CytomX Therapeutics

43rd Annual J.P. Morgan Healthcare Conference

Sean McCarthy, *D.Phil.*
Chief Executive Officer and Chairman

January 15, 2025

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.

Company Snapshot

Addressing Major Unmet Need in Oncology

CytomX® THERAPEUTICS

South San Francisco, CA

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

Clinical Programs:

- **Wholly-Owned:** CX-2051 (EpCAM ADC) and CX-801 (IFN-α2b)
- **Partnered:** CX-904 (EGFR-CD3) – Amgen Co-development

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

Financials: ~$118M cash balance as of Q3 2024 with cash runway into Q2 2026, excluding any potential milestones or new business development

Organization: ~70 employees; integrated R&D capabilities

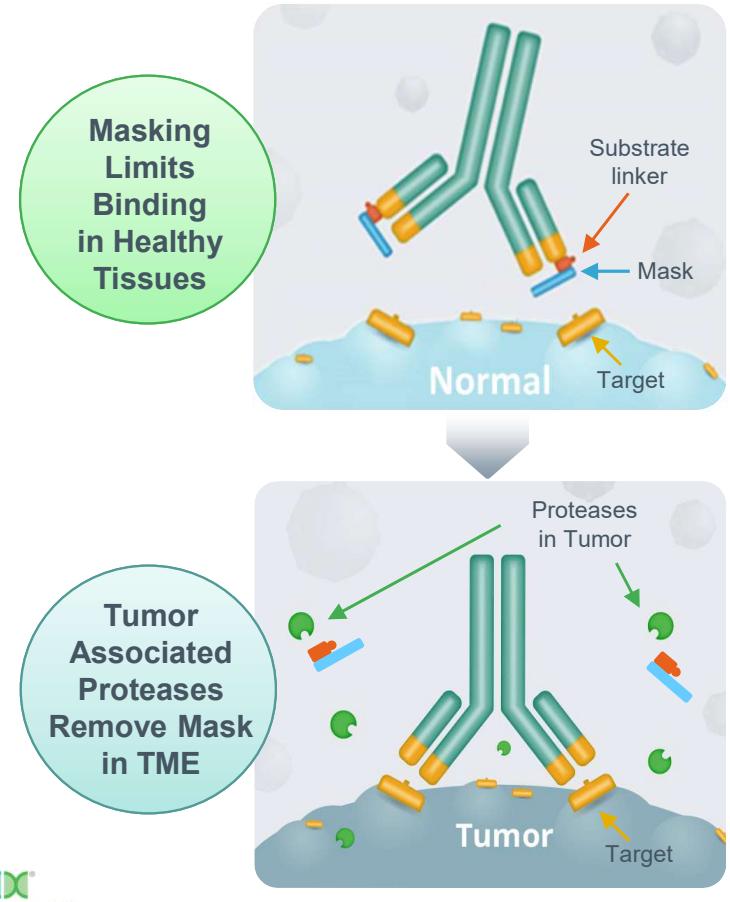
Multi-Modality Pipeline of Masked PROBODY® Therapeutics

2025 Priority Focus on Development of CX-2051 (EpCAM ADC) in CRC

Product Candidate	Target	Indication	Phase 1a	Phase 1b/2	2025 Milestones	Commercial Rights
CX-2051	EpCAM	Advanced CRC			❑ Initial Phase 1 data in CRC in the first half of 2025 ❑ Determine Phase 1b dose(s)	CytomX
CX-801	IFN-α2b	Advanced Melanoma			❑ Initiate Keytruda® combination ❑ Initial Phase 1 data in advanced melanoma in the second half of 2025	CytomX
CX-904	EGFRxCD3	EGFR+ Solid Tumors			❑ Plans for Ph1a completion and potential Ph1b are pending resourcing and discussions with development partner, Amgen	Amgen / CytomX

— Clinical pipeline entering a data rich period in focused indications with high unmet need —

PROBODY® Platform Technology Enhances Therapeutic Index for Potent Biologics By Reducing On Target Toxicity



The First Masking Platform to:

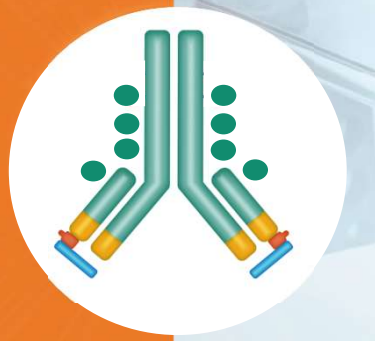
- ✓ Demonstrate clinical responses
- ✓ Demonstrate molecular activation in patient biopsies
- ✓ Achieve TCE clinical responses with minimal CRS

Industry Leading Platform Expertise:

- ✓ Clinically validated & proprietary substrate library
- ✓ Multiple fit-for-purpose proprietary masking technologies
- ✓ Application across multiple modalities (T-cell engagers, Antibody Drug Conjugates, Cytokines)

CytomX® Therapeutics

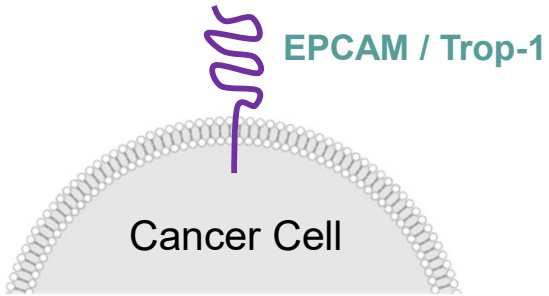
CytomX® THERAPEUTICS

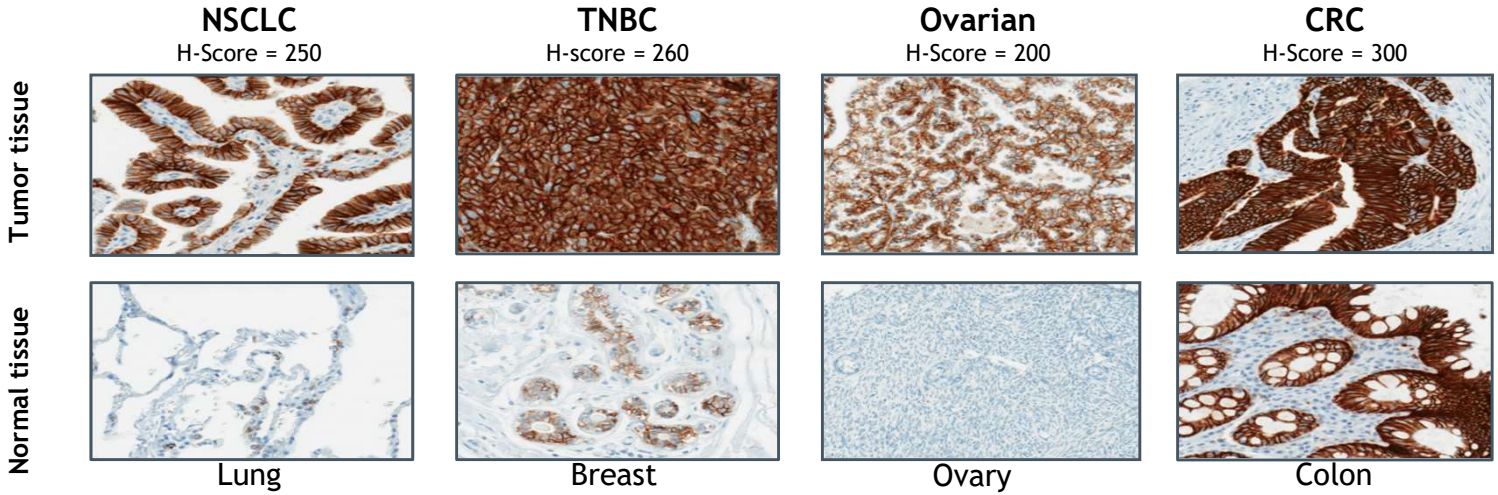


CX-2051: Masked PROBODY® ADC Targeting EpCAM

EpCAM (Epithelial Cell Adhesion Molecule) has Potential as a Pan-Tumor ADC Target with High Expression in Colorectal Cancer (CRC)

