CytomX Therapeutics

REIMAGINING THERAPEUTIC ANTIBODIES FOR THE TREATMENT OF CANCER

ASCO20 Virtual Scientific Program Presentation Review

MAY 29, 2020

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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; 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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Our Agenda

INTRODUCTION

Sean McCarthy, D. Phil. President CEO and Chairman

ASCO20: FIRST-IN-CLASS PROGRAMS: CX-2029 AND CX-2009

Alison L. Hannah, M.D., Chief Medical Officer

ASCO20: BEST-IN-CLASS PROGRAMS: BMS-986249 AND CX-072

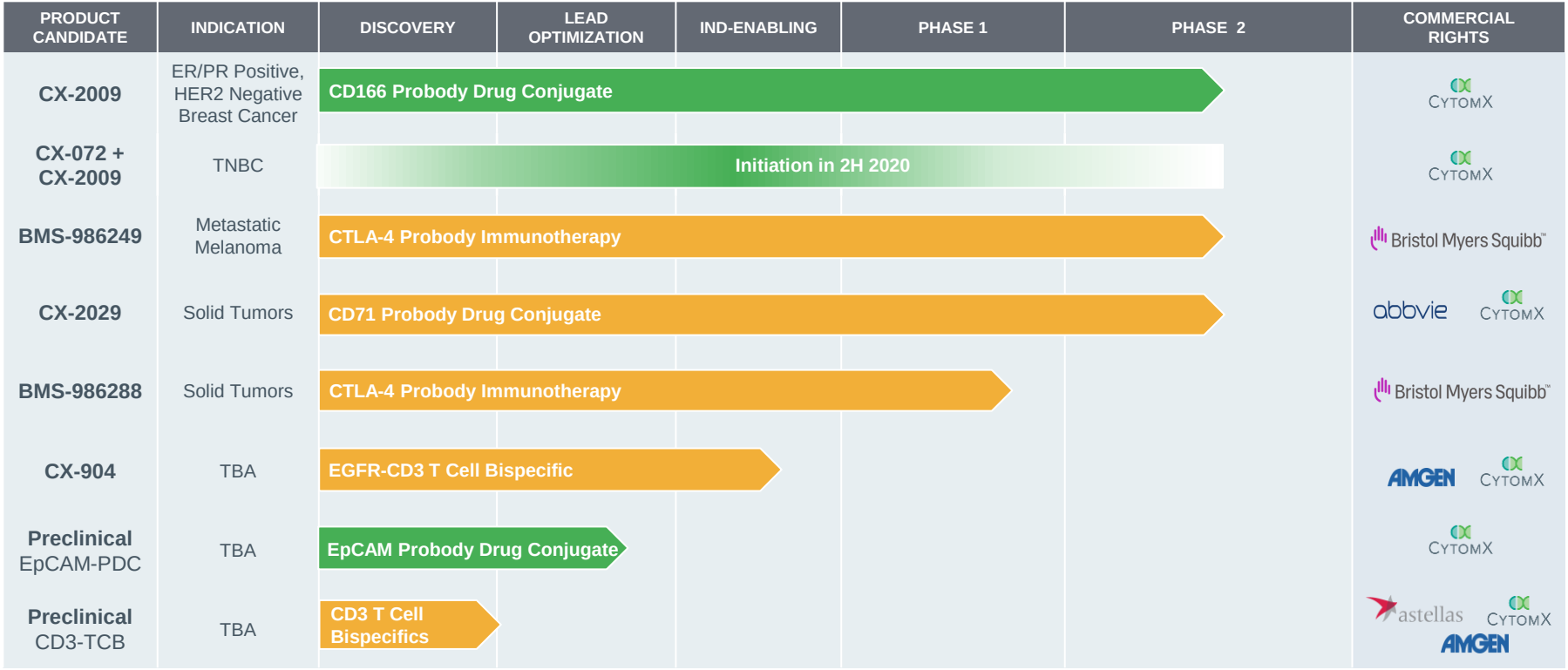
Amy Peterson, M.D., Chief Development Officer

CONCLUDING REMARKS

Sean McCarthy, D. Phil. President CEO and Chairman

QUESTIONS & ANSWERS

Probody Therapeutic Pipeline Advancing Across Multiple Stages of Development with Strong Progress in Wholly Owned and Partnered Programs



ASCO®20 Virtual SCIENTIFIC PROGRAM

Data Presentation from Four Clinical-Stage Probody Programs

First Clinical Data for CX-2029 Targeting Undruggable Target CD71

PROCLAIM CX-2029

CX-2029, a PROBODY Drug Conjugate Targeting CD71 (Transferrin Receptor): Results from a First-in-Human Study (PROCLAIM-CX-2029) in Patients (Pts) With Advanced Cancer (Oral Presentation)

abbvie

Updated Phase 1 and PK Data for CX-2009 Targeting Undruggable Target CD166

PROCLAIM CX-2009

CX-2009, A CD166-Directed PROBODY Drug Conjugate (PDC): Results From the First-in-Human Study in Patients With Advanced Cancer Including Breast Cancer

Preliminary Clinical Pharmacokinetics and Dose-Response to Support a Phase 2 Dose Selection for CX-2009: A Masked PROBODY Drug Conjugate to CD166

First Clinical Data for BMS-986249 Targeting CTLA-4

Anti–CTLA-4 Probody BMS-986249 Alone or in Combination with Nivolumab in Patients with Advanced Cancers: Initial Phase 1 Results

Bristol Myers Squibb

Updated Phase 1/2 Data for CX-072 (anti-PD-L1)

PROCLAIM CX-072

PROCLAIM-CX-072: Analysis of Patients With Advanced Solid Tumors Receiving Long-Term Treatment With CX-072, a PD-L1 PROBODY Therapeutic, as a Single Agent or in Combination With Ipilimumab (Oral Presentation)

Preliminary Population Pharmacokinetics Supports Phase 2 Dose Selection for Masked Anti–PD-L1 Antibody CX-072

Evidence of Intratumoral Localization, Activation, and Immunomodulatory Effect of CX-072, a PROBODY Therapeutic Targeting PD-L1, in a Phase 1/2 Trial

CytomX THERAPEUTICS

ASCO20: Broad Progress Across Our Pipeline

Growing evidence Probody Platform can unlock clinical potential in previously undruggable targets and enable improved immune checkpoint inhibition

Phase 1 data for CX-2029 (Anti-CD71) underpin recent $40 million AbbVie milestone and support Phase 2 expansion studies

- CX-2029 global co-development alliance with AbbVie with 35% US commercial rights retained

Phase 2 data for CX-2009 (Anti-CD166) support Breast Cancer Phase 2 Strategy
CX-2009 remains wholly-owned by CytomX

Continued progress with Probody Checkpoint Inhibitor programs

- BMS-986249 (Anti-CTLA4) Phase 1 data support ongoing randomized Phase 2 expansion in melanoma
- CX-072 (Anti-PD-L1) durable clinical benefit in multiple tumor types with favorable tolerability profile

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QUESTIONS & ANSWERS

Targeting Undruggable Targets with Probody Drug Conjugates

CX-2029 and CX-2009 and *Potential First-in-Class Agents with Demonstrated Single-Agent Clinical Activity*

ALISON L. HANNAH, M.D., CHIEF MEDICAL OFFICER

CX-2029, a PROBODY Drug Conjugate Targeting CD71 (Transferrin Receptor): Results From a First-in-Human study (PROCLAIM-CX-2029) in Patients With Advanced Cancer

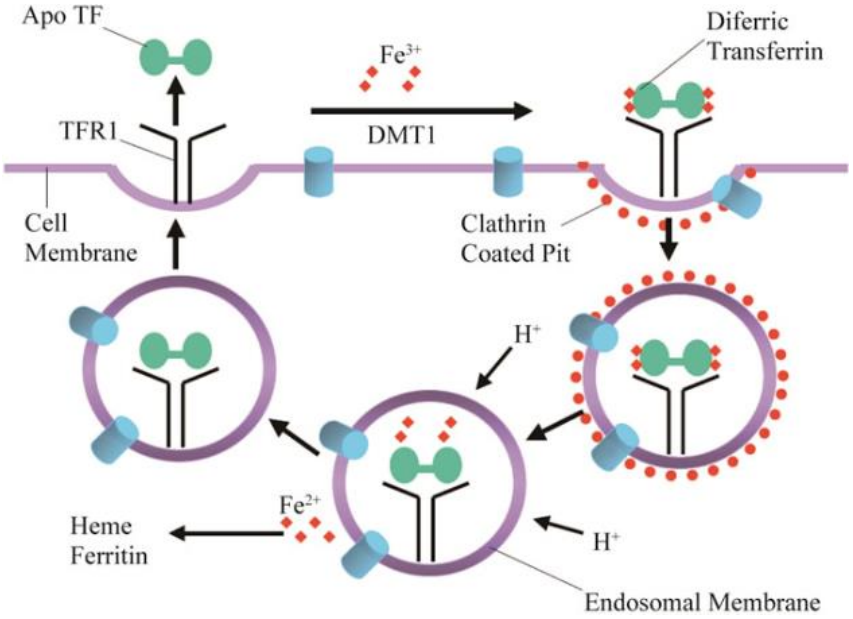
Melissa Johnson,[1] Anthony El-Khoueiry,[2] Navid Hafez[3,],Nehal Lakhani,[4] Hirva Mamdani,[5] Jordi Rodon,[6] Rachel E. Sanborn,[7] Thang Ho,[8] Rachel Li,[8] Jana Waldes,[8] and Alexander Spira[9]

[1]Sarah Cannon Research Institute, Nashville, TN; [2]University of Southern California, Los Angeles, CA; [3]Yale University, New Haven, CT; [4]START Midwest, Grand Rapids, MI; [5] Barbara Ann Karmanos Cancer Institute, Detroit, MI; [6]MD Anderson University, Houston, TX; [7]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR; [8]CytomX Therapeutics, Inc., South San Francisco, CA; [9]Virginia Cancer Specialists, US Oncology Research, Fairfax, VA

May 29, 2020

PROBODY Therapeutics: Investigating Undruggable Targets

- CD71 (transferrin receptor 1): attractive target for a PROBODY drug conjugate
  - CD71 is a transmembrane glycoprotein that efficiently internalizes iron-bound transferrin
  - Highly expressed on malignant cells
  - Expressed in healthy tissue with high iron requirements (e.g., rapidly dividing cells; hematopoietic precursors)
- CD71 expression in normal cells prohibits development of a traditional antibody drug conjugate (ADC) due to lethal on-target toxicity
- Probody therapeutics: recombinant antibody prodrugs designed to remain inactive in healthy tissue; activated in the tumor microenvironment by tumor-associated proteases



