CytomX® THERAPEUTICS

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

November 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.

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Company Snapshot

Addressing Major Unmet Need in Oncology

South San Francisco, CA

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

Pipeline: >15 therapeutic 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

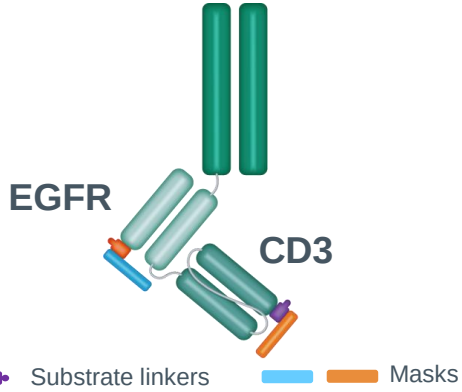
Financials: ~$118M cash balance as of Q3 2024 with cash runway to the end of 2025, excluding any potential milestones or new business development

CytomX Pipeline Addresses Multiple Large Oncology Indications

Multi-Modality, Tumor-Localized Probody® Therapeutics

CX-904 (EGFRxCD3)

PROBODY® T-Cell Engager



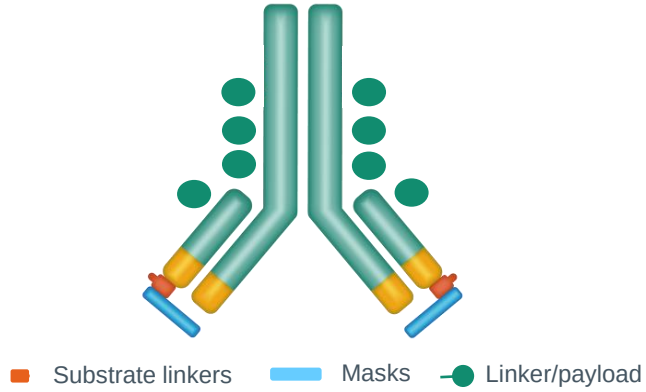
Utilize EGFR expression as an "address" to localize T-cells to solid tumors

OPPORTUNITY

Broad applicability in EGFR+ tumors regardless of mutational status

CX-2051 (EpCAM)

PROBODY® ADC



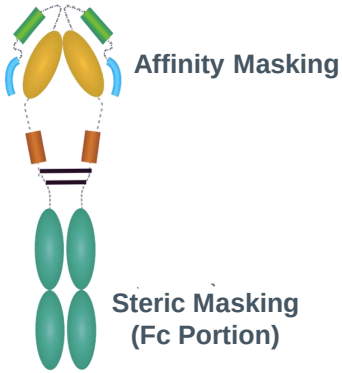
Increase therapeutic index for EpCAM through tumor localization and tailored Topo-1 linker-payload

OPPORTUNITY

EpCAM+ tumors including CRC

CX-801 (IFNα2b)

PROBODY® Cytokine



Harness IFNα2b activity to preferentially impact the tumor microenvironment

OPPORTUNITY

Designed to be a cornerstone of combination therapy

CytomX Therapeutics

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	❑ Decision to Initiate Phase 1b, in Conjunction with Amgen in 2025
CX-2051 (EpCAM ADC)	Phase 1 Dose Escalation	☑ Phase 1 Initiation in EpCAM+ tumors including CRC in 1H 2024 ☑ Enrolling the 5th Dose Escalation Cohort	❑ Initial Phase 1 Data in 1H 2025
CX-801 (IFNα2b)	Phase 1 Dose Escalation	☑ Phase 1 Initiation focused in Melanoma ☑ Merck supply agreement for KEYTRUDA®	❑ Initial Phase 1 Data in 2H 2025
Research Collaborations	Preclinical	☑ $10 million in Astellas milestones achieved in 2024 year-to-date • More than 10 ongoing preclinical programs with partners; majority are T-cell engagers • Additional research milestones achievable in 2024 – 2025 and beyond	

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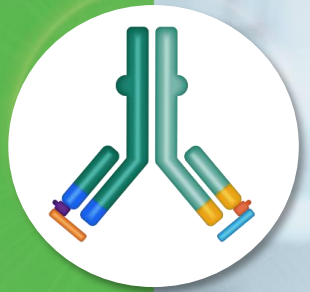
CytomX® THERAPEUTICS

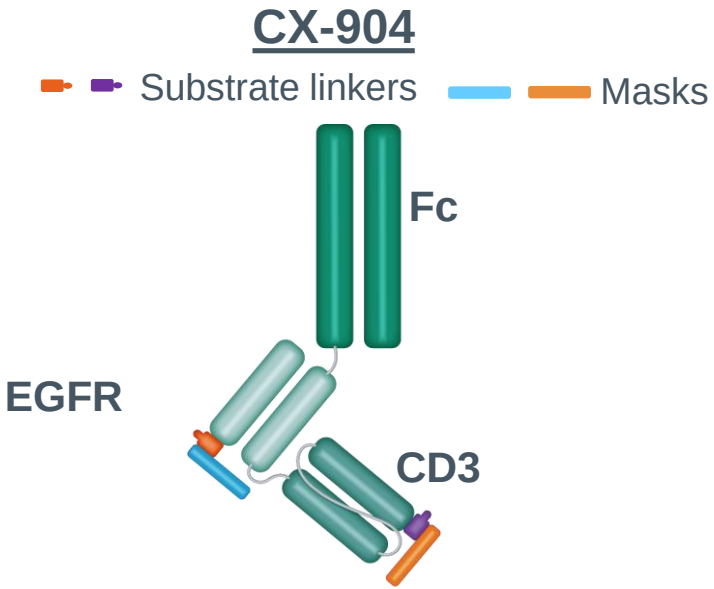
AMGEN



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

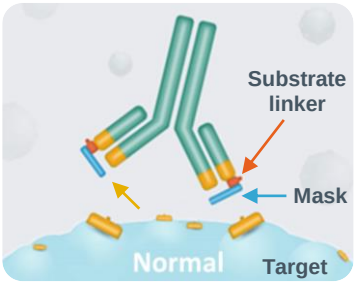
CX-904: Masked PROBODY® T-Cell Engager Targeting EGFR and CD3

