CytomX Therapeutics

Conditionally Activated Therapeutics

for the treatment of cancer

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, inability to obtain and costs of obtaining 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.

Company Snapshot

Clinical-Stage Oncology Focused Biopharma Company

Conditionally Activated Therapeutics

- Innovative targeting strategy
- Leverages tumor microenvironment
- Opens previously undruggable target space

Key Milestones

- CX-2029 initial Phase 2 expansion cohort data
- IND filing for CX-904
- CX-2009 initial Phase 2 data in breast cancer

Foundational Partnerships

- AbbVie, Amgen, Astellas & BMS
- Retained certain US rights

Strong Balance Sheet

- $336M cash at end of Q3 2021
- No debt

Experienced Leadership

Sean A. McCarthy, D. Phil.
President, Chief Executive Officer and Chairman
>20 years of experience in biotech with roles in R&D, business development, financing and general management

Amy C. Peterson, M.D.
EVP, Chief Development Officer
>15 years of leadership experience in oncology drug development

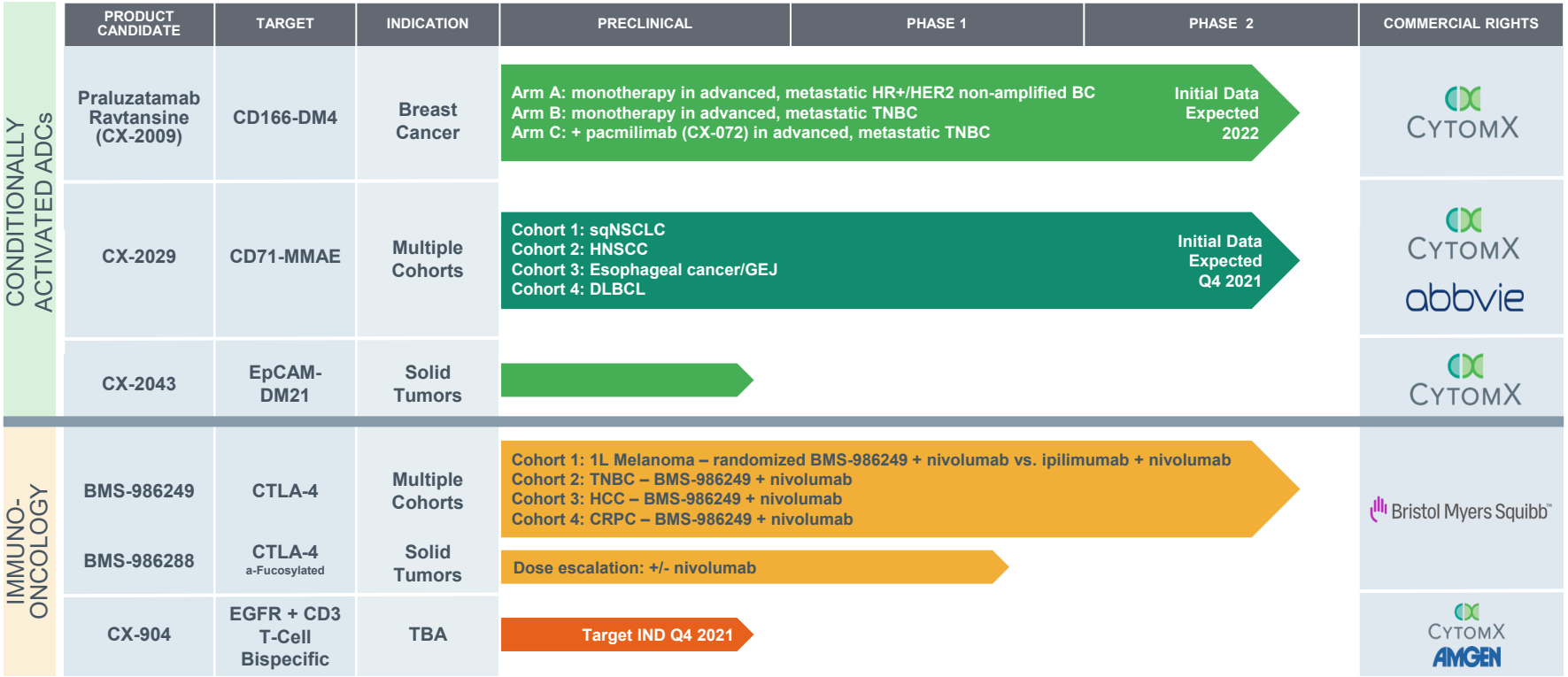
Alison L. Hannah, M.D.
SVP, Chief Medical Officer
>30 years of experience in investigational cancer therapy development

Carlos Campoy
SVP, Chief Financial Officer
>30 years of financial and leadership experience, mostly with publicly-held healthcare and biopharmaceutical companies

Marcia P. Belvin, Ph.D.
SVP, Head of Research
>20 years of experience in preclinical pipeline discovery and development in oncology

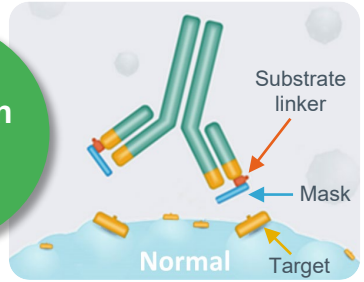
CytomX Therapeutics

Broad Clinical and Preclinical Pipeline with Multiple Phase 2 Readouts 2021+

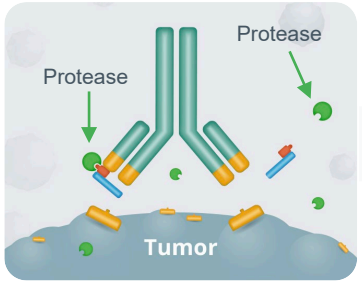


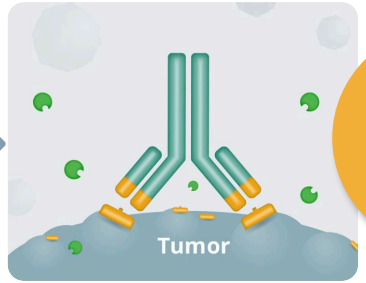
The Probody® Therapeutic Platform:
Multiple Modalities of Conditionally Activated Therapeutics

