CytomX Therapeutics

# 40th Annual J.P. Morgan Healthcare Conference

**Sean McCarthy, D.Phil.**

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

**January 12, 2022**

# 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.

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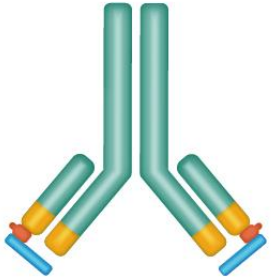
CytomX Therapeutics

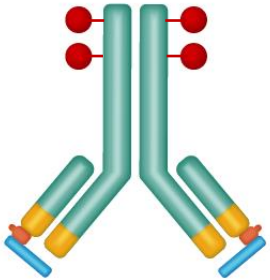
# Destroying Cancer. Differently.

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

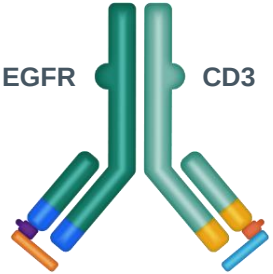
**Antibodies**



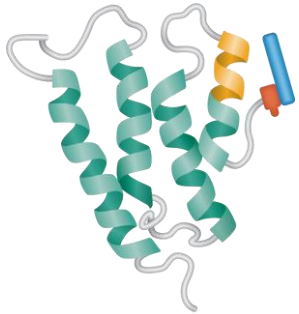
**Antibody-Drug Conjugates**



**T-cell Bispecifics**



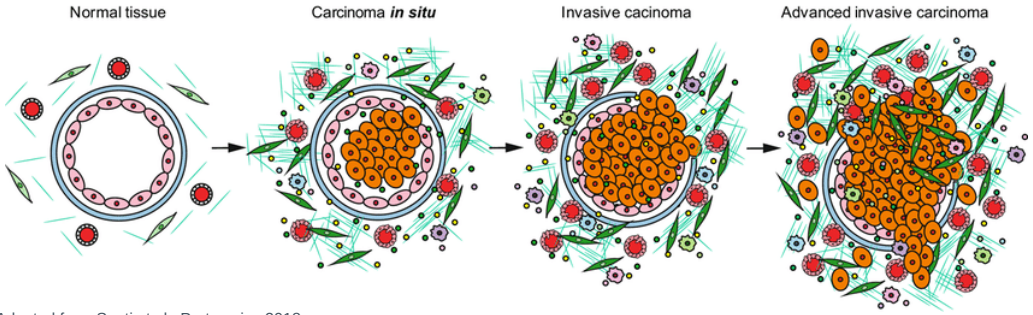

**Cytokines**



## Our Value Proposition

*The Leading Paradigm of Biologics Localization,*
*Opening Unparalleled Opportunity for More Effective and Safer Cancer Therapeutics*

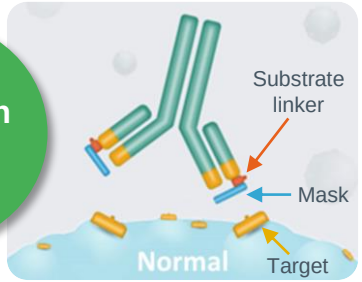
# The Probody® Therapeutic Platform – Exploiting Cancer's Achilles' Heel



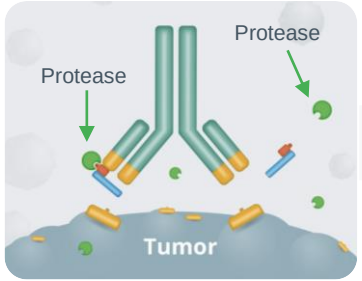

Adapted from Santi et al., Proteomics 2018

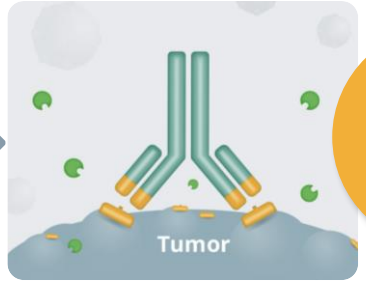
Upregulated protease activity is a hallmark of cancer