Format and Therapeutic Concept

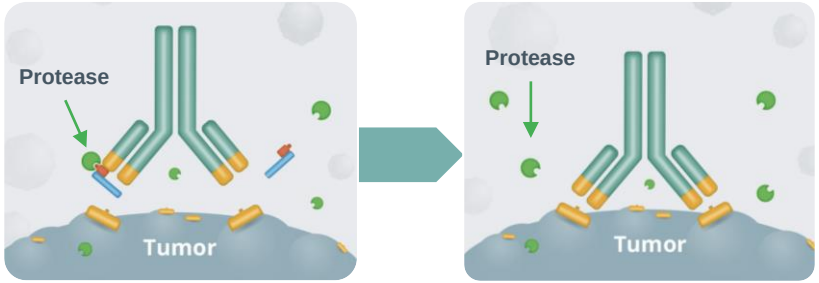


- Finely tuned masks and protease substrates
- Distinct “Prodomains” on EGFR and CD3 to optimize therapeutic window
- Fc domain to mimic PK of approved T-cell engagers

“Masking” limits PROBODY therapeutic binding to healthy tissues



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



CytomX Therapeutics

CX-904 Phase 1a Dose Escalation Current Status

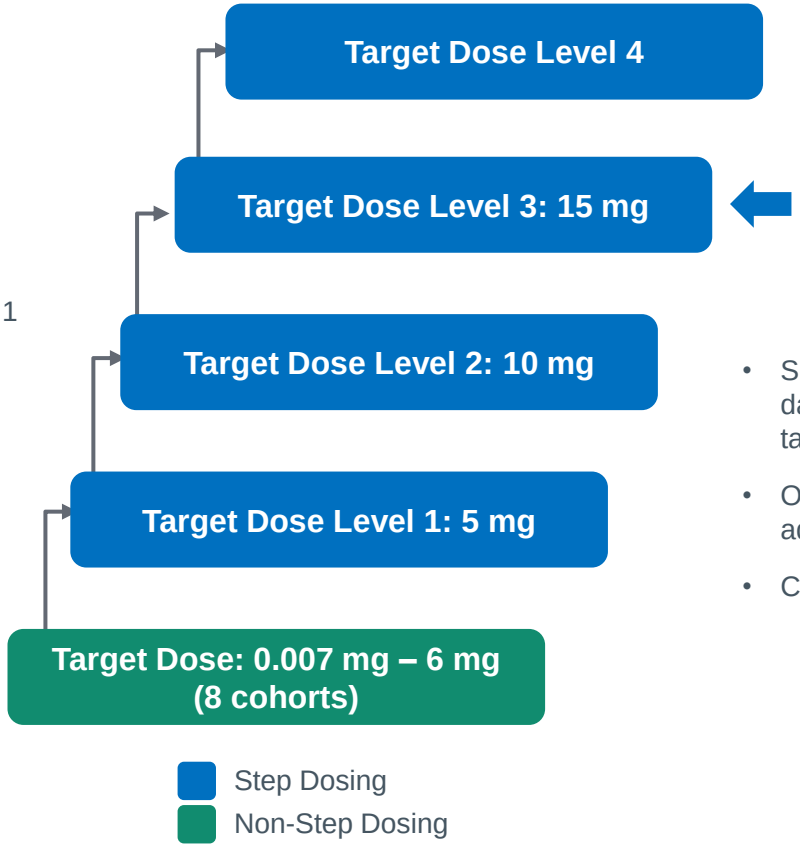
Dose escalation continues

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



Announced on November 7th, 2024 that 15 mg dose level had been cleared.

- 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

Source: 1.CytomX Internal Data

CytomX Therapeutics

CTMX-904-101 Phase 1a Baseline Characteristics

35 patients enrolled through 10 mg Target Dose

CytomX Initial Phase 1a Update, May 8, 2024

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%)

**17 of 18 patients MSS CRC*

Data cutoff as of 16 Apr 2024

CytomX Therapeutics

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

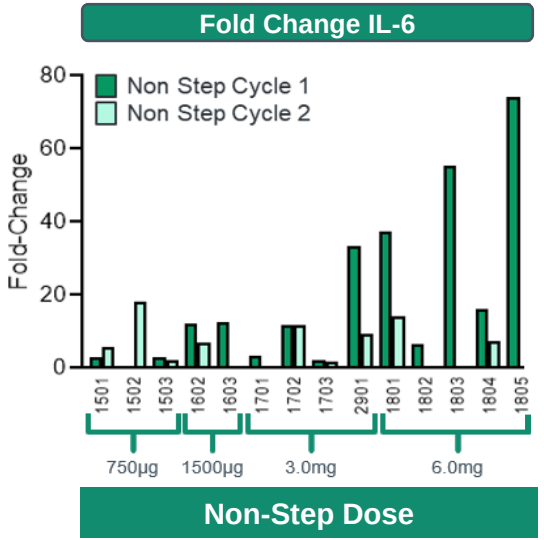
No CRS observed through 3 mg, no grade >1 CRS at 6 mg

