatic adenocarcinoma
  - CD8+ margination and tumor infiltration
- **Determine RP2D (ongoing)**
  - Dose escalation continues
  - Currently enrolling at 15mg target dose

CX-904 Phase 1a Clinical Study Update

Dr. Wayne Chu, M.D.
Chief Medical Officer

CX-904 Dose Escalation Status and Current Enrollment

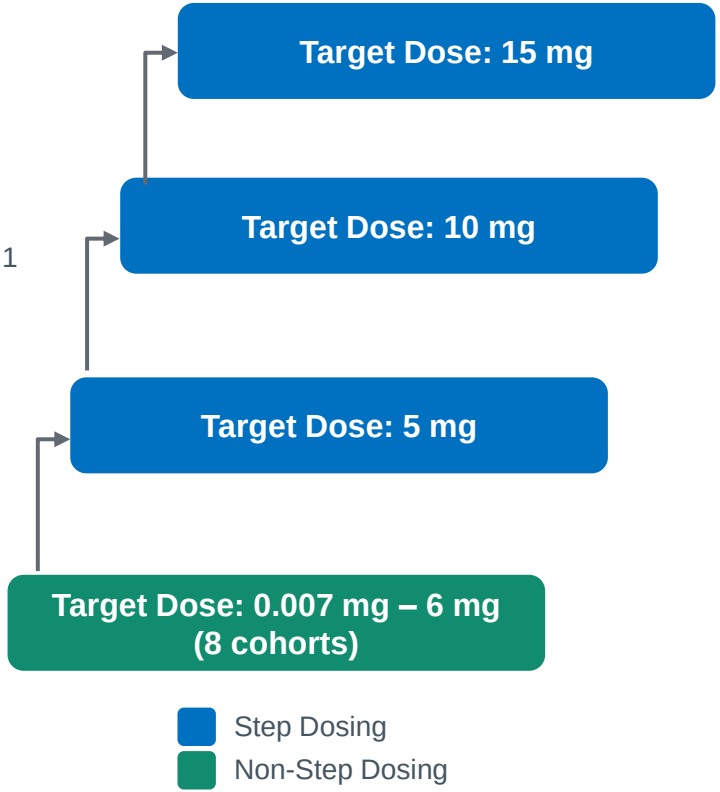
Dose ranges consistent with biologically effective dose modeling[1]

Key Eligibility Criteria

- Age ≥ 18 years
- Locally advanced/metastatic disease
- Tumors with known EGFR expression; unselected
- Measurable disease per RECIST 1.1
- Adequate organ function
- ECOG 0-1

Key Objectives

- Primary
  - Safety and tolerability
  - Determine MTD and RP2D
- Secondary
  - Anti-tumor activity
  - Pharmacokinetics



- Schedules tested with 1 or 2 steps with 7 or 14 days between successive doses to achieve target dose
- Once target dose is reached, subsequent doses administered Q2W
- Current step-dosing schedule:
  - **3 mg - *7d* - 5 mg - *7d* – target dose**
  - Data cutoff through 10 mg target dose
  - Currently enrolling cohort with 15 mg target dose

CytomX Therapeutics

Source: 1.CytomX Internal Data

CTMX-904-101 Phase 1a Baseline Characteristics

35 Patients enrolled through 10 mg Target Dose

Patient Characteristics: *Advanced late-line refractory disease*	Non-Step Dosing (n = 19)	Step Dosing (n = 16)	Total Safety Evaluable (N =35)
Median Age (range)	58 (36, 77)	54 (35, 79)	58 (35, 79)
Indication:			
CRC*	11 (58%)	7 (44%)	18 (51%)
Pancreatic	2 (11%)	5 (31%)	7 (20%)
NSCLC	3 (16%)	-	3 (9%)
HNSCC	-	3 (19%)	3 (9%)
Gastric	1 (5%)	1 (6%)	2 (6%)
Esophageal	1 (5%)	-	1 (3%)
Other	1 (5%)	-	1 (3%)
Prior cancer therapies, median (range)	**4 (1, 8)**	**3 (2, 5)**	**4 (1, 8)**
Refractory (PD) to last prior therapy	13 (68%)	5 (31%)	18 (51%)
Prior EGFRi	5 (26%)	3 (19%)	8 (23%)
Prior PD-(L)1	7 (37%)	3 (19%)	10 (29%)

