CX-2051: A Novel EpCAM-Directed ADC

Phase 1 Interim Clinical Data in Advanced Colorectal Cancer

May 12, 2025

Forward-Looking Statements

This presentation may contain projections and other forward-looking statements regarding future events, including those related to CX-2051. 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 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, including CX-2051, 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, including data for CX-2051, 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, including CX-2051; 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.

On Today's Call

Speakers

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

Wayne Chu, MD
Chief Medical Officer

Chris Ogden
Chief Financial Officer

CytomX® THERAPEUTICS

Addressing Major Unmet Need in Oncology

Introduction

Sean McCarthy, D.Phil.
Chairman and CEO, CytomX Therapeutics

Colorectal Cancer Remains One of the Biggest Unmet Needs in Oncology

~1.9M patients per year, increasing to 3M by 2040

2nd leading cause of cancer death worldwide

5-year survival rate of 13% in mCRC

Abbreviation: mCRC = metastatic colorectal cancer. Sources: World Health Organization, interactive data; Biller and Schrag, 2021, JAMA; American Cancer Society

The Current Standard of Care in 3L+ Metastatic CRC Is Highly Inadequate

Poor response rates and limited survival benefit

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

Abbreviations: DCR = disease control rate; ORR = overall response rate; OS = overall survival; PFS = progression free survival.
Sources: Lonsurf® (trifluridine and tipiracil) Fruzaqla® (fruquintinib), Stivarga® (regorafenib) package inserts; Dasari et al. 2023; Grothey et al. 2013; Prager et al. 2023.

Antibody Drug Conjugates are Transforming Cancer Care

CX-2051 aims to bring the promise of ADCs to colorectal cancer

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

Nectin-4 / Bladder

Seagen/Pfizer -
$43B Acquisition

CX-2051*
PROBODY® ADC

EpCAM / CRC

CytomX Therapeutics

ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

HER2 / Breast, Lung**

Daiichi/Astra Zeneca -
2024 Sales ~$3.8B

ELAHERE™
mirvetuximab soravtansine-gynx
injection 100 mg

FRα / Ovarian

Immunogen/AbbVie -
$10B Acquisition

TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

TROP2 / Breast

Immunomedics/Gilead -
$21B Acquisition

CytomX THERAPEUTICS

* CX-2051 is not an approved product and is in an ongoing Phase 1 clinical trial. **Enhertu select indications only. Sources: Company announcements.

Today's Update: Positive Phase 1 Clinical Data Observed for CX-2051

Pan-CRC Target

High EpCAM expression in all tested tumors

No Patient Selection Needed

Robust Clinical Activity in mCRC*

- 28% confirmed ORR
- 94% disease control
- 5.8 mo. preliminary PFS

Potential New Standard of Care in Late-line CRC

Favorable Safety

- No dose limiting toxicities
- EpCAM target enabled by masking

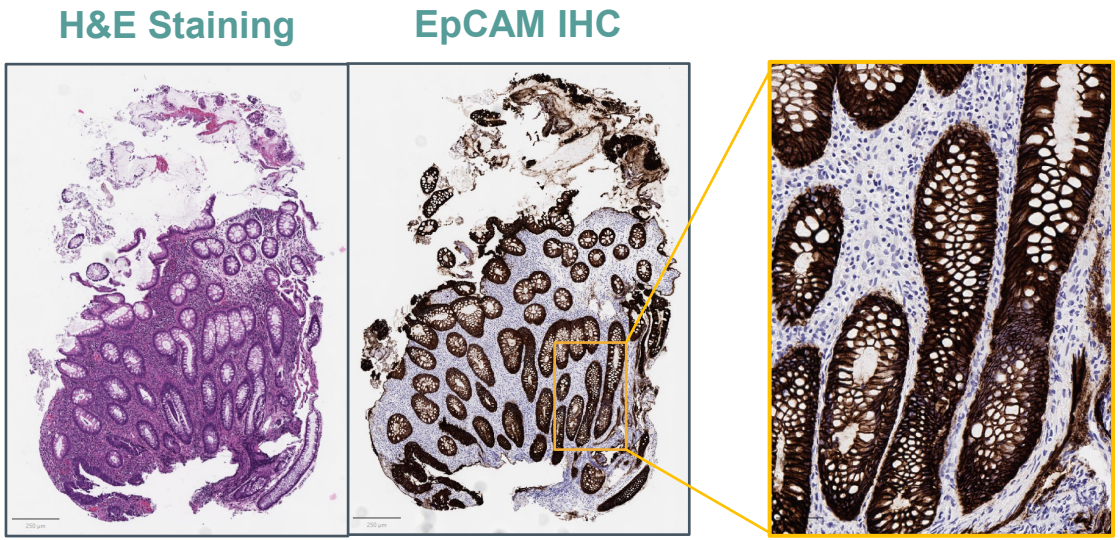
Supports Development of Combinations in Earlier Lines of Therapy

*Based on Interim Data cutoff 4/7/2025

CX-2051 Molecular Design and Phase 1 Clinical Strategy

EpCAM (Epithelial Cell Adhesion Molecule)

