



REIMAGINING THERAPEUTIC ANTIBODIES FOR THE TREATMENT OF CANCER

Goldman Sachs 41st Annual Global Healthcare Conference



JUNE 10, 2020

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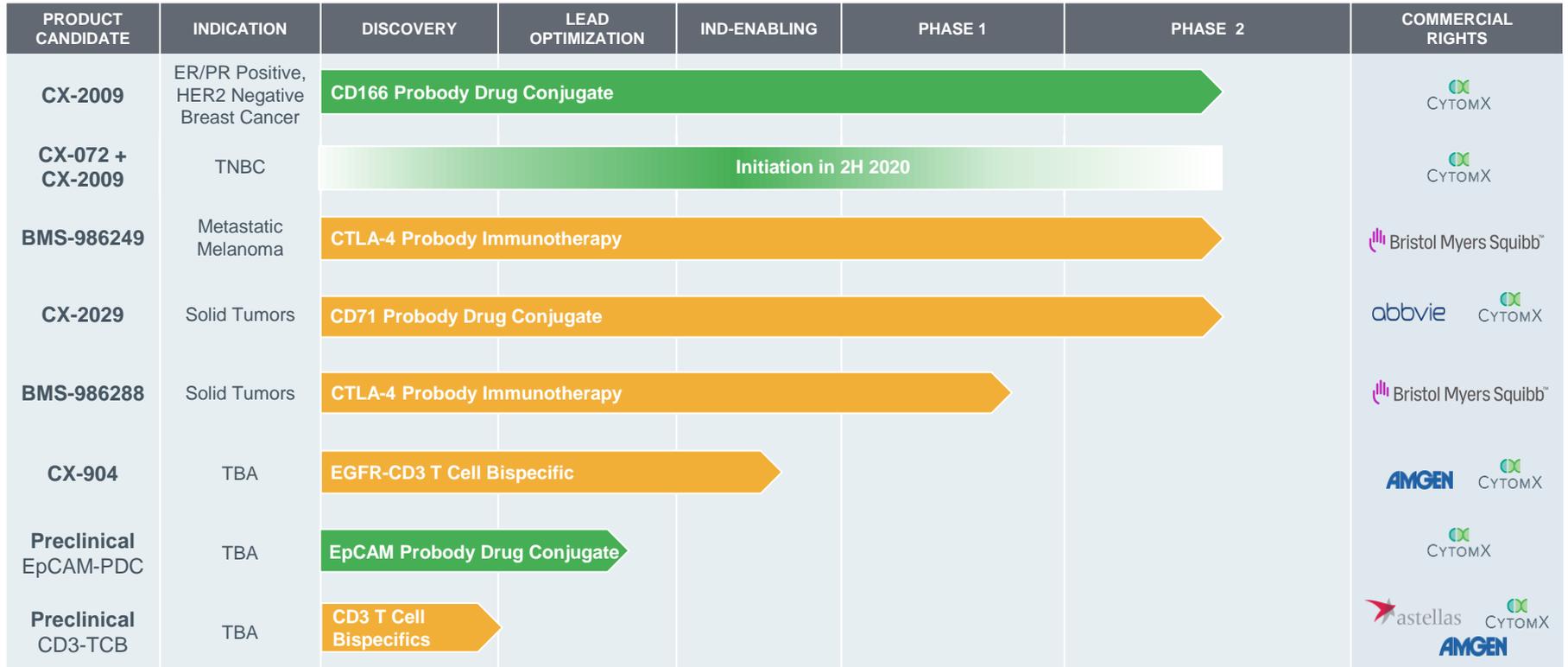
Company Summary

