

### **REIMAGINING THERAPEUTIC ANTIBODIES**

Bank of America Merrill Lynch 2019 Health Care Conference





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This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). No representation is made as to their safety or effectiveness for the purposes for which they are being investigated.



### **Reimagining Therapeutic Antibodies**

#### ANTIBODIES ARE A SUCCESSFUL CLASS OF THERAPEUTICS

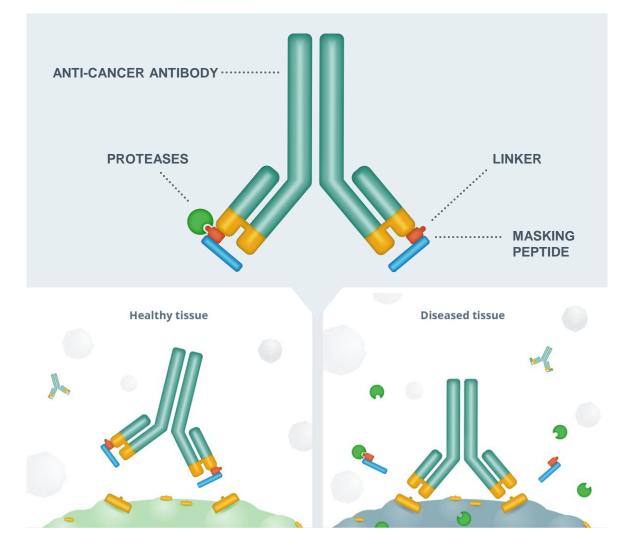
- Powerful, potent modalities; > \$100 billion WW sales 2018
- Potency can be a liability for widely distributed targets
- Major opportunity to improve targeting and localize antibody pharmacology

#### CYTOMX PROBODY™ PLATFORM IS DESIGNED TO LOCALIZE TARGET BINDING TO TUMOR

- Maintaining potency
- Reducing side effects
- Enabling new target opportunities

#### PROBODY PLATFORM BUILT ON A DECADE OF "HIGH SCIENCE" RESEARCH AT CYTOMX

- Deep knowledge of tumor microenvironment biology
- Innovative antibody engineering and IP to create Probody<sup>™</sup> therapeutics, a unique class of localized, antibody prodrugs





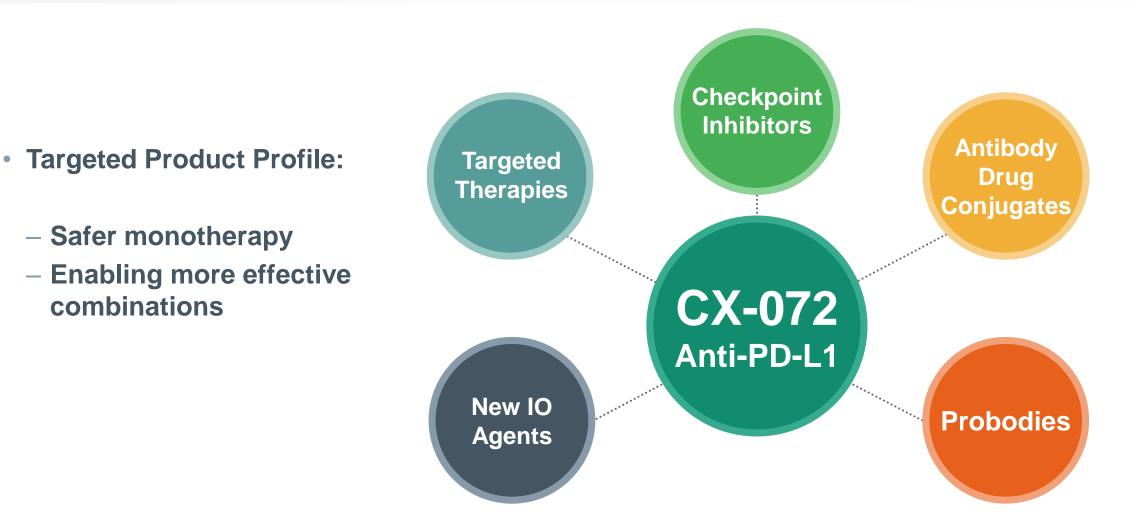
### **Deep and Differentiated Probody Pipeline**

