CytomX® THERAPEUTICS

Unmasking Advances in Oncology

44th Annual JP Morgan Healthcare Conference

Dr. Sean McCarthy, CEO and Chairman

January 14, 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:

- Varsetatug masetecan (EpCAM PROBODY® Topo-1 ADC)* for Colorectal Cancer
- CX-801 (PROBODY® IFN-α2b) for Melanoma

Financials: Cash runway to Q2 2027, excluding any potential milestones or new business development

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

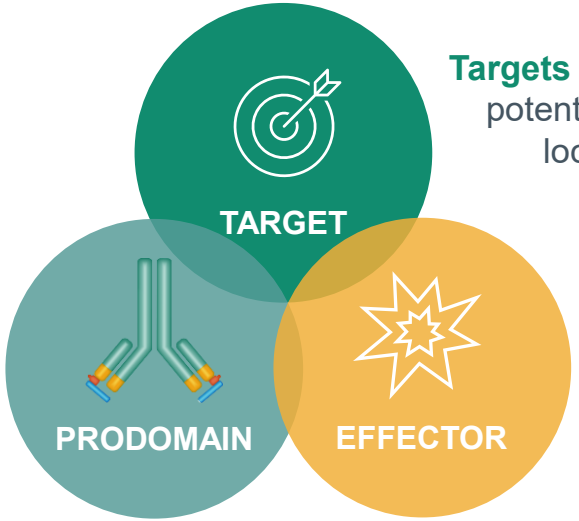
Organization: ~70 employees; integrated R&D capabilities

*Varsetatug masetecan ("Varseta-M") - (formerly CX-2051)

PROBODY® Therapeutic Design

Right Target, Right Tumor, Right Effector Mechanism

Optimized selection of target, pro-domain and effector function



Targets with anti-tumor potential that need localization

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

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

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

*CytomX Commercial Rights include wholly-owned molecules or molecules in which CytomX has full development and commercial control

Varsetatug masetecan (CX-2051)

A Novel EpCAM-Directed ADC Focused in Colorectal Cancer (CRC)

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

FRα / Ovarian

Immunogen/AbbVie -
$10B Acquisition

TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

TROP2 / Breast

Immunomedics/Gilead -
$21B Acquisition

CytomX THERAPEUTICS

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

Colorectal Cancer Remains One of the Biggest Unmet Needs in Oncology

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

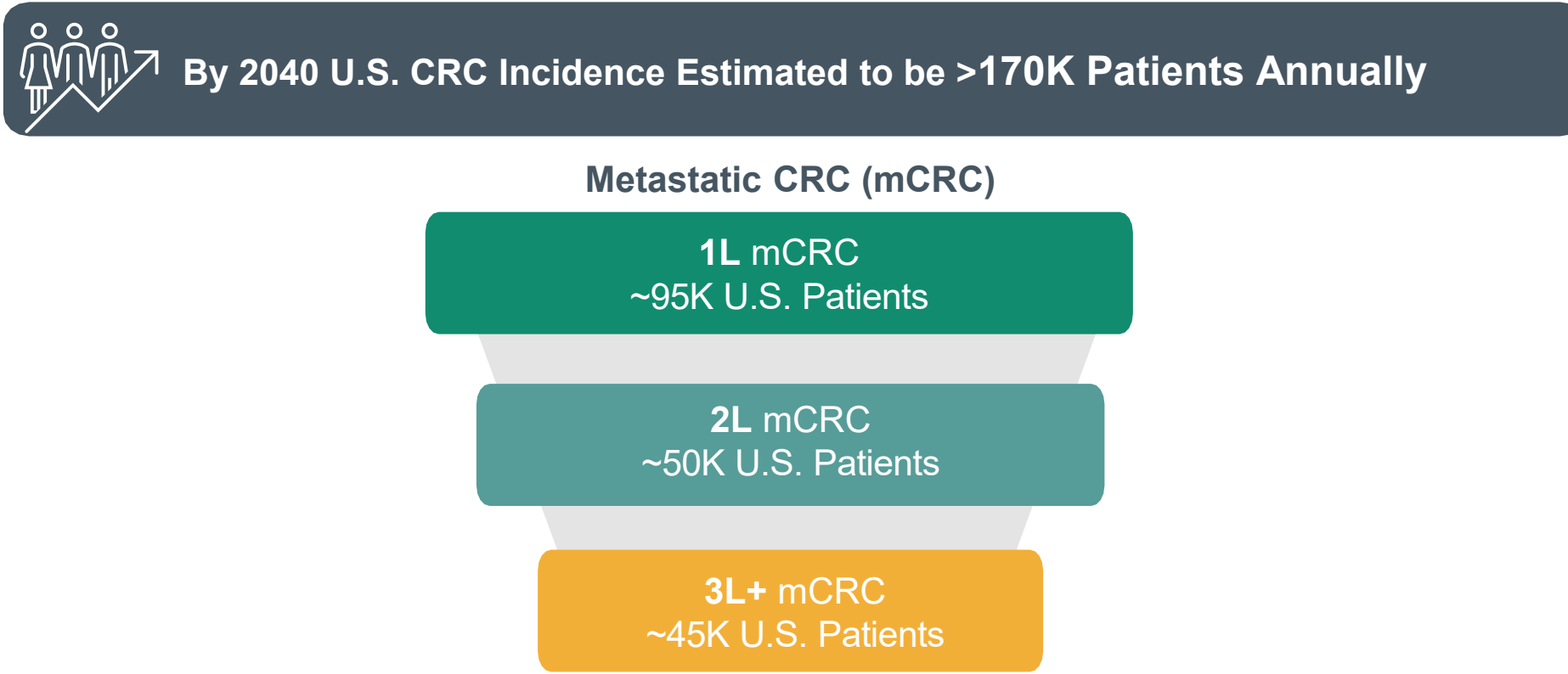
2nd leading cause of cancer death worldwide