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

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



 Wholly Owned

 Partnered

ASCO 2020: 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



Targeting Undruggable Targets with Probody Drug Conjugates

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



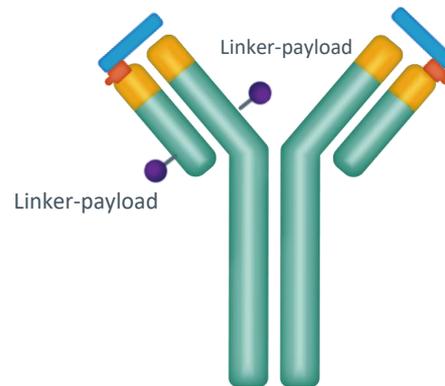
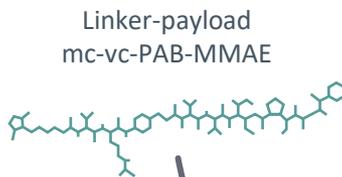
CX-2029: Probody Drug Conjugate Against CD71 with MMAE Warhead

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

CD71- DIRECTED PROBODY

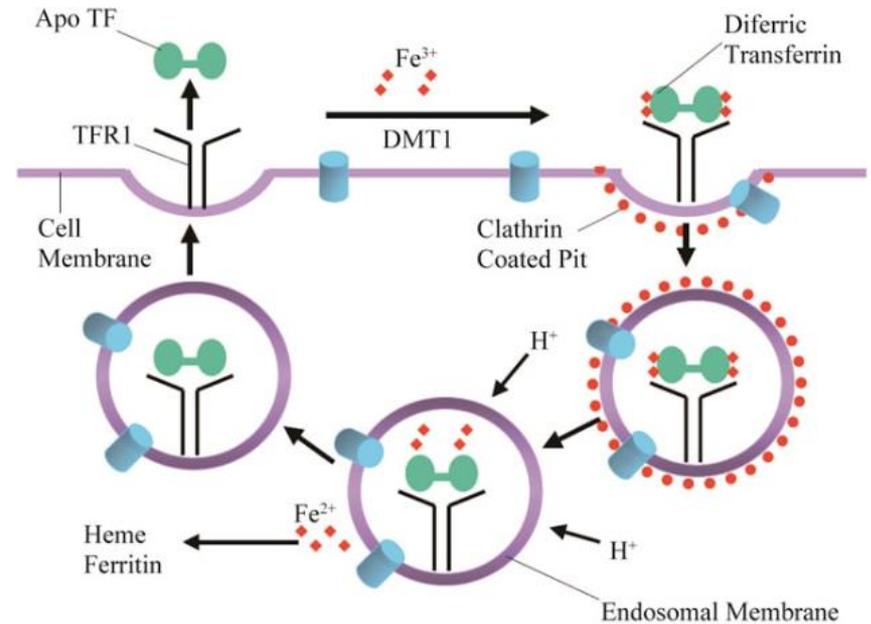


CX-2029 PDC

TME, tumor microenvironment.

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.