CytomX Therapeutics

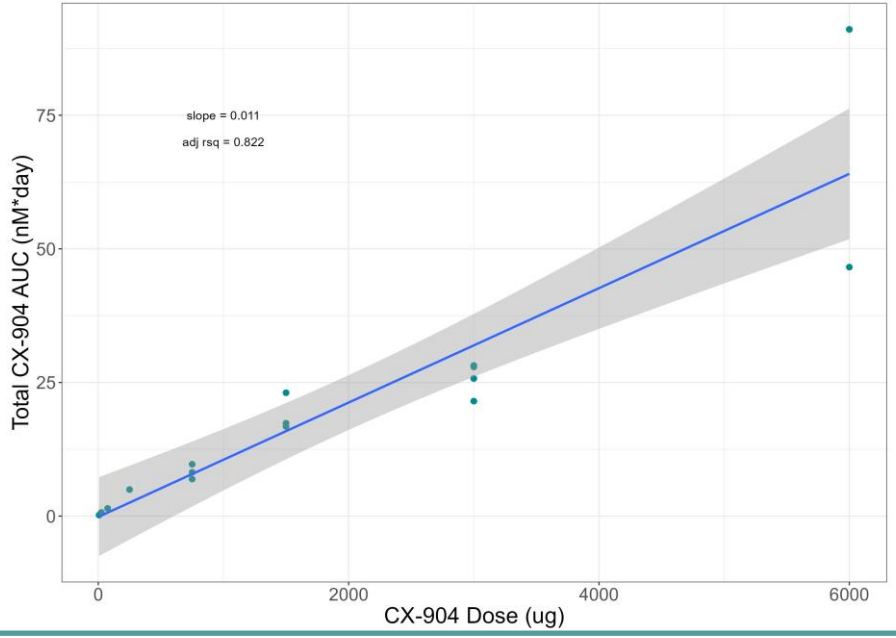
**17 of 18 patients MSS CRC*

Data cutoff as of 16 Apr 2024

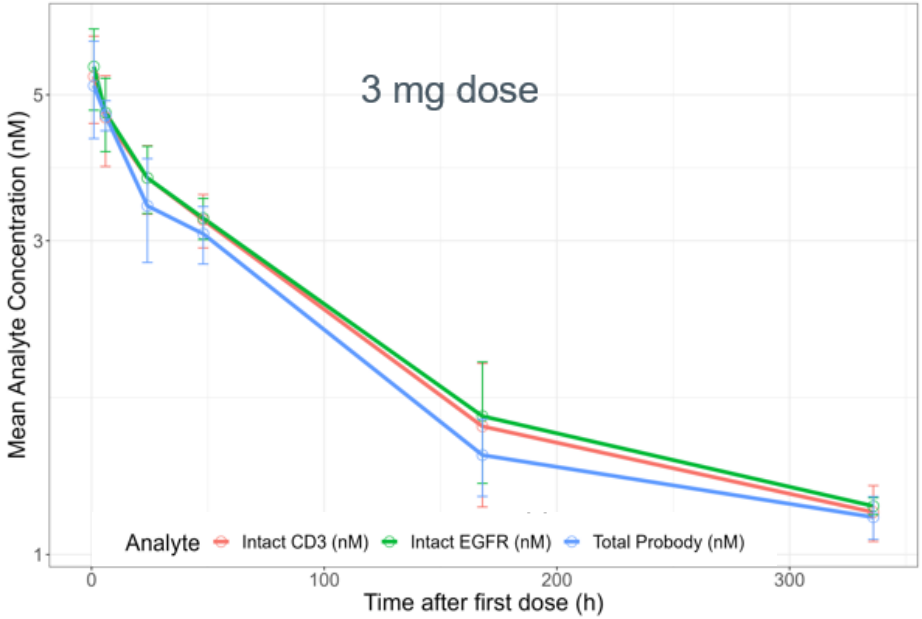
Ph1 Clinical PK Data is Consistent with CX-904 PROBODY TCE Design

CX-904 exposure increases linearly with dose and remains masked in circulation

- Total CX-904 exposure (Cmax and AUC) increase linearly with increasing dose
  - No apparent change in clearance with dose
  - No apparent Target Mediated Drug Disposition (TMDD)



- Circulating CX-904 is predominantly intact (masked)
  - Preliminary estimates of half-life is between 2.8-5.3 days



Summary data presented as mean, SD

30 November 2023

Source: CytomX Internal Data

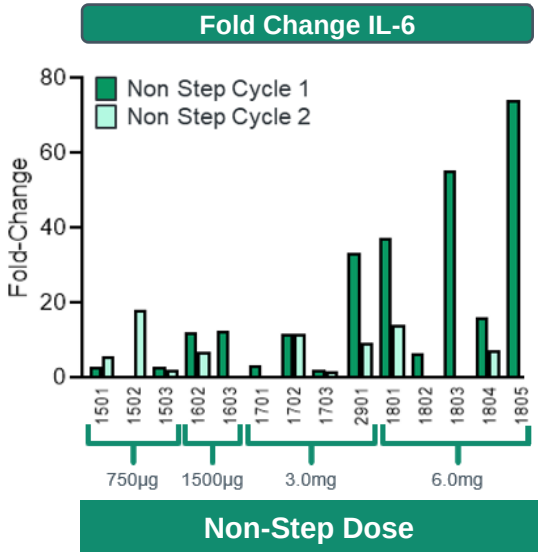
Initial CX-904 Non-Step Dosing Was Well Tolerated Through 3 mg

No CRS observed through 3 mg, no grade >1 CRS at 6 mg

No prophylaxis administered for CRS

Preferred Term, Treatment-Related AEs in >1 patient or DLT	Non-Step 0.007 mg - 3 mg (n = 14)			Non-Step 6 mg (n = 5)			Total (n = 19)
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3	All Grades
Arthralgia	3 (21%)	2 (14%)	-	-	2 (40%)	-	7 (37%)
CRS	-	-	-	5 (100%)	-	-	5 (26%)
Arthritis	-	1 (7%)	-	-	1 (20%)		2 (11%)
Rash[a]	-	-	-	1 (20%)	-	1 (20%)	2 (11%)
Vomiting	-	-	-	2 (40%)	-	-	2 (11%)
Tenosynovitis	-	-	-	-	-	1 (20%)	1 (5%)

[a] *Includes the preferred terms rash maculopapular, dermatitis acneiform, rash pustular, and skin exfoliation*



Source: CytomX Internal Data

- *Emerging musculoskeletal AEs were associated with dose dependent IL-6 elevation*
- *DLTs at 6 mg non-step dose were tenosynovitis, rash (maculopapular)*
- *No ICANS was observed*

