



Leading the Field of Localized Biologic Therapies

November 2023

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 COVID-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 localized
biologic therapies

Multi-Modality
Platform

**Probody®
Platform**

**Deep
Pipeline**

3 Clinical-stage assets

2 INDs expected in Q4 2023

\$194M Cash as
of Q3 2023

Broad IP
portfolio

**Robust
Financing
and IP**

**Strong
Partners**

5 major partnerships

2 molecules in the clinic



 Bristol Myers Squibb™

AMGEN

 astellas

REGENERON

moderna

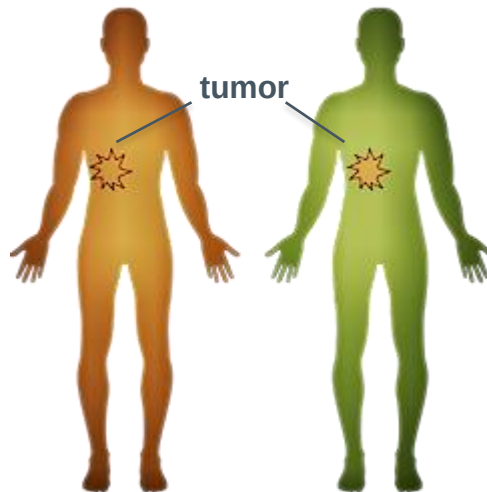
The Promise of Conditionally Active, Localized Biologic Therapies

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**

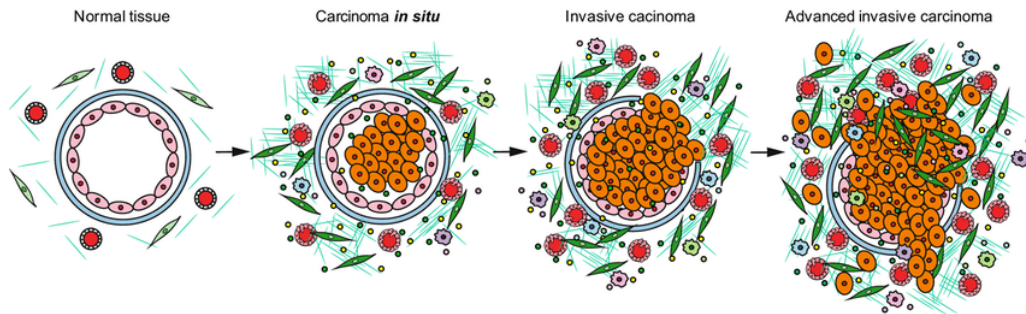


Active Antibody



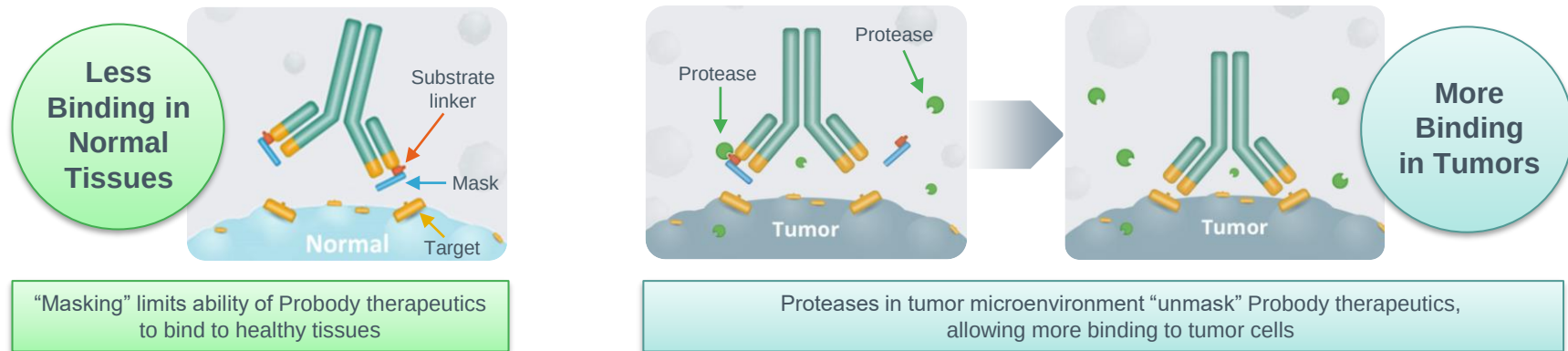
Masked Probody Tx

The Probody[®] Therapeutic Platform – Exploiting Cancer’s Achilles’ Heel



Adapted from Santi et al., Proteomics 2018

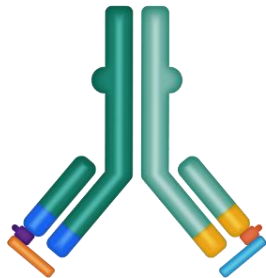
Upregulated protease activity is a hallmark of cancer



Leading Platform for Localized Biologic Therapies

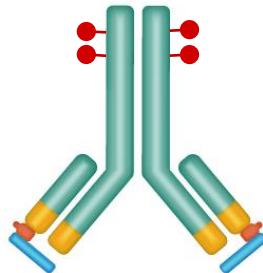
Addressing Major Challenges in Today's Cancer R&D Landscape