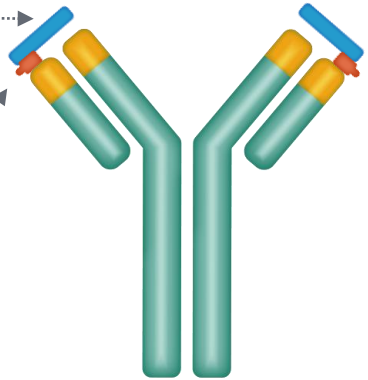
Elliott and Head. *J Cancer Ther. 2012;3:278-311.*

CX-2029: Probody Drug Conjugate Against CD71 with MMAE Warhead

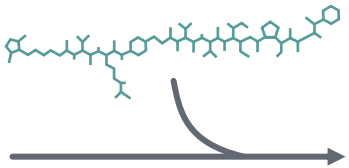
MONOMETHYL AURISTATIN E (MMAE):
POTENT CYTOTOXIC MICROTUBULE INHIBITOR, BLOCKING CELL DIVISION

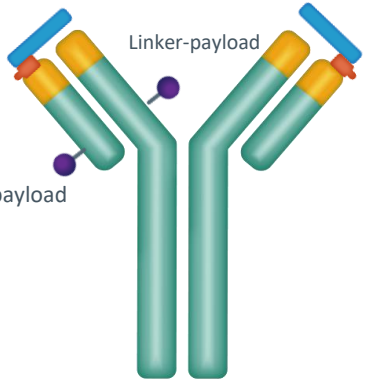
Mask prevents/ significantly reduces binding in normal tissue

Proteases cleave **substrate**, remove mask and allow target engagement in the TME



Linker-payload
mc-vc-PAB-MMAE





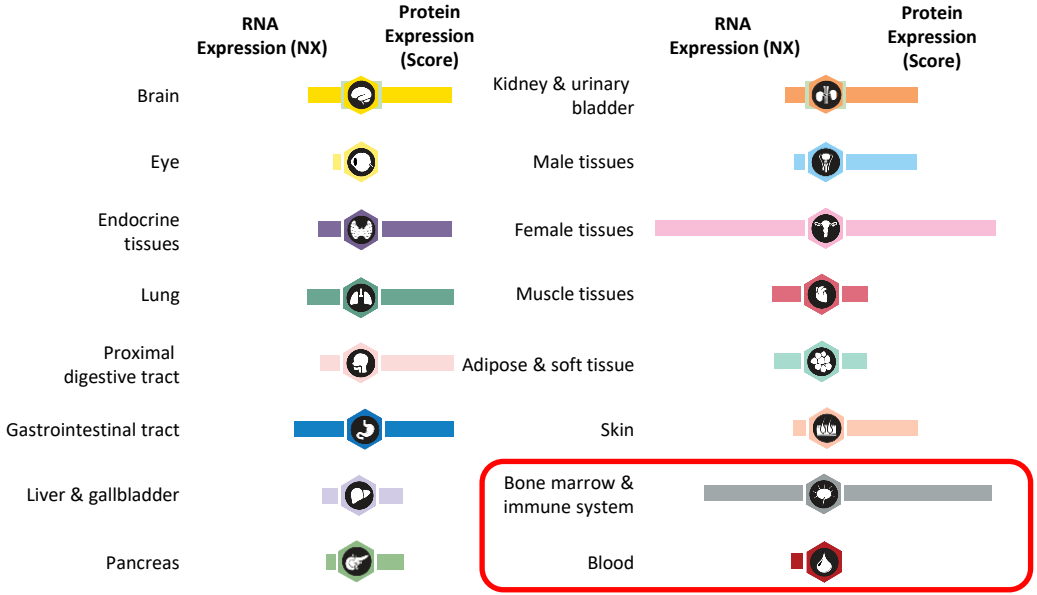
CD71- DIRECTED PROBODY

CX-2029 PDC

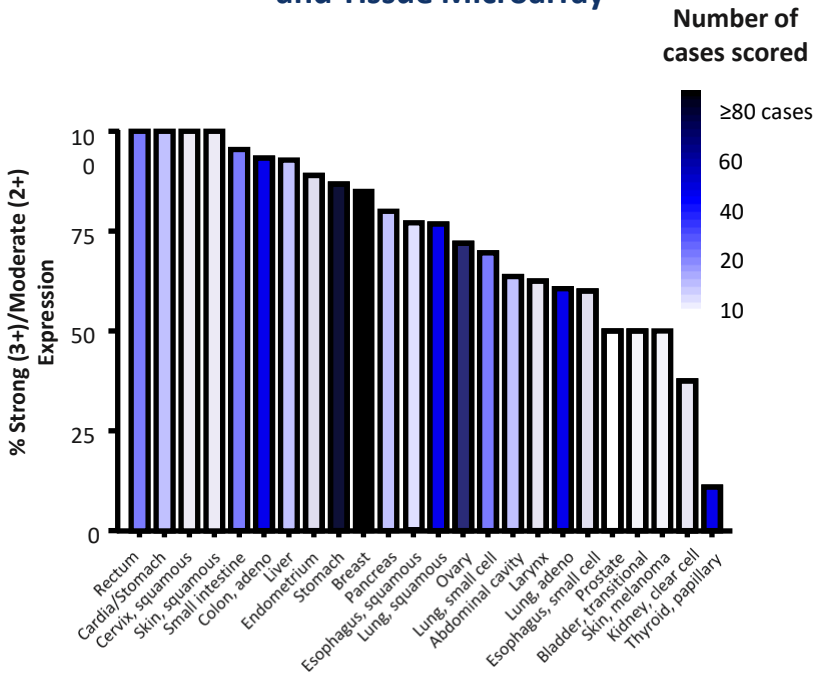
TME, tumor microenvironment.

Expression of CD71 in Healthy Tissue and Multiple Cancers

RNA and Protein Expression in Healthy Tissue



Expression by IHC using Commercial Antibody and Tissue Microarray



Adapted from The Human Protein Atlas
RNA and Protein Expression Summary/TRC available from proteinatlas.org/ENSG00000072274-TFRC/tissue.

Phase 1 Dose-Escalating Clinical Trial

Starting Dose

- Given nonclinical toxicity, broad expression of CD71, and novelty of target and platform, the starting dose was ~1/20 the HNSTD in the monkey
- Predicted toxicities (based on MMAE payload): hematopoietic suppression, neuropathy
- Nonclinical PK and toxicology predicted dose range of 2–4 mg/kg in patients

Key Eligibility Criteria

- Metastatic or locally advanced unresectable solid tumor
- ECOG 0 or 1
- 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

Intravenous Dose (every 3 weeks)	TOTAL (n)
0.1 mg/kg	3
0.25 mg/kg	3
0.5 mg/kg	6
1.0 mg/kg	3
2.0 mg/kg	8
3.0 mg/kg	12
4.0 mg/kg	6
5.0 mg/kg	4

13

HNSTD: Highest non severely toxic dose.

Demographics and Exposure

	All Cohorts (n=45)
Age, median (min, max)	60 (31, 75)
Sex, male / female (%)	62 / 38
Number of prior cancer treatments, median (min, max)	3 (1, 16)
Baseline ECOG 0 / 1, %	29 / 71
CD71 staining,* n (%)	
High expression [2+/3+ by IHC]	15 (33)
Low expression [0/1+ by IHC]	16 (36)
Unknown	14 (31)
Tumor types, n (%)	
NSCLC	9 (20)
HNSCC	8 (18)
Colorectal cancer	7 (16)
Soft tissue sarcoma	4 (9)
Prostate cancer	3 (7)
Other**	14 (31)
Number of CX-2029 doses administered, median (min, max)	3 (1, 12)
Duration of exposure in weeks, median (min, max)	9 (3, 36)

*CD71 expression was defined by overall tumor staining using a proprietary antibody.

**Other tumor types include adenoid cystic carcinoma of parotid gland (n=2); ovarian cancer (n=2); cutaneous melanoma (n=1); endometrial cancer (n=1); hepatocellular carcinoma (n=1); mesothelioma (n=1); ocular melanoma (n=1); oncocytic carcinoma of parotid gland (n=1); pancreatic cancer (n=1); perivascular epithelioid cell tumor (n=1); thymoma/thymic cancer (n=1); thyroid cancer (n=1).

Treatment-Related AEs (>10% of Patients; N=45)

	Patients, n (%)				
	CX-2029 1.0 mg/kg (n=3)	CX-2029 2.0 mg/kg (n=8)	CX-2029 3.0 mg/kg (n=12)	CX-2029 4.0 mg/kg (n=6)	CX-2029 5.0 mg/kg (n=4)
Infusion-related reaction	3 (100)	8 (100)	9 (75)	6 (100)	3 (75)
Anemia	2 (67)	6 (75)	9 (75)	5 (83)	4 (100)
Neutropenia	0	0	4 (33)	3 (50)	3 (75)
Fatigue	1 (33)	2 (25)	2 (17)	2 (33)	2 (50)
Leukopenia	1 (33)	0	3 (25)	2 (33)	2 (50)
Nausea	0	1 (13)	4 (33)	2 (33)	0
Decreased appetite	1 (33)	0	1 (8)	1 (17)	1 (25)
Vomiting	0	0	3 (25)	0	1 (25)

MMAE-predicted toxicity: anemia, neutropenia, thrombocytopenia

- Polatuzumab (grade 3 neutropenia 40%, anemia 11%)[1]
- Brentuximab (grade 3 neutropenia 20%, anemia 6%)[2]

MMAE-associated neuropathy: rarely seen to date (1 patient each with grade 1–2 neuropathy at 1 and 3 mg/kg)

- May be confounded by limited duration of CX-2029 therapy

1. Palanca-Wellis et al. *Lancet Oncol.* 2015;16:704. **2.** Younes et al. *J Clin Oncol.* 2012;30(18):2183.

Analysis combines Preferred Terms (eg, "neutropenia" and "decreased neutrophil count").