CytomX Initial Phase 1a Update, May 8, 2024

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*

CytomX Therapeutics

Data cutoff as of 16 Apr 2024

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

No CRS or ICANS of any grade; dose escalation continues

CytomX Initial Phase 1a Update, May 8, 2024

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

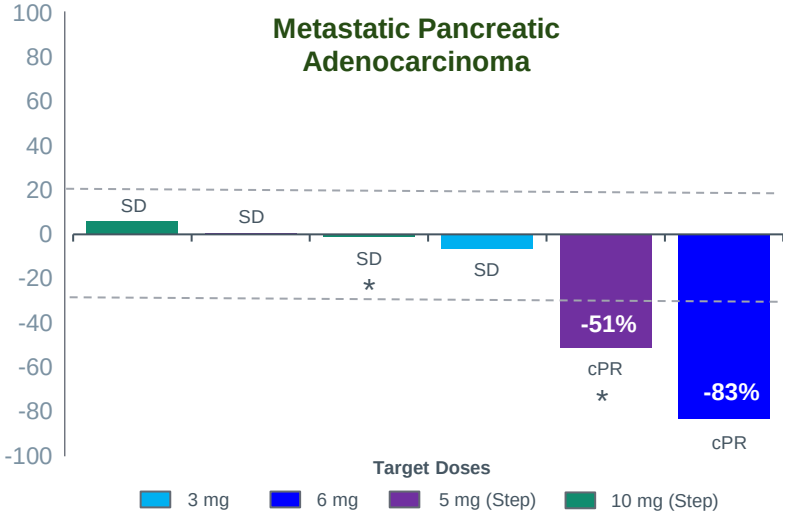
Phase 1a Initial Anti-Tumor Activity for CX-904

Confirmed objective responses and disease control observed in pancreatic cancer

CytomX Initial Phase 1a Update, May 8, 2024

CX-904 Initial Phase 1a Actvity - Best Reponse Per Recist 1.1
Target Doses ≥ 0.75 mg (n=26)

Efficacy Evaluable Patients *Advanced late-line disease N=25*[1]	Confirmed Objective Response	Stable Disease	Progressive Disease	Measurable Reductions in Tumor Burden
CRC (n=13)[1]	-	3 (23%)	9 (69%)	2 (15%)
Pancreatic (n=6)	2 (33%)	4 (67%)	-	4 (67%)
NSCLC (n=2)	-	1 (50%)	1 (50%)	1 (50%)
HNSCC (n=2)	-	-	2 (100%)	-
Gastric (n=2)	-	-	2 (100%)	-
Esophageal (n=1)	-	1 (100%)		1 (100%)



[1] *One CRC patient was not evaluable because tumor assessment was performed prior to minimum time requirement for categorical response of SD per RECIST 1.1*

Data cutoff as of 16 Apr 2024

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

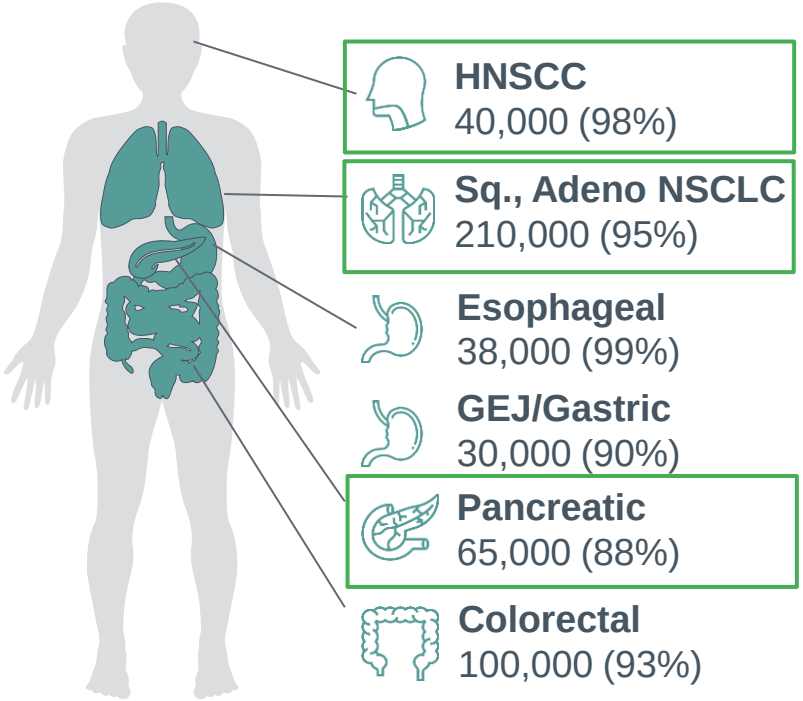
CX-904 Can Potentially Address Multiple Indications With High Unmet Need

CX-904 - High Potential TCE for EGFR+ Tumors

- CX-904 has demonstrated a favorable initial safety profile with non-step and step dosing schedules
- Promising early signs of efficacy, including confirmed RECIST 1.1 responses in pancreatic cancer
- Prevalent EGFR expression in many cancer types positions CX-904 to potentially address large unmet need in oncology
- Dose escalation currently focused in Pancreatic, NSCLC, and HNSCC to inform Phase 1b strategy