T-Cell Bispecifics



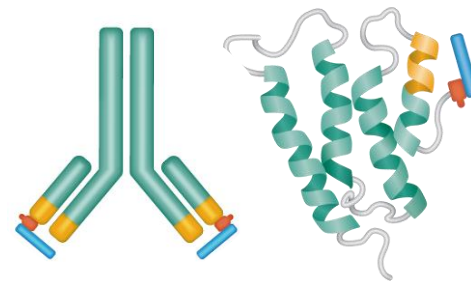
Localizing T-cell engaging bispecifics to attack solid tumors

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

Broad, Multi-Modality Probody® Pipeline

Economics	Product Candidate	Target	Indication	Preclinical	Phase 1	Phase 2	Partner
Wholly-Owned or Retained US Rights*	CX-904	EGFRxCD3	EGFR+ Solid tumors				 
	CX-2051	EpCAM/Trop-1	EpCAM+ Solid tumors		IND expected Q4 2023		
	CX-801	IFN-α2b	Solid Tumors		IND expected Q4 2023		
	Probody TCBs	Undisclosed	TBD				 
Fully Partnered**	BMS-986288	CTLA-4 (a-fucosylated)	Solid tumors	 +/- nivolumab			
	Probody TCBs	Undisclosed	TBD				  
	Various	Undisclosed	TBD				
	mRNA	Undisclosed	Oncology & Non-oncology				



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

** Milestone payments and royalties payable to CytomX

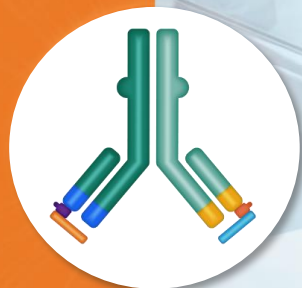
Company Priorities and Milestones in 2023 and 2024



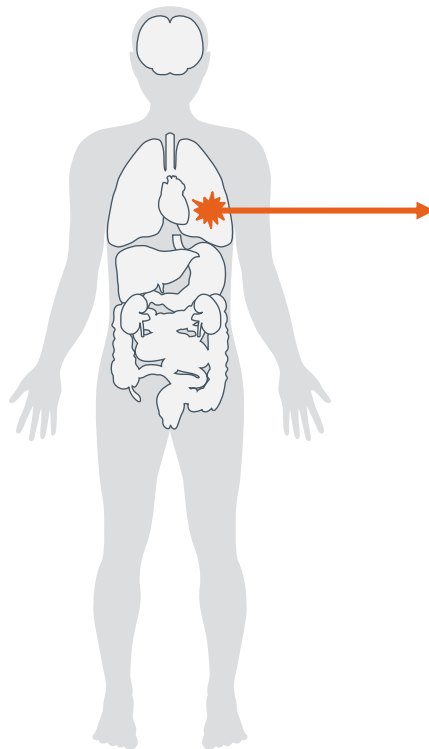
- **CX-904 (EGFRxCD3):**
 - **2023:** Continue Phase 1a dose escalation
 - **2024:** Phase 1a dose escalation data in 1st half of 2024; Potential decision to initiate Phase 1b expansion
- **CX-2051 (EpCAM):** File IND by the end of 2023 and begin Phase 1 dose escalation in 2024
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- **BMS CTLA-4:** Continued clinical progress for BMS-986288 including proof-of-concept studies in MSS CRC and NSCLC. BMS anticipates data from the study will be available in 2024.
- **Collaborations:** Continuation of drug discovery activities with Bristol Myers Squibb, Amgen, Astellas, Regeneron, and Moderna



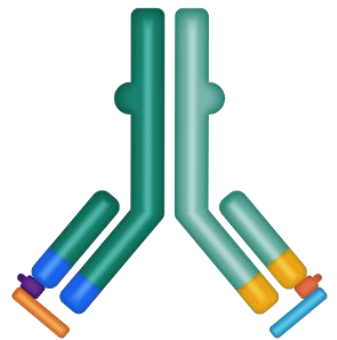
CX-904 (EGFRxCD3 T-cell Bispecific)



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 malignancies^{1,2}
 - EGFR plays a crucial role in cancer, and is one of the most frequently altered oncogenes in solid tumors¹
 - 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

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

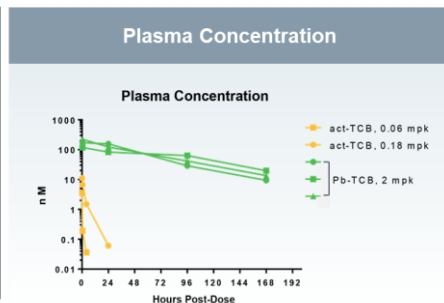
Increases MTD

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

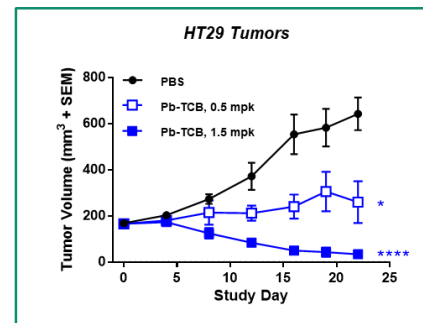
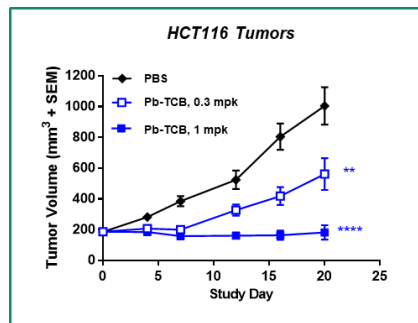
MTD increases by >60-fold with conditionally activated TCB (Pb-TCB)