- **EpCAM highly expressed on cancer cells**
- **Moderate expression in normal tissue**
- **Functional role in cancer signaling**





EpCAM Has Been Clinically Validated But Not as a Systemic Therapy

Systemic therapies limited by high grade gastrointestinal toxicities

Locally administered EpCAM therapies have been validated in the clinic

- **Vicineum™ fusion protein:** anti-EpCAM scFv linked to a truncated form of Pseudomonas exotoxin A
- Delivered by intravesical administration
- ~40% 3-month complete response in bladder cancer

Sesen Bio

- **Removab®:** EpCAM x CD3 bispecific
- Delivered by intraperitoneal infusion
- Approved for treatment of malignant ascites
  - Being relaunched in Europe by Pharmanovia

Insys Therapeutics

Prior systemic EpCAM approaches discontinued due to on-target toxicity

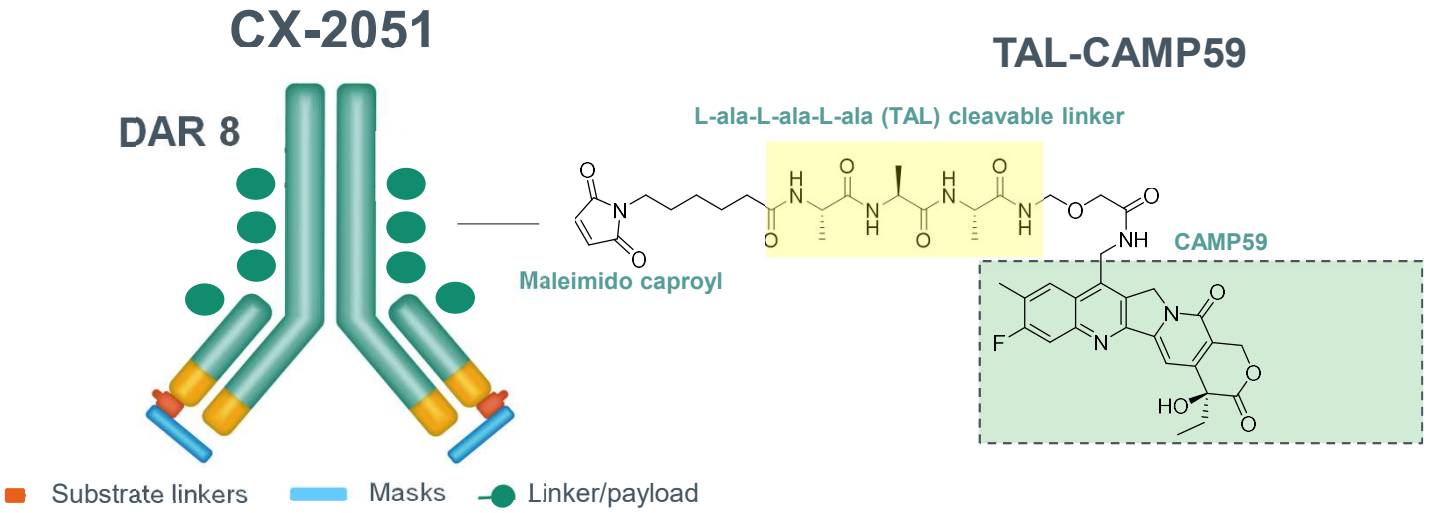
Asset	Company	MOA	Phase	DLTs*
Solitomab	Amgen	EpCAM x CD3 BiTE	1	• Grade 3+ diarrhea from upper GI inflammation • Grade 3+ elevation in liver enzymes
ING-1	XOMA	EpCAM mAb	1	• Pancreatitis
3622W94	GSK	EpCAM mAb	1	• Pancreatitis

**Sources: Kebenko, et.al. 2018; de Bono, et. al. 2004*

CytomX Therapeutics

CX-2051: A First in Class EpCAM Targeting ADC

Topo-1 inhibitor payload selected for EpCAM-expressing indications including CRC



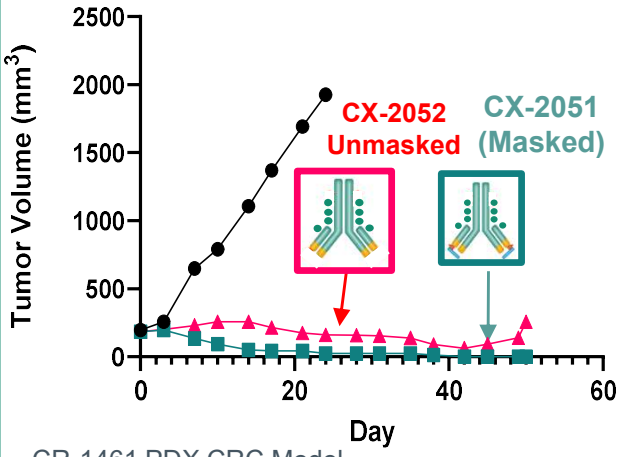
- High affinity EpCAM antibody with masking efficiency >100x by ELISA
- Validated protease-cleavable linker and with broad cleavability across multiple tumors
- TAL payload-antibody linker designed to have similar cleavability profile as deruxtecan (DXd) and optimized for bystander effect
- CAMP59 payload shows similar potency to DXd in multiple cell lines and preclinical models including CRC

Sources: Wei Let, et. al 2019, CytomX Internal Data

CX-2051 Leverages Masking to Open a Therapeutic Window for EpCAM

Masking designed to mitigate on target EpCAM toxicities

Equivalent Efficacy



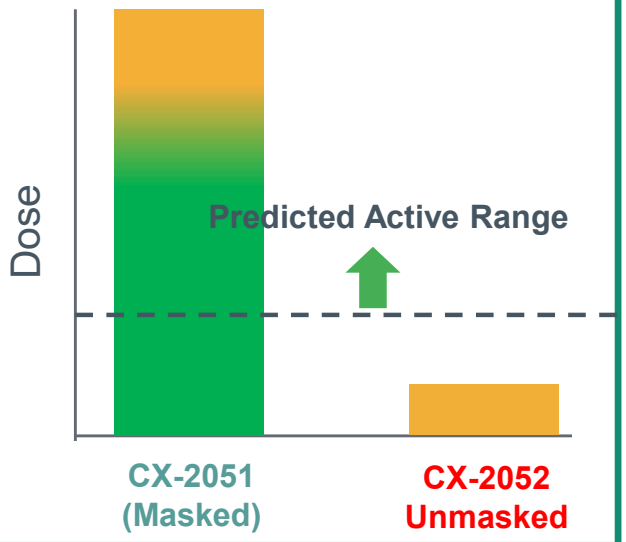
CR-1461 PDX CRC Model
Dosing regimen: 6 mg/kg Q2W x 3

Improved Tolerability

Dose (Q2Wx3)	CX-2051 (Masked)	CX-2052 (Unmasked)
90 mpk	Not tolerated	
60 mpk	Tolerated	
30 mpk	Tolerated	
10 mpk	Tolerated	Not tolerated