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

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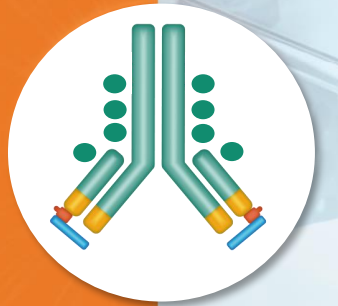
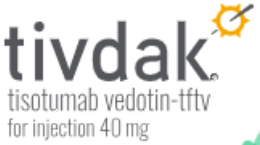


CX-2051:
Masked PROBODY® ADC Targeting EpCAM

Antibody Drug Conjugates, a Growing and Potent Modality in Solid and Liquid Tumors

Approved Solid Tumor ADCs



TF1

HER2

TROP2

HER2

Nectin4

FRα

Approved Liquid Tumor ADCs

CD79b

CD19

CD30

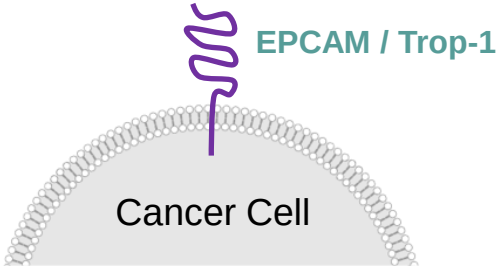
CD22

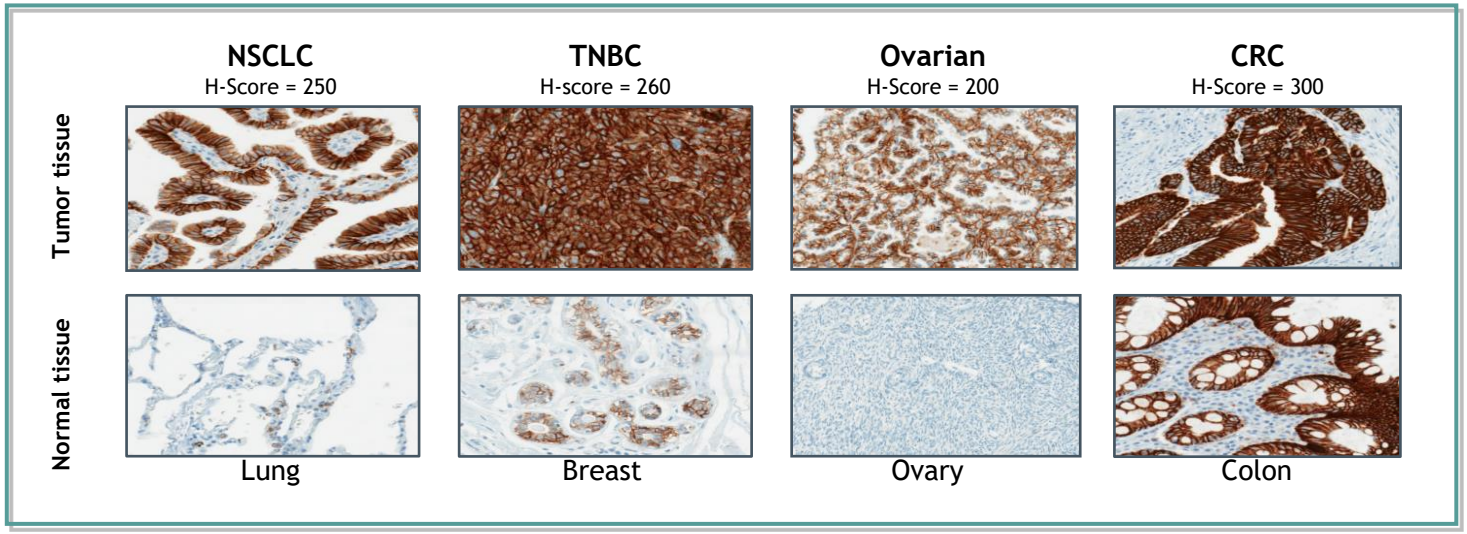
CD33

CytomX Therapeutics

EpCAM (Epithelial Cell Adhesion Molecule) has Potential as a Pan-Tumor ADC Target with Very High Expression 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

EpCAM Has Been Clinically Validated But Not as a Systemic Therapy

Systemic therapies limited by high grade gastrointenstinal 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 but later withdrawn for commercial reasons