PRODUCT CANDIDATE	LEAD OPTIMIZATION	IND-ENABLING	PHASE 1/2	COMMERCIAL RIGHTS
CX-072	PD-L1 Probody Immunotherapy			СутомХ
CX-2009	CD166 Probody Drug Conjugate			СутомХ
<b>BMS-986249</b>	CTLA-4 Probody Immunotherapy			Bristol-Myers Squibb
CX-2029	CD71 Probody Drug Conjugate			abbvie CytomX
Probody Drug Conjugate	EpCAM PDC			immun•gen
Pb T Cell Bispecific	EGFR-CD3 PbTCB			AMGEN CYTOMX
Additional PDCs, IO, TCBs				СутомХ
	Immunotherapies	Probody Drug Conjugates	Pb T Cell Engaging Bispecifics	Multiple Programs

\$396M in cash at end of Q1 2019

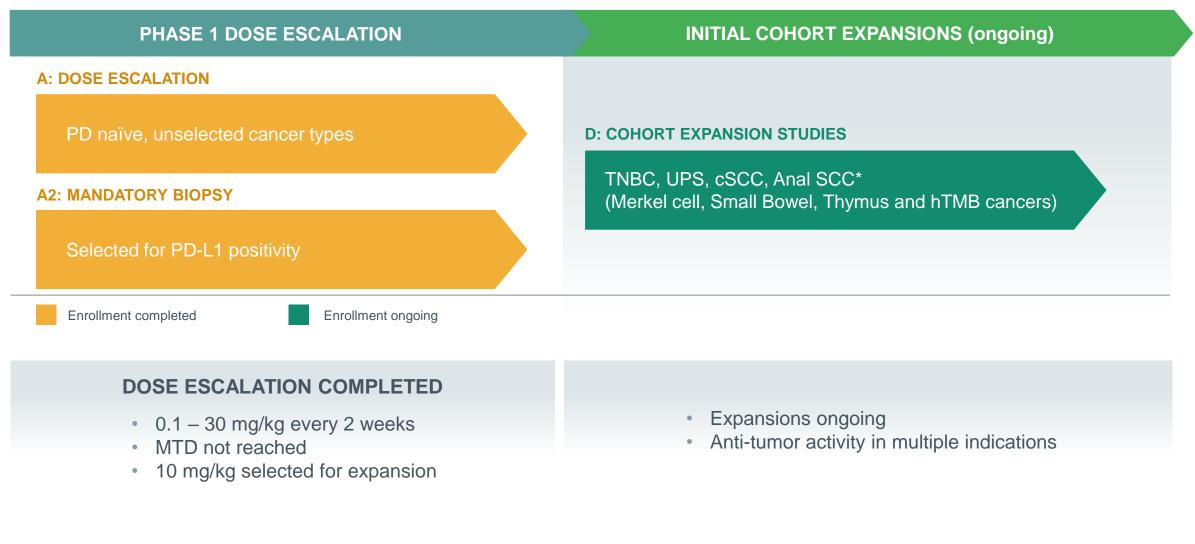


## CX-072: Potential as a Differentiated anti-PD-L1 Centerpiece of Cancer Combination Therapy



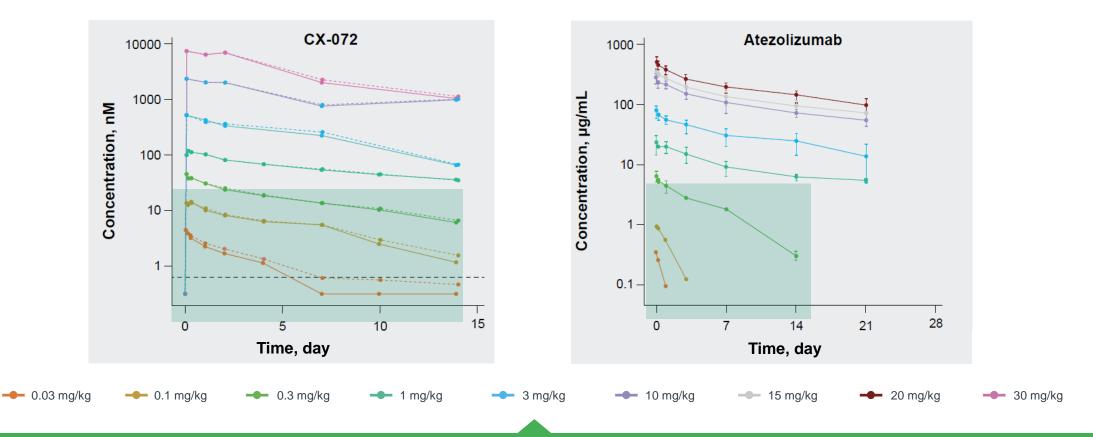








