CytomX Therapeutics

Destroying Cancer. Differently.

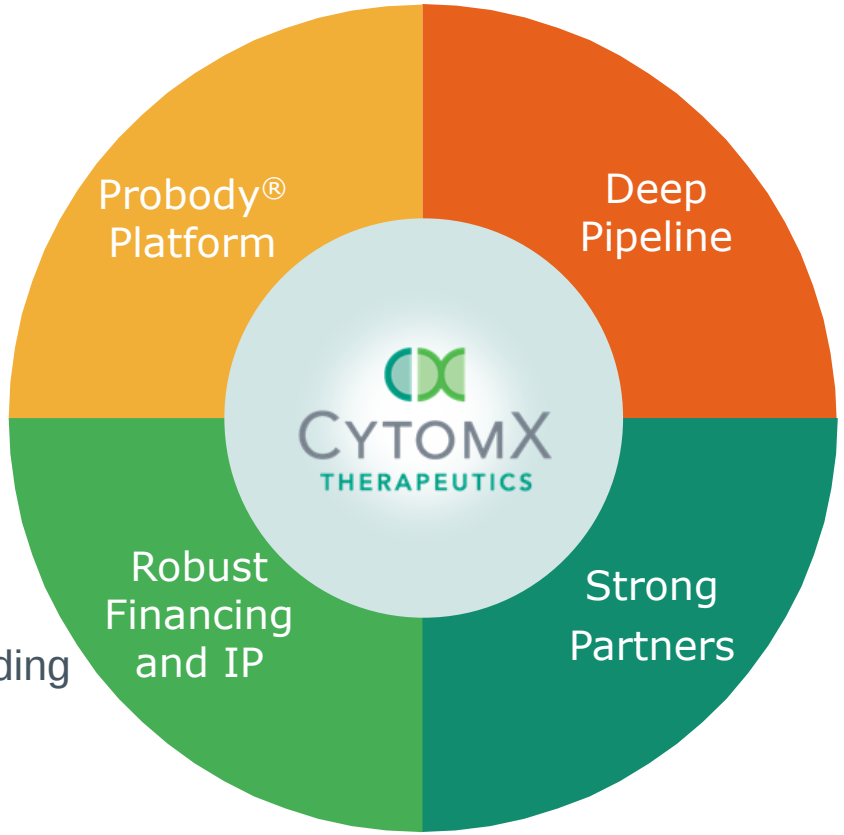
Forward-Looking Statements

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.

This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). No representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Integrated Business Model for Long-Term Value Creation

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



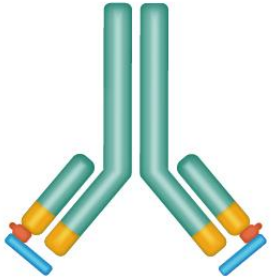
- Robust & diverse portfolio
- Phase 2 assets across multiple cancer types
- 2 new INDs expected in 2023

- Strong balance sheet
- $228M end Q2 2022
- >550 issued and pending patents worldwide

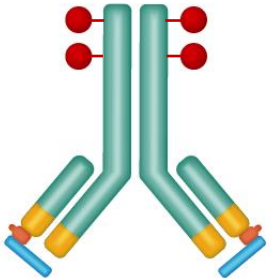
- 4 global partnerships
- 3 partnered programs in clinic

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

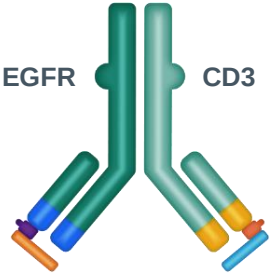
Antibodies



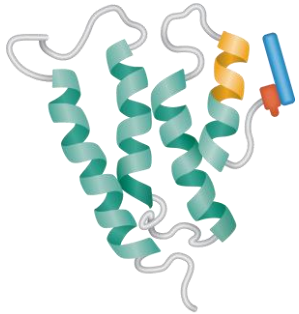
Antibody-Drug Conjugates



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

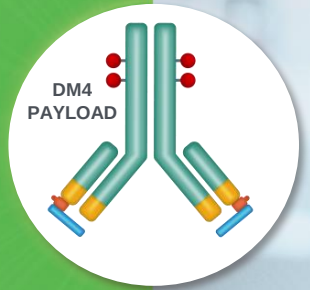
CytomX THERAPEUTICS

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



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.

