CytomX Therapeutics

Destroying Cancer. Differently.

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Forward-Looking Statements

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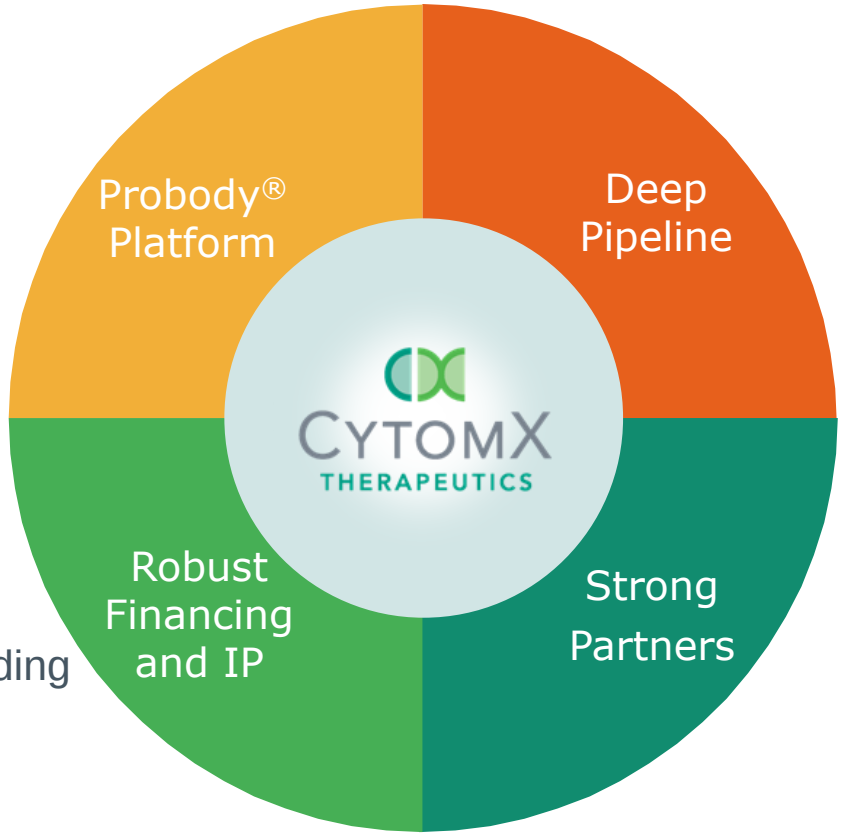
Integrated Business Model for Long-Term Value Creation

- Leader in conditional activation of biologics
- Tunable platform
- Multi-modality



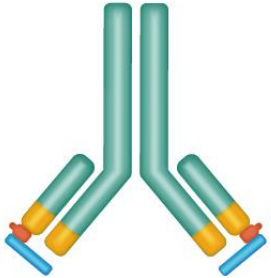
- Robust & diverse portfolio
- Phase 2 assets across multiple cancer types
- 2 new INDs expected in 2023

- Strong balance sheet
- $194M end Q3 2022
- >550 issued and pending patents worldwide

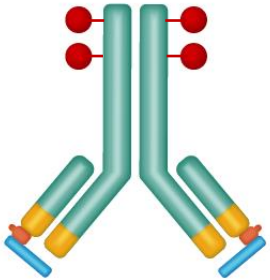
- 4 global partnerships
- 3 partnered programs in clinic

CytomX has Pioneered a Multi-Modality Platform for Conditional Activation and Tissue Localization of Potent Biologic Drug Candidates

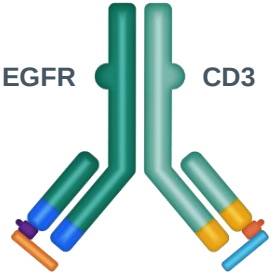
Antibodies



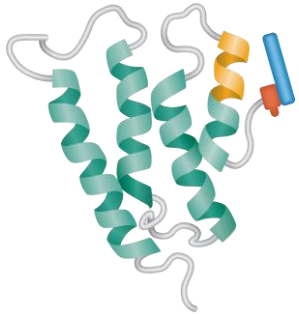
Antibody-Drug Conjugates



T-cell Bispecifics



Cytokines



Our Value Proposition

The Leading Paradigm of Biologics Localization
Addressing Major Challenges in Today's Cancer R&D Landscape

Substrate linkers | Masks | Linker payload

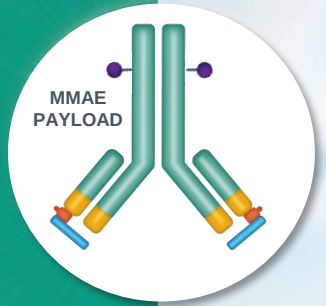
CytomX THERAPEUTICS

Leading Platform, Deep Pipeline, Broad Clinical Experience

7 Therapeutic Candidates, 3 in Phase 2 Studies Across Multiple Cancer Types

Modality	Product Candidate	Target-Payload	Indication	Preclinical	Phase 1	Phase 2	Commercial Rights/Partner
Antibody-Drug Conjugate	CX-2029	CD71-MMAE	SqNSCLC, Esophageal/ GEJ				CytomX abbvie
	CX-2051	EpCAM	Solid tumors				CytomX
	Praluzatamab ravtansine (CX-2009)	CD166-DM4	HR+/HER2-non-amp BC				CytomX
Immuno-Oncology	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			
	CX-801	IFN alpha-2b	TBD				CytomX
TCB	CX-904	EGFRxCD3	Solid tumors				CytomX AMGEN
	Various	Undisclosed	TBD				CytomX astellas

