CytomX Therapeutics

41st Annual J.P. Morgan Healthcare Conference

Sean McCarthy, *D.Phil.*
Chief Executive Officer and Chairman

January 11, 2023

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CytomX Therapeutics

Leading the Field of Localized Biologic Therapies

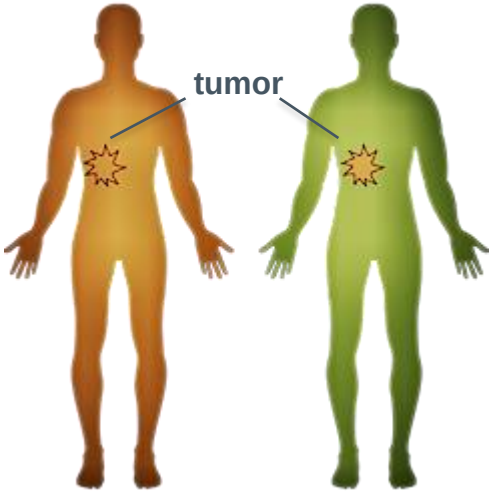
The Promise of Conditionally Active, Localized Biologic Therapies

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

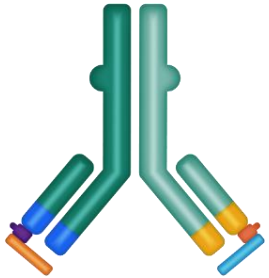
- **Designed to localize anti-cancer efficacy and decrease systemic toxicities**



Leading Platform for Localized Biologic Therapies

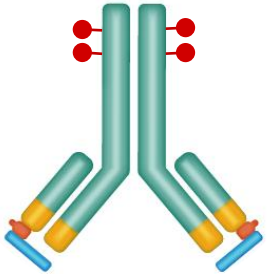
Addressing Major Challenges in Today's Cancer R&D Landscape

T-Cell Bispecifics



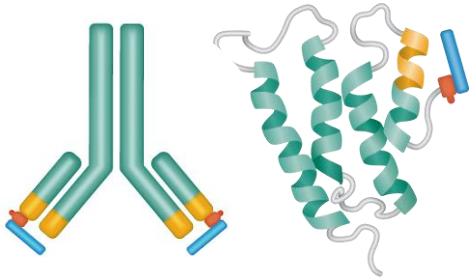
Localizing T-cell engaging bi-specifics to attack solid tumors

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

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

Robust Financing and IP

- $194M Cash as of Q3 2022
- Broad IP portfolio

Strong Partners

- 6 major partnerships
- 4 molecules in the clinic

Bristol Myers Squibb™ abbvie AMGEN astellas REGENERON moderna

Broad, Multi-Modality Probody® Pipeline

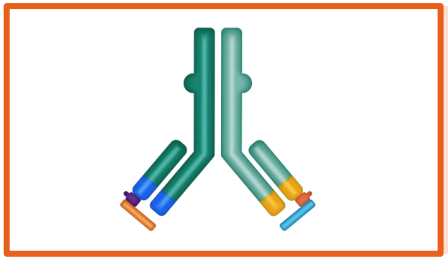
Economics	Product Candidate	Target	Indication	Preclinical / Phase 1 / Phase 2	Partner
Wholly-Owned or US Rights*	CX-2029	CD71-MMAE	SqNSCLC, Esophageal / GEJ		CytomX, abbvie
	CX-904	EGFRxCD3	Solid tumors		CytomX, AMGEN
	CX-2051	EpCAM	Solid tumors		CytomX
	CX-801	IFN-α2b	TBD		CytomX
	Various	Undisclosed	TBD		CytomX, astellas
Collaborator Directed Pipeline	BMS-986249	CTLA-4	1L Melanoma	+ nivolumab vs. ipi + nivo	Bristol Myers Squibb
			TNBC, HCC, CRPC	+ nivolumab	
	BMS-986288	CTLA-4 (a-fucosylated)	Solid tumors	+/- nivolumab	
	Probody TCBs	Undisclosed	TBD		AMGEN, astellas, REGENERON
	Various	Undisclosed	TBD		Bristol Myers Squibb, abbvie
	Various	Undisclosed	TBD		moderna

