

# **CX-2029, a Probody Drug Conjugate Targeting CD71 in Patients with Selected Tumor Types: PROCLAIM-CX-2029 Dose Expansion Phase**

Melissa Johnson<sup>1</sup>, Jordi Rodon Ahnert<sup>2</sup>, Nehal Lakhani<sup>3</sup>, Rachel E. Sanborn<sup>4</sup>, Anthony El-Khoueiry<sup>5</sup>, Navid Hafez<sup>6</sup>,  
Hirva Mamdani<sup>7</sup>, Valentina Boni<sup>8</sup>, Henry Castro<sup>9</sup>, Alison L. Hannah<sup>9</sup>, Alexander Spira<sup>10</sup>

<sup>1</sup>Sarah Cannon Research Institute, Nashville, TN, USA; <sup>2</sup>MD Anderson Cancer Center, Houston, TX, USA; <sup>3</sup>START Midwest, Grand Rapids, MI, USA;

<sup>4</sup>Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; <sup>5</sup>USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA;

<sup>6</sup>Yale University School of Medicine, New Haven, CT, USA; <sup>7</sup>Barbara Ann Karmanos Cancer Institute, Detroit, MI, USA; <sup>8</sup>START Madrid CIOCC Madrid, Spain,

<sup>9</sup>CytomX Therapeutics, Inc., South San Francisco, CA, USA; <sup>10</sup>Virginia Cancer Specialists, Fairfax, VA, USA



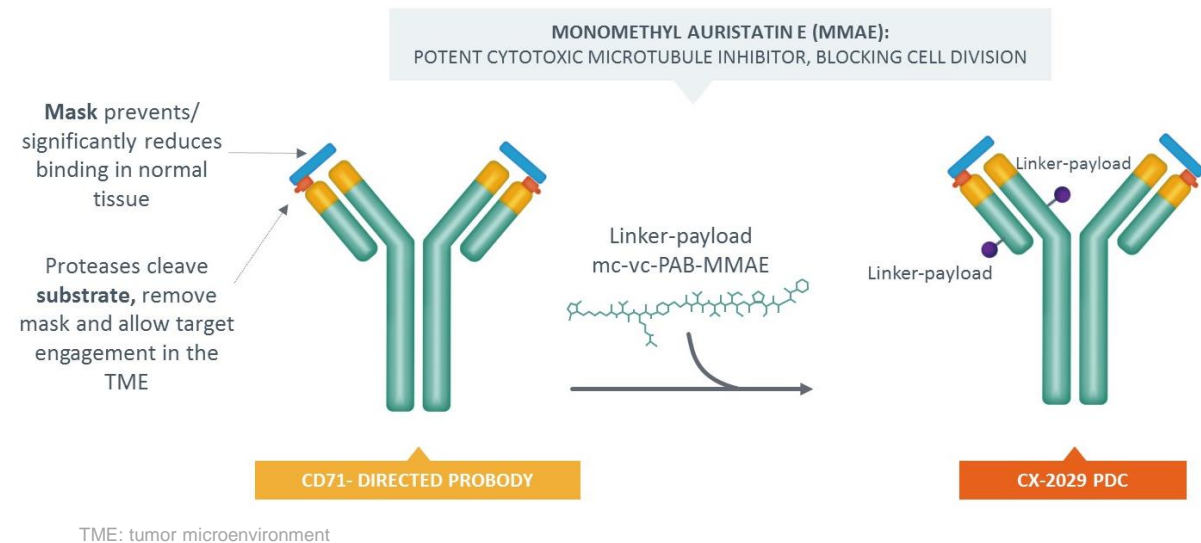
2020 World Conference  
on Lung Cancer Singapore

JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT

# Background

## Introduction

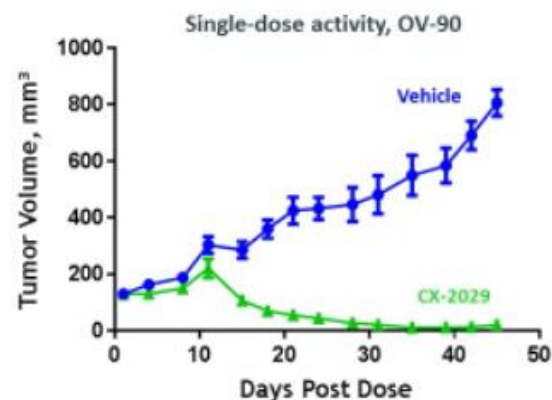
- Probody<sup>®</sup> drug conjugates (PDCs) are conditionally activated masked ADCs, unmasked by tumor-associated proteases, thereby restricting target engagement to the tumor.
- Iron is essential to fundamental metabolic processes of human cells. Regulation of iron metabolism involves transferrin (Tf), among other proteins.<sup>1</sup>
- CD71, also known as Tf receptor 1 (TfR1), is a transmembrane glycoprotein that facilitates cellular uptake of iron through the binding and internalization of iron-bound Tf.<sup>2</sup>
- CD71 is highly expressed on the surface of malignant cells and healthy cells with high iron requirements (eg, rapidly dividing cells, hematopoietic precursors).<sup>2,3</sup>
- CD71 expression on normal cells precludes the use of "traditional" antibody-drug conjugate (ADC) targeting due to lethal on-target toxicity.
- CX-2029 is a PDC directed against CD71 that contains monomethyl auristatin E (MMAE), a potent microtubule inhibitor.



