



Varsetatug masetecan (CX-2051)
Unlocking EpCAM as a Cancer Target
via a Masked EPCAM-Directed Topo1 ADC

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

World ADC London
February 25th, 2026

Forward-Looking Statements

This presentation may contain projections and other forward-looking statements regarding future events, including those related to varsetatug masetecan and CX-801. 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 varsetatug masetecan and CX-801, 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 varsetatug masetecan and CX-801, 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 varsetatug masetecan and CX-801; 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

Unmasking Advances in Oncology



CYTOMX[®]
THERAPEUTICS



South San Francisco, CA

PROBODY[®] Platform: Leading the field of masked therapeutics

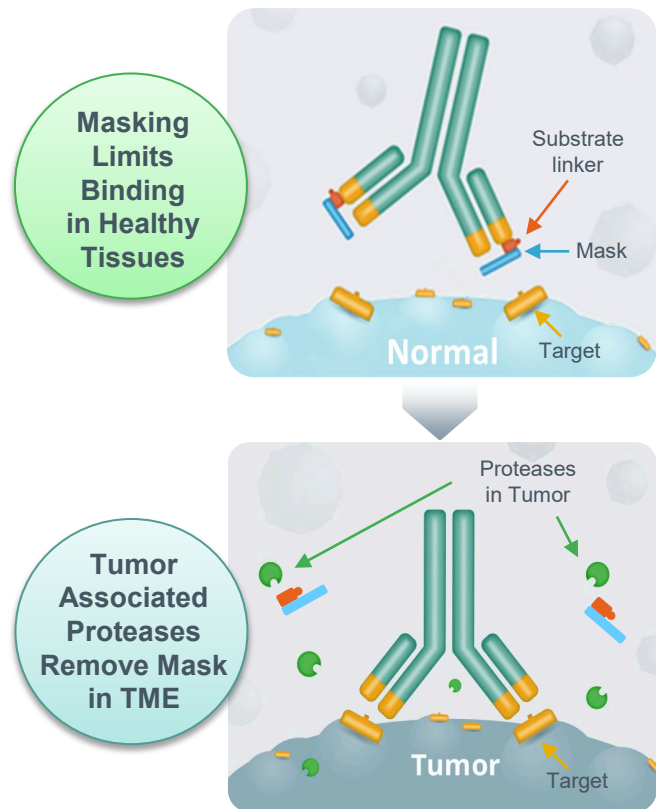
Clinical Programs:

- CX-2051 Varsetatug masetecan for Colorectal Cancer (EpCAM PROBODY[®] Topo-1 ADC)*
- CX-801 for Melanoma (PROBODY[®] IFN- α 2b)

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

Organization: ~70 employees; integrated R&D capabilities

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

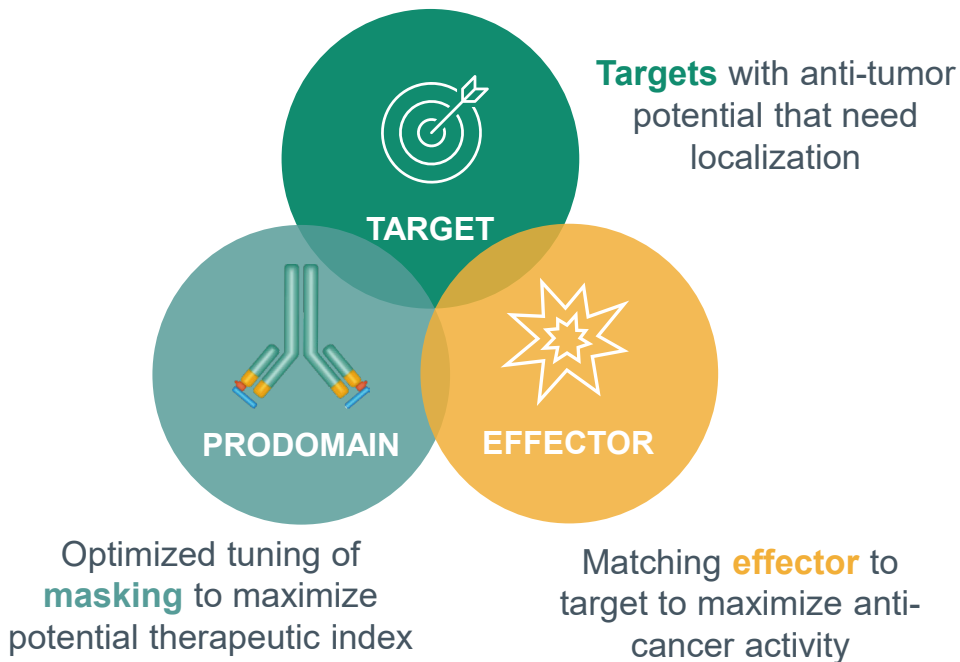
Industry Leading Platform Expertise:

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

PROBODY[®] Therapeutic Design

Right Target, Right Tumor, Right Effector Mechanism

Optimized selection of target, pro-domain and effector function



● Industry Leading platform:

- Proprietary masking technologies
- Applicable across multiple modalities
- Drives novel pipeline programs

Varsetatug masetecan
EpCAM PROBODY[®] ADC

❖ *Lead Indication: Colorectal Cancer*

CX-801
PROBODY[®] INTERFERON ALPHA-2b

❖ *Lead Indication: Melanoma*

PROBODY® Platform Drives Highly Differentiated Pipeline

Economics	Product Candidate(s)	Indication(s)	Preclinical	Phase 1	Phase 1 Expansion	Commercial Rights*
Clinical Pipeline	Varseta-M EpCAM Topo-1 ADC	3L+ metastatic CRC (mCRC)	Phase 1 expansion data expected in Q1 2026			CYTOMX
	Varseta-M + bevacizumab	2L/3L mCRC	Initiating in Q1 2026			CYTOMX
	Varseta-M	Additional EpCAM+ indications	Initiating in 2H 2026			CYTOMX
	CX-801 (IFNα2b)	Advanced Melanoma	Phase 1 data CX-801 + KEYTRUDA® by 2026 Year-End			CYTOMX
Preclinical Programs	CX-908 (P-Cadherin x CD3)	Solid Tumors				CYTOMX
	PROBODY® TCBs	Solid Tumors				astellas REGENERON Bristol Myers Squibb
	PROBODY® mRNAs	Oncology & Non-oncology				moderna