CytomX Therapeutics



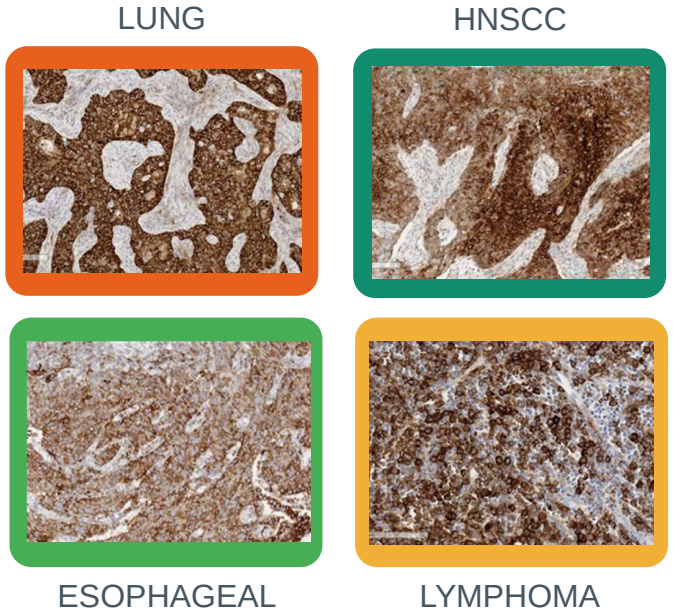
CX-2029

First-in-Class Antibody-Drug Conjugate (ADC) Directed Toward CD71 (Transferrin Receptor) for Multiple Cancer Types

CD71 is a High Potential ADC Target With High Tumor Expression

- Undruggable target with conventional ADC due to central role in iron metabolism
- CX-2029 is a CD71-directed MMAE conjugated conditionally activated ADC
- Anti-cancer agent with first-in-class potential

CD71 Expression by IHC



Data generated by CytomX

Ongoing Multi-Cohort CX-2029 Phase 2 Expansion Study

3 mg/kg Q3W Selected as Phase 2 Dose

Patient Enrollment Met Objectives in All Three Solid Tumor Indications

Key Eligibility	Cancer Type	Endpoints
• Prior platinum and checkpoint inhibitor required • Documented progression after at least one systemic regimen for advanced disease	**sqNSCLC** n~25* **HNSCC** n~25* **Esophageal/GEJ** n~25*	**Primary:** Overall Response Rate (ORR) by local investigator **Secondary**: PFS, DCR, CBR24, DoR, OS, Safety, PK, ADA, TTR **Exploratory:** Biomarker correlation with outcome **Readout:** Preliminary data for sqNSCLC and HNSCC reported Dec 2021

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

CX-2029 Preliminary Phase 2 ORR of 18.8% in 3L+ SqNSCLC

Enrollment Complete – Data Update Expected in Fourth Quarter 2022

No Current Standard-of-Care in 3L+ Post-Checkpoint Inhibitor Setting

Study	Treatment	Phase	Line	N	Sq NSCLC ORR (%)
CX-2029[1]	**CX-2029**	**2**	**3rd**	**16**	**18.8**
CheckMate 063[2]	Nivolumab	2	3rd	117	14.5
REVEL[3]	Docetaxel	3	2nd	171	10.5
CheckMate 017[4]	Nivolumab	3	2nd	135	20.0
	Docetaxel			137	8.8
OAK[5,6]	Atezolizumab	3	2nd	112	11.6
	Docetaxel			110	8.2

Sources: 1) CytomX press release, 12/20/2021; 2) Rizvi NA, Lancet Oncol 2015; 3) Garon EB, Lancet 2014; 4) Brahmer J, NEJM 2015; 5) Rittmeyer A, Lancet 2017; 6) Cortinovis D, Annals Oncol 2017 Supplement 2, ii32

Preliminary Takeaways from Ongoing Phase 2 Expansion Study

- Heavily-pretreated and unselected sqNSCLC patients (n=16*)
  - Median # prior therapies = 2
  - All received prior checkpoint inhibition
  - Response durability: 5.6 months for 1 PR and two PRs still on therapy**
- HNSCC cohort fully enrolled (n=25*)
  - 4% ORR
- Safety profile consistent with Phase 1 observations
  - No new safety signals identified
  - Anemia most common Grade 3+ adverse event (67%)
  - Low TRAE discontinuation rate, all due to anemia (5.8%)

* Efficacy Evaluable; ** As of data cut off on October 29, 2021

CytomX Therapeutics

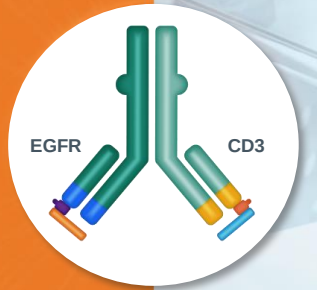
Emerging Opportunity for CX-2029 in 3L+ SqNSCLC

Potential to Replace Chemotherapy in Early Line Therapies

Metastatic SqNSCLC Treatment (2021 US and EU5 Patients)		
First Line (81K patients)	**Second Line (49K patients)**	**Third Line (20K patients)**
Chemotherapy	Chemotherapy	Physician's choice / salvage
PD-(L)1 inhibitors +/- chemotherapy	PD-(L)1 monotherapy	**CX-2029 Monotherapy 3L**
Nivolumab + ipilimumab +/- chemotherapy	Targeted therapies +/- chemotherapy	

Sources: NCCN NSCLC Guidelines, 2021; DRG NSCLC Treatment 2021; DRG Breast Cancer Epidemiology 2021; CytomX analysis