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

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

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

Progress to-date

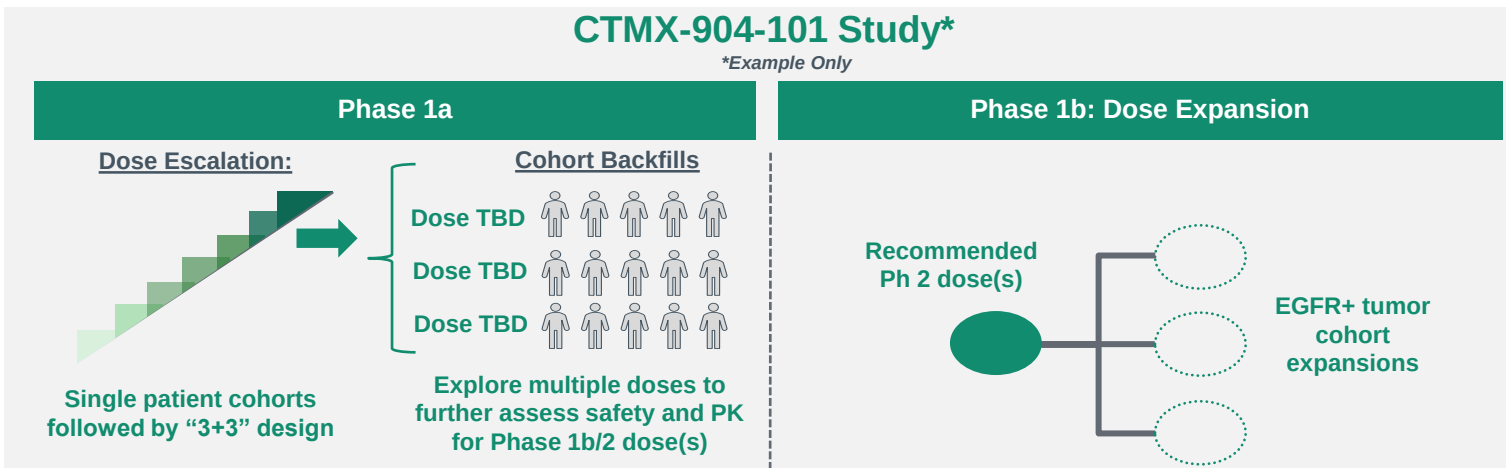
- ✓ First Patient Dosed in May 2022
- ✓ Advanced through single patient cohorts
- ✓ 3+3 Dose Escalation Ongoing
- ✓ Backfilling of certain dose escalation cohorts initiated in Q4 2023

Focus Areas

- Continue Phase 1 dose escalation
- Robust biomarker and translational science effort to optimize patient selection strategies
- Initial Phase 1a Dose Escalation Data anticipated in 1H 2024
- Decision to initiate Phase 1b expansion cohorts in certain EGFR positive tumor types anticipated in 2024

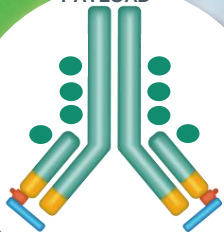
CTMX-904-101 Study*

**Example Only*





NEXT-GEN
CAMPTOTHECIN
PAYLOAD



CX-2051: EpCAM ADC

First-in-Class Conditionally Activated ADC With Next Generation Camptothecin Analog Linker-Payload



Antibody Drug Conjugates Have Emerged as a Growing and Potent Modality in Both Solid and Liquid Tumors

Approved Solid Tumor ADCs

tivdak
tisotumab vedotin-tftv
for injection 40 mg

TF1

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

HER2

TRODELVY
sacituzumab govitecan-hziy
180 mg for injection

TROP2

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

HER2

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

Nectin4

ELAHERE
mirvetuximab soravtansine-gynx
injection 100 mg

FR α

Approved Liquid Tumor ADCs

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

CD79b

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

CD19

ADCETRIS
brentuximab vedotin | injection 50 mg

CD30

BESPONSA
inotuzumab ozogamicin INJECTION
0.9 mg single-dose vial

CD22

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

CD33

Targeting EpCAM with CX-2051

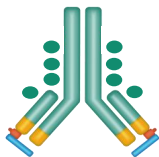
A conditionally activated ADC with a next-gen camptothecin analog linker-payload



ADC target options are limited by normal tissue expression. Conditional activation can allow ADC technology to be applied to a wider set of targets.