Antibody Drug Conjugates are Transforming Cancer Care

Varseta-M brings 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

Varseta-M^{*}

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

FR α / Ovarian

Immunogen/AbbVie -
\$10B Acquisition

 **TRODELVY**[®]
sacituzumab govitecan-hziy
180 mg for injection

TROP2 / Breast

Immunomedics/Gilead -
\$21B Acquisition

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



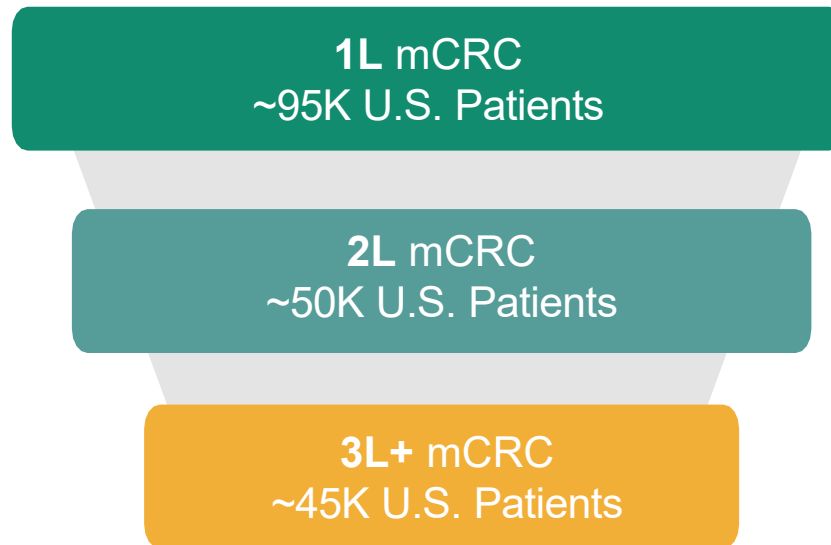
5-year survival rate of
13% in mCRC

Varseta-M has the Potential to Address a Large Patient Population due to Broad and Consistent EpCAM Expression in CRC



By 2040 U.S. CRC Incidence Estimated to be >170K Patients Annually

Metastatic CRC (mCRC)

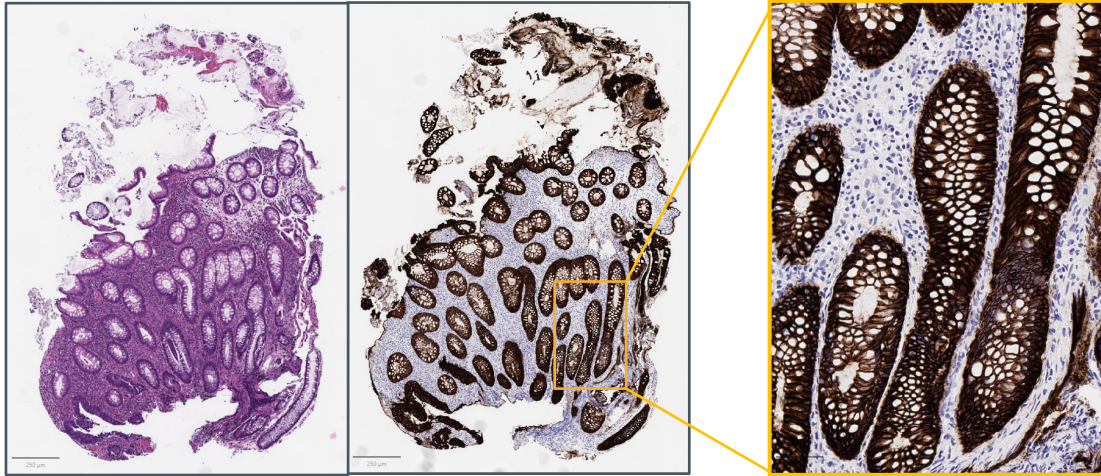


EpCAM (Epithelial Cell Adhesion Molecule)

An ideal CRC target enabled by the CytomX PROBODY[®] platform

H&E Staining

EpCAM IHC

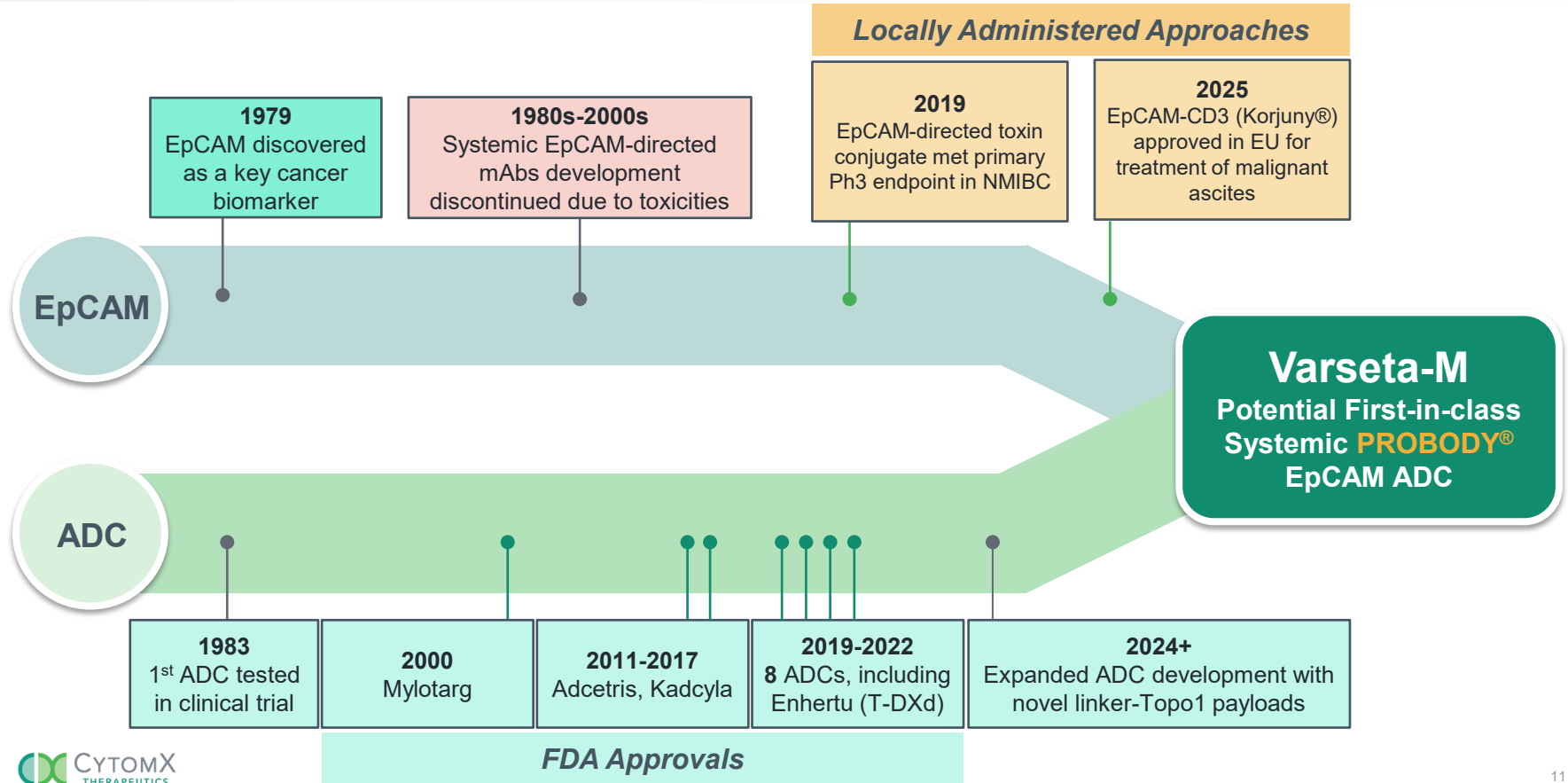


- **Uniformly high expression across CRC**
- **EpCAM expression across all stages of CRC**
- **Expression in normal tissues has limited drug development**