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

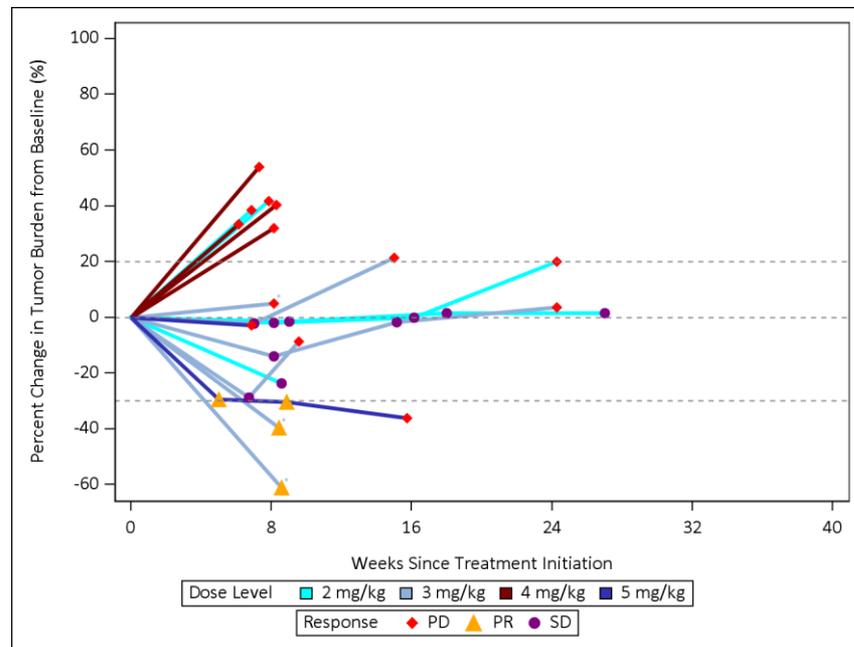
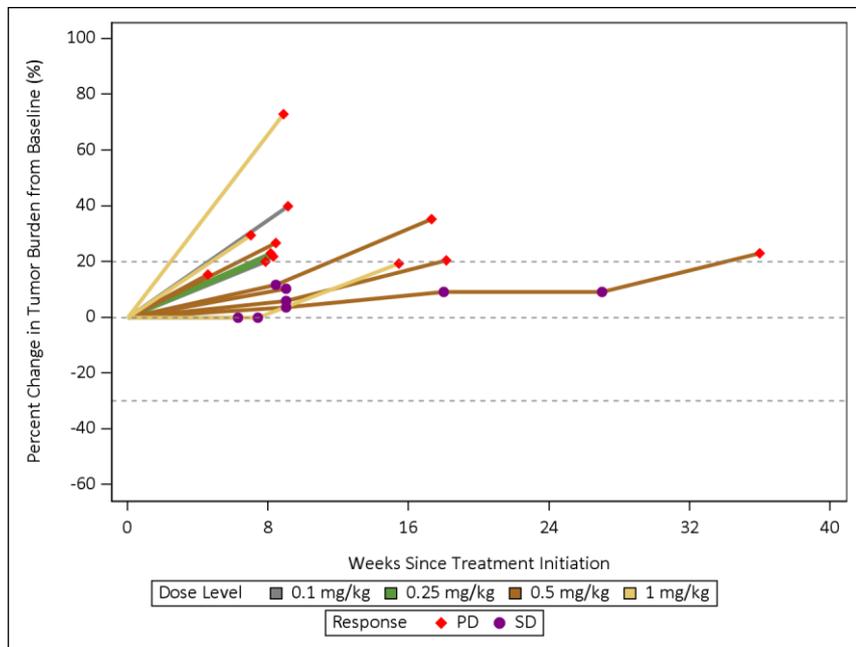
HNSTD: Highest non severely toxic dose.

	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).

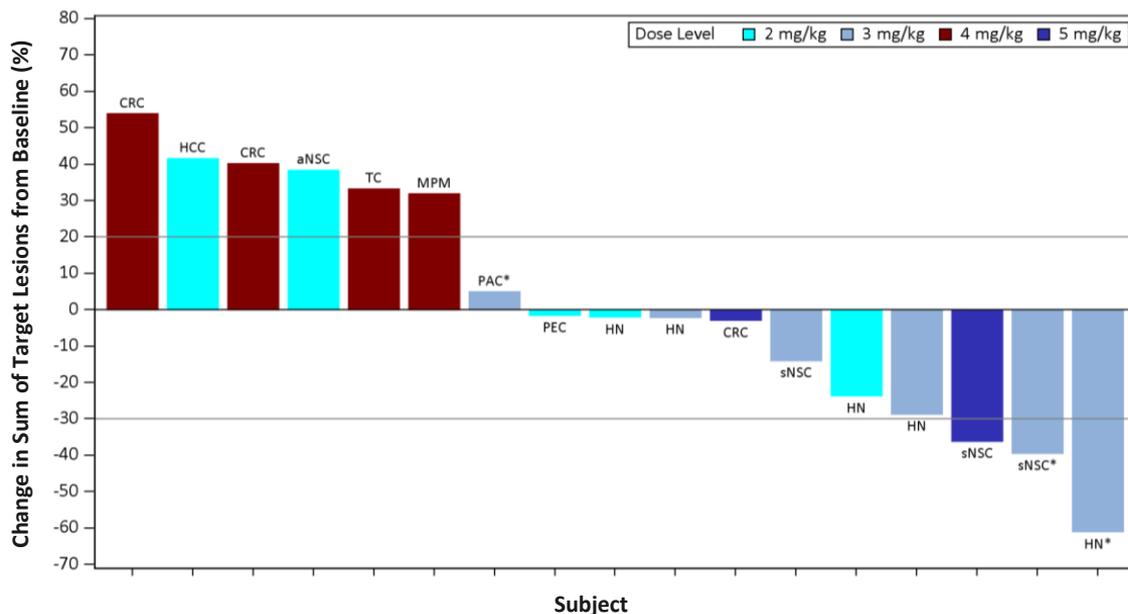
Clinical Activity at CX-2029 Doses ≥ 2 mg/kg