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

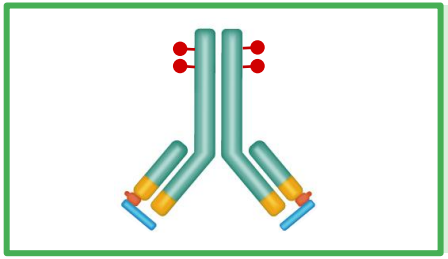
CytomX THERAPEUTICS

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

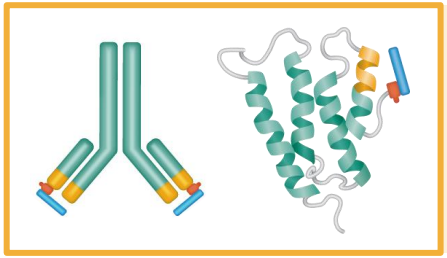
Pipeline Review



Expanding R&D Activities in T-cell Engaging Bispecifics



Probody® Antibody Drug Conjugates



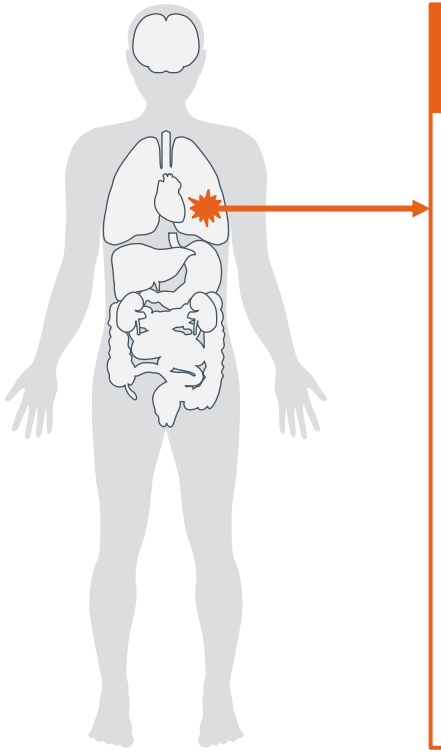
Probody® Immunotherapies

CytomX Therapeutics

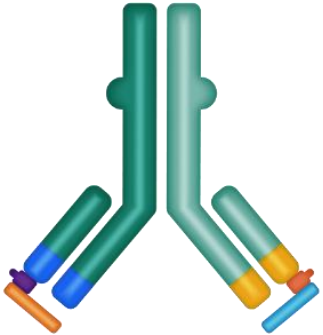
Expanding R&D Activities in T-cell Engaging Bispecifics

- CX-904 (EGFRxCD3) Phase 1 Progress AMGEN
- Astellas: Progress in TCB Collaboration astellas
- Regeneron Collaboration REGENERON

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

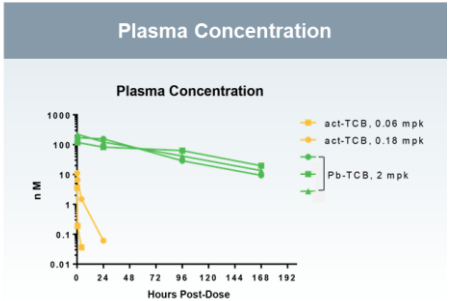
Increases MTD

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

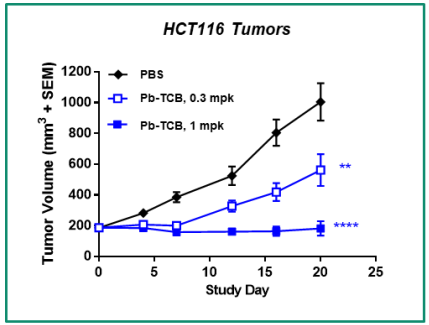
MTD increases by >60-fold with conditionally activated TCB (Pb-TCB)

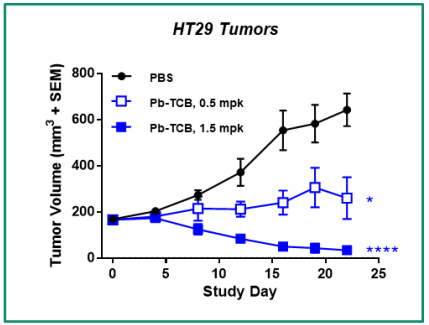
Extends PK



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 AACR-NCI-EORTC International Conference on Molecular Targets 2017

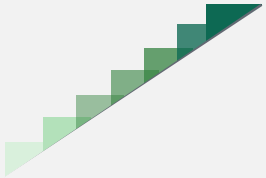
CX-904 Progress-to-date and Clinical Path Forward

2022 Progress

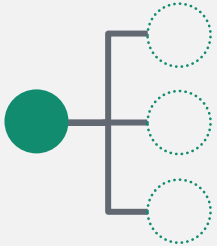
- ✓ First Patient Dosed in May 2022
- ✓ Advanced through single patient cohorts
- ✓ 3+3 Dose Escalation Ongoing