Less Binding in Normal Tissues



"Masking" limits ability of conditionally activated antibody to bind to healthy tissues

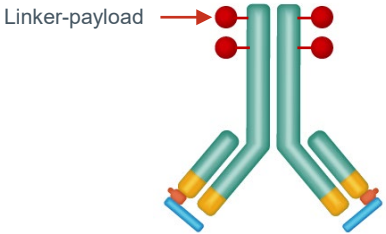




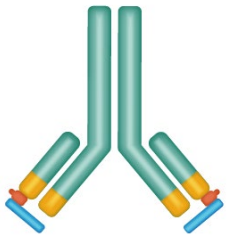
More Binding in Tumors

Proteases in tumor microenvironment "unmask" conditionally activated antibody, allowing more binding to tumor cells

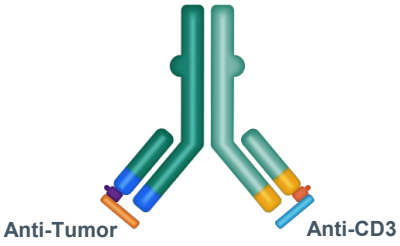
Antibody-Drug Conjugate



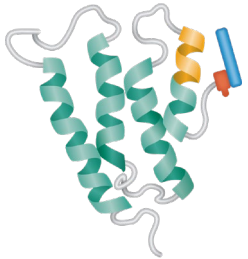
Immune Modulator/ Checkpoint Inhibitor



T-Cell Bispecific



Cytokine



Antibody-Drug Conjugates for Cancer are a Major Opportunity

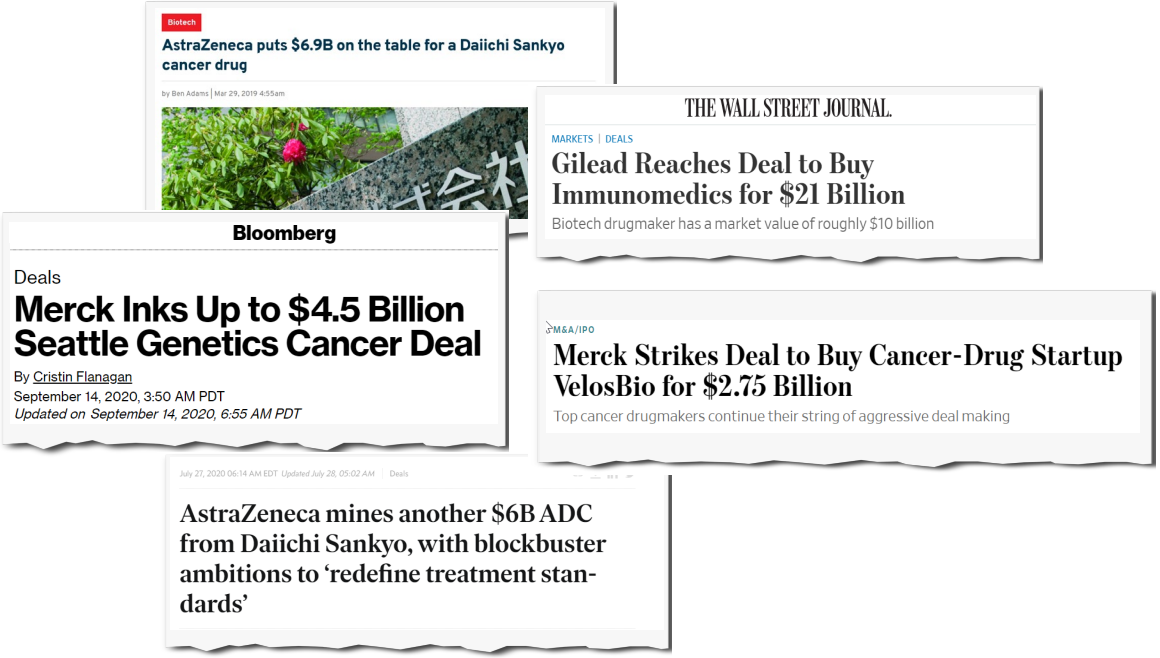
Recent Approvals and Transactions Underscore High Potential of Class

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

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

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

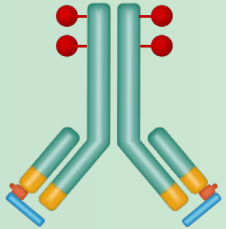
TRODELVY™
sacituzumab govitecan-hziy
180 mg for injection



Conditionally Activated ADCs Expand ADC Target Landscape

Antibody-drug conjugates

Limited druggable space for conventional ADCs



CytomX Conditionally Activated ADCs

Broad opportunity for new first-in-class therapies

Convert undruggable target to druggable target by opening therapeutic window

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Praluzatamab Ravtansine (CX-2009)