**Less Binding in Normal Tissues**




"Masking" limits ability of Probody therapeutics to bind to healthy tissues



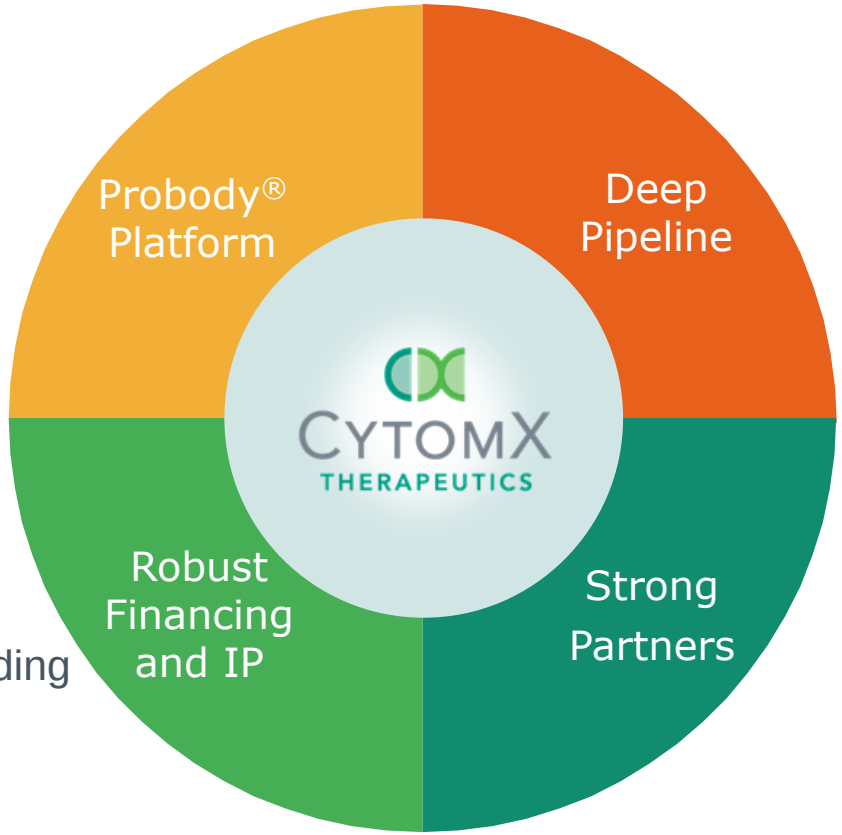




**More Binding in Tumors**

Proteases in tumor microenvironment "unmask" Probody therapeutics, allowing more binding to tumor cells

# Integrated Business Model for Long-Term Value Creation

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




- Robust & diverse portfolio
- 6 INDs
- 4 Phase 2 assets in 9 cancer types

- Strong balance sheet
- $336M end Q3 2021
- >450 issued and pending patents worldwide

- 4 global partnerships
- 3 partnered programs in clinic
- Raised >$500M non-dilutive capital to date

# Experienced Leadership Team

**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*

**Jeff Landau**
SVP, Head of Strategy and Chief Business Officer
*>20 years of biopharmaceutical experience in corporate development, corporate strategy and new product strategy/planning*

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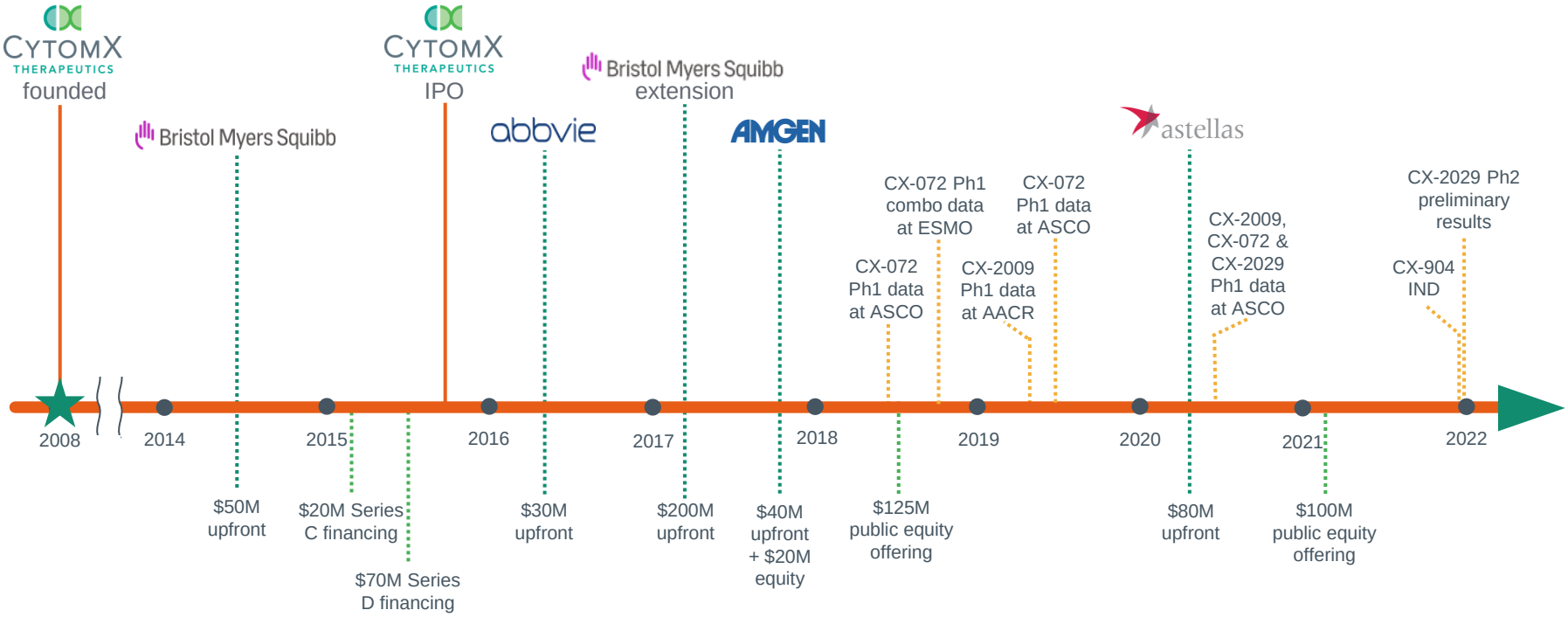
# Strong Track Record of Execution Towards Our Vision