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

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

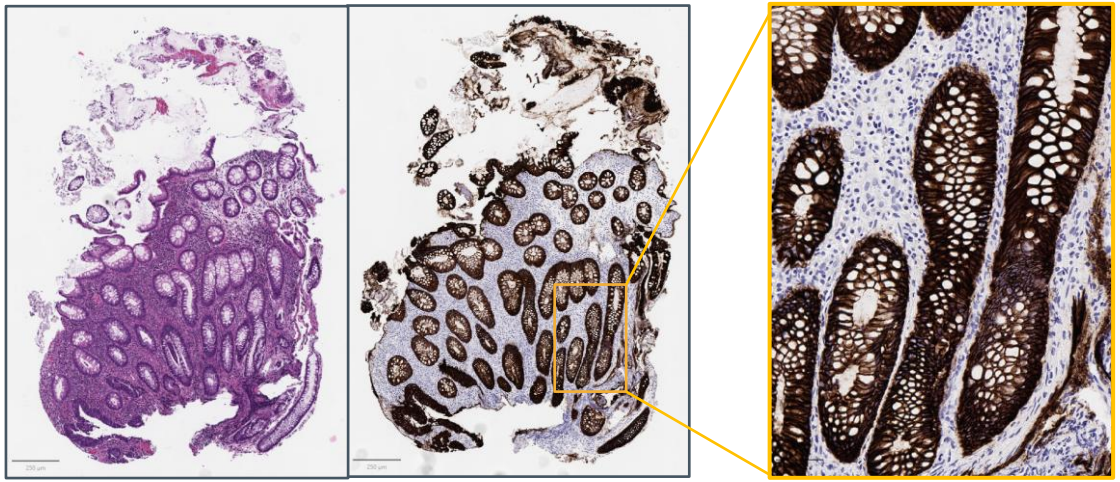


Sources and assumptions: DRG epidemiology; Company estimates

EpCAM (Epithelial Cell Adhesion Molecule)

An ideal CRC target enabled by the CytomX PROBODY® platform

H&E Staining **EpCAM IHC**



IHC Staining of CRC Patient Biopsy from Ongoing Phase 1 Study

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

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

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

EpCAM Has Been Clinically Validated But Not as a Systemic Therapy

EpCAM is clinically validated with a locally administered therapy

KORJUNY® (catumaxomab): EpCAM x CD3

- Delivered by intraperitoneal infusion
- Approved by EMA for treatment of malignant ascites
- Launched in Germany in December 2025

Pharmanovia

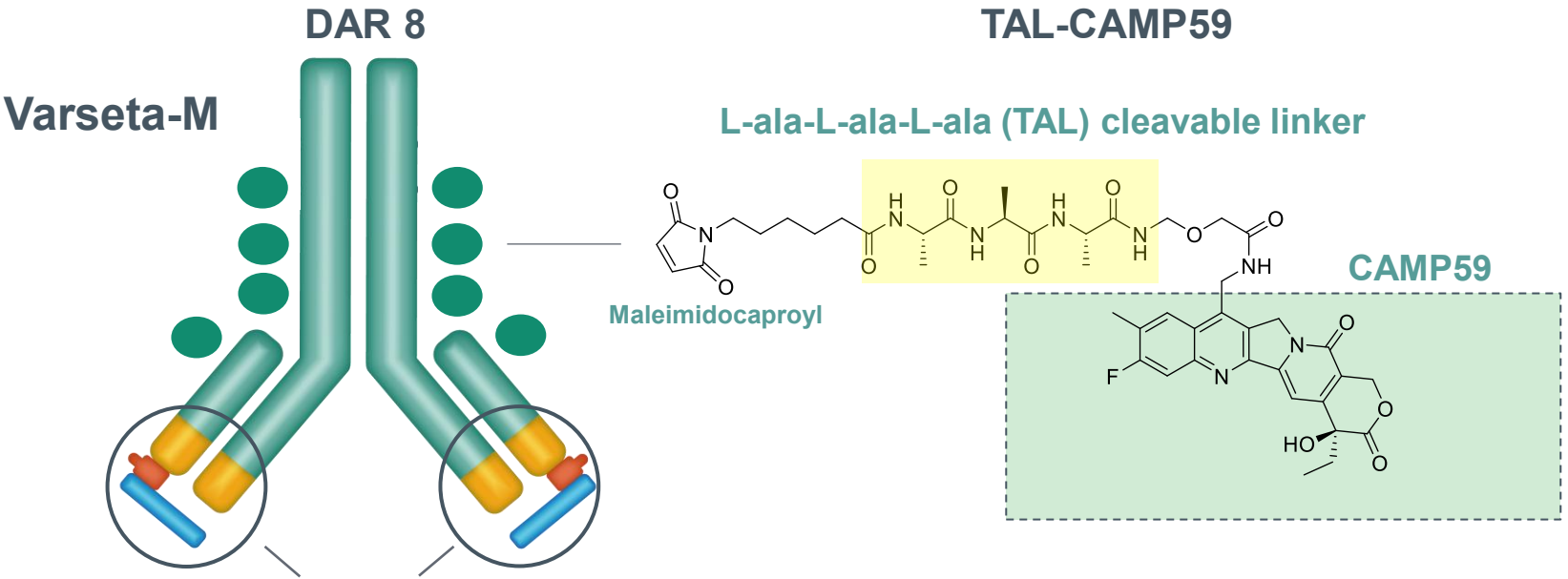
Systemic EpCAM approaches have been limited by toxicity

Asset	Company	MOA	Stage	Status
Solitomab	Amgen	EpCAM x CD3 BiTE	Ph 1	GI tox; liver tox discontinued
ING-1	XOMA	EpCAM mAb	Ph 1	Pancreatitis; discontinued
3622W94	GSK	EpCAM mAb	Ph 1	Pancreatitis; discontinued

Sources: Pharmanovia.com; de Bono et. All; de Bono et al. 2004; Gires et al. 2020

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***

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

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*[1]**	3L	6%	77%	5.6	10.8

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

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.