NHP Pilot tox

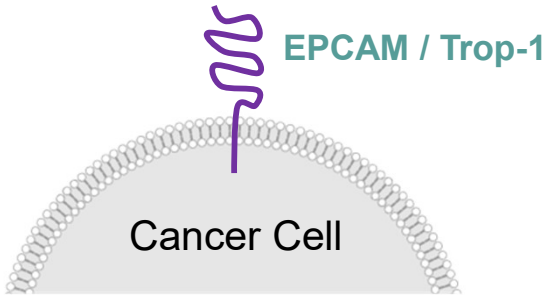
Open Therapeutic Window

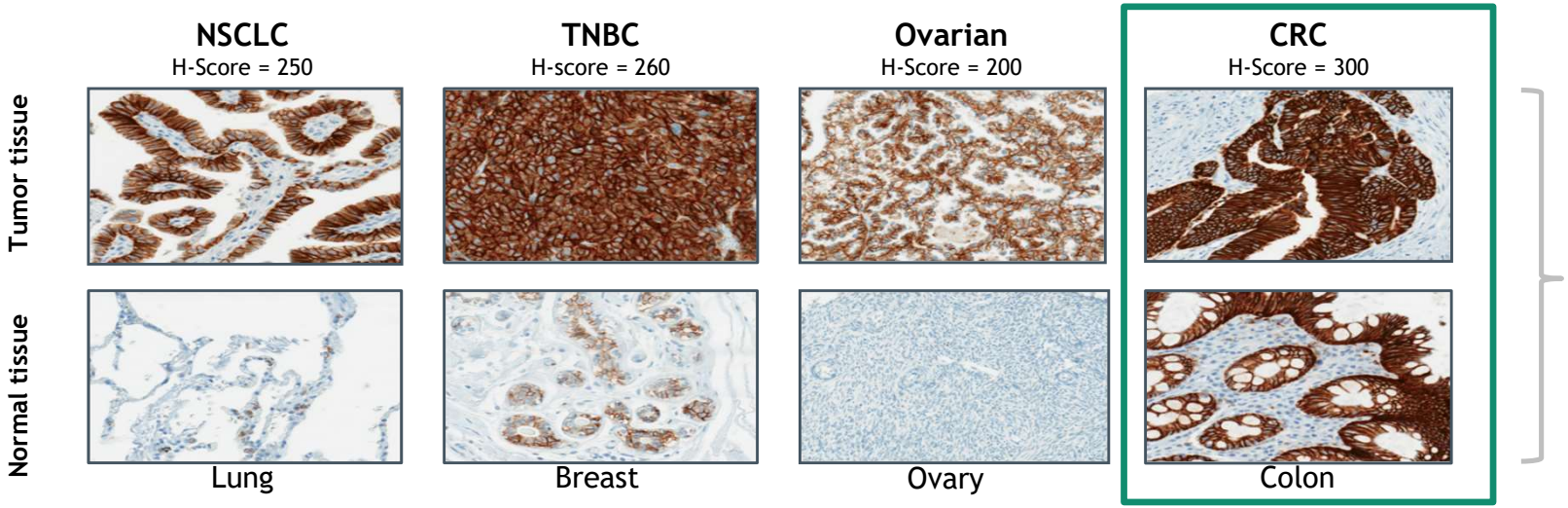


*Sources: World ADC 2023, CytomX Internal Data

CX-2051 Development Strategy Initially Focused in CRC

- **EpCAM highly expressed on cancer cells**
- **Moderate expression in normal tissue**
- **Functional role in cancer signaling**





Masked PROBODY ADCs are designed to preserve the therapeutic index when target is expressed in normal tissue

CytomX Therapeutics

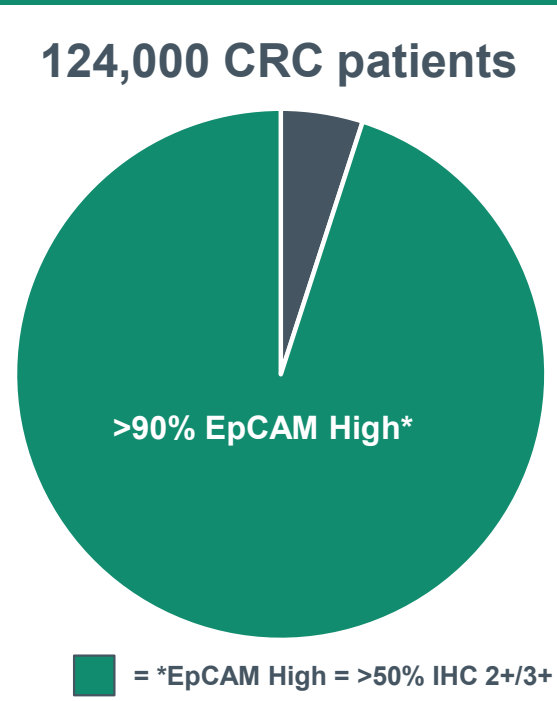
The CRC Market is Large with Significant Unmet Need

EpCAM expressed at high levels in >90% of patients

Significant Unmet Need In Colorectal Cancer

- 124,000 CRC drug treatable cases in the U.S. annually
- Over 90% of CRC cases estimated to have high EpCAM expression
- CRC is 2nd leading cause of cancer death in the U.S.
- Increased incidence and mortality in patients 50 years and younger
- Increasing percentage of CRC cases classified as advanced at diagnosis

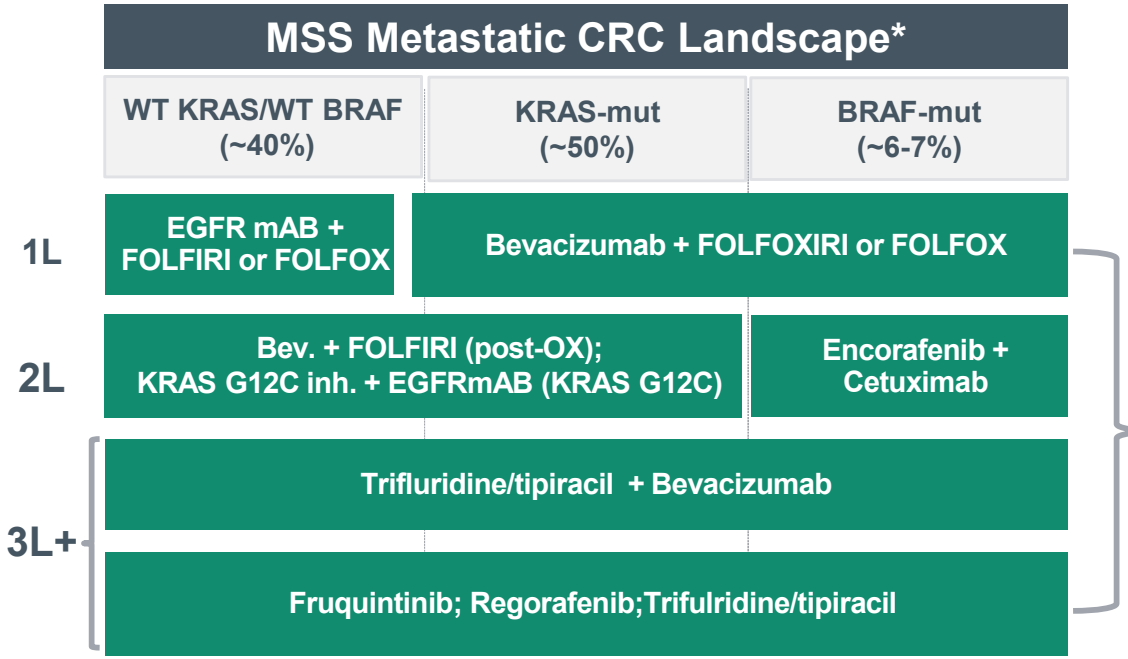
CX-2051
Initial Development Focus in CRC