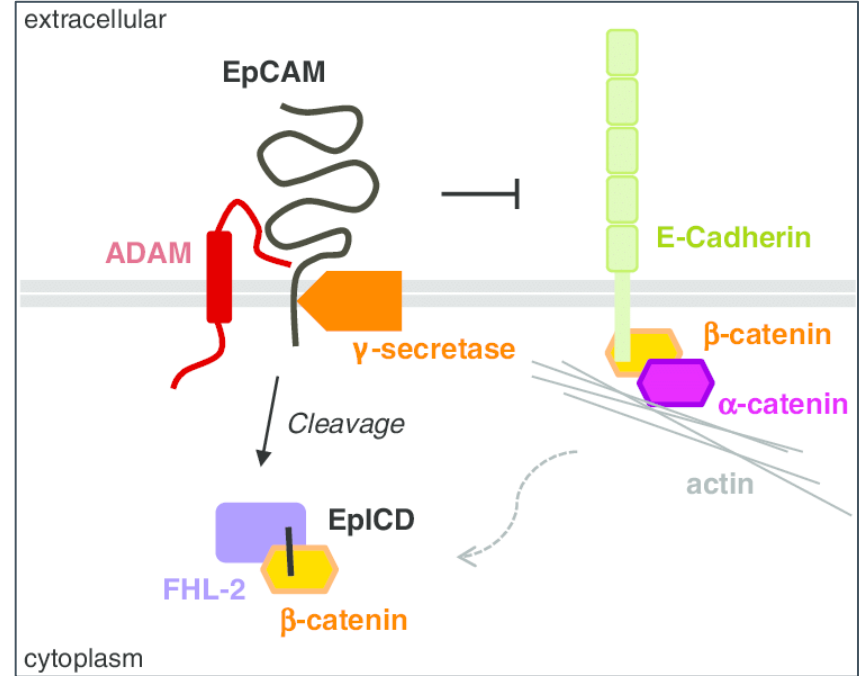
Conditional activation using Probody[®] Therapeutic technology restricts molecular activity to the site of the tumor.



CX-2051 uses Probody[®] technology to direct an ADC to one of the most promising cancer targets, EpCAM

EpCAM (Epithelial Cell Adhesion Molecule / Trop1) is an Attractive ADC Target

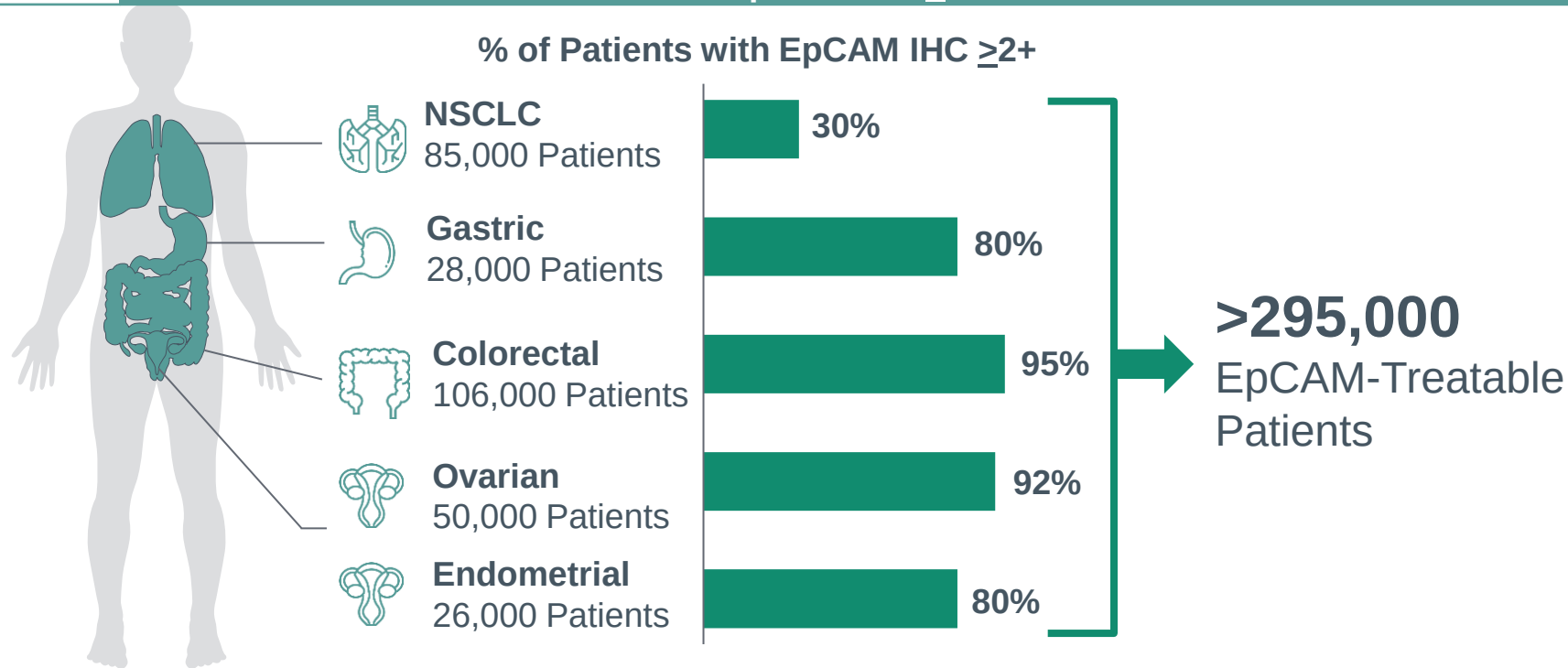
- **Highly expressed on cancer cells**
 - Overexpressed in multiple cancer indications
 - Expressed in both adeno and squamous histologies
- **Functional role in cancer signaling**
 - Internalizes and binds to β -catenin
 - Upregulates c-myc, cyclins
- **Expressed on circulating tumor cells**
 - Associated with cancer stem / progenitor cells