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

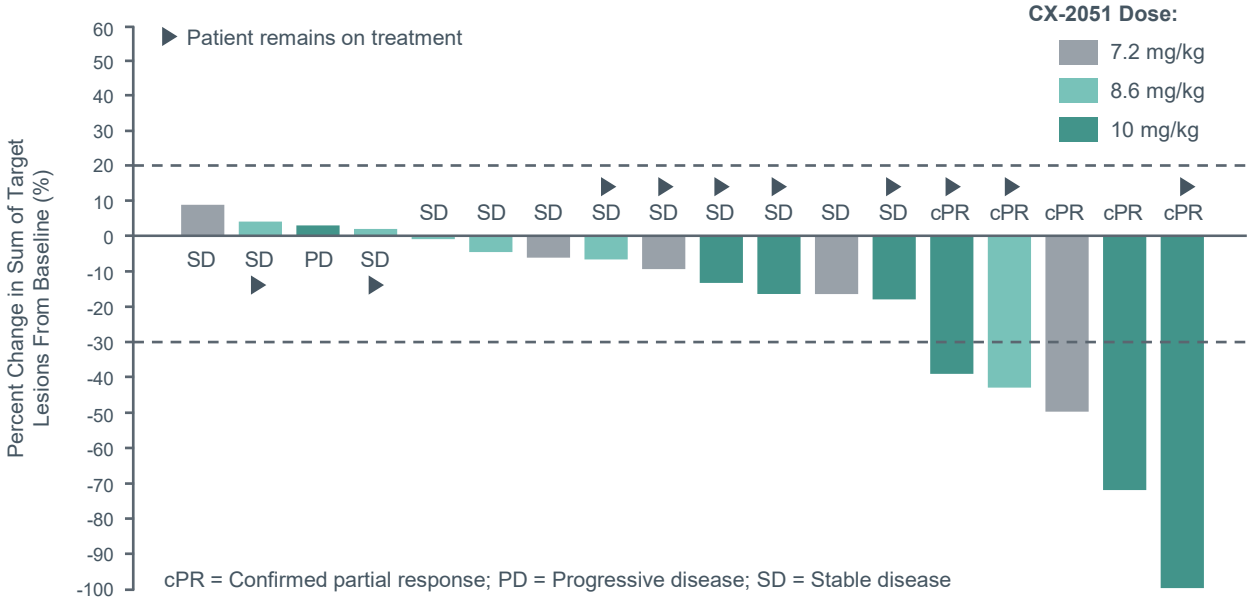
- No dose limiting toxicities
- EpCAM target enabled by masking

Supports Development of Combinations in Earlier Lines of Therapy

*Based on Interim Data cutoff 4/7/2025

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	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

CytomX Therapeutics

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%**	**5.8** [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*[2]	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 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 Varseta-M 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.

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 Therapuetics May 12, 2025 Varseta-M Data Presentation

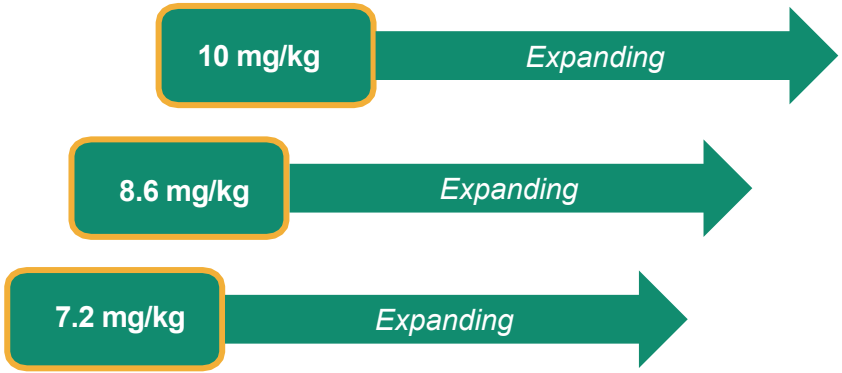
**As of the clinical data reported on May 12, 2025. Varseta-M GR3+ AEs were GR3 only as of April 7th data cutoff. As reported subsequently in August 2025, a* single Grade 5 treatment-related acute kidney injury occurred in a patient with a complex medical history including having a solitary kidney.