An ideal CRC target enabled by the CytomX PROBODY® platform



- **High and uniform expression across CRC**
- **Expression in normal tissues has limited drug development**

IHC Staining of CRC Patient Biopsy from Ongoing Phase 1 Study

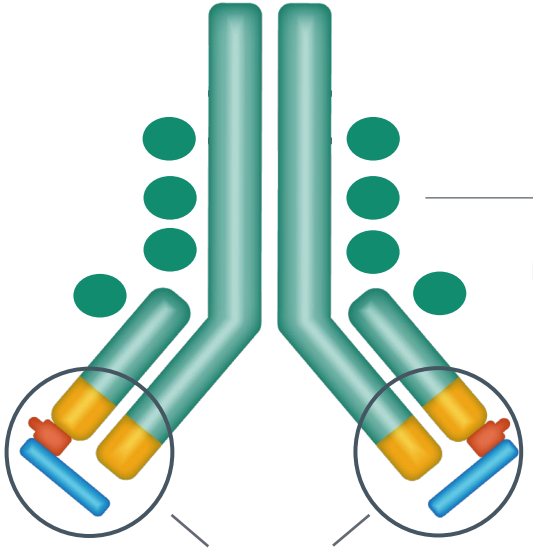
Maximum H-score of 300 (100% cells 3+ by IHC)

Abbreviations: IHC = immunohistochemistry; H&E = hematoxylin and eosin. Source: CytomX Internal Data, CTMX-2051-101 Study Patient Biopsy.

CX-2051: A Novel EpCAM Targeting ADC

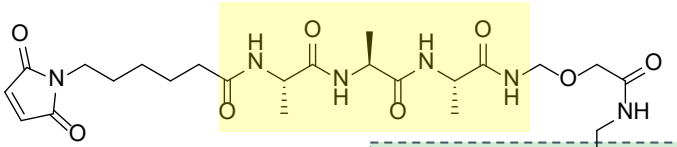
The Right Target, The Right Payload

DAR 8



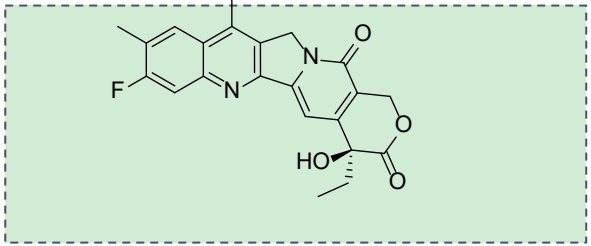
TAL-CAMP59

L-ala-L-ala-L-ala (TAL) cleavable linker



Maleimidocaproyl

CAMP59



Masking domains designed to reduce EpCAM binding in normal tissues

Abbreviations: DAR = drug antibody ratio. CX-2051 antibody and linker-payload licensed through collaboration with Immunogen.

CX-2051 Phase 1 Dose Escalation Study Current Status

Focused in late-line mCRC. Dose expansions in progress.

CX-2051 Administered Q3W

Study Commenced April 2024

Patient Data Presented Today:

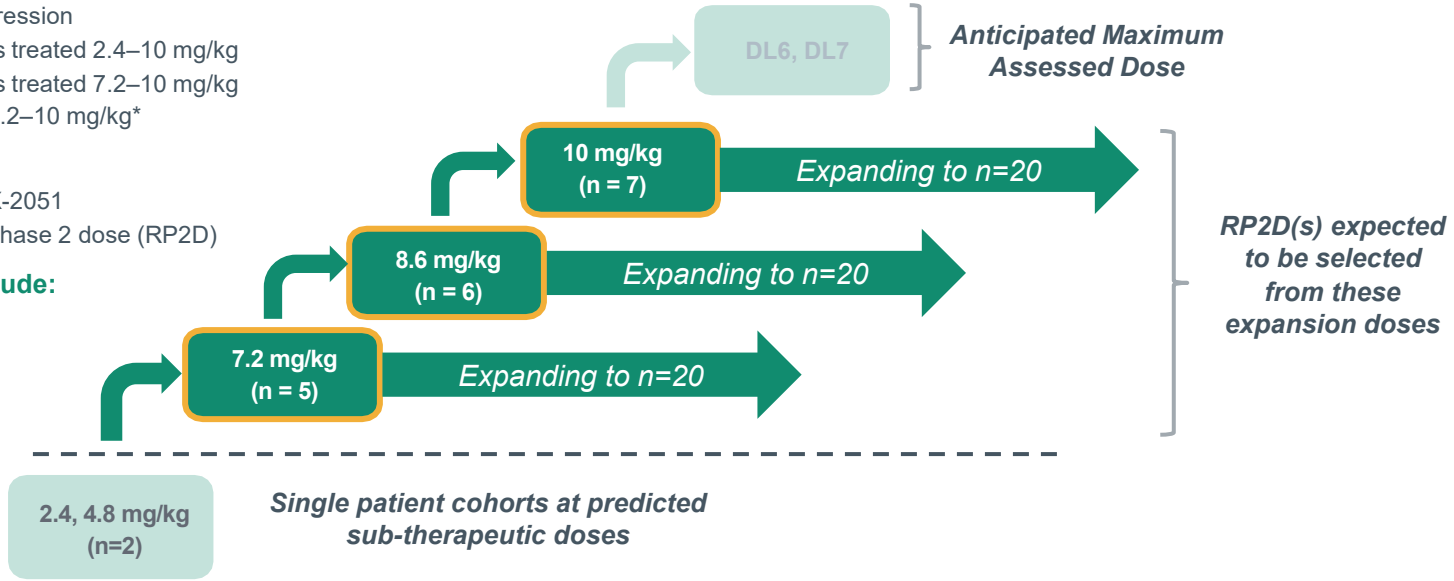
- Unselected for EpCAM expression
- 25 safety-evaluable patients treated 2.4–10 mg/kg
- 23 safety-evaluable patients treated 7.2–10 mg/kg
  - 18 efficacy-evaluable at 7.2–10 mg/kg*