Treatment-Related Grade 3+ AEs; Transfusions

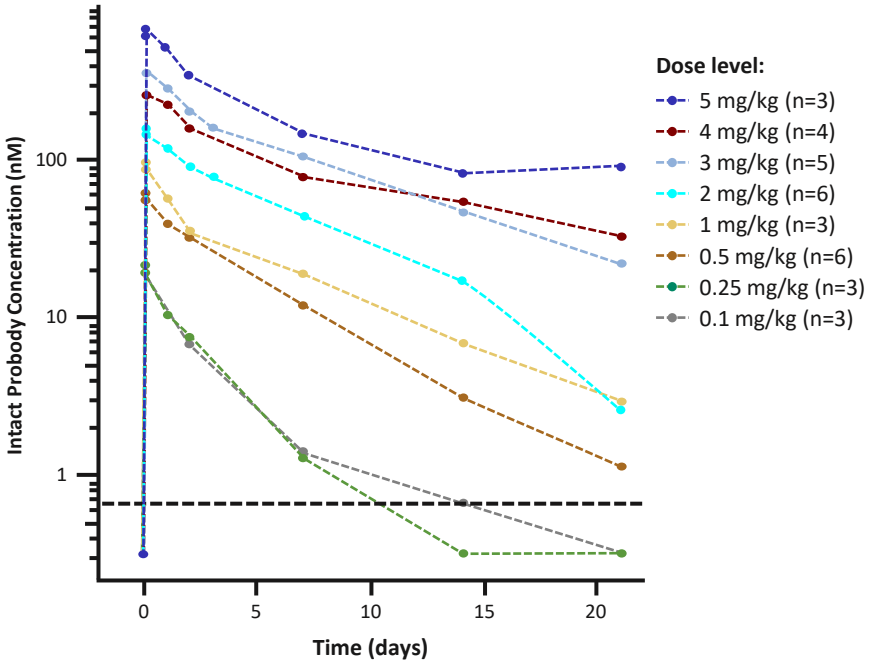
Treatment-Related Grade 3+ AEs (≥2 patients)	Patients, n (%)				
	CX-2029 1.0 mg/kg (n=3)	CX-2029 2.0 mg/kg (n=8)	CX-2029 3.0 mg/kg (n=12)	CX-2029 4.0 mg/kg (n=6)	CX-2029 5.0 mg/kg (n=4)
Anemia	1 (33)	5 (63)	7 (58)	5 (83)	4 (100)
Neutropenia	0	0	4 (33)	3 (50)	3 (75)
Leukopenia	0	0	1 (8)	2 (33)	2 (50)
Infusion-related reaction	0	1 (13)	0	1 (17)	0
PRBC Transfusions					
Patients with ≥1 RBC transfusion , n (%)	1 (33)	6 (75)	10 (83)	5 (83)	4 (100)
Number of RBC transfusions received, median	1	2	2	2	2
Time to first RBC transfusion, median, days	36	38	34	37	15

- No treatment-related deaths occurred
- Etiology of anemia is under active investigation

Analysis combines Preferred Terms (eg, “neutropenia” and “decreased neutrophil count”).

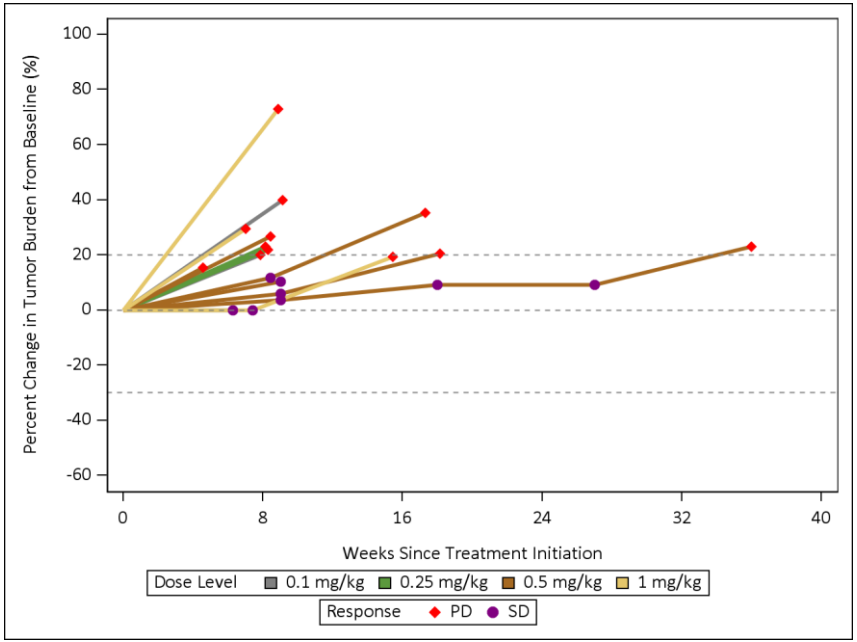
Pharmacokinetics

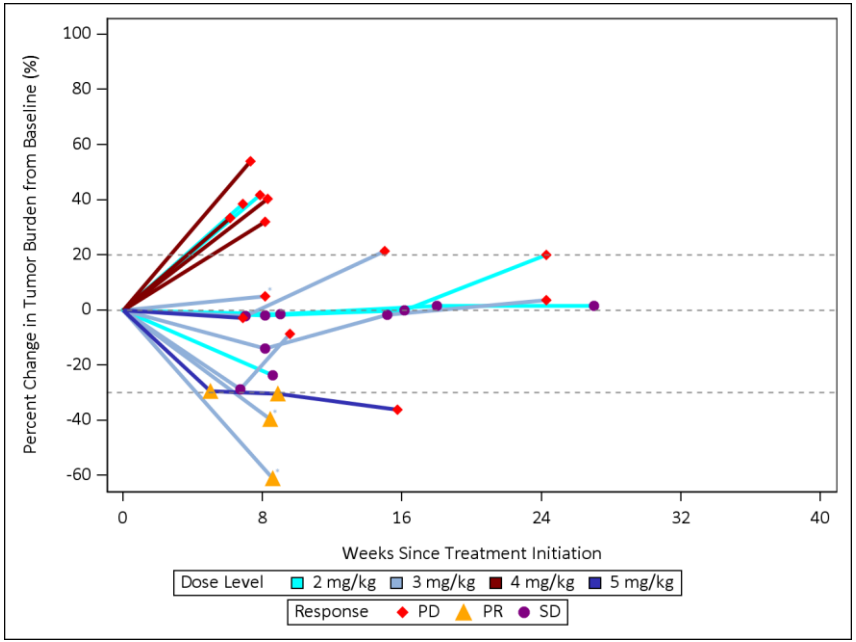
- Following 0.25–5.0 mg/kg, CX-2029 circulates predominantly as intact CX-2029 (>90%)
- For intact CX-2029:
  - No trends from dose-proportionality
  - Clearance 0.55–2.7 L/day
  - Volume of distribution 3.2–10.6 L
  - Terminal half-life 2.3–9.8 days
- Free MMAE circulates <4.3% of Total CX-2029



Spider Plot (Doses 0.1–1 and 2-5 mg/kg)

Clinical Activity at CX-2029 Doses ≥2 mg/kg

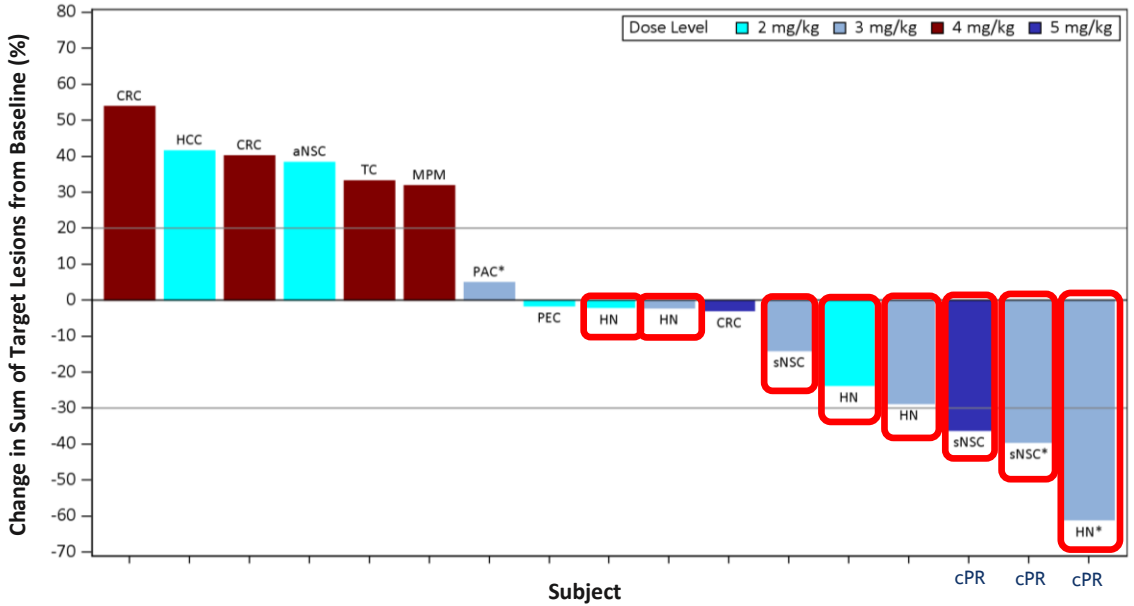




PD, progressive disease; PR, partial response; SD, stable disease.
*Patient on treatment as of data cut-off.

Data cut-off: April 20, 2020.

Waterfall Plot (Doses 2–5 mg/kg)



Activity predominantly seen in patients with tumors of squamous histology

aNSC = non–small cell lung cancer (adenocarcinoma), CRC = colorectal cancer, HCC = hepatocellular carcinoma, HN = head and neck squamous cell carcinoma, MPM = malignant pleural mesothelioma, PAC = pancreatic cancer, PEC = perivascular epithelioid cell tumor, sNSC=non–small cell lung cancer (squamous cell carcinoma), TC = thyroid carcinoma.

*Denotes subjects still on treatment.

13 patients not included due to (a) 5 patients ongoing without first on-study scan; (b) 6 patients discontinued without on-study scan; (c) 1 patient without measurable disease at baseline, and (d) 1 patient diagnosed with new lesion without target lesion(s) assessed.

All 3 patients with Target Lesions Shrinkage >30% are confirmed partial responses

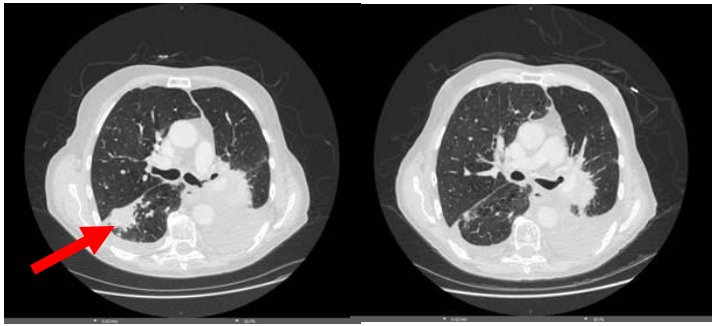
Data cut-off: April 20, 2020.