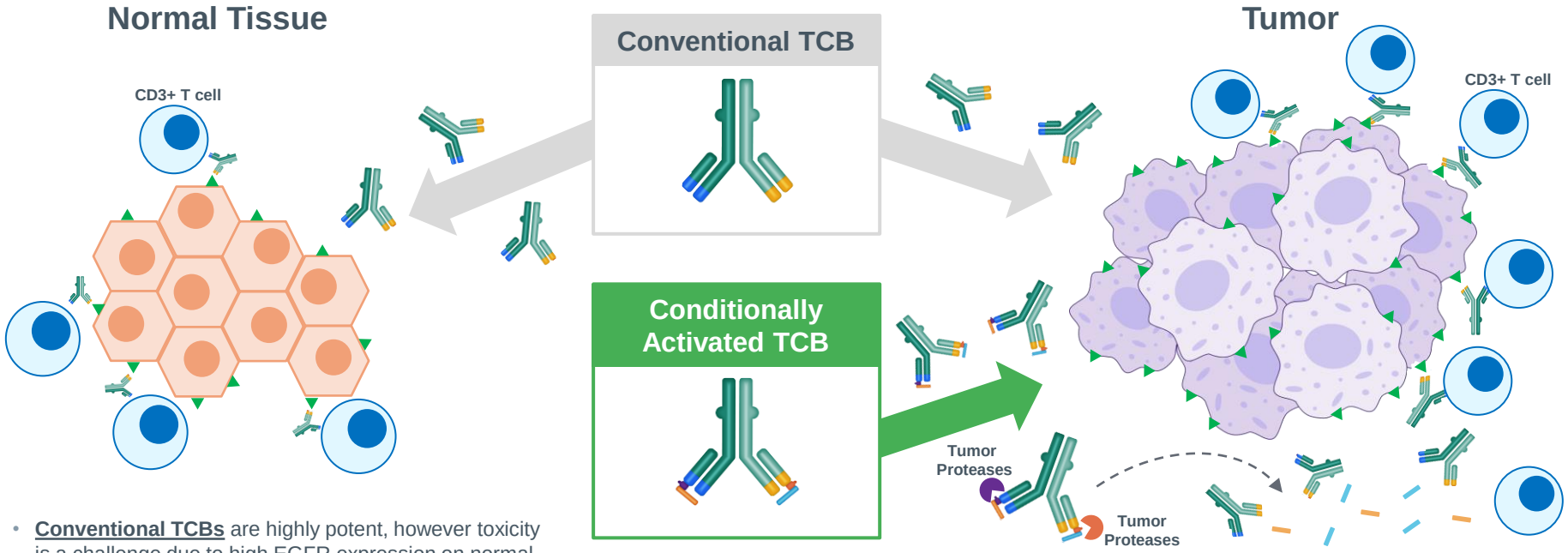
CytomX Therapeutics



CX-904

Conditionally Activated EGFR x CD3 T-Cell-Engaging Bispecific Antibody (TCB)

Conditionally Activated TCBs Open Target Landscape for Solid Tumors



- **Conventional TCBs** are highly potent, however toxicity is a challenge due to high EGFR expression on normal tissues
- Limited TCB targets and narrow therapeutic window

- **Conditionally activated TCBs** designed to retain potent anti-tumor activity while having less systemic toxicities by avoiding T-cell engagement outside of tumor
- Potentially expands TCB target landscape and widens therapeutic window

Source: Image adapted from Middelburg et al. Cancers. 2021

Key: ▲ = EGFR = Normal cells = CD3+ T cells = Tumor cells = Proteases

CytomX Therapeutics

EGFR: A High Potential Target for Conditionally Activated TCB Modality

- **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 mAbs approved (cetuximab, panitumumab, nimotuzumab, and necitumumab)
- **Prevalent EGFR expression**
  - EGFR x CD3 conditionally activated TCB has opportunity in both high- and low-expressing cancers
- **Conditionally activated TCBs 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 agents

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

Conditionally Activated EGFRxCD3 TCB Induces Tumor Regressions and Increases MTD in Preclinical Studies

Increases MTD

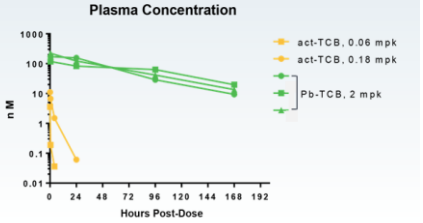
TCB*	Dose (mg/kg)	Clinical Observations
Act-TCB	0.06 *(MTD)*	Moderate
Act-TCB	0.18	Severe
Pb-TCB	0.6	None
Pb-TCB	2.0	Mild
Pb-TCB	4.0 *(MTD)*	Moderate

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

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

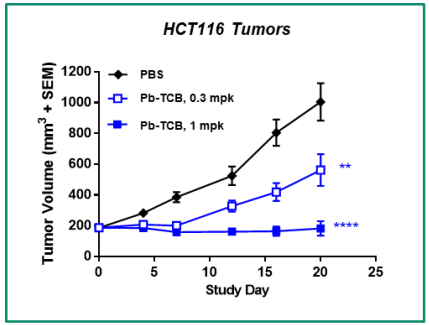
Extends PK

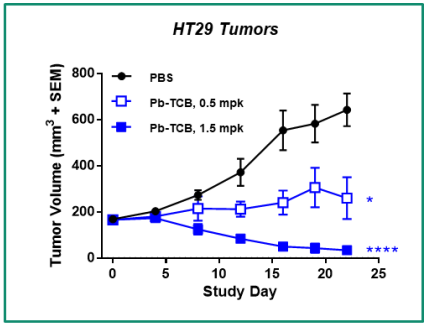
Plasma Concentration



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 AACR-NCI-EORTC International Conference on Molecular Targets 2017

