CytomX Therapeutics

# 39th Annual J.P. Morgan Healthcare Conference

**Sean McCarthy, D.Phil.**

**President, Chief Executive Officer, and Chairman**

**JANUARY 14, 2021**

CytomX Therapeutics

# Conditionally-Active Antibody 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-Active Antibodies

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

## Key 2021 Milestones

- CX-2009 initial Phase 2 data in breast cancer
- CX-2029 initial Phase 2 expansion cohort data
- Next IND filings

## Foundational Partnerships

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

## Strong Balance Sheet

- $321M cash at end of Q3 2020
- 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*

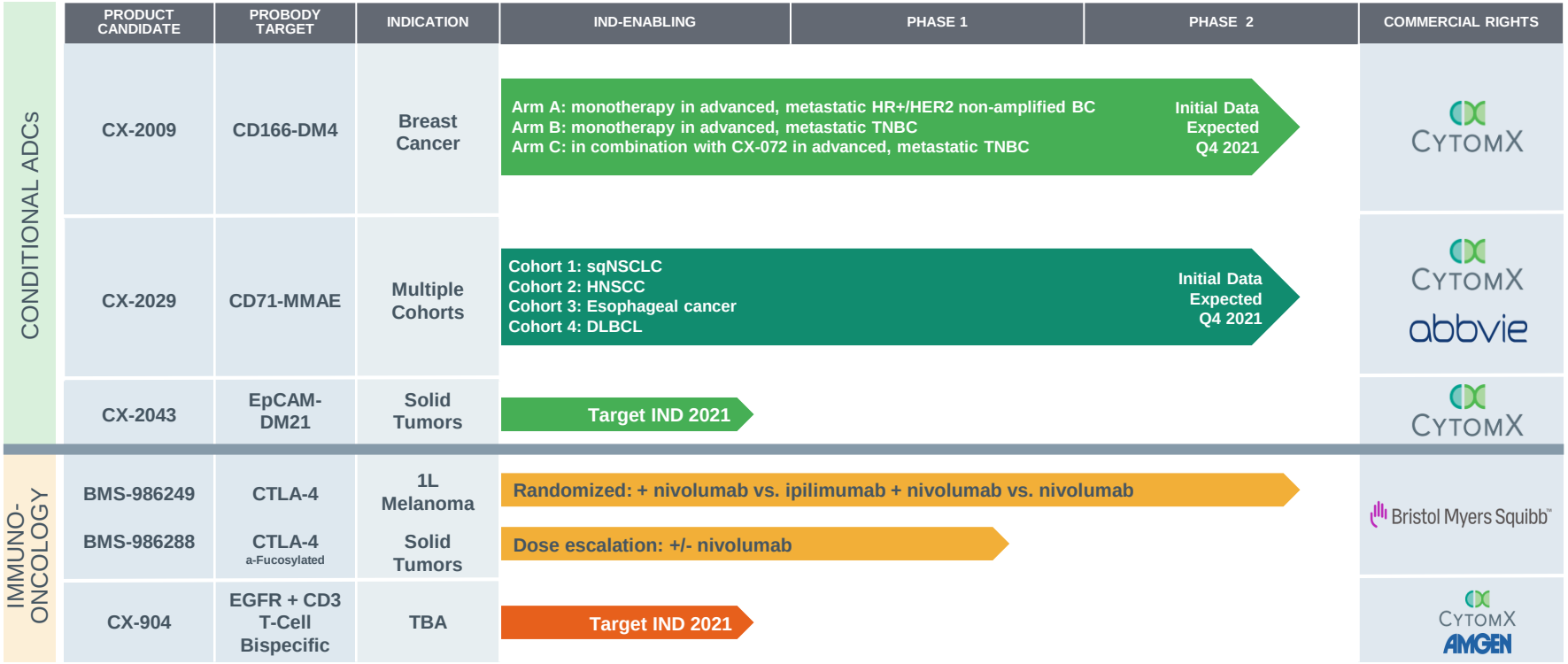
**Amy C. Peterson, M.D.**
EVP, Chief Development Officer
*>15 years of leadership experience in oncology drug development*

**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*

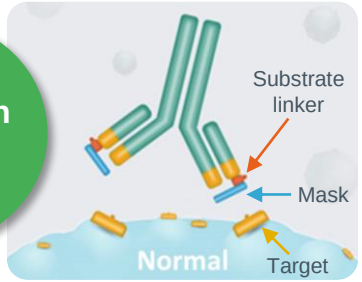
**Marcia P. Belvin, Ph.D.**
SVP, Head of Research
*>20 years of experience in preclinical pipeline discovery and development in oncology*

