CytomX Therapeutics

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

January 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; the uncertainties inherent in the initiation and enrollment of clinical trials; the uncertainties associated with the COVD-19 pandemic; expectations of expanding on-going clinical trials; availability and timing of data from clinical trials; the unpredictability of the duration and results of regulatory review; 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; and possible safety or efficacy concerns, 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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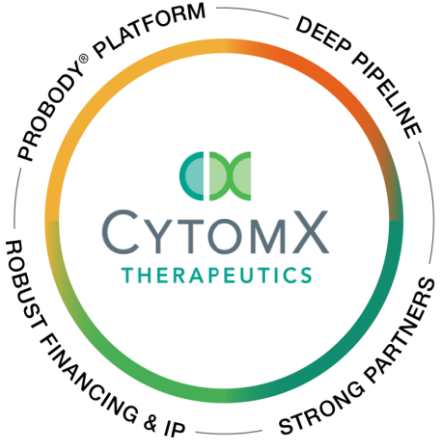
Company Snapshot

Addressing Major Unmet Need in Oncology



South San Francisco, CA

Probody® Platform: Unique antibody engineering strategy for tumor localization and enhancement of therapeutic index

Pipeline: >15 Probody programs in multiple therapeutic modalities; 4 clinical-stage molecules, 3 with retained commercial rights

Lead Programs: CX-904 (EGFR-CD3), CX-2051 (EpCAM ADC), CX-801 (IFN-α2b), BMS-986288 (CTLA-4-NF)

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

Financials: $194M cash balance as of Q3 2023 with cash runway to the 2nd half of 2025, excluding any potential milestones or new business development

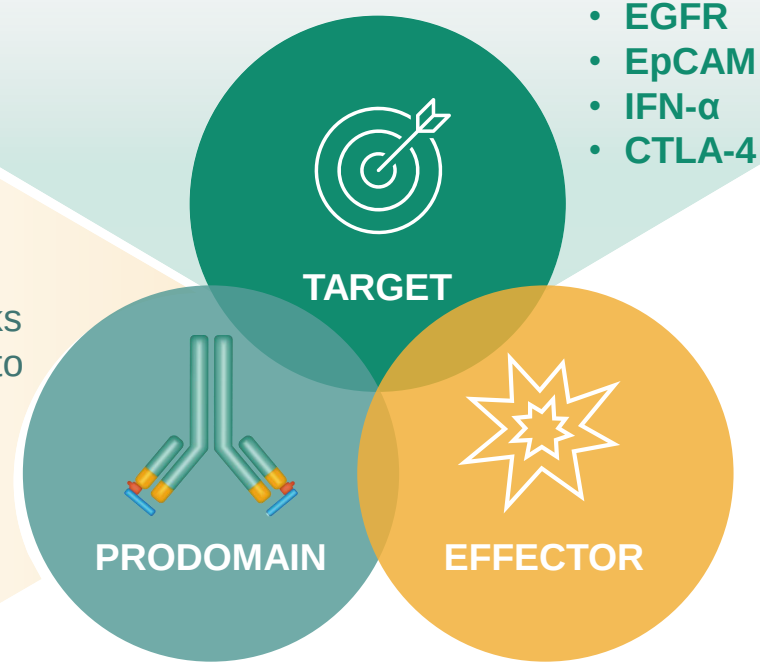
Organization: ~120 employees; seasoned executive team with ~200 years of collective biotech experience; integrated R&D capabilities to support wholly-owned and collaboration programs

CytomX Product Design Strategy Leverages the Probody® Platform

Optimized Selection of Target, Prodomain and Effector Function

Targets with **validated anti-tumor efficacy** that need localization to unlock potential

- **EGFR**
- **EpCAM**
- **IFN-α**
- **CTLA-4**



Optimized tuning of masks and protease substrates to **maximize potential therapeutic index**

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

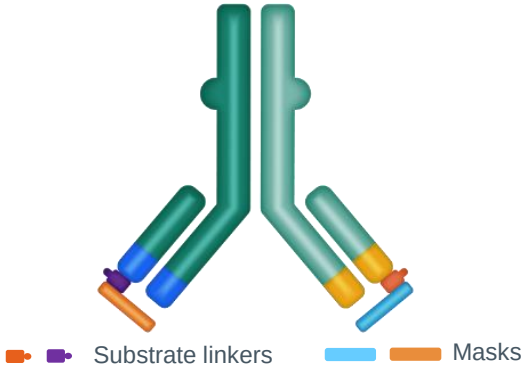
- **TCE**
- **ADC**
- **Cytokine**
- **Fc**

CytomX Pipeline Addresses Multiple Large Oncology Indications

Multi-modality, Tumor-Localized Probody® Therapeutics

CX-904 (EGFRxCD3)

Probody® T-Cell Engager



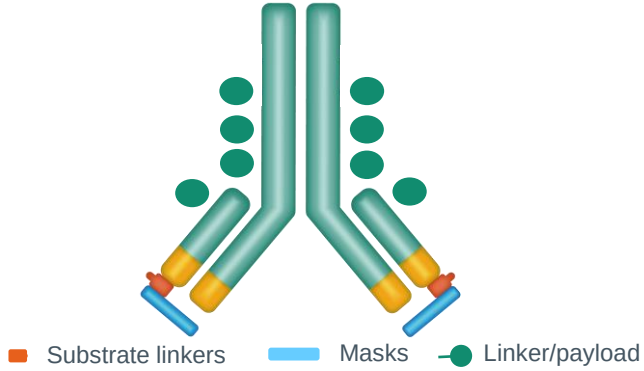
Utilize EGFR expression as an "address" to localize T-cells to solid tumors