First-in-human Study Evaluating Safety, Tolerability & Activity of CX-904

First Patient Dosed in May 2022

Key Eligibility

- Patients with metastatic or locally advanced solid tumors who have exhausted or are not eligible for standard-of-care therapy
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Measurable disease per RECIST 1.1
- Positive for EGFR expression or consent to obtain a screening biopsy
- Patients with asymptomatic brain metastases that are ≤1 cm may be eligible
- Adequate organ and bone marrow function

Design

Accelerated Escalation:
Single patient cohorts followed by 3+3 design

Dose Expansion:
Cohorts (~20 each) TBD

Objectives/Endpoints

Primary:
Tolerability and determination of recommended Phase 2 dose and schedule

Secondary:
Investigator assessed activity including ORR, DoR, PFS and OS

Other:
Characterization of pharmacokinetics, pharmacodynamics and anti-drug antibodies

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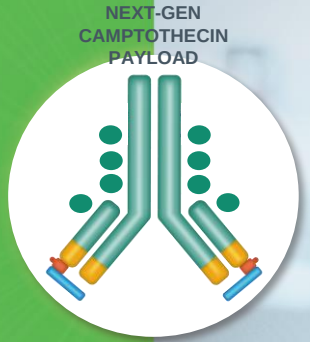
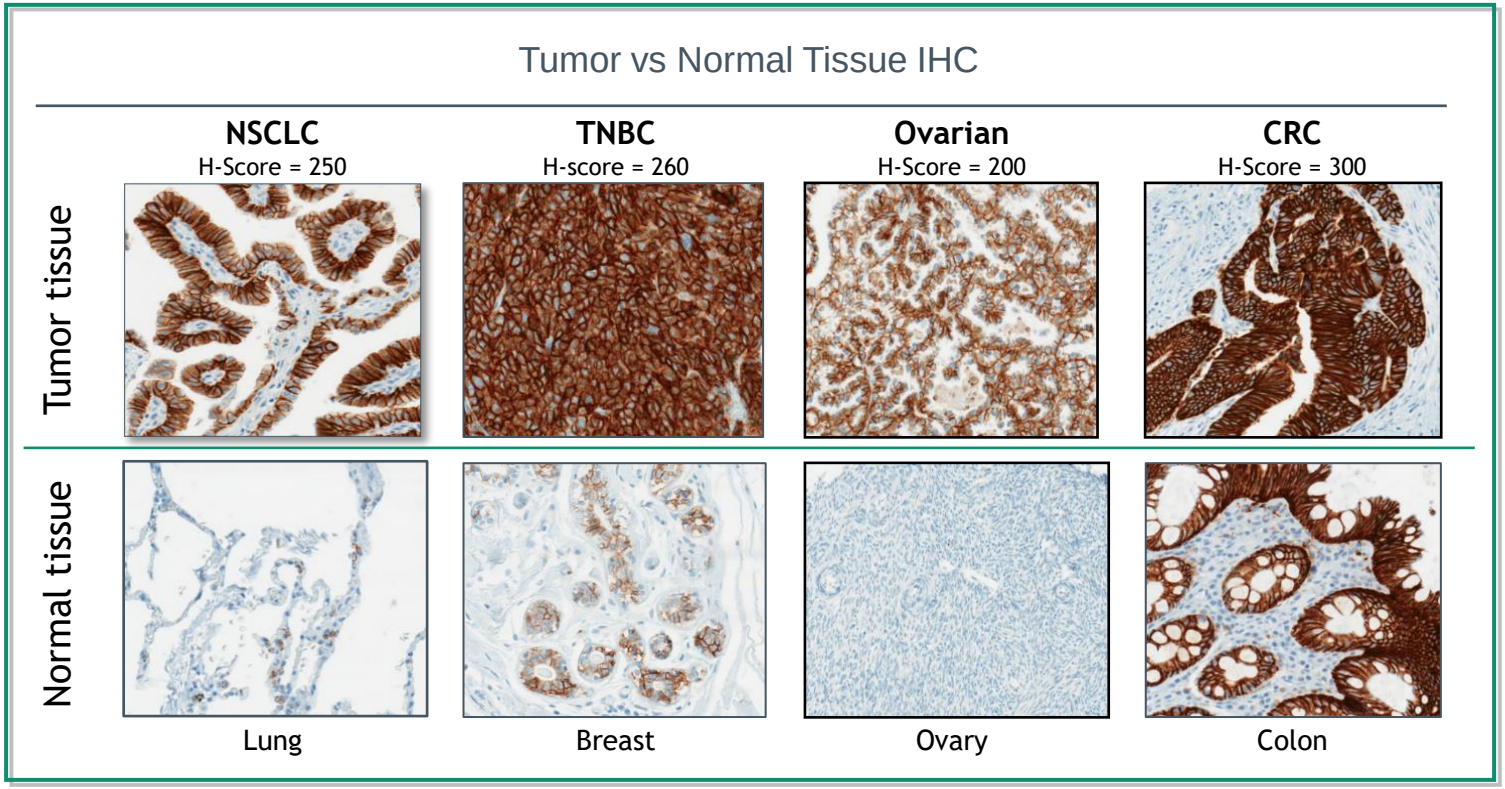


CX-2051

First-in-Class Antibody-Drug Conjugate (ADC) Directed Toward Epithelial Cell Adhesion Molecule (EpCAM)