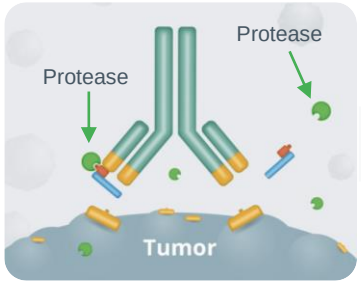
# Broad Clinical and Preclinical Pipeline with Multiple Phase 2 Readouts 2021+

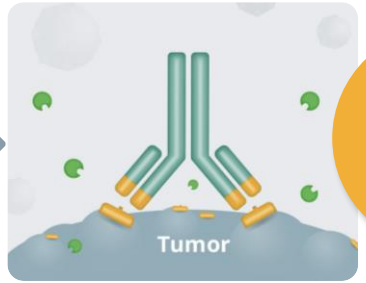


# The Probody® Therapeutic Platform: *Conditionally-Active Antibodies*

**Less Binding in Normal Tissues**



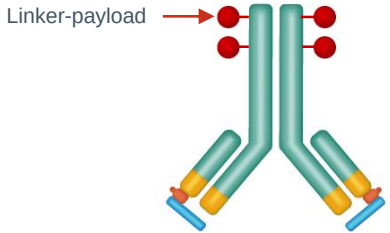




**More Binding in Tumors**

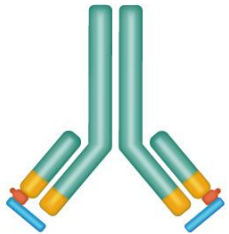
"Masking" limits ability of conditionally-active antibody to bind to healthy tissues

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

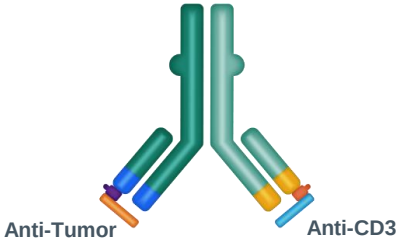
**Antibody-Drug Conjugate**




**Immune Modulator/ Checkpoint Inhibitor**



**T-Cell Bispecific**

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# 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 30MG | 140MG

TRODELVY™
sacituzumab govitecan-hziy
180 mg for injection

Biotech

**AstraZeneca puts $6.9B on the table for a Daiichi Sankyo cancer drug**

by Ben Adams | Mar 29, 2019 4:55am

THE WALL STREET JOURNAL.

MARKETS | DEALS

**Gilead Reaches Deal to Buy Immunomedics for $21 Billion**

Biotech drugmaker has a market value of roughly $10 billion

Bloomberg

Deals

**Merck Inks Up to $4.5 Billion Seattle Genetics Cancer Deal**

By Cristin Flanagan
September 14, 2020, 3:50 AM PDT
*Updated on September 14, 2020, 6:55 AM PDT*

M&A/IPO

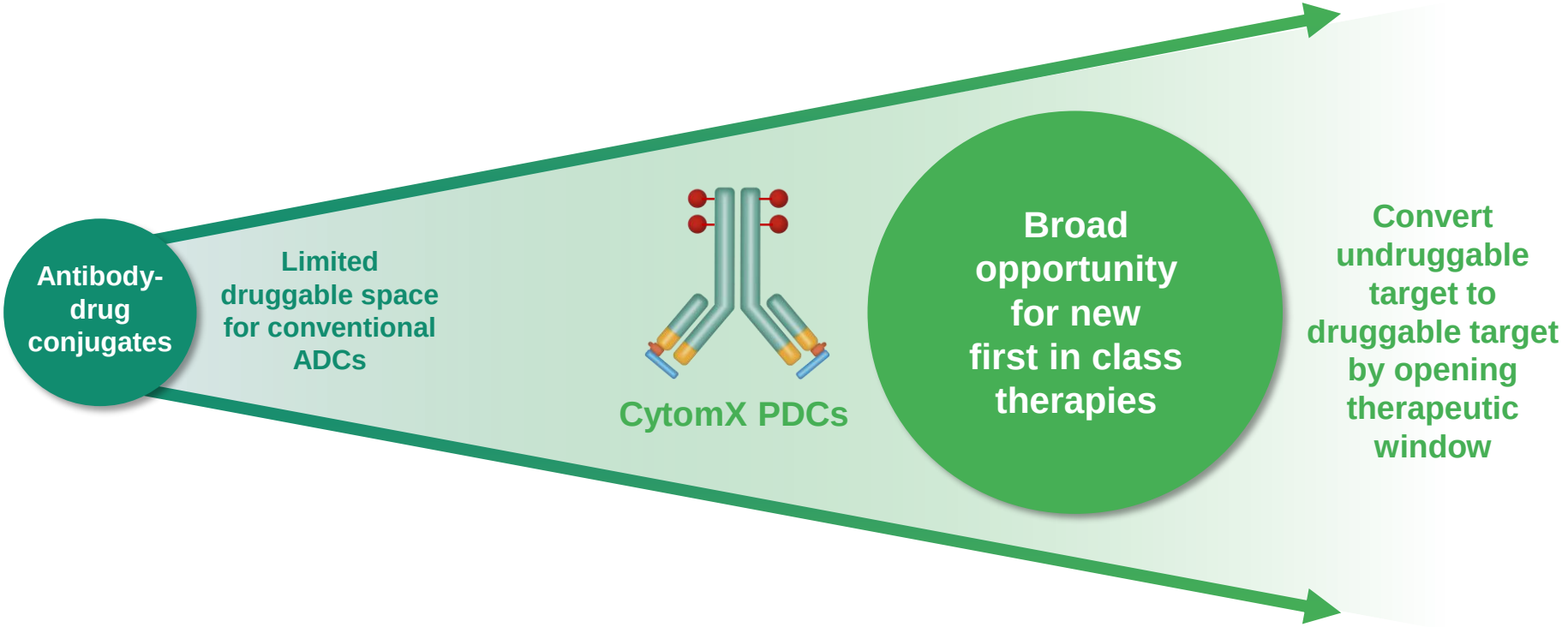
**Merck Strikes Deal to Buy Cancer-Drug Startup VelosBio for $2.75 Billion**