Primary Objectives:

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

Secondary Objectives include:

- Objective response rate
- Disease control rate
- Progression free survival



*5 patients not efficacy-evaluable: 4 pts on treatment that have not reached a post-treatment scan; 1 patient at 10 mg/kg dose discontinued for clinical progression prior to first post-treatment scan.

CX-2051 Phase 1 Interim Results

Wayne Chu, MD
Chief Medical Officer, CytomX Therapeutics

CX-2051 Phase 1 Baseline Characteristics

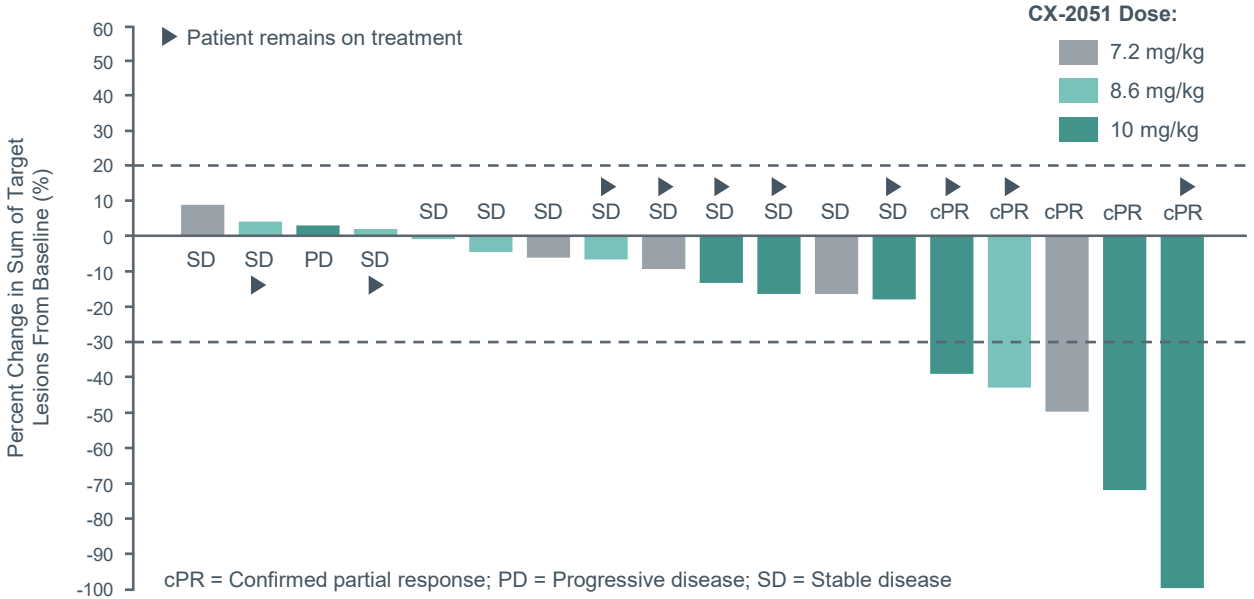
Heavily pre-treated advanced CRC population; median 5th line

Baseline Characteristics	N=25 (Safety evaluable) [1]
Number of prior lines of anti-cancer therapy, median (range)	4 (1-10)
Prior irinotecan, n (%)	25 (100)
Liver metastases, n (%)	16 (64)
KRAS mutation, n (%)	16 (64)
MSS, n (%)	24 (96)

[1] Patients treated with at least one CX-2051 dose between 2.4 mg/kg and 10 mg/kg.
MSS = microsatellite stable.

CX-2051 Anti-Tumor Activity at Doses Selected for Expansion

Confirmed ORR: 28% (5/18) overall, 43% (3/7) at 10 mg/kg



Prior lines of systemic therapy	3	4	9	3	3	4	4	3	6	4	6	3	8	4	5	3	5	10
KRAS mutation (Y/N)	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	N	Y
Liver metastases (Y/N)	Y	Y	Y	Y	Y	N	Y	Y	Y	N	N	N	N	Y	N	Y	Y	Y
Baseline EpCAM H-Score[1]																		

H-Score > 280

Not evaluable

[1] Maximum immunohistochemistry (IHC) H-Score is 300; H-score captures the proportion of EpCAM+ cells in the biopsy and intensity of EpCAM expression.