CTMX-904-101 Study

Dose Escalation:



Dose Expansion:



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

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

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**

CytomX and Regeneron Collaboration on Bispecific Immunotherapies

CytomX THERAPEUTICS | REGENERON

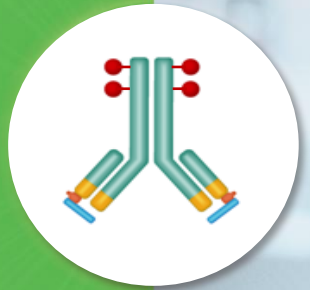
November 2022

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**

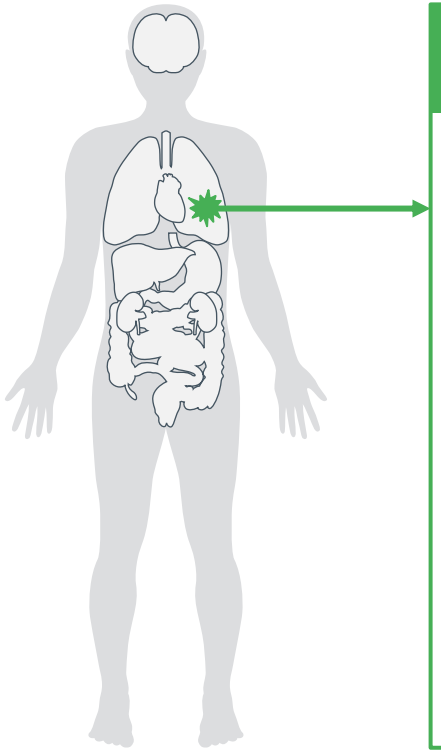
CytomX Therapeutics



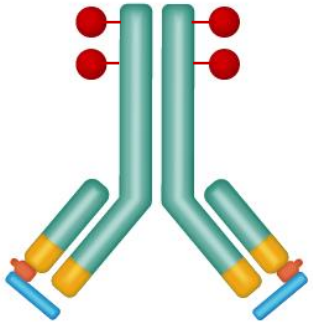
Probody® ADCs