Top cancer drugmakers continue their string of aggressive deal making

July 27, 2020 06:14 AM EDT *Updated July 28, 05:02 AM* | Deals

**AstraZeneca mines another $6B ADC from Daiichi Sankyo, with blockbuster ambitions to 'redefine treatment stan-dards'**

# Probody Drug Conjugates Expand ADC Target Landscape



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# CX-2009 (Praluzatamab ravtansine)

## Anti-CD166 Conditional 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**

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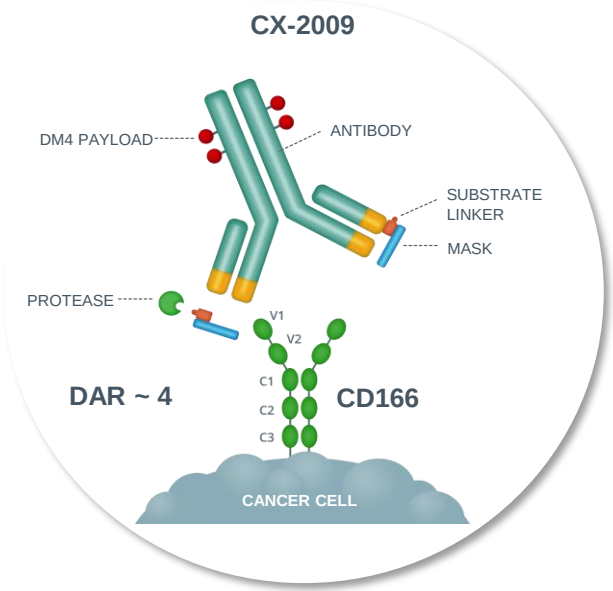
1. Cancer Statistics, 2020; Siegel CA Cancer J Clin 2020;70:7-30

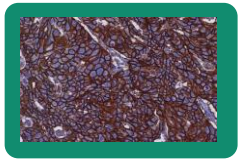
# CX-2009: A Probody Drug Conjugate Targeting CD166 (ALCAM*)



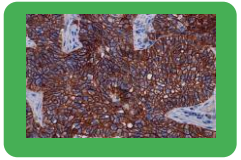

- CD166 expression in normal cells limits development of a conventional ADC (e.g., Lung, GI tissues, Liver)
- CX-2009 is a first-in-class anti-CD166 Probody conjugated to the maytansinoid cytotoxic payload DM4
- Designed to target CD166 towards tumor tissue, away from healthy tissue
- CD166 expressed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

