CytomX Therapeutics

Leading the Field of Localized Biologic Therapies

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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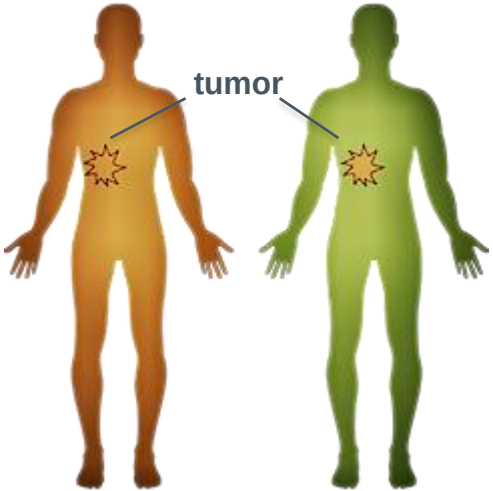
The Promise of Conditionally Active, Localized Biologic Therapies

R&D Challenge

- **Next Generation Biologic Therapies have evolved to highly potent formats including:**
  - T-Cell Engagers (TCBs)
  - Antibody Drug Conjugates (ADCs)
  - Immunotherapies
- **Separating potency from toxicity is a key challenge for optimizing therapeutic effectiveness**

CytomX Probody® Therapeutics

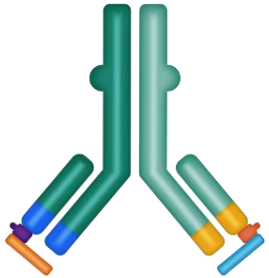
- **Designed to localize anti-cancer efficacy and decrease systemic toxicities**



Leading Platform for Localized Biologic Therapies

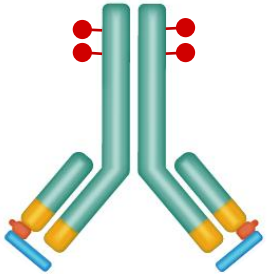
Addressing Major Challenges in Today's Cancer R&D Landscape

T-Cell Bispecifics



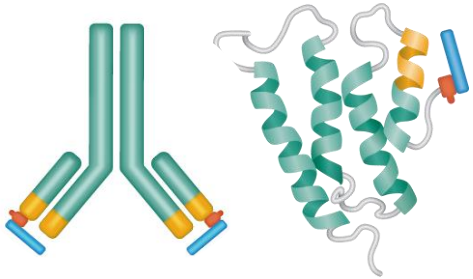
Localizing T-cell engaging bi-specifics to attack solid tumors

Antibody-Drug Conjugates



Unlocking new ADC targets through localization in disease tissue

Immunotherapies



Harnessing immunotherapy through preferential activity in the tumor microenvironment

Substrate linkers Masks Linker payload

Integrated Business Model for Long-Term Value Creation

Probody® Platform

- Leader in localized biologic therapies
- Multi-Modality Platform

Deep Pipeline

- 3 Clinical-stage assets
- 2 INDs expected in 2023

Robust Financing and IP

- $194M Cash as of Q4 2022*
- Broad IP portfolio

Strong Partners

- 5 major partnerships
- 3 molecules in the clinic

Bristol Myers Squibb™ AMGEN astellas REGENERON moderna

**Does not include $35 million payment from Moderna collaboration received in Q1 2023*

Broad, Multi-Modality Probody® Pipeline

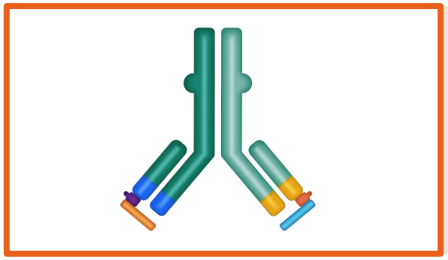
Economics	Product Candidate	Target	Indication	Preclinical / Phase 1 / Phase 2	Partner
Wholly-Owned or Retained US Rights*	CX-2029	CD71-MMAE	Squamous Esophageal		CytomX
	CX-904	EGFRxCD3	EGFR+ Solid tumors		CytomX, Amgen
	CX-2051	EpCAM	EpCAM+ Solid tumors		CytomX
	CX-801	IFN-α2b	Solid Tumors		CytomX
	Probody TCBs	Undisclosed	TBD		CytomX, Astellas
Fully Partnered**	BMS-986288	CTLA-4 (a-fucosylated)	Solid tumors	+/- nivolumab	Bristol Myers Squibb
	Probody TCBs	Undisclosed	TBD		Amgen, Astellas, Regeneron
	Various	Undisclosed	TBD		Bristol Myers Squibb
	mRNA	Undisclosed	Oncology & Non-oncology		moderna

Probody® Modality: TCBs | ADCs | Immunotherapy | mRNA | Undisclosed

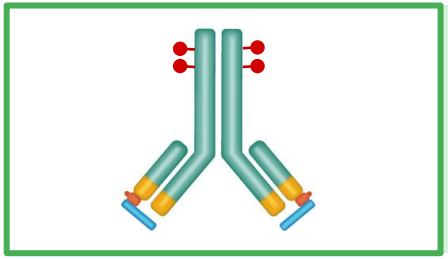
*US Rights include wholly-owned molecules or collaboration molecules in which CytomX has a right or option to share in U.S. commercial profits

** R&D milestone payments and royalties payable to CytomX

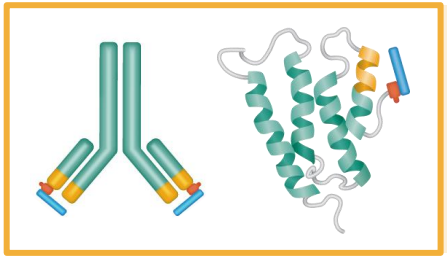
Pipeline Modalities



Expanding R&D Activities in T-cell Engaging Bispecifics



Probody® Antibody Drug Conjugates



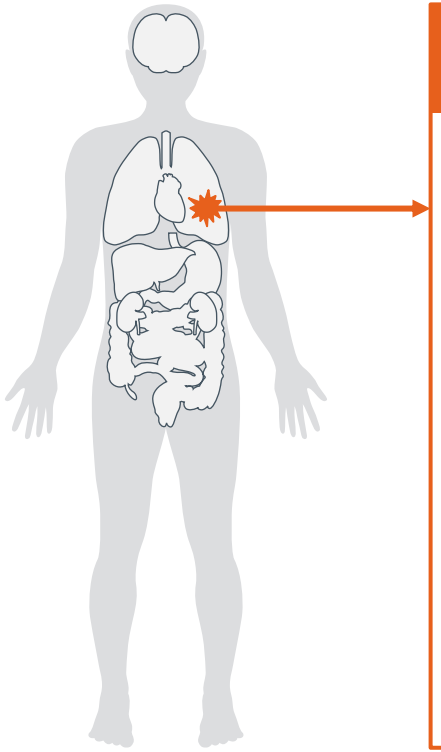
Probody® Immunotherapies

CytomX Therapeutics

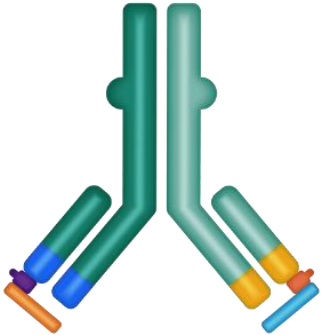
R&D Activities in T-cell Engaging Bispecifics