### PROCLAIM<br/>CX-072Phase 1 Dose Escalation: CX-072 Remains Effectively<br/>Masked in the Circulation of Cancer Patients

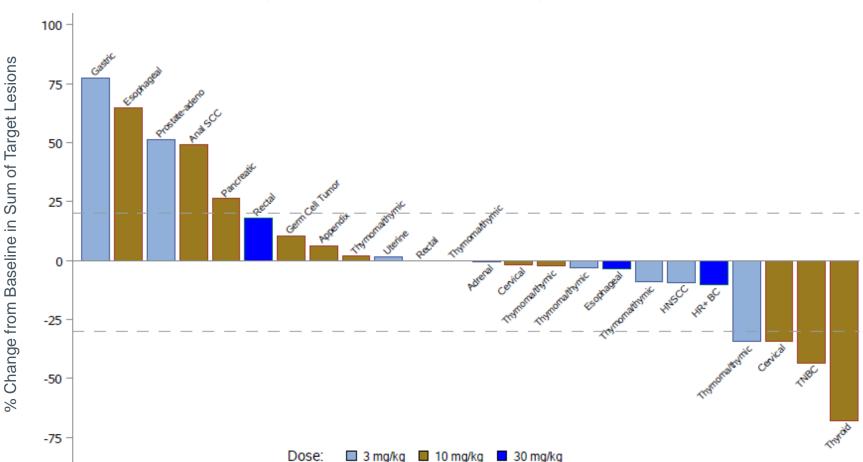


• Single-dose CX-072 PK data and PK modelling suggest that CX-072 circulates predominantly as the intact prodrug species

• Clearance is minimally influenced by target mediated drug disposition



## **PROCLAIM**<br/>CX-072Monotherapy Anti-Cancer Activity<br/>at $\geq$ 3mg/kg from Dose Escalation



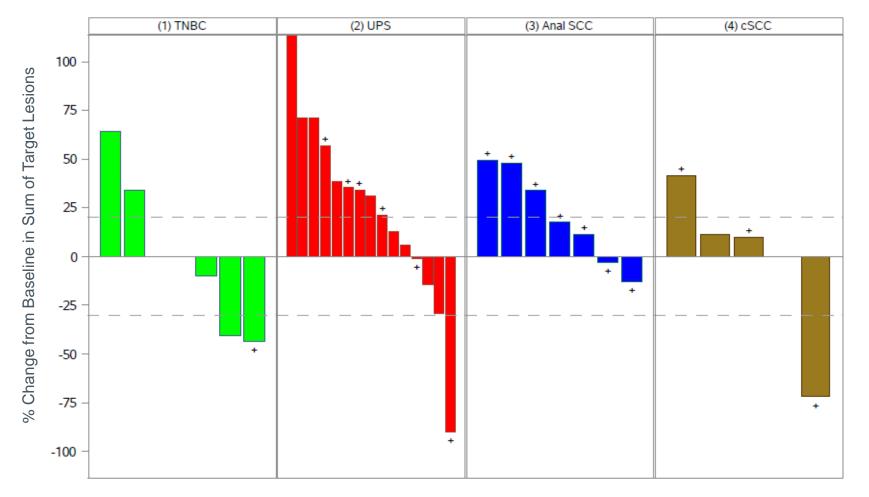
**Best Percent Change from Baseline in Sum of Target Lesion Measurements** 



triple negative breast cancer (TNBC), head and neck squamous cell carcinoma (HNSCC), HR+ breast cancer (HR+ BC), anal squamous cell carcinoma (SCC) Data cutoff as of February 6, 2019