EpCAM: A Compelling Target for a Conditionally Activated ADC

High Expression in Tumors; Moderate Expression in Normal Tissues



EpCAM Has Been Clinically Validated But Not As a Systemic Therapy

Locally administered EpCAM therapies have demonstrated impressive efficacy

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

Insys Therapeutics

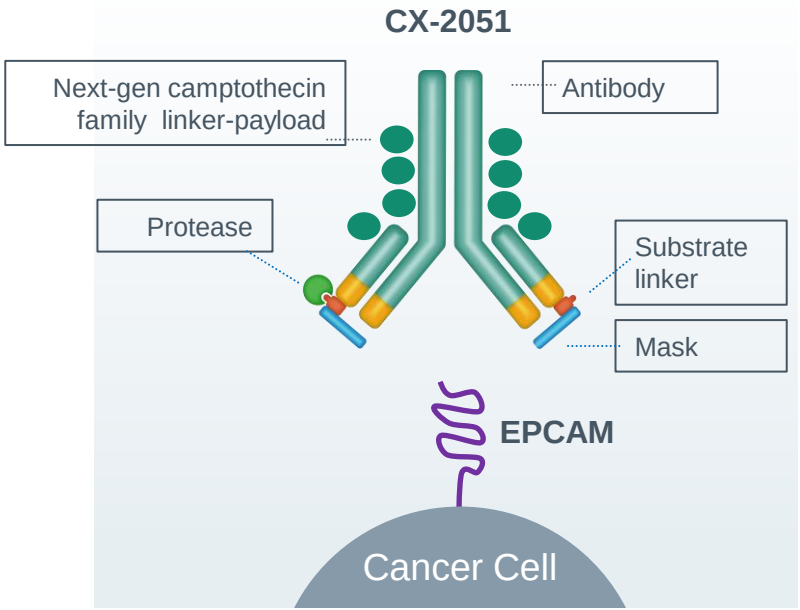
- Vicineum fusion protein: anti-EpCAM scFv linked to a truncated form of Pseudomonas exotoxin A
- Delivered by intravesical administration
- Phase 3 in bladder cancer

Sesen Bio

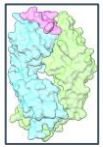
Systemic EpCAM therapies have demonstrated clinical toxicity

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

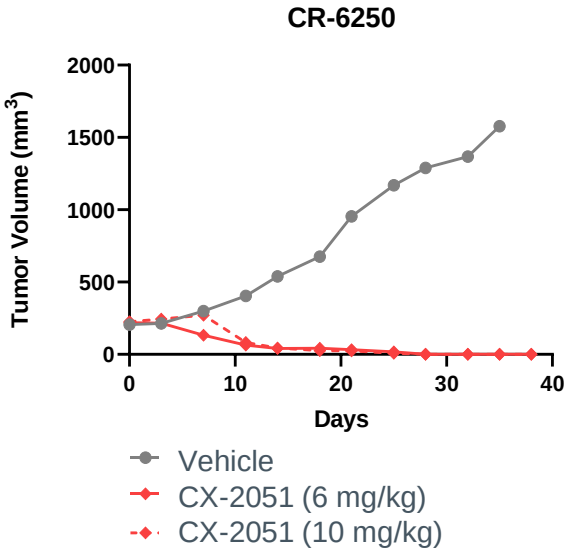


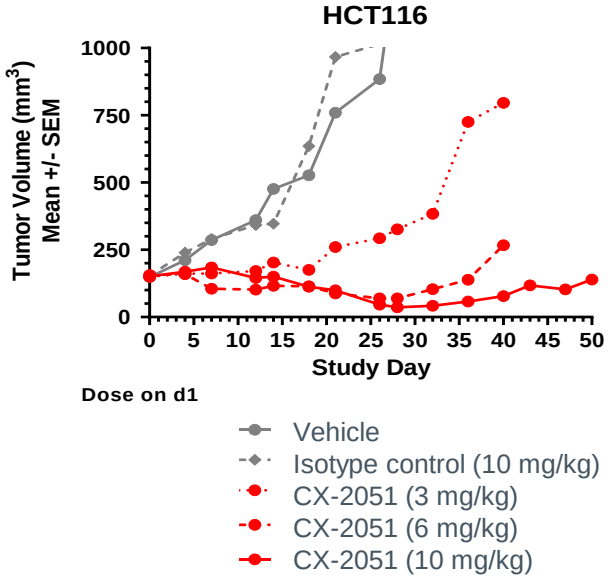
- Anti-EpCAM MAb with cross-reactivity to cynomolgus monkey
- Probody peptide mask with >60X masking efficiency (by ELISA)
- Protease-cleavable substrate with broad cleavability profile across multiple tumor types
- Next-gen camptothecin linker-payload (licensed from Immunogen)
- Optimized linker drives large bystander effect
- Inter-chain cysteine conjugation DAR8
- Crystal structure of mask interaction with antibody has been solved



Program licensed from ImmunoGen

CX-2051 Demonstrates Strong Activity in Preclinical Models





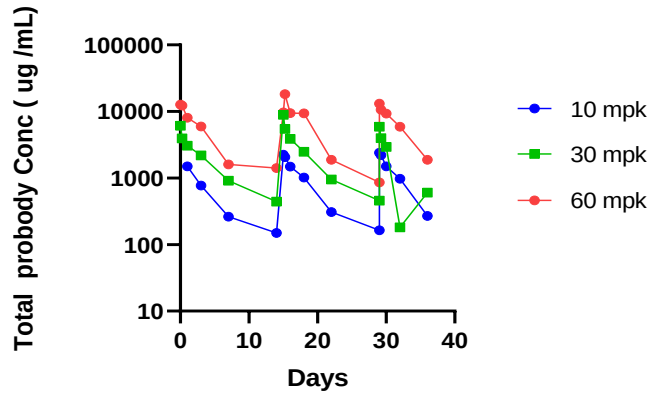
PDX: Patient derived xenograft; CDX: Cell derived xenograft
CR-6250 and HCT116: Colorectal cancer models