75-Year-Old Patient With Squamous NSCLC (3 mg/kg)

- **Patient:** diagnosed with stage III squamous NSCLC in August 2017
- **Prior therapy**: Carboplatin/paclitaxel with radiation (2 mo.); durvalumab (10 mo.); gemcitabine (2 mo.); docetaxel/ramucirumab (8 mo.; SD then PD)
- **Toxicity**: Cycle 2 and cycle 3 grade 3 anemia
- **Response**: confirmed partial response seen on Week 8 (12Mar20) and Week 16 (4May20) scans

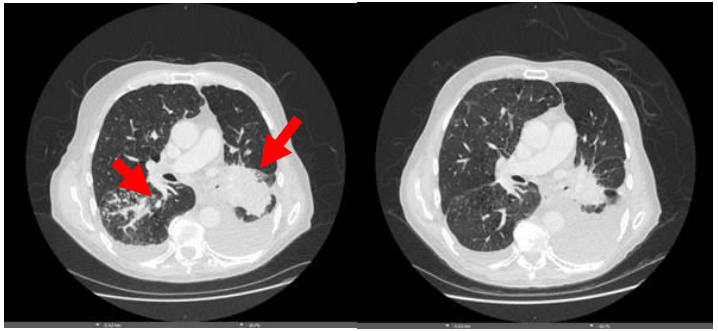
20 Jan 2020 **12 Mar 2020**

Near-resolution of right perifissural lesion (target lesion #2)



20 Jan 2020 **12 Mar 2020**

Improvement in LLL lesion (target lesion #1),
with marked improvement in RLL nodular lesions (nontarget lesions)



(Images are courtesy of Navid Hafez, MD)

66-Year-Old Patient with Squamous Head and Neck Carcinoma (3 mg/kg)

Cancer History

- Diagnosed with nasopharyngeal carcinoma in February 2018
- Prior therapy included: docetaxel/5FU/cisplatin with radiation (3 mo.); high-dose cisplatin (1 mo.); investigational agent (sEPHB4-HAS) + pembrolizumab (3 mo.; PD)

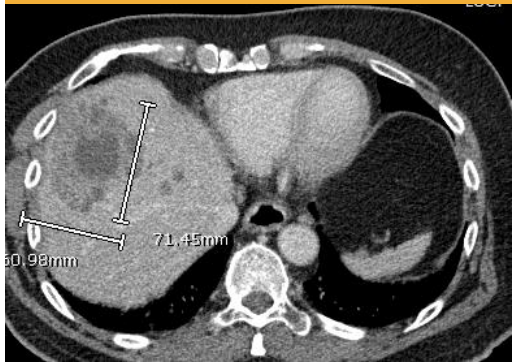
Relevant Past Medical History:

anemia, increased LFTs, HTN, neuropathy, dyspnea

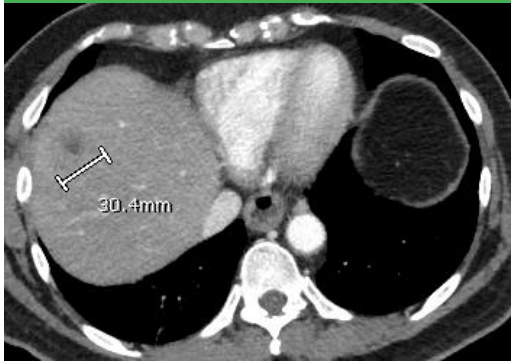
Initiated CX-2029: [14 Jan 2020]

- **Toxicity:** Cycle 1 grade 4 neutropenia (Neulasta) and grade 2 anemia; Cycles 2-4 grade 3 anemia managed with PRBCs, transfusions and **dose reduction to 2 mg/kg**; darbepoetin initiated Cycle 6
- **Response**: Partial response at Week 8 (13 Mar 2020) confirmed 8 weeks later (8 May 2020)

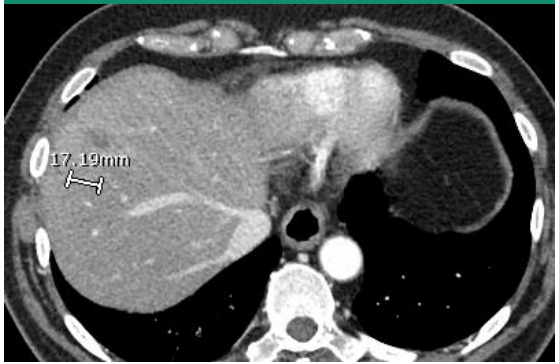
18 Dec 2019



13 Mar 2020 (43% ↓)



8 May 2020 (78% ↓)



CytomX Therapeutics

PROCLAIM® CX-2029

Summary and Conclusions

First-in-human trial results of CX-2029 validate CD71 (transferrin receptor 1) as a viable therapeutic target in cancer

Probody technology enables administration of an antibody drug conjugate against CD71, a previously undruggable ADC target, at tolerable doses with clinical anti-tumor activity

Dose-dependent hematologic toxicities consistent with MMAE payload

- Anemia, most common hematologic toxicity, is also seen in non-clinical species
- The etiology of the anemia is under investigation, but is likely multifactorial in nature, including both MMAE-associated toxicity and CD71 expression on RBC precursors.

Clinical activity was observed at doses of 2 mg/kg and higher

- Consistent with PK prediction
- Activity to date was observed in squamous histologies

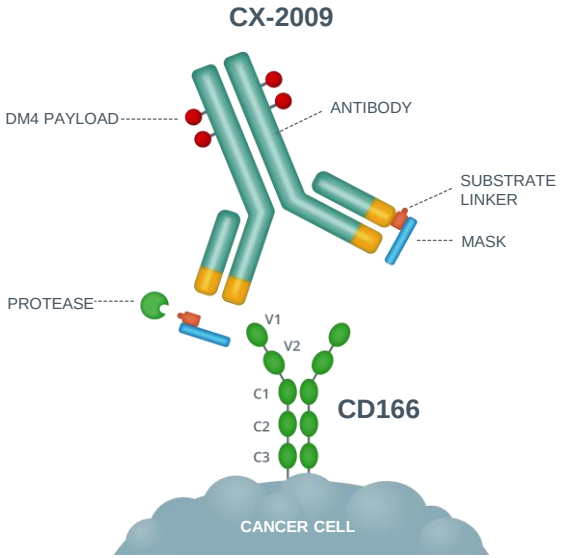
CX-2029, 3mg/kg, will be further evaluated in dose-expansion cohorts

- Including cohorts of HNSCC and squamous NSCLC

CytomX Therapeutics

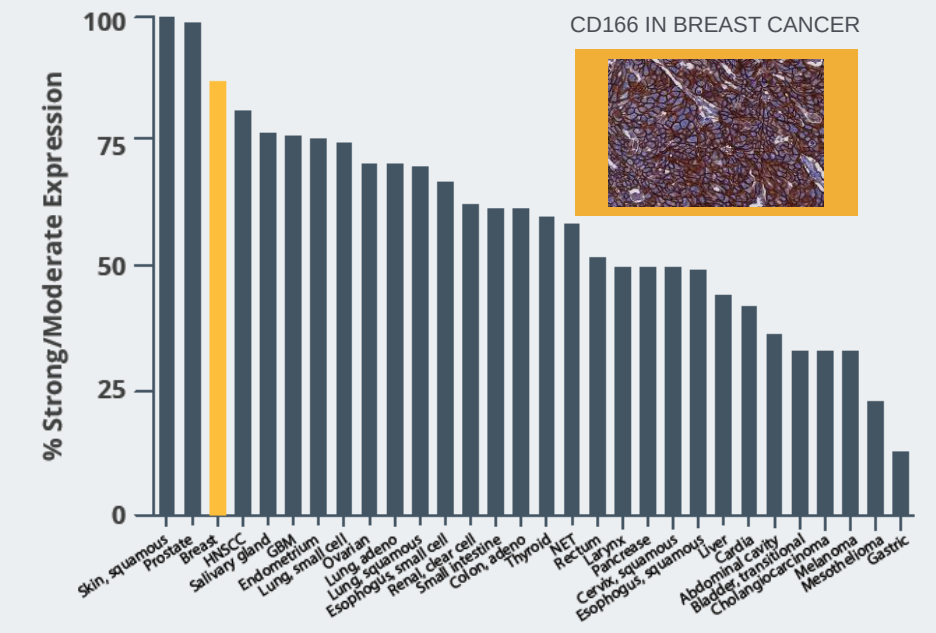
Targeting Undruggable Targets With Probody Drug Conjugates: CX-2009

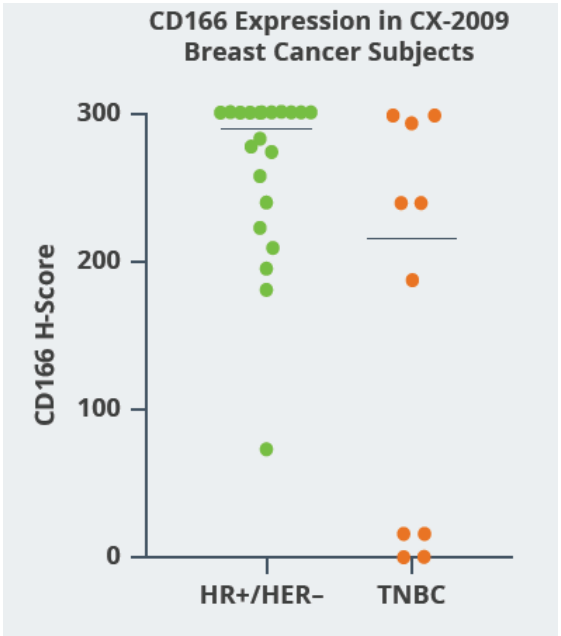
CX-2009: A Probody Drug Conjugate Targeting CD166 (ALCAM)



- CD166 (activated leukocyte cell adhesion molecule) is a transmembrane protein that functions as a junctional adhesion molecule, and facilitates cell migration, differentiation, and hematopoiesis.
- CD166 is a broadly and highly expressed tumor antigen
- CD166 is also present on normal tissues (eg GI, Liver, lung, pancreas)
- CX-2009 PDC applies our Probody technology to a proprietary anti-CD166 antibody coupled with a DM 4 payload
- DM4-maytansine payload
  - Microtubule inhibitor known to be active against a variety of cancers
  - Ocular, neuropathic and hepatic toxicities are well characterized DM4 related toxicities

High CD166 Expression is >80% for ER+/HER2–Breast Cancer and ~50% for Triple-negative Breast Cancer (TNBC)





GBM, glioblastoma; HNSCC, squamous cell carcinoma of the head and neck; NET, neuroendocrine tumor; TNBC, triple-negative breast cancer.