Sources: Siegel, et. al, 2023, American Cancer Society, Colorectal Caner Statistics, 2023; 2029 Drug-treatable patient by tumor type from DRG
CytomX Internal prevalence study, EpCAM High ≥50% cells with 2+/3+ EpCAM Intensity

CRC Treatment Landscape

CX-2051 has the potential to be a foundational CRC therapy



*Excludes HER2 and NTRK mutations estimated at 5 – 7% of patients

CX-2051 CRC Development Opportunities

- ❖ Replace irinotecan (IRI) in 1L/2L
- ❖ Novel combinations
- ❖ Monotherapy, e.g. in late-line CRC

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Source: Package Inserts; Epidemiology data source: DRG

Significant Unmet Need and Poor Patient Outcomes in Late-line CRC

Treatment	Treatment Line	ORR (%)	DCR (%)	Median PFS (months)	Median OS (months)
Trifluridine/tipiracil	3L+	2%	44%	2.0	7.1
Trifluridine/tipiracil + Bevacizumab	3L	6%	77%	5.6	10.8
Regorafenib	2/3L+	1%	41%	2.0	6.4
Fruquitinib	4L	2%	56%	3.7	7.4

- **Single Agent ORR in 4th line CRC in low single digit percentages and less than 4 months progression free survival (PFS)**
- **CX-2051 could potentially improve upon the approved standard of care in 3L/4L+ CRC**
- **Future combinations provide opportunity to move to earlier lines of therapy**

CytomX® THERAPEUTICS

Sources: Lonsurf®, Fruzaqla®, Stivarga® package inserts.

CX-2051 Phase 1 Designed to Demonstrate Proof of Concept in CRC

Study commenced Q2 2024. Encouraging progress to date. Escalation continues.

CTMX-2051-101 Overview

Part 1:Dose Escalation; Part 2: Dose Expansion

Patient Population:

- Metastatic or locally advanced, unresectable disease
- Measurable disease by RECIST v1.1
- Unselected for EpCAM expression
- No prior treatment with Topo-1 ADC

Primary Objectives:

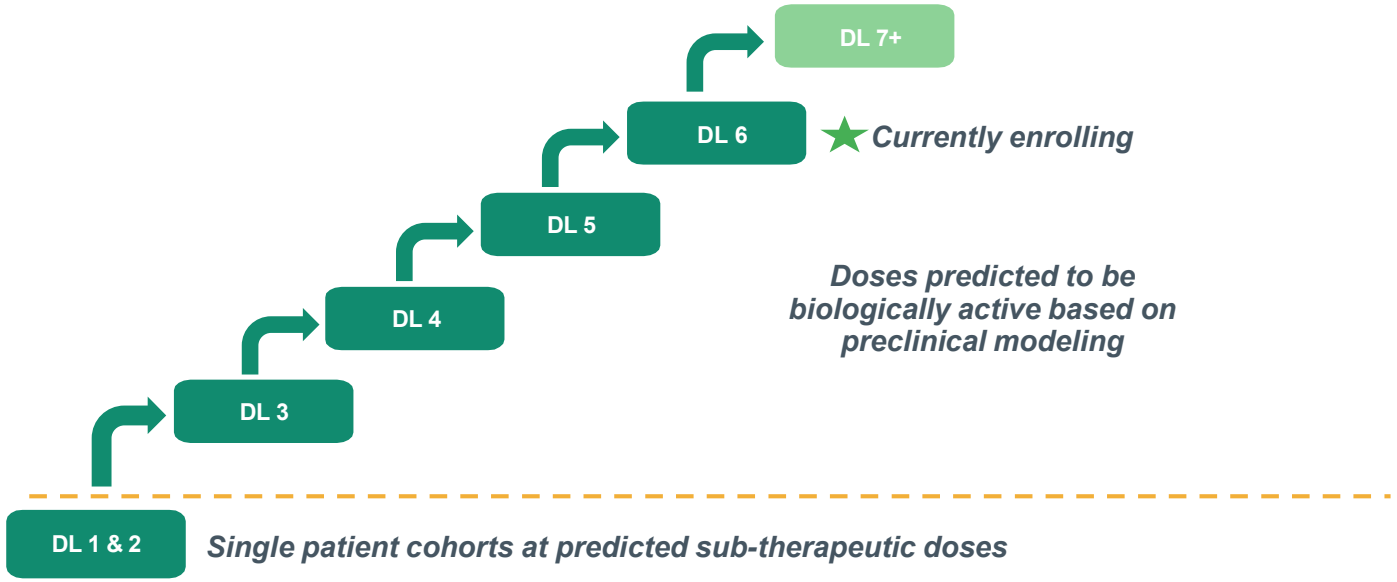
- Safety and tolerability of CX-2051
- Determine the recommended Phase 2 dose (RP2D)

Secondary Objectives include:

- Objective response rate, Duration of response, Progression free survival, Disease control Rate, Overall survival

Part 1: Phase 1 Dose Escalation, Q3W

- ***Enrolling unselected, advanced CRC, generally 4L+***
- ***Currently enrolling 6th dose level; limited backfilling initiated***
- ***Current dose levels (DL) predicted to be in biologically active range***
- ***MTD/RP2D expected to be driven by potential Topo-1 payload toxicities including cytopenias, nausea/vomiting, diarrhea***



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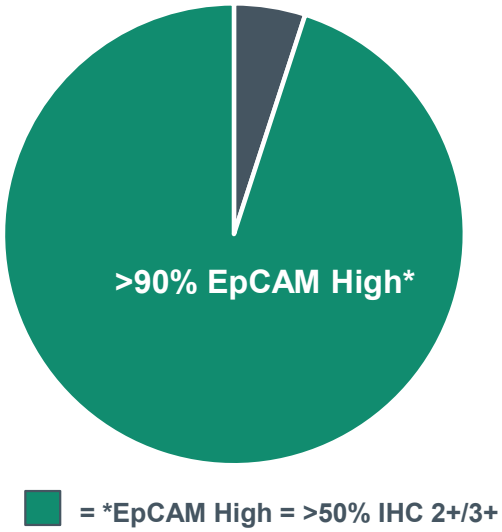
Beyond CRC: CX-2051 is a “Pipeline in a Product” Opportunity