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

• Data cut-off: April 20, 2020.

Phase 1: Waterfall Plot (Doses 2–5 mg/kg)



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.

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)

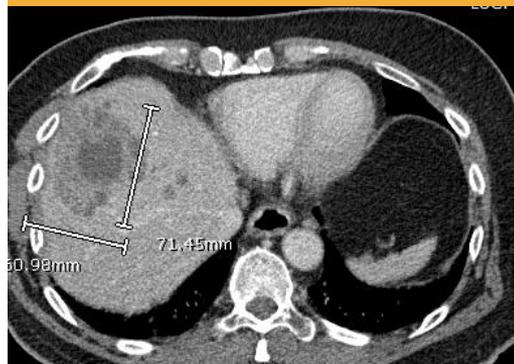
Relevant Past Medical History:

anemia, increased LFTs, HTN, neuropathy, dyspnea

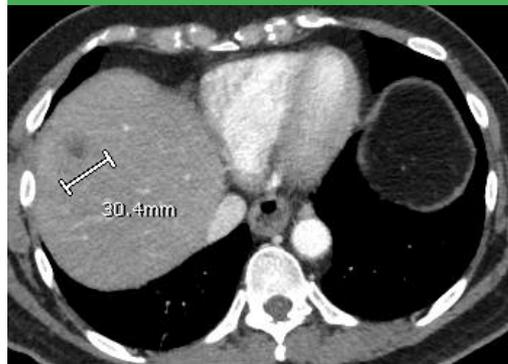
Initiated CX-2029: [14 Jan 2020]

- **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



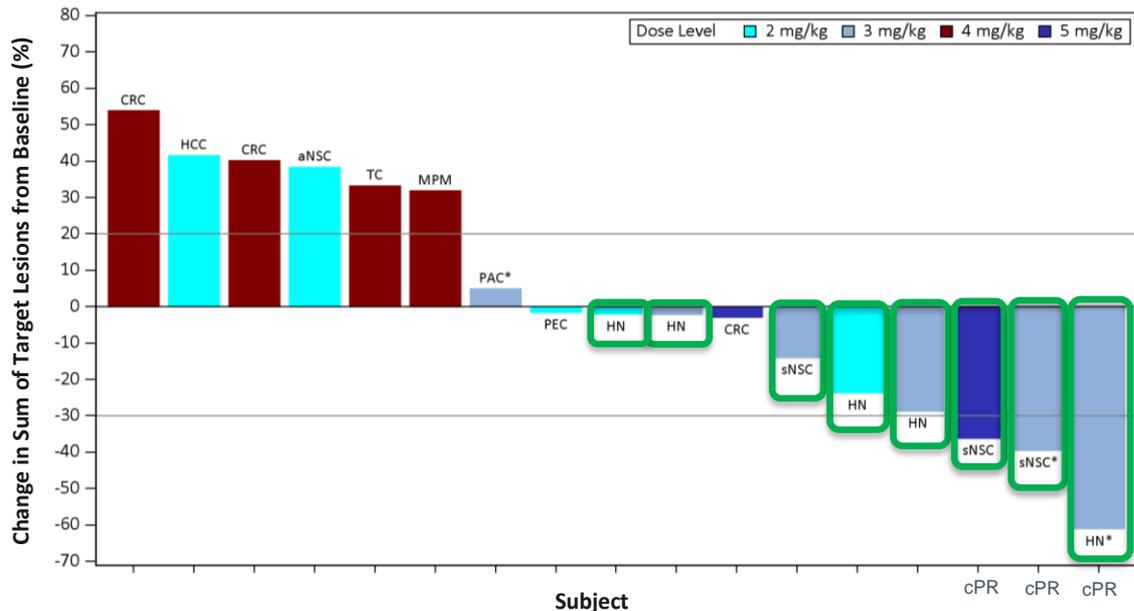
13 Mar 2020 (43% ↓)