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

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



Probody® Antibody Drug Conjugates



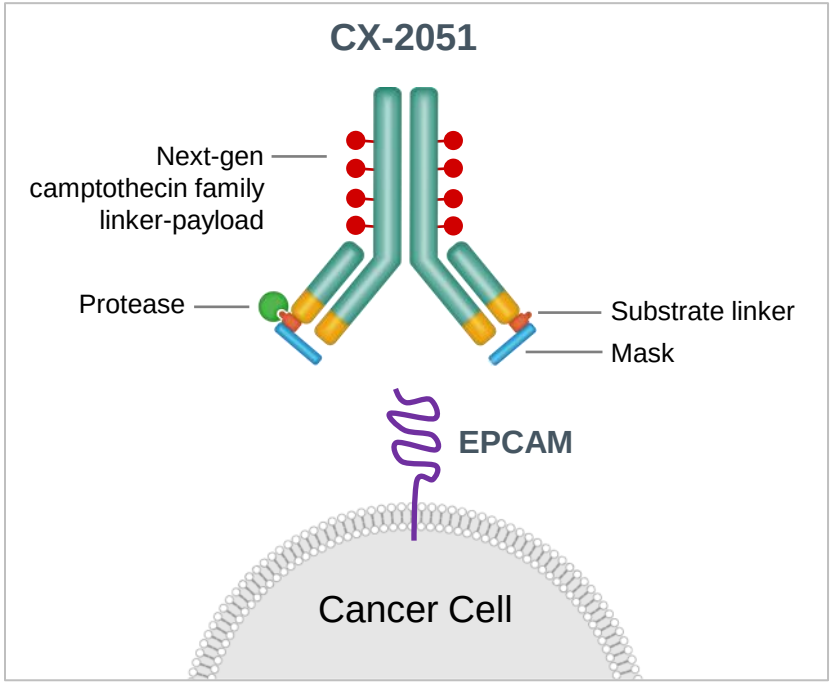
Substrate linkers

Masks

Linker payload

- **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

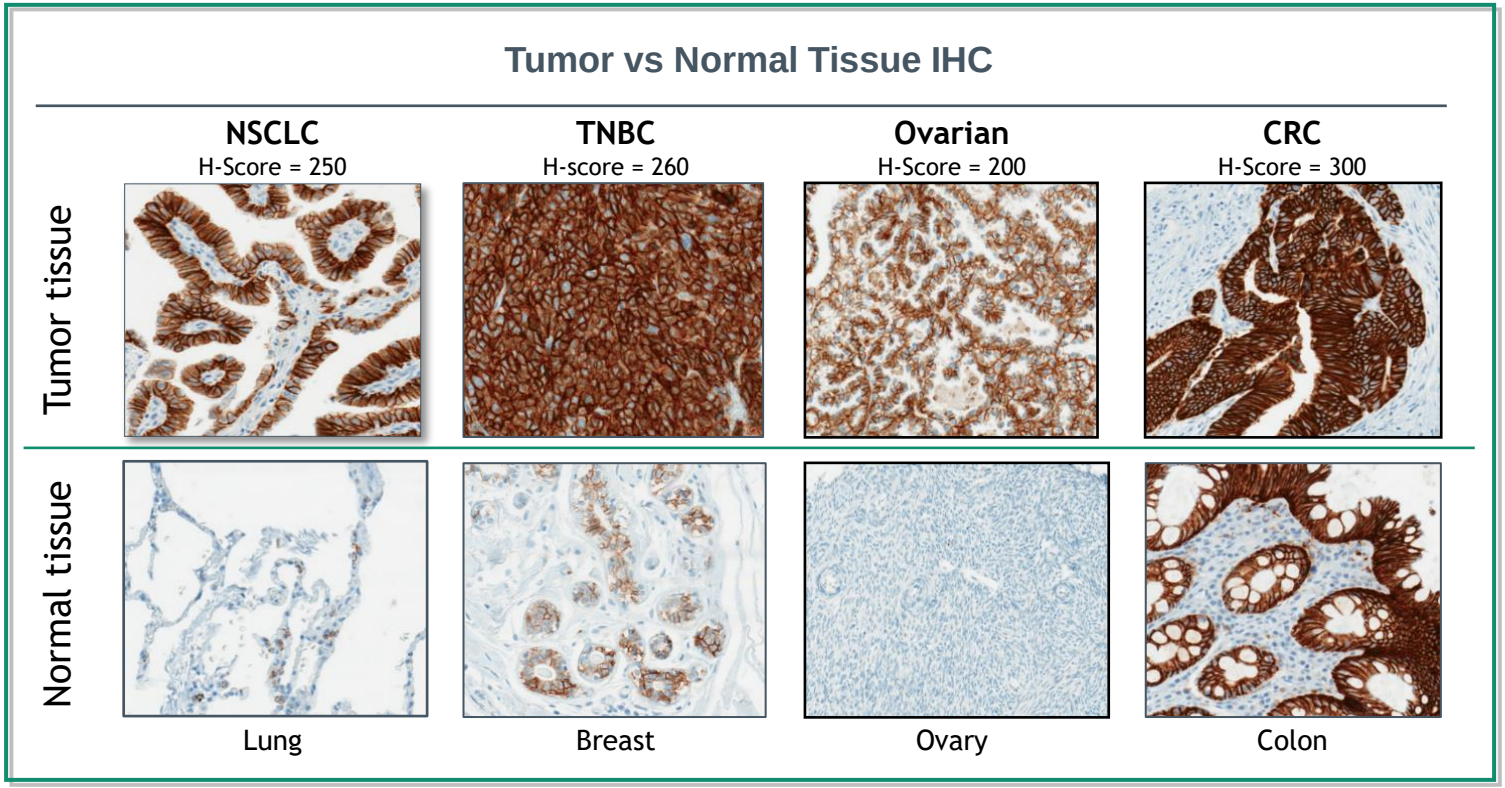
Sesen Bio

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

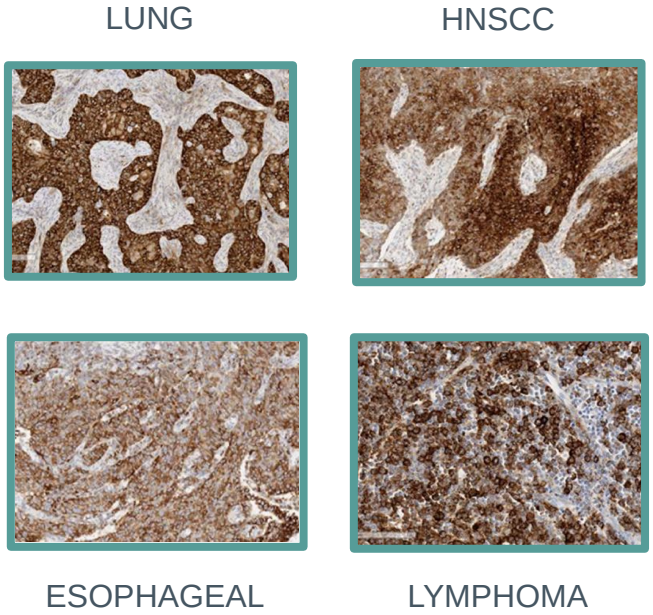
IND Filing Anticipated 2H 2023



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 Fully Enrolled

3 mg/kg Q3W Phase 2 Dose

Study Design:

Part A – 3+3 Dose escalation

- 0.1 mg/kg to 5 mg/kg Q3W

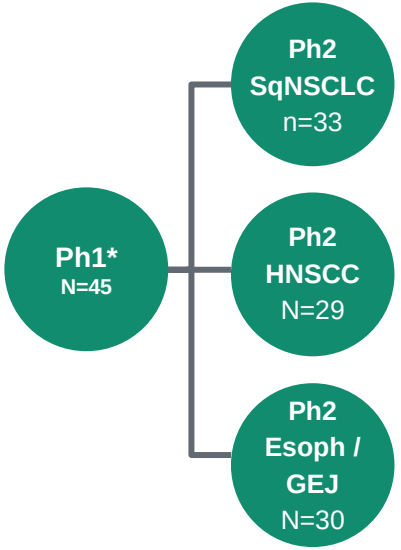
Part B – Tumor Biopsy Cohort

- 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

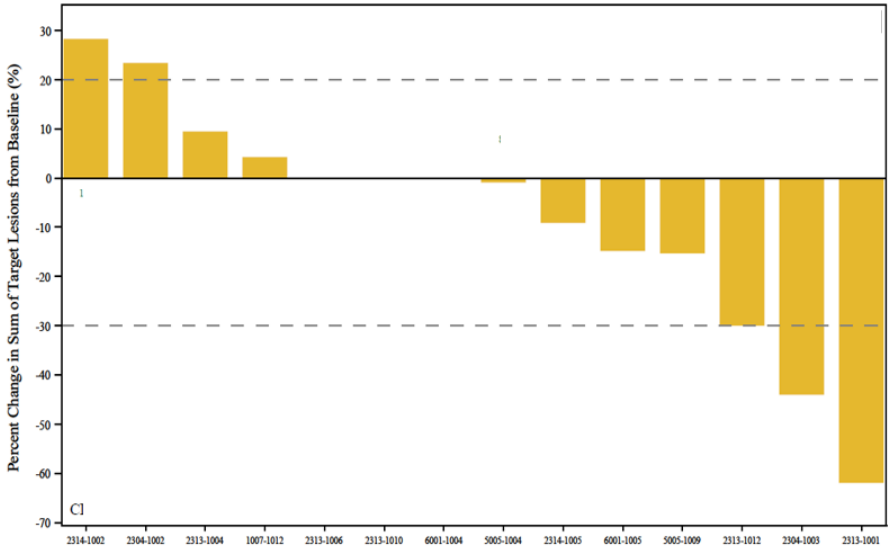


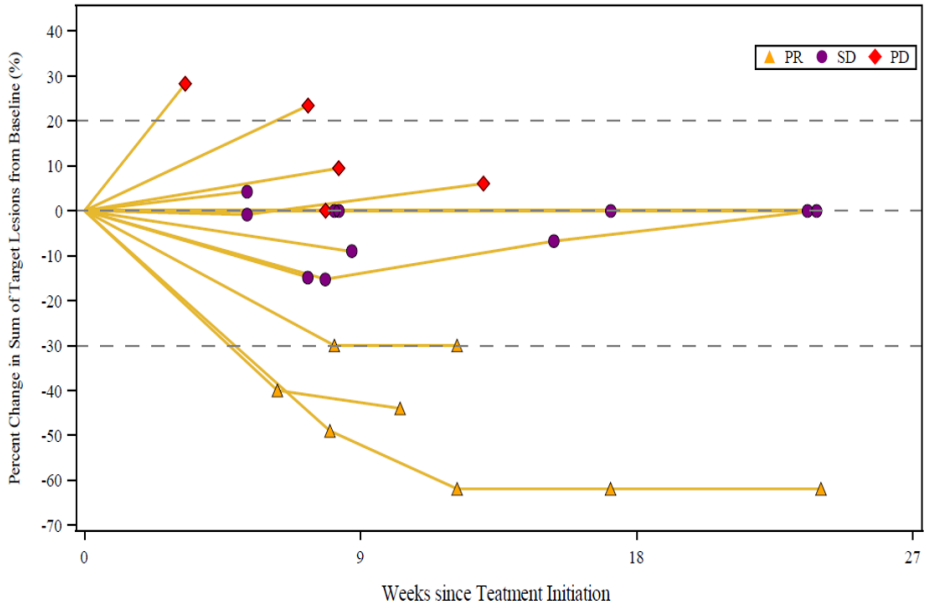
Note: Phase 2 Expansion includes 5 Patients from Part B dosed at 3mg/kg Q3W; 2 patients with sqNSCLC and 3 HNSCC