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

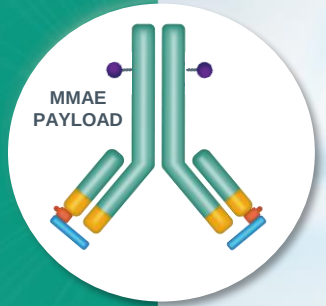
Arm B – triple-negative breast cancer (TNBC)

- 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

(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

CytomX Therapeutics



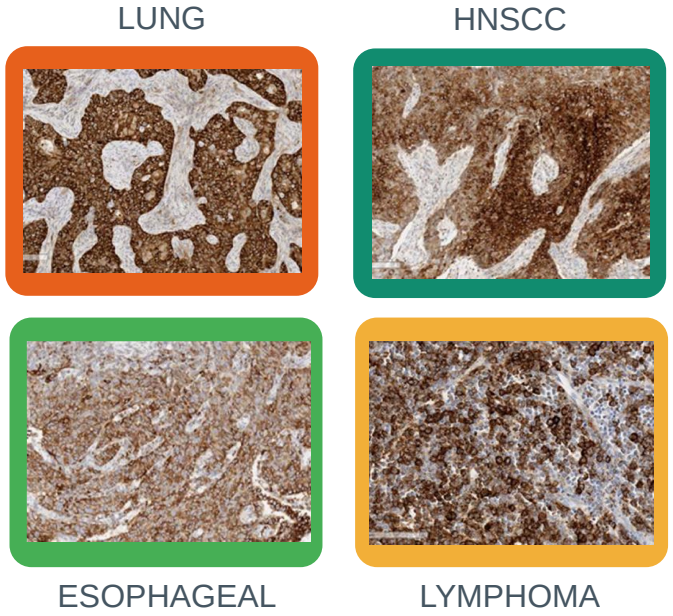
CX-2029

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

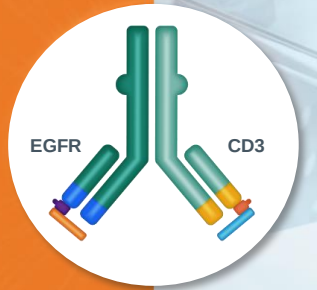
Emerging Opportunity for CX-2029 in 3L+ SqNSCLC