Insys Therapeutics

Prior systemic EpCAM approaches discontinued due to on-target toxicity

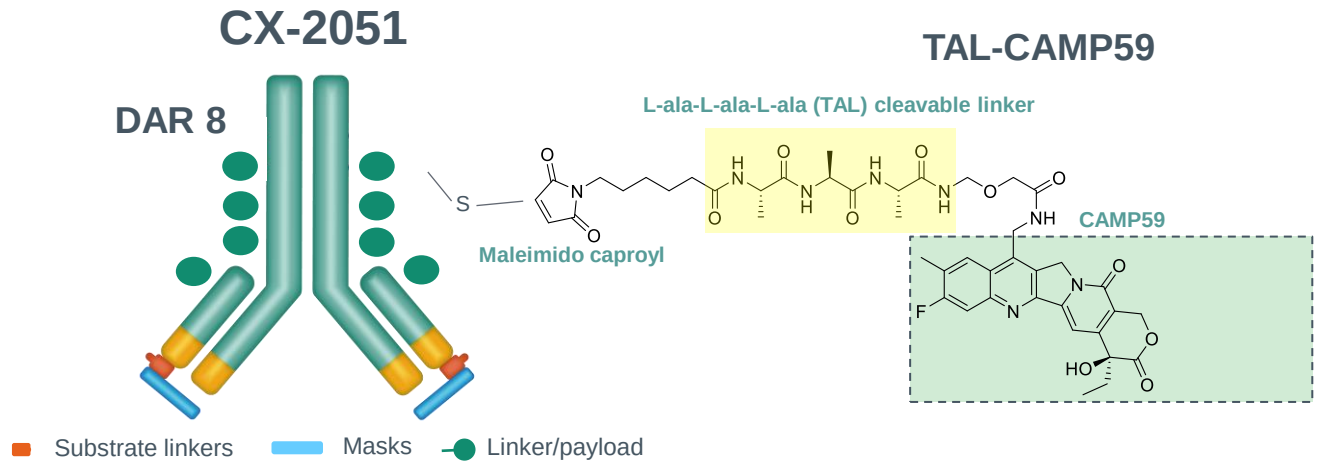
Asset	Company	MOA	Phase	DLTs*
Solitomab	Amgen	EpCAM x CD3 BiTE	1	• Grade 3+ diarrhea • Grade 3+ elevation in liver enzymes
ING-1	XOMA	EpCAM mAb	1	• Pancreatitis
3622W94	GSK	EpCAM mAb	1	• Pancreatitis

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

CytomX Therapeutics

CX-2051 Tailored to EpCAM Expressing Indications, Including CRC

Designed with next-generation topo-1 linker-payload (TAL-CAMP59)



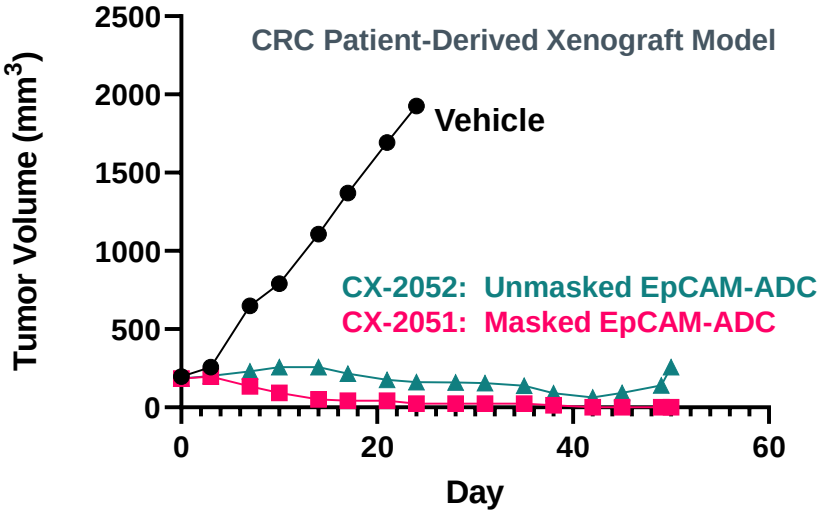
- High affinity EpCAM antibody with masking efficiency >100x by ELISA
- Protease-cleavable linker and with broad cleavability across multiple tumors
- TAL payload-antibody linker designed to have similar cleavability profile as deruxtecan (DXd) and is optimized for bystander effect
- CAMP59 shows similar potency to DXd in multiple cell lines and preclinical models
- EpCAM target highly expressed in CRC and other cancer types that are known to be sensitive to the payload mechanism of action

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

CytomX Therapeutics

CX-2051 Shows Equivalent Anti-Tumor Efficacy as Unmasked EpCAM ADC With Substantially Improved Tolerability Compared to the Unmasked ADC

CX-2051 is efficiently unmasked and activated in the tumor microenvironment



Dosing regimen: 6 mg/kg, Q2W x 3

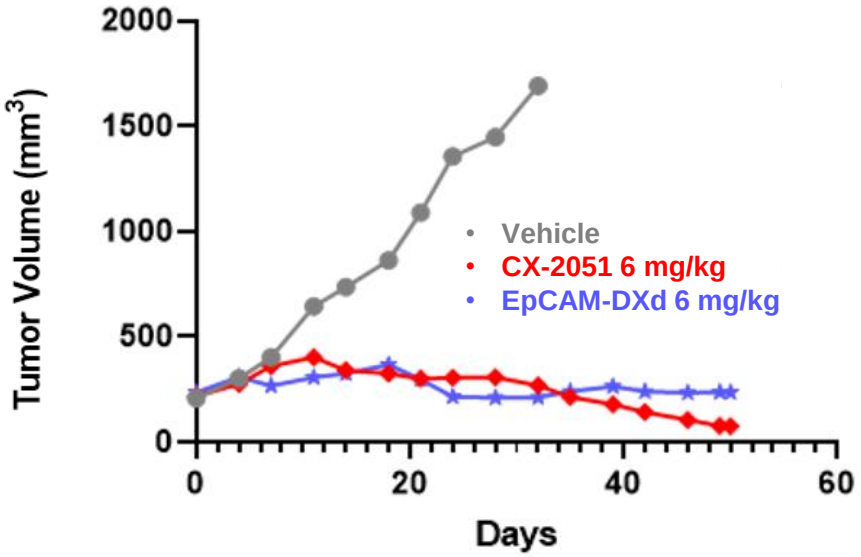
Tolerability in Cyno Toxicology Study

Dosing (3 x Q2W)	CX-2051 (Masked)	CX-2052 (Unmasked)
10 mpk	Tolerated	Not tolerated
30 mpk	Tolerated	
60 mpk	Tolerated	
90 mpk	Not Tolerated	