IHC Staining of CRC Patient Biopsy from Ongoing Phase 1 Study

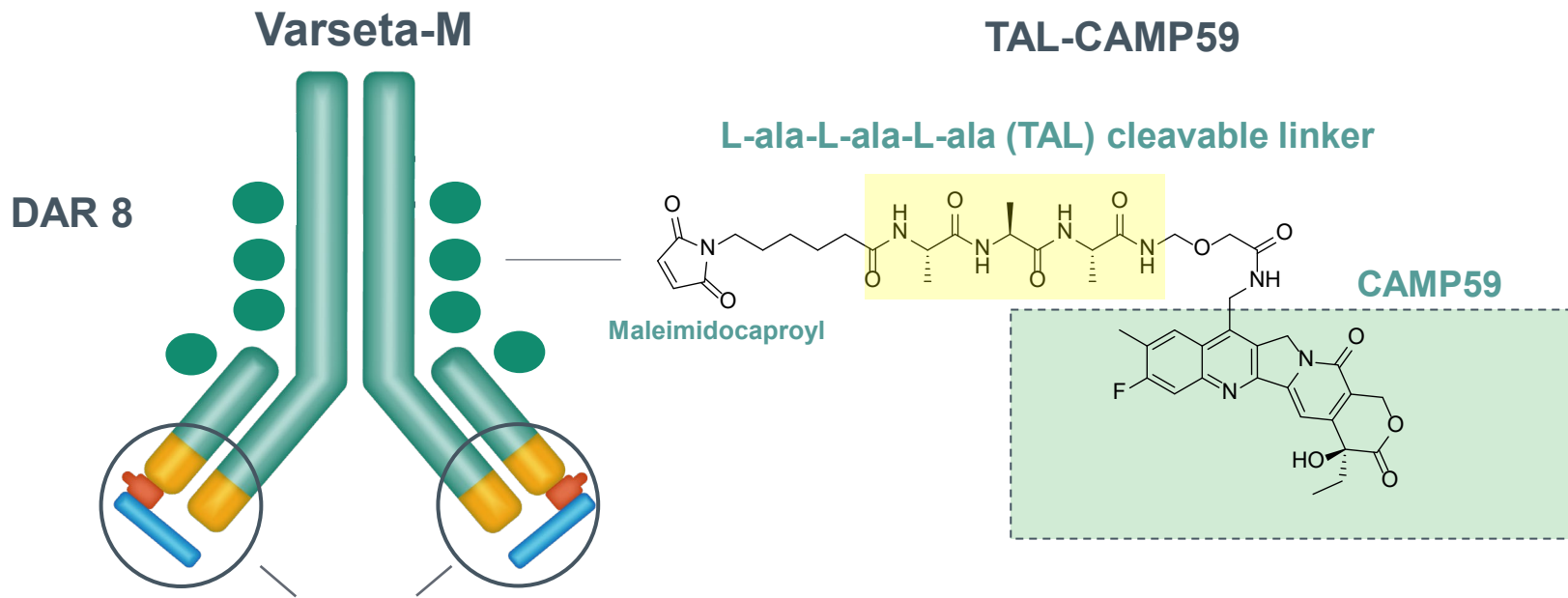
Maximum H-score of 300 (100% cells 3+ by IHC)

Varseta-M Brings Decades of EpCAM and ADC History Together



Varsetatug masetecan: A Novel EpCAM Targeting PROBODY[®] ADC

The Right Target, The Right Payload

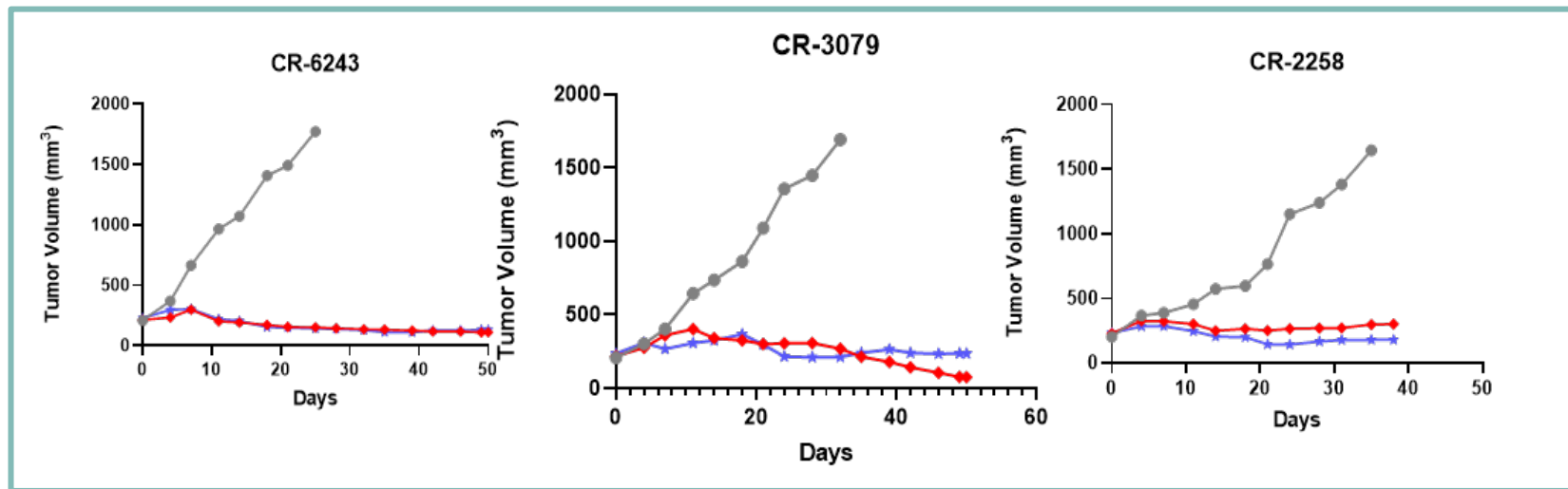


- *Masking domains designed to reduce EpCAM binding in normal tissues*
- *Unmasked antibody or ADC not expected to have a therapeutic window due to systemic toxicity*

Next-Gen Linker-Payload in Varseta-M Is Equally Efficacious as DXd Linker-Payload in Murine Cancer Models