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

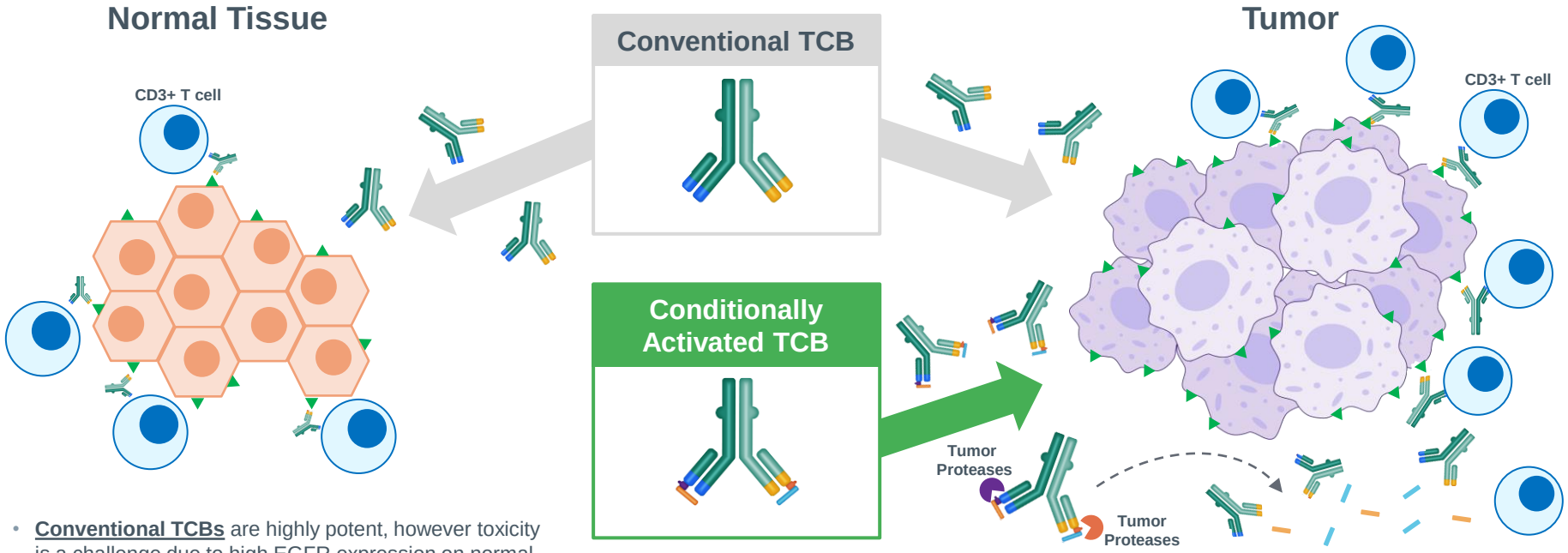
CytomX Therapeutics



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

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

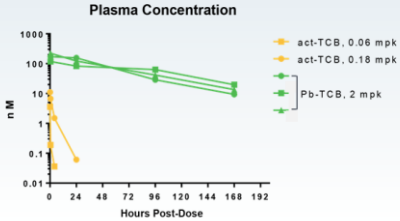
TCB*	Dose (mg/kg)	Clinical Observations
Act-TCB	0.06 *(MTD)*	Moderate
Act-TCB	0.18	Severe
Pb-TCB	0.6	None
Pb-TCB	2.0	Mild
Pb-TCB	4.0 *(MTD)*	Moderate