**CD166 Expression by IHC**

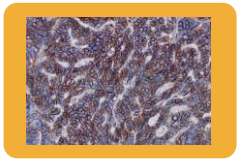
**Breast Cancer**



**Lung Cancer**



**Ovarian Cancer**

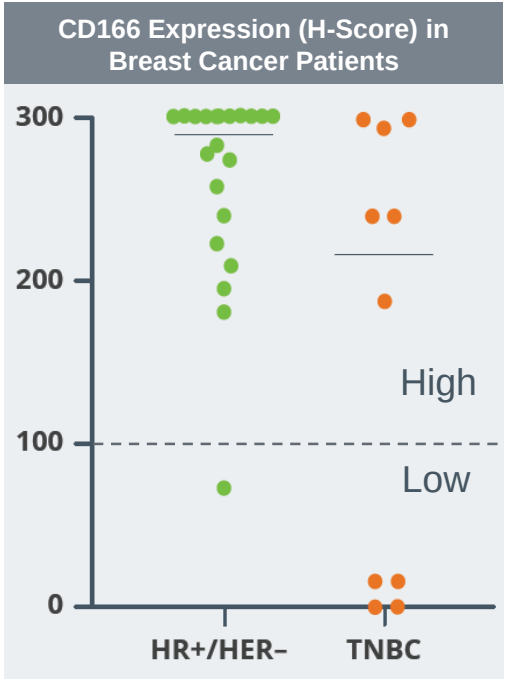


* ALCAM - Activated Leukocyte Cell Adhesion Molecule

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

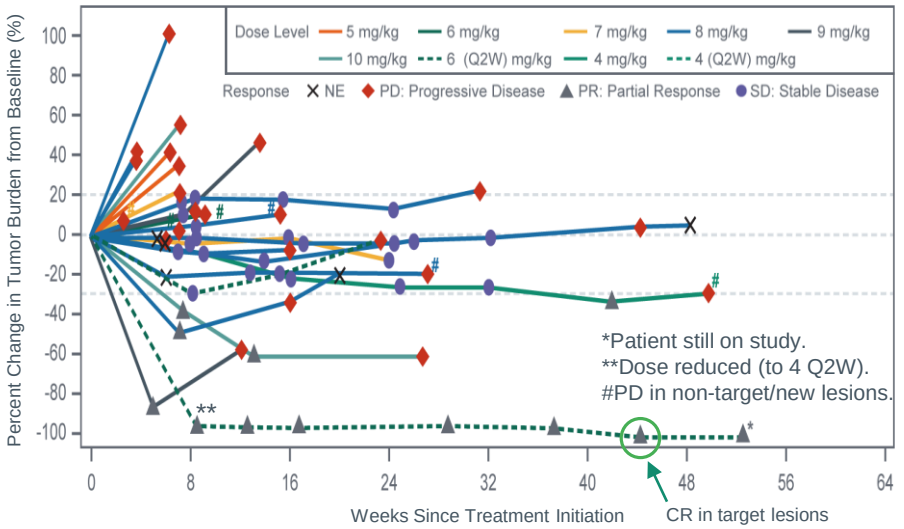
| | Overall (n=39) | HR+/HER2- (n=28) | TNBC (n=11) |
|---|---|---|---|
| **Median age, years (range)** | 53 (31-77) | 54 (37-77) | 45 (31-68) |
| **White/Asian/Hawaiian/Unk/Other, n** | 30/1/1/5/2 | 21/0/1/5/1 | 9/1/0/0/1 |
| **ECOG PS 0/1** | 17/22 | 12/16 | 5/6 |
| **Median no. of prior regimens, (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



# 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) |

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

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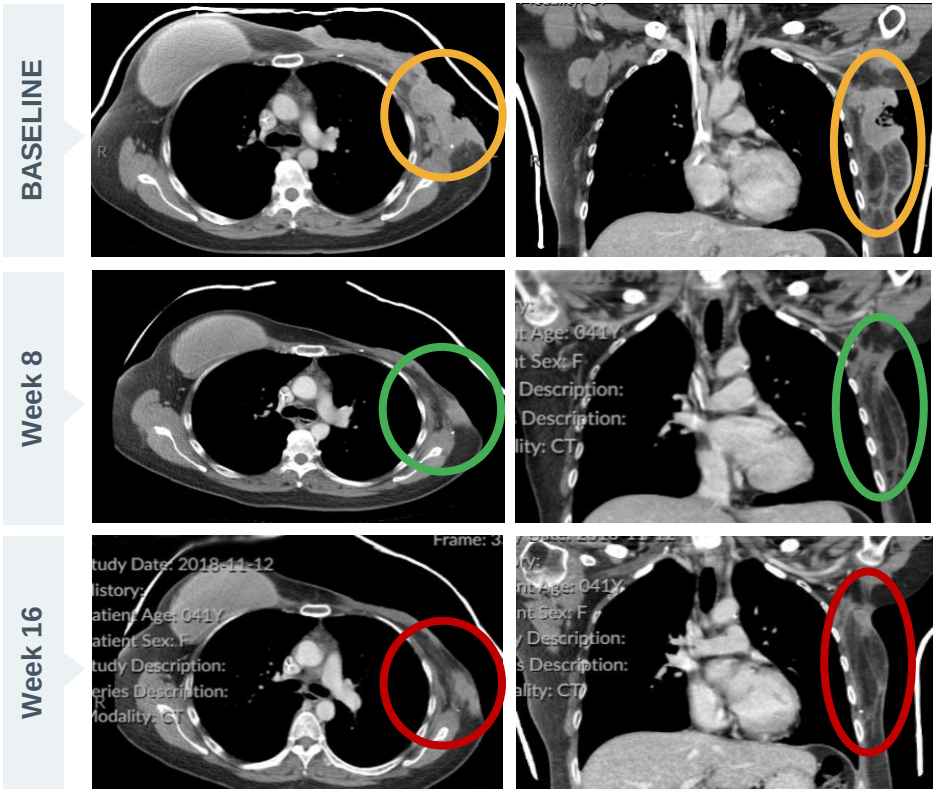
Data presented SABCS 2020