## Becoming a Sustainable, Commercial Stage Oncology Leader

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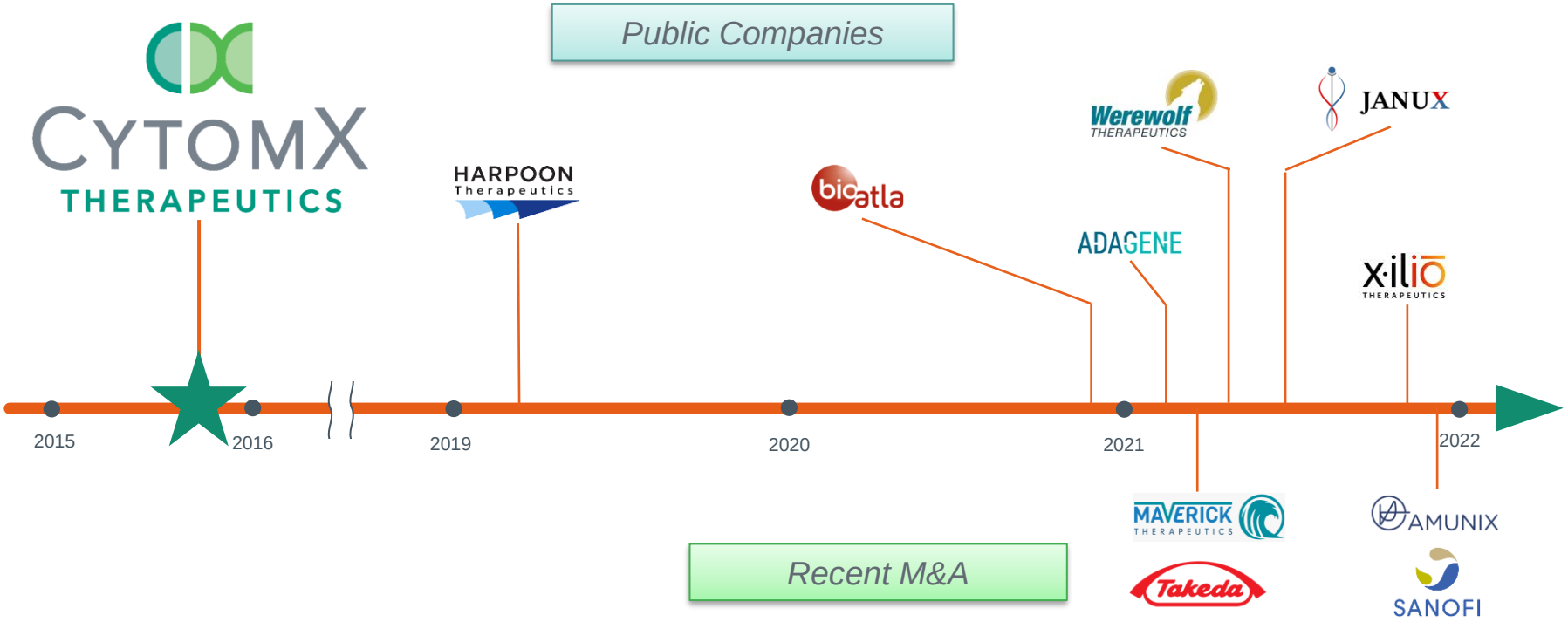
Alliance  Clinical  Financials

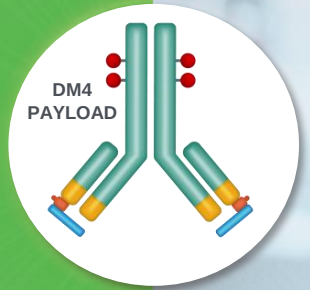
# CytomX Leadership has Established Conditional Activation as a Highly Strategic Area of Biologics Research and Development



# Leading Platform, Deepest Pipeline, Broadest Clinical Experience

## 4 Assets in 11 Phase 2 Studies in 9 Cancer Types

| Modality | Product Candidate | Target-Payload | Indication | Preclinical | Phase 1 | Phase 2 | Commercial Rights |
|---|---|---|---|---|---|---|---|
| Antibody-Drug Conjugate | Praluzatamab ravtansine (CX-2009) | CD166-DM4 | HR+/HER2-non-amp BC | | | | CytomX |
| | | | TNBC | | | | |
| | | | + pacmilimab (CX-072) | | | | |
| | CX-2029 | CD71-MMAE | Squamous NSCLC | | | | CytomX abbvie |
| | | | HNSCC | | | | |
| | | | Esophageal/GEJ | | | | |
| | | | DLBCL | | | | |
| | CX-2043 | EpCAM-DM21 | Solid tumors | | | | CytomX |
| Immuno-Oncology | BMS-986249 | CTLA-4 | 1L Melanoma | | | | Bristol Myers Squibb |
| | | | TNBC, HCC, CRPC | | | | |
| | BMS-986288 | CTLA-4 (a-fucosylated) | Solid tumors | | | | |
| TCB | CX-904 | EGFRxCD3 | TBD | IND filed | | | CytomX AMGEN |
| Cytokine | TBD | IFN-a2b | TBD | | | | CytomX |