CytomX THERAPEUTICS

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

Phase 1 expansion data update on track for Q1 2026

Phase 1 Expansions Ongoing

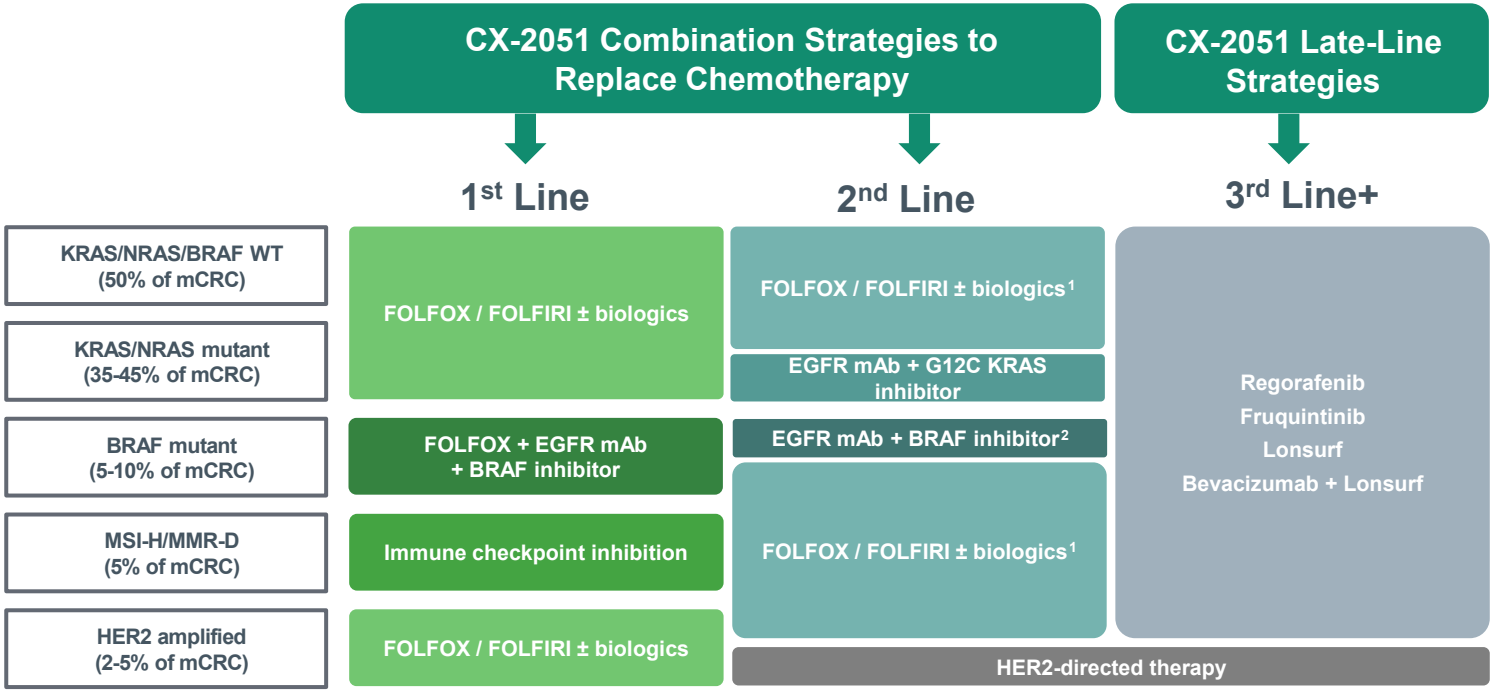


Q1 2026 Phase 1 Expansion Update:

- 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

Combo study with bevacizumab starting in Q1 2026 to enable earlier lines of therapy

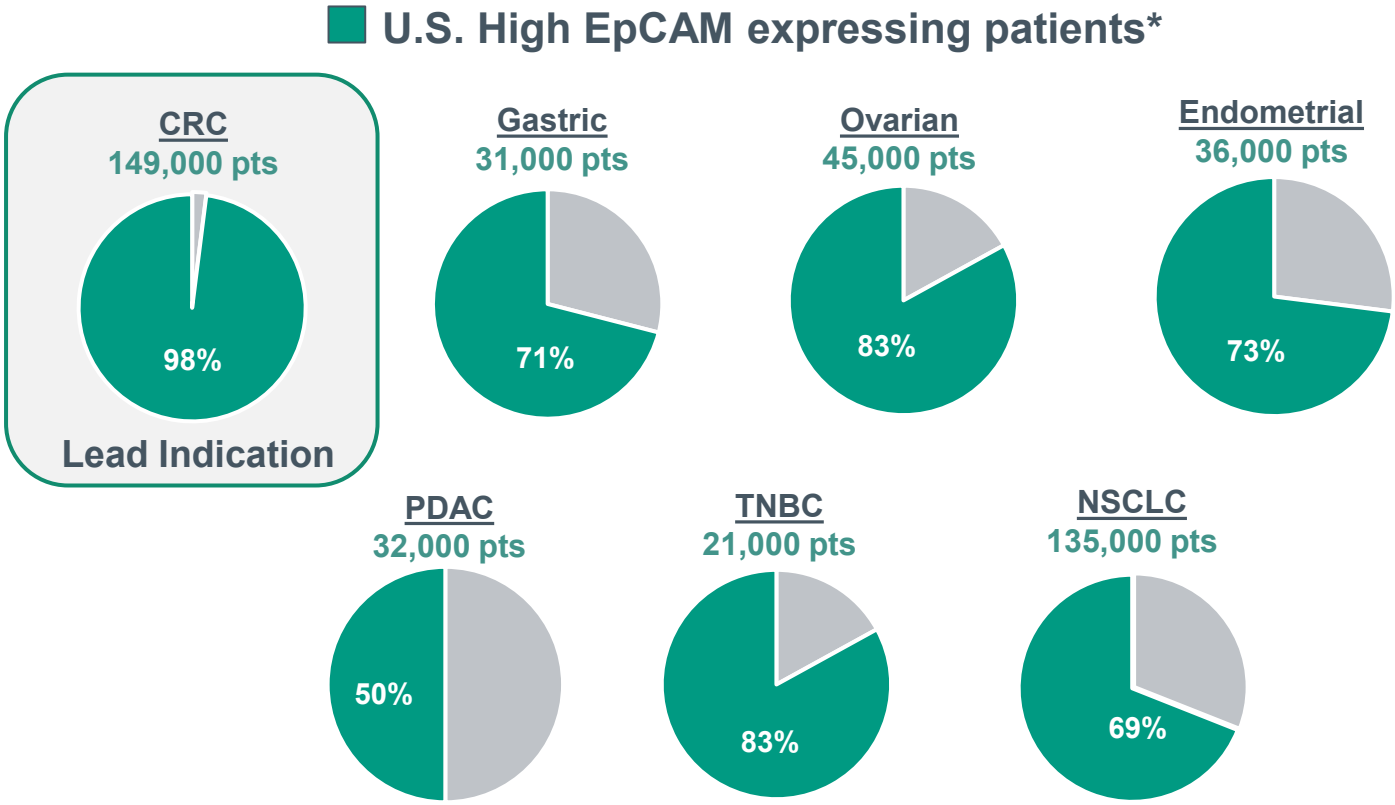


[1] Whichever regimen that was not previously given in 1L. [2] If BRAF inhibitor not previously given in 1L.
Abbreviations: FOLFIRI = fluorouracil, folinic acid, irinotecan; FOLFOX = fluorouracil, folinic acid, oxaliplatin. mAb = monoclonal antibody.
Adapted from Biller and Schrag, 2021