- CX-904 (EGFRxCD3) Phase 1 Progress
- Astellas Collaboration
- Regeneron Collaboration

CytomX Probody® Bispecifics are Designed to Localize T-cell Engaging Antibodies to the Tumor Microenvironment



Probody® Bispecifics



Substrate linkers

Masks

- **Conventional Bispecifics** are highly potent, however toxicity is a significant challenge
- **Probody® Conditionally Activated Bispecifics** retain potent anti-tumor activity while having less systemic toxicities

CX-904 Targets EGFR: A High Potential Target for Localized T-Cell Bi-specific

- **Epidermal Growth Factor Receptor (EGFR)**
  - EGFR is a tyrosine kinase receptor involved in homeostatic regulation of normal cells and carcinogenesis of epithelial malignacies[1,2]
  - EGFR plays a crucial role in cancer, and is one of the most frequently altered oncogenes in solid tumors[1]
  - Multiple EGFR targeting mAbs and small molecules approved
- **Prevalent EGFR expression in many cancer types**
  - EGFR x CD3 conditionally activated TCB has opportunity across a multitude of solid tumors
- **CX-904 designed to unlock EGFR potential**
  - Mechanism of action does not rely on EGFR signaling blockade
  - Less impacted by acquired resistance, e.g., activating mutations in NSCLC, KRAS/BRAF mutations in CRC
  - Opportunity to combine with IO or other targeted agents including EGFR tyrosine kinase inhibitors

Sources: 1) Thomas and Weihua. Front Oncol. 2019; 2) Cai et al. Front. Oncol. 2020

Localized EGFRxCD3 TCB Induces Tumor Regressions and Increases MTD in Preclinical Studies

Increases MTD

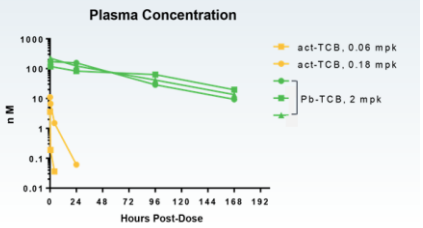
TCB*	Dose (mg/kg)	Clinical Observations
Act-TCB	0.06 *(MTD)*	Moderate
Act-TCB	0.18	Severe
Pb-TCB	0.6	None
Pb-TCB	2.0	Mild
Pb-TCB	4.0 *(MTD)*	Moderate

* Act-TCB: Protease activated, unmasked TCB; Pb-TCB: Conditionally activated, masked TCB

MTD increases by >60-fold with conditionally activated TCB (Pb-TCB)

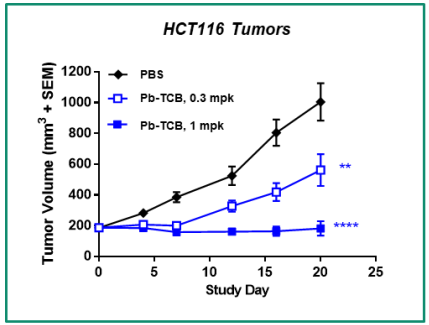
Extends PK

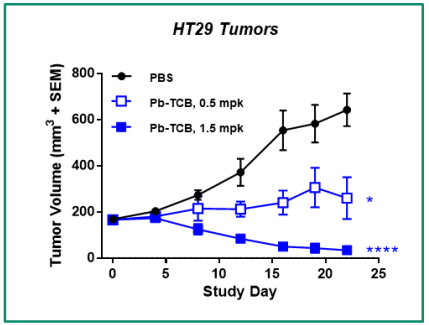
Plasma Concentration



Masking markedly extends PK relative to the unmasked TCB (no TMDD)

Single Agent Efficacy in Human PBMCs engrafted into HCT116 and HT29 Tumor-bearing NSG mice





Conditionally Activated EGFRxCD3 TCB Demonstrates Efficacy in Animal Models

Source: Boustany, L. et al. Cancer Res. 2022 Nov 15; 82(22):4288-4298.

CX-904 Progress-to-date and Clinical Path Forward

Phase 1a Goal: Assess Safety and Determine Phase 1b/2 dose(s)

Progress to-date

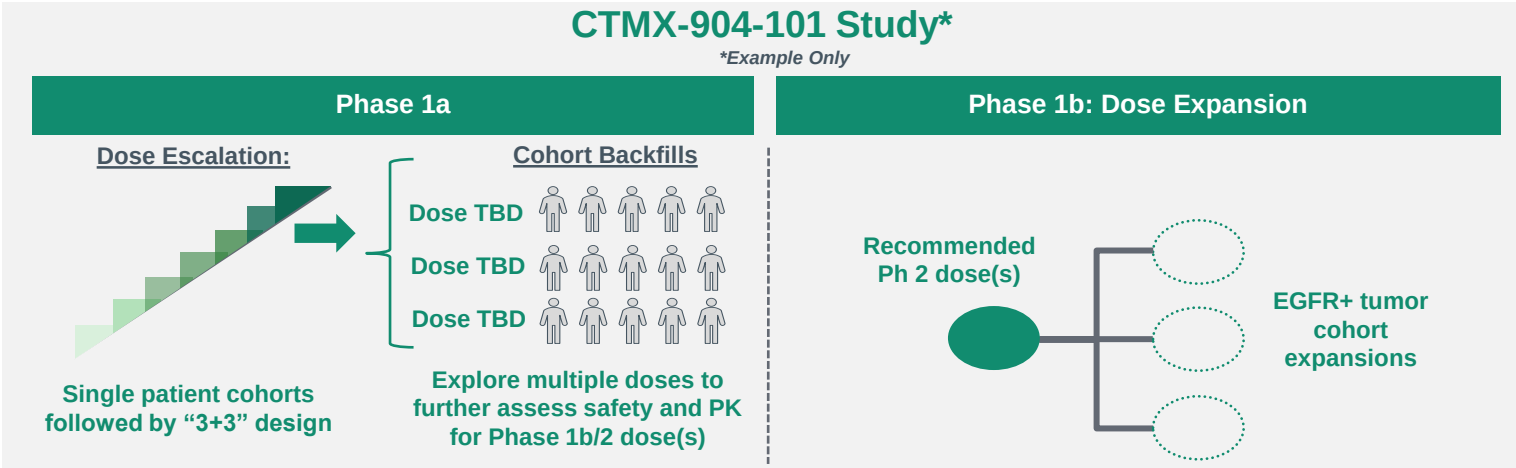
- ✓ First Patient Dosed in May 2022
- ✓ Advanced through single patient cohorts
- ✓ 3+3 Dose Escalation Ongoing