Source: CytomX Internal Data; 14th Annual World ADC Conference, October 2023

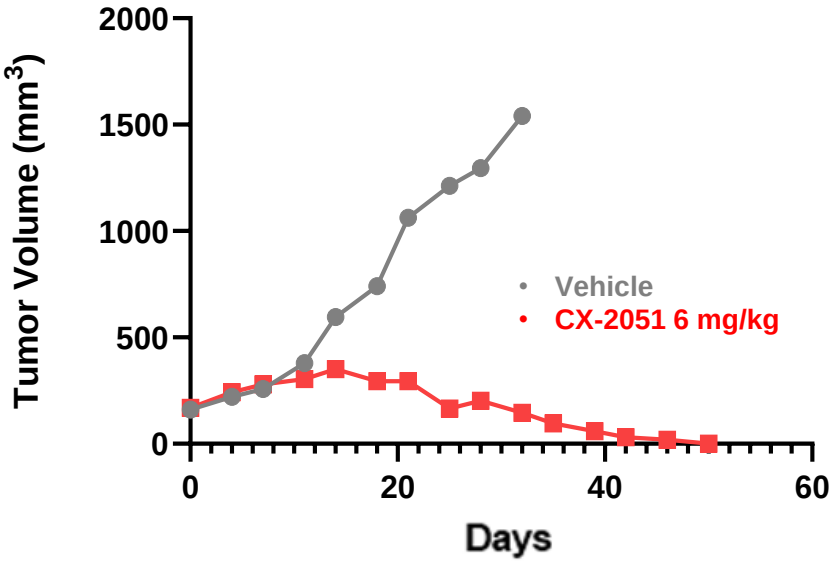
Preclinical Profile of CX-2051 Shows Deruxtecan-Like Potency and Efficacy in Irinotecan-Resistant Models

CX-2051 payload shows equivalent preclinical activity to deruxtecan (DXd)



Dosing regimen: 6 mg/kg, Q2W x 3

CX-2051 preclinical efficacy in irinotecan-resistant CRC PDX model



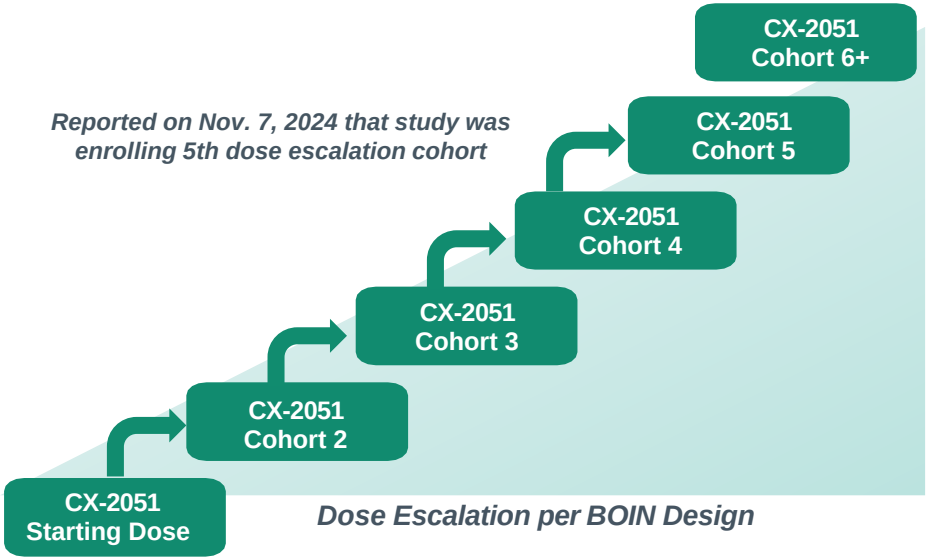
Dosing regimen: 6 mg/kg, Q2W x 3

Source: 14th Annual World ADC Conference, October 2023, CytomX Internal Data

CX-2051 Phase 1 Strategy Designed to Rapidly Demonstrate Proof of Concept in CRC and Other EpCAM Expressing Tumors

Part 1: Dose Escalation

Advanced/metastatic solid tumors with known/documented EpCAM expression focused in CRC



- Determine dose(s) for indication specific expansions; assess for early evidence of anti-tumor activity

Part 2: Dose Expansion

Indication-Specific Expansion Cohorts

*Advanced/Metastatic CRC**

CX-2051 ≤ MTD/MAD

EpCAM+ Cancer #2

CX-2051 ≤ MTD/MAD

EpCAM+ Cancer #3

CX-2051 ≤ MTD/MAD

- Evaluate safety and tolerability and efficacy in multiple EpCAM+ tumors

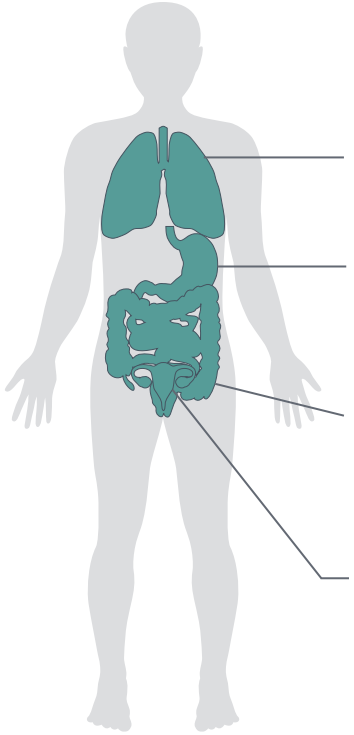
BOIN = Bayesian optimal interval; MAD = Maximum assessed dose; MTD = Maximum tolerated dose