OPPORTUNITY

Broad applicability in EGFR+ tumors regardless of mutational status

CX-2051 (EpCAM)

Probody® ADC



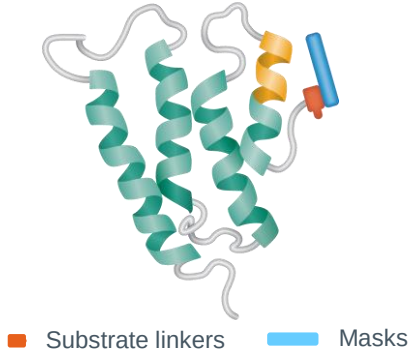
Increase therapeutic index for EpCAM through tumor localization and tailored Topo-1 linker-payload

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

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CytomX Multi-Modality Clinical Pipeline of Probody® Therapeutics

Company Entering a Milestone-Rich Period Starting in 2024

Program	Effector	Indications	Preclinical	Phase 1	Phase 2	2024 Milestones
CX-904 (EGFR)	T-Cell Engager (CD3)	EGFR+ Solid tumors	CytomX / Amgen — *Shared U.S. Commercial Rights*			❑ Phase 1a Data ❑ Decision to Expand to Phase 1b
CX-2051* (EpCAM)	ADC Topo1 Payload	EpCAM+ Tumors incl. CRC	CytomX — *Wholly-Owned*			☑ IND Filed in Dec ‘23 ❑ Phase 1 initiation
CX-801 (IFNα2b)	Cytokine IFNα2b	Solid Tumors incl. Melanoma, Renal, HNSCC	CytomX — *Wholly-Owned*			☑ IND Filed in Dec ‘23 ❑ Phase 1 initiation
BMS-986288 (CTLA-4)	Non-Fucosylated CTLA-4	Solid Tumors	Bristol Myers Squibb — *Milestones & Royalties to CytomX*			❑ POC Trials in NSCLC & MSS CRC Ongoing ❑ Data Anticipated in ‘24

*Licensed from Immunogen

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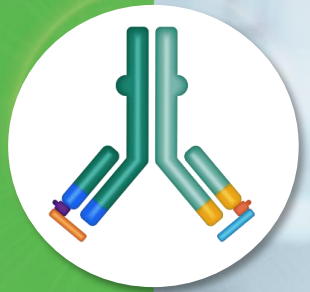
AMGEN

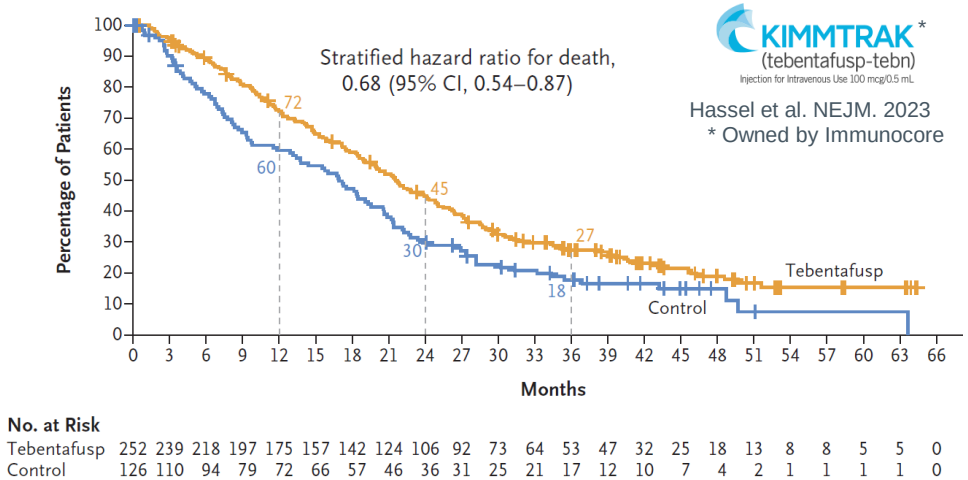


CX-904: Conditionally Activated Probody® T-cell Engager Targeting EGFR and CD3

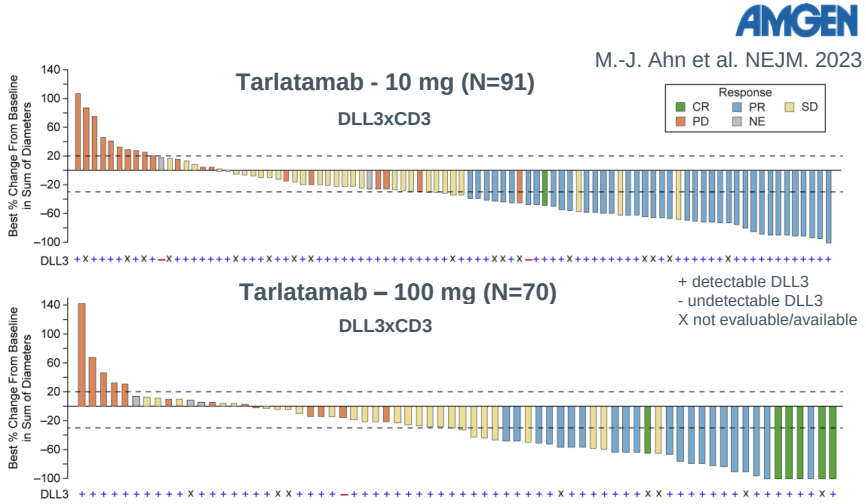
Landscape for T-Cell Engagers (TCEs) for Solid Tumors