2023 Focus Areas

- Continued dose escalation
- Potential exploration of multiple Phase 2 doses to optimize Phase 1b/2 success
- Robust biomarker and translational science effort to optimize patient selection strategies

CTMX-904-101 Study*

**Example Only*



CytomX Therapeutics

AMGEN

Astellas Collaboration: Progress with T-Cell Engaging Bi-specifics

CytomX Therapeutics | astellas

March 2020

Probody® T-Cell Engaging Bispecific Collaboration

Collaboration Highlights

- **Multiple pre-clinical programs in progress**
- **CytomX retains U.S. Co-Commercialization and profit share rights to a select number of programs**
- **Research funded by Astellas**
- **First clinical candidate milestone ($5 million) reached Q1 2023**

CytomX and Regeneron Collaboration on Bispecific Immunotherapies

CytomX THERAPEUTICS | REGENERON

November 2022

Probody ® Conditional Bispecifics for the Treatment of Cancer

Collaboration Highlights

- **Enables development of bispecific immunotherapies using CytomX's Probody® and Regeneron's Veloci-Bi® platforms**
- **Potentially addresses tumors that are unresponsive to immunotherapy**
- **$30 million upfront payment, up to ~$2 billion in milestones, tiered royalties on global net sales**
- **Research funded by Regeneron**

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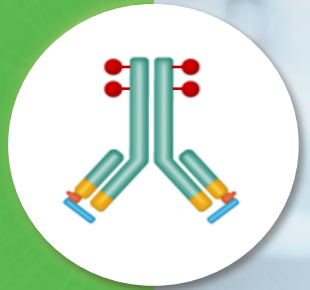
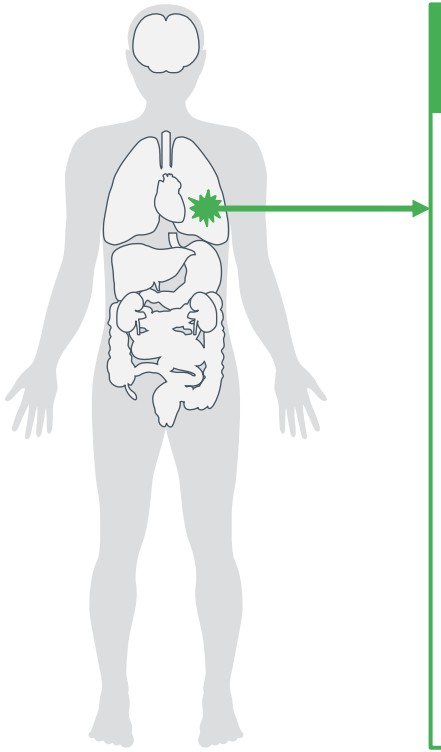


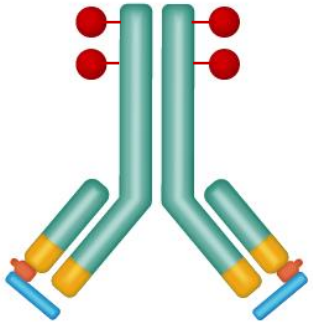
Probody® ADCs

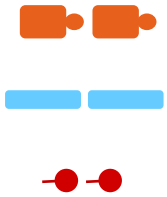
- **CX-2051**: First-in-Class ADC Directed Toward Epithelial Cell Adhesion Molecule (EpCAM)
- **CX-2029**: First-in-Class ADC Directed Toward CD71 (Transferrin Receptor)

CytomX Probody® ADCs are Designed to Localize the Potent Anti-Tumor Activity of Cytotoxic Payloads



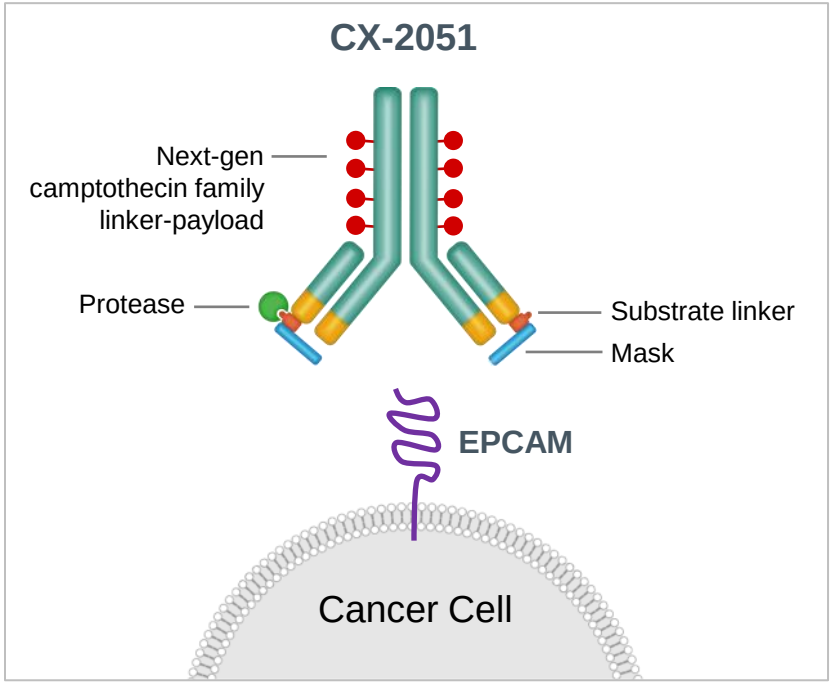
Probody® Antibody Drug Conjugates





- **Conventional ADCs** are highly potent, however On-Target, Off-Tumor effects can cause significant adverse events
- **Probody® Conditionally Activated ADCs** retain potent anti-tumor activity while having less systemic toxicities

CX-2051: EpCAM-Directed Conditionally Activated ADC with Next Generation Camptothecin Payload



Conditionally-Activated EpCAM ADC

- **Probody peptide mask with >60X masking efficiency**
- **Protease-cleavable substrate with broad cleavability across multiple tumor types**
- **Next-gen camptothecin linker-payload**
- **Optimized linker drives bystander effect**
- **Inter-chain cysteine conjugation DAR8**