# Introduction (Cont'd)

- CX-2029 demonstrated antitumor activity in mouse tumor models, suggesting proteolytic cleavage, unmasking, CD71 target engagement, and delivery of MMAE preferentially in the tumor microenvironment.
- CX-2029 is tolerated by cynomolgus monkeys up to 6 mg/kg whereas CD71 ADC is lethal at 2.0 mg/kg due to neutropenic sepsis.

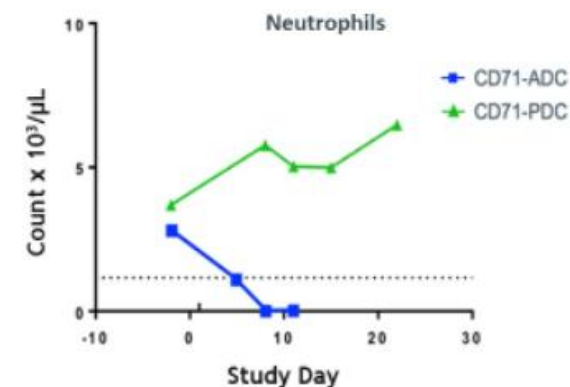
PDC REGRESSES TUMORS AFTER A SINGLE DOSE IN MICE



PDC HAS EFFICACY ACROSS MULTIPLE CELL LINE / PDX NON-CLINICAL MODELS

Models Type	Regression or Stasis
Cell-line derived (unselected)	15/21 (71%)
Patient-derived (high CD-71 expressing)	30/36 (83%)

IN NON-HUMAN PRIMATES, PDC BROADENS THERAPEUTIC INDEX

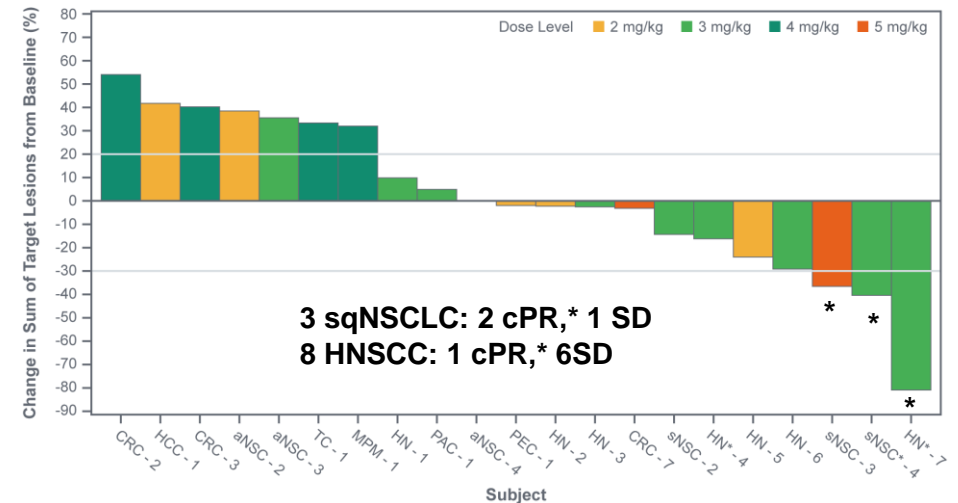


ADC, antibody-drug conjugate  
PDC, Probody-drug conjugate

# PROCLAIM-CX-2029 Dose Escalation

- PROCLAIM-CX-2029 is an open-label, phase 1/2 study (**NCT03543813**) evaluating CX-2029 in patients with advanced solid tumors or diffuse large B-cell lymphoma (DLBCL).
- Results from the dose-escalation phase were previously reported.<sup>4</sup> Clinical activity was observed at doses of 2 mg/kg and higher (all confirmed responses were observed in squamous histologies: non-small cell lung cancer [NSCLC] and head and neck squamous cell cancer [HNSCC]).
- CX-2029 produced dose-dependent hematologic toxicities consistent with MMAE. Anemia was the most common hematologic toxicity.
- The recommended phase 2 dose (RP2D) of CX-2029, 3 mg/kg, will be studied in the dose-expansion phase.