Data cutoff 4/7/2025

ORR: Overall Response Rate

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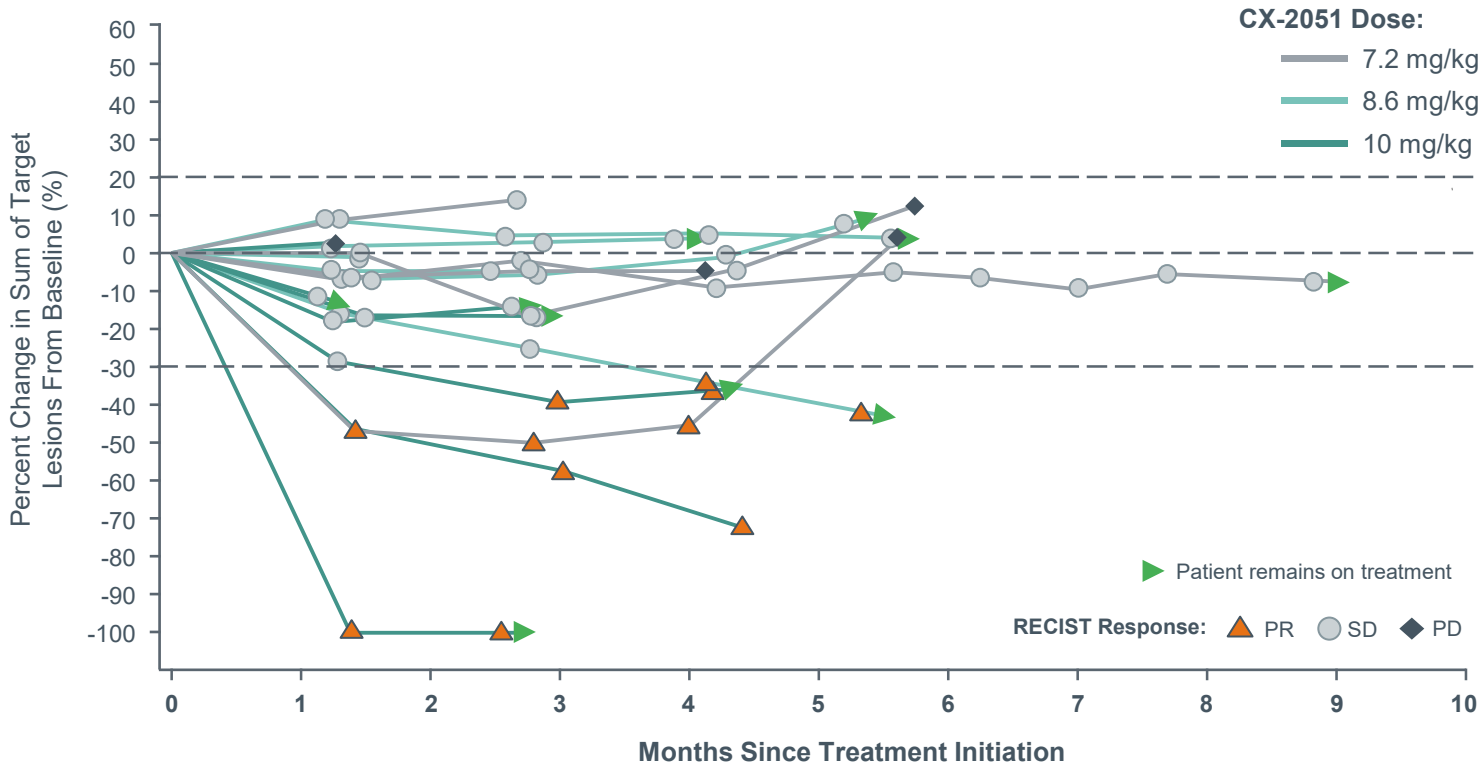
CX-2051 Anti-Tumor Activity 7.2-10 mg/kg