8 May 2020 (78% ↓)



Phase 1: 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.

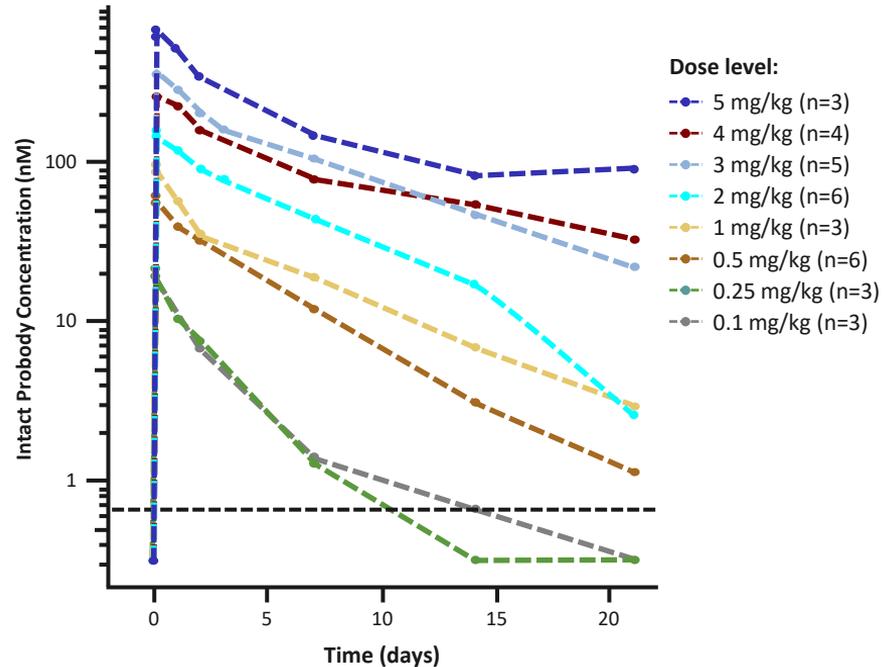
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All 3 patients with Target Lesions Shrinkage >30% are confirmed partial responses

Data cut-off: April 20, 2020.

- 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



	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 (≥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”).

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.

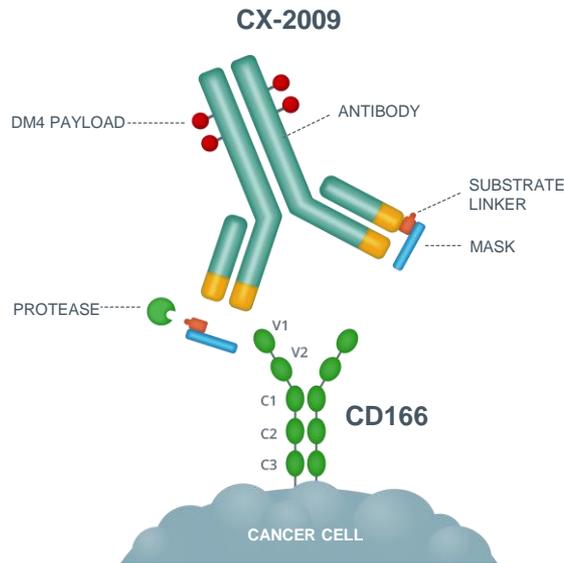
Clinical activity was observed at doses of 2 mg/kg and higher