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

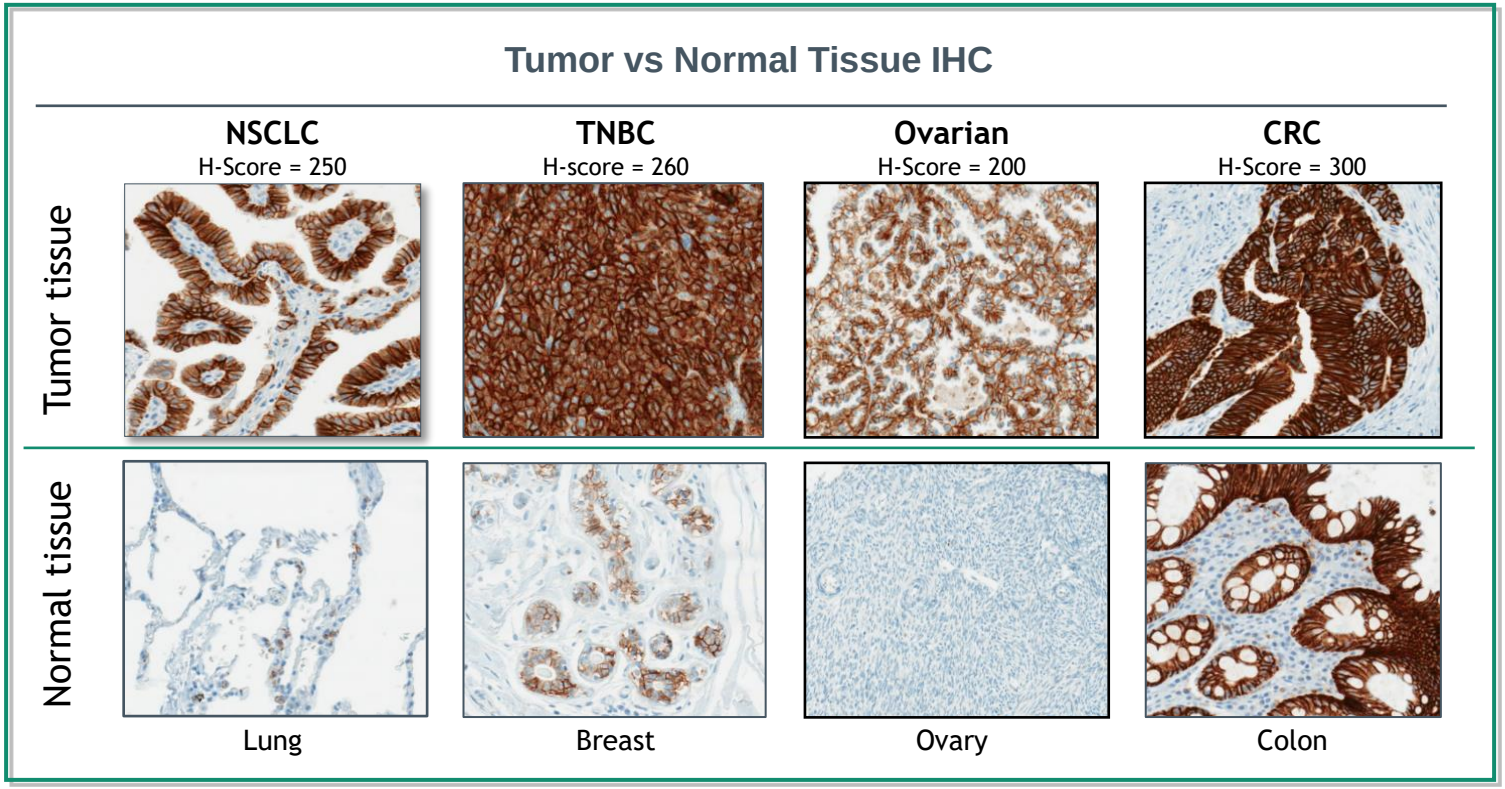
- **Vicineum fusion protein:** anti-EpCAM scFv linked to a truncated form of Pseudomonas exotoxin A
- Delivered by intravesical administration
- ~40% 3-month complete response in bladder cancer

Sesen Bio

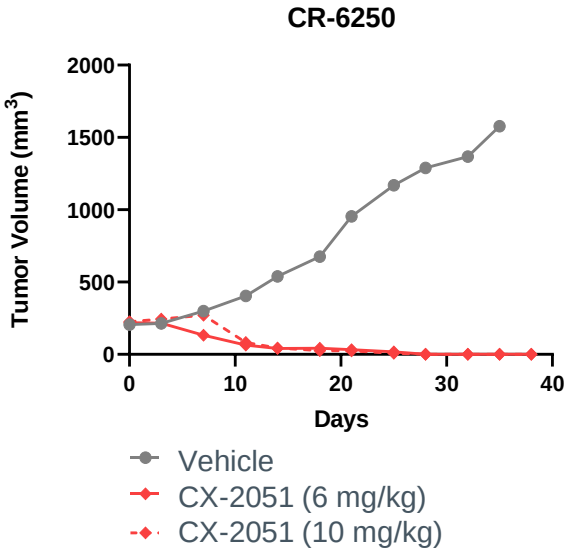
Systemic EpCAM approaches have significant toxicity concerns

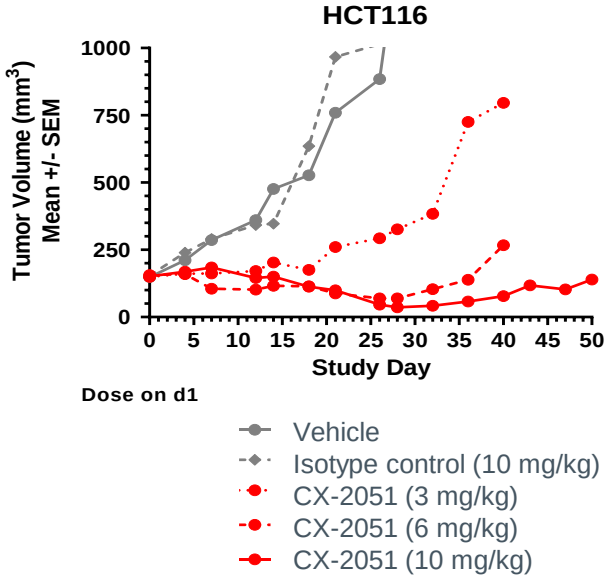
Asset	Company	MOA	Stage	Status
Solitomab	Amgen	EpCAM x CD3 BiTE	Ph 1	GI tox reported; discontinued
ING-1	XOMA	EpCAM mAb	Ph 1	Pancreatitis reported; discontinued
3622W94	GSK	EpCAM mAb	Ph 1	Pancreatitis reported; discontinued

EpCAM: A Compelling Target with Multiple Tumor Opportunities



CX-2051 Demonstrates Strong Activity in Preclinical Models Including Colorectal Cancer





PDX: Patient derived xenograft; CDX: Cell derived xenograft
CR-6250 and HCT116: Colorectal cancer models

Dosing regimen: Q2W x 3

- **Regression observed in multiple preclinical models**
- **Efficacy is dependent on target engagement**

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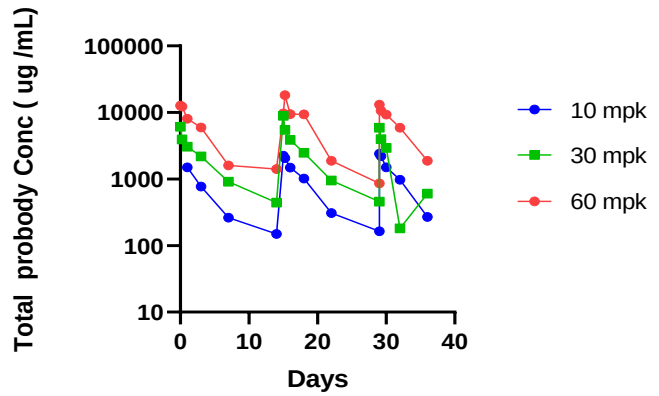
CX-2051 Shows Dose Proportional PK in Cynomolgus Monkey