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

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

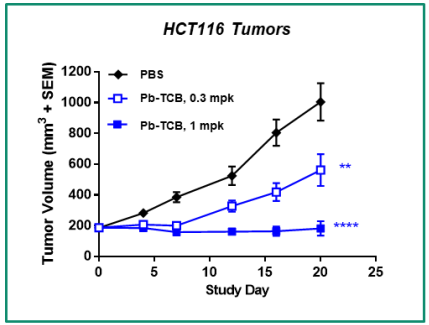
Extends PK

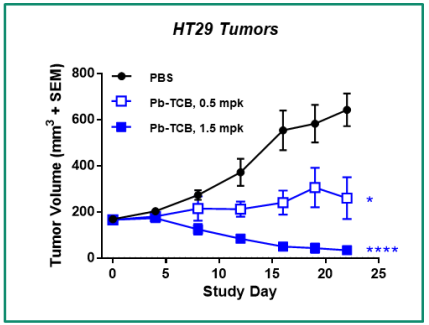
Plasma Concentration



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

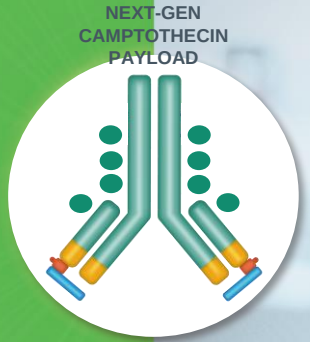
Objectives/Endpoints

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

CytomX Therapeutics

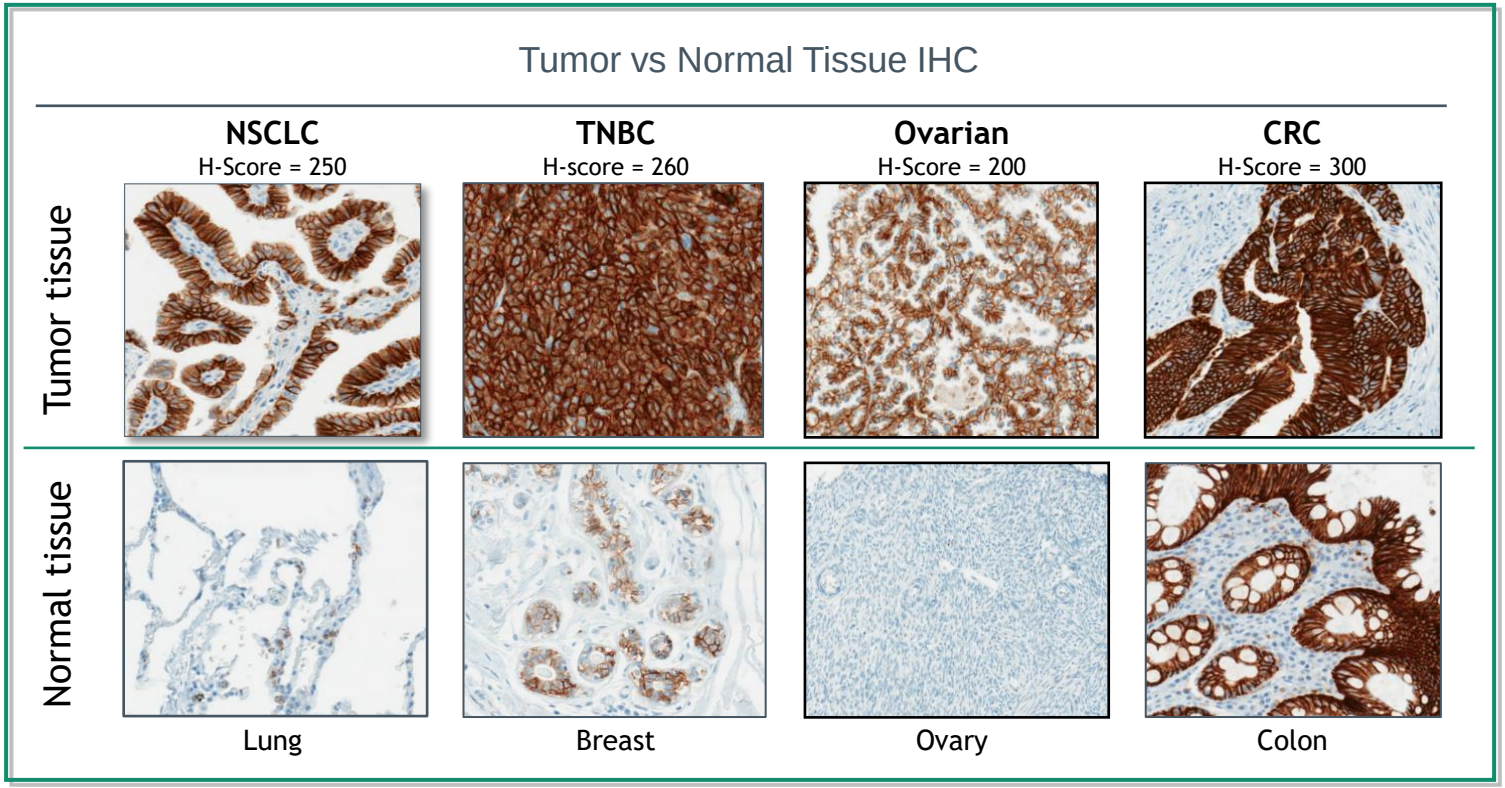


CX-2051

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

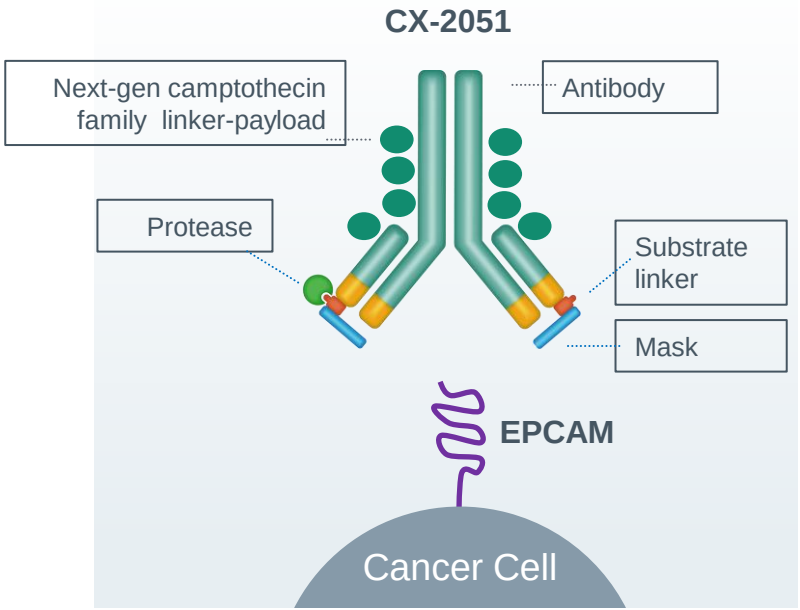
- Vicineum fusion protein: anti-EpCAM scFv linked to a truncated form of Pseudomonas exotoxin A