CX-904 Remained Well Tolerated Through 10 mg with Step-Dosing

No CRS or ICANS of any grade; dose escalation continues

Preferred Term, Treatment-Related AEs in >1 patient	Step-Dosing 5 mg target (n=10)			Step-Dosing 10 mg target (n = 6)			Total (n =16)
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3	All Grades
Rash[a]	3 (30%)	3 (30%)	-	6 (100%)	-	-	12 (75%)
Arthralgia	2 (20%)	1 (10%)	1 (10%)	-	1 (17%)	1 (17%)[b]	6 (38%)
Pruritus	2 (20%)	-	-	3 (50%)	-	-	5 (31%)
Arthritis	-	1 (10%)	-	-	1 (17%)	1 (17%)[b]	3 (19%)
Vomiting	1 (10%)	-	-	1 (17%)	1 (17%)	-	3 (19%)
Nausea	-	1 (10%)	-	-	2 (33%)	-	3 (19%)
CRS or ICANS	-	-	-	-	-	-	-

[a] *Includes the preferred terms rash maculo-papular, dermatitis acneiform, rash pustular, and skin exfoliation*
[b] *Not protocol-defined DLTs*

Step-Dosing and Tocilizumab Prophylaxis Implemented

- Step-dosing enabled escalation to higher target doses
- Tocilizumab has activity in ICI-induced arthritis[1,2,3,4]
- Tocilizumab shown not to impact TCE anti-tumor activity[5]

Summary of Safety and Tolerability

- No change in arthralgia incidence and severity with higher target dose
- No Grade 3 rash
- No related adverse events leading to treatment discontinuation
- No mandatory hospitalization required for monitoring at cleared dose levels

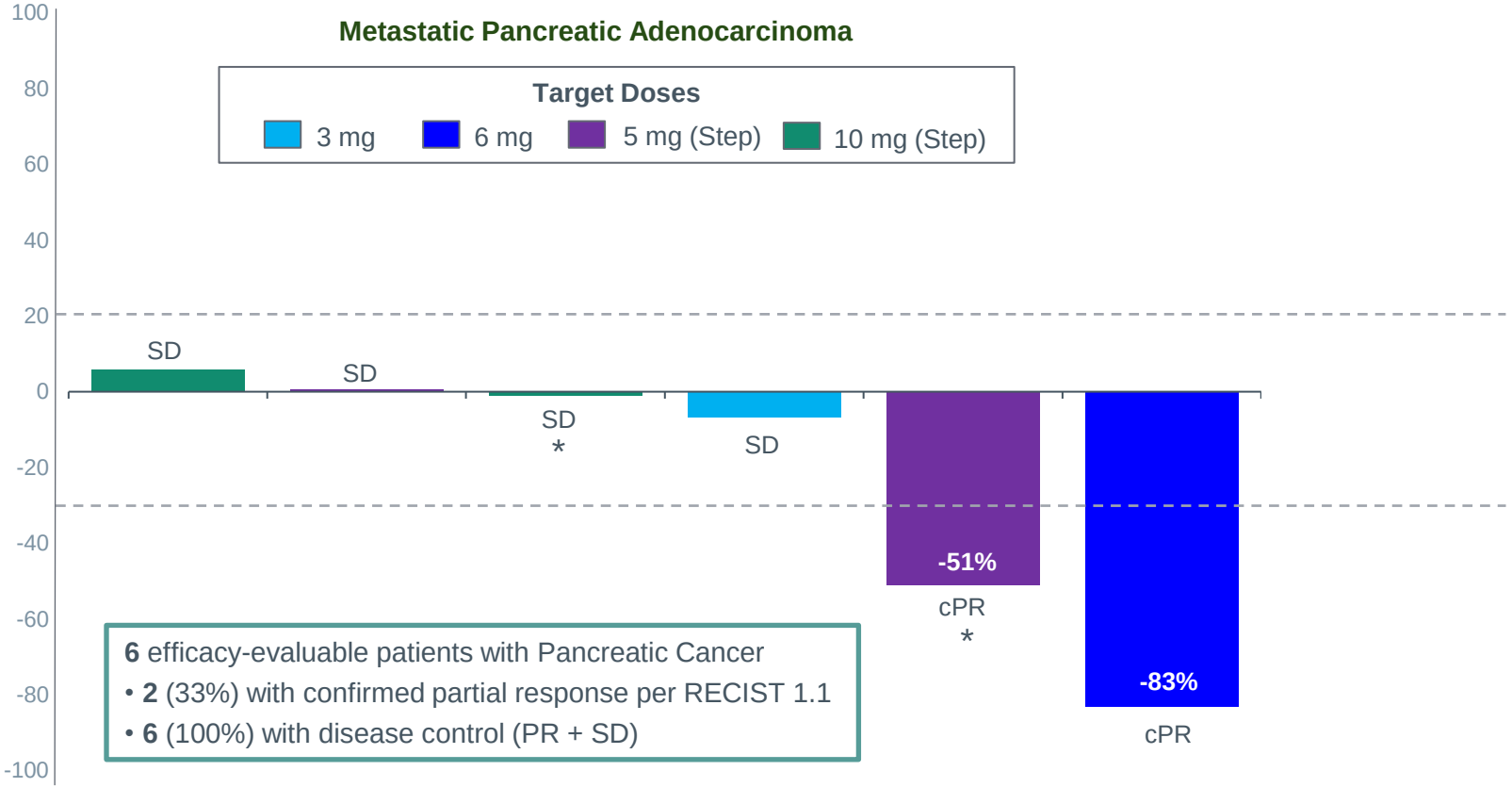
CytomX Therapeutics

Sources: [1] Kim et al. 2022 ; [2] Actemra product insert; [3] Fleischmann et al. 2009; [4] Holmstroem et al. 2022; [5] Kauer et al. 2022