94% (17/18) disease control rate

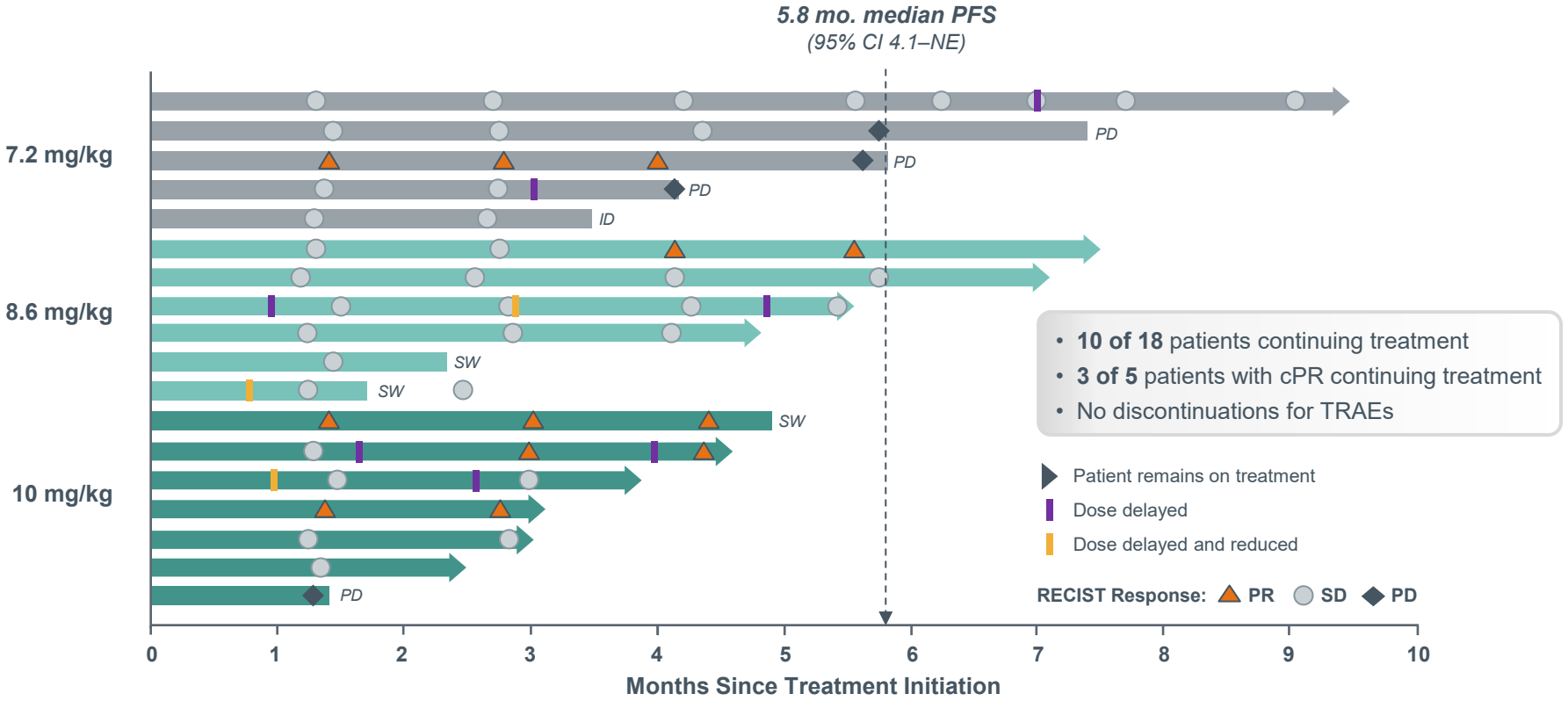


Abbreviations: PD = progressive disease; PR = partial response; SD = stable disease.

Data cutoff 4/7/2025

Emerging Durability Results with CX-2051

Preliminary median progression free survival 5.8 months

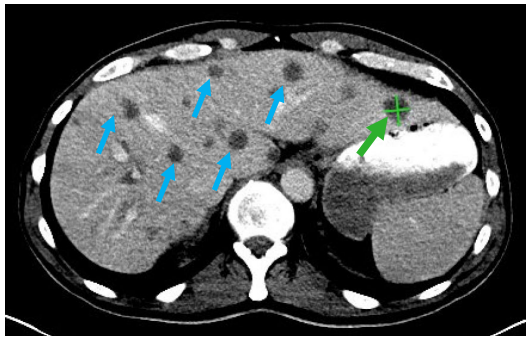
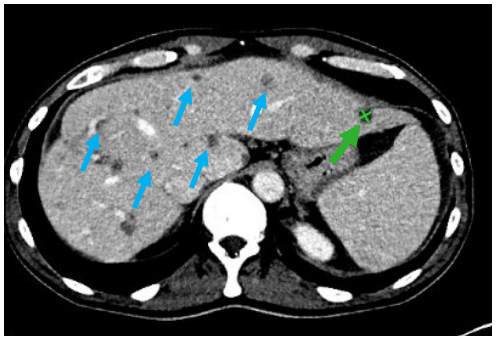
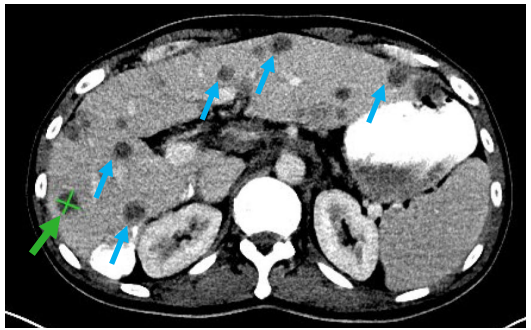
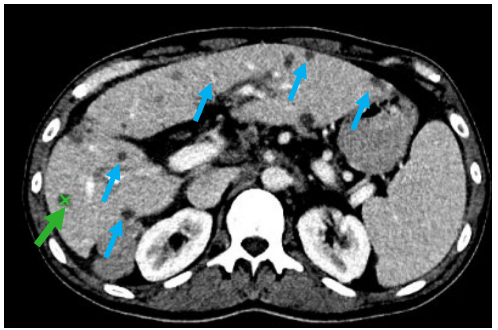


Abbreviations: ID = investigator decision; PD = progressive disease; PR = partial response; SD = stable disease; SW = subject withdrawal. Data cutoff 4/7/2025.