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

# Partial Response to CX-2009 in Patient with TNBC Refractory to Pembrolizumab+Paclitaxel and to Sacituzumab Govitecan




- 41-year-old treated at 8 mg/kg
- Prior treatment for metastatic disease:
  - Pembrolizumab + paclitaxel (best response = PD)
  - Sacituzumab govitecan (best response = PD)
- Baseline: **ulcerating skin lesions** on chest wall and axillary nodal metastasis
- First scan (Week 8): 48% reduction in **target lesions**
- Dose interruption (week 9 -16) for keratitis (resolved), **disease progressed** before treatment could be re-initiated

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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 (7mg/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 Q4 2021

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

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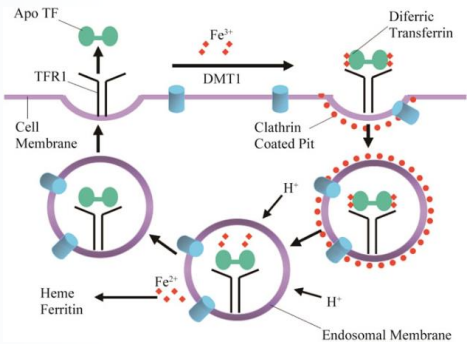
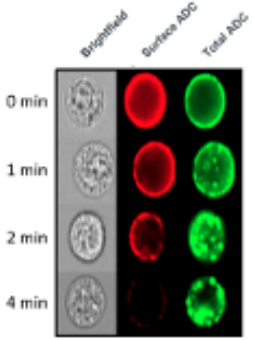
# CX-2029

## Anti-CD71 (Transferrin Receptor) Conditional ADC

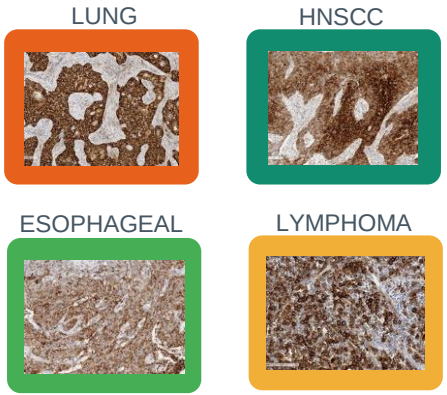
# CD71 (Transferrin Receptor)

- 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
- Probody strategy – open therapeutic window by limiting normal tissue binding
- Potentially paradigm shifting anti-cancer agent with first in class potential