- Exposure is maintained after each dose (3 x Q2W)
- Consistent exposure across individuals
- Well-behaved pharmacokinetic profile
- Increased exposure with increase dose
- No evidence of decreased exposure upon repeat dosing

Multidose Exploratory Toxicology Study (3 x Q2W)

Dosing	CX-2051	Isotype
10 mg/kg	Tolerated (2/2)	
30 mg/kg	Tolerated (2/2)	
60 mg/kg	Tolerated (3/3)	Tolerated (2/2)
90 mg/kg	Not Tolerated (1/2)	

- CX-2051 up to 60 mg/kg is well tolerated
- No evidence of pulmonary tox (including post-recovery)

IND submission for CX-2051 expected in 2H 2023

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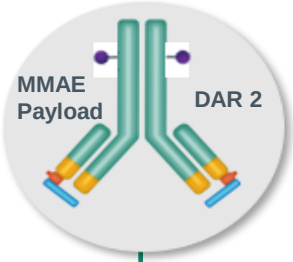
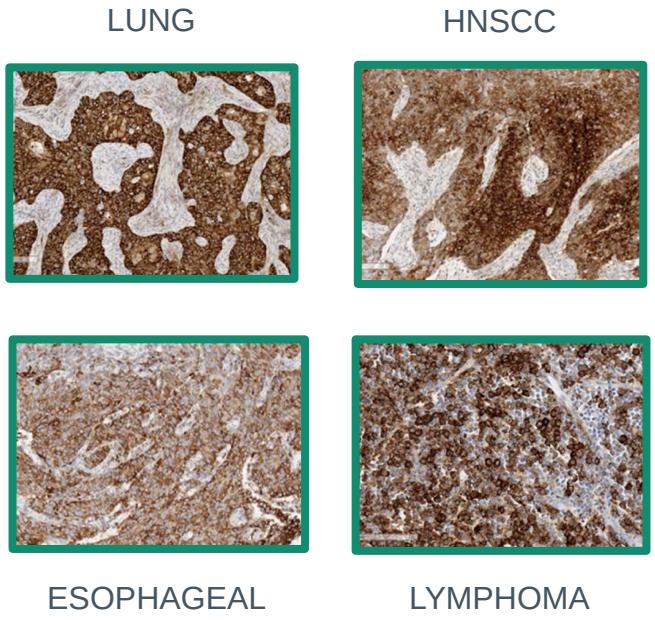
CX-2029: CD71-Directed Conditionally Activated ADC with Clinically Proven MMAE Payload



- CD71 was previously an undruggable target with conventional therapeutics due to central role in iron metabolism
- CX-2029 is a CD71-directed MMAE conjugated conditionally activated ADC
- CX-2029 is the first-in-class CD71 targeted therapeutic candidate

CD71 Tumor Expression by IHC



Data generated by CytomX

Multi-Cohort CX-2029 Phase 2 Expansion Study
3 mg/kg Q3W Phase 2 Dose

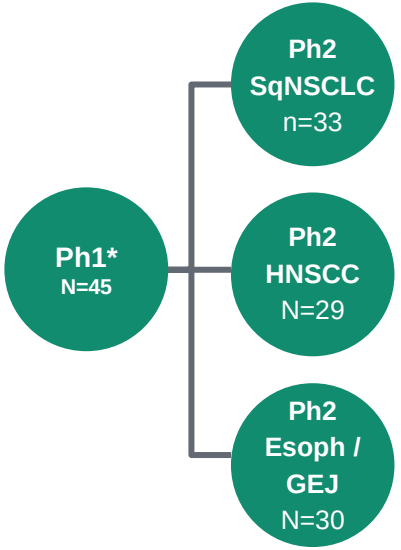
Study Design:

Part A – 3+3 Dose escalation
- 0.1 mg/kg to 5 mg/kg Q3W

Part B – Tumor Biopsy Cohort
- Doses of 2 and 3 mg/kg Q3W evaluated

Part C – Phase 2 Expansion Cohorts
- 3mg/kg Q3W Phase 2 dose

PROCLAIM-CX-2029-101

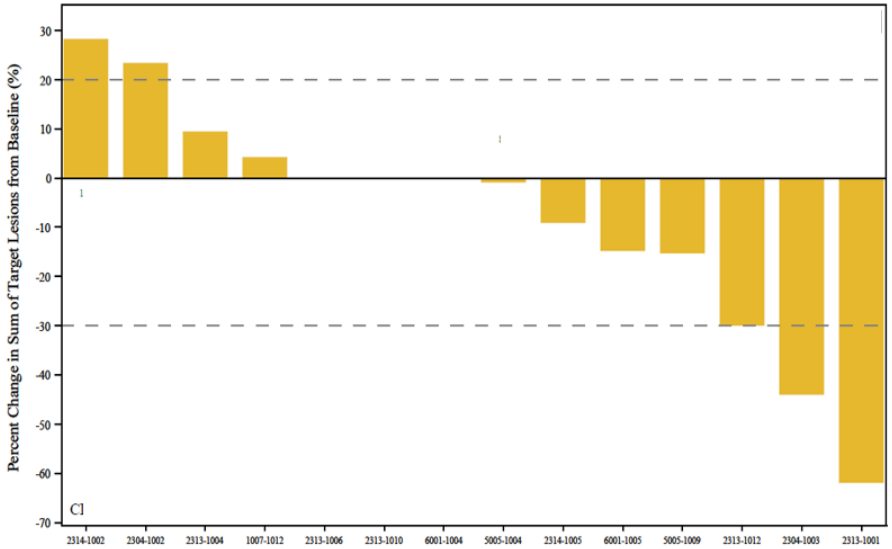


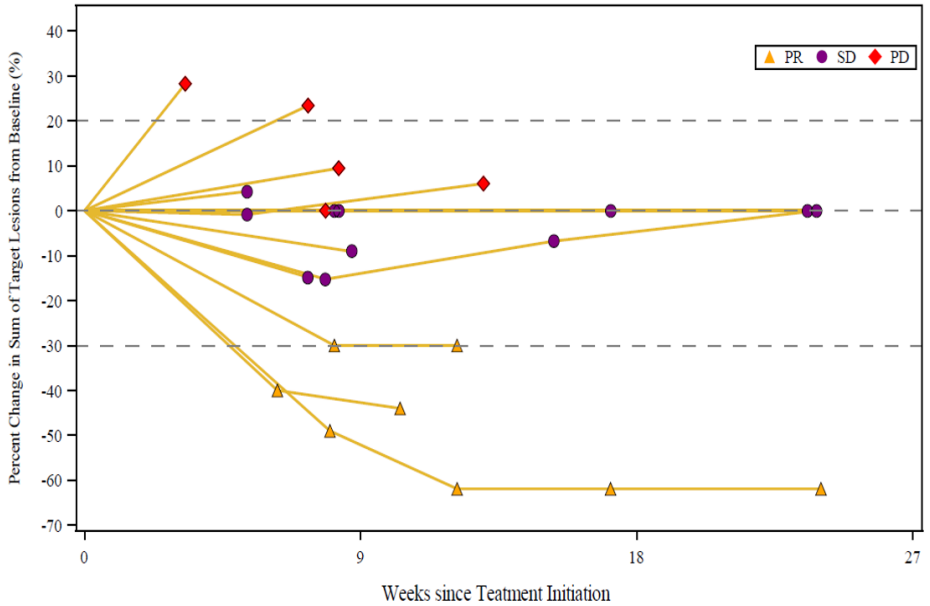
Note: Phase 2 Expansion includes 5 Patients from Part B dosed at 3mg/kg Q3W; 2 patients with sqNSCLC and 3 HNSCC