Case Study: Confirmed Partial Response in mCRC

CX-2051 7.2 mg/kg Q3W

- **46 y.o. male with metastatic CRC**
  - KRAS wild-type
  - Microsatellite Stable (MSS)
  - Baseline tumor burden: liver, lung, lymph node
- **Prior therapies**
  - Panitumumab + FOLFOX
  - Bevacizumab + FOLFIRI
  - Bevacizumab + trifluridine/tipiracil
- **Clinical Course on CX-2051 (7.2 mg/kg)**
  - No dose modifications for adverse events
  - Partial response at 6-week tumor assessment with 47% reduction in liver target lesions
  - Clinical improvement - discontinuation of cancer-related pain medication
  - Partial response maintained through ~6 mos.

Baseline	Partial Response at 6-Week Scan (47% Reduction)
	
Target Lesion #1: **21 mm**	Target Lesion #1: **11 mm**
	
Target Lesion #2: **18 mm**	Target Lesion #2: **10 mm**

↗ Non-target Liver Lesions

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Most Frequent Treatment Related Adverse Events (TRAE) Observed

AEs generally manageable and reversible; no grade 4-5 TRAE

Preferred Term, n (%)	2.4–4.8 mg/kg (n = 2)		7.2–10 mg/kg (n = 23)	
	All grade	Grade 3	All grade	Grade 3
Hematologic Adverse Events (in > 1 patient)				
Anemia	0	0	5 (21.7)	3 (13.0)
Neutrophil count decreased	0	0	2 (8.7)	2 (8.7)
Neutropenia	0	0	2 (8.7)	1 (4.3)
Non-hematologic Adverse Events (in > 1 patient)				
Diarrhea	0	0	18 (78.3)	5 (21.7)
Nausea	0	0	11 (47.8)	1 (4.3)
Vomiting	0	0	8 (34.8)	0
Fatigue	0	0	8 (34.8)	1 (4.3)
Hypokalemia	0	0	3 (13.0)	1 (4.3)
Abdominal pain	0	0	3 (13.0)	0
Alanine aminotransferase increased	0	0	2 (8.7)	0
Aspartate aminotransferase increased	0	0	2 (8.7)	0
Decreased appetite	0	0	2 (8.7)	0
Weight decreased	0	0	2 (8.7)	0
Serious Adverse Events* (all patients)	0	0	5 (21.7)	4 (17.4)

*Serious adverse events occurred in 5 patients: Grade 3 Diarrhea (n=1); Grade 3 Anemia (n=1); Grade 3 colitis (n=1); Grade 3 Diarrhea and Acute kidney injury (n=1); Grade 2 Asthenia (n=1)

Data cutoff 4/7/2025

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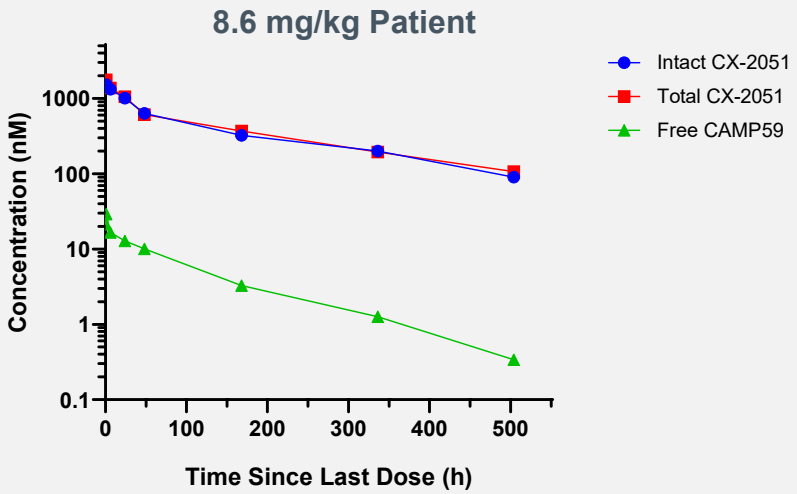
CX-2051 Preliminary Pharmacokinetics Observed



Interim Analysis of Cycle 1 Pharmacokinetics

- Rate of payload deconjugation was low and in line with other Topo I inhibitor ADCs (1 – 5%)
- CX-2051 remained masked in circulation
- Half life of approximately 5.9 days
- CX-2051 showed dose linearity with respect to AUC and C_{max}

Total CX-2051 reflects masked + unmasked forms of ADC; Intact CX-2051 reflects only masked ADC

Initial Phase 1 Data Supports Competitive Results for CX-2051

3L+ CRC Landscape

Treatment	ORR (%)	DCR (%)	Median PFS (months)	Median OS (months)
CX-2051 (7.2–10 mg/kg)	**28%**	**94%**	**5.8** [1]	**N/A**
Fruquintinib	2%	56%	3.7	7.4
Regorafenib	1%	41%	2.0	6.4
Trifluridine/tipiracil	2%	44%	2.0	7.1
Trifluridine/tipiracil + *Bevacizumab*	6%	77%	5.6	10.8

[1] Preliminary PFS as of 4/7/2025 data cutoff.