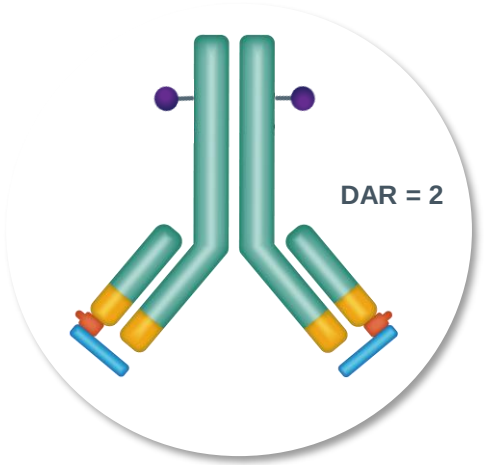




Elliott and Head. *J Cancer Ther. 2012;3:278-311.*

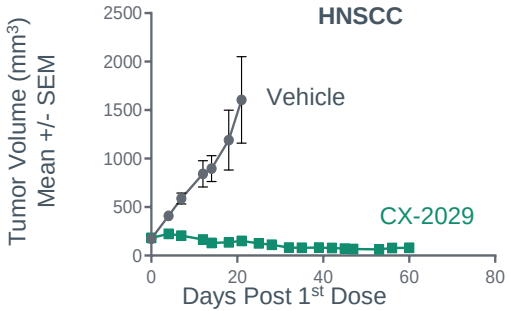



**CD71 Expression by IHC**

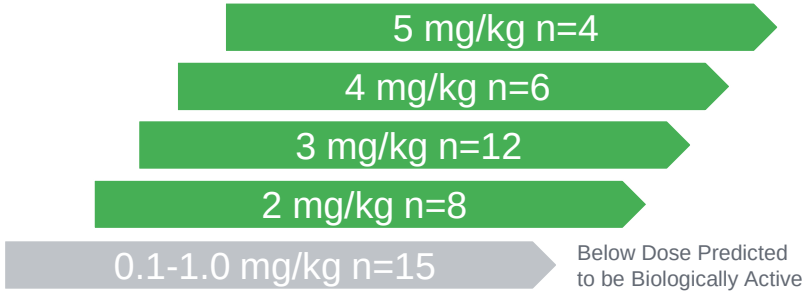
# CX-2029: Potentially Paradigm Shifting Anti-Cancer Agent




- Unmasked ADC is lethal in preclinical models at sub-therapeutic doses
- Therapeutic range for CX-2029 conditional ADC 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

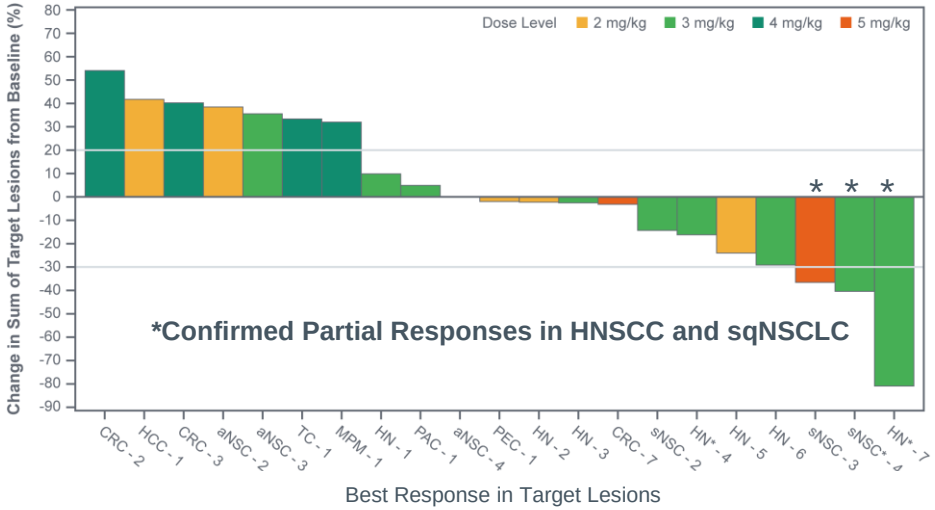
**Exclusions:**
- Transfusion-dependent anemia or iron metabolism disorders
- Grade 2 or higher neuropathy

| 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) |

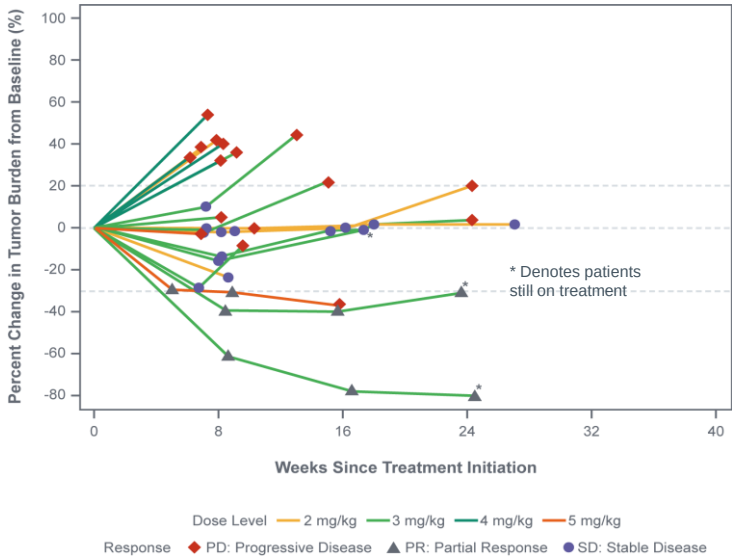
*Other tumor types include sarcoma (4), Prostate (3), parotid gland (3); ovarian (2); melanoma (n=1); endometrial (1); hepatocellular (1); mesothelioma (1); ocular melanoma (1); pancreatic (1); perivascular epithelioid (1); thymoma (1); thyroid (1).