- 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

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

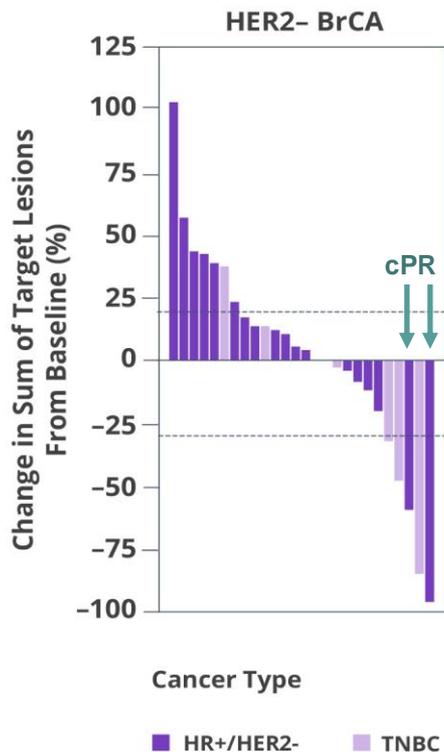


- CD166 (activated leukocyte cell adhesion molecule) is a transmembrane protein that functions as a junctional adhesion molecule, and facilitates cell migration, differentiation, and hematopoiesis.
- CD166 is a broadly and highly expressed tumor antigen
- CD166 is also present on normal tissues (eg GI, 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

	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)

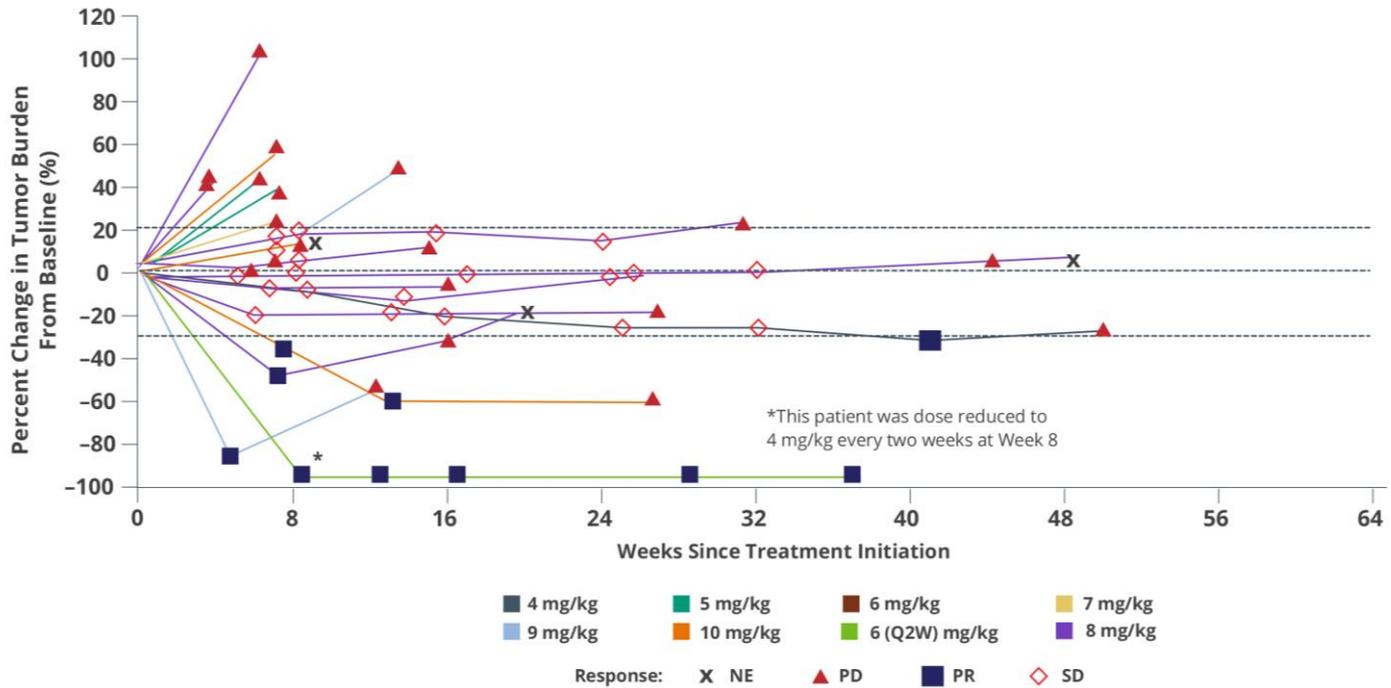
CX-2009 Phase 1: Evidence of Clinical Benefit in Patients with Breast Cancer Treated ≥ 4 mg/kg Q3W