PROCLAIM CX-2009

Demographics and Baseline Characteristics

	Total N=96
Median age (range)	58.5 (31–79)
Male/female, n	21/75
White/Asian/African American/Other, n	78/5/2/11
ECOG PS 0/1, n	31/65
Cancer type, n (%)	
Breast cancer	42 (44)
Epithelial ovarian cancer	22 (23)
Non–small cell lung cancer	13 (14)
Head and neck squamous cell carcinoma	9 (9)
Cholangiocarcinoma	5 (5)
Endometrial carcinoma	3 (3)
Castration-resistant prostate cancer	2 (2)
Median no. prior treatments (range)	5 (1–9)
Median no. CX-2009 doses (range)	2 (1–15)

	TNBC (n=11)	HR+/HER2– (n=25)	Overall (n=36)
Median age, range	45 (31–68)	54 (37–77)	53 (31–77)
ECOG PS 0/1, n	4/7	11/14	15/21
CD166 by IHC, high/low/unknown, n	6/4/1	23/1/1	29/5/2
Median no. prior treatments (range)	7 (3–11)	8 (4–16)	7 (3–16)
Platinum, n	9	4	13
Microtubule inhibitor, n	11	24	35
PD-L1/PD-1 inhibitor, n	4	1	5
CDK 4/6 inhibitor, n	0	16	16
Median no. CX-2009 doses (range)	2 (1–16)	2 (1–16)	2 (1–14)

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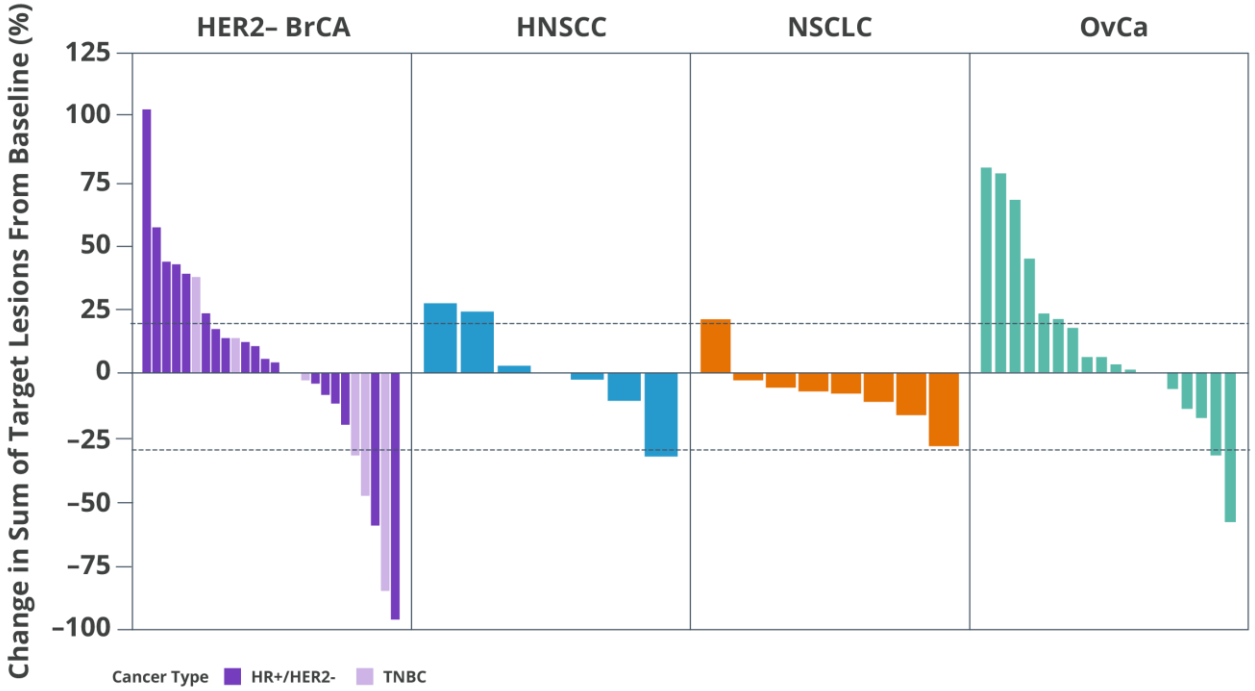
PROCLAIM CX-2009

Summary of Overall Adverse Events

Category, n	CX-2009 Dose (mg/kg)							
	≤4 Q3W (n=20)	5 Q3W (n=9)	6 Q3W (n=9)	7 Q3W (n=9)	8 Q3W (n=22)	9 Q3W (n=9)	6 Q2W (n=6)	10 Q3W (n=8)
TRAE	14	9	9	9	21	9	6	7
Grade 3+	1	3	2	2	14	5	3	4
Causing discontinuation	0	3	2	0	3	2	0	1
DLT	0	0	0	0	1	0	2	0
TRAE death	0	0	0	0	1*	0	0	0
Ocular AE	2	6	2	3	13	5	5	6
Grade 3+	0	1	0	0	3	3	2	1
Neuropathy	1	6	2	2	8	3	3	2
Grade 3+	0	1	1	1	0	1	1	0
Hepatic disorder	1	0	2	1	9	3	2	3
Grade 3+	0	0	0	0	4	0	1	3
Blood/lymphatic system disorders	1	0	0	1	6	0	1	0
Grade 3+	1	0	0	0	4	0	0	0

PROCLAIM CX-2009

Patients Receiving CX-2009 ≥4 mg/kg Every 3 Weeks



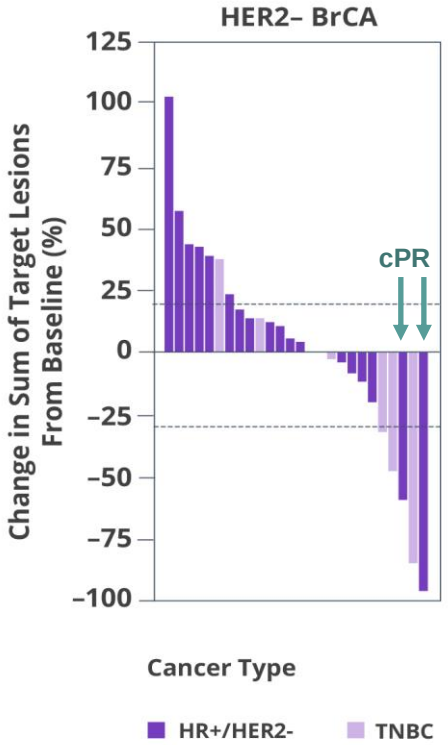
HER2- BrCA: HER 2 negative breast cancer; HNSCC: Head and neck squamous cell carcinoma; NSCLC: Non-small cell lung cancer; OvCa: Ovarian cancer; TNBC: Triple negative breast cancer

CytomX Therapeutics

ASCO 20 Virtual Scientific Program

PROCLAIM CX-2009

Evidence of Clinical Benefit in Patients with Breast Cancer Treated ≥4 mg/kg Every 3 Weeks



	Evaluable Breast Cancer Patients		
	TNBC (n=8)	HR+/HER2– (n=18)	All (n=26)
Response, n			
Confirmed PR	0	2	2
Unconfirmed PR	3	0	3
SD	1	8	9
PD	4	8	12
CBR16	4	6	10 (39%)
CBR24	4	5	9 (35%)

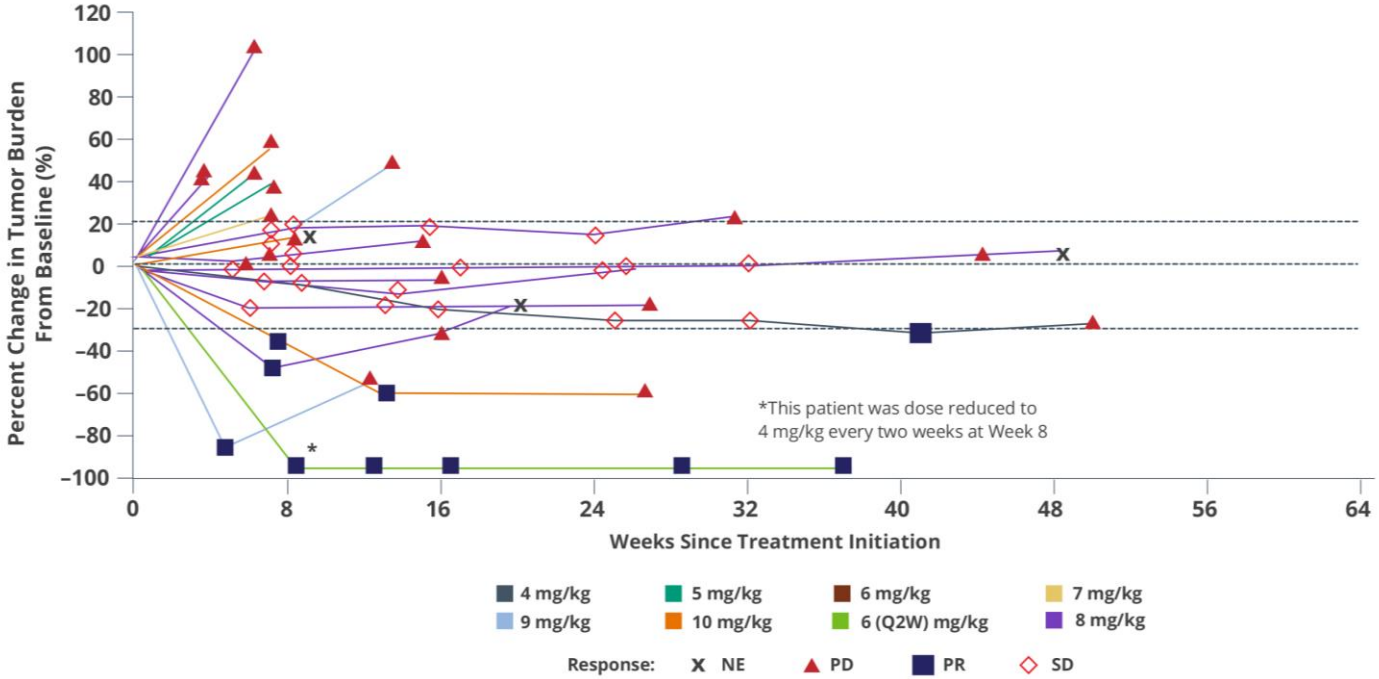
HER2- BrCA: HER 2 negative breast cancer; TNBC: Triple negative breast cancer

ASCO20 Virtual SCIENTIFIC PROGRAM

CytomX THERAPEUTICS

PROCLAIM CX-2009

Evidence of Clinical Benefit in Patients with Breast Cancer Treated ≥4 mg/kg Every 3 Weeks



ASCO20 Virtual SCIENTIFIC PROGRAM

CytomX THERAPEUTICS

PROCLAIM CX-2009

Summary

- First-in-Human trial results validate CD166 as a viable First-in-Class therapeutic target in cancer
- Probody platform works as designed, enabling administration of an antibody drug conjugate against CD166, a previously undruggable ADC target
- Toxicities observed are consistent with the DM4 payload and were manageable at a dose of 7mg/kg Q3W
- Confirmed partial responses and clinically meaningful disease control observed in patients with Her2 negative breast cancer
- CX-2009 is being further explored as monotherapy in patients with HR+/HER2- breast cancer and will be evaluated in a separate study both as monotherapy and in combination with CX-072 (an anti-PD-L1 Probody) in patients with TNBC.