Anti-CD166 Conditionally Activated ADC for HER2 non-Amplified Breast Cancer

Substantial Unmet Need Remains in Breast Cancer

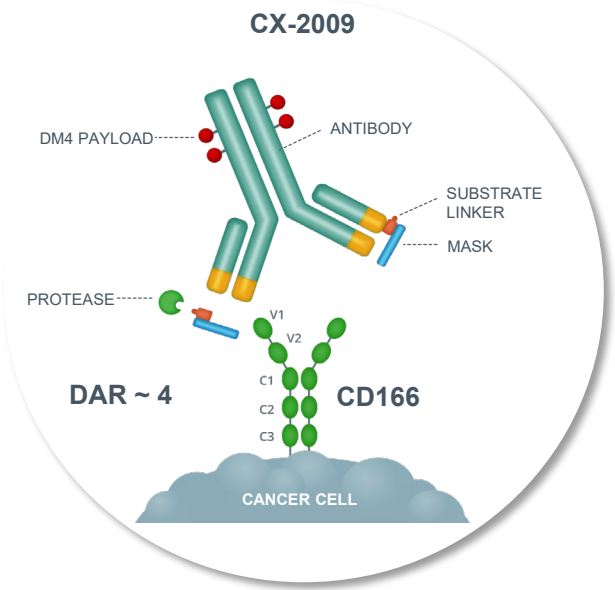
30% of all cancer in females with an estimated **~276k** new cases and **~42k** deaths in the United States in 2020

Breast cancer is the 2nd leading cause of cancer deaths in women[1]

- **~80% of breast cancer is HER2 non-amplified**
- **Despite recent advances, new therapies are needed, especially in the metastatic setting**
- **CD166 is broadly and highly expressed in HER2 non-amplified breast cancer**

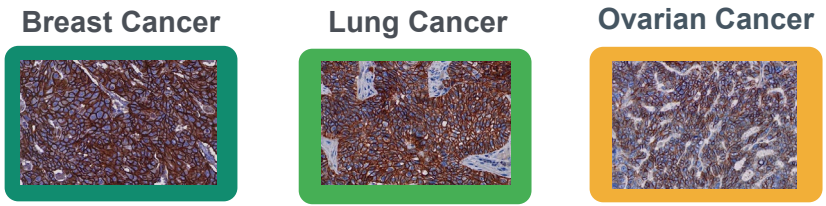
1. Cancer Statistics, 2020; Siegel CA Cancer J Clin 2020;70:7-30

CX-2009: Conditionally Activated ADC Targeting CD166 (ALCAM*)



- CD166 expression in normal cells limits development of a conventional ADC (e.g., Lung, GI tissues, Liver)
- CX-2009 is a first-in-class anti-CD166 conditionally activated antibody conjugated to the maytansinoid cytotoxic payload DM4
- Designed to target CD166 towards tumor tissue, away from healthy tissue
- CD166 expressed on many other cancer types → future opportunity (e.g., Ovarian, Lung, HNSCC)

CD166 Expression by IHC



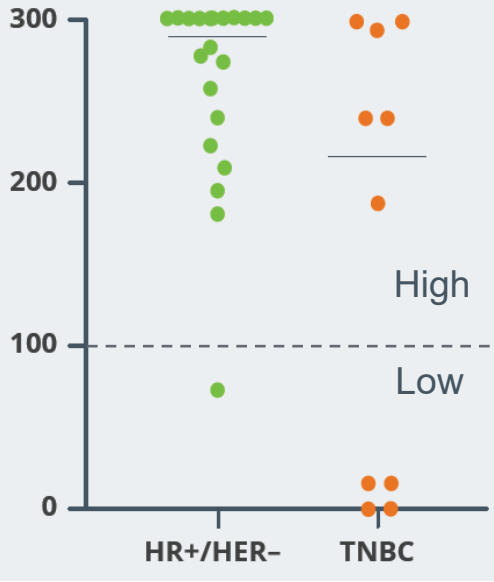
* ALCAM - Activated Leukocyte Cell Adhesion Molecule

Phase 1 Enrolled 39 Patients with Breast Cancer at Doses 0.25-10 mg/kg

	Overall (n=39)	HR+/HER2- (n=28)	TNBC (n=11)
Median age, years (range)	53 (31-77)	54 (37-77)	45 (31-68)
White/Asian/Hawaiian/Unk/Other, n	30/1/1/5/2	21/0/1/5/1	9/1/0/0/1
ECOG PS 0/1	17/22	12/16	5/6
Median no. of prior regimens, (range)	7.5 (3-16)	8 (4-16)	7 (3-11)
Prior platinum, n (%)	15 (38.5%)	6 (21.4%)	9 (81.8%)
Prior microtubule inhibitor, n (%)	37 (94.9%)	26 (92.9%)	11 (100%)
Prior CDK4/6 inhibitor, n (%)	17 (43.6%)	17 (60.7%)	0
Prior anti-PD-l or PD-L1, n (%)	6 (15.4%)	2 (7.1%)	4 (36.4%)
CD166 High/Low/Unknown	32/5/2	26/1/1	6/4/1
Median no. of CX-2009 doses (range)	2 (1-25)	2.5 (1-25)	2 (1-14)

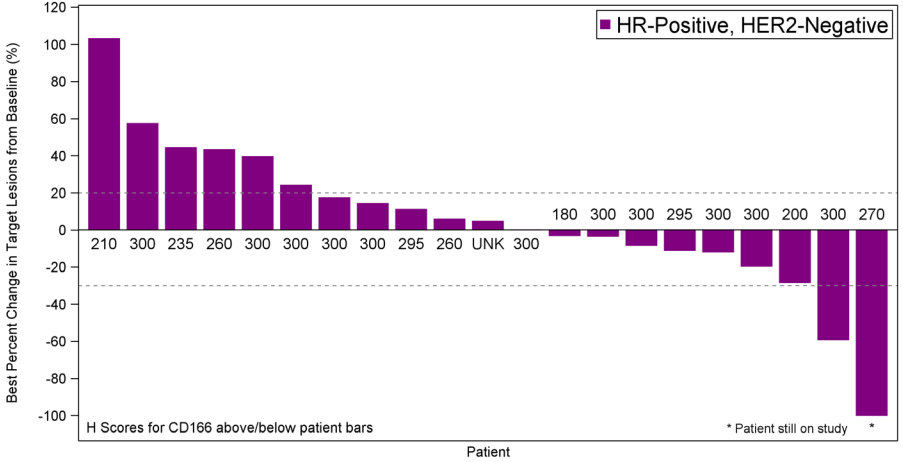
HR+/HER2- : Hormone Receptor positive and HER2 non-amplified breast cancer;
TNBC: Triple negative breast cancer