## **PROCLAIM**<br/>CX-072Cohort Expansions: Monotherapy CX-072 is Active<br/>in Multiple Tumor Types at 10 mg/kg

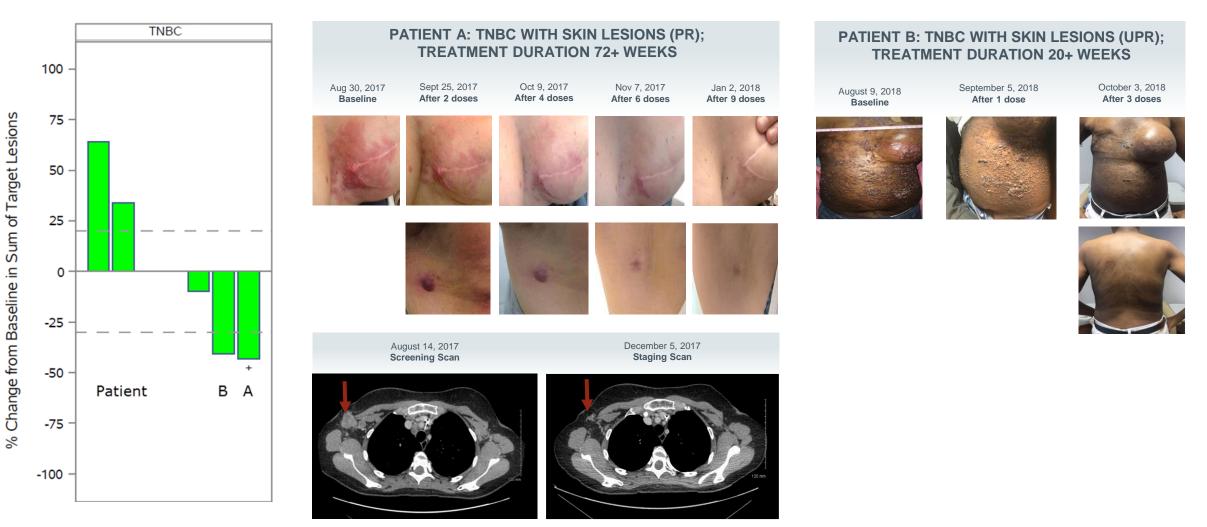
Best Percent Change from Baseline in Sum of Target Lesion Measurements, by Cancer Classification





+ denotes PD-L1 positive, defined as tumor proportion score ≥1% of membranous staining based on DAKO PD-L1 IHC 22C3 pharmDx. Data cutoff as of February 6, 2019