- Delivered by intravesical administration
- Phase 3 in bladder cancer

Sesen Bio

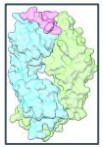
Systemic EpCAM therapies have demonstrated clinical toxicity

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

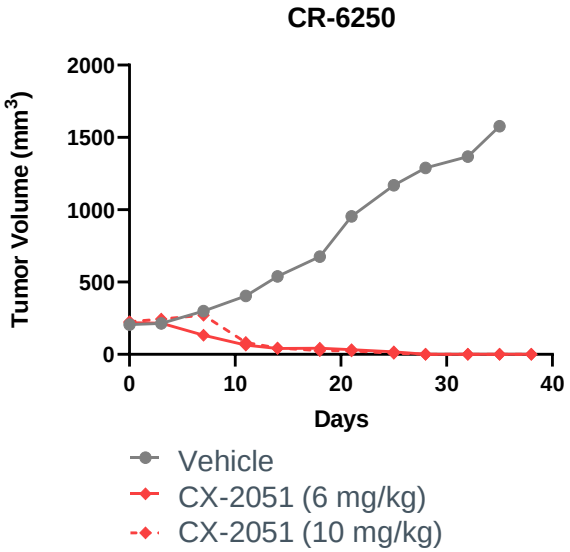


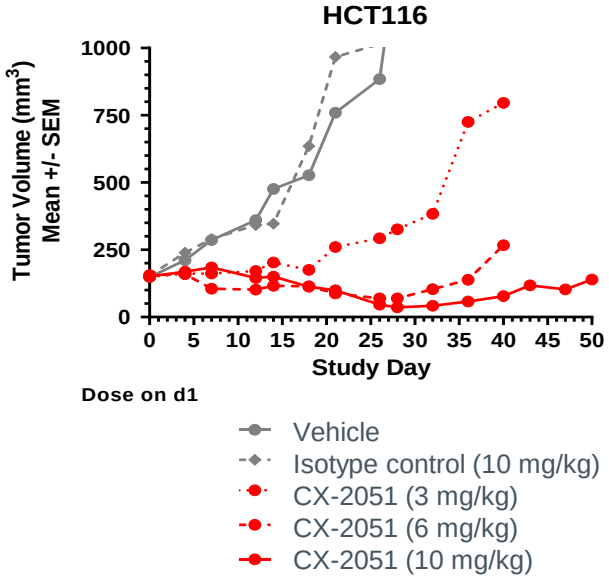
- Anti-EpCAM MAb with cross-reactivity to cynomolgus monkey
- Probody peptide mask with >60X masking efficiency (by ELISA)
- Protease-cleavable substrate with broad cleavability profile across multiple tumor types
- Next-gen camptothecin linker-payload (licensed from Immunogen)
- Optimized linker drives 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