# 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**

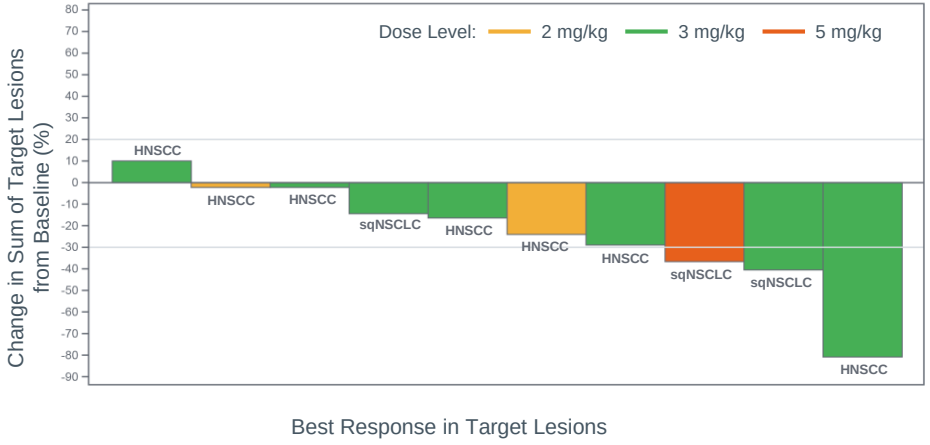


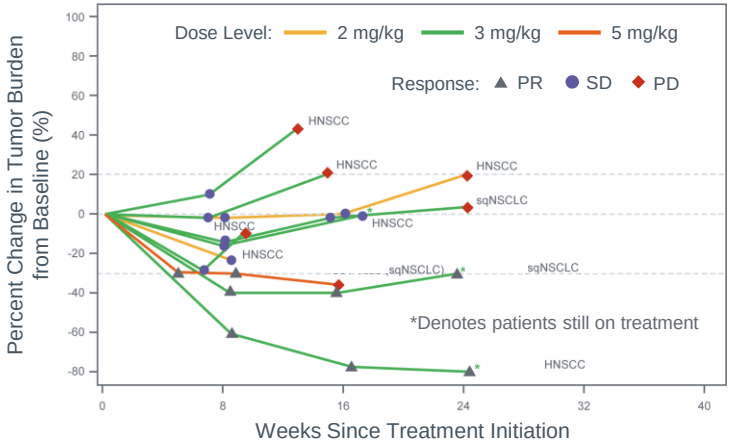

CRC=Colorectal Cancer, HCC=Hepatocellular carcinoma, aNSC=Non-small cell lung adenocarcinoma, TC=Thyroid carcinoma MPM=Malignant pleural mesothelioma, HN=Head and neck squamous cell carcinoma, PAC=Pancreatic cancer, PEC=Perivascular epithelioid cell tumor, sNSC=Non-small cell lung squamous carcinoma



# 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**



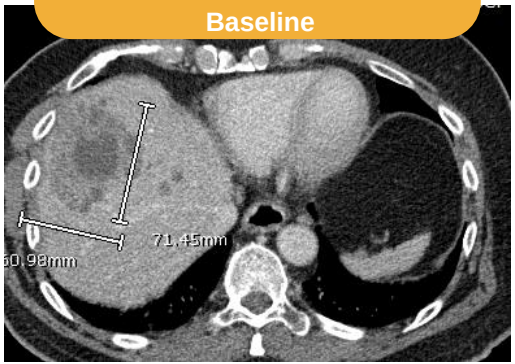

1 patient with sqNSCLC was dosed at 1 mg/kg; 1 patient with HNSCC came off study without a post-baseline assessment

*Data cut-off: August 2020*

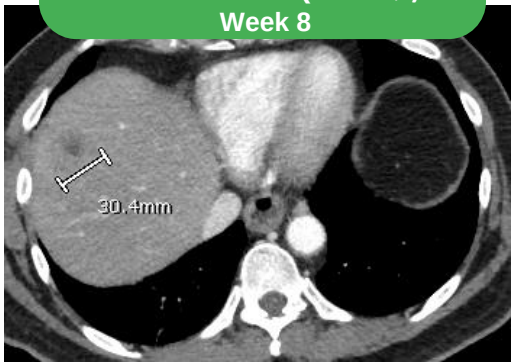
# CX-2029 Case Study: Patient with HNSCC

- 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.