Colorectal cancer patient-derived xenograft models

- Vehicle
- **CX-2051 6 mg/kg**
- **EpCAM-DXd 6 mg/kg**



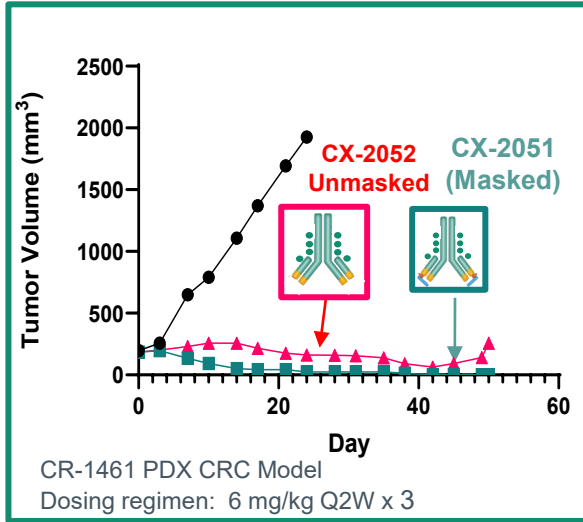
CX-2051 is equally efficacious preclinically as EpCAM-DXd

Dosing regimen: Q2W x 3

Varseta-M Leverages Masking to Open a Therapeutic Window for EpCAM

Masking designed to mitigate on target EpCAM toxicities

Equivalent Efficacy

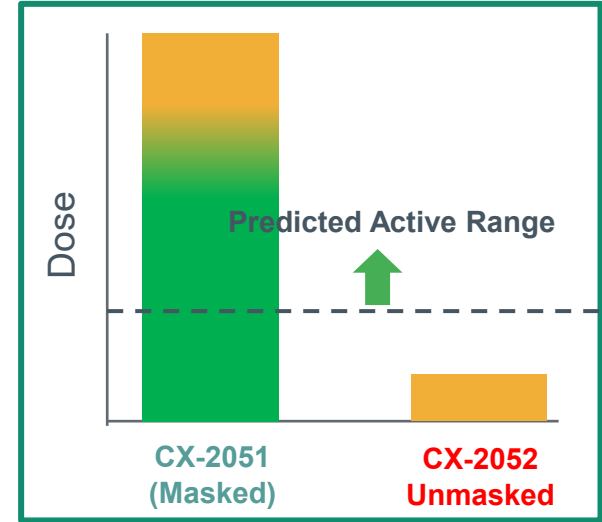


Improved Tolerability

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



CX-2051 Can Address High Unmet Need in Metastatic CRC

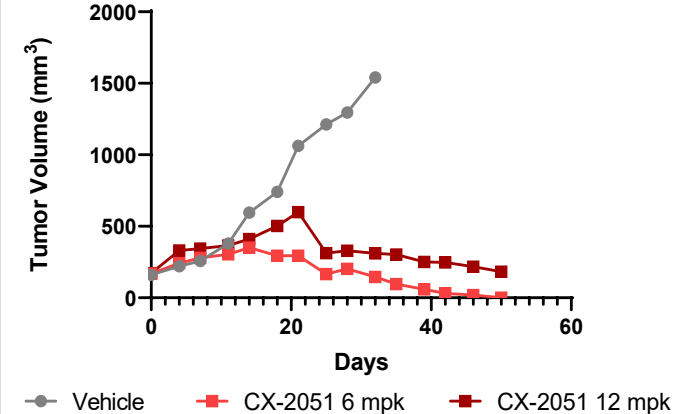


Broad Opportunity for Topo I Based ADCs in CRC

1L	FOLFOX (folinic acid, fluorouracil, oxaliplatin) / FOLFIRI (folinic acid, fluorouracil, irinotecan) + bevacizumab / cetuximab / panitumumab	53 – 65% ORR 24 – 30 mo. OS
2L	FOLFIRI / FOLFOX +/- bevacizumab / aflibercept / ramucirumab / cetuximab / panitumumab	13 – 22% ORR 10 – 14 mo. OS
3L	regorafenib / trifluridine & tipiracil +/- bevacizumab	1 – 6% ORR 6 – 10 mo. OS

Strong preclinical anti-tumor activity even in irinotecan resistant setting

CRC PDX Model (CR-0029)
(Irinotecan resistant model)



Varseta-M Phase 1 Study Currently Focused in Late-Line CRC

Phase 1 enrollment expected to be ~100 patients by Q1 2026

CX-2051 Administered Q3W

Study Commenced April 2024

Patient Data Presented in May 2025:

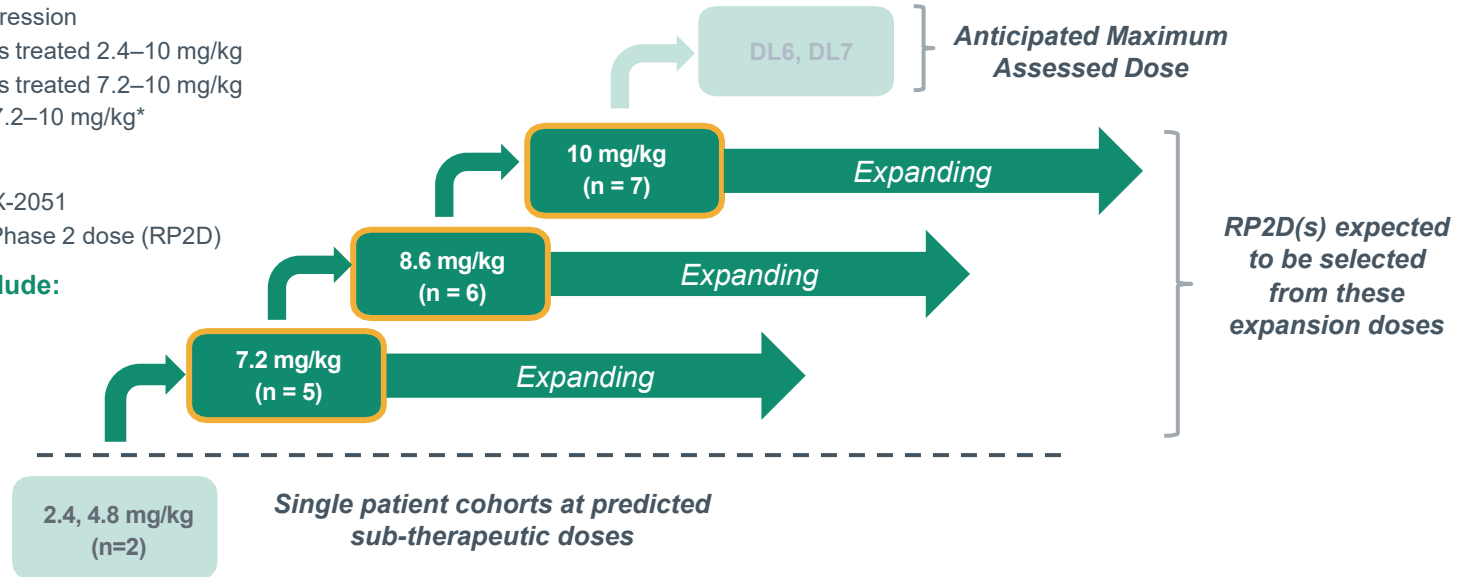
- Unselected for EpCAM expression
- 25 safety-evaluable patients treated 2.4–10 mg/kg
- 23 safety-evaluable patients treated 7.2–10 mg/kg
 - 18 efficacy-evaluable at 7.2–10 mg/kg*

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.