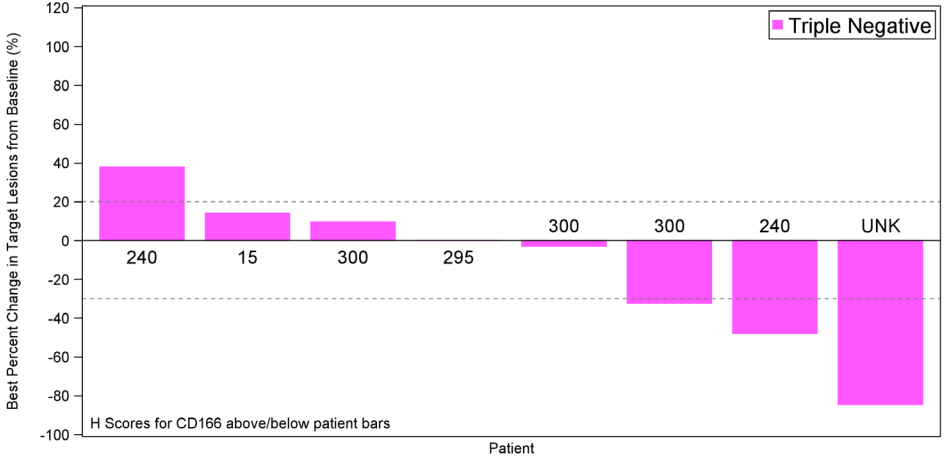
CD166 Expression (H-Score) in Breast Cancer Patients



Observed Clinical Activity in Breast Cancer with CX-2009 at Doses ≥4 mg/kg Q3W

Breast cancer patients with measurable disease who received ≥ 4 mg/kg CX-2009 and had a post-baseline assessment





Parameter	Evaluable* Breast Cancer Patients		
	Overall (n=32)	HR+/HER2- (n=22)	TNBC (n=10)
CBR16	13 (41%)	9	4
CBR24	9 (28%)	5 (2 cPR)	4 (3 uPR)

*Includes those with non-measurable but evaluable (e.g. bone-only) disease

CBR= clinical benefit rate (CR, PR or SD for 16 or 24 wks);
cPR= confirmed partial response;
uPR= unconfirmed Partial Response
UNK = Unknown

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Data presented SABCS 2020

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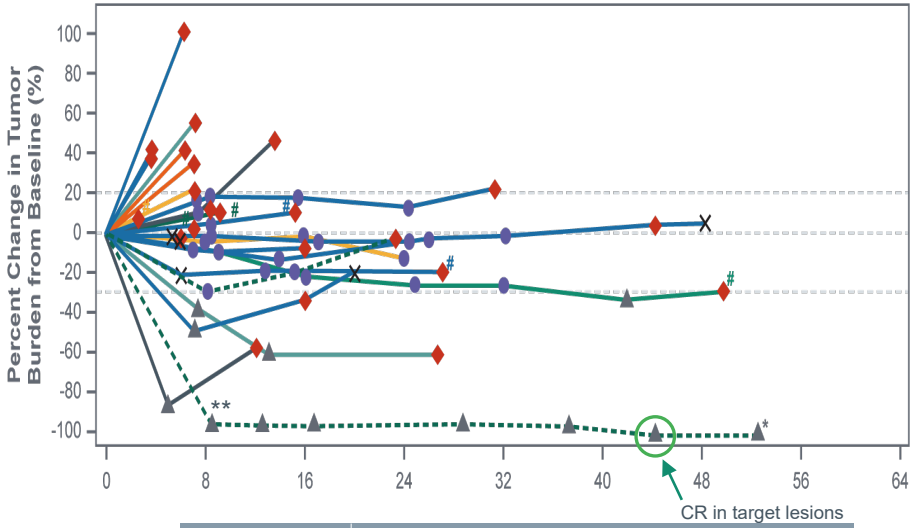

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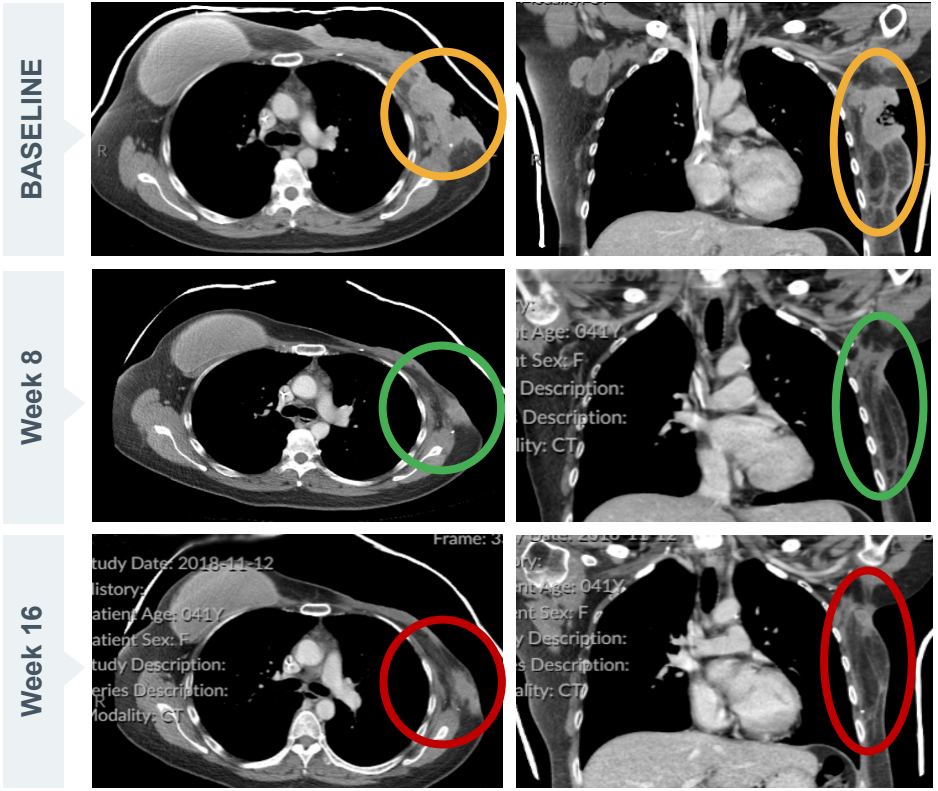
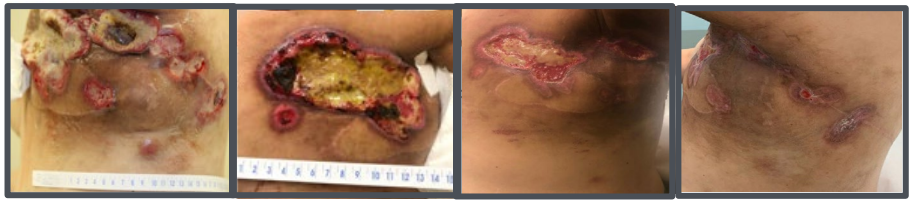
Data presented SABCS 2020