## CX-2029 >: Confirmed Partial Responses in HNSCC and sqNSCLC



ACP=Adenoid cystic carcinoma of parotid gland, CRC=Colorectal Cancer, HCC=Hepatocellular carcinoma, HN=Head and neck squamous cell carcinoma, MPM=Malignant pleural mesothelioma, NSC=Non-small cell lung carcinoma, aNSC=Non-small cell lung carcinoma (Adenocarcinoma), sNSC=Non-small cell lung carcinoma (Squamous cell carcinoma), OC=Ovarian cancer, OCP=Oncocytic carcinoma of parotid gland, OM=Ocular melanoma, PAC=Pancreatic cancer, PC=Prostate cancer, PEC=Perivascular epithelioid cell tumor, STS=Soft tissue sarcoma, TCC=Bladder Cancer, TC=Thyroid carcinoma, TH=Thymoma or thymic cancers. RC, CRC, and HCC are less/not sensitive to microtubule inhibitors (MTIs). \* Denotes patients still on treatment.

Data cut-off: Aug 14, 2020.

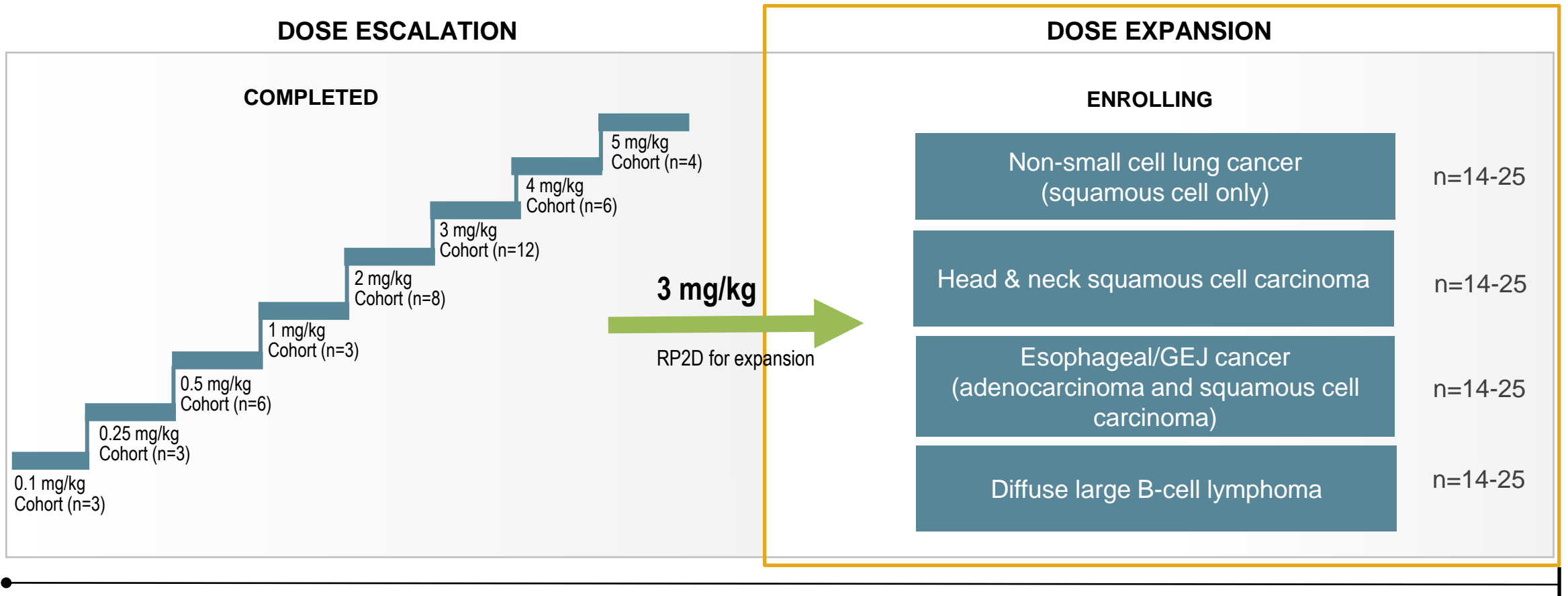
# PROCLAIM-CX-2029 Dose Expansion Phase

## Objective

- Evaluate the antitumor activity of CX-2029 in patients with histologically or cytologically confirmed metastatic or locally advanced squamous NSCLC, HNSCC, esophageal/gastroesophageal junction (GEJ) and DLBCL in expanded cohorts using the maximum tolerated dose (MTD)/RP2D.

# Study Schema

- In the dose-expansion phase, patients will have one of 4 selected tumor types (Figure).
- The initial cohorts will enroll up to 14 patients in each tumor type. An additional 11 patients may be enrolled in each of cohorts up to a maximum of 25 patients per tumor type.
  - A Simon's 2-stage optimal design is being employed, the enrollment of these additional 11 patients will require 1 or more responders observed from the initial dose cohort of 14 patients, including any patients in Part B treated at the MTD/RP2D, if appropriate.
- CX-2029 will be administered at 3 mg/kg by intravenous infusion every 21 days until disease progression, unacceptable toxicity, or other reason for discontinuation.