CytomX Therapeutics

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

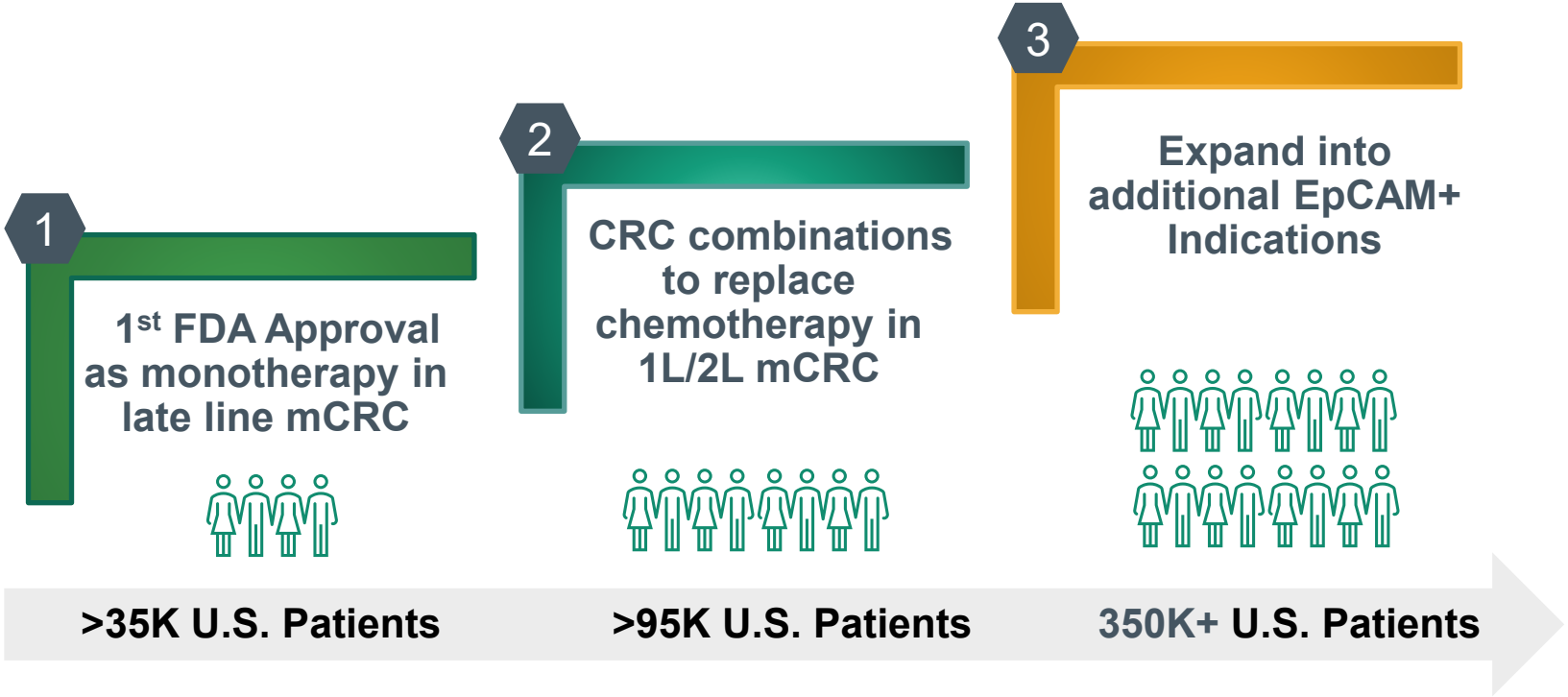
EpCAM is broadly expressed in many solid tumors in addition to CRC



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

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



Sources and assumptions: DRG epidemiology forecast, internal estimates

CX-801 PROBODY® IFNα-2b

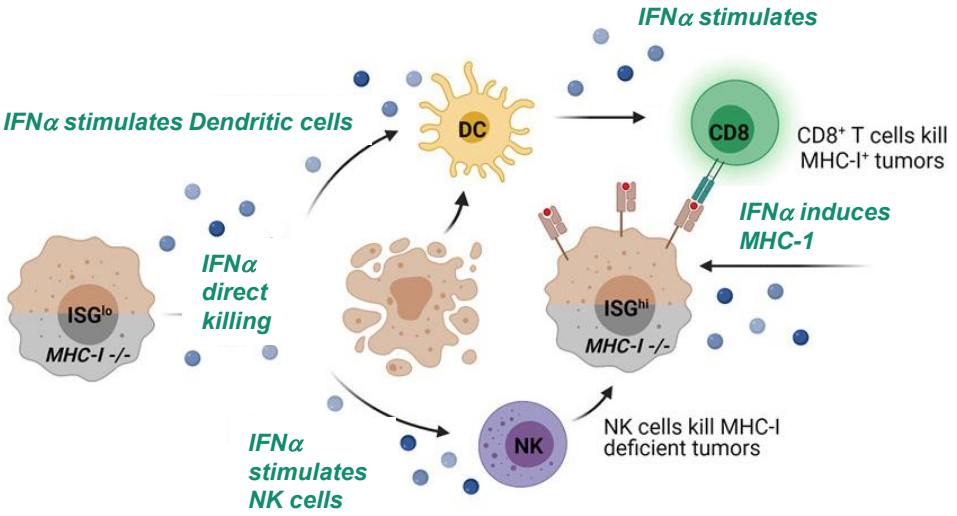
A Novel Immunotherapy Focused in Melanoma

IFNα-2b is a Powerful Cancer Immunotherapy With Ideal Properties to Combine with Checkpoint Inhibitor Therapy

Why IFNα-2b?