Broad Opportunity Across Multiple Indications



2023 US Metastatic, Drug-Treatable Patients EpCAM IHC $\geq 2+$



EpCAM Has Been Clinically Validated But Not As a Systemic Therapy

Locally administered EpCAM therapies have been validated in the clinic

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

Insys Therapeutics

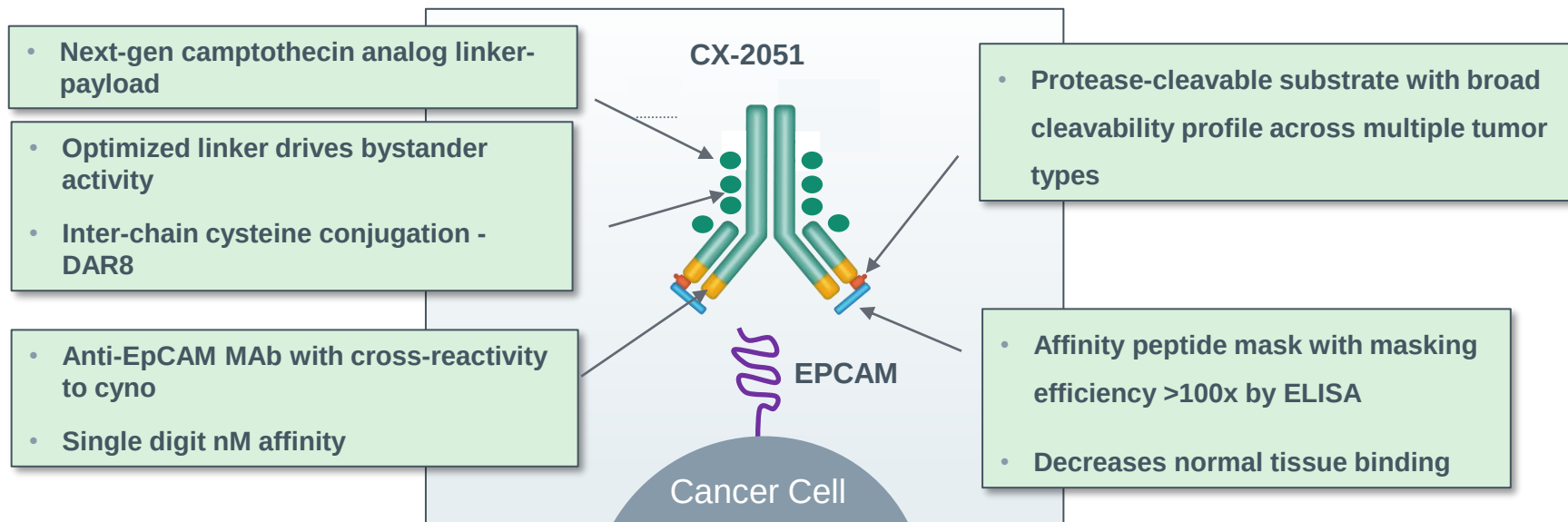
- **Vicineum fusion protein:** anti-EpCAM scFv linked to a truncated form of Pseudomonas exotoxin A
- Delivered by intravesical administration
- ~40% 3-month complete response in bladder cancer

Sesen Bio

Systemic EpCAM approaches have significant toxicity concerns

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

CX-2051: EpCAM Probody[®] ADC with Next Generation Camptothecin Analog Linker-Payload

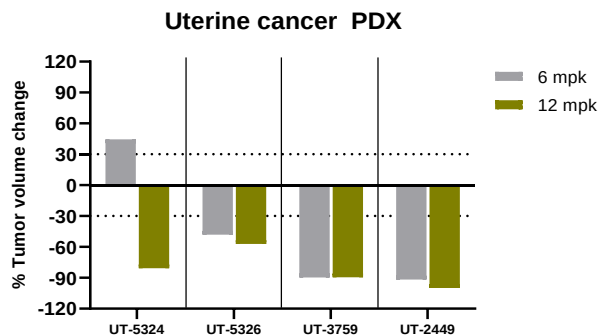
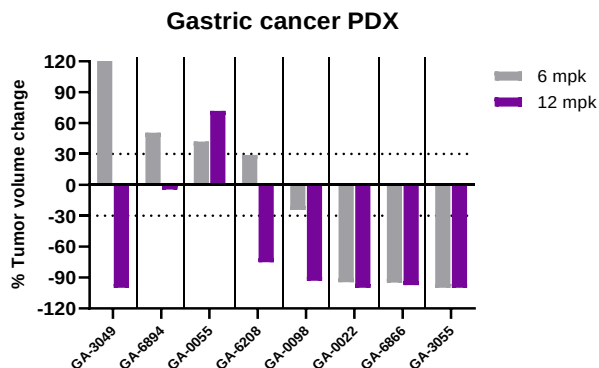
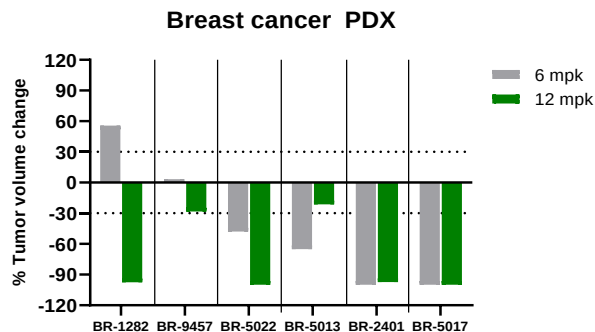
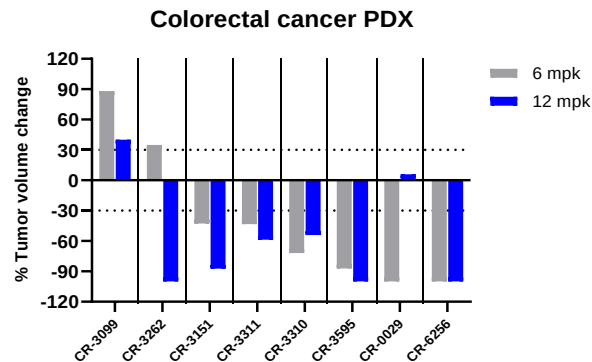