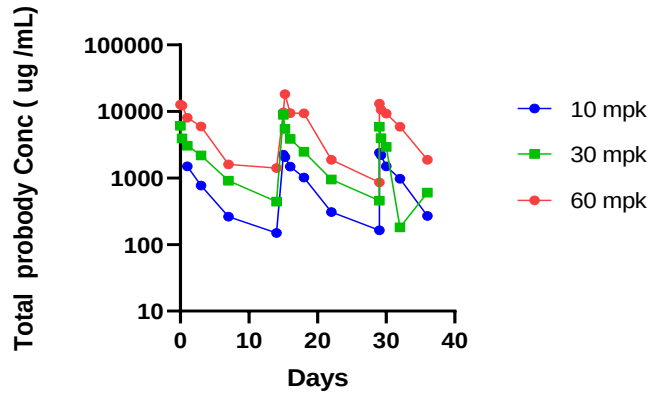
PDX: Patient derived xenograft; CDX: Cell derived xenograft
CR-6250 and HCT116: Colorectal cancer models

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)

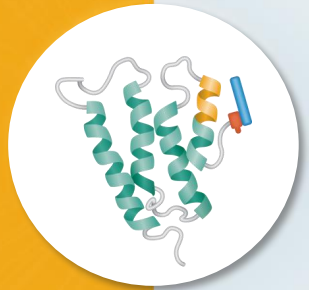
Dosing	CX-2051	Isotype
10 mg/kg	Tolerated (2/2)	
30 mg/kg	Tolerated (2/2)	
60 mg/kg	Tolerated (3/3)	Tolerated (2/2)
90 mg/kg	Not Tolerated (1/2)	

- 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

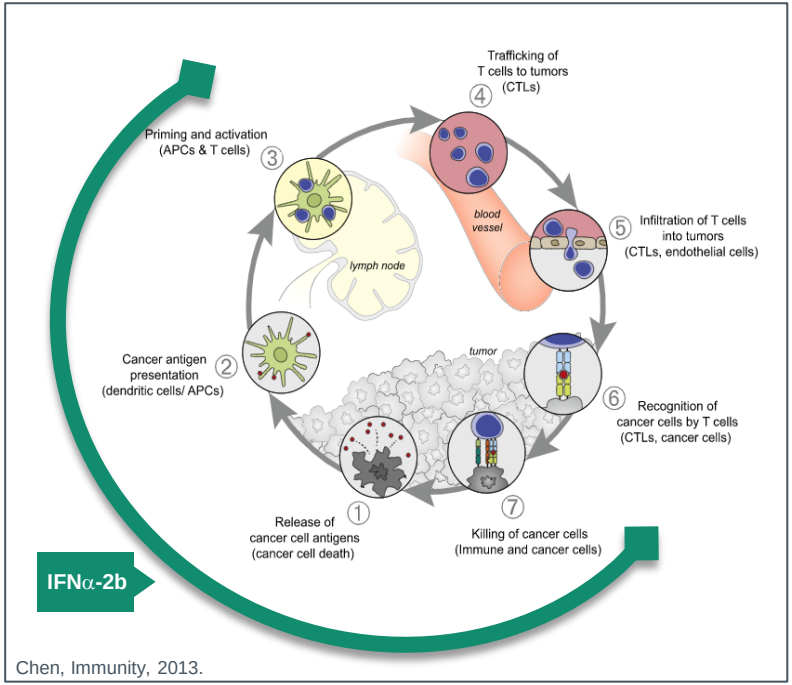
Conditionally Activated Interferon Alpha-2b