IFNα-2b Mechanism of Action

- Kills cancer cells directly leading to immunogenic cell death
- Stimulates antigen presenting cells to activate tumor-reactive T cells
- Modulates NK, stromal and vascular cells
- Approved for treating melanoma (Sylatron™), renal (Avastin® + IFN), and bladder cancer (Adstiladrin®)
- Potential to treat checkpoint resistant / refractory indications



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

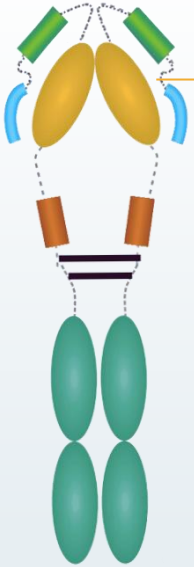
CX-801: Dually-Masked, Conditionally Activated PROBODY® IFNα2b

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

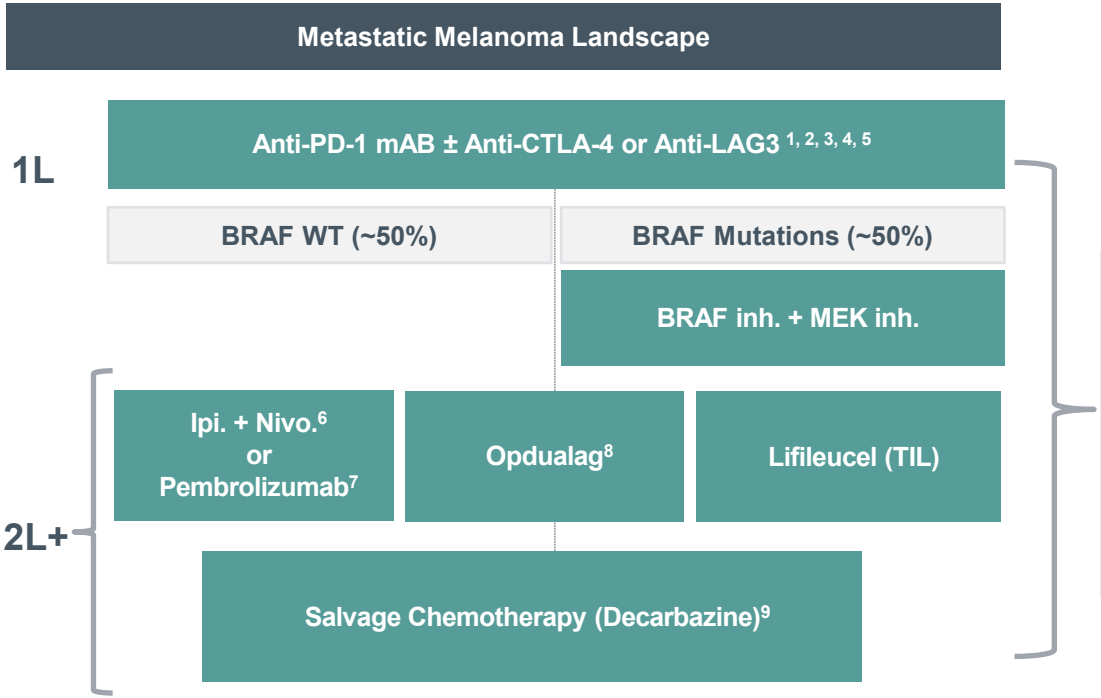
Masking & Substrates Design Strategy

- Dual-masking strategy with steric and affinity mask (peptide)
- 1000X masking efficiency based on preclinical models

CytomX Therapeutics

High Unmet Need in PD-1 Refractory Melanoma Patients

CX-801 has potential to enhance responsiveness to checkpoint inhibitors



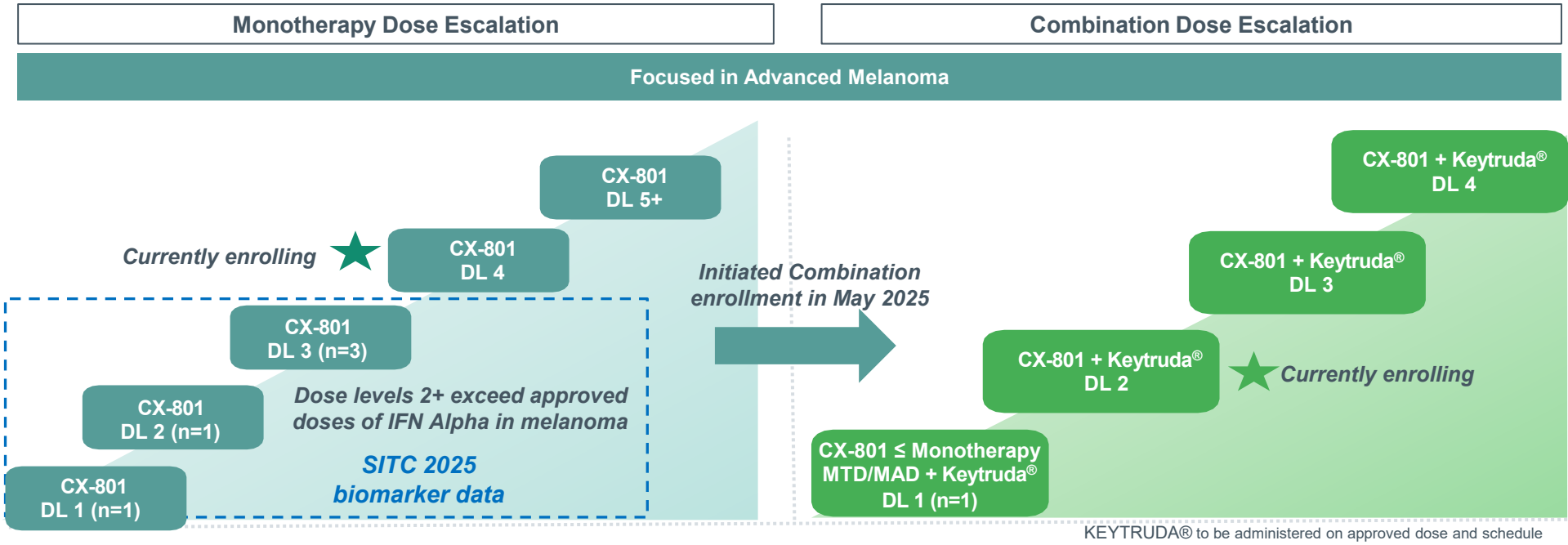
CX-801 Development Opportunities in Melanoma