CX-2051 is a conditionally activated EpCAM ADC designed to be active preferentially in the tumor microenvironment with limited activity in normal tissues

Program licensed from

immunogen

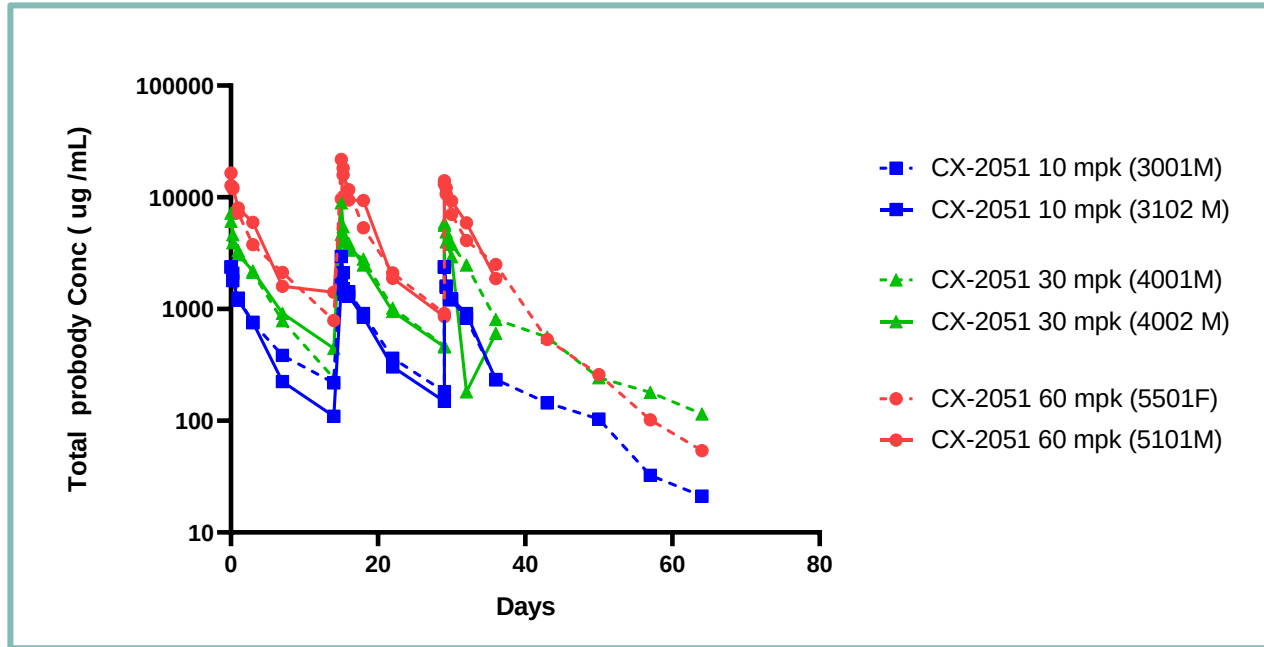
CX-2051 Shows Broad Preclinical Activity Across Multiple Tumor Types



- High percentage of deep regressions across multiple PDX tumor models
- High percentage of regressions even at lower doses

CX-2051 Shows Dose Proportional Pharmacokinetics in Non-Human Primates

Pharmacokinetic Profile of CX-2051 in Cyno



- Exposure is maintained after each dose (Q2Wx3)

CX-2051 Is Tolerated in Non-Human Primates at >6x Unmasked EpCAM ADC

Tolerability of CX-2051 in Cyno Pilot Tox Study

Dosing (3 x Q2W)	CX-2051 (Masked)	CX-2052 (Unmasked)
10 mpk	Tolerated	Not tolerated
30 mpk	Tolerated	
60 mpk	Tolerated	
90 mpk	Not Tolerated	

CX-2052: Unmasked EpCAM-ADC
CX-2051: Masked EpCAM-ADC

- CX-2051 Shows Substantially Improved Safety Profile Over Unmasked ADC

CX-2051 Can Address High Unmet Need in Metastatic CRC



**Broad Opportunity for
Topo I Based ADCs in CRC**

1L

FOLFOX (folinic acid, fluorouracil,
oxaliplatin) / FOLFIRI (folinic acid,
fluorouracil, **irinotecan**)

+

bevacizumab / cetuximab / panitumumab

53 – 65% ORR
24 – 30 mo. OS

2L

FOLFIRI / FOLFOX

+/-

bevacizumab / aflibercept / ramucirumab /
cetuximab / panitumumab

13 – 22% ORR
10 – 14 mo. OS

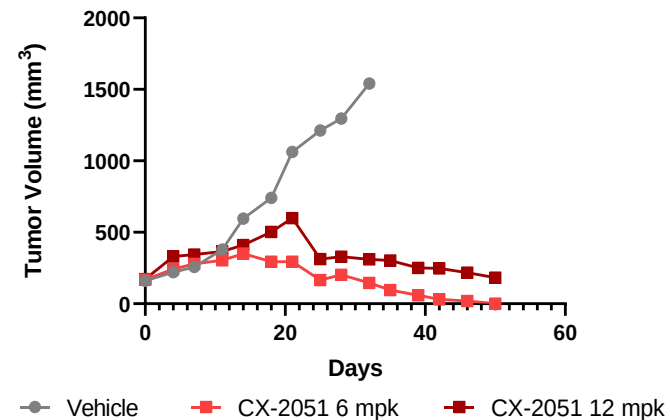
3L

regorafenib / trifluridine & tipiracil +/-
bevacizumab

1 – 6% ORR
6 – 10 mo. OS

**Strong preclinical anti-tumor activity
even in irinotecan resistant setting**

CRC PDX Model (CR-0029)
(Irinotecan resistant model)