Anti-CTLA-4 Program

BMS-986249 and BMS-986288

Probody Therapeutics with Best-in-Class Potential

AMY C. PETERSON, M.D., CHIEF DEVELOPMENT OFFICER

Leveraging the Probody Platform for Potentially Safer and More Effective anti-CTLA-4 Therapy

BMS-986249: Ipilimumab Probody

- Initial Phase 1 Data
- Advanced by BMS into randomized 5 arm Phase 2 Expansion Cohort in Metastatic Melanoma in Q1 2020
- Additional Preclinical Data at AACR 2020 (June)
  - Abstract 4551 / Poster 19

BMS-986288: a CytomX-designed Probody of a non-fucosylated version of Ipilimumab

- Ongoing Phase 1 dose escalation study in solid tumors
- Initial Preclinical Data at AACR 2020 (June)
  - Abstract 4551 / Poster 19

ASCO20 Presentation

ABSTRACT 3508

Anti–CTLA-4 Probody BMS-986249 Alone or in Combination With Nivolumab in Patients With Advanced Cancers: Initial Phase 1 Results

Presenter: Martin Gutierrez, M.D. Hackensack University Medical Center, Hackensack, New Jersey

ClinicalTrials.Gov Identifier #NCT03369223

Bristol Myers Squibb™

CytomX Therapeutics

ASCO20 Virtual Scientific Program

Summary

Monotherapy evaluated 5 doses of BMS986249: 240,800,1600 or 2400 Q4W or 1600 Q8W (≈3,10,20 or 30 mpk)

- No grade 5 TRAEs
- TRAE leading to discontinuation was 10% (n=4)
- Grade 3–4 TRAES occurred in 23%
  - Grade 4 TRAE: 1 each hyponatremia, lipase increase, encephalitis all resolved with treatment
  - No grade ≥ 3 TRAEs or IMAEs were reported at 240 mg
  - Rates of grade ≥ 3 TRAEs and IMAEs were lower with Q8W dosing than with Q4W dosing
- 2 DLTS resolved ≈ 1 week: 1600 mg Q4W: grade 3 diarrhea; 1600 mg Q8W: grade 4 hyponatremia

Combination of 480mg nivo Q4W + 4 doses of BMS986249: 240, 800 or 1200 Q4W or 800 Q8W (≈3,10 or 15 mpk)

- No grade 4 or 5 TRAEs were reported
- TRAE leading to discontinuation was 9% (n=4)
- Rates of TRAEs and IMAEs were lower with 800 mg on a Q8W compared with Q4W regimen
- 1 DLT of grade 3 encephalitis at 800 mg Q4W + NIVO 480 mg resolved ≈week

No new safety signals were reported

Data presented at ASCO 2020 Abstract # 3508 (NCT03369223) Bristol Myers Squibb Sponsored Trial

Key Conclusions

The plasma PK profile of the total Probody BMS-986249 at 240 mg and 800 mg was similar to that of IPI at 3 mg/kg and 10 mg/kg respectively

The safety profile of BMS-986249 allowed for assessment of higher doses as monotherapy and in combination with full dose nivolumab than previously tested

The types of AEs were consistent with those reported for ipilimumab

- incidence of grade ≥ 3 events was supportive of the probody mechanism of action

BMS-986249 represents a novel therapeutic strategy to enhance CTLA-4 exposure in the tumor microenvironment while potentially sparing systemic toxicity.

Preliminary data from the dose escalation phase was supportive of the proposed MOA and provides confidence for further clinical evaluation.

Data presented at ASCO 2020 Abstract # 3508 (NCT03369223) Bristol Myers Squibb Sponsored Trial

CX-072 Anti-PDL1 Probody

Potentially Best-in-Class Checkpoint Inhibitor Combination Agent

PROCLAIM CX-072

Updated CX-072 Data at ASCO 2020

ORAL PRESENTATION ABSTRACT #3005

PROCLAIM-CX-072: Analysis of Patients With Advanced Solid Tumors Receiving Long-Term Treatment With CX-072, a PD-L1 PROBODY Therapeutic, as a Single Agent or in Combination With Ipilimumab

Presenter: Fiona C. Thistlethwaite, MB, MChir, Ph.D, The Christie NHS Foundation Trust, University of Manchester, United Kingdom

POSTER #172

Evidence of Intratumoral Localization, Activation, and Immunomodulatory Effect of CX-072, a PROBODY Therapeutic Targeting PD-L1, in a Phase 1/2 Trial

Presenter: Susan K. Lyman, Ph.D. CytomX Therapeutics

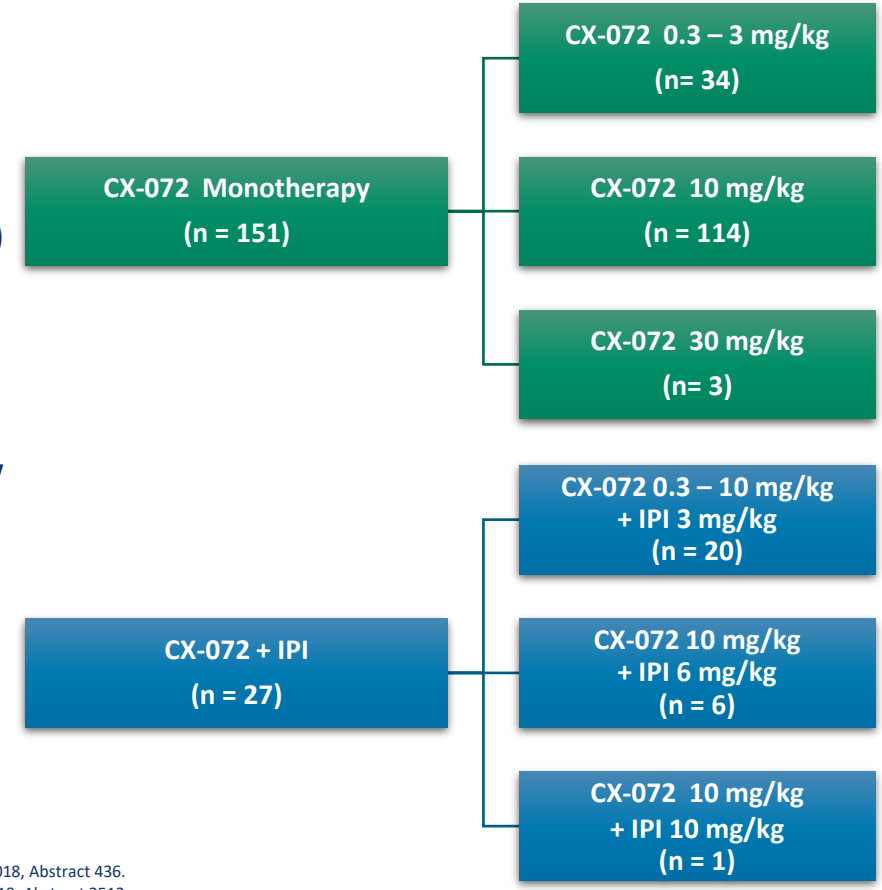
POSTER #332

Preliminary Population Pharmacokinetics Supports Phase 2 Dose Selection for Masked Anti–PD-L1 Antibody CX-072

Presenter: Mark Stroh, Ph.D., CytomX Therapeutics

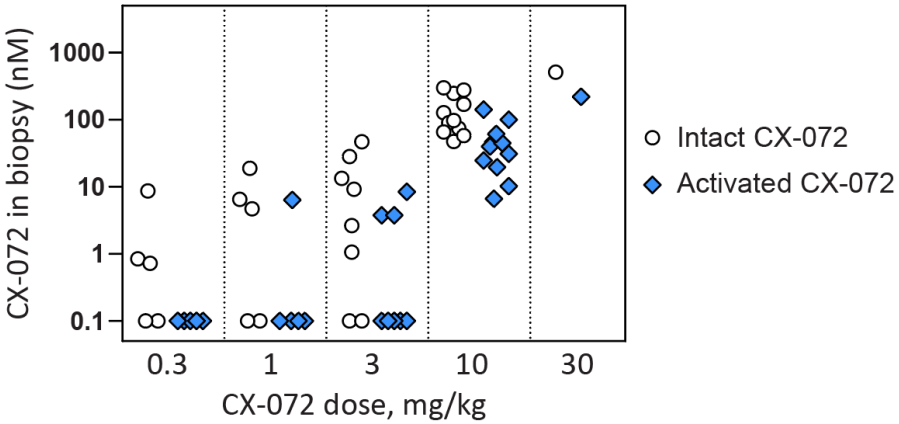
CX-072 Clinical Trial Design

- Phase 1: monotherapy q2w[1-2]
  - CX-072 0.03 – 30 mg/kg (MTD was not reached)
- Phase 1: combination with ipilimumab (IPI)[3-4]
  - MTD was CX-072 10 mg/kg + IPI 3 mg/kg
- Phase 2 (monotherapy)[5]: CX-072 10 mg/kg q2w
  - Anal squamous cell carcinoma (aSCC)
  - Cutaneous squamous cell carcinoma (cSCC)
  - Triple negative breast cancer (TNBC)
  - Small bowel adenocarcinoma (SBA)
  - Undifferentiated pleomorphic sarcoma (UPS)
  - High tumor mutational burden (hTMB)[6]
  - Thymoma or thymic cancers