Abbreviations: DCR = disease control rate; ORR = overall response rate; OS = overall survival; PFS = progression free survival.
Sources: Lonsurf® (trifluridine and tipiracil) Fruzaqla® (fruquintinib), Stivarga® (regorafenib) package inserts; Dasari et al. 2023; Grothey et al. 2013; Prager et al. 2023.

CX-2051 is an investigational early-phase therapy. Information in tables above is not intended to be a direct comparison to approved treatments. Additionally, information provided in the tables above is for illustrative purposes only and no head-to-head comparison of CX-2051 has been conducted against any product or investigational therapy. Differences exist between study or trial designs and subject characteristics, and caution should be exercised when comparing data across unrelated studies.

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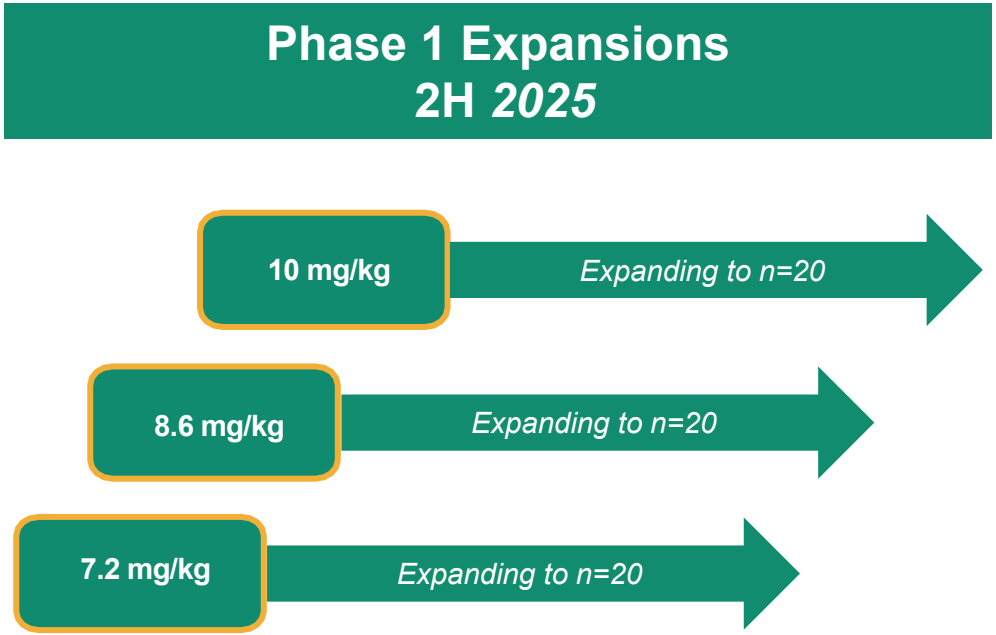
CX-2051 Monotherapy Dose Expansions Underway in Late-line CRC

Plan to Initiate Phase 2 Study in 1H 2026



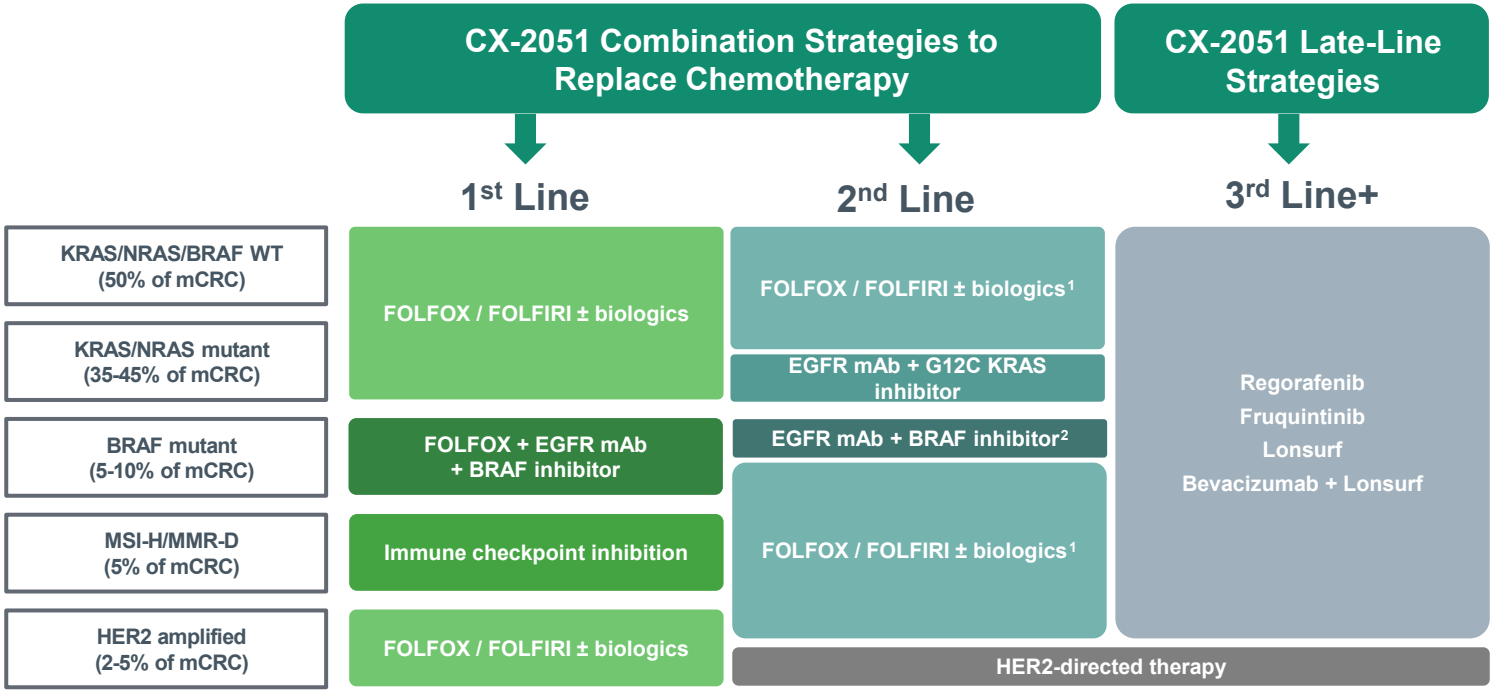
70+ patient Phase 1 data update and Phase 2 design anticipated in Q1 2026