Increasing Clinical Validation, Major R&D Investment Across the Industry

Tebentafusp in Uveal Melanoma



Tarlatamab in SCLC



Solid Tumor TCEs are a Key Focus Area for Global Oncology Leaders

AMGEN · astellas · Roche · Pfizer · REGENERON · abbvie · Boehringer Ingelheim

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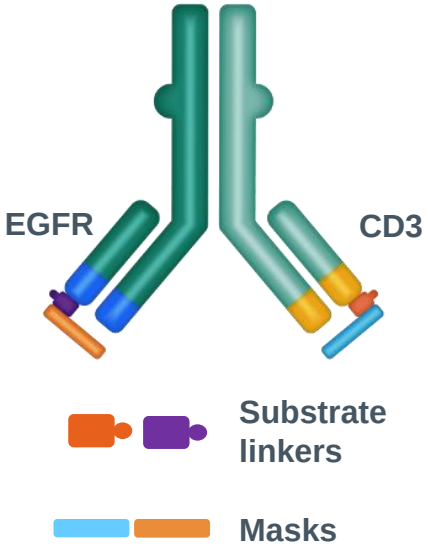
CytomX Probody® T-cell Engagers are Designed to Address Key Limitations of Conventional TCEs in Solid Tumors

Probody® T-Cell Engagers



- **Conventional T-cell engagers** are highly potent, but their use in solid tumors is significantly limited by:
  - Systemic toxicities such as CRS and ICANS
  - On-target, off-tumor toxicity
- **Conditionally activated Probody® T-cell engagers** are designed to retain potent anti-tumor activity while having less systemic toxicities
- CytomX has a **broad pipeline of partnered Probody TCE programs** with retained commercial rights on select programs, including CX-904

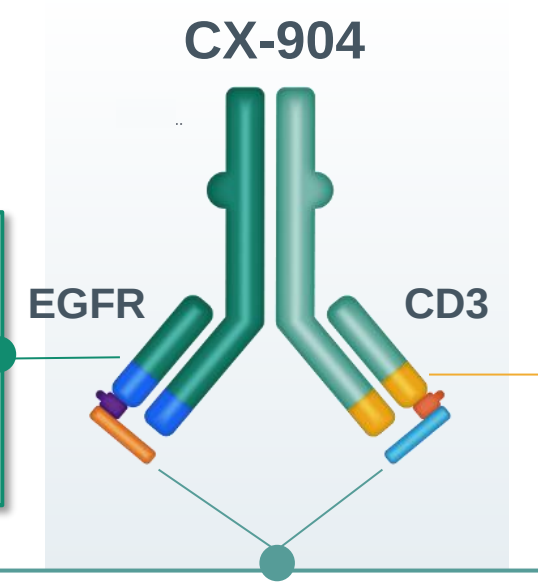
CX-904: Optimized Design

Conditionally Activated Probody® T-Cell Engager Targeting EGFR and CD3

TARGET

Validated, High Potential Target

- Broad expression across solid tumors
- Clinical validation across multiple modalities
- Limited therapeutic index (e.g., skin rash, gastrointestinal toxicities)



EFFECTOR

TCE – CD3

- Potent anti-tumor activity across hematological malignancies
- Growing validation in solid tumors

PRODOMAIN

Optimized Masking

- Customized masks and protease cleavable linkers for EGFR and CD3 binding domains
- >60-fold increase in MTD preclinically for Probody TCE vs. unmasked EGFR TCE

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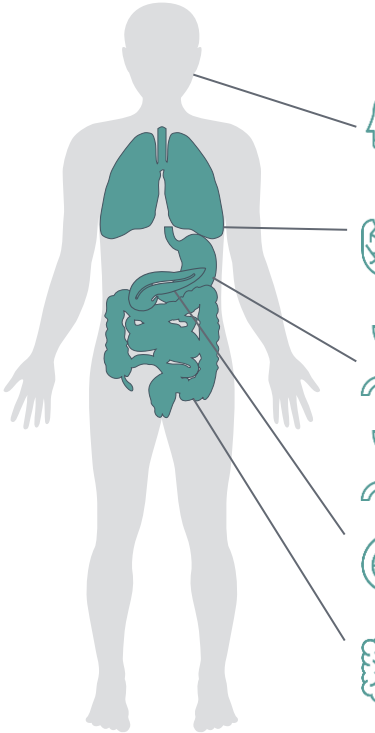
CX-904 – Broad Market Opportunity Across Multiple Indications

2023 US Metastatic, Addressable Patients



% of Patients with EGFR+ Tumors (TPM 8+)