* Example

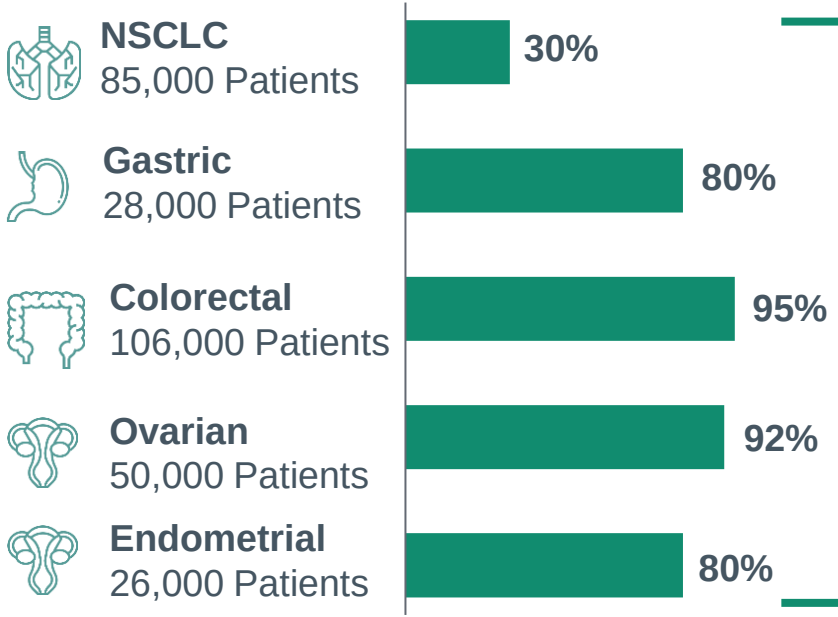
CytomX Therapeutics

CX-2051 – Broad Opportunity Across Multiple EpCAM+ Indications

2023 US Metastatic, Addressable Patients



% of Patients with EpCAM+ Tumors (IHC ≥ 2+)



>295,000
EpCAM+
Addressable Patients

Source: DRG Epidemiology & Forecast Dashboards, 2021 – 2023

CytomX Therapeutics

CytomX® THERAPEUTICS

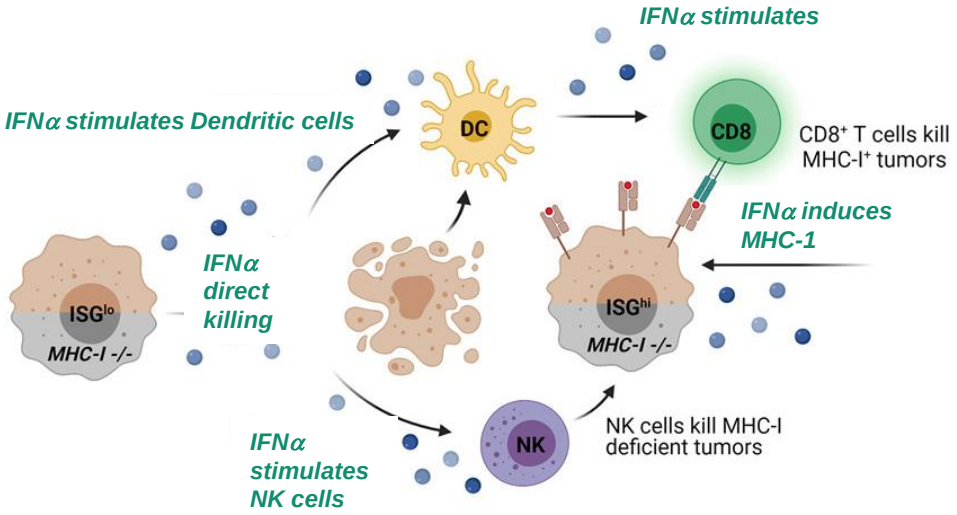
CX-801:
Dually-Masked PROBODY® Cytokine, IFNα-2b

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

CytomX Therapeutics

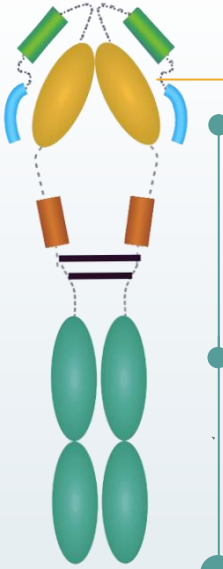
CX-801: Dually-Masked, Conditionally Activated PROBODY® IFNα2b

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

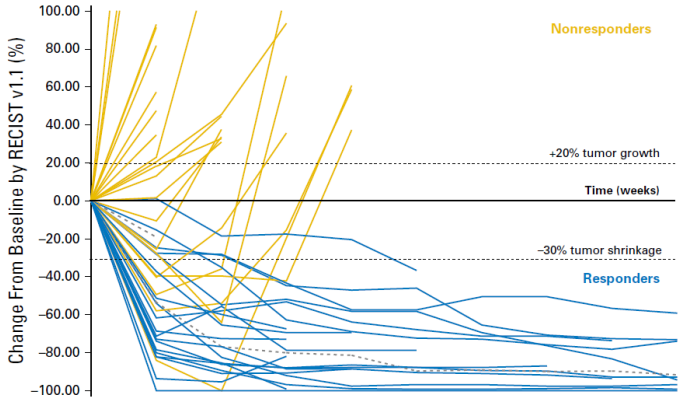
- Dual-masking strategy with steric and affinity mask (peptide)
- 1000X masking efficiency based on preclinical models
- Preclinically, Probody IFNα is effectively unmasked in the tumor