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



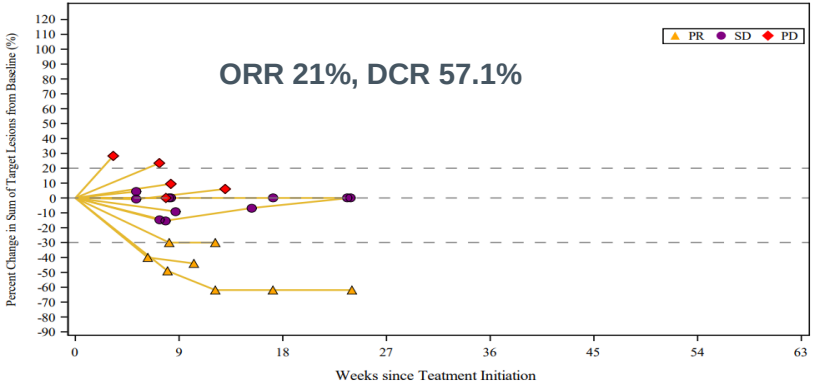


Data snapshot cutoff date for efficacy: 2022 October 4

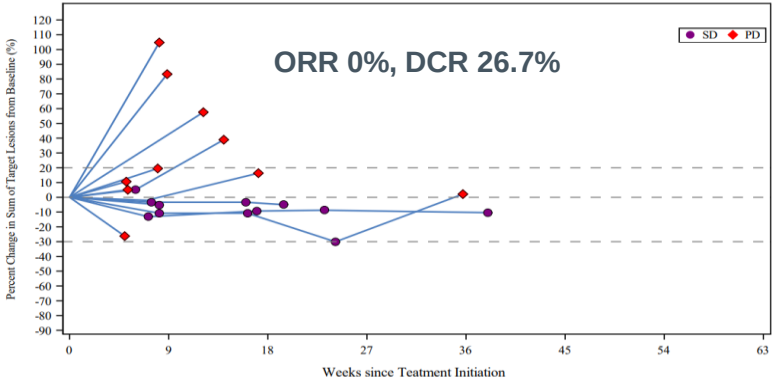
CX-2029 Responses Observed in Squamous Tumors

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

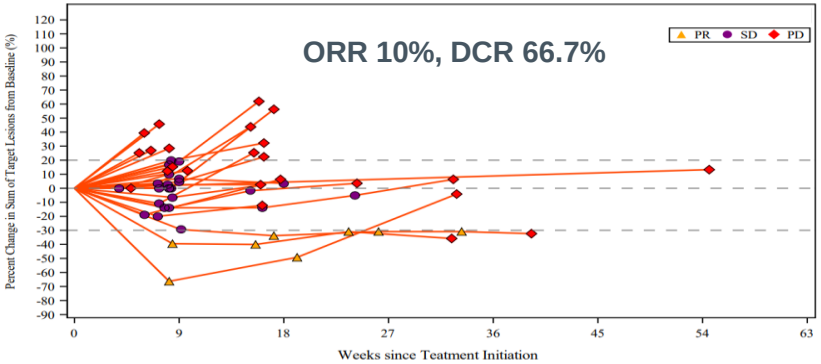
Squamous Esophageal



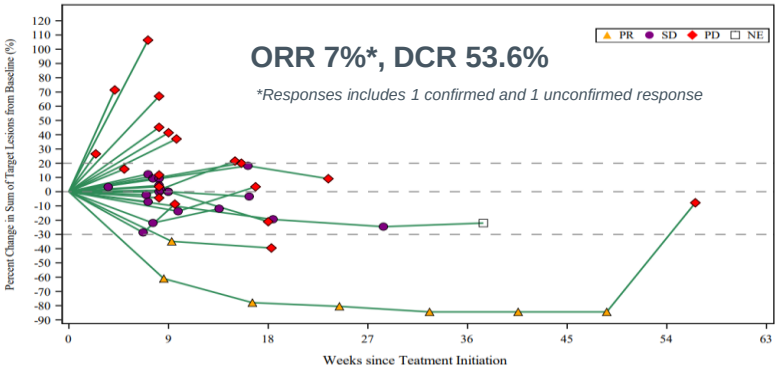
Adeno Esophageal



Squamous NSCLC



Squamous Head & Neck



CytomX Therapeutics

Data snapshot cut date for efficacy: 2022 October 4

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)