Patient with TNBC Refractory to Pembrolizumab + Paclitaxel and Sacituzumab Govitecan





Week 1 Week 5 Week 10 Week 13

- 41-year-old treated at 8 mg/kg
- Disease progression after
  - Pembrolizumab + Paclitaxel
  - Sacituzumab govitecan
- Baseline: **ulcerating lesions** chest wall, axilla
- First scan: 48% reduction in **target lesions**
- Dose interruption for keratitis (resolved), **disease progressed** before treatment could be re-initiated

Baseline

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Data presented SABCS 2020

CX-2009: Phase 1 Tolerability Supports Phase 2 Dose of 7 mg/kg

	< 6 mg/kg (n=38)	RP2D 7 mg/kg (n=12)	8 mg/kg (n=22)	9 mg/kg (n=9)	10 mg/kg (n=8)
TRAE (Grade 3+)	16%	33%	64%	56%	50%
TEAE leading to Discontinuation	13%	8%	14%	22%	13%
DLT (n)	0	0	1	0	0
TR SAEs	0	17%	27%	22%	13%
Ocular Toxicity (any grade)*	26%	25%	59%	56%	75%
Ocular Toxicity (Grade 3+)	3%	0	14%	33%	13%

RP2D= Recommended Phase 2 Dose
*Ocular prophylaxis was optional; future studies will incorporate mandatory ocular prophylaxis

- CX-2009 was generally well tolerated at doses ≤ 7 mg/kg (toxicity profile consistent with payload: ocular, neuropathic and hepatic)
- Ocular toxicities appeared dose dependent in frequency and severity
- Selection of 7 mg/kg Q3W as RP2D is supported by activity, tolerability and PK/PD modeling

CX-2009 Breast Cancer Phase 2 Study Design

Monotherapy (7 mg/kg Q3W) and Combination with Pacmilimab (CX-072; anti-PD-L1) In Advanced, HER2-non-Amplified Breast Cancer

Key Eligibility

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

Breast Cancer SubType

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**

Endpoints

Primary: Overall Response Rate (ORR) by central review

Secondary: ORR (Inv), PFS, DCR, CBR24, DoR, OS, Safety, PK, ADA

Exploratory: Biomarker correlation with outcome

Readout: Initial data expected 2022

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*Evaluable, **https://meetinglibrary.asco.org/record/186711/abstract

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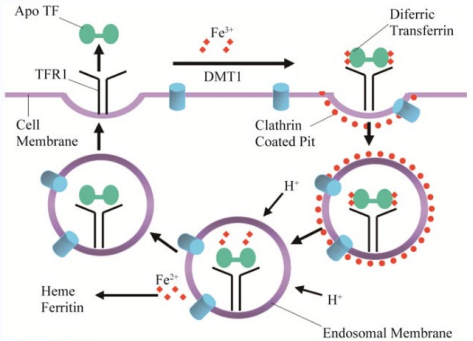
CX-2029

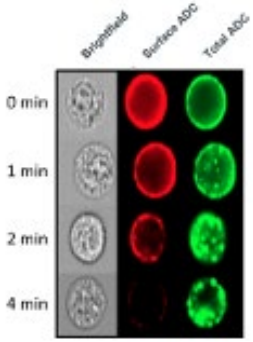
Anti-CD71 (Transferrin Receptor) Conditionally Activated ADC

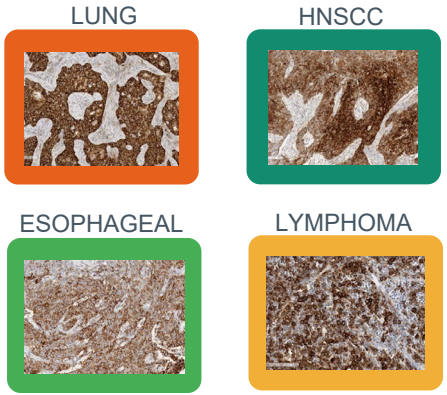
CD71 (Transferrin Receptor)

- Highly expressed tumor antigen
- “Professional internalizer” ideally suited to delivery of cytotoxic payloads to cancer cells
- Undruggable target with conventional antibody approaches due to normal tissue biology
- Conditional activation strategy – open therapeutic window by limiting normal tissue binding
- Potentially paradigm shifting anti-cancer agent with first in class potential