CytomX® THERAPEUTICS

IFN-α2b has Proven Activity in Combination with PD-1 but Has Been Limited Due to Toxicity

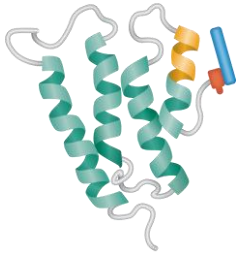
Peginterferon + PD-1 in Melanoma

(Davar et al., J Clin. Onc., 2018)



- ⊕ Potent activity (60.5% ORR)
- ⊖ Significant, dose limiting adverse events (49% Grade 3/4 AEs)

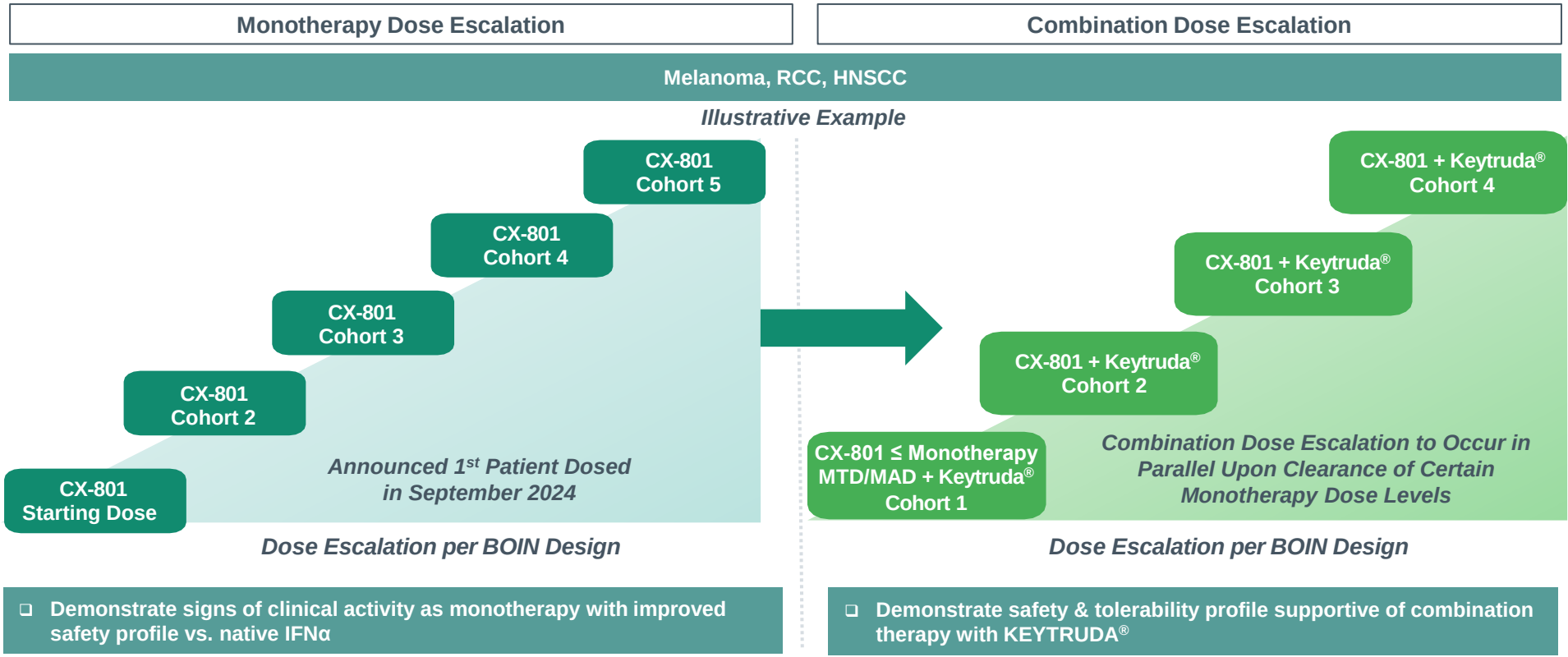
CX-801 (Conditionally-Activated IFN-α2b)



- ⊕ Less systemic toxicity
- ⊕ Better Exposure
- ⊕ Systemic Delivery
- ⊕ Increased Therapeutic Index
- ⊕ Improved Combination Therapies

CytomX Therapeutics

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



- Demonstrate signs of clinical activity as monotherapy with improved safety profile vs. native IFNα
- Demonstrate safety & tolerability profile supportive of combination therapy with KEYTRUDA®

NOTE: PD-1 Inhibitor administered on approved dose and schedule, BOIN = Bayesian Optimal Interval; MTD = Maximum tolerated dose; MAD = Maximum assessed dose

CytomX Therapeutics: Building for the Future

- **Differentiated PROBODY® Platform**
- **Robust Multi-Modality Pipeline of Masked Biologics**
- **Large Market Opportunities**
- **High-Quality Partners**
- **Strong Financial Position**
- **Talented Organization**