Dosing regimen: Q2W x 3

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

CytomX Therapeutics

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)

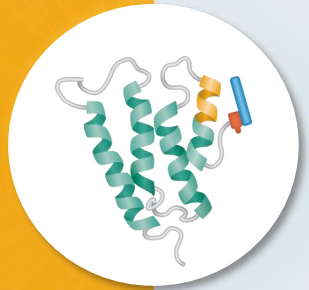
Dosing	CX-2051	Isotype
10 mg/kg	Tolerated (2/2)	
30 mg/kg	Tolerated (2/2)	
60 mg/kg	Tolerated (3/3)	Tolerated (2/2)
90 mg/kg	Not Tolerated (1/2)	

- 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

CytomX Therapeutics

CytomX Therapeutics



CX-801

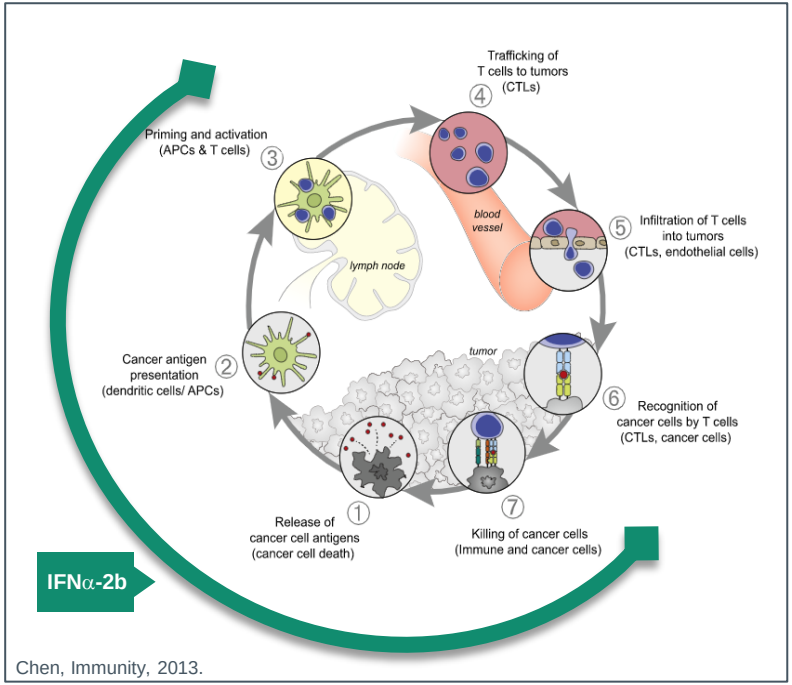
Conditionally Activated Interferon Alpha-2b

CX-801 is Designed to Activate Anti-Tumor Immunity in “Cold” Tumors

Why IFNα-2b?

MOA

- 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*
- The combination of IFNα-2b and CPI has the potential to **unlock classically CPI-resistant indications**



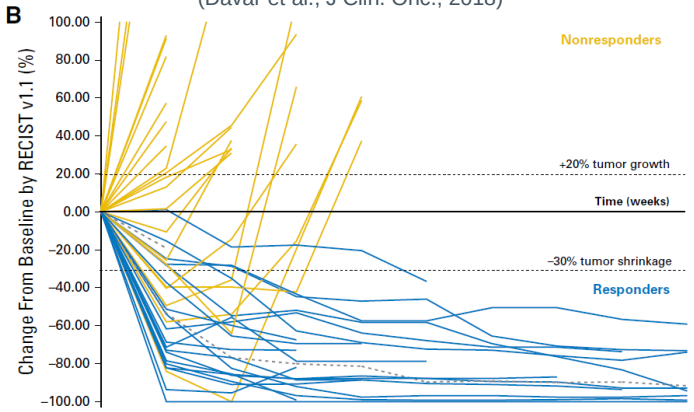
Chen, Immunity, 2013.

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)

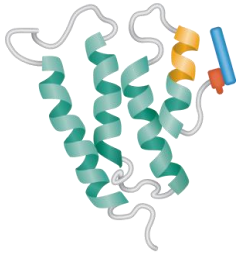


- **Potent activity (60.5% ORR)**
- **Significant, dose limiting adverse events (49% Grade 3/4 AEs)**

CX-801 (Probody Interferon-α2b)