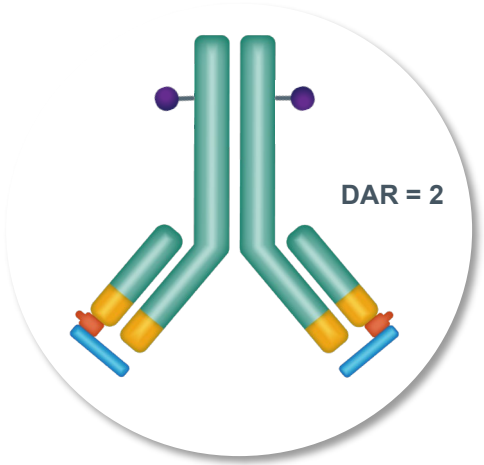
Elliott and Head. *J Cancer Ther. 2012;3:278-311.*



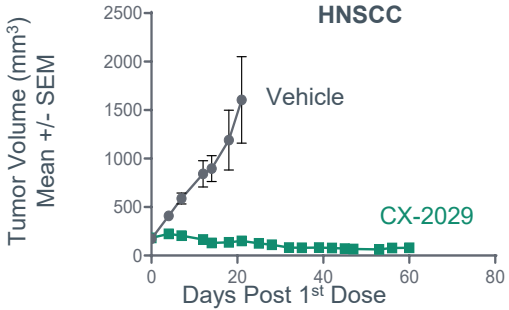


CD71 Expression by IHC

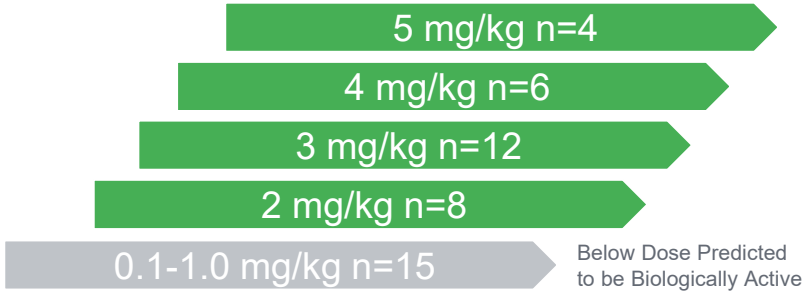
CX-2029: Potentially Paradigm Shifting Anti-Cancer Agent



- Unmasked ADC is lethal in preclinical models at sub-therapeutic doses
- Therapeutic range for CX-2029 predicted in patients 2-4 mg/kg
- Hematologic toxicity dose limiting in preclinical studies



Phase 1 Dose Escalation Study Evaluated CX-2029 Q3W in 45 Patients with Solid Tumors



Key Eligibility Criteria
- Metastatic or locally advanced unresectable solid tumor
- Archival tissue or biopsy available for tissue analyses
- Stable brain metastases permitted

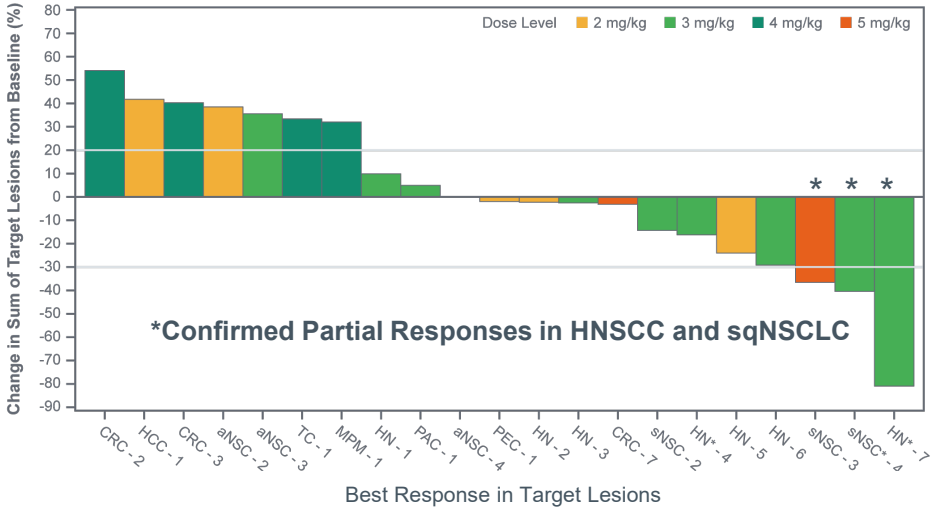
Exclusions:
- Transfusion-dependent anemia or iron metabolism disorders
- Grade 2 or higher neuropathy

Key Patient Demographics	All Cohorts (n=45)
Age, median (min, max)	60 (31, 75)
Baseline ECOG 0 / 1, %	29 / 71
CD71 IHC staining, n (%)	
High expression [2+/3+]	15 (33)
Low expression [0/1+]	16 (36)
Unknown	14 (31)
Tumor types, n (%)	
NSCLC	9 (20)
Squamous NSCLC	4 (9)
HNSCC	8 (18)
Colorectal cancer	7 (16)
Other*	21 (46)
Median priors (min, max)	3 (1, 16)

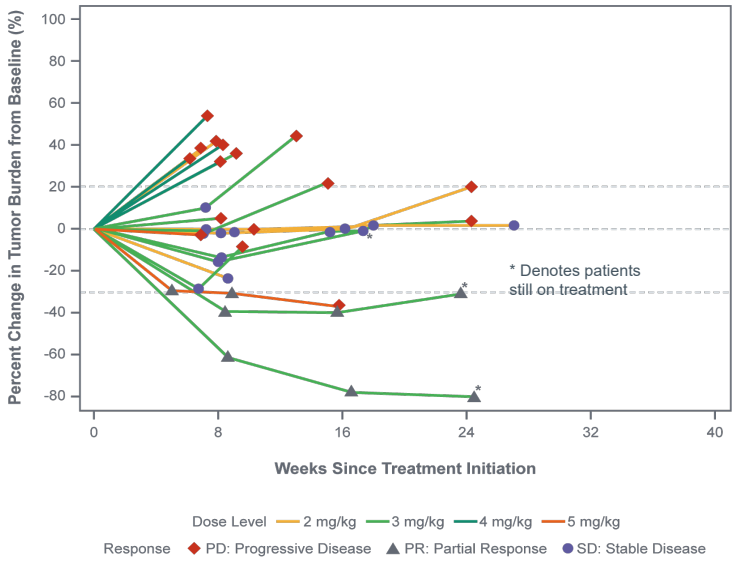
*Other tumor types include sarcoma (4), Prostate (3), parotid gland (3); ovarian (2); melanoma (n=1); endometrial (1); hepatocellular (1); mesothelioma (1); ocular melanoma (1); pancreatic (1); perivascular epithelioid (1); thymoma (1); thyroid (1).