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

	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%)

Phase 1: Evidence of Clinical Benefit in Patients with Breast Cancer Treated ≥ 4 mg/kg Q3W



Phase 1 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

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.

Cancer Immunotherapy Programs

- Anti-CTLA-4
- Anti-PD-L1



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

Summary of Safety Findings for BMS-986249 Phase 1

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

Key Conclusions from BMS-986249 Phase 1

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.

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

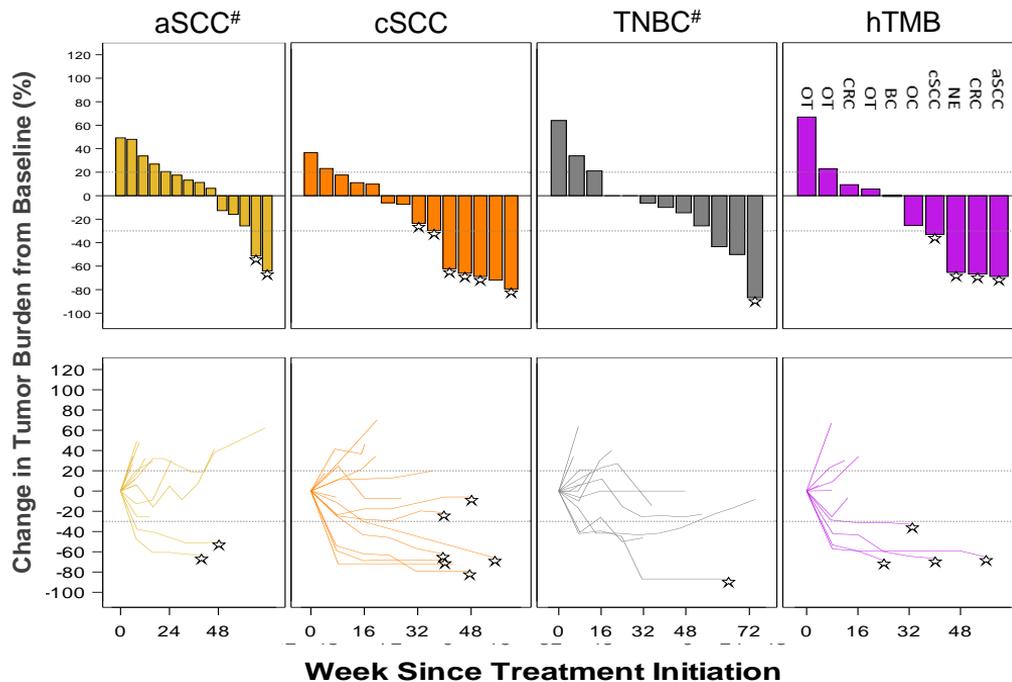
Presenter: Susan K. Lyman, Ph.D. CytomX Therapeutics