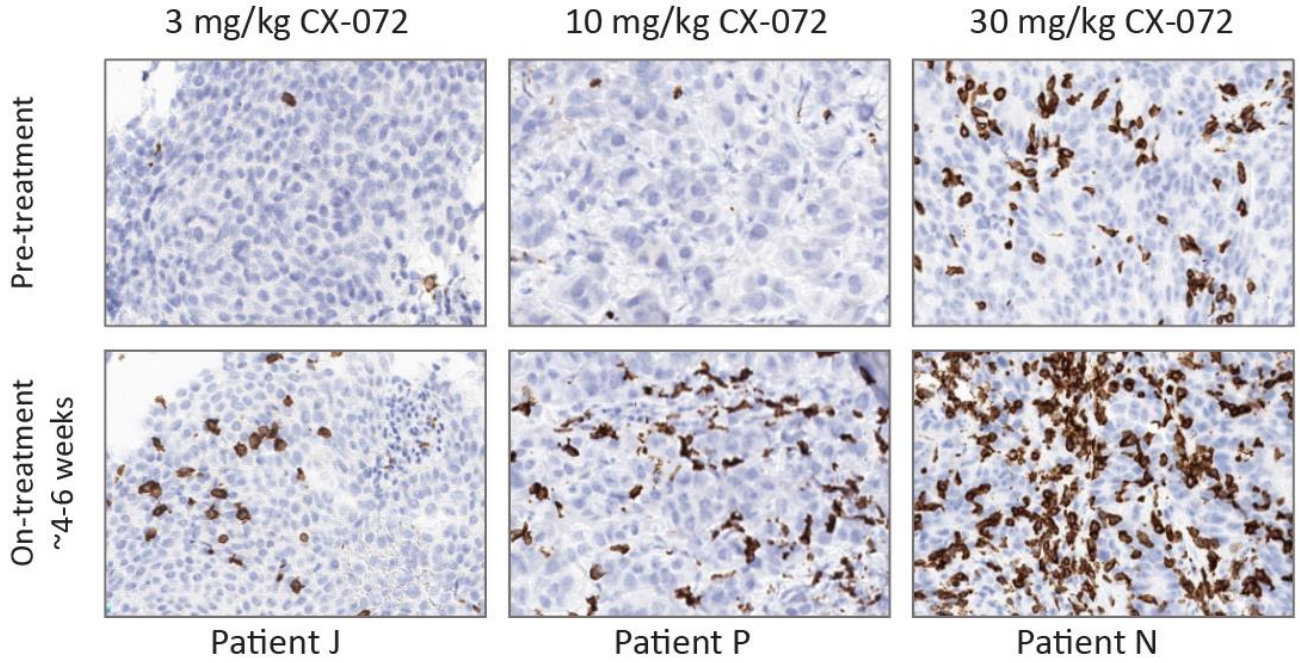
1. Autio, Arkenau, O'Neil et al. ASCO 2018, Abstract 3071
2. Boni, Garcia-Corbacho, Ott et al, ESMO 2018, Abstract 435
3. Sanborn, Menke, Autio et al. ASCO 2018. Abstract 3072
4. Plummer, Sanborn, DeVries et al. ESMO 2018, Abstract 436.
5. Naing, Thistlethwaite, Spira et al. ASCO 2019, Abstract 2513
6. hTMB status as assessed locally

Activated CX-072 Detected in Patient Biopsies at Doses ≥1 mg/kg



CX-072 Dose (mg/kg)	Median Molar Ratio Activated CX-072:PD-L1	Median Calculated Target Occupancy
30 (n=1 biopsy sample)	Not available	**99.97%**
10 (11/11 biopsies had detectable activated CX-072)	**259x** Range: 14–12430x	**99.70%**
3 (3/8 biopsies had detectable activated CX-072)	**7x** Range: 7–984x	**98.18%**

CX-072 Treatment Associated with Increased CD8 Levels in Some Patient Tumors



Poster reference

CX-072 Clinical Trial Design

- Phase 1: monotherapy q2w[1-2]
  - CX-072 0.03 – 30 mg/kg (MTD was not reached)
- Phase 1: combination with ipilimumab (IPI)[3-4]
  - MTD was CX-072 10 mg/kg + IPI 3 mg/kg
- Phase 2 (monotherapy)[5]: CX-072 10 mg/kg q2w
  - Anal squamous cell carcinoma (aSCC)
  - Cutaneous squamous cell carcinoma (cSCC)
  - Triple negative breast cancer (TNBC)
  - Small bowel adenocarcinoma (SBA)
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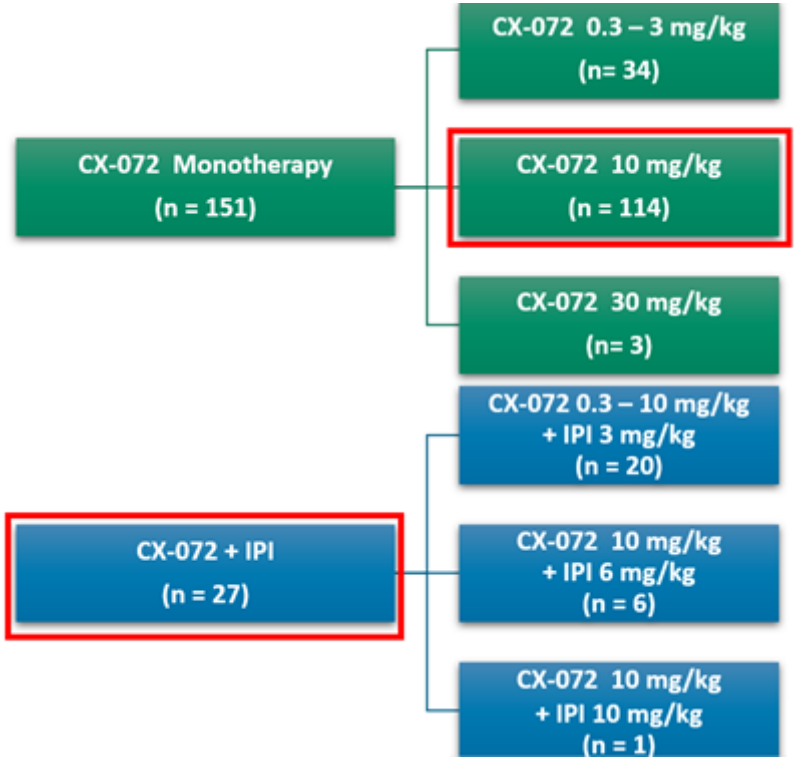
  - High tumor mutational burden (hTMB)[6]
  - Thymoma or thymic cancers



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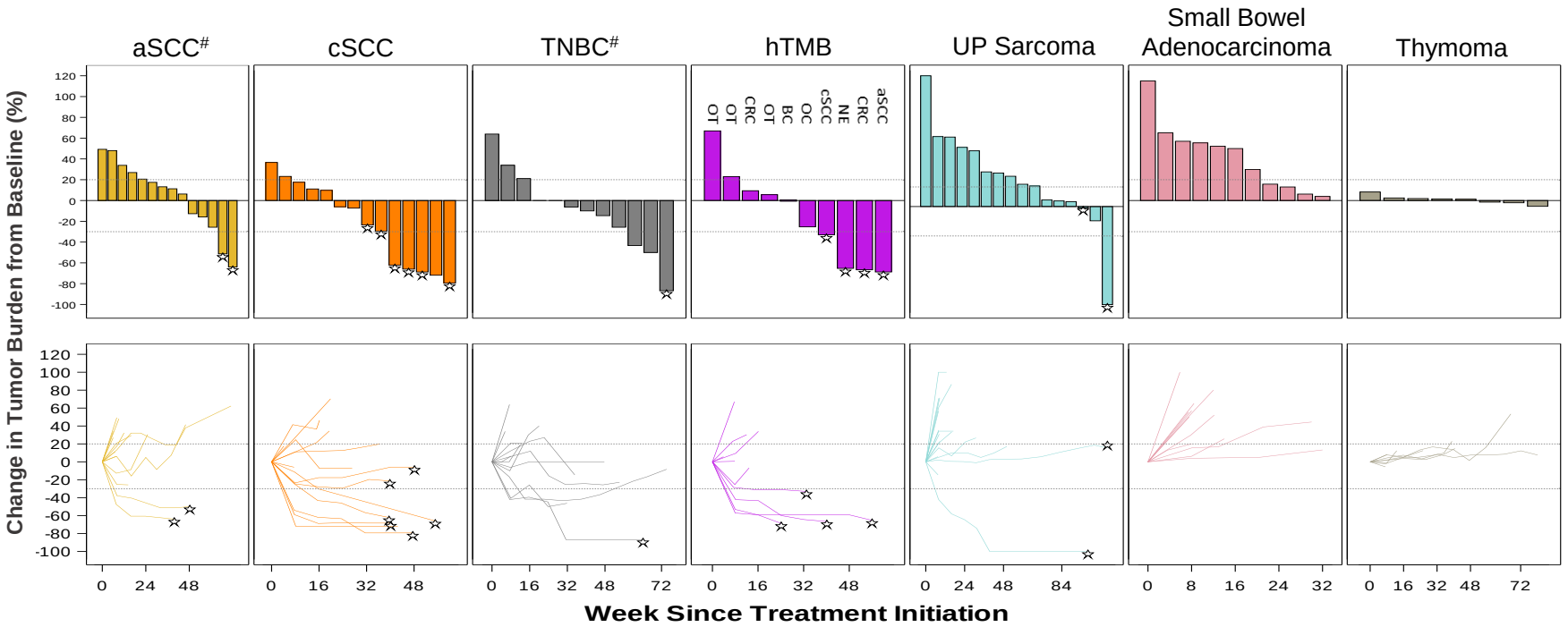
5. Naing, Thistlethwaite, Spira et al. ASCO 2019, Abstract 2513
6. hTMB status as assessed locally

Demographics
Majority of patients enrolled had low or no tumor expression of PD-L1

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Age – median (min, max)	59.5 (32, 83)	63.5 (32, 83)	56 (28, 70)	54.5 (39, 68)
Sex – Male / Female, %	39 / 61	41 / 59	43 / 57	33 / 67
# prior cancer treatments – median (min, max)	2.5 (0, 12)	2 (0, 5)	3 (1, 10)	4 (1, 4)
Baseline ECOG – 0 / 1, %	31 / 69	56 / 44	43 / 57	33 / 67
PD-L1 status, %				
High expression	15.0	29.4	4.8	0
Low expression	30.0	32.4	19.0	16.7
No expression	50.0	26.5	52.4	66.7
Unknown / NE	3.8 / 1.3	11.8 / 0	19.0 / 4.8	16.7 / 0
Tumor Types, n (%)				
Undifferentiated pleiomorphic sarcoma	16 (20)	4 (11.8)	0	0
TNBC	10 (12.5)	5 (14.7)	1 (4.8)	0
Anal SCC	10 (12.5)	5 (14.7)	0	1 (16.7)
Cutaneous SCC	6 (7.5)	8 (23.5)	0	0
Small bowel adenocarcinoma	13 (16.3)	1 (2.9)	0	0
Thymoma or thymic cancers	6 (7.5)	4 (11.8)	0	0
hTMB	8 (10.0)	2 (5.9)	0	0
Other	11 (13.8)	5 (14.7)	20 (95.2)	5 (95.2)

Data cutoff: 20-Apr-2020

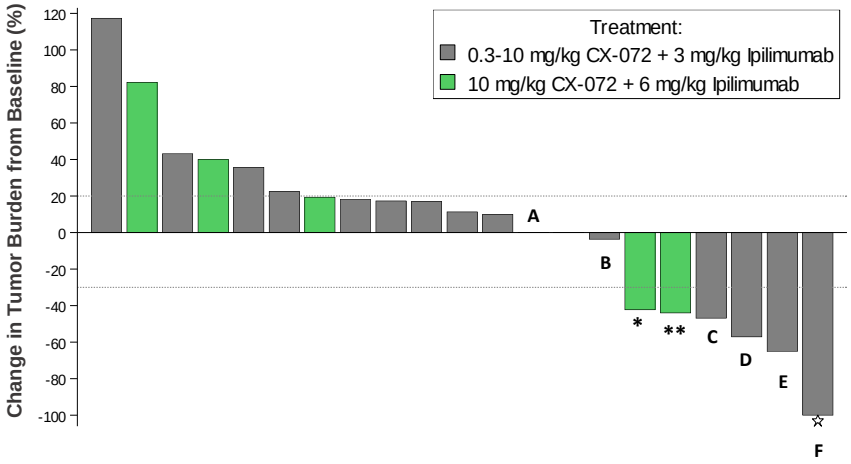
Activity Observed in IO-Responsive Tumors: CX-072 Monotherapy (10 mg/kg)