Observed Clinical Activity with CX-2029 at Doses ≥2 mg/kg Q 3 Weeks

Patients with measurable disease who received ≥ 2 mg/kg CX-2029 and had a post-baseline assessment

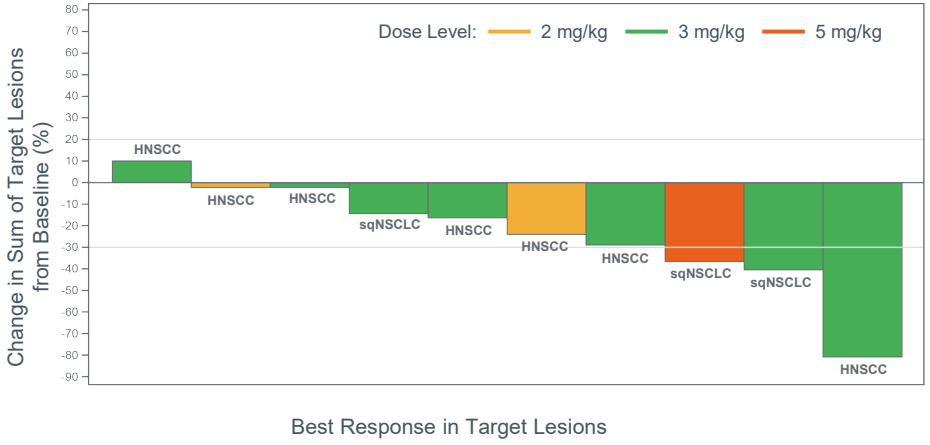


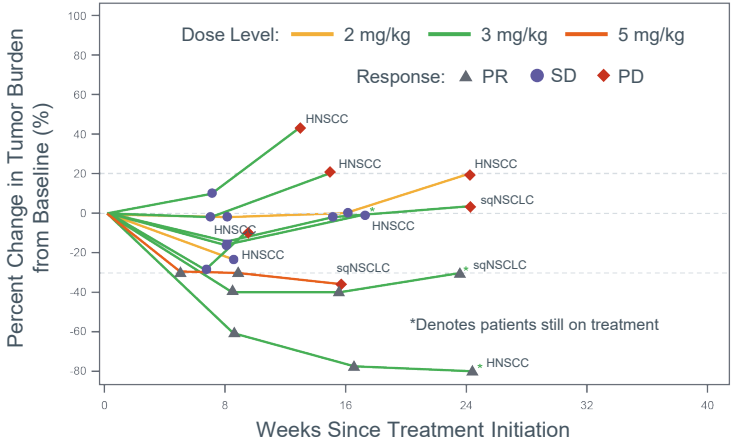
CRC=Colorectal Cancer, HCC=Hepatocellular carcinoma, aNSC=Non-small cell lung adenocarcinoma, TC=Thyroid carcinoma MPM=Malignant pleural mesothelioma, HN=Head and neck squamous cell carcinoma, PAC=Pancreatic cancer, PEC=Perivascular epithelioid cell tumor, sNSC=Non-small cell lung squamous carcinoma



Observed Clinical Activity in sqNSCLC and HNSCC with CX-2029 at Doses ≥2 mg/kg Q 3 Weeks

sqNSCLC or HNSCC patients with measurable disease, received ≥ 2 mg/kg CX-2029, and had a post-baseline assessment



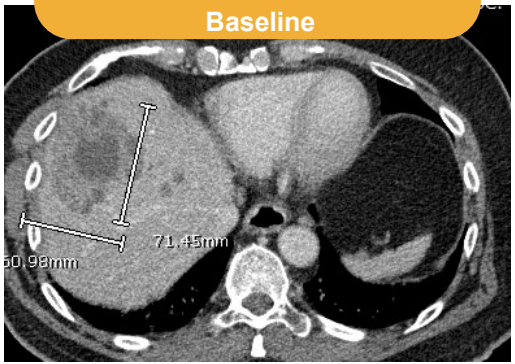


1 patient with sqNSCLC was dosed at 1 mg/kg; 1 patient with HNSCC came off study without a post-baseline assessment

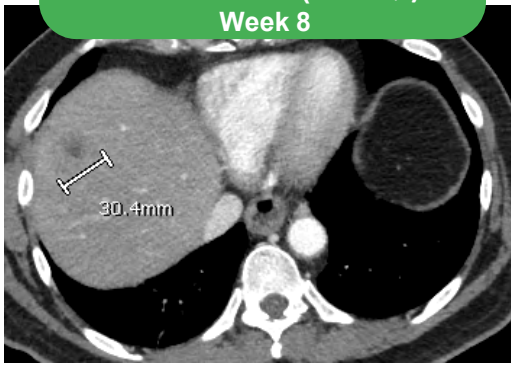
CX-2029 Case Study: Patient with HNSCC

- Nasopharyngeal carcinoma (Diagnosed in February 2018)
- Prior therapies: docetaxel/5FU/cisplatin with radiation; high-dose cisplatin; investigational agent (sEphB4-HSA) + pembrolizumab (best response was PD)
- CX-2029 treatment initiated (January 2020)
- Partial response at Week 8 confirmed 8 weeks later. Dose reduced to 2 mg/kg; additional shrinkage of liver target lesion seen.