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

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



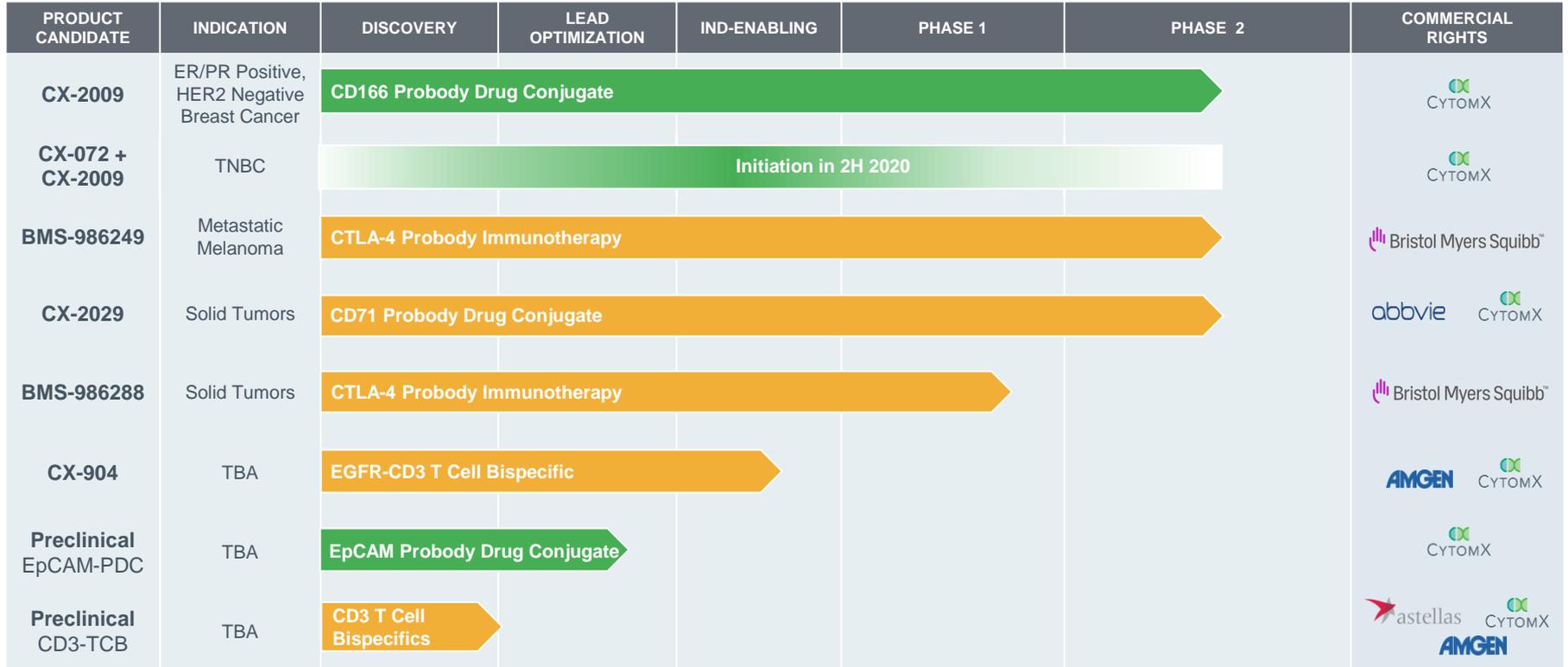
☆ Denotes patient considered to be on treatment as of data cut-off date; evaluable patients include those in the safety population with post-baseline response assessment. # Includes all evaluable patients from dose escalation at 10 mg/kg (n=2, TNBC and anal SCC) and dose expansion. aSCC: anal squamous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

Data cutoff: 20-Apr-2020

CLINICAL SUMMARY

- ✓ 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
- ✓ Next steps include Phase 2 combination with CX-2009

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



 Wholly Owned

 Partnered

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 Phase 2 HR+/HER2- Breast Cancer
- CX-2009 + CX-072 Phase 2 TNBC
- CX-2029 Phase 2 expansions
- BMS-986249 randomized Phase 2
- CX-904 (EGFR-CD3) IND
- Additional IND(s) from internal and partnered discovery programs



REIMAGINING THERAPEUTIC ANTIBODIES FOR THE TREATMENT OF CANCER

Goldman Sachs 41st Annual Global Healthcare Conference



JUNE 10, 2020