Concluding Remarks

Sean McCarthy, D.Phil.
Chairman and CEO, CytomX Therapeutics

Broad Development Opportunity for CX-2051 in Metastatic CRC

Pan-CRC design offers broad development potential across the treatment paradigm



[1] Whichever regimen that was not previously given in 1L. [2] If BRAF inhibitor not previously given in 1L.
Abbreviations: FOLFIRI = fluorouracil, folinic acid, irinotecan; FOLFOX = fluorouracil, folinic acid, oxaliplatin. mAb = monoclonal antibody.
Adapted from Biller and Schrag, 2021

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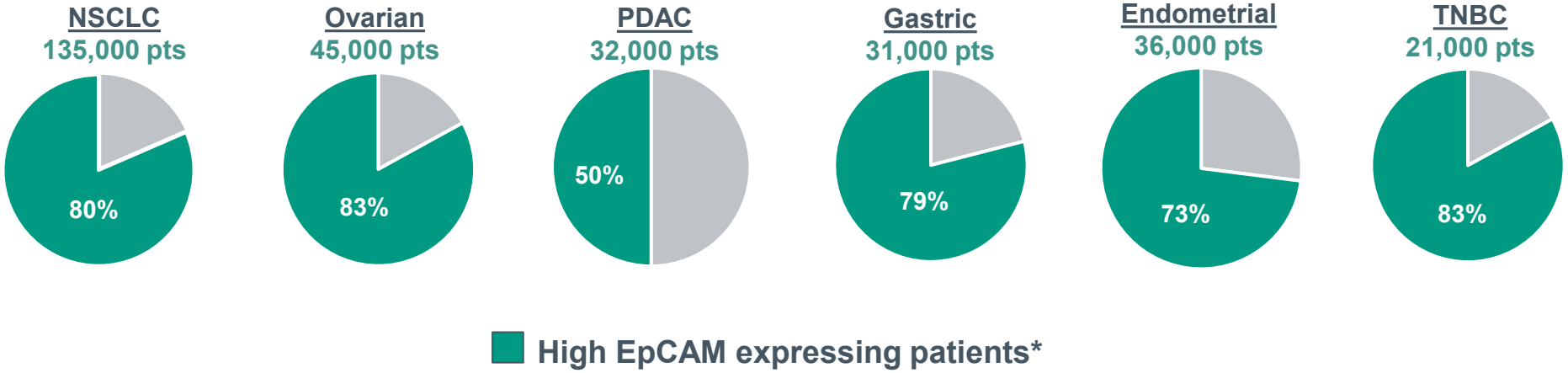
Beyond CRC: CX-2051 is a “Pan-Tumor” Opportunity

EpCAM is broadly expressed in many solid tumors in addition to CRC

Select Non-CRC EpCAM Addressable Patients in U.S.



Sources: *CytomX Internal prevalence study, ≥50% cells with 2+/3+ EpCAM Intensity or >10% 3+; 2029 Drug-treatable patient by tumor type from DRG.

CX-2051 Phase 1 Interim Data Summary & Next Steps

Clinical PoC Demonstrated in CRC for EpCAM Topo-1 ADC

Potential First-in-Class ADC Could Present a Multi-billion Annual Sales Opportunity

Top Priority is Advancement Towards Potential 1st Approval in mCRC

Potential Parallel Advancement into Combination Regimens in CRC in Earlier Lines and Exploration of Additional Tumor Opportunities

CX-2051: A Novel EpCAM-Directed ADC

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