HNSCC
40,000 Patients — 98%

Sq., Adeno NSCLC
210,000 Patients — 95%

Esophageal
38,000 Patients — 99%

GEJ/Gastric
30,000 — 90%

Pancreatic
65,000 — 88%

Colorectal
100,000 Patients — 93%

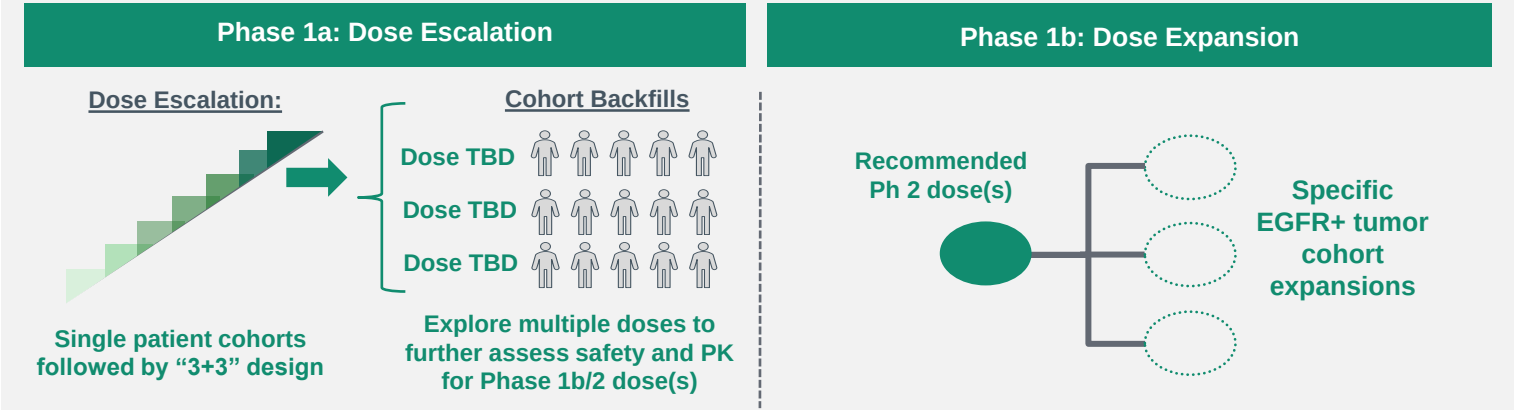
>450,000
EGFR+
Addressable Patients

Source: TPM 8+ equivalent to 2+ by IHC (internal prevalence study); TPM = Transcripts per million; TCGA RNA Seq Data; Epidemiology data from DRG

CX-904 Progress and 2024 Milestones

- Phase 1a ongoing in patients with advanced solid tumors with known EGFR expression
- Backfilling of certain dose escalation cohorts initiated in Q4 2023
- Initial Phase 1a data anticipated in the 2nd half of 2024
- Potential decision (to be taken with Amgen) to initiate Phase 1b expansion cohorts in specific EGFR positive tumor types is anticipated in 2024

Study CTMX-904-101*



*Illustrative Example

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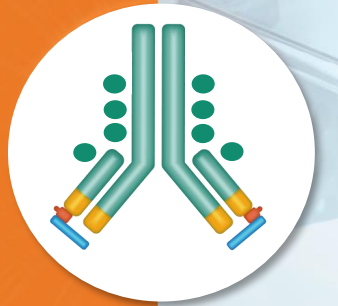


CX-2051: Conditionally Activated Probody® ADC Targeting EpCAM

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

Approved Solid Tumor ADCs

tivdak
tisotumab vedotin-tftv
for injection 40 mg

TF1

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

HER2

TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

TROP2

Kadcyla®
ado-trastuzumab emtansine
20 mg/mL INJECTION FOR INTRAVENOUS USE

HER2

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

Nectin4

ELAHERE™
mirvetuximab soravtansine-gynx
injection 100 mg

FRα

Approved Liquid Tumor ADCs

POLIVY™
polatuzumab vedotin-piiq
INJECTION FOR INTRAVENOUS USE 30 MG | 140 MG

CD79b

Zynlonta®
loncastuximab tesirine-lpyl
for injection, for intravenous use • 10mg

CD19

ADCETRIS®
brentuximab vedotin | injection 50 mg

CD30

BESPONSA™
inotuzumab ozogamicin INJECTION FOR IV INFUSION
0.9 mg single-dose vial

CD22

MYLOTARG™
gemtuzumab ozogamicin injection for IV infusion
4.5 mg single-dose vial

CD33

CytomX THERAPEUTICS

EpCAM Has Been Clinically Validated But Not as a Systemic Therapy

Locally administered EpCAM therapies have been validated in the clinic

- **Removab® (catumaxomab):** EpCAM x CD3 bispecific
- Delivered by intraperitoneal infusion
- Approved for treatment of malignant ascites (but later withdrawn for commercial reasons)

Insys Therapeutics

- **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

Systemic EpCAM approaches have significant toxicity concerns

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

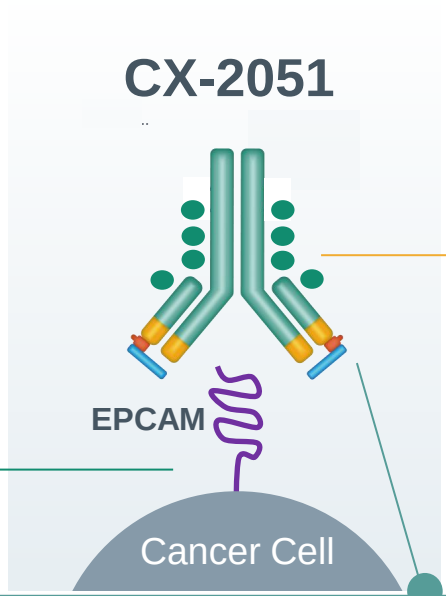
CX-2051: Optimized Design

Conditionally Activated EpCAM Probody® ADC with Topoisomerase-1 Linker-Payload

TARGET

Validated, High Potential Target

- Broad expression profile
- Proven localized anti-cancer activity
- Limited therapeutic index that requires masking



EFFECTOR

Tailored Payload

- Next-gen camptothecin analog (Topo-1) linker-payload, DAR8
- Optimized to drive bystander activity
- Payload known efficacy in EpCAM+ tumor types

PRODOMAIN

Optimized Masking

- Protease-cleavable substrate with broad cleavability across multiple tumors
- Peptide mask with masking efficiency >100x by ELISA