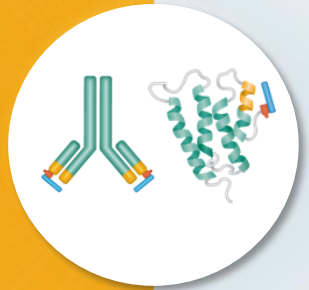
AE Grades are based on CTCAE v 5.0; AEs w missing relationship are considered related to CX-2029
Subjects are only counted only at the maximum severity grade experienced w each preferred term
Neutropenia includes the following preferred terms: 'Neutropenia',' Neutrophil count decreased', 'Febrile neutropenia' 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 and AbbVie to determine next steps for CX-2029 in 2023

CytomX Therapeutics



Probody® Immunotherapies

- **CX-801**: Conditionally Activated IFNα-2b
- **BMS-986249**: First-in-class Conditionally Activated Antibody Targeting Cytotoxic T Lymphocyte Antigen-4 (CTLA-4)

Cytokine Therapeutics Are Potent, But Associated With Safety Issues

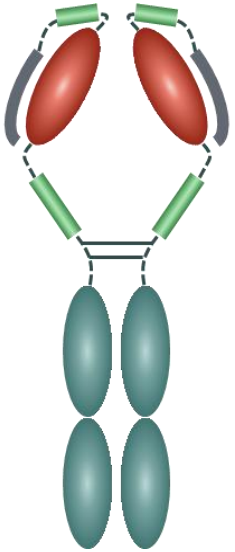
Cytokines and Cytokine Therapeutics

- 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

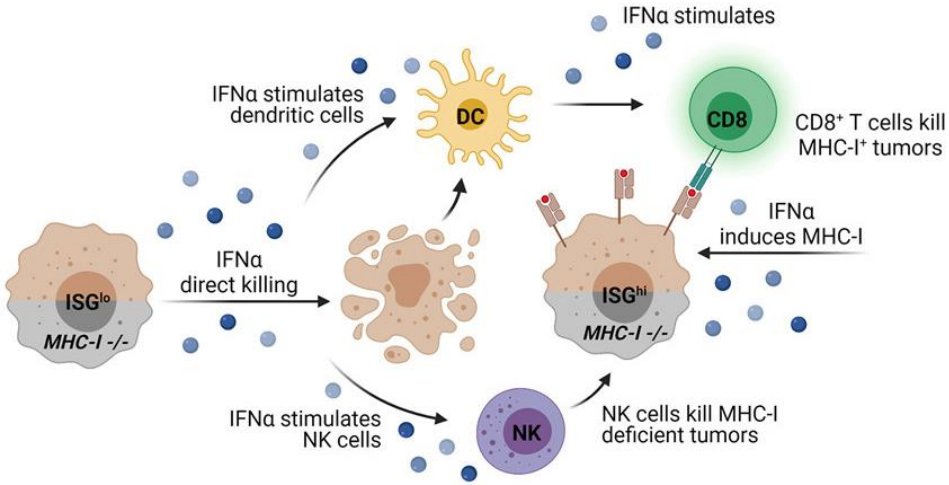


IFNα-2b is a Powerful Mediator of Immune Activation with Ideal Properties for Cancer Immunotherapy

Why IFNα-2b?

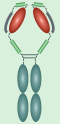
Mechanism of Action

- 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

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



CX-801
Potential Best in Class

1 **Best-in-Class Profile**

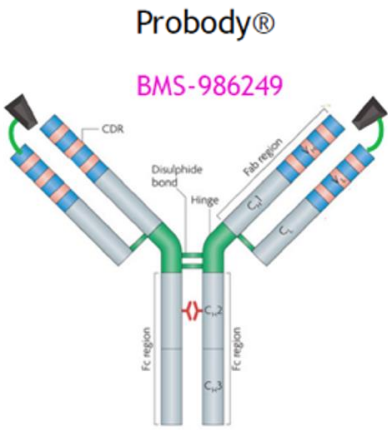
- Differentiated molecule with attractive preclinical efficacy and tolerability profile
- Well tolerated in multi-dose pilot NHP tox study up to 60 mg/kg