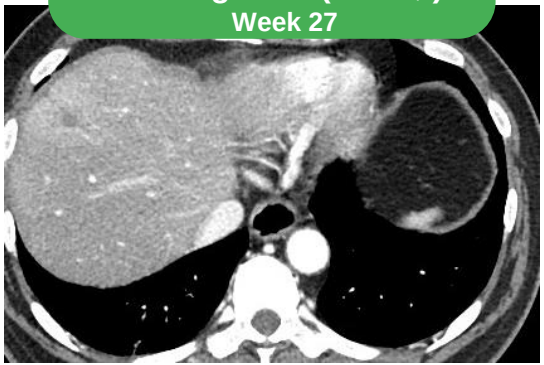
**18 Dec 2019**
**Baseline**




**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

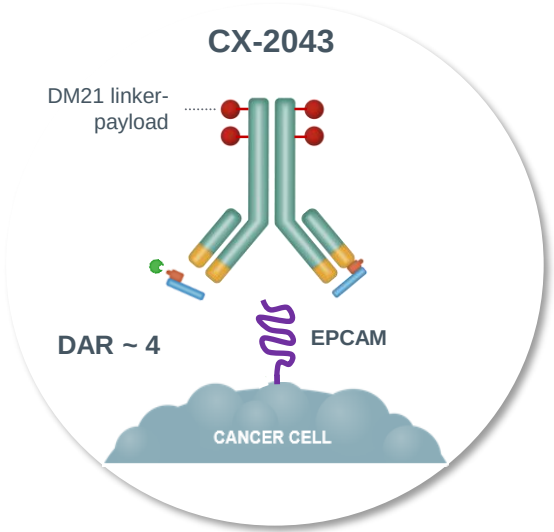
**Readout:** Initial data expected Q4 2021

CytomX Therapeutics

# CX-2043

## Anti-EpCAM (TROP-1) Conditional ADC

# CX-2043: Conditional ADC Targeting EpCAM/TROP-1

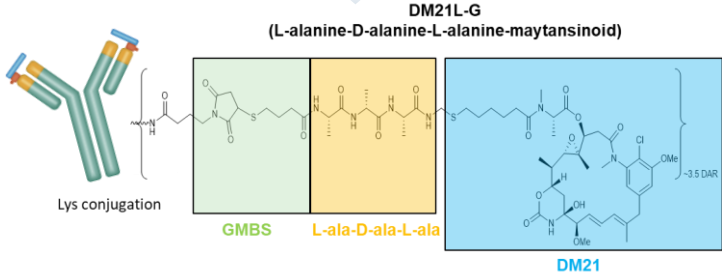



- CX-2043 generated in collaboration with Immunogen
- CytomX retains WW development and commercial rights

## Target Background

- Epithelial cell marker; Highly expressed on solid tumors
- EpCAM-targeted therapies can be active when delivered locally
- On-target / off-tumor toxicities limit systemic delivery

## CX-2043: EpCAM-targeting PDC

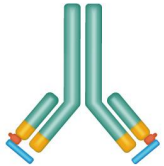



- Next-generation linker-payload system with enhanced stability and improved bystander activity
- Probody platform alleviates on-target / off-tumor toxicity (pancreatitis, GI tox)

CytomX Therapeutics

# Alliances and Financials

# Strong Alliances Advancing Multiple Programs and Probody Formats



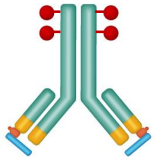
Bristol Myers Squibb™

**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**



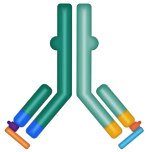
abbvie

**PROBODY DRUG CONJUGATES**

**LEAD PROGRAM: CD71 (CX-2029)**

**Global co-development alliance**

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



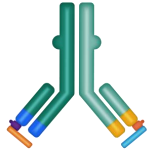
AMGEN

**T-CELL BISPECIFICS**

**LEAD PROGRAM: CX-904**

**EGFR-CD3 conditional T-Cell bispecific**

**IND enabling studies for potential 2021 IND**



astellas

**T-CELL BISPECIFICS**

**Conditional T-Cell Bispecifics**

**Alliance formed March 2020**

**$80 million upfront**

# Strong Balance Sheet to Support Pipeline and Operations

- $321M in cash as of Sept. 30th 2020
- $130M of non-dilutive capital in 2020
  - $80M upfront from Astellas
  - $40M CX-2029 milestone from AbbVie
  - $10M anti-CTLA-4 milestone from BMS
- No debt
- 46.2M shares outstanding

# Leadership in Conditionally-Active Antibodies with Validated Platform

## Summary

- Versatile, multi-modality platform
- Five clinical stage assets
- 2 conditional ADCs in Phase 2
  - CX-2009, CX-2029
- 2 conditional checkpoint inhibitors in Phase 2
  - CX-072 (+ CX-2009)
  - BMS-986249
- Emerging T-cell bispecifics
- 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 Q4 2021
- Patient enrollment into CX-2029 Ph 2 expansions
  - sqNSCLC, HNSCC, esophageal, DLBCL
  - Initial data expected Q4 2021
- IND submission
  - CX-2043
  - CX-904
- 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

# Questions and Answers