Varseta-M Interim Phase 1 Clinical Data in May 2025 Demonstrated an Encouraging Clinical Profile in Late-line Metastatic CRC



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



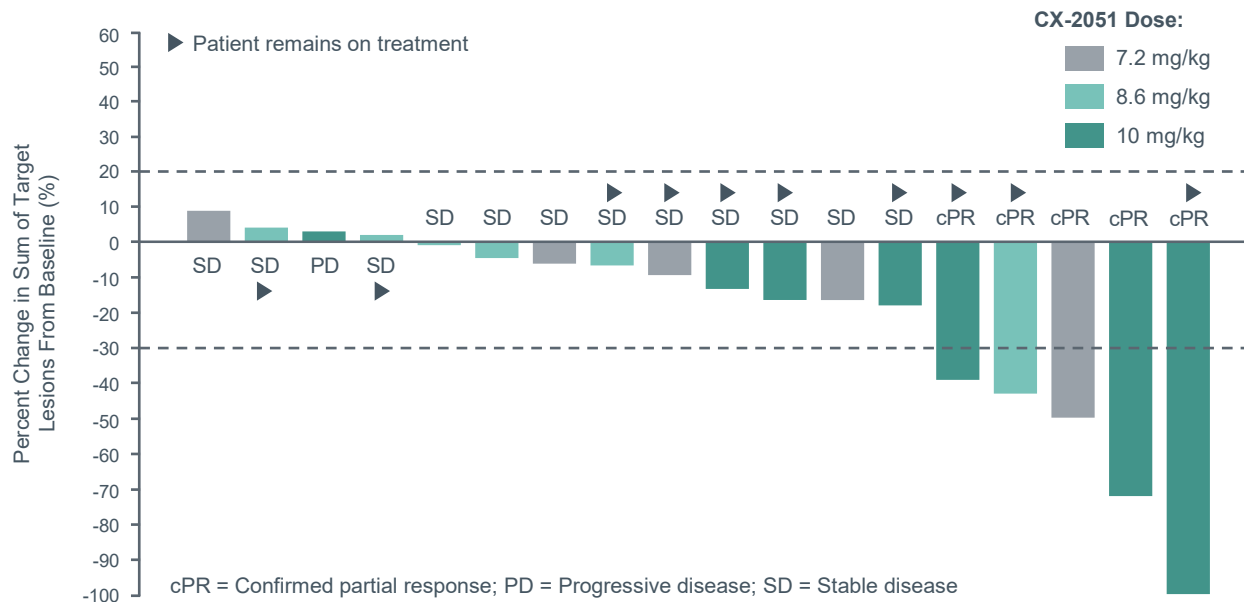
Favorable Safety

- No dose limiting toxicities
- EpCAM target enabled by masking

Supports Development of
Combinations in Earlier Lines
of Therapy

Varseta-M 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

KRAS mutation (Y/N)

Liver metastases (Y/N)

Baseline EpCAM H-Score¹

3	4	9	3	3	4	4	3	6	4	6	3	8	4	5	3	5	10
N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	N	Y
Y	Y	Y	Y	Y	N	Y	Y	Y	N	N	N	N	Y	N	Y	Y	Y
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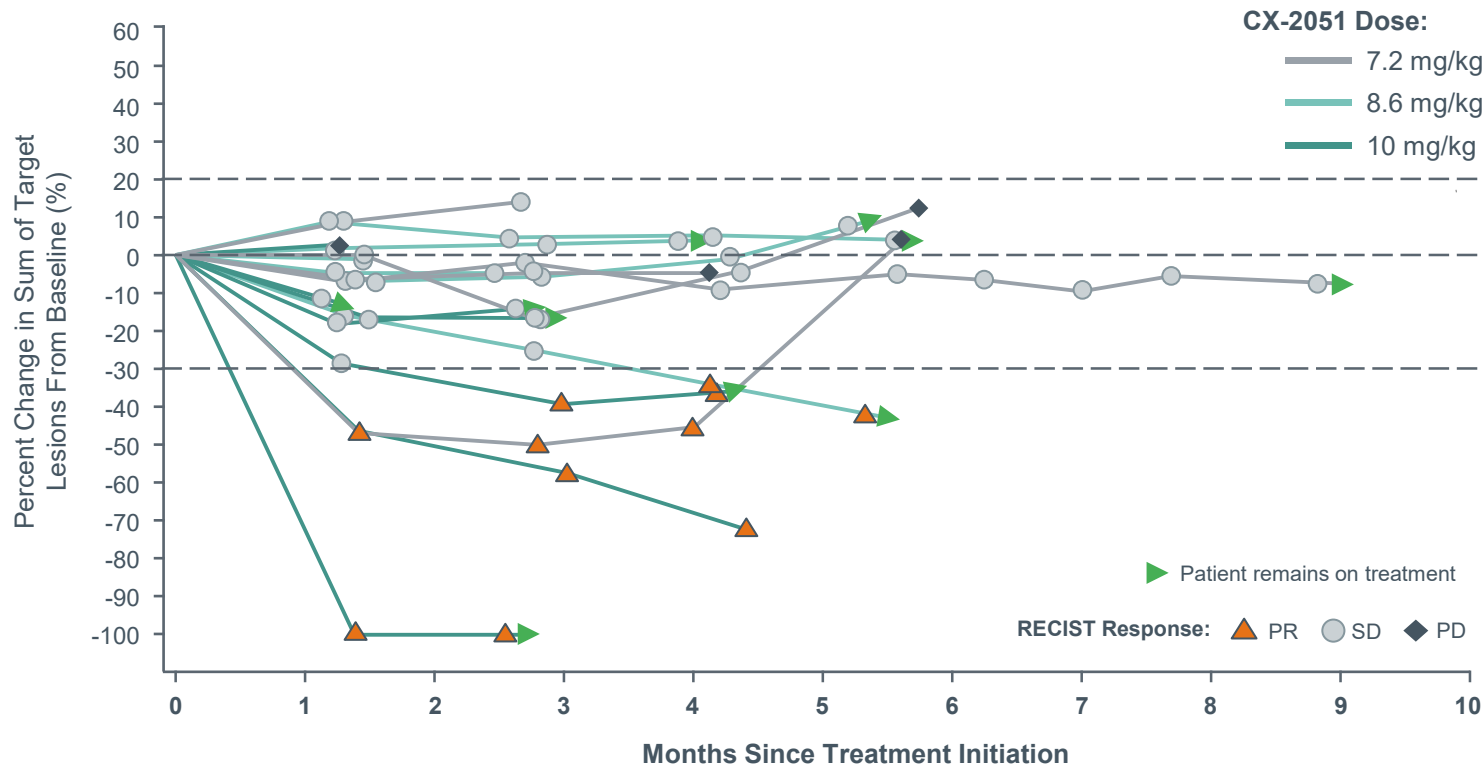
■ H-Score > 280

▨ 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.