Broad development potential in EpCAM+ indications

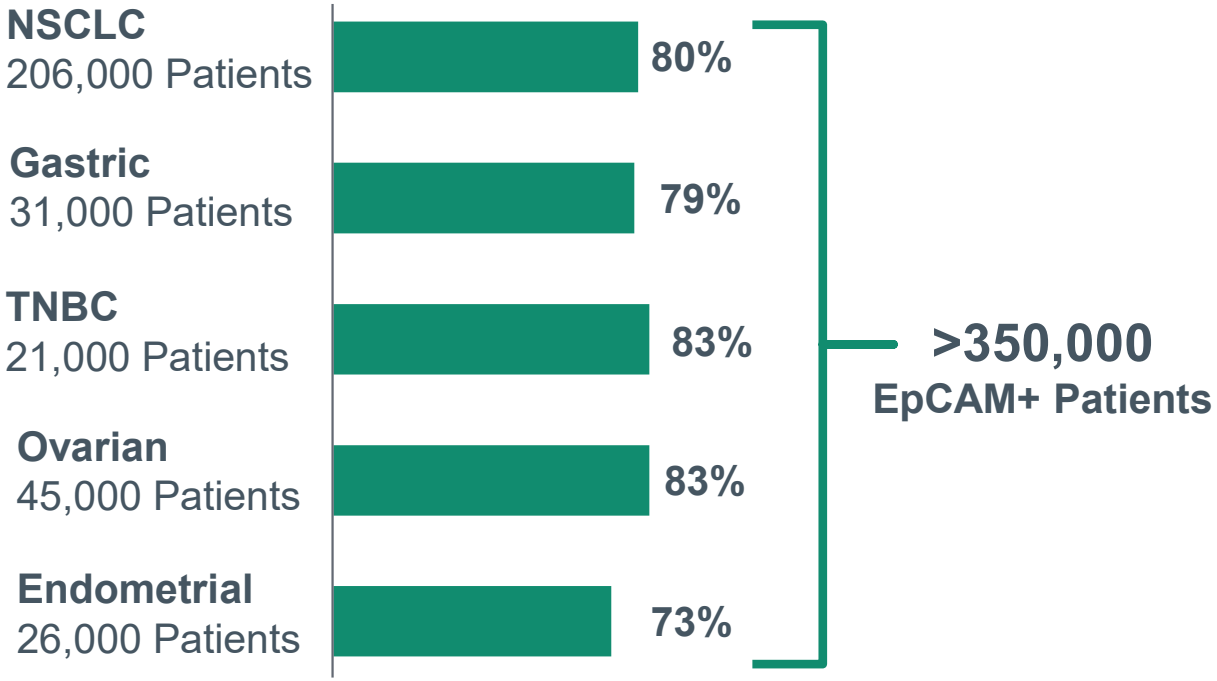
Initial Development Focus in CRC

124,000 CRC patients



Potential Future Development Areas

% of Patients with EpCAM High Tumors (>50% IHC ≥ 2+/3+)



CytomX Internal prevalence study, ≥50% cells with IHC 2+/3+ EpCAM Intensity
2029 Drug-treatable patient by tumor type from DRG

CX-2051 Phase 1a Goals & Next Steps

2025 Goals:

- Continued Phase 1 Dose escalation and potential backfills focused in advanced metastatic CRC
- Initial Phase 1 data in advanced metastatic CRC in first half of 2025
  - **Safety:** Determine safety/tolerability profile, including characterization of on-target and payload toxicities
  - **Efficacy:** Initial signs of disease control and tumor reductions
- Determine Phase 1b dose(s)

Additional Development Opportunities:

- CRC combinations including in earlier lines of therapy
- Additional EpCAM-expressing indications beyond CRC, potentially selecting for EpCAM expression level

CytomX® THERAPEUTICS

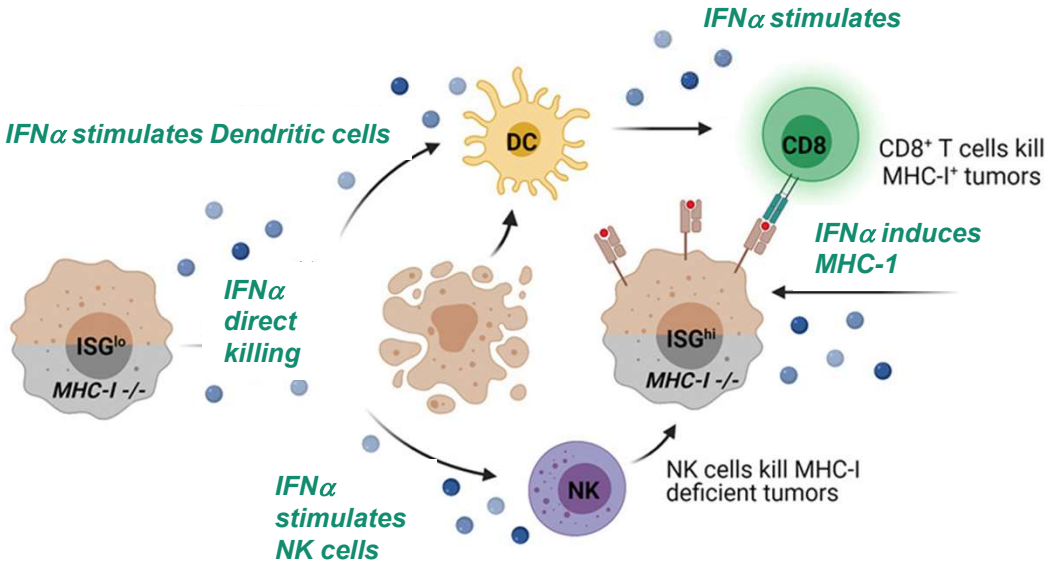
CX-801: Masked PROBODY® Cytokine, IFNα-2b

IFNα-2b is a Powerful Cancer Immunotherapy With a Dual Mechanism of Action and Ideal Properties to Combine with PD-1 Therapy

Why IFNα-2b?

Mechanism of Action

- IFNα-2b provides an **orthogonal activity to IL-12, IL-2 and IL-15** in the cancer immunity cycle
  - IFNα-2b can **kill cancer cells directly** leading to immunogenic cell death, and
  - IFNα-2b **stimulates antigen presenting cells to activate T cells** – *distinct from IL-2, IL-12, and IL-15 that are restricted to proliferative effects via IFNγ*
- Approved for treating melanoma (Sylatron™), renal (Avastin® + IFN), and bladder cancer (Adstiladrin®)
- Potential to treat **CPI-resistant indications**



Adapted from Green et al., Mol. Ther. Onc. 2021

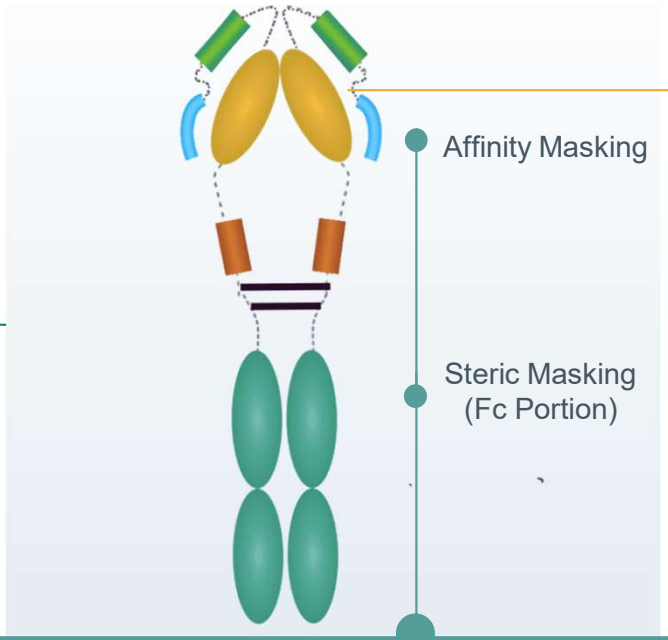
CX-801: Dually-Masked, Conditionally Activated PROBODY® IFNα2b

TARGET

Validated, High Potential Target

- Approved immunotherapy in multiple tumors
- Enhanced anti-cancer activity in combination with PD-1
- Limited clinical use due to poor tolerability

CX-801



EFFECTOR

IFNα2b

- Dual-mechanism of action
- Proven single agent activity
- Increases APCs to enhance PD-1 blockade