CX-2051

Tailoring the target, payload, and tumor type maximizes the potential therapeutic index

1

CX-2051 demonstrates strong preclinical activity and tolerability, with a favorable predicted therapeutic index

- Next-gen camptothecin payload with linker optimized for bystander effect
- CX-2051 design builds upon CytomX's prior experience with masked ADCs

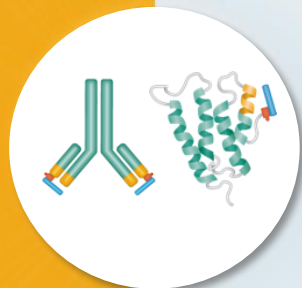


Clear Therapeutic Applications

- EpCam expression and tecan sensitive tumors provide path forward

2023

CX-2051 IND anticipated by the end of 2023 with clinical initiation in 2024



Probody[®] Immunotherapies

- **CX-801**: Conditionally Activated IFN α -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

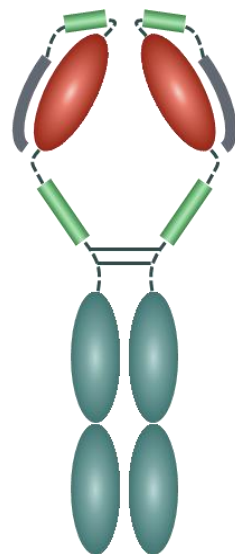
Cytokines and Cytokine Therapeutics

- 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

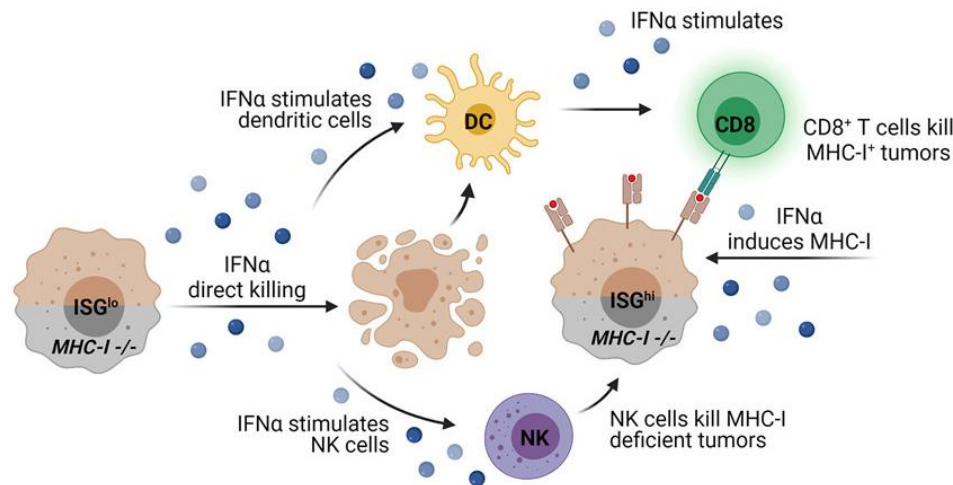


IFN α -2b is a Powerful Mediator of Immune Activation with Ideal Properties for Cancer Immunotherapy

Why IFN α -2b?

Mechanism of Action

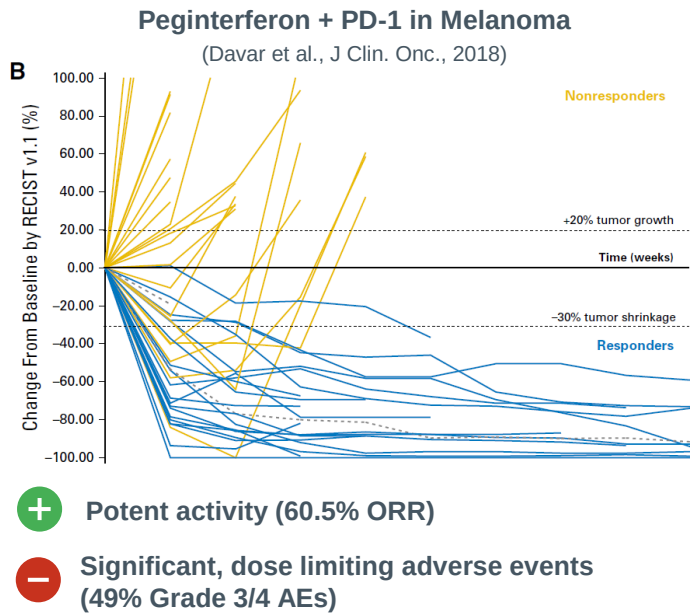
- IFN α -2b provides an **orthogonal activity to IL-12, IL-2 and IL-15** in the cancer immunity cycle
 - IFN α -2b can **kill cancer cells directly** leading to immunogenic cell death, and
 - IFN α -2b **stimulates antigen presenting cells to activate T cells** – *distinct from IL-2, IL-12, and IL-15 that are restricted to proliferative effects via IFN γ*
- Potential to **unlock classically CPI-resistant indications**