Phase 1 Data: Johnson M. et al. Clin Cancer Res. 2021 Aug 15;27(16):4521-4530.

Squamous Esophageal: 21% Confirmed ORR and 57% DCR

N = 14 Efficacy Evaluable Patients



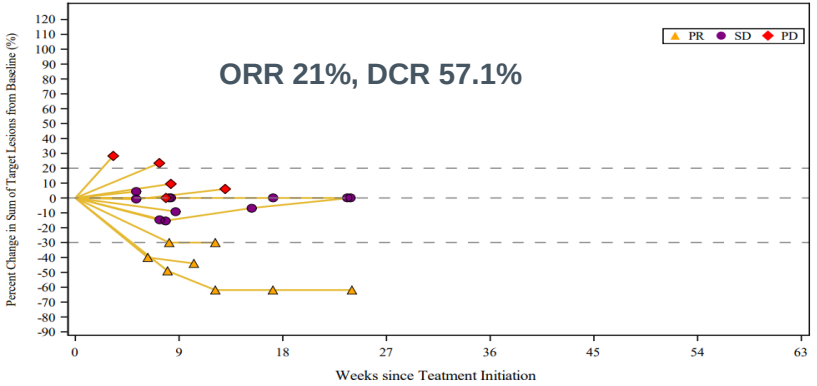


Data snapshot cutoff date for efficacy: 2022 October 4

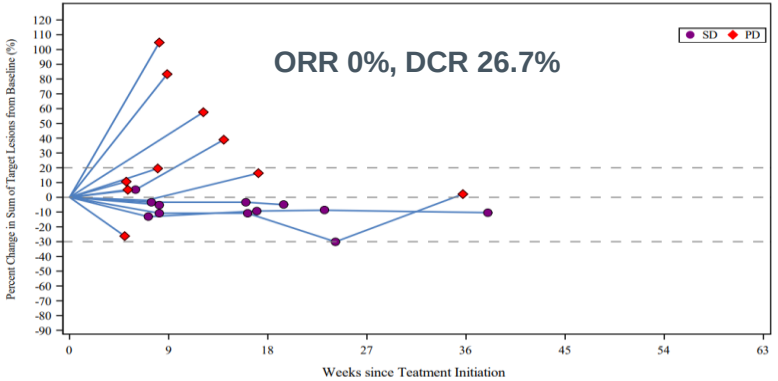
CX-2029 Responses Observed in Squamous Tumors

Durable Responses in Heavily Pretreated and Refractory ESCC, HNSCC, and sqNSCLC

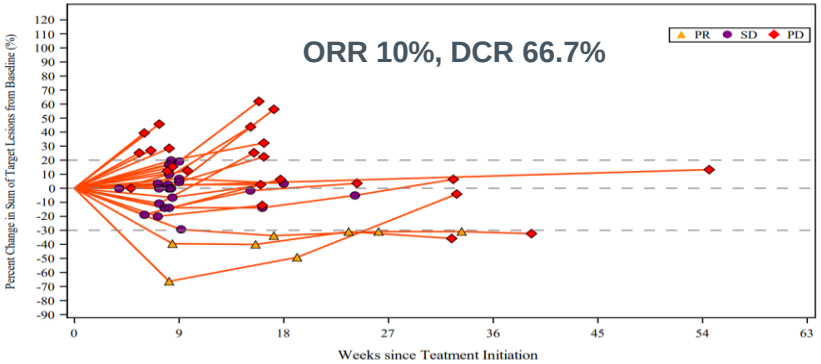
Squamous Esophageal



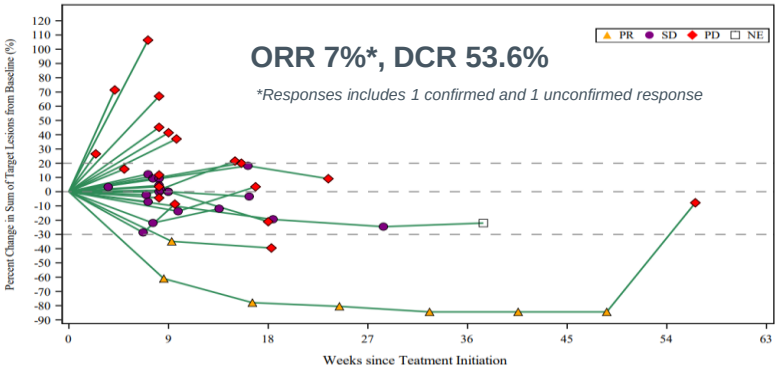
Adeno Esophageal



Squamous NSCLC



Squamous Head & Neck



CytomX Therapeutics

Data snapshot cut date for efficacy: 2022 October 4

CX-2029: Anemia Remains Most Common Treatment Related Adverse Event

Predictable and Managed with Transfusions, Dose Delays and/or Reductions

Preferred Term	Parts B & C 3 mg/kg (n=92)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All Grades
Subjects w at least 1 related TEAE	0	13 (14.1)	70 (76.1)	7 (7.6)	0	90 (97.8)
Anemia	**2 (2.2)**	**4 (4.3)**	**70 (76.1)**	**0**	**0**	**76 (82.6)**
Infusion related reaction	11 (12.0)	51 (55.4)	3 (3.3)	0	0	65 (70.7)
Neutropenia	2 (2.2)	4 (4.3)	9 (9.8)	7 (7.6)	0	22 (23.9)
Fatigue	4 (4.3)	11 (12.0)	1 (1.1)	0	0	16 (17.4)
Nausea	6 (6.5)	5 (5.4)	1 (1.1)	0	0	12 (13.0)
Diarrhea	9 (9.8)	1 (1.1)	0	0	0	10 (10.9)

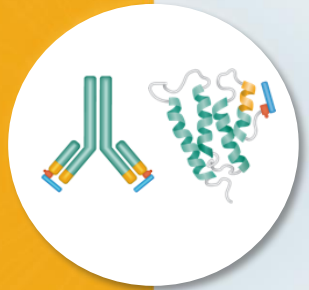
AE Grades are based on CTCAE v 5.0; AEs w missing relationship are considered related to CX-2029
Subjects are only counted only at the maximum severity grade experienced w each preferred term
Neutropenia includes the following preferred terms: 'Neutropenia',' Neutrophil count decreased', 'Febrile neutropenia' and 'Pancytopenia