PRODOMAIN

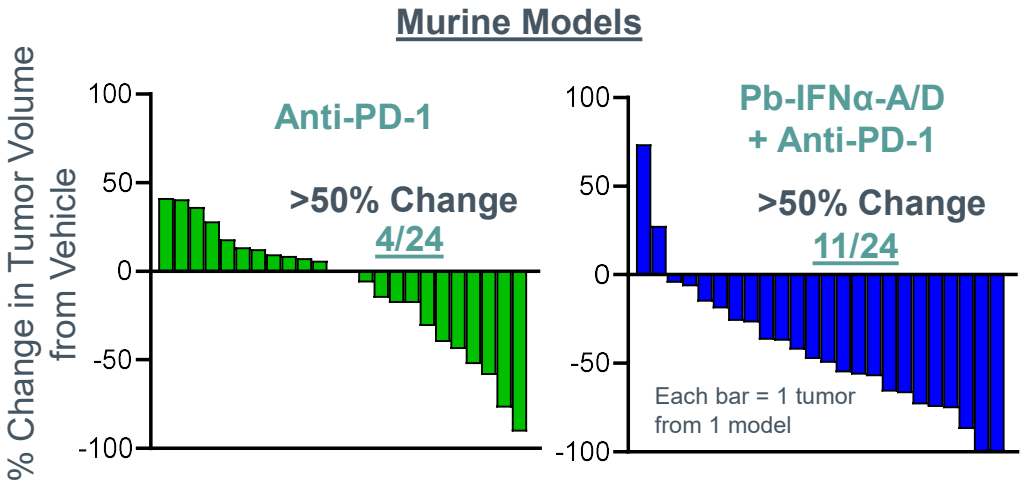
Masking & Substrates Design Strategy

- Dual-masking strategy with steric and affinity mask (peptide)
- 1000X masking efficiency based on preclinical models
- Preclinically, Probody IFNα is effectively unmasked in the tumor

CytomX Therapeutics

CX-801 Preclinical Profile Suggests Clinical Synergy with PD-1 and Enhanced Safety Compared to Unmasked IFNα2b

Single Agent and Synergistic Activity with PD-1 Observed with Probody IFNα2B in Preclinical Models



Masking of IFNα Significantly Increases Tolerability and Lowers Peripheral Activity

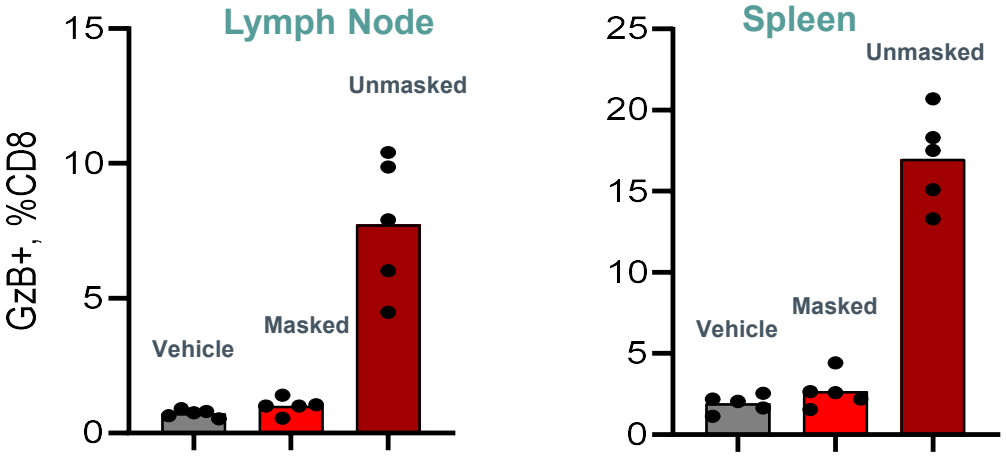
Dose	Pb-IFNa-A/D (Masked)	IFNa-A/D (Unmasked)
2400 μg	Not tolerated	
1200 μg	Tolerated	
500 μg	Tolerated	
20 μg		Not Tolerated
5 μg		Tolerated

Source: Povinelli, et. al. SITC 2023

CX-801 Preferentially Inflames the Tumor Microenvironment and Demonstrates Synergistic Activity with Anti-PD-1

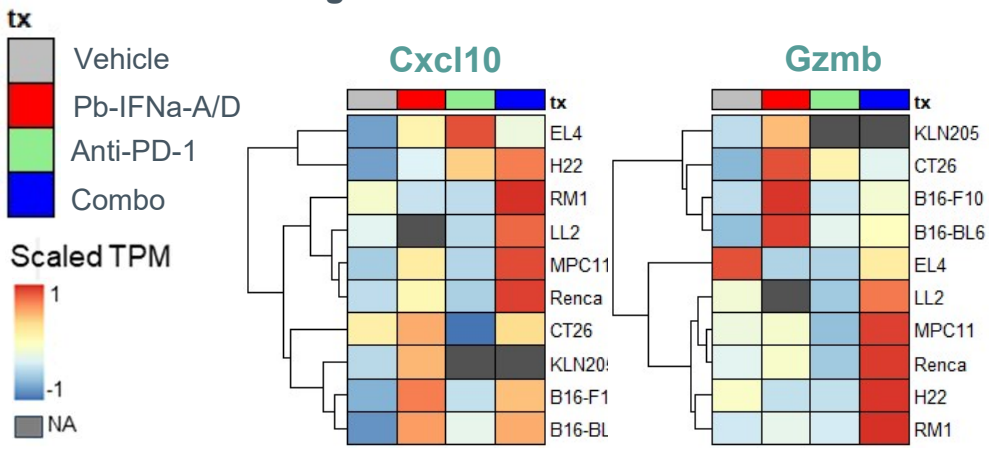
CX-801 Stimulates T-Cell Activation Preferentially to Tumor Microenvironment