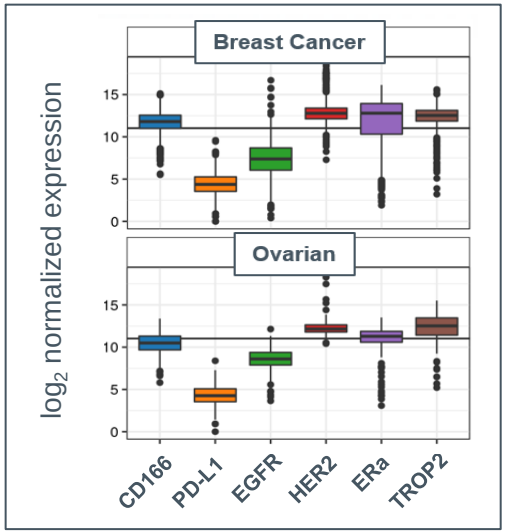

# Praluzatamab Ravtansine (CX-2009)

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

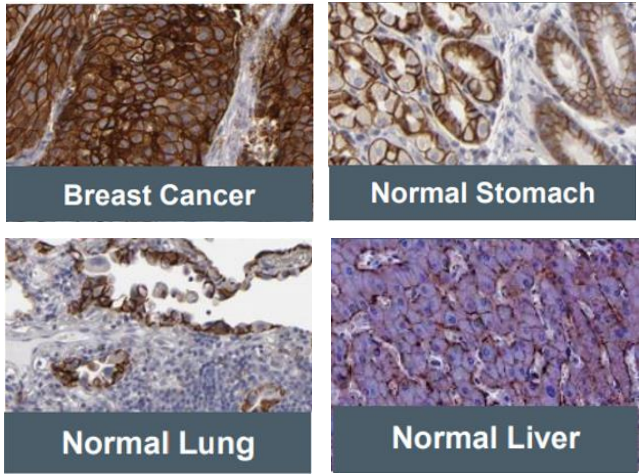
# CD166 is a Novel ADC Target with High Tumor Expression

## Undruggable Using Conventional ADC Because of High Expression on Normal Tissue

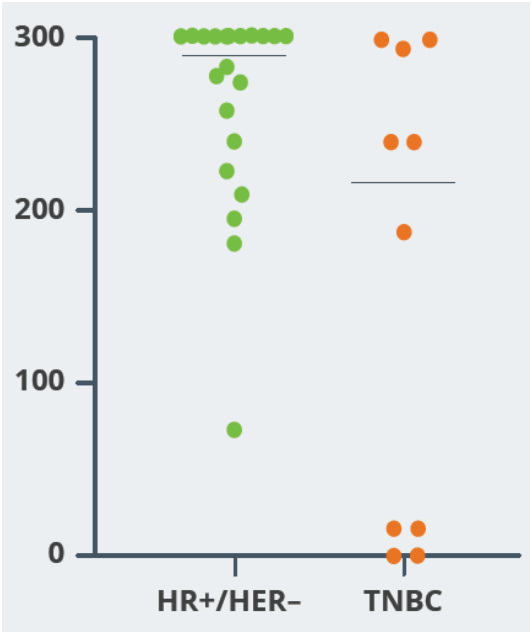
### High Expression on Tumors




### High CD166 Expression by IHC



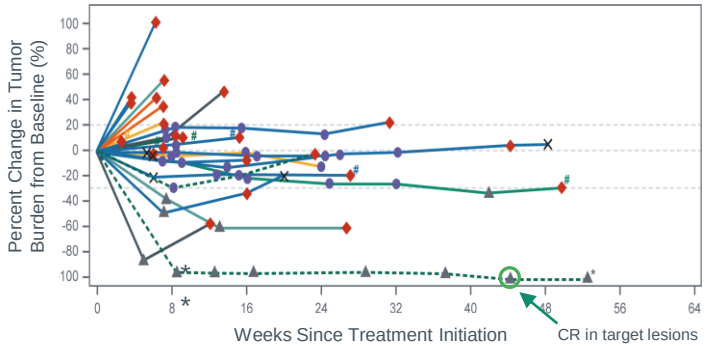

### CD166 Expression (H-Score) in Breast Cancer Patients




Source: Lui J. et al SABCS 2020; PS 11-07

# Praluzatamab Ravtansine Demonstrated Meaningful Clinical Benefit in Breast Cancer in Phase 1

**Heavily pretreated patients with measurable disease who received ≥ 4 mg/kg CX-2009**




| 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

## Other Key Takeaways from Phase 1 Study

- **Recommended Phase 2 dose**
  - 7 mg/kg Q3W
- **Toxicity profile consistent with DM4 payload**
  - Ocular, neuropathic and hepatic