Data cut date: 5 August 2022

CX-2029 Summary: CD71 Targeted for First Time with an ADC

- Responses in squamous tumors including heavily pre-treated ESCC
- Encouraging duration of response in patients with a confirmed partial response or stable disease
- Biomarker evaluation for future patient selection strategies continues
- Ongoing work on potential anemia mitigation strategies
- CytomX to determine next steps for CD71 program, including CX-2029

CytomX Therapeutics



Probody® Immunotherapies

- **CX-801**: Conditionally Activated IFNα-2b
- **BMS-986288**: First-in-class non-fucosylated Probody Targeting Cytotoxic T Lymphocyte Antigen-4 (CTLA-4)

Cytokine Therapeutics Are Potent, But Associated With Safety Issues

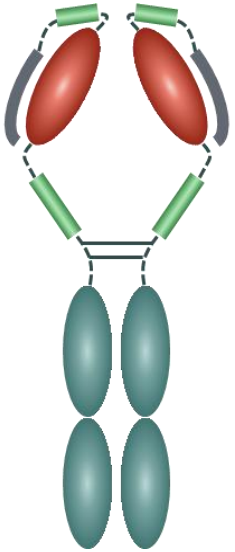
Cytokines and Cytokine Therapeutics

- Major regulators of innate and adaptive immune system
- Broad anti-tumor activity demonstrated in the clinic
- ***Clinical success to date limited by systemic toxicity or poor exposure***

Potential Advantages for Conditional Cytokine Therapeutics

- ✓ **Less systemic toxicity**
- ✓ **Better exposure** (reduced TMDD)
- ✓ **Systemic delivery** (versus IT injection)
- ✓ **Increased therapeutic index**
- ✓ **Improved combination therapies**

Probody® Cytokines

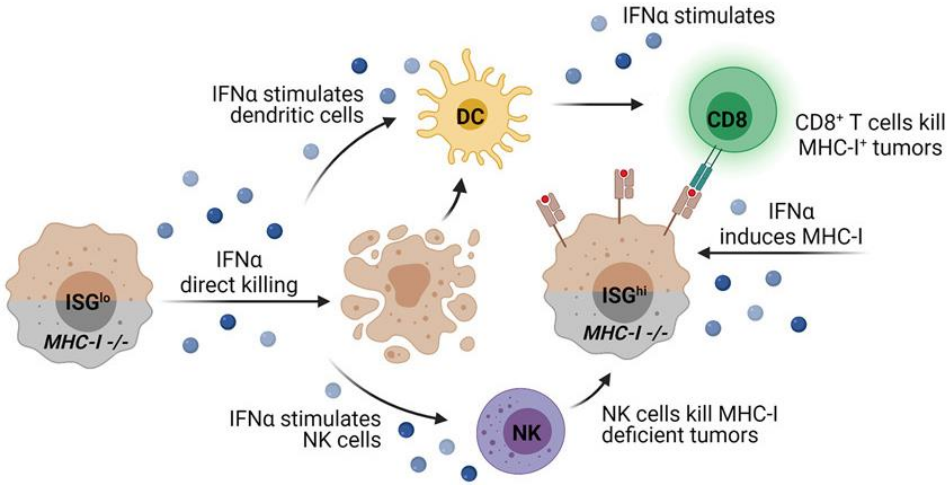


IFNα-2b is a Powerful Mediator of Immune Activation with Ideal Properties for Cancer Immunotherapy

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*
- Potential to **unlock classically CPI-resistant indications**



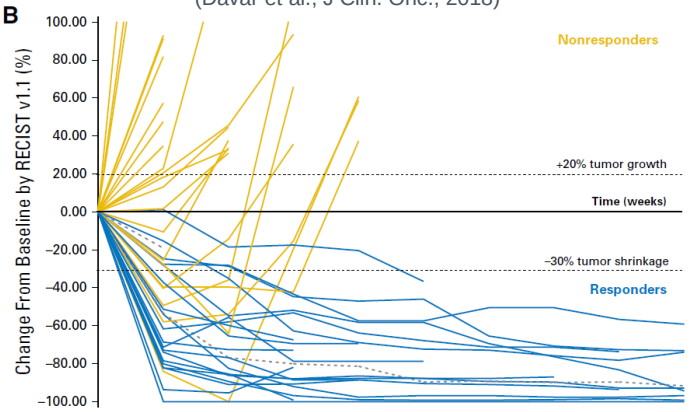
Adapted from Green et al., Mol. Ther. Onc. 2021

Probody-IFN-α2b has Potential to Harness Powerful Activity of Cytokines by Increasing Therapeutic Window

IFN-α2b - Significant Unmet Need

Peginterferon + PD-1 in Melanoma

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

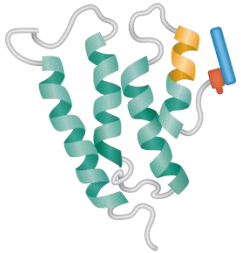


- **Potent activity (60.5% ORR)**
- **Significant, dose limiting adverse events (49% Grade 3/4 AEs)**

CX-801 (Probody Interferon-α2b)

Potentially Best-in-Class Conditionally-Activated IFN-α2b

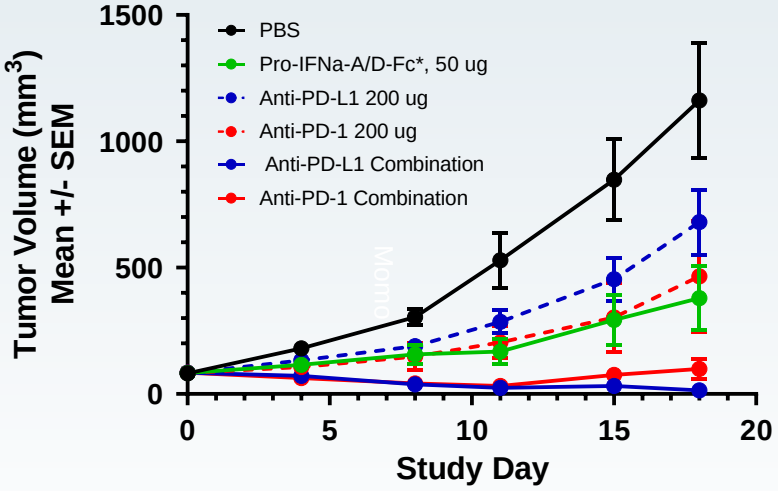
Advantages of CX-801



- **Less systemic toxicity**
- **Better Exposure** (reduced TMDD)
- **Systemic Delivery**
- **Increased Therapeutic Index**
- **Improved Combination Therapies**