Data cutoff as of 16 Apr 2024

Metastatic Pancreatic Adenocarcinoma Anti-Tumor Activity for CX-904

2 of 6 (33%) Efficacy-evaluable patients with confirmed objective response



** Patient still on study treatment as of data cutoff*

Data cutoff as of 16 Apr 2024

Case Study 1: Confirmed PR in Metastatic Pancreatic Adenocarcinoma

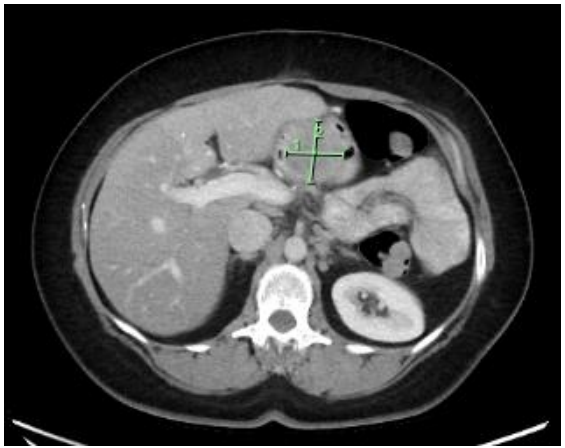
Patient remains on CX-904 treatment (>3 months as of data cutoff)

Patient Background:

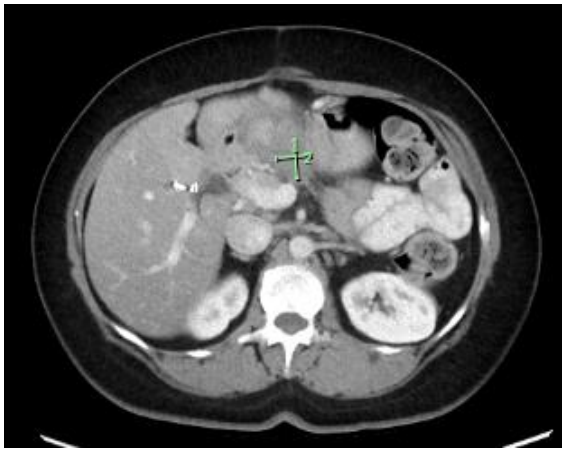
- 49 y/o female
- Surgery, radiotherapy, three prior lines of systemic chemotherapy

Dosing and clinical course on CX-904:

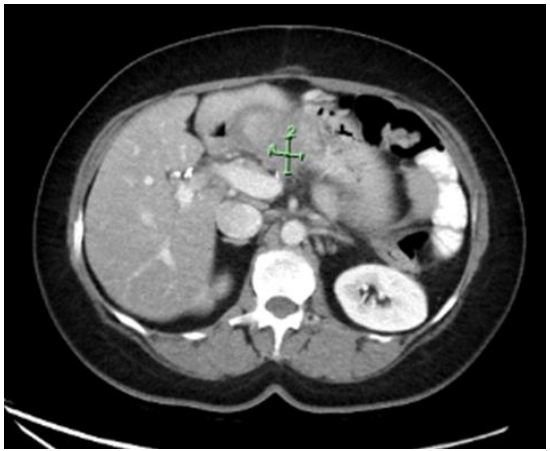
- 1.5 mg on D1, 5 mg on D8 and Q2W thereafter
- No CRS; G3 related arthralgia resolved to G1 after 1-cycle dose delay and corticosteroids
- PR per RECIST 1.1 at 6- and 12-week tumor assessments



43 × 41 mm
Baseline target lesion



23 × 19 mm
-46.5% reduction at 6 weeks



21 × 20 mm
-51.2% reduction at 12 weeks

CytomX Therapeutics

Data cutoff as of 16 Apr 2024

Case Study 2: Durable Stable Disease in Metastatic Pancreatic Adenocarcinoma

Patient remains on 10 mg CX-904 treatment (>3.5 months as of data cutoff)

Patient Background:

- 59 y/o female
- 3 prior lines of systemic therapies: FOLFIRI; gemcitabine and abraxane; liposomal irinotecan and 5-FU

Dosing and clinical course:

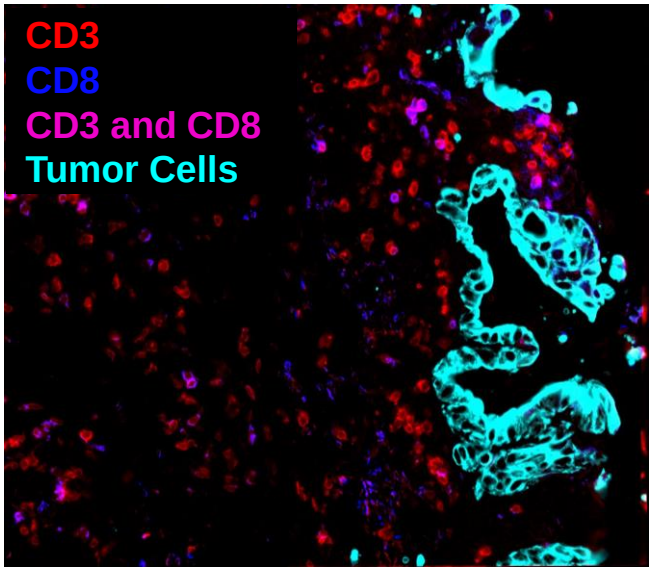
- 1.5 mg on D1, 5 mg on D8, 10 mg on D15 and then Q2W
- No CRS or musculoskeletal adverse events; G1 papulopustular rash resolved with topical management