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Source: Lui J. et al SABCS 2020; PS 11-07

# Ongoing Multi-Arm Breast Cancer Phase 2 Study

## Initial Data Readout Expected in 2022

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

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*Efficacy evaluable, ** Naing, A. et al. J Immunother Cancer 2021;9:e002447

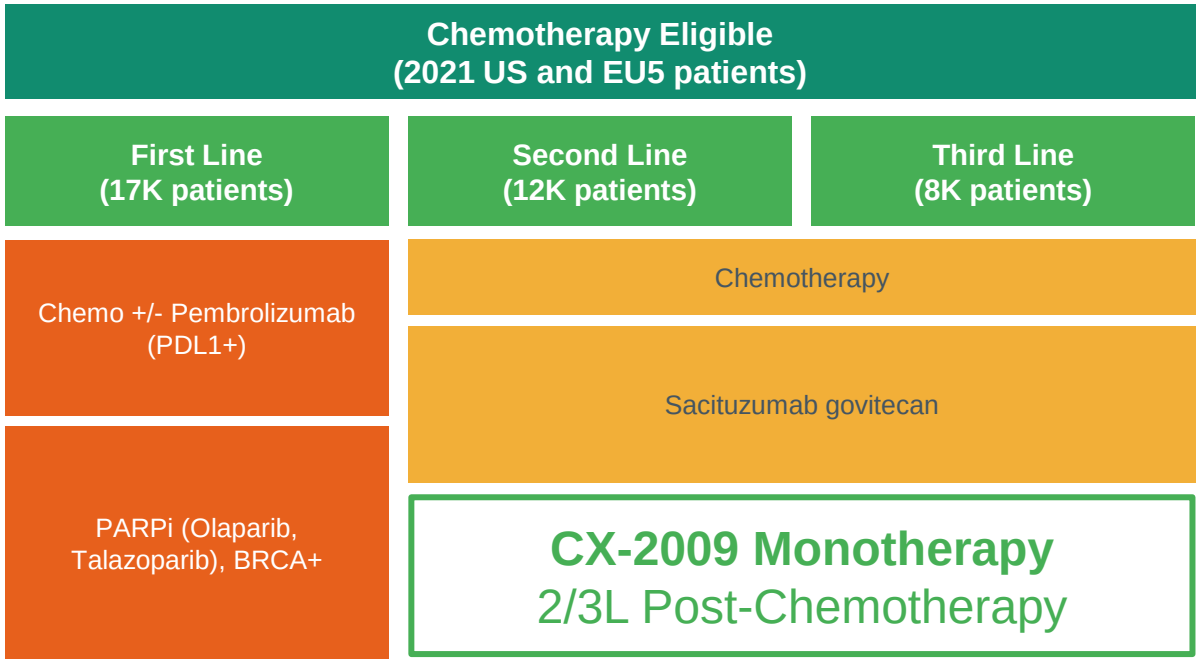
# Praluzatamab Ravtansine Has Broad Potential in Current HR+/HER2– Treatment Paradigm

| Hormone Therapy Eligible (2021 US and EU5 patients) | |
|---|---|
| **First Line (82K patients)** | **Second Line (53K patients)** |
| Hormone therapy +/- CDK4/6 (Abemaciclib, ribociclib, Palbociclib) | Hormone therapy +/- PI3K (Alpelisib) |
| | Hormone therapy +/- mTOR (Everolimus) |
| | PARPi (Olaparib, Talazoparib) +/- Hormone therapy, |

| Chemotherapy Eligible (2021 US and EU5 patients) | | |
|---|---|---|
| **Chemo-Naïve* (88K patients)** | **Post One Line Chemo (78K patients)** | **Post Two Lines Chemo (63K patients)** |
| **CX-2009 monotherapy** 0-2 prior lines of chemotherapy, post-endocrine therapy | | |

Sources: NCCN Breast Cancer Guidelines, 2021; DRG Breast Cancer Treatment 2021; GlobalData HER2- Epidemiology and Forecast 2020; CytomX analysis

# Praluzatamab Ravtansine Has Broad Potential in Current TNBC Treatment Paradigm




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

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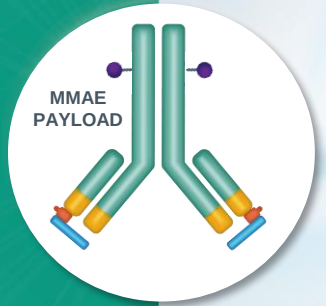