Program licensed from immunogen

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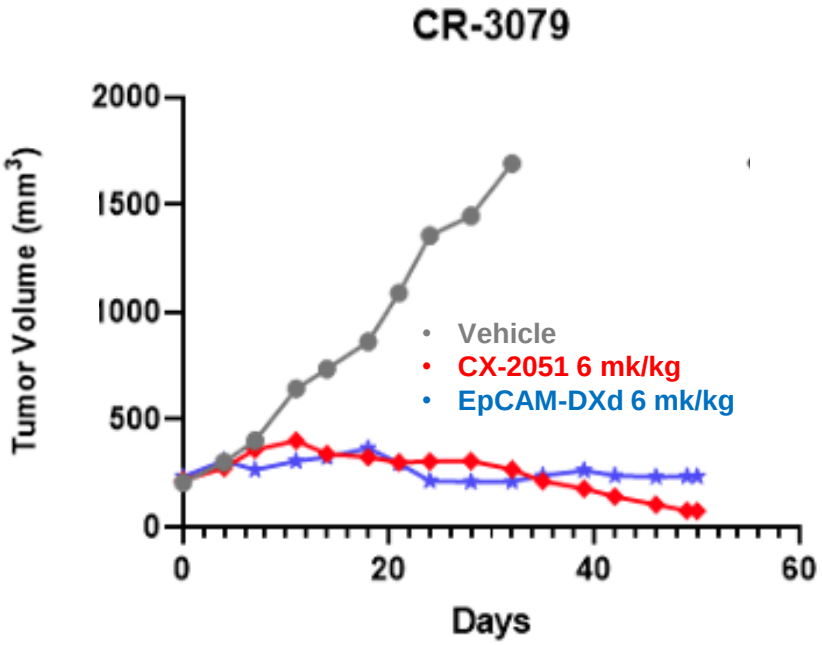
Preclinical Profile of CX-2051 Shows DXd-like Potency with Substantially Improved Tolerability Compared to the Unmasked ADC

Anti-Tumor Xenograft Activity in CRC Model



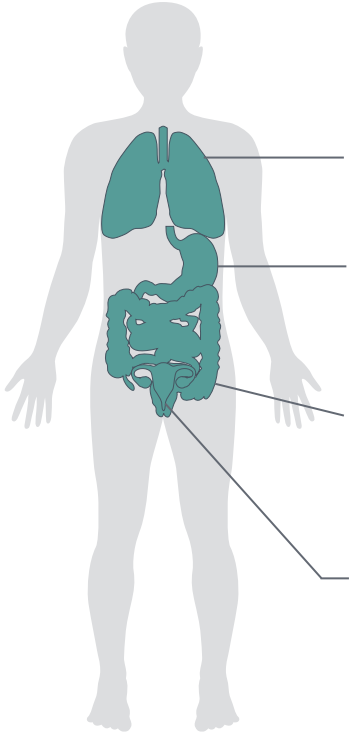
Tolerability in Cyno Toxicology Study

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	

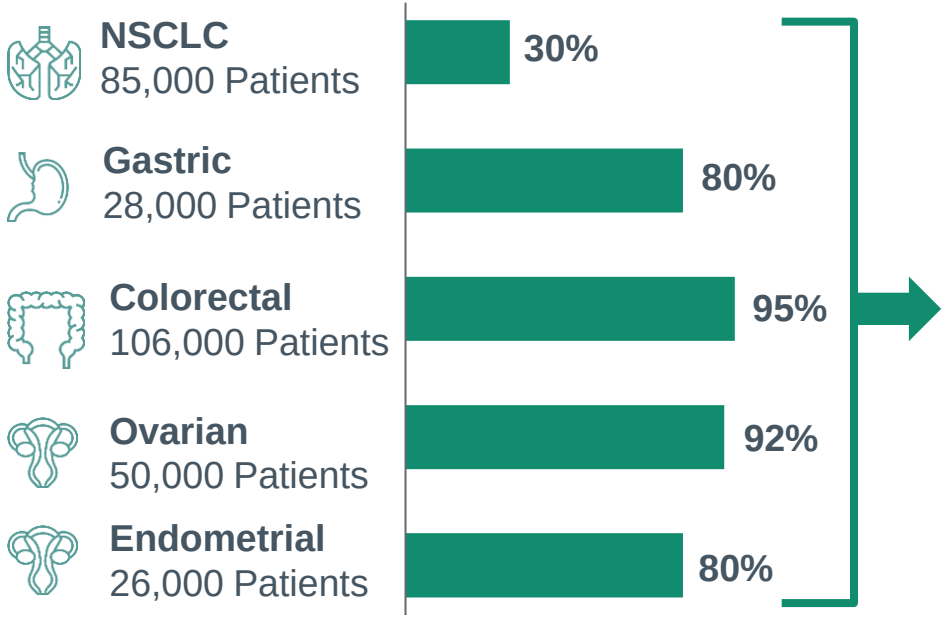
Source: 14th Annual World ADC Conference, October 2023

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

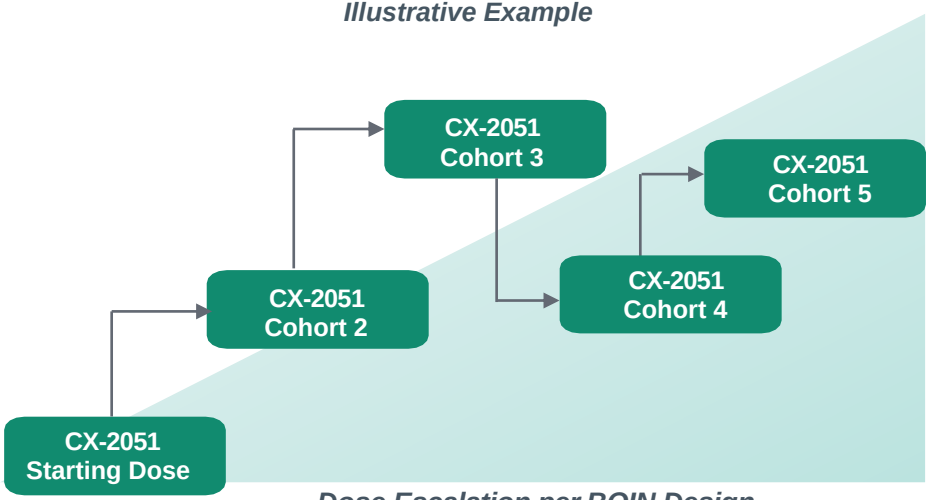
Source: DRG Epidemiology & Forecast Dashboards, 2021 – 2023