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**



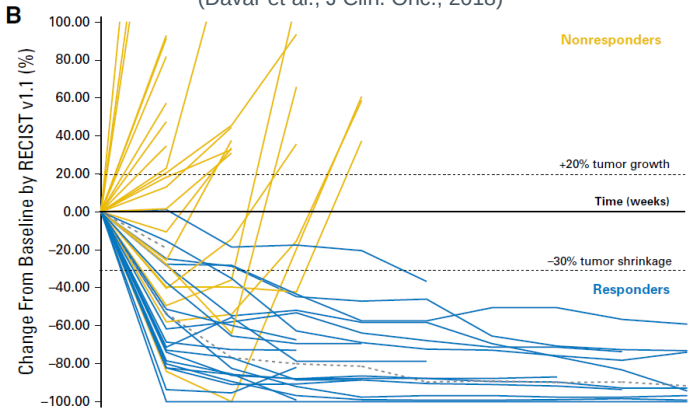
Chen, Immunity, 2013.

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)

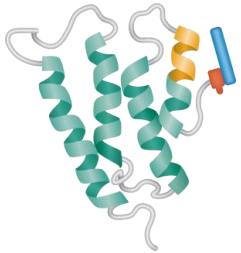


- **Potent activity (60.5% ORR)**
- **Significant, dose limiting adverse events (49% Grade 3/4 AEs)**

CX-801 (Probody Interferon-α2b)

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

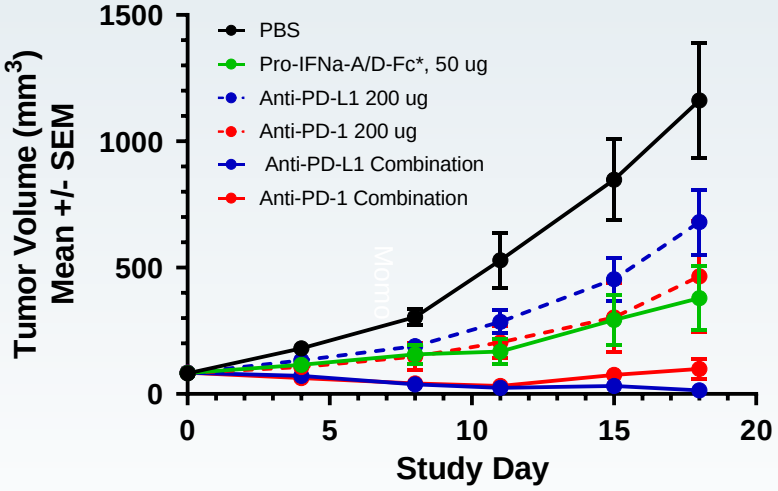
Advantages of CX-801



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

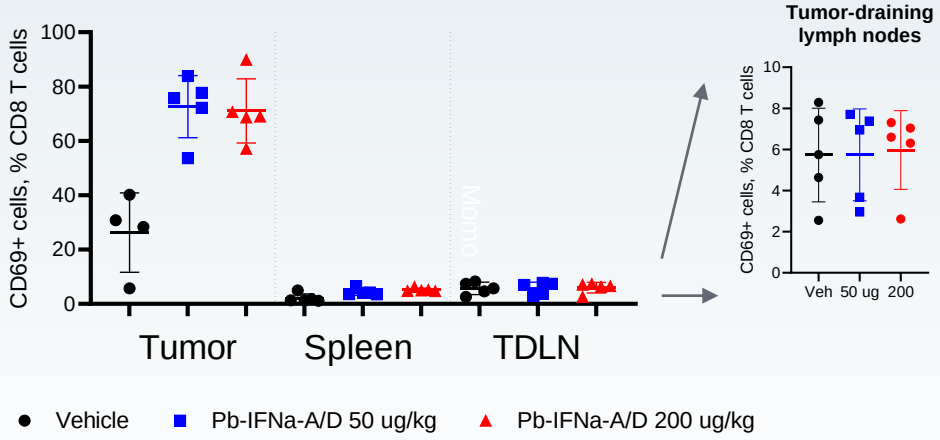
Combination of Dual Masked IFN-αA/D-Fc* and anti-PD-(L)1 Induces Substantially Enhanced Efficacy in MC38 Tumor Model