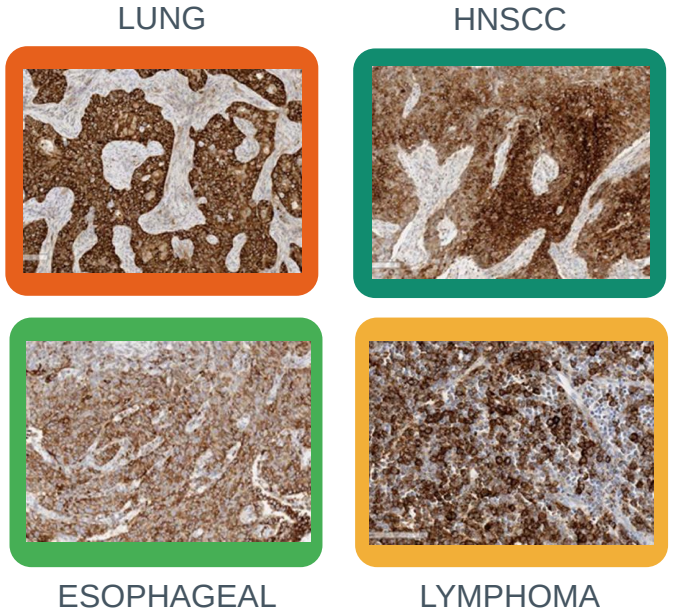

# CX-2029

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

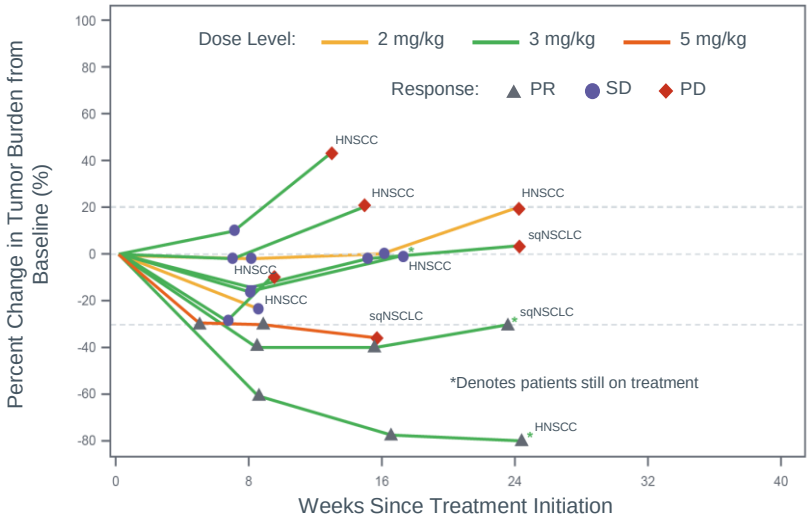
**CD71 Expression by IHC**




Data generated by CytomX

# CX-2029 Phase 1 Clinical Activity in Squamous Cancers

**sqNSCLC or HNSCC patients with measurable disease who received ≥ 2 mg/kg CX-2029**




- **> 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**

Source: Johnson M. et al Clin Cancer Res. 2021; 1078-0432.CCR-21-0194

# Ongoing Multi-Cohort CX-2029 Phase 2 Expansion Study

## Monotherapy at 3 mg/kg Every Three Weeks (Q3W)

### Key Eligibility

**sqNSCLC, HNSCC and esophageal/GEJ**

- Prior platinum and checkpoint inhibitor required
- Documented progression after at least one systemic regimen for advanced disease

**DLBCL**

- ≥2 prior regimens (including 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*

### 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:**
Preliminary data for sqNSCLC and HNSCC reported Dec 2021

*Efficacy evaluable

# CX-2029 Interim Phase 2 ORR of 18.8% in 3L+ SqNSCLC
## Enrollment Continues

### 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

### Interim 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

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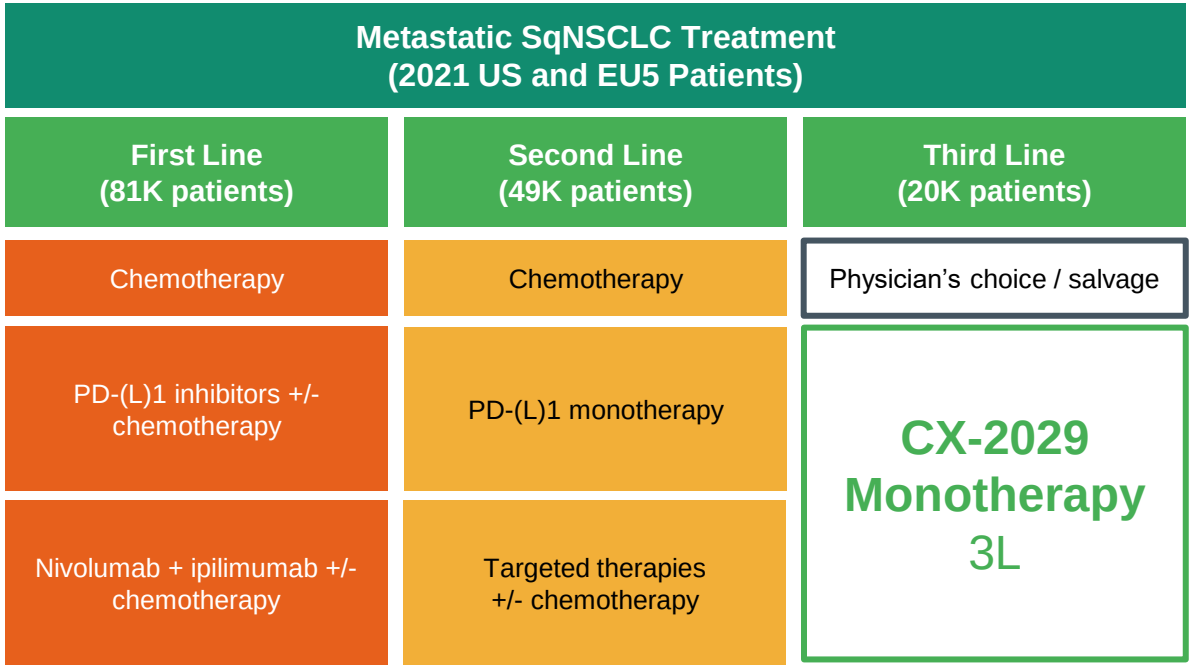
# Emerging Opportunity for CX-2029 in 3L+ SqNSCLC