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

Part 1: Dose Escalation

Advanced/metastatic solid tumors with known/documented EpCAM expression

Illustrative Example



Dose Escalation per BOIN Design

- 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

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CX-801: Conditionally Activated Probody® Cytokine, IFNα-2b

Immuno-oncology Treatment Landscape

Significant Unmet Need Remains, Creating Major Opportunity for CX-801

IO Sensitive Tumors

Indications where PD-(L)1s are Approved


Melanoma & Non-Melanoma


NSCLC & SCLC


Gastric / GEJ & Esophageal


Bladder


HNSCC


MSI-H / Pan Tumor


Renal


Endometrial & Cervical


Liver


TNBC

10 – 50% **Overall Response Rates with Single-Agent PD-(L)1[1,2]**

IO Resistant Tumors

Insensitive to PD-(L)1s / CPI


MSS CRC


HR+/- Breast


Prostate


Ovarian


Pancreatic

< 10% **Overall Response Rates with Single-Agent PD-(L)1[1,2]**

Significant Opportunities for CX-801

- Increase frequency and durability of responses in **IO-sensitive tumors**
- Establish or restore efficacy in **IO-resistant tumors**

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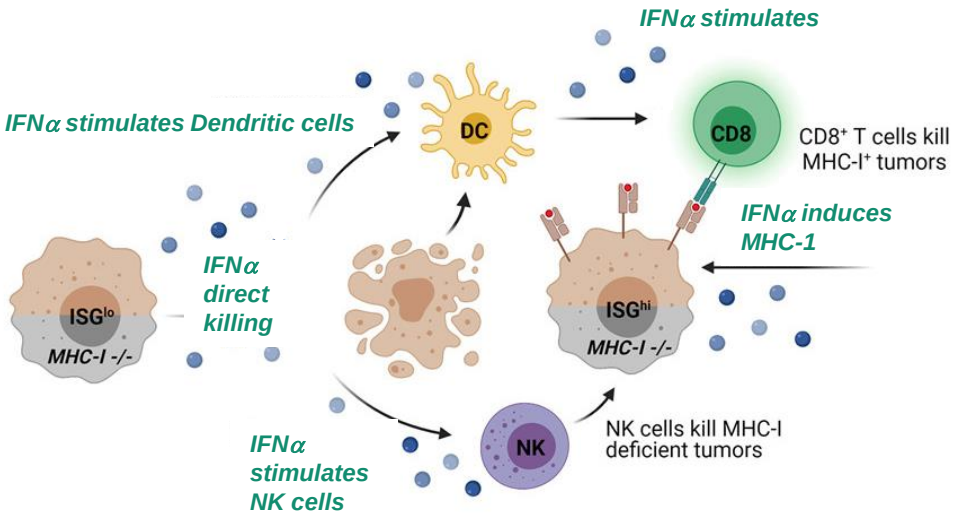
Source: [1]Sun et al. Biomarker Research. 2020; [2]DFCI and NCI Data Commons

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 **unlock classically CPI-resistant indications**

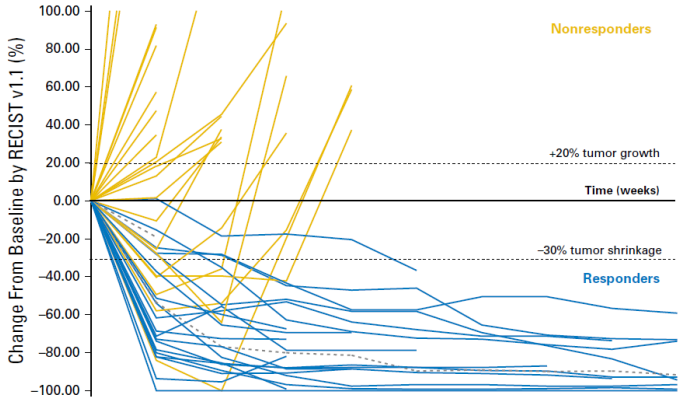


Adapted from Green et al., Mol. Ther. Onc. 2021

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

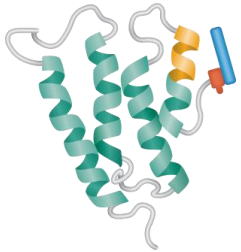
Peginterferon + PD-1 in Melanoma

(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

CX-801: Optimized Design

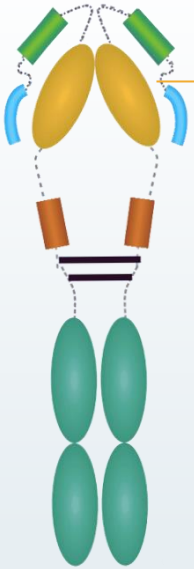
Dually-Masked, Conditionally Activated Probody® IFNα2b