- **Combine with anti-PD-1 inhibitors in post-PD-1 setting**
  - Improve on activity of PD-1 inhibitors (7% ORR)[9]
  - Safe and tolerable alternative to TIL therapy
- **Novel IO combinations to enhance activity in earlier-line settings**

[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

CytomX Therapeutics

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



KEYTRUDA® to be administered on approved dose and schedule

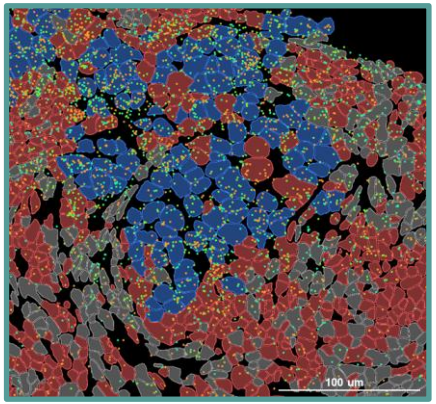
- **Combination dose escalation commenced in May 2025**
- **Initial biomarker data presented at SITC 2025**
- **Phase 1 CX-801 + Keytruda® combination data in 2026**

Source: Package Insert - SYLATRON™

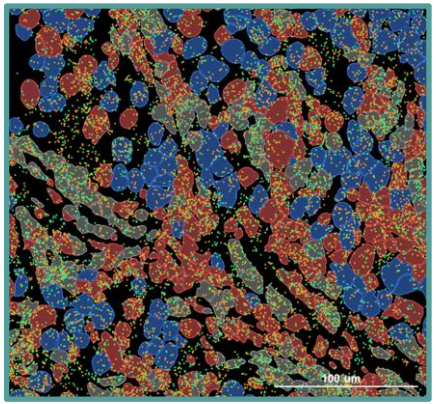
CX-801 Monotherapy Shows Intended MOA in Tumor Biopsies

Strong induction of interferon stimulated genes in multiple cell types

Baseline



On-Treatment

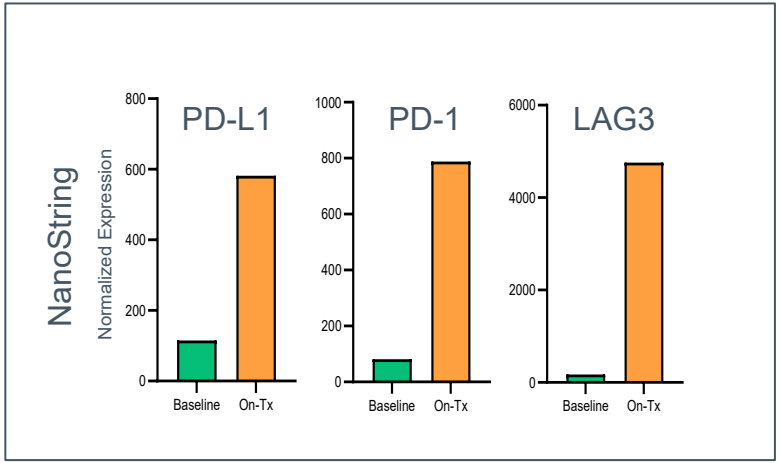


Cell Type

- Melanoma Cells
- Immune Cells
- Stromal Cells

ISG Transcript	Transcript Count Baseline	On-Tx
ISG15	1,061	2,886
MX1	1,185	5,189
IFIT3	882	2,602

Induction of Checkpoint Gene Expression



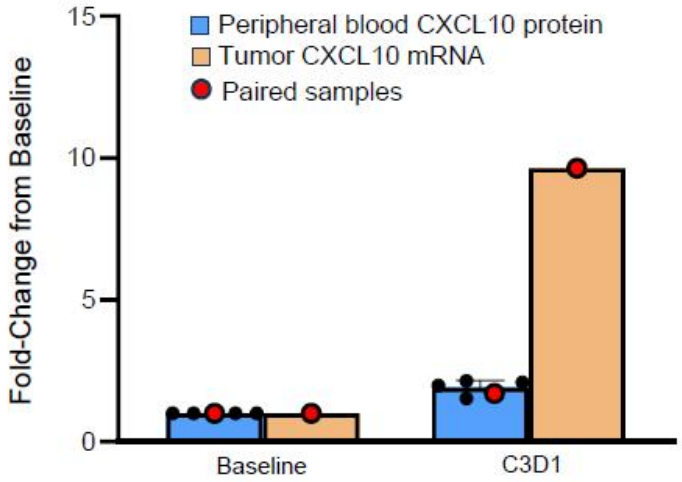
Checkpoint gene expression represented by PD-L1, PD-1, and LAG3 induced by CX-801 measured by NanoString platform (RNA).