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

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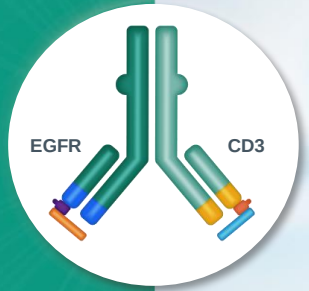
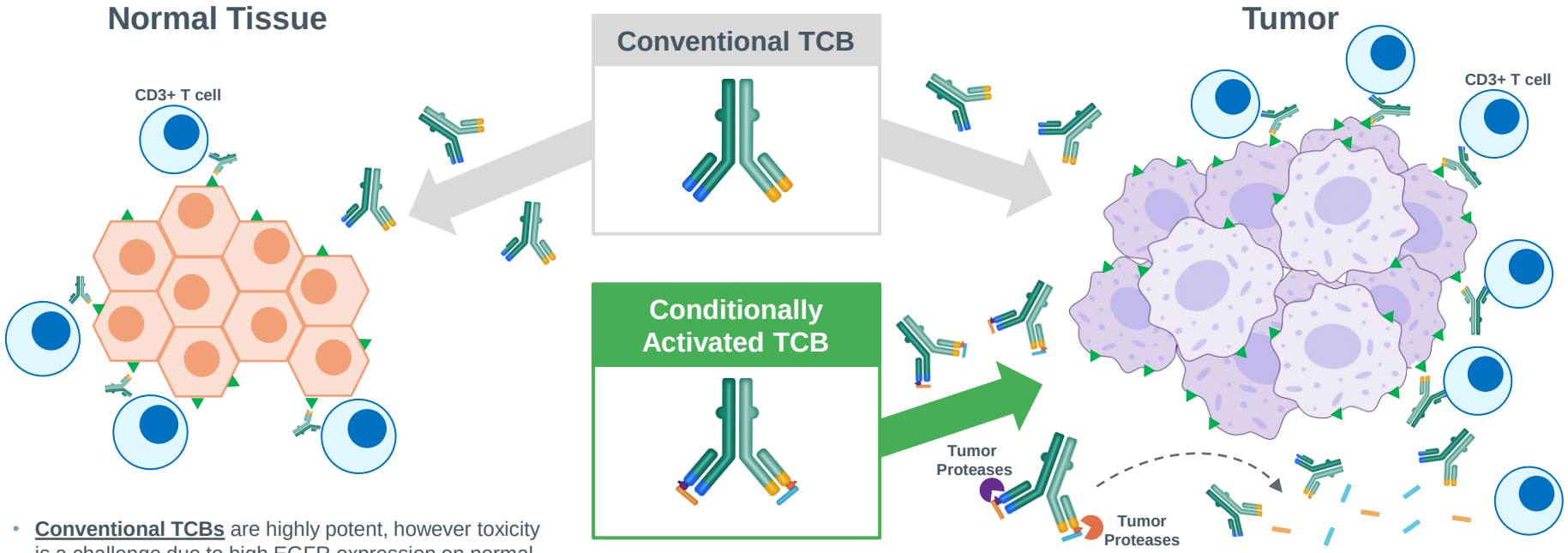



# CX-904

## 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

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# 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

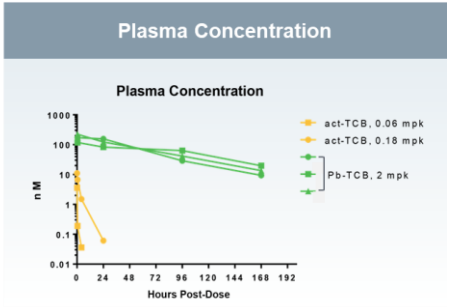
## Increases MTD

| 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

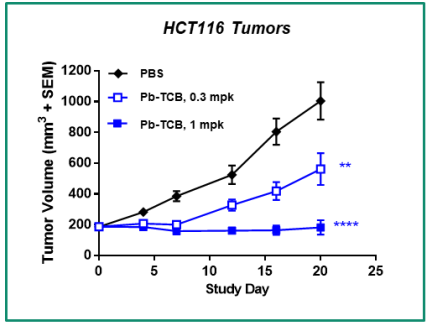
MTD increases by >60-fold with conditionally activated TCB (Pb-TCB)