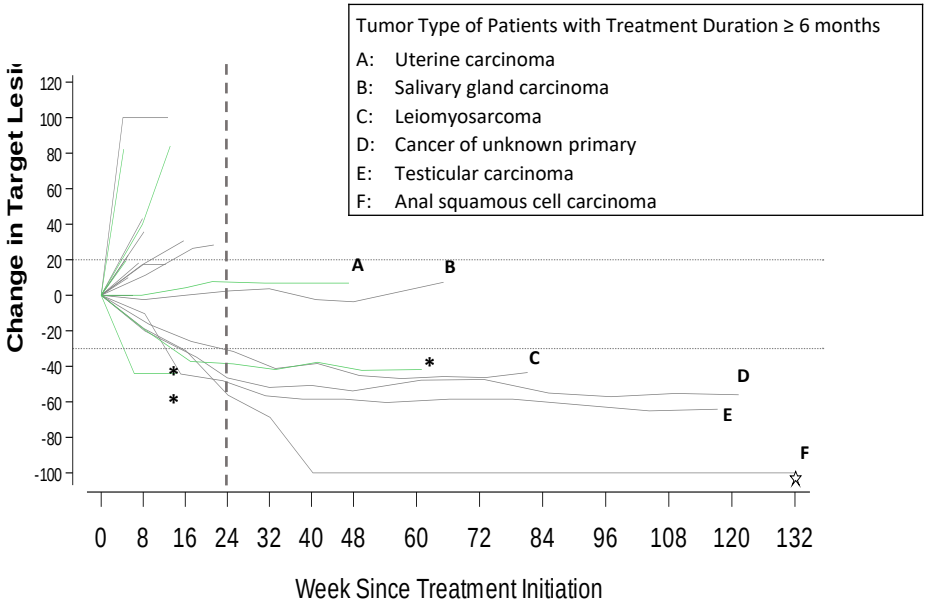


☆ Denotes patient considered to be on treatment as of data cut-off date; evaluable patients include those in the safety population with post-baseline response assessment. # Includes all evaluable patients from dose escalation at 10 mg/kg (n=2, TNBC and anal SCC) and dose expansion. aSCC: anal squamous cell carcinoma, cSCC: cutaneous squamous cell carcinoma, TNBC: triple-negative breast cancer, hTMB: high tumor mutational burden; UP: undifferentiated pleiomorphic, CRC: colorectal cancer, NE: neuroendocrine carcinoma, OC: ovarian cancer, BC: breast cancer, OT: other tumor type

Data cutoff: 20-Apr-2020

Activity Observed in Phase 1 Dose Escalation Unselected Patients Treated with CX-072 + Ipilimumab





☆Denotes patient considered to be on treatment as of data cut-off date; evaluable patients include those in the safety population with post-baseline response assessment.
* Patient with cervical cancer discontinued due to AE on day 43, but continues to have stable disease on follow-up tumor scans
** Patient with mesothelioma
CR: complete response

Data cutoff: 20-Apr-2020

Treatment Related Grade 3+ AE (≥ 1 patient)
Grade 3+ events were uncommon

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Subjects with at least one Related Grade 3+ TEAE, n (%)	**8 (10.0)**	**2 (5.9)**	**7 (33.3)**	**2 (33.3)**
Colitis	0	0	2 (9.5)**	0
GGT increased	2 (2.5)	0	0	0
Aspartate transferase increased	1 (1.3)	0	1 (4.8)	0
Alanine transferase increased	0	0	1 (4.8)**	0
Transaminases increased	0	0	1 (4.8)	0
Lipase increased	1 (1.3)	1 (2.9)*	0	1 (16.7)*
Amylase increased	0	0	0	1 (16.7)*
Diarrhea	0	0	1 (4.8)	0
Pneumonitis	0	0	1 (4.8)**	0
Dyspnea	0	0	1 (4.8)**	0
Guillain Barré syndrome	0	0	1 (4.8)	0
Hyponatremia	0	0	0	1 (16.7)*
Rash Maculopapular	1 (1.3)	0	0	0
Hypoxia	0	0	1 (4.8)**	0
Infusion related reaction	0	0	1 (4.8)	0
Neutropenia	0	0	1 (4.8)	0
Enterocutaneous fistula	0	1 (2.9)*	0	0
Fatigue	1 (1.3)	0	0	0
Hypertension	1 (1.3)	0	0	0
Myocarditis	1 (1.3)	0	0	0

* Events reported during first 6 months of treatment

** One patient was treated with CX-072 0.3mg/kg + IPI 3 mg/kg

Data cutoff: 20-Apr-2020

Immune-related AE (≥ 2 patients or ≥ 1 patient for Grade 3+) Rates were low across all groups and no Grade 3+ events were reported in long-term patients

	CX-072 10 mg/kg < 6 months (n=80)		CX-072 10 mg/kg ≥ 6 months (n=34)		CX-072 + IPI < 6 months (n=21)		CX-072 + IPI ≥ 6 months (n=6)	
	All Grade	Grade 3+	All Grade	Grade 3+	All Grade	Grade 3+	All Grade	Grade 3+
Subjects with at least one irAE, n (%)	**9 (11.3)**	**2 (2.5)**	**7 (20.6)**	**0**	**11 (52.4)**	**6 (28.6)**	**5 (83.3)**	**0**
Alanine aminotransferase increased	3 (3.8)	0	1 (2.9)	0	0	0	0	0
Aspartate aminotransferase increased	3 (3.8)	0	2 (5.9)	0	1 (4.8)	0	0	0
Transaminases increased	0	0	0	0	1 (4.8)	1 (4.8)	0	0
Hypothyroidism	2 (2.5)	0	2 (5.9)	0	1 (4.8)	0	1 (16.7)	0
Rash	2 (2.5)	0	1 (2.9)	0	0	0	3 (50.0)	0
Rash maculo-papular	2 (2.5)	1 (1.3)	0	0	3 (14.3)	0	1 (16.7)	0
Pruritus	0	0	0	0	3 (14.3)	0	1 (16.7)	0
Colitis	0	0	0	0	2 (9.5)	2 (9.5)**	0	0
Diarrhea	0	0	0	0	2 (9.5)	1 (4.8)*	0	0
Hyperthyroidism	0	0	0	0	1 (4.8)	0	1 (16.7)	0
Pneumonitis	0	0	0	0	1 (4.8)	1 (4.8)**	0	0
Myocarditis	1 (1.3)	1 (1.3)	0	0	0	0	0	0
Neutropenia	0	0	0	0	1 (4.8)	1 (4.8)*	0	0
Guillain-Barré syndrome	0	0	0	0	1 (4.8)	1 (4.8)	0	0

* Events reported in the same patient
** One patient was treated with CX-072 0.3mg/kg + IPI 3 mg/kg

Data cutoff: 20-Apr-2020

PROCLAIM CX-072

Summary

TRANSLATIONAL/PLATFORM

- ✓ Protease activity was detectable in the majority of PROCLAIM-CX-072 patient tumor biopsies
- ✓ CX-072 was unmasked/activated in tumor biopsies, and PD-L1 target occupancy exceeded 98% at the 10 mg/kg at doses ≥3 mg/kg
- ✓ On-treatment pharmacodynamic changes were consistent with PD-1/PD-L1 pathway activation

CLINICAL

- ✓ Consistent with other checkpoint inhibitors, CX-072 showed highly durable objective responses in multiple tumor types
- ✓ CX-072 was well tolerated alone or in combination with ipilimumab administered at doses ≥3 mg/kg
- ✓ Long term patients experienced fewer irAEs and had no grade 3+ irAEs suggesting that tolerability early on can impact duration of treatment

Overall Summary ASCO 2020

Taken together,

- Data presented in 7 abstracts today at ASCO establish that our Probody therapeutic platform performs as designed when applied to IO agents, or as Probody drug conjugates to previously undruggable targets like CD71 and CD166

- Clinical activity and tolerability as presented across all 4 clinical stage programs support Phase 2 exploration with each molecule, specially:
  - CX-2029 in HNSCC, SqNSCLC, Esophageal and DLBCL
  - CX-2009 ±CX-072 in HR+/Her2- and Triple Negative Breast Cancers
  - BMS986249 +nivolumab in metastatic melanoma

Thank you

to the patients and their families and caregivers

Thank you

to the investigators, the study nurses and staff

CytomX Therapeutics

Concluding Remarks

SEAN MCCARTHY, D.PHIL, PRESIDENT, CEO AND CHAIRMAN

Company Summary

Clinical-stage biopharmaceutical company advancing first-in-class and best-in-class cancer treatments with a novel therapeutic antibody platform:

Probody® Therapeutics

- Leader in field of “conditional activation” of therapeutic antibodies with broad platform and discovery engine
- Initial clinical proof of concept established for platform
- Pipeline advancing from Phase 1 to Phase 2
- Potential first-in-class programs against previously undruggable targets: Probody Drug Conjugates to CD166 (CX-2009) and CD71 (CX-2029)
- Potential best-in-class programs against validated targets: CX-072 (anti-PD-L1), BMS-986249, BMS-986288 (anti-CTLA-4)
- Major Partnerships (BMS, AbbVie, Amgen, Astellas)
- Strong balance sheet; $248 million at end of Q1 2020; additional $130 million in milestone and upfront payments achieved in Q1 and received in Q2

Recent Achievements and Future Milestones

1H 2020 ACHIEVEMENTS

- ✓ CX-2029 Phase 2 Advancement
  - HNSCC, NSCLC, DLBCL, Esophageal
- ✓ CX-2009 Phase 2 Advancement
  - HR+/HER2- Breast Cancer (paused)
- ✓ BMS-986249 Phase 2 Advancement
  - Melanoma
- ✓ New Alliance with Astellas
  - Probody T-cell Bispecifics; $80M Upfront
- ✓ CX-904 Advancement towards IND
  - EGFR-TCB (in partnership with Amgen)

FUTURE MILESTONES

- CX-2009 Ph2 Breast Cancer readout
- CX-2009 + CX-072 TNBC Ph 2 initiation
- CX-2029 Ph2 expansion readouts
- BMS-986249 randomized Ph 2 readout
- CX-904 IND Advancing into Phase 1
- Additional IND(s) from internal and partnered discovery programs

Question and Answer Session

CytomX Therapeutics

REIMAGINING THERAPEUTIC ANTIBODIES FOR THE TREATMENT OF CANCER

ASCO20 Virtual Scientific Program Presentation Review

MAY 29, 2020