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

IFN- α 2b is an approved immunotherapeutic therapy that has shown efficacy as a single agent and in combination with PD-1, but has been limited due to toxicity

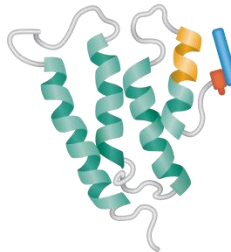
IFN- α 2b - Significant Unmet Need



CX-801 (Probody Interferon- α 2b)

Potentially Best-in-Class
Conditionally-Activated IFN- α 2b

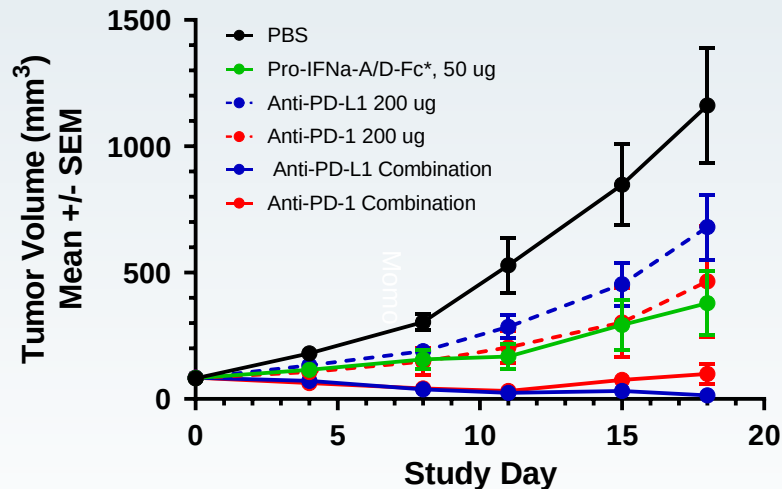
Advantages of CX-801



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

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

Efficacy

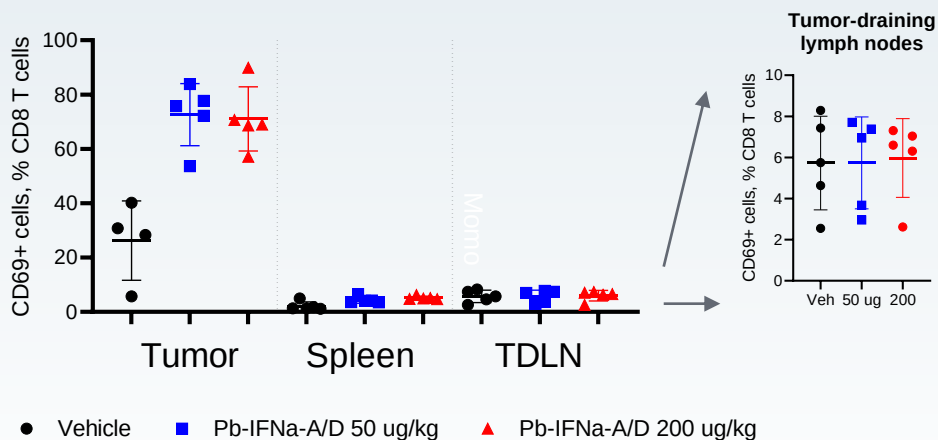


Doses

PBS, ProC1023: d0, d4, d8, d11, d15

Anti-PD-L1, Anti-PD-1: d0,d8, d15

Pharmacodynamic Activity is Restricted to Tumors



Probody[®] IFN- α 2b (CX-801) has Significantly Improved Tolerability Compared to Unmasked Interferon in Non-Human Primates

Protection in multi-dose tolerability study is $\geq 30x$

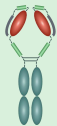
Historical Peginterferon Data

Dosing ($\mu\text{g}/\text{m}^2$) (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

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

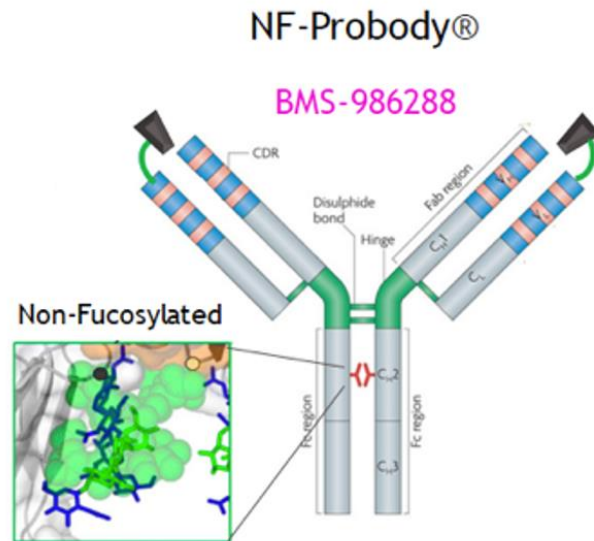
2023

CX-801 IND anticipated by the end of 2023 with clinical initiation in 2024

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 and includes proof-of-concept studies in MSS CRC and NSCLC
- Designed to enhance CD16 binding and increase APC-mediated T cell priming



Non-Fucosylated Probody®
with increased CD16 affinity

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