Varseta-M Anti-Tumor Activity 7.2-10 mg/kg

94% (17/18) disease control rate; Preliminary median progression free survival 5.8 months



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

Data cutoff 4/7/2025

Case Study: Confirmed Partial Response in mCRC

Varseta-M 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

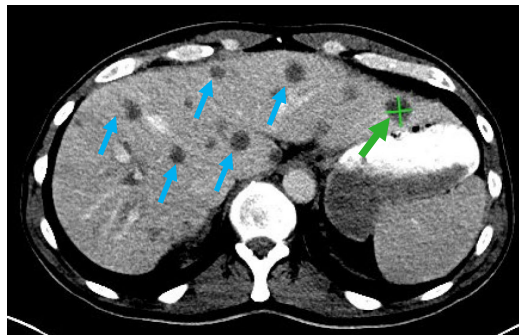
- **Prior therapies**

- Panitumumab + FOLFOX
- Bevacizumab + FOLFIRI
- Bevacizumab + trifluridine/tipiracil

- **Clinical Course on CX-2051 (7.2 mg/kg)**

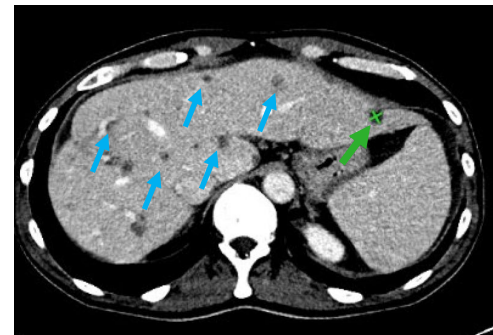
- No dose modifications for adverse events
- Partial response at 6-week tumor assessment with 47% reduction in liver target lesions
- Clinical improvement - discontinuation of cancer-related pain medication
- Partial response maintained through ~6 mos.

Baseline

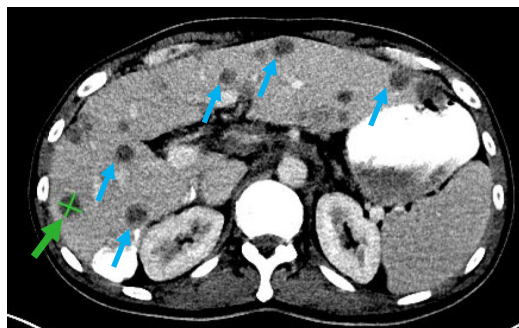


Target Lesion #1: 21 mm

Partial Response at 6-Week Scan
(47% Reduction)



Target Lesion #1: 11 mm



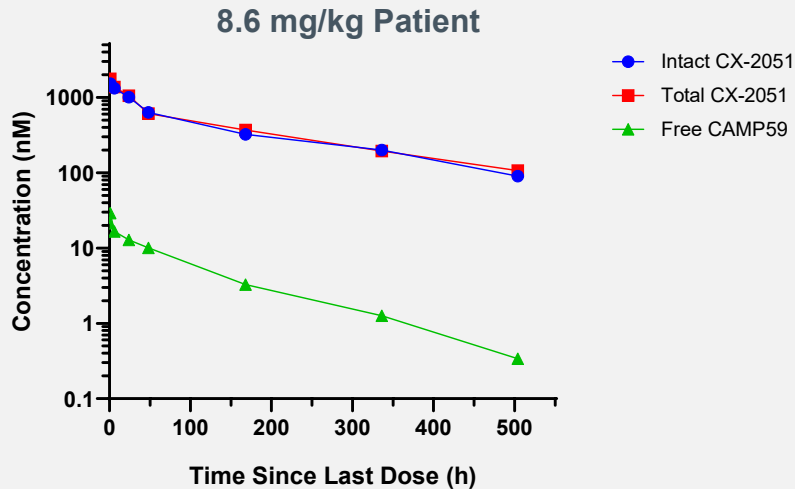
Target Lesion #2: 18 mm



Target Lesion #2: 10 mm

➤ Non-target Liver Lesions

Varseta-M Preliminary Pharmacokinetics



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

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}

Varseta-M Initial Safety Profile* Presented in May 2025 is Encouraging and Enabled by Masked PROBODY[®] ADC Design

Varseta-M Phase 1 Safety Profile*

- Adverse events (AEs) generally manageable and reversible with most events Grade 1/2
- No signs of pancreatitis or serious liver toxicity which have limited prior EpCAM antibodies
- No evidence of interstitial lung disease (ILD) observed
- Hematologic profile may be attractive for future combinations
- Diarrhea was the most common treatment-related adverse event (22% Grade 3)
Prophylaxis implemented in Phase 1 expansions.

Sources: CytomX Therapeutics May 12, 2025 Varseta-M Data Presentation

**As of the clinical data reported on May 12, 2025. Varseta-M GR3+ AEs were GR3 only as of April 7th data cutoff. As reported subsequently in August 2025, a single Grade 5 treatment-related acute kidney injury occurred in a patient with a complex medical history including having a solitary kidney.*

Initial Phase 1 Data Supports Competitive Profile for Varseta-M

3L+ CRC Landscape

Treatment	ORR (%)	DCR (%)	Median PFS (months)	Median OS (months)
Varseta-M (7.2–10 mg/kg)	28%	94%	5.8¹	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 + <i>Bevacizumab²</i>	6%	77%	5.6	10.8

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

² SUNLIGHT study total patients; Patients previously treated with prior bevacizumab had median PFS of 4.5 months and OS of 9.0 months