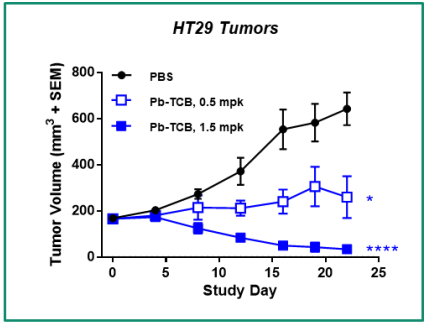
## Extends PK




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

**Initiating First-in-Human Phase 1 Dose-Escalation Study of CX-904 in 2022**

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Source: Boustany L. et al AACR-NCI-EORTC International Conference on Molecular Targets 2017

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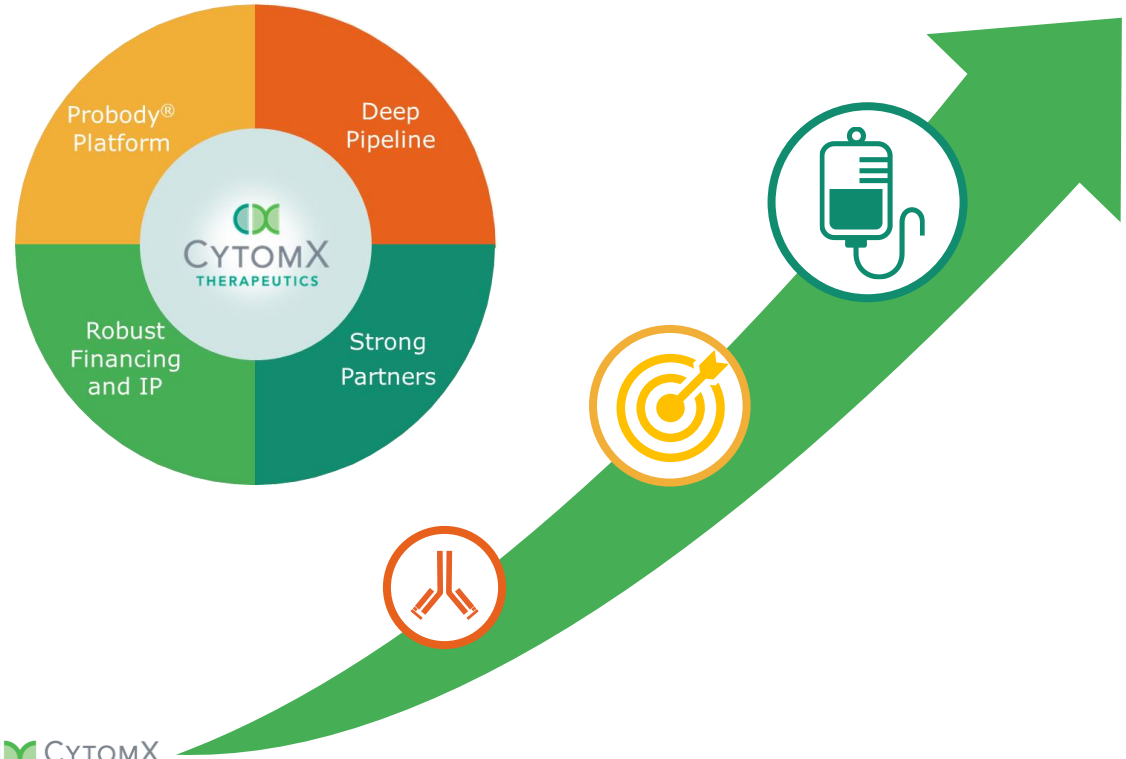
# Summary and Milestones

# Leading Platform, Deepest Pipeline, Broadest Clinical Experience

## 4 Assets in 11 Phase 2 Studies in 9 Cancer Types

| Modality | Product Candidate | Target-Payload | Indication | Preclinical | Phase 1 | Phase 2 | Commercial Rights |
|---|---|---|---|---|---|---|---|
| Antibody-Drug Conjugate | Praluzatamab ravtansine (CX-2009) | CD166-DM4 | HR+/HER2-non-amp BC | | | | CytomX |
| | | | TNBC | | | | |
| | | | + pacmilimab (CX-072) | | | | |
| | CX-2029 | CD71-MMAE | Squamous NSCLC | | | | CytomX abbvie |
| | | | HNSCC | | | | |
| | | | Esophageal/GEJ | | | | |
| | | | DLBCL | | | | |
| | CX-2043 | EpCAM-DM21 | Solid tumors | | | | 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 | |
| TCB | CX-904 | EGFRxCD3 | TBD | IND filed | | | CytomX AMGEN |
| Cytokine | TBD | IFN-a2b | TBD | | | | CytomX |

# Continued Leadership and Execution in 2022




## 2022 Outlook

- Initial praluzatamab ravtansine (CX-2009) Phase 2 data in breast cancer (Arms A & B)
- Expansion phase completion for CX-2029 and new data updates
- CX-904 Phase 1 study initiation
- Early-stage pipeline progress including cytokine program

# Questions and Answers