GEJ, gastroesophageal junction; RP2D, recommended phase 2 dose



# Endpoints (Dose Expansion)

## Primary Endpoint

- Overall response rate by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 or modified Lugano classification for DLBCL.

## Secondary Endpoints

- Duration of response
- Time to response
- Progression-free survival
- Overall survival
- Safety
- Pharmacokinetics of CX-2029 (total and intact) and MMAE (conjugated and unconjugated)
- Antidrug antibody formation to CX-2029

## Exploratory Endpoints

- Predictive biomarker analysis (eg, CD71 expression in tissue samples collected prior to treatment, and cancer molecular/mutation signatures)
- Protease activity and cleavage of CX-2029 in tumor biopsies and peripheral blood



# Eligibility Criteria

## Key Inclusion Criteria for Patients Entering Dose Expansion

- Age  $\geq$ 18 years
- Histologically or cytologically confirmed metastatic or locally advanced unresectable HNSCC, NSCLC (squamous cell histology only), or esophageal cancer (esophageal adenocarcinoma [EAC], esophageal squamous cell carcinoma [ESCC], or gastroesophageal junction [GEJ] cancer) and DLBCL
- Measurable disease per RECIST v1.1 or for DLBCL must have at least one bi-dimensionally measurable disease site
- Eastern Cooperative Oncology Group performance status 0 to 1
- Treated and stable brain metastases permitted
- Agree to provide tumor tissue

# Key Inclusion Criteria for Patients Entering Dose Expansion (cont'd)

- Documented progression or relapse after at least 1 prior systemic therapy and patients must have exhausted available life-prolonging therapies
  - Squamous NSCLC: must have received prior treatment with platinum-based therapy (unless intolerant or not suitable) and a PD-1/PD-L1 inhibitor. A checkpoint inhibitor should have been administered if approved for the patient's indication in their locality, alone or in combination with other therapy. If appropriate, patient should have received targeted therapy and progressed or shown intolerance to the therapy prior to enrollment.
  - HNSCC and esophageal cancer: must have received a platinum-containing regimen (unless intolerant or not suitable) and a programmed cell death protein 1 (PD-1) inhibitor if approved for patient's indication in their locality.
  - Esophageal cancer: should have received at least 1 line of systemic chemotherapy or chemoradiation, unless intolerant or not suitable. Patients with known human epidermal growth factor receptor 2 (HER2)-overexpressing tumors should have received treatment with HER2-targeted therapy.
  - DLBCL: must have relapsed or refractory disease after 2 lines of systemic therapy. At least 1 line should contain anti-CD20–based immunochemotherapy, and patients should not be candidates for autologous hematopoietic stem cell transplantation.

# Key Exclusion Criteria

- Neuropathy grade  $\geq 1$
- Unresolved acute toxicity grade  $>1$  (or baseline, whichever is greater) from prior anticancer therapy
- Chemotherapy, non-biological anticancer therapies and radiotherapy within 14 days prior to study drug initiation; biologics (monoclonal antibodies) within 30 days prior to study drug initiation
- Clinically significant iron metabolism disorders (eg, sickle cell anemia)
- Transfusion-dependent anemia with transfusion of at least one unit of packed red blood cells required every 90 days to maintain hemoglobin  $>10$  g/dL over the past 12 months
- Use of iron chelators

# Study Status

- Enrollment in the dose expansion phase is currently underway.
- The study is currently enrolling in the US, UK, and Spain.\*
  - United States
    - Los Angeles, California
    - New Haven, Connecticut
    - Hattiesburg, Mississippi
    - New York, New York
    - Portland, Oregon
    - Nashville, Tennessee
    - Houston, Texas
    - Fairfax, Virginia
  - Spain
    - Barcelona
    - Madrid
  - United Kingdom
    - Withington, Manchester Greater
    - Glasgow

\*Enrollment as of January 11<sup>th</sup>, 2021

# References

1. Hentze MW, Muckenthaler MU, Galy B, et al. *Cell*. 2010; 142:24-38.
2. Elliott RL, Head JF. *J Cancer Ther*. 2012;3:278-311.
3. Trowbridge IS, Omary MB. *Proc Natl Acad Sci USA*. 1981;78:3039-3043.
4. Johnson M, El-Khoueiry A, Hafez N, et al. Presented at the American Society of Clinical Oncology Virtual Scientific Program. May 29, 2020. Abstr 3502.

# Acknowledgements

- This study was sponsored by CytomX Therapeutics in partnership with AbbVie, Inc. Editorial assistance funded by the study sponsor was provided by Phillips Gilmore Oncology.