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

Optimized Masking & Substrates

- 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

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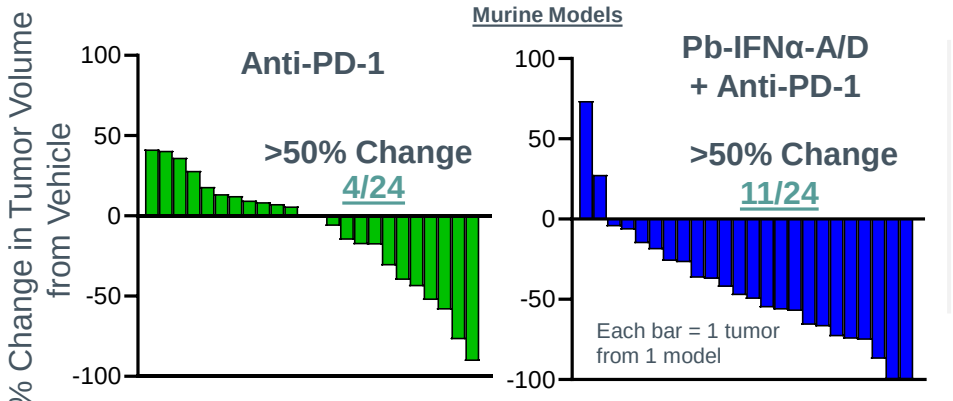
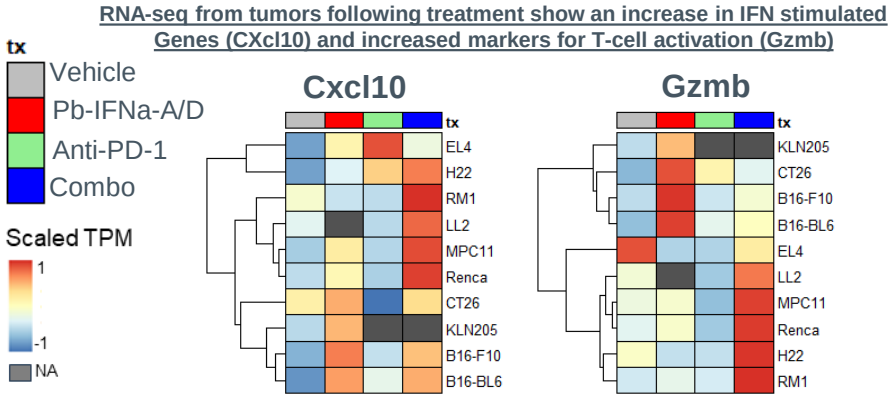
CX-801 Preclinical Profile Suggests Clinical Synergy with PD-1 and Enhanced Tolerability Compared to Unmasked IFNα

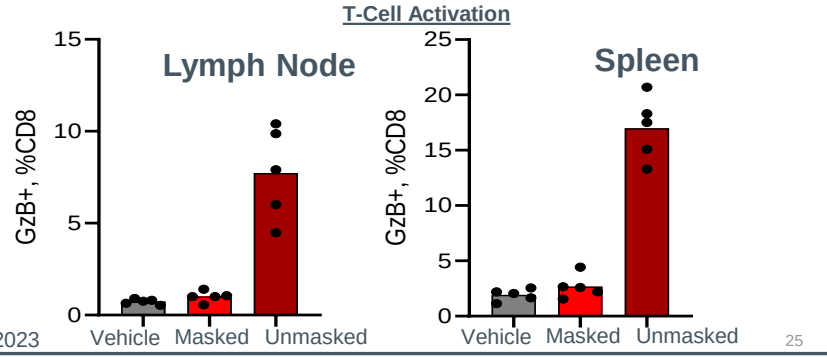
Single Agent and Synergistic Activity with PD-1 Observed with Probody IFNα2B in Preclinical Models





Masking of IFNα Significantly Increases Tolerability and Lowers Peripheral Activity (Murine Models)

	5 ug	20 ug	600 ug	1200 ug	2400 ug
Pb-IFNa-A/D (Masked)			Tolerated	Tolerated	Not tolerated
IFNa-A/D (Unmasked)	Tolerated	Not tolerated			