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

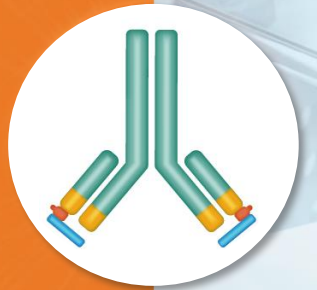
Dosing (μg/m²) (15 x Q2D)	Dosing (mpk) (15 x Q2D)	Dosing (mpk/w)	Peginterferon (SQ)
1414	0.1 mpk	0.35	Tolerated (6/6)
4329	0.3 mpk	1.05	Tolerated (6/6)
14126	1 mpk	3.5	Not Tolerated (5/6)

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

CytomX Therapeutics



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

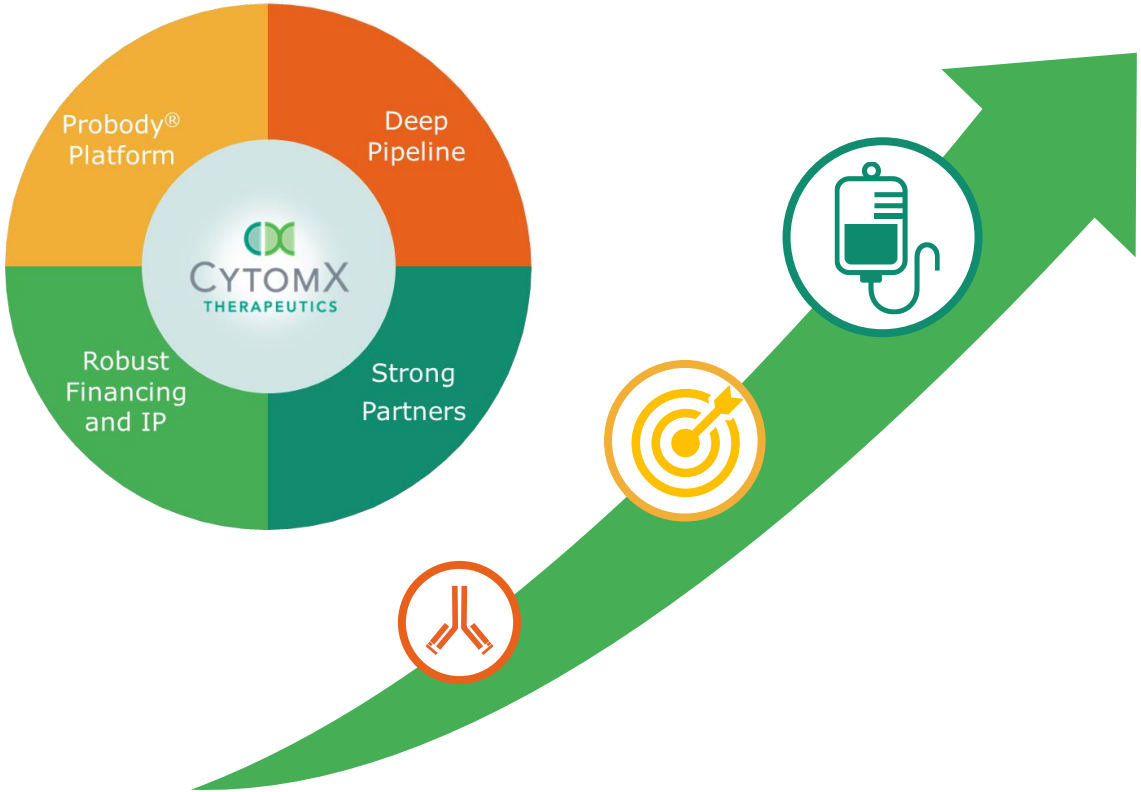
Summary and Milestones

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