T-cell Activation



RNA-seq from Tumors

IFN stimulated genes and markers of T-cell activation

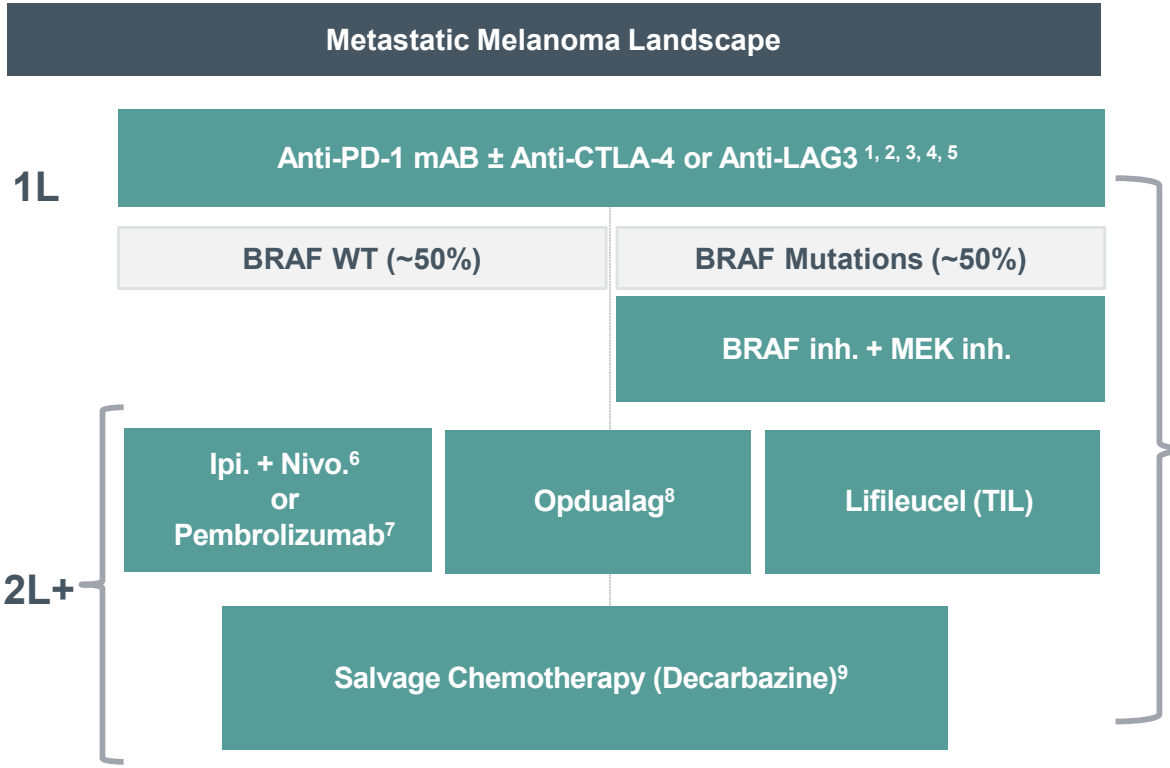


Phase 1 translational data key focus for clinical proof of concept

Source: Povinelli, et. al. SITC 2023

High Unmet Need in PD-1 Refractory Melanoma Patients

CX-801 has potential to enhance responsiveness to checkpoint inhibitors



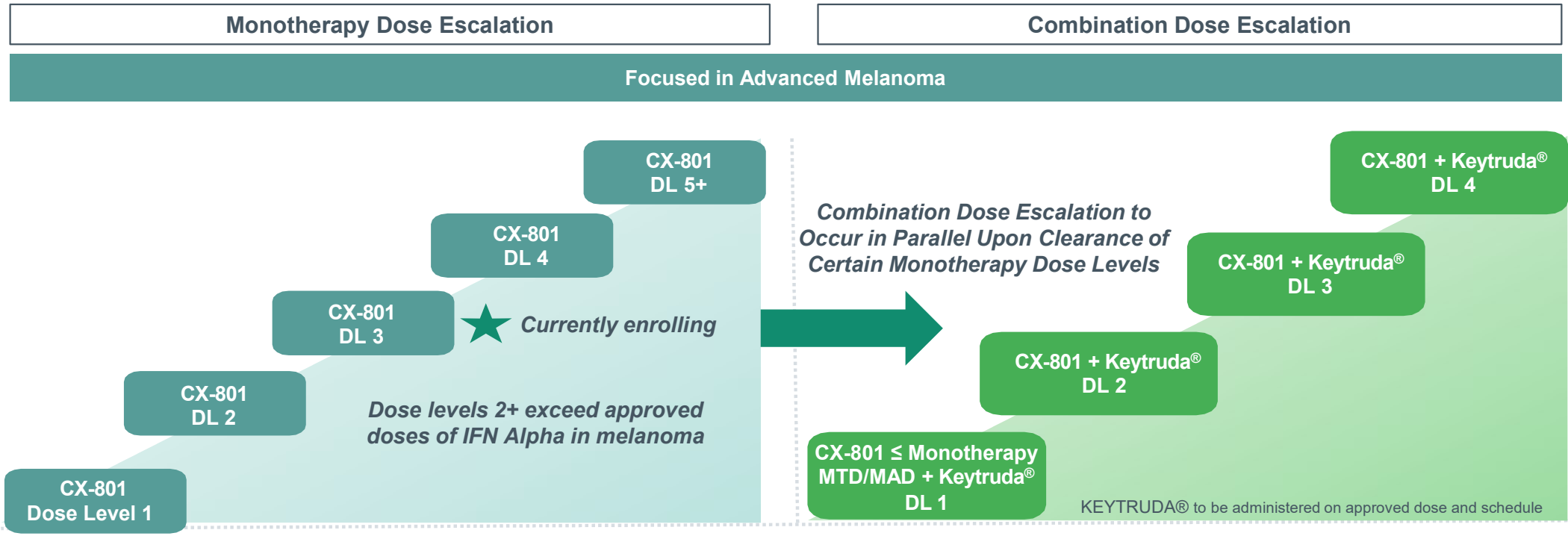
CX-801 Development Opportunities in Melanoma

- Combine with anti-PD-1 inhibitors in post-PD-1 setting
  - Improve on activity of PD-1 inhibitors (7% ORR)[10]
  - Safe and tolerable alternative to TIL therapy
- Novel IO combinations to enhance activity in earlier-line settings

CytomX Therapeutics

[1] Robert et al. 2015; [2] Robert et al. 2023; [3] Tawbi et al. 2022; [4] Wolchock et al. 2017; [5] Wolchock et al.2022; [6] VanderWalde et al.; [7] Olson et al. 2021 2023; [8] Ascierto et al. 2023; [9] Robert et al. 2011

Phase 1 Dose Escalation is Designed to Assess CX-801 Clinical Profile as Monotherapy and in Combination with KEYTRUDA®



- **Announced 1st Patient Dosed in September 2024**
- **Initial CX-801 Phase 1 translational data expected in the 2nd half of 2025**

CytomX Therapeutics

Source: Package Insert - SYLATRON™

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

CX-801 Phase 1a Goals & Next Steps

2025 Goals:

- Continued Phase 1 Dose escalation as monotherapy
- Initiate CX-801 combination with KEYTRUDA®
- Initial Phase 1 data in advanced melanoma in the second half of 2025
  - **Safety:** Determine safety/tolerability profile including vs. unmasked interferon
  - **Efficacy:** Translational and pharmacodynamic data consistent with interferon MOA

Additional Development Opportunities:

- Earlier lines of therapy in melanoma in combination with PD-(L)1
- Other indications with known clinical activity such as RCC and HNSCC
- Indications not responsive or refractory to immunotherapies

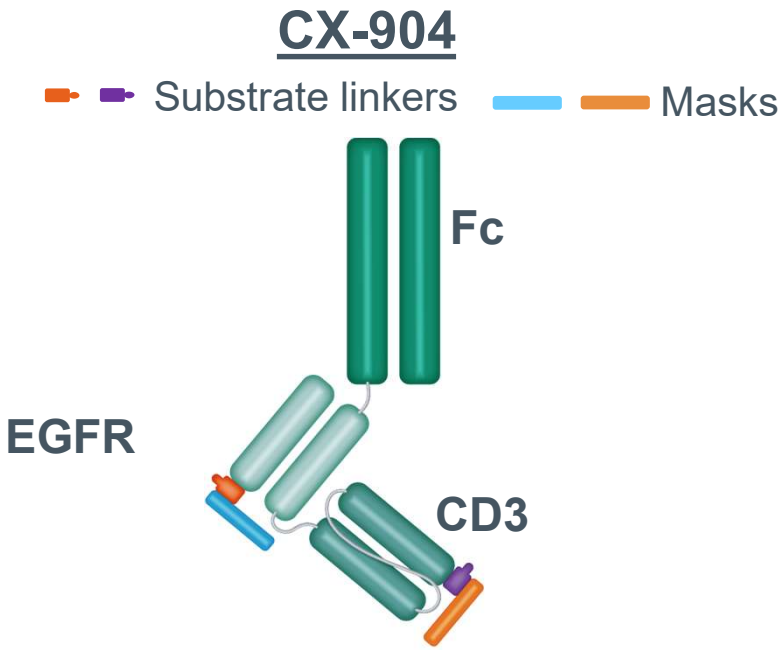
CytomX® THERAPEUTICS

AMGEN

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

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

Format and therapeutic concept



- Finely tuned masks and protease substrates
- Distinct “Prodomains” on EGFR and CD3 to optimize therapeutic window
- Fc domain to mimic PK of approved T-cell engagers