Varseta-M Monotherapy Dose Expansions Underway in Late-line CRC

Phase 1 expansion data update on track for Q1 2026

Phase 1 Expansions Ongoing

10 mg/kg

Expanding

8.6 mg/kg

Expanding

7.2 mg/kg

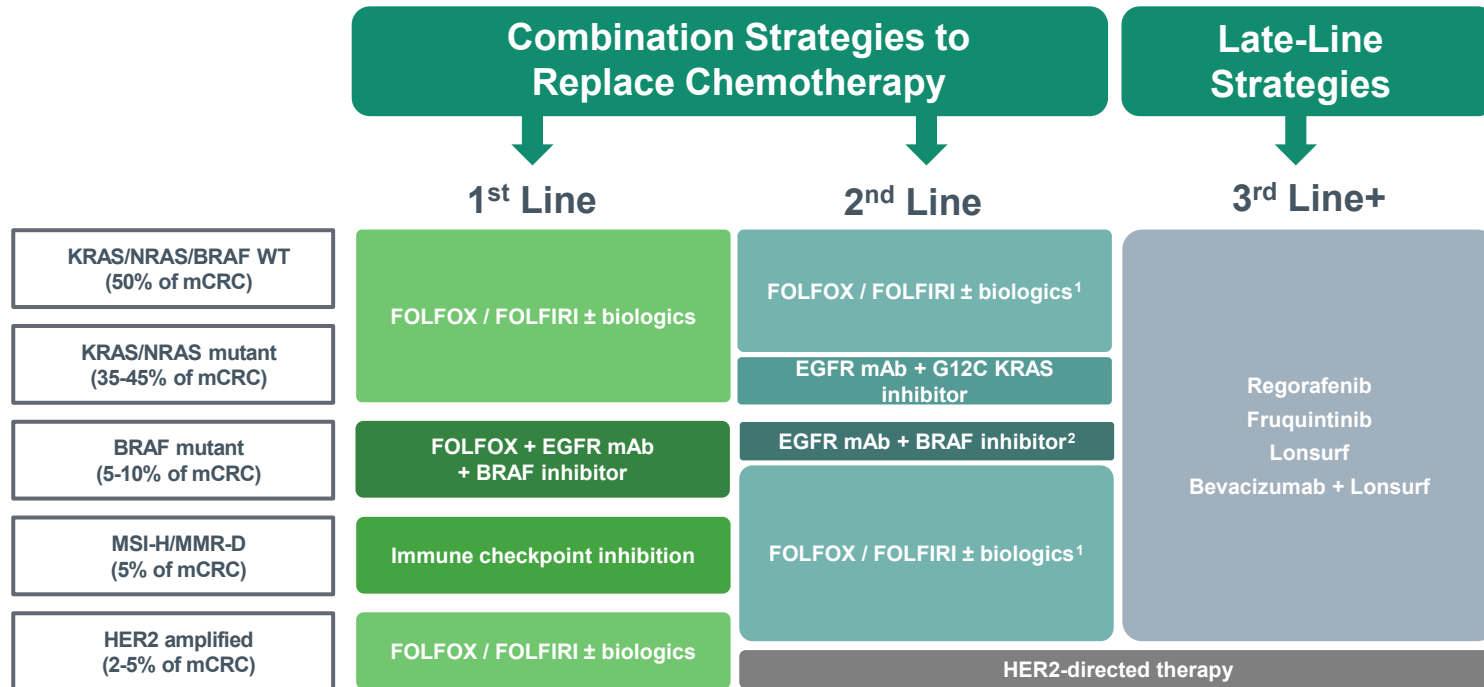
Expanding

Q1 2026 Phase 1 Expansion Update:

- 73 patients enrolled as of August 2025, projected to enroll ~100 patients by Q1 data update
- Goals for Phase 1 Expansion Data Update:
 - Evaluate efficacy profile in larger sample size
 - Characterize AE profile in larger number of patients, including GI AE management strategies utilized to-date
- **2026 Goal:**
 - Select a dose or doses for a potential registrational study in late-line CRC

Broad Development Opportunity for Varseta-M in Metastatic CRC

Combination Phase 1 study with bevacizumab initiating in Q1 2026



¹ Whichever regimen that was not previously given in 1L. ² If BRAF inhibitor not previously given in 1L.

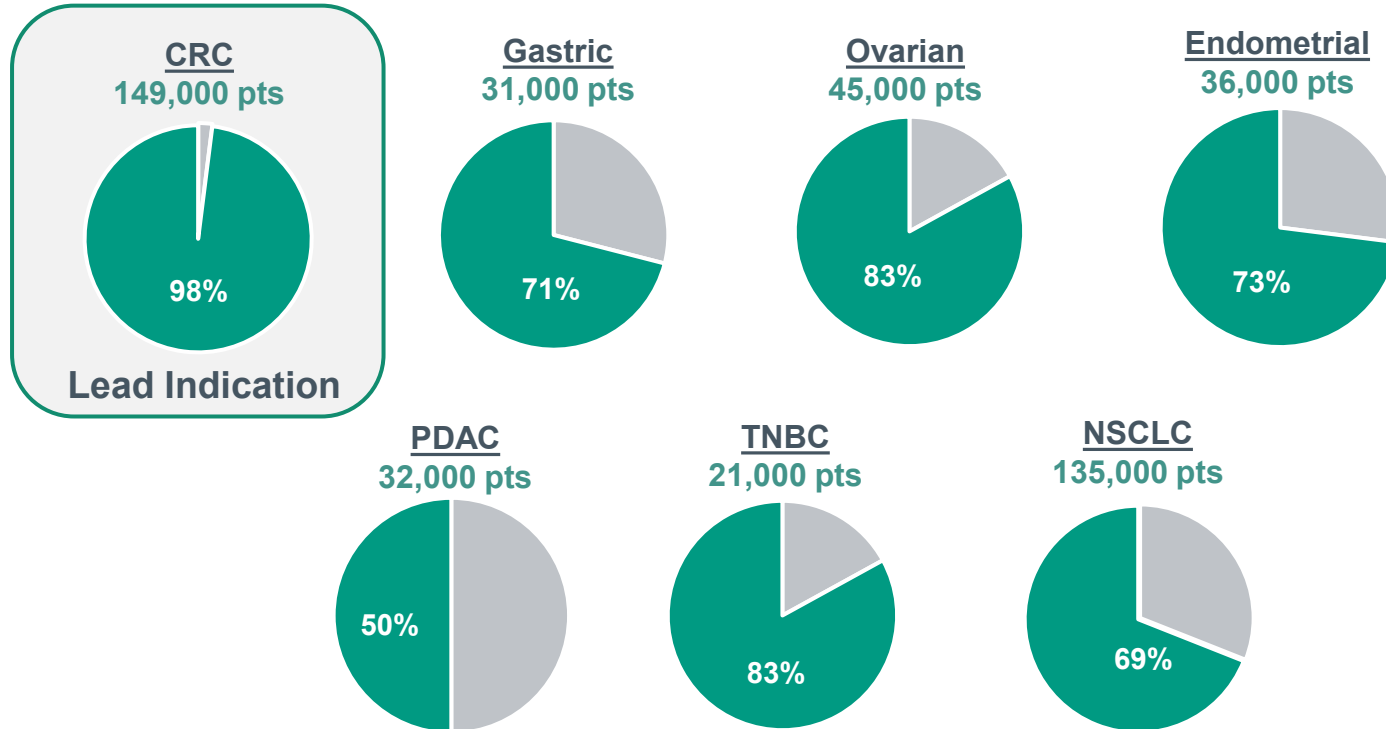
Abbreviations: FOLFIRI = fluorouracil, folinic acid, irinotecan; FOLFOX = fluorouracil, folinic acid, oxaliplatin. mAb = monoclonal antibody.