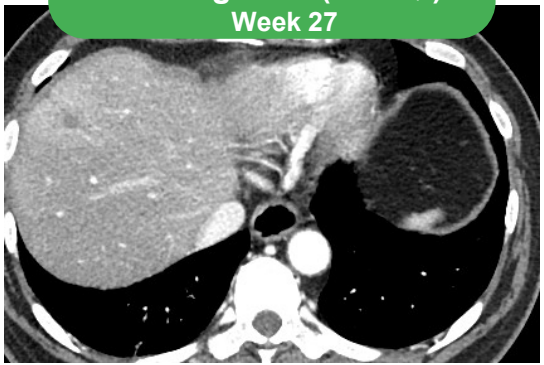
18 Dec 2019
Baseline



13 Mar 2020 (43% ↓)
Week 8



28 Aug 2020 (84% ↓)
Week 27



Data cut-off: August 2020.

CX-2029 Phase 1 Tolerability Supports Phase 2 Dose of 3mg/kg

Generally Well Tolerated to 3 mg/kg with Manageable Adverse Events

Treatment-Related Grade 3+ AEs (≥2 patients)	1.0 mg/kg (n=3)	2.0 mg/kg (n=8)	RP2D 3.0 mg/kg (n=12)	4.0 mg/kg (n=6)	5.0 mg/kg (n=4)
Anemia	33%	63%	58%	83%	100%
Neutropenia	0	0	33%	50%	75%
Leukopenia	0	0	8%	33%	50%
Infusion-related reaction	0	13%	0	17%	0

- > 90% masking maintained in circulation
- Most frequent Grade 3+ AE was anemia
  - Managed with red blood cell transfusions, growth factor support and/or dose delays/reductions
  - Likely multi-factorial including CD71 biology and MMAE payload
- 3 mg/kg Q3W selected as Phase 2 dose

Data cut-off: August 2020

Phase 2 Expansion Underway to Evaluate CX-2029 in Four Cohorts

Monotherapy at 3 mg/kg Q3W

Eligibility

sqNSCLC, HNSCC and esophageal

- Prior therapy must include prior platinum and a checkpoint inhibitor (alone or in combination; if approved by the local Health Authority).
- For esophageal: squamous, adenocarcinoma or GE junction; prior HER2-targeted therapy if tumor is HER2+
- Documented progression after at least one prior regimen for advanced disease

DLBCL

- Progression after at least 2 prior regimens (one of which must be anti-CD20 based therapy); not a candidate for stem cell transplant

Cancer Type

sqNSCLC
n~25*

HNSCC
n~25*

Esophageal/GEJ
n~25*

DLBCL
n~25*

*Evaluable

Endpoints

Primary: Overall Response Rate (ORR) by local investigator

Secondary: PFS, DCR, CBR24, DoR, OS, Safety, PK, ADA, TTR

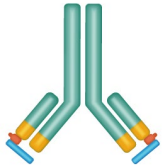
Exploratory: Biomarker correlation with outcome

Readout: Initial data expected Q4 2021

CytomX Therapeutics

Alliances and Financials

Strong Alliances Advancing Multiple Programs and Probody Formats



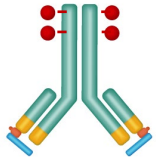
Bristol Myers Squibb™

CHECKPOINT INHIBITORS

LEAD PROGRAMS: Expanding therapeutic window for CTLA-4

BMS-986249 ipilimumab Probody in melanoma Phase 2

BMS-986288 non-fucosylated ipilimumab Probody in Phase 1



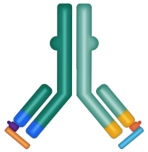
abbvie

CONDITIONALLY ACTIVATED ANTIBODY-DRUG CONJUGATES

LEAD PROGRAM: CD71 (CX-2029)

Global co-development alliance

CytomX retained US rights (35%) and >20% royalties ex-US



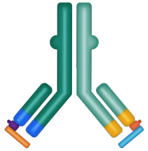
AMGEN

T-CELL BISPECIFICS

LEAD PROGRAM: CX-904

EGFR-CD3 conditionally activated T-cell bispecific

IND enabling studies for potential 2021 IND



astellas

T-CELL BISPECIFICS

Conditionally activated T-cell Bispecifics

Alliance formed March 2020

$80 million upfront

Strong Balance Sheet to Support Pipeline and Operations

- $336M in cash as of September 30, 2021
- No debt
- 65M shares outstanding as of September 30, 2021

Leadership in Conditionally Activated Therapeutics with Validated Platform

Summary

- Versatile, multi-modality platform
- Five clinical stage assets
- 2 conditionally activated ADCs in Phase 2
  - CX-2009, CX-2029
- 2 Probody checkpoint inhibitors in Phase 2
  - CX-072 (+ CX-2009)
  - BMS-986249
- Emerging T-cell bispecifics and cytokines
- Robust platform and preclinical pipeline
- Strong alliances

2021 Priorities

- Patient enrollment into CX-2009 Ph 2 study
  - HR+/HER2-non-amplified breast cancer
  - TNBC +/– CX-072
  - Initial data expected 2022
- Patient enrollment into CX-2029 Ph 2 expansions
  - sqNSCLC, HNSCC, esophageal/GEJ, DLBCL
  - Initial data expected Q4 2021
- IND submission
  - CX-904 expected Q4 2021
- Continued progress within partnerships

CytomX Therapeutics Inc.

Our **VISION**

Create
a new approach to the treatment of cancer by improved tumor targeting

Our **PLATFORM**

Lead
in conditional activation of antibody-drug conjugates and other modalities

Our **PRODUCTS**

Advance
a broad clinical pipeline of anti-cancer therapies in areas of significant unmet need

Our **TOMORROW**

Build
a long-term, commercial stage, multi-product enterprise