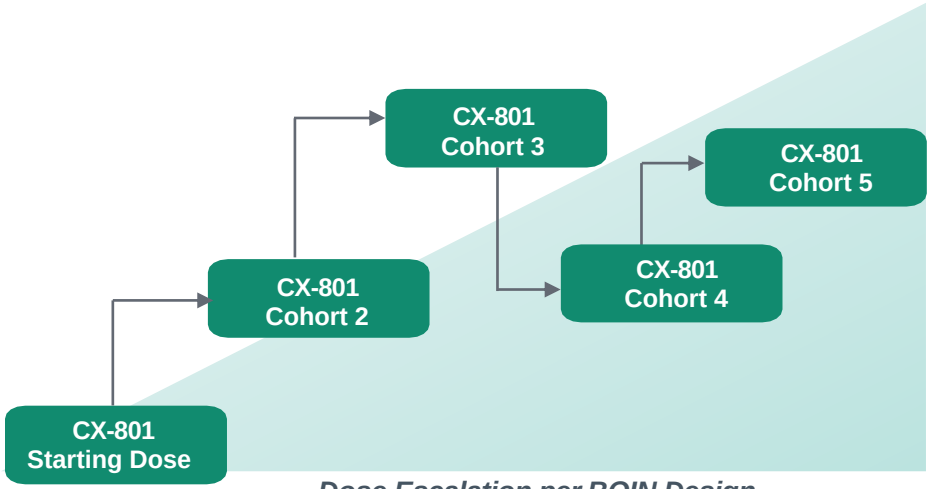
Source: Povinelli, et. al. SITC 2023

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

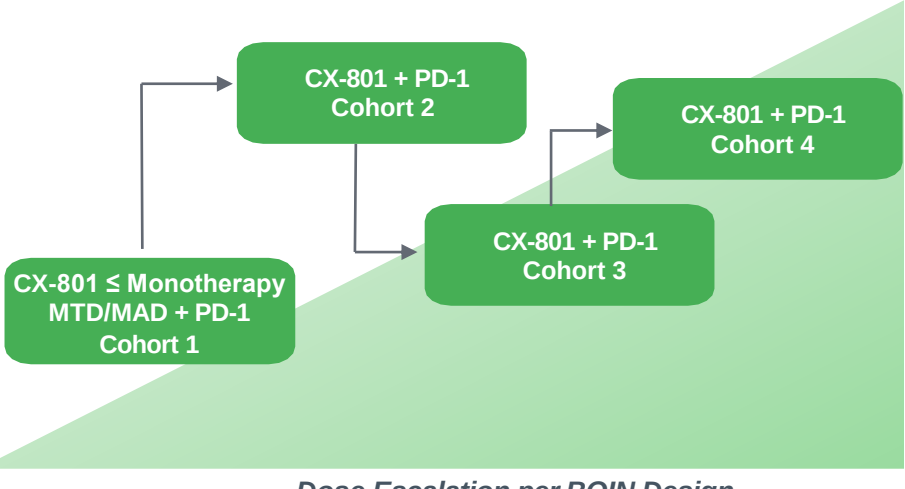
Monotherapy Dose Escalation	Combination Dose Escalation

Melanoma, RCC, HNSCC

Illustrative Example



Dose Escalation per BOIN Design



Dose Escalation per BOIN Design

- ❑ **Demonstrate signs of clinical activity as monotherapy with improved safety profile vs. native IFNα**
- ❑ **Demonstrate safety & tolerability profile supportive of combination therapy with PD-1 inhibition**

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

CytomX Therapeutics

Strategic Partnerships

Business Development as a Strategic Engine for Value Creation

Bristol Myers Squibb™	AMGEN	astellas	REGENERON	moderna
Multiple Modalities	*T-Cell Engagers*	*T-Cell Engagers*	*Bispecific Immunotherapies*	*MRNA Oncology & Other Diseases*
• **BMS-986288** Anti-CTLA-4 **Phase 2**	• **CX-904** EGFRxCD3 **Phase 1***	• **Multiple Programs****	• **Multiple Programs**	• **Multiple MRNA Programs**
• **Multiple Programs**	• **Preclinical Programs**			

> $500M of funds raised through collaborations

> 10 Active, Preclinical Collaboration Programs

Commercial Rights, Near- and Long-term milestones

**Co-development & Commercialization with retained U.S. Rights*
***CytomX retains US rights on select programs*

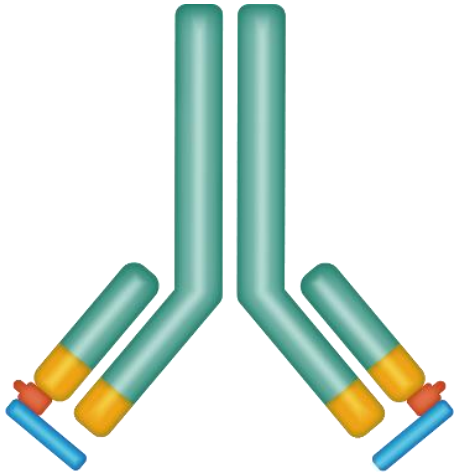
CytomX THERAPEUTICS

Next Generation CTLA-4 Program

*PoC Trials in NSCLC & MSS CRC; Data Anticipated in 2024**

Bristol Myers Squibb™

BMS-986288 (CTLA-4)



Non-Fucosylated (NF) Probody® Therapeutic with increased CD16 affinity

- CTLA-4: established MOA, with Yervoy approved across solid tumors
- Challenges (toxicity and patient selection) associated with targeting CTLA-4 have limited development
- BMS-986288 is a next-generation CTLA-4 designed to improve the benefit/risk:
  - NF (enhanced CD16 binding) biology increases immune priming via Fc engagement enhancing anti-tumor response
  - Improves safety profile with Probody® technology added to NF allowing for combinations and moving to earlier lines of therapy

* Bristol Myers Squib 2023 R&D Day, September 14, 2023

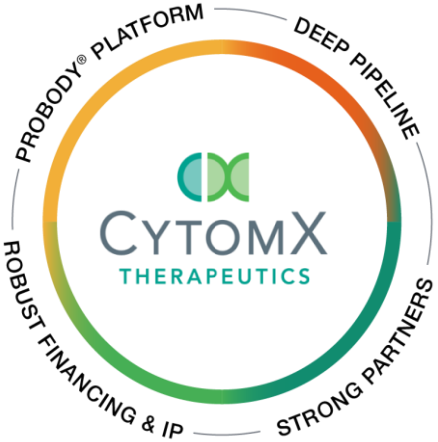
Outlook & Milestones

CytomX is Entering a Catalyst Rich Period

2024 & 2025 Potential Milestones

Program	Stage	2024	2025
CX-904 (EGFR TCB)	Phase 1 Dose Escalation	❑ Phase 1a Data in 2H 2024 ❑ Decision to Expand to Phase 1b in Conjunction with Amgen	❑ Phase 1b Initiation
CX-2051 (EpCAM ADC)	✓ IND Filed (Dec ‘23)	❑ Phase 1 Initiation in EpCAM+ tumors including CRC in 1H 2024	❑ Initial Phase 1 Data
CX-801 (IFNα2b)	✓ IND Filed (Dec ‘23)	❑ Phase 1 Initiation in Solid Tumors including Melanoma, Renal and HNSCC in 1H 2024	❑ Initial Phase 1 Data
BMS-986288 (CTLA-4)	Phase 2	❑ POC Trials in NSCLC & MSS CRC Ongoing ❑ Data Anticipated in ‘24	❑ Continued Updates by BMS
Research Collaborations	Preclinical	• More than 10 ongoing preclinical research programs with partners • Research milestones achievable across 2024 – 2025 and beyond	

CytomX Therapeutics: Building for the Future



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