Ongoing Stable Disease:

- CT scans at 4 weeks and 11 weeks on study treatment showed SD per RECIST 1.1
- No evidence of tumor growth
- Reductions in CA19-9 from 59K U/mL (baseline) to 20K U/mL (at ~11 weeks on study)
- ECOG PS improved from 1 to 0

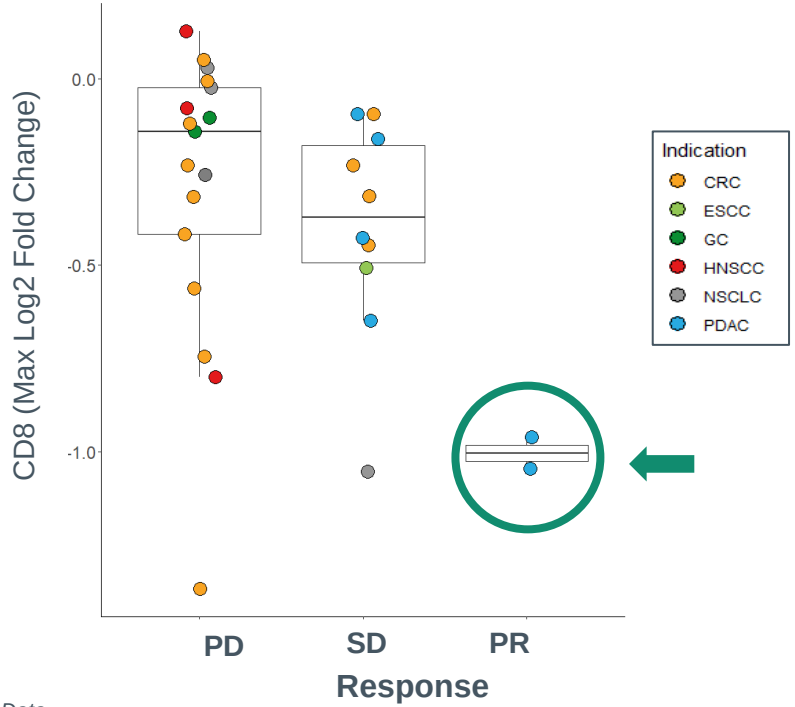
CX-904 Mechanism of Action in Pancreatic Responses Supported by Preliminary T-Cell Pharmacodynamics

Pre-treatment biopsy immunofluorescence
Pancreatic patient with cPR (83% tumor reduction)



Pre-treatment biopsy shows high level of CD8+ cells in the tumor microenvironment

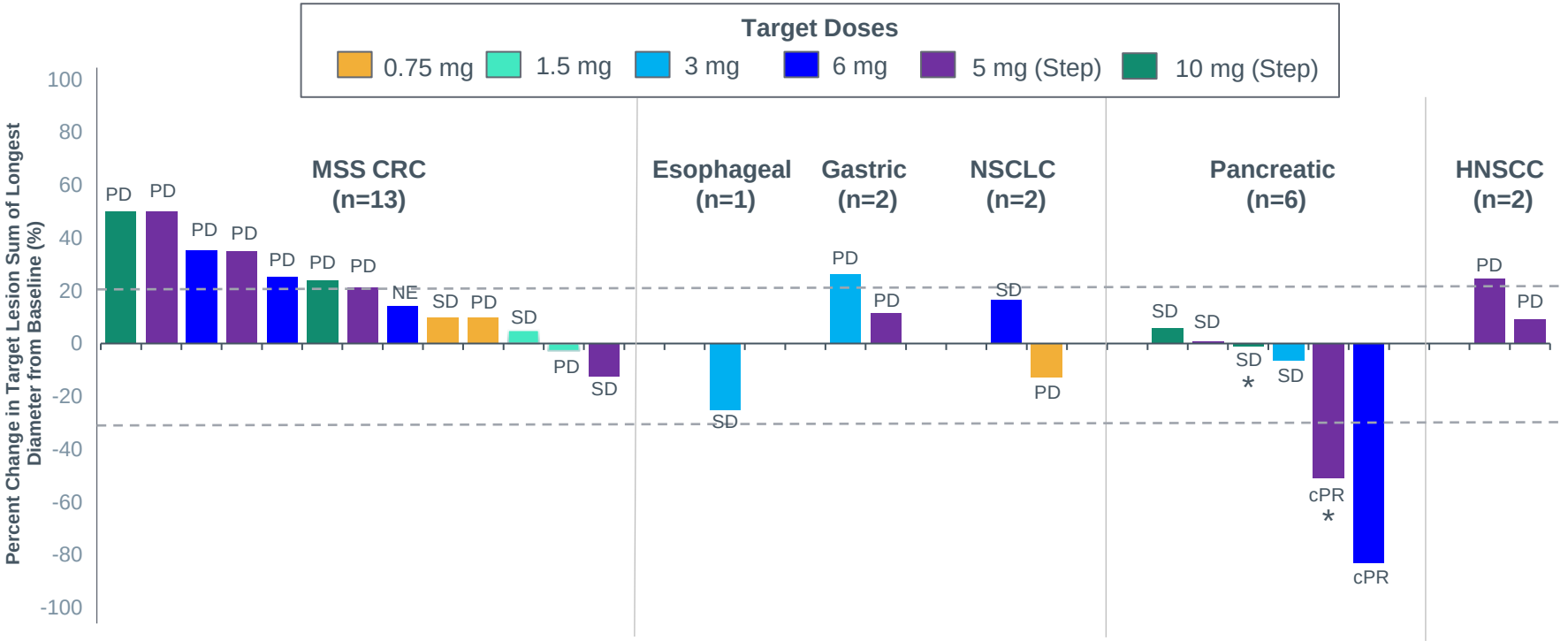
Reduced CD8+ in Periphery Shows Preliminary Correlation With Response



Source:CytomX Internal Data

CX-904 Anti-tumor Activity for Patients Dosed at ≥0.75 mg

Enrollment continues for Pancreatic, NSCLC, HNSCC, Gastric, Esophageal



Best overall response per RECIST 1.1 is shown for each efficacy evaluable patient

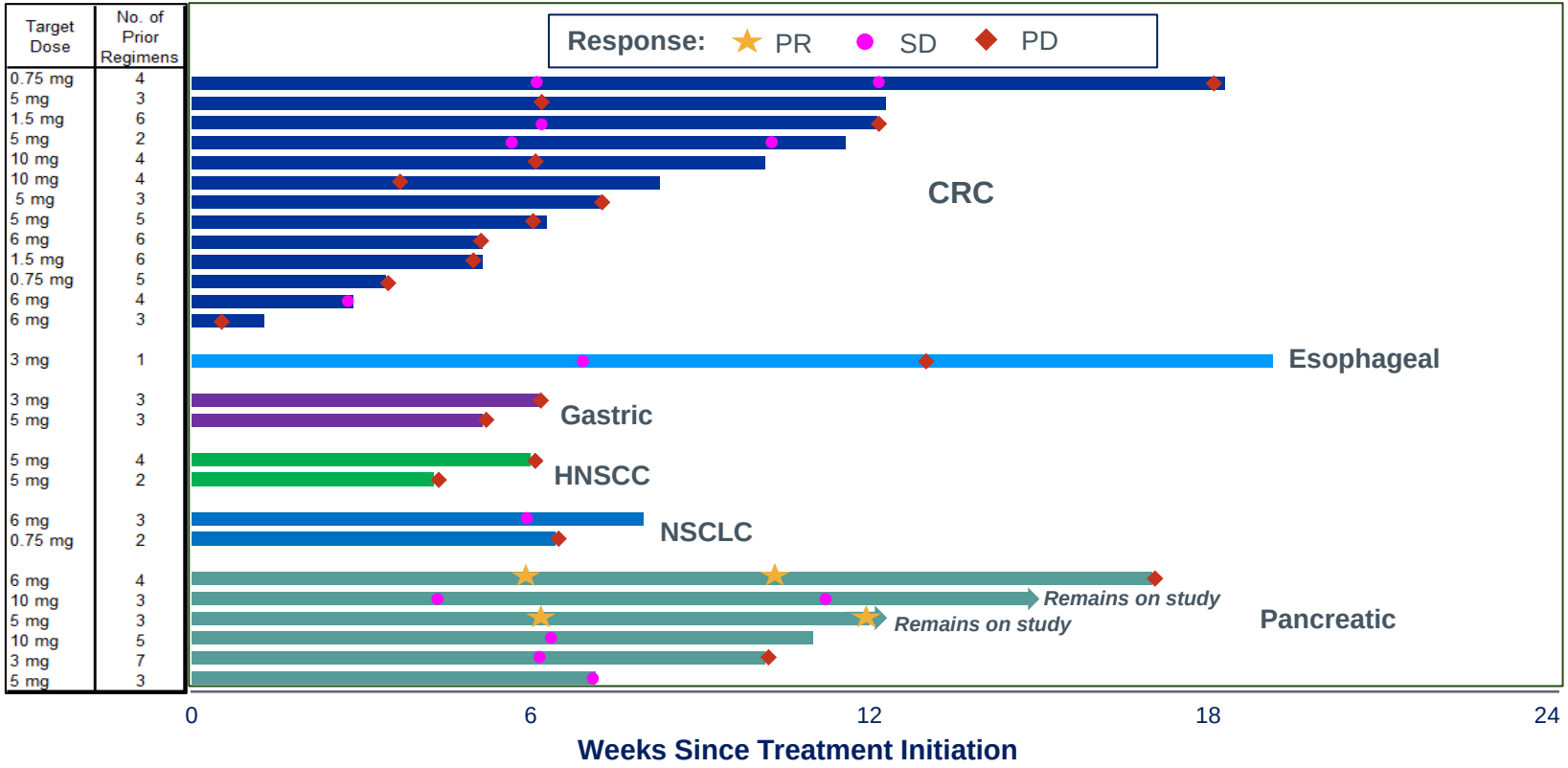
CytomX Therapeutics

** Patient still on study as of data cutoff*

Data cutoff as of 16 Apr 2024

CX-904 Treated Patients Time on Study

Efficacy evaluable patients treated ≥ 0.75 mg



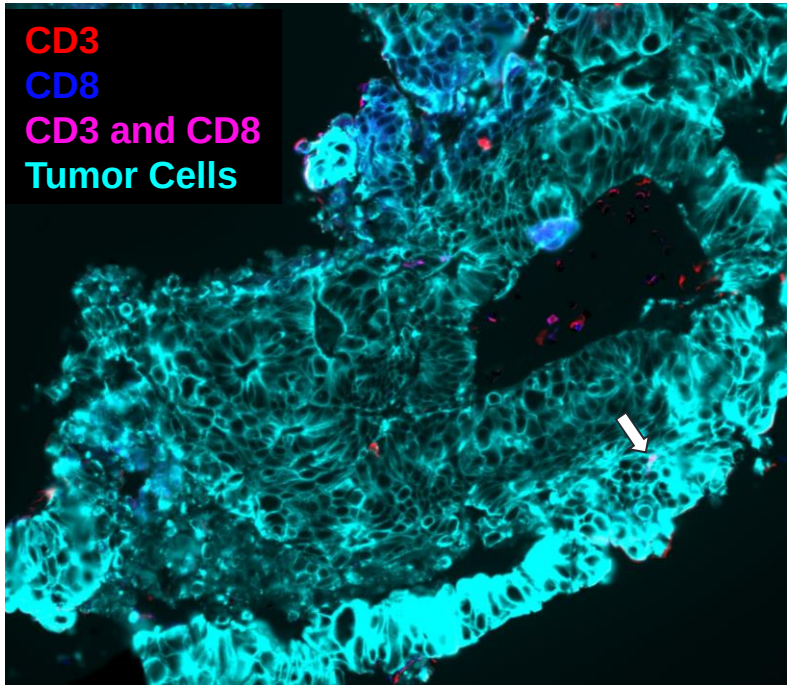
Data cutoff as of 16 Apr 2024

Increased Intratumoral T-Cells with CX-904 in MSS CRC Patient

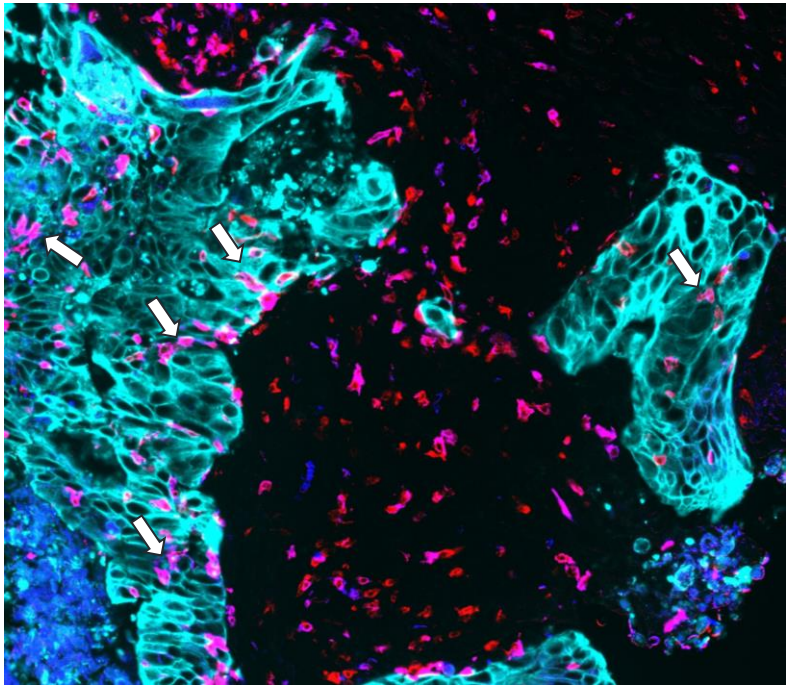
Demonstrates MOA and potential combination strategies

Increased Intratumoral CD8+ T-Cells After CX-904 Treatment

Pre-treatment



On treatment (Cycle 4 Day 1)



Source:CytomX Internal Data

CX-904 EGFR-CD3 PROBODY® TCE Phase 1a Initial Data

Summary and Next Steps

CX-904 Demonstrates a Favorable Safety Profile

- Masking is maintained in circulation
- No CRS or ICANS observed with step-dosing
- Treatment-related AEs are manageable with no discontinuations
- CX-904 can be administered in out-patient setting

Promising Early Efficacy and Pharmacodynamic activity

- Confirmed RECIST 1.1 PRs in 2 of 6 (33%) metastatic pancreatic adenocarcinoma patients
- CD8+ margination and tumor infiltration consistent with mechanism of action

Future Monotherapy Enrollment Focused on Determining RP2D

- Continued enrollment in Pancreatic, NSCLC, HNSCC, GEJ/Gastric, and Esophageal to inform Phase 1b strategy
- Combination strategies under consideration

Concluding Remarks

Dr. Sean McCarthy, *D.Phil*
Chairman and CEO

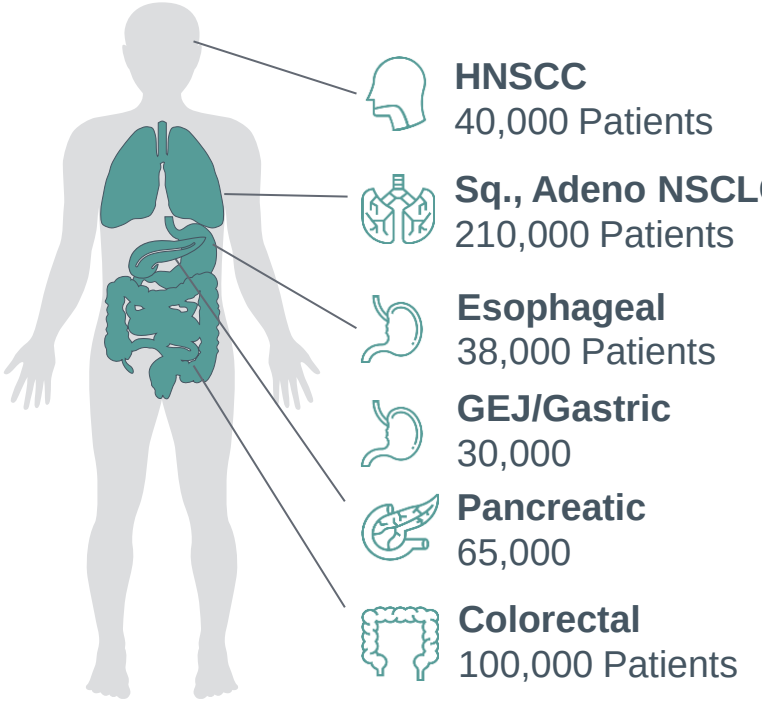
CX-904 Can Potentially Address Multiple Indications With High Unmet Need