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

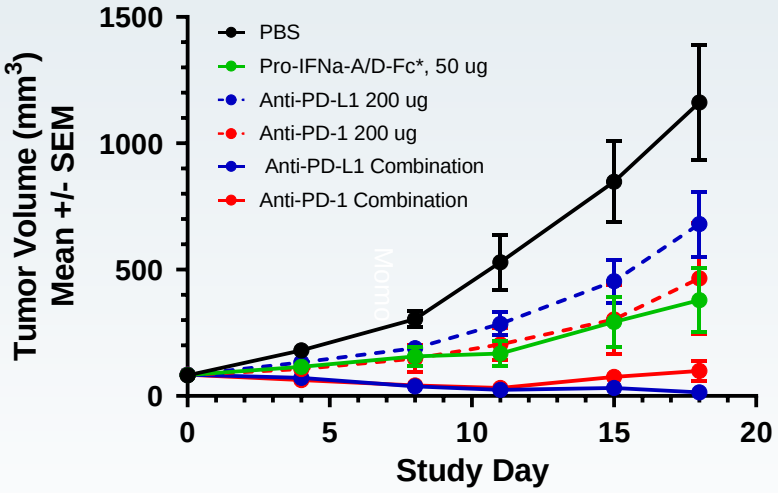
Advantages of CX-801



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

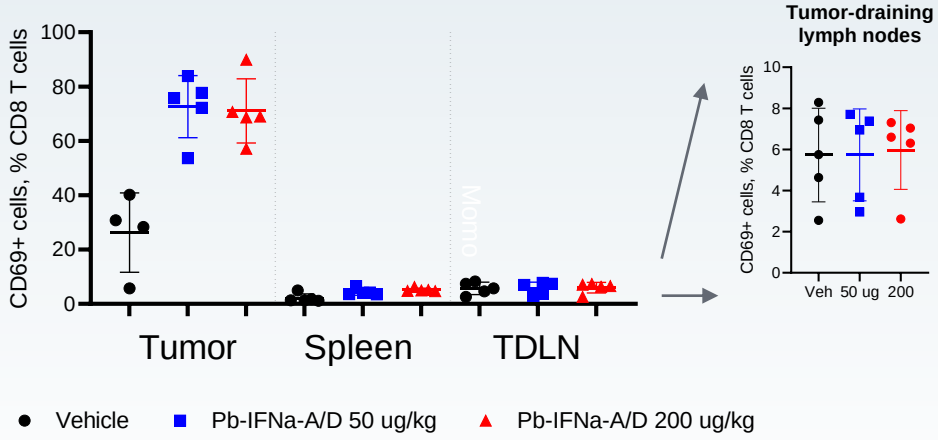
Combination of Dual Masked IFN-αA/D-Fc* and anti-PD-(L)1 Induces Substantially Enhanced Efficacy in MC38 Tumor Model

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

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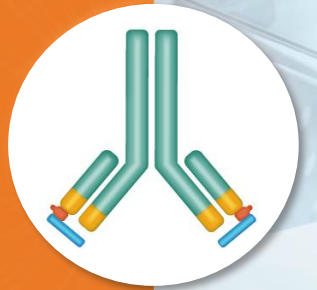

BMS-986249

First-in-class Conditionally Activated Antibody Targeting Cytotoxic T Lymphocyte Antigen-4 (CTLA-4)

Bristol Myers Squibb™

Updated Phase 1 Results at ESMO 2022 Support Ongoing Randomized Phase 2 in 1L Advanced Melanoma

- **BMS-986249 dose tested ranged from 240 – 2400 mg (~3 – 30 mg/kg)**
- **Encouraging early efficacy reported**
  - 38% disease control rate across all dose levels in patients who received BMS-986249 + nivolumab
  - 26% disease control rate across all dose levels in patients treated with BMS-986249 monotherapy
- **No unexpected safety signals with the combination across all tested dose levels**
  - Treatment-related adverse event incidence and severity appeared to be dose-dependent
- **Randomized Phase 2 study ongoing**
  - Study compares BMS-986249 + nivolumab vs. ipilimumab + nivolumab in 1L advanced melanoma
  - Study expanded to include three single-arm cohorts in advanced hepatocellular carcinoma, metastatic castration-resistant prostate cancer, and advanced triple-negative breast cancer

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

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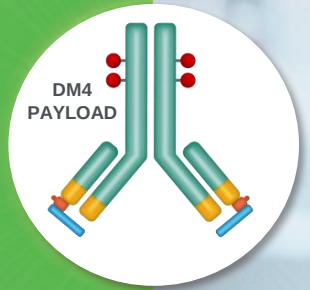

Praluzatamab Ravtansine (CX-2009)

First-in-Class Antibody-Drug Conjugate (ADC) Directed Toward CD166 for HER2-non-Amplified Advanced Breast Cancer

Multi-Arm Breast Cancer Phase 2 Study Design

Monotherapy and Combination with Pacmilimab (CX-072; anti-PD-L1) In Advanced, HER2-non-Amplified Breast Cancer

Key Eligibility	Breast Cancer SubType	Endpoints
Ocular prophylaxis required **HR+/HER2 non-amplified** • 0 – 2 prior cytotoxics for advanced disease • Measurable disease required • No active corneal disease **TNBC** • CD166 High • ≥ 1 and ≤ 3 priors for advanced disease • Measurable disease required • Treated/stable brain metastases allowed • No active corneal disease • **Arm C exclusion criteria:** – PD-L1 negative/unknown – I/O refractory – History of or active autoimmune condition	**Arm A** HR+/HER2 non-amp (n~40*) CX-2009 **Arm B** TNBC (n~40*) CX-2009 **Arm C** TNBC (n~40*) CX-2009 + CX-072**	**Primary:** Overall Response Rate (ORR) by central review **Secondary**: ORR (Inv), PFS, DCR, CBR24, DoR, OS, Safety, PK, ADA **Exploratory:** Biomarker correlation with outcome

*Efficacy evaluable, ** Naing, A. et al. J Immunother Cancer 2021;9:e002447, Phase 1 Data: Boni V. et al. Clin Cancer Res. 2022 May 13;28(10):2020-2029.