# **PROCLAIM**<br/>CX-072Case Study:<br/>Anti-Tumor Activity at 10 mg/kg in TNBC





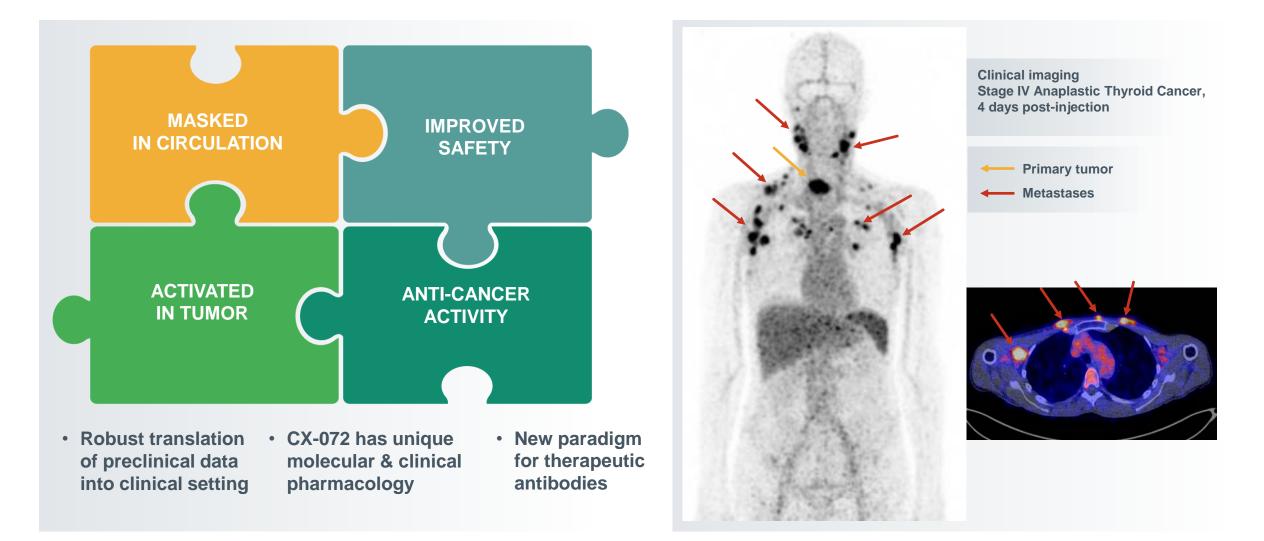
## PROCLAIMPreliminary Safety: Monotherapy at 10 mg/kgCX-072Limited Grade 3/4 TRAEs and Immune-related AEs

	Total (N=50)*
NUMBER (%) OF SUBJECTS EXPERIENCING	3
TEAE Grade 3+	21 (42.0)
Related to CX-072 (TRAE)	2 (4.0)
TEAE Leading to CX-072 Discontinuation	1 (2.0)
Related to CX-072 (TRAE)	0
TEAE Leading to Death	1 (2.0)
Related to CX-072 (TRAE)	0
IRRs	3 (6.0)
Grade 3+	0
IRAEs Grade 3+	2 (4.0)

\* triple negative breast cancer (TNBC), undifferentiated pleomorphic sarcoma (UPS), cutaneous squamous cell carcinoma (cSCC) and anal squamous cell carcinoma (SCC) patients treatment emergent adverse event (TEAE), treatment related adverse event (TRAE) infusion-related reactions (IRR), immune related adverse event (irAE) infusion rela



### Clinical and Translational Data Support Probody Platform Proof-of-Concept





## **PROCLAIM**<br/>CX-072Clinical Data Presentations at<br/>2019 ASCO Annual Meeting\*

Abstract #2513/ Poster #157

CX-072, a PD-L1 Probody Therapeutic, as Monotherapy in Patients with Advanced Solid Tumors: Preliminary Results of PROCLAIM-CX-072

- Presenter: Aung Naing, M.D., FACP, MD Anderson Cancer Center
- Session: Developmental Immunotherapy and Tumor Immunobiology
- Date/Time: Saturday, June 1, 8:00 11:00 a.m.

Poster Discussion Session

CX-072, a PD-L1 Probody Therapeutic, as Monotherapy in Patients with Advanced Solid Tumors: Preliminary Results of PROCLAIM-CX-072

- Presenter: David B. Page, M.D., Providence Portland Medical Center
- Session: Developmental Immunotherapy and Tumor Immunobiology
- Date/Time: Saturday, June 1, 1:15 2:45 p.m.

<sup>\*</sup> Data presentations at ASCO will reflect a data cutoff of April 5, 2019.





### CX-072 + Ipilimumab (anti-CTLA-4) Combination



Sydnia

CYTOMX THERAPEUTICS

CYTOMX

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# Full Potential for Combination Immunotherapy is Limited by Immune-Related Toxicities

#### **CHECKMATE 67: COMBINATION TOXICITIES**

	Nivolumab Mono	lpilimumab Mono	Nivo + Ipi Combo¹
	melanoma	melanoma	melanoma
	3mg/kg every 2 weeks	3mg/kg every 3 weeks	nivo 1mg/kg + ipi 3mg/kg every 3 weeks
ORR	44%	19%	58%
Treatment related Grade 3/4 AEs	16%	27%	55%
Discontinued Drug	8%	15%	36%

#### **RESULTS FROM MSKCC EXPANDED ACCESS PROGRAM**<sup>2</sup>