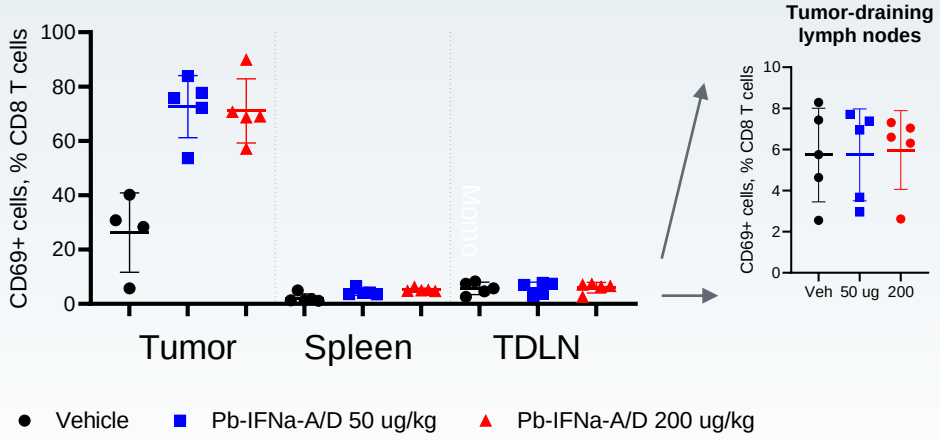
Combination of Dual Masked IFN-αA/D-Fc* and anti-PD-(L)1 Induces Substantially Enhanced Efficacy in MC38 Tumor Model

Efficacy



Doses
PBS, ProC1023: d0, d4, d8, d11, d15
Anti-PD-L1, Anti-PD-1: d0,d8, d15

Pharmacodynamic Activity is Restricted to Tumors



Data presented at 2022 AACR, *IFNαA/D is a chimeric human IFNα that binds murine IFNα receptors; Human IFNα2a$_{1-62}$Human IFNα1$_{64-166}$

Probody® IFN-α2b (CX-801) has Significantly Improved Tolerability
Compared to Unmasked Interferon in Non-Human Primates

Protection in multi-dose tolerability study is ≥ 30x

Historical Peginterferon Data

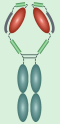
Dosing (μg/m²) (15 x Q2D)	Dosing (mpk) (15 x Q2D)	Dosing (mpk/w)	Peginterferon (SQ)
1414	0.1 mpk	0.35	Tolerated (6/6)
4329	0.3 mpk	1.05	Tolerated (6/6)
14126	1 mpk	3.5	Not Tolerated (5/6)

Dosing (3 x QW, IV)	CX-801*
7.5 mpk/w	Tolerated (4/4)
15 mpk/w	Tolerated (4/4)
30 mpk/w	Tolerated (4/4)
60 mpk/w	Tolerated (4/4)

* Histopathology pending

IND submission for CX-801 expected in 2H 2023

CX-801: Expanding the Reach of I/O Therapy



CX-801
Potential Best in Class

1 **Best-in-Class Profile**

- Differentiated molecule with attractive preclinical efficacy and tolerability profile
- Well tolerated in multi-dose pilot NHP tox study up to 60 mg/kg

Broad Therapeutic Applications

- Enhance IO therapy and expand the reach of IO agents to more patients

2023 **CX-801 IND anticipated in 2H 2023**

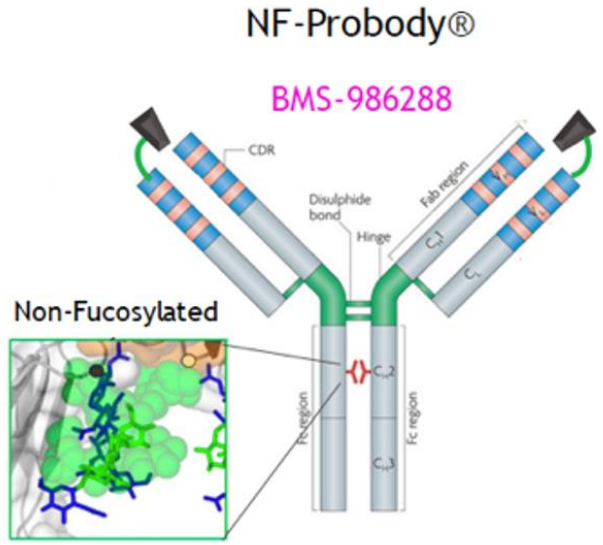
Next Generation Probody® CTLA-4 Program

Bristol Myers Squibb™

BMS CTLA-4 Probody® Summary

BMS-986288, a Probody version of anti-CTLA-4 Non-Fucosylated antibody (BMS-986218)

- **Advanced to Phase 2 in February 2023**
- **Designed to enhance CD16 binding and increase APC-mediated T cell priming**



Non-Fucosylated Probody® with increased CD16 affinity

CytomX Therapeutics

CytomX and Moderna Announce Strategic Collaboration to Research and Develop Messenger RNA-Based Conditionally Activated Therapeutics

CytomX THERAPEUTICS | moderna

January 2023

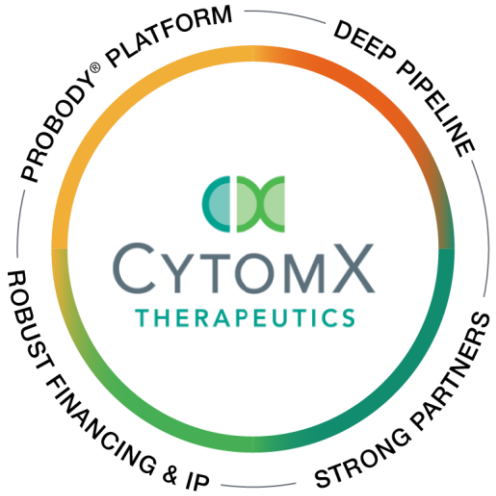
Conditionally Activated mRNA Therapies in Cancer and Other Diseases

Collaboration Highlights

- **Collaboration will combine CytomX's Probody® Platform with Moderna's mRNA technologies**
- **Collaboration Scope includes oncology and non-oncology conditions**
- **CytomX received $35 million upfront payment, including $5 million of prefunded R&D**
- **Potential for up to approximately $1.2 billion in research, milestones, tiered royalties on global net sales**
- **Research funded by Moderna**
- **Moderna option to participate in a future financing**

Transforming Lives with Safer, More Effective Therapies

Potential 2023 Events and Milestones



- **CX-904 (EGFRxCD3):** Continue Phase 1 dose escalation, initiate backfill cohorts by end of year ahead of potential 2024 Phase 1b initiation
- **File 2 New INDs:** CX-801 (IFNa2b) and CX-2051 (EpCAM) in the second half of 2023
- **CX-2029 (CD71):** Determine next steps for CD71 Program, including CX-2029
- **BMS CTLA-4:** Continued clinical progress by BMS for BMS-986288 (advanced to Phase 2 in Feb 2023)
- **Collaborations:** Continuation of drug discovery activities within R&D alliances including newest collaborators, Regeneron and Moderna