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Phase 2 CX-2009 Results[1] Support Single-Agent Activity in HR+ BC

Seeking Partnership to Further Develop Program

Arm A – HR+/HER2-non-amplified breast cancer

- Confirmed ORR at 15% met primary efficacy endpoint
- 47 primary efficacy evaluable patients [2]
- 40% CBR24[3], clinical benefit rate at 24 weeks
- 2.6 months median progression-free survival (mPFS)
- All patients treated at initial Phase 2 starting dose of 7 mg/kg, Q3W
- 30% patients discontinued treatment for an adverse event
  - grade 3+ ocular and neuropathic toxicities 15% and 10%, respectively

Arm B – triple-negative breast cancer (TNBC)

- Did not pass futility boundary (ORR<10%); enrollment discontinued
- Evaluated 7 mg/kg and 6 mg/kg starting doses
- Toxicity profile of 7 mg/kg starting dose consistent with Arm A
- No patients discontinued treatment for an AE in 6 mg/kg cohort
  - 3% Grade 3+ ocular and neuropathic events 3% and 0%, respectively

- mPFS does not support further evaluation at 7 mg/kg
- Encouraged by the emerging safety profile of 6 mg/kg
- Data update to be presented at San Antonio Breast Cancer Symposium in December 2022

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(1) As of the data cutoff on May 13, 2022; (2) Unselected for CD166 expression; (3) Per protocol, any response (confirmed or unconfirmed) or stable disease for 24 weeks

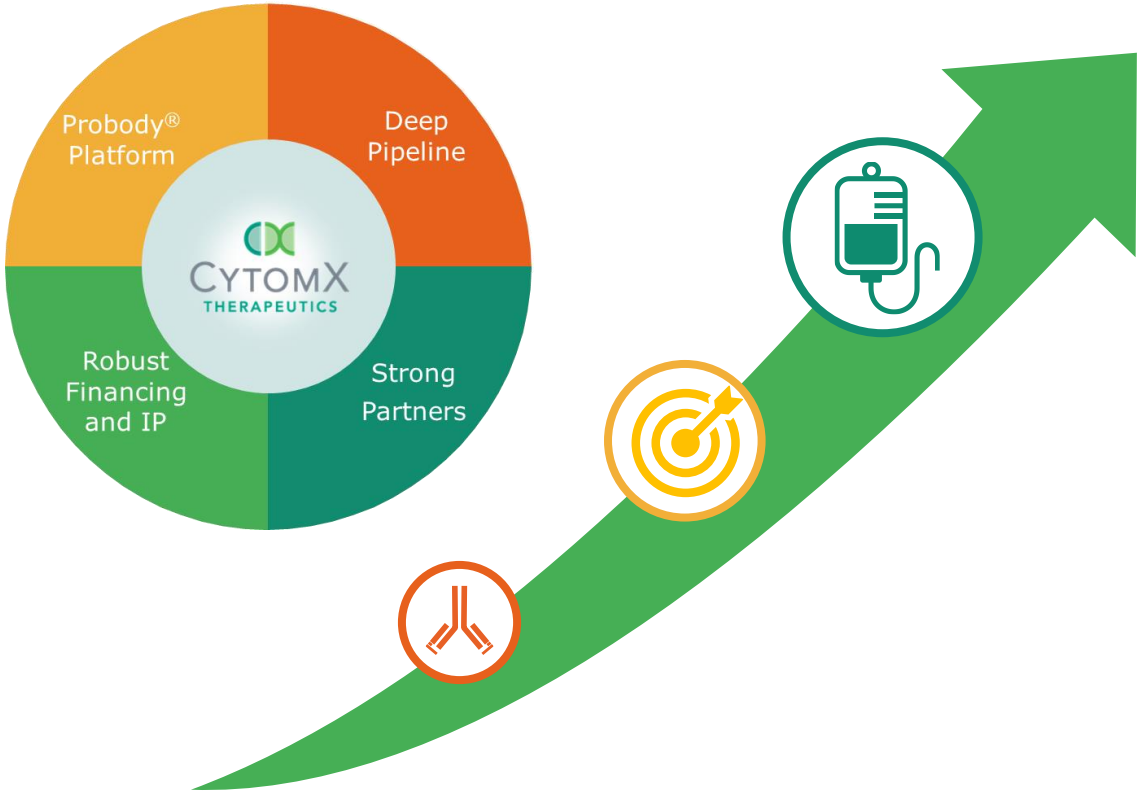
Summary and Milestones

Leading Platform, Deep Pipeline, Broad Clinical Experience

7 Therapeutic Candidates, 3 in Phase 2 Studies Across Multiple Cancer Types

Modality	Product Candidate	Target-Payload	Indication	Preclinical / Phase 1 / Phase 2	Commercial Rights/Partner
Antibody-Drug Conjugate	CX-2029	CD71-MMAE	SqNSCLC, Esophageal/ GEJ		CytomX, abbvie
	CX-2051	EpCAM	Solid tumors		CytomX
	Praluzatamab ravtansine (CX-2009)	CD166-DM4	HR+/HER2-non-amp BC		CytomX
Immuno-Oncology	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	
	CX-801	IFN alpha-2b	TBD		CytomX
TCB	CX-904	EGFRxCD3	Solid tumors		CytomX, AMGEN
	Various	Undisclosed	TBD		CytomX, astellas

Continued Leadership and Innovation in 2022 / 2023



2022 / 2023 Priorities

- Data update for CX-2029 in sqNSCLC in Q4 2022
- Updated data for praluzatamab ravtansine in advanced BC in Q4 2022
- Continue patient enrollment in CX-904 Phase 1 study
- Submit INDs for CX-801 and CX-2051 in 2H 2023
- Ongoing progress with BMS-986249