Adapted from Biller and Schrag, 2021

Beyond CRC: Varseta-M is a “Pan-Tumor” Opportunity

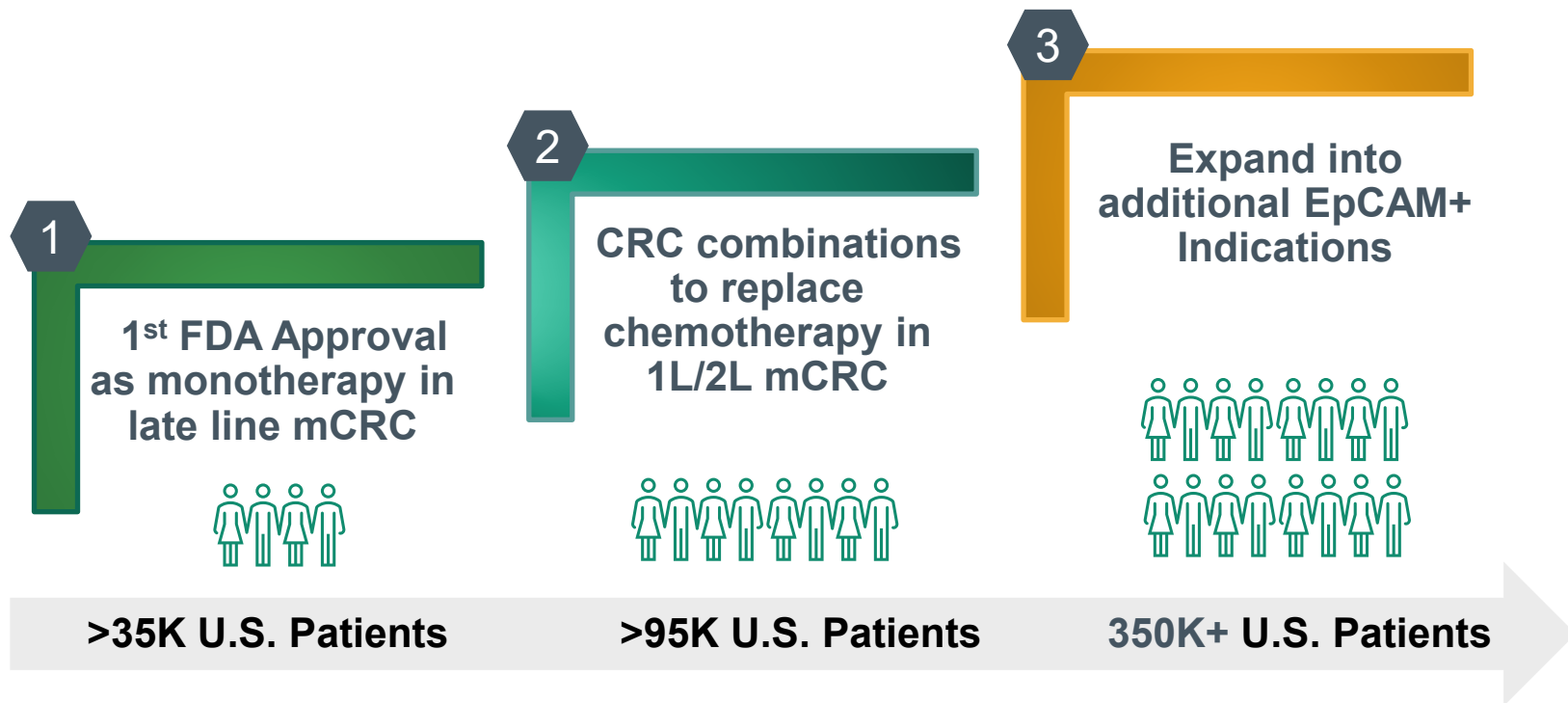
EpCAM is broadly expressed in many solid tumors in addition to CRC

■ U.S. High EpCAM expressing patients*



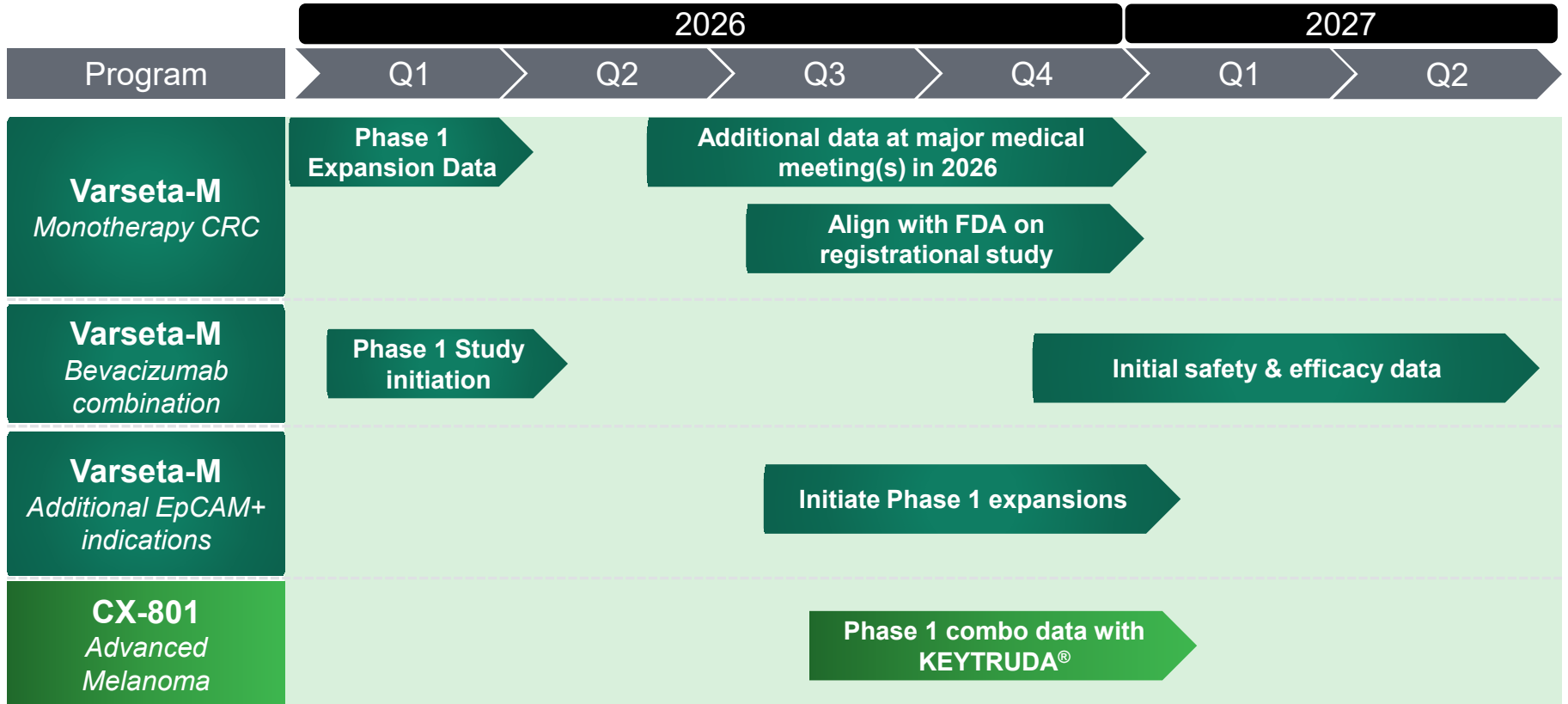
Varseta-M is a Differentiated, First-in-Class ADC Positioned to Address a Broad EpCAM+ Patient Population

Varseta-M: Unlocking Multiple Layers of Value Creation



CytomX Has Significant Pipeline Momentum Entering 2026

Multiple milestones expected while advancing toward later phase development





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via a Masked EPCAM-Directed Topo1 ADC

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