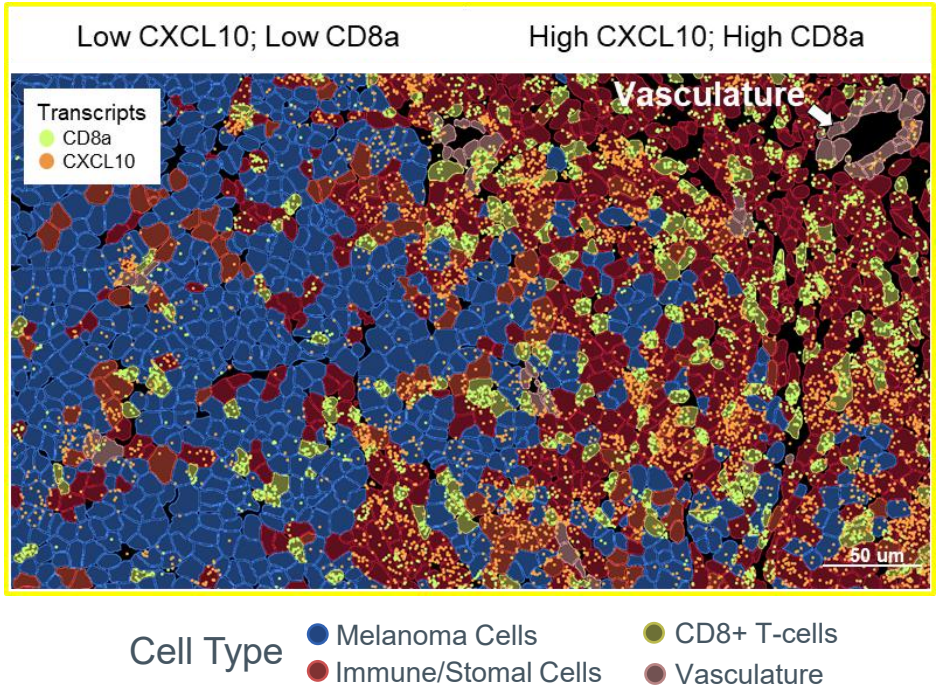
CytomX Therapeutics

40th ANNIVERSARY sitc 2025 Society for Immunotherapy of Cancer Nov. 5–9 | National Harbor, MD

CX-801 Promotes Chemokine Induction in the Tumor Microenvironment Driving Lymphocyte Infiltration into Tumor Tissue

CX-801 Activates Cytotoxic T-cells

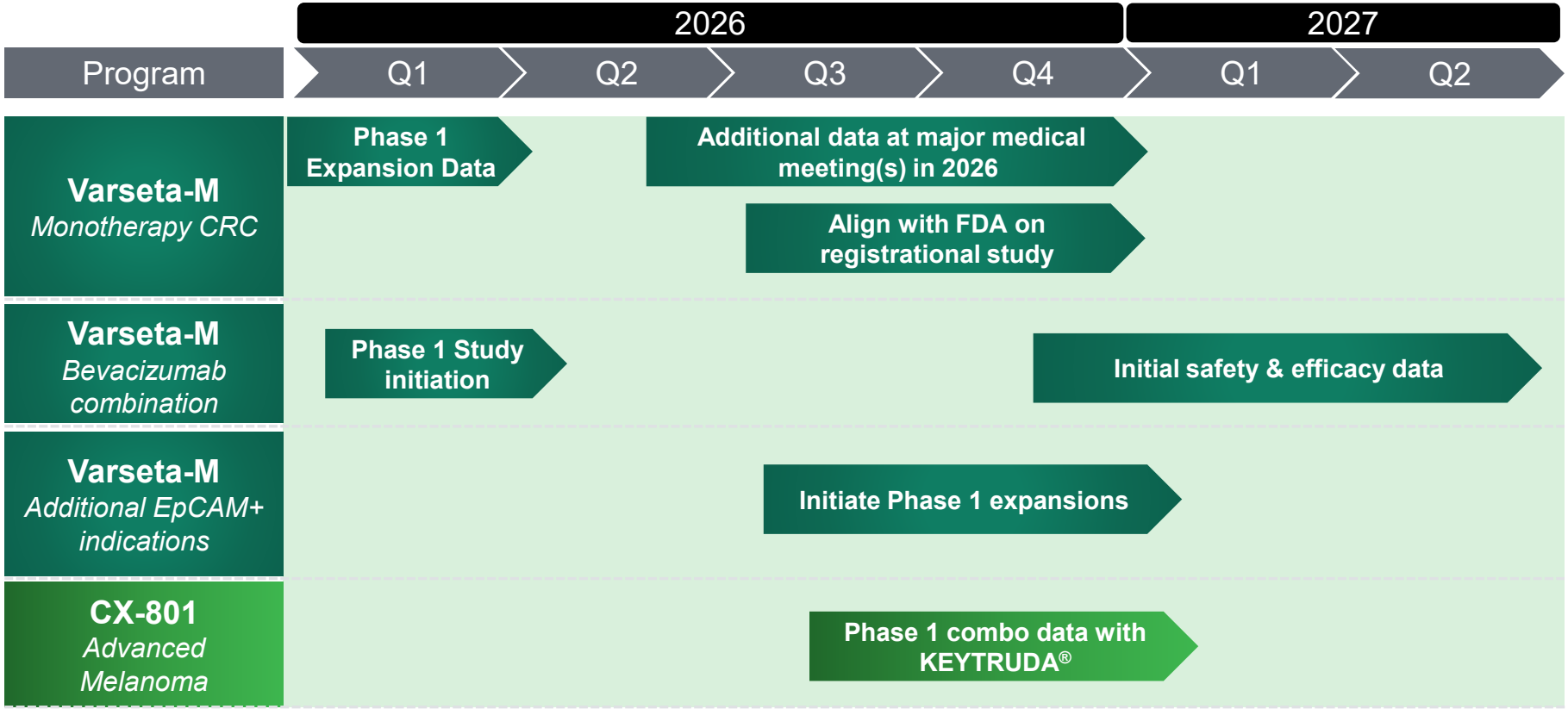




2026 Milestones and Outlook

CytomX Has Significant Pipeline Momentum Entering 2026

Multiple milestones expected while advancing toward later phase development



Appendix

Most Frequent Treatment Related Adverse Events (TRAE) Observed in Varseta-M Phase 1 Interim Dose Escalation Data Presented on May 12, 2025

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

CytomX Therapeutics