Broad Therapeutic Applications

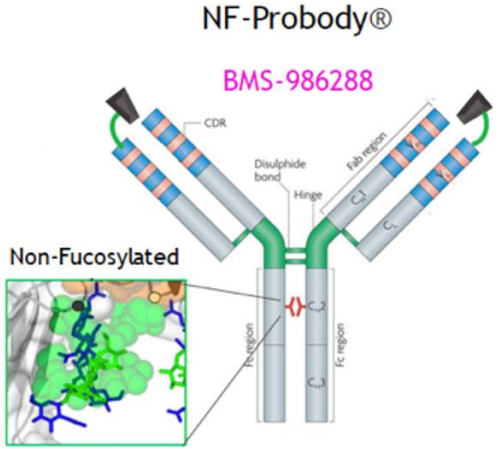
- Enhance IO therapy and expand the reach of IO agents to more patients

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

Next Generation Probody® CTLA-4 Programs



Ipilimumab Probody® with a protease cleavable mask to localize activity to the tumor



Non-Fucosylated Probody® with increased CD16 affinity

BMS CTLA-4 Probody® Summary

BMS-986249, a Probody version of Ipilimumab

- Phase 1 doses tested ranged from 240 mg – 2400 mg
- Early efficacy reported with no unexpected safety signals
- Randomized Phase 2 ongoing

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

- Phase 1/2 study ongoing
- Designed to enhance CD16 binding and increase APC-mediated T cell priming

Bristol Myers Squibb™

Annals of Oncology (2022) 33 (suppl_7): S331-S355. 10.1016/annonc/annonc1058

CytomX Therapeutics

Society for Immunotherapy of Cancer's (SITC) webinar Targets for Cancer IO: A Deep Dive in Enhanced CTLA-4 blockade, Nicholas Wilson, Ph.D, October 5, 2022

CytomX THERAPEUTICS

Moderna Alliance and Closing Comments

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 to receive $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**

Broad, Multi-Modality Probody® Pipeline

Economics	Product Candidate	Target	Indication	Preclinical / Phase 1 / Phase 2	Partner
Wholly-Owned or US Rights*	CX-2029	CD71-MMAE	SqNSCLC, Esophageal / GEJ		CytomX, abbvie
	CX-904	EGFRxCD3	Solid tumors		CytomX, AMGEN
	CX-2051	EpCAM	Solid tumors		CytomX
	CX-801	IFN-α2b	TBD		CytomX
	Various	Undisclosed	TBD		CytomX, astellas
Collaborator Directed Pipeline	BMS-986249	CTLA-4	1L Melanoma	+ nivolumab vs. ipi + nivo	Bristol Myers Squibb
			TNBC, HCC, CRPC	+ nivolumab	
	BMS-986288	CTLA-4 (a-fucosylated)	Solid tumors	+/- nivolumab	
	Probody TCBs	Undisclosed	TBD		AMGEN, astellas, REGENERON
	Various	Undisclosed	TBD		Bristol Myers Squibb, abbvie
	Various	Undisclosed	TBD		moderna

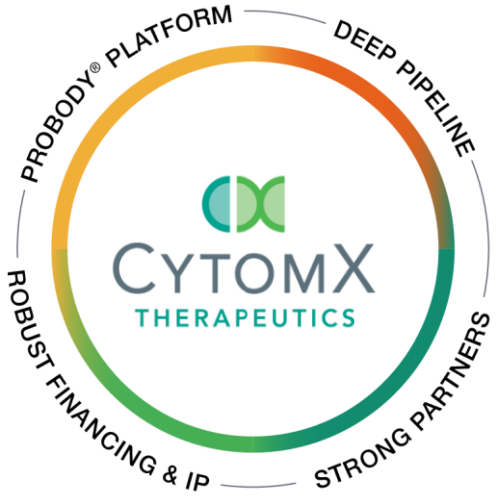
Probody® Modality: TCBs | ADCs | Immunotherapy | mRNA | Undisclosed

CytomX THERAPEUTICS

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

Transforming Lives with Safer, More Effective Therapies

Potential 2023 Events and Milestones



- **CX-904 (EGFRxCD3):** Continue patient enrollment and dose escalation in ongoing Phase 1 study
- **File 2 New INDs:** CX-801 (IFNa2b) and CX-2051 (EpCAM) in the second half of 2023
- **CX-2029 (CD71):** Determine next steps with AbbVie
- **BMS CTLA-4:** Continued clinical progress for BMS-986249 and BMS-986288
- **Collaborations:** Initiation of R&D activities with our newest collaborators, Regeneron and Moderna