EGFR – High Potential TCE Target

- Prevalent EGFR expression in many cancer types
- CX-904 masked EGFR TCE designed to address large unmet need and market opportunity
- Monotherapy activity demonstrated
- Opportunity to combine with immunotherapy or other targeted agents

2023 US Metastatic, Addressable Patients

Patients with EGFR+ Tumors



Source: TPM 8+ equivalent to 2+ by IHC (internal prevalence study); TPM = Transcripts per million; TCGA RNA Seq Data; Epidemiology data from DRG

Pancreatic Cancer Incidence & Treatment Landscape

Remains critical area of high unmet need

Estimated Incidence

66,440 new cases in 2024

51,750 deaths estimated in 2024

- 2nd leading cause of cancer deaths
- 80% of patients present with unresectable disease
- Overall, the survival rate is 13% at 5 years

Treatment Landscape

- Patients with localized disease: surgical resection
- Patients with recurrent or metastatic disease
  - SOC chemo includes gemcitabine combo with Abraxane (nab-paclitaxel, albumin bound paclitaxel) or FOLFIRINOX (if eligible)
  - Historically unresponsive to anti-EGFR mAbs[1] or immunotherapy
- Benchmark[2] in 2L+ metastatic pancreatic cancer:
  - ORR: 7.7%
  - mPFS: 3.1 months
  - OS: 6.1 months

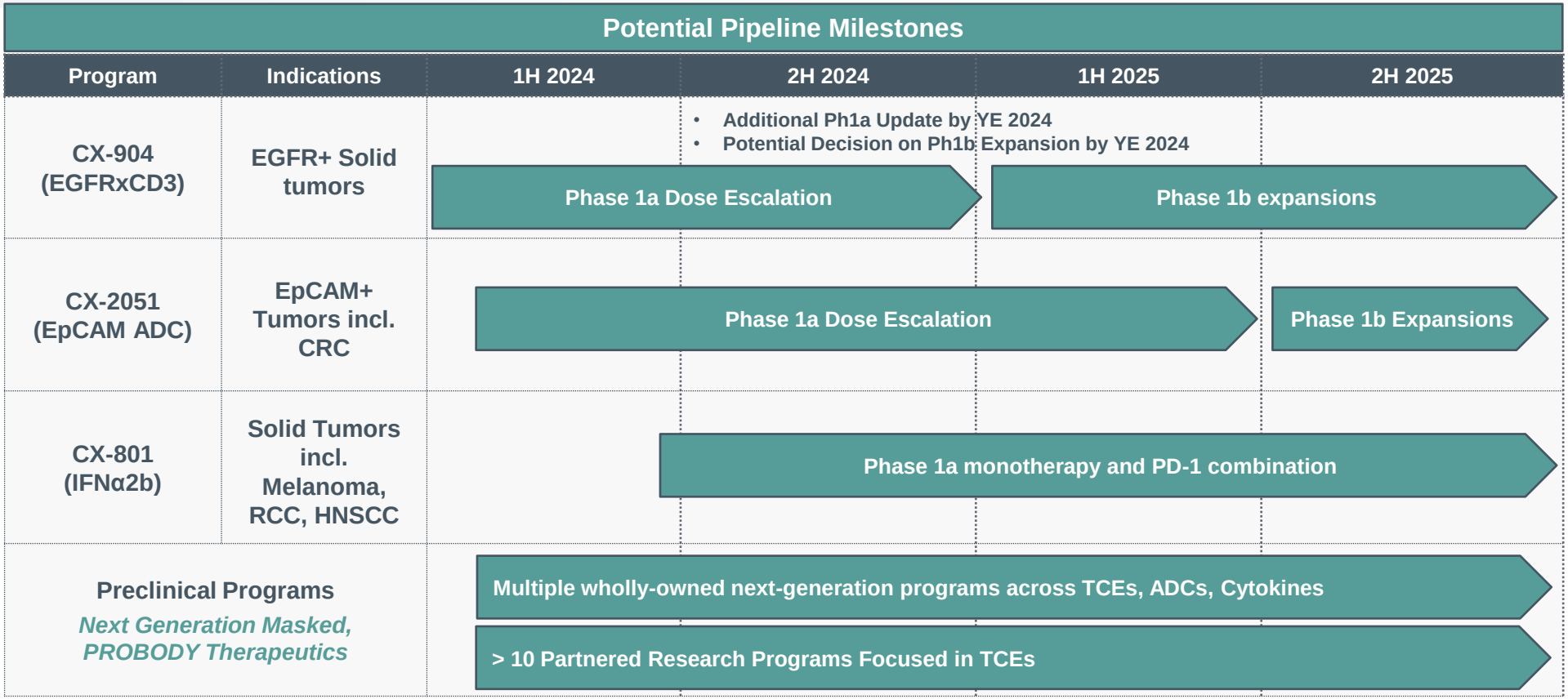
CytomX Therapeutics

Sources: Surveillance and Health Equity Science, American Cancer Society (2023 stats) & SEER through National Cancer Institute. 2023 Cowen Therapeutics Categories Outlook

Sources: [1] Forster, et al. 2020; [2]ONIVYDE® Package Insert

CytomX Therapeutics: Building for the Future

Transforming Lives with Safer, More Effective Therapies

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