TCE Designed to Address EGFR+ Tumors

- Prevalent EGFR expression in many cancer types
- CX-904 masked EGFR TCE designed to address large unmet need and market opportunity
- Initial Phase 1a safety and monotherapy activity demonstrated supportive of masking
- Opportunity to combine with immunotherapy or other targeted agents

CytomX® THERAPEUTICS

CX-904 Phase 1a Current Status

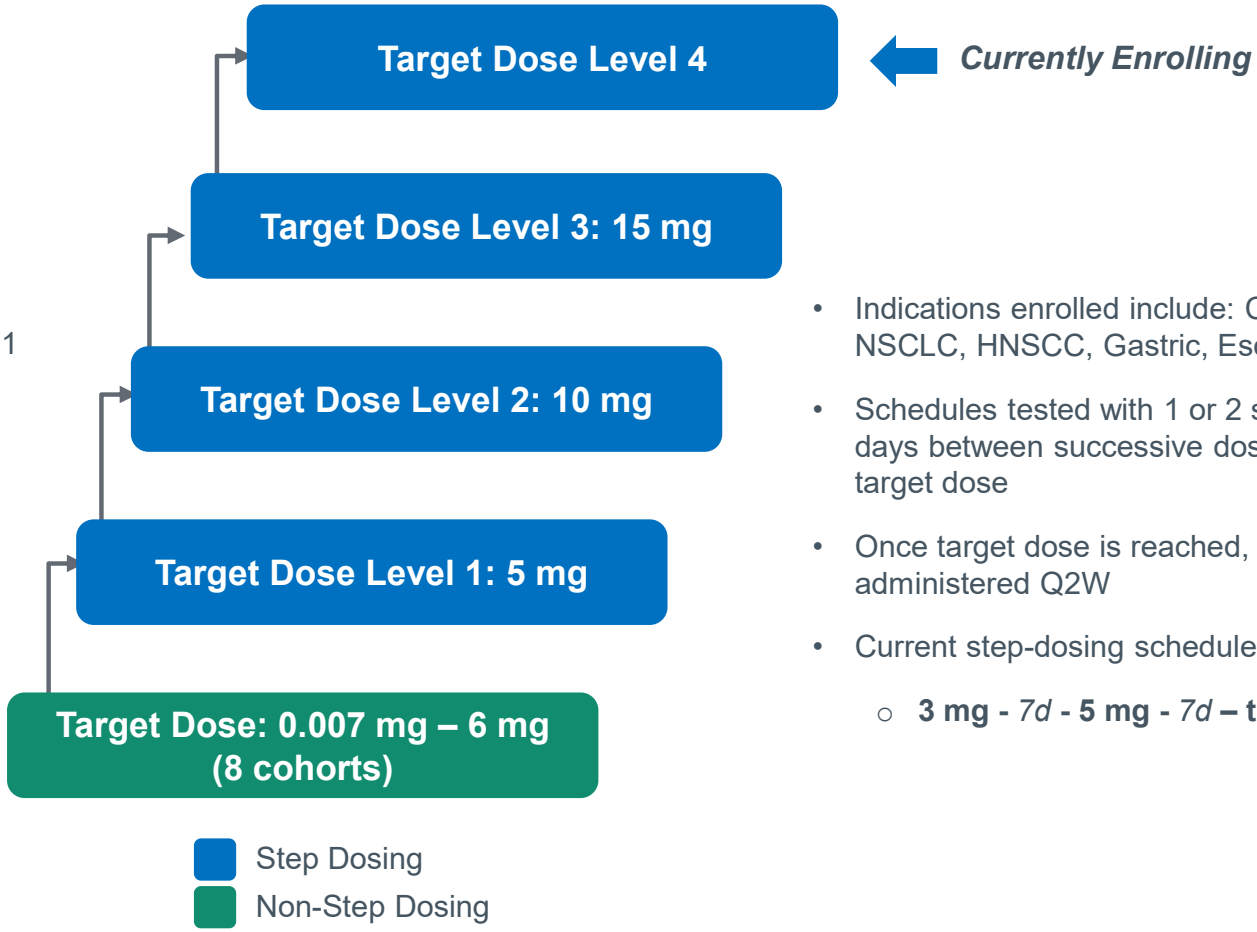
>70 Patients enrolled to date, current focus on escalating to higher doses

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



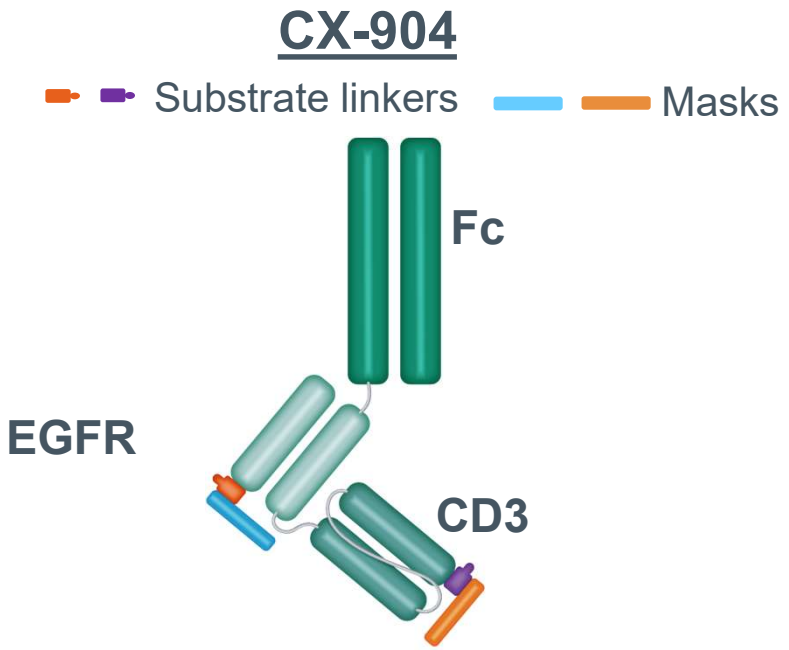
- Indications enrolled include: CRC, PDAC, NSCLC, HNSCC, Gastric, Esophageal
- Schedules tested with 1 or 2 steps with 7 or 14 days between successive doses to achieve target dose
- Once target dose is reached, subsequent doses administered Q2W
- Current step-dosing schedule:
  - **3 mg - *7d* - 5 mg - *7d* – target dose**

Source: 1.CytomX Internal Data

CytomX Therapeutics

CX-904 Phase 1 Summary & Next Steps

- Over 70 patients enrolled to date. The 15 mg target step-dose level has been cleared and the maximum tolerated dose has not been reached.
- Current and 2025 enrollment prioritizing escalation to higher dose levels based on ongoing clinical observations to-date.
- Plans for Phase 1a completion and potential advancement to Phase 1b are pending ongoing consideration of 2025 program resourcing given CytomX current capital constraints and discussions with our partner Amgen.



Company Priorities and 2025 Milestones

Multi-Modality Pipeline of Masked PROBODY® Therapeutics

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CX-904	EGFRxCD3	EGFR+ Solid Tumors			❑ Plans for Ph1a completion and potential Ph1b are pending resourcing and discussions with development partner, Amgen	Amgen / CytomX

— Clinical pipeline entering a data rich period in focused indications with high unmet need —

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CytomX Therapeutics

43rd Annual J.P. Morgan Healthcare Conference

Sean McCarthy, *D.Phil.*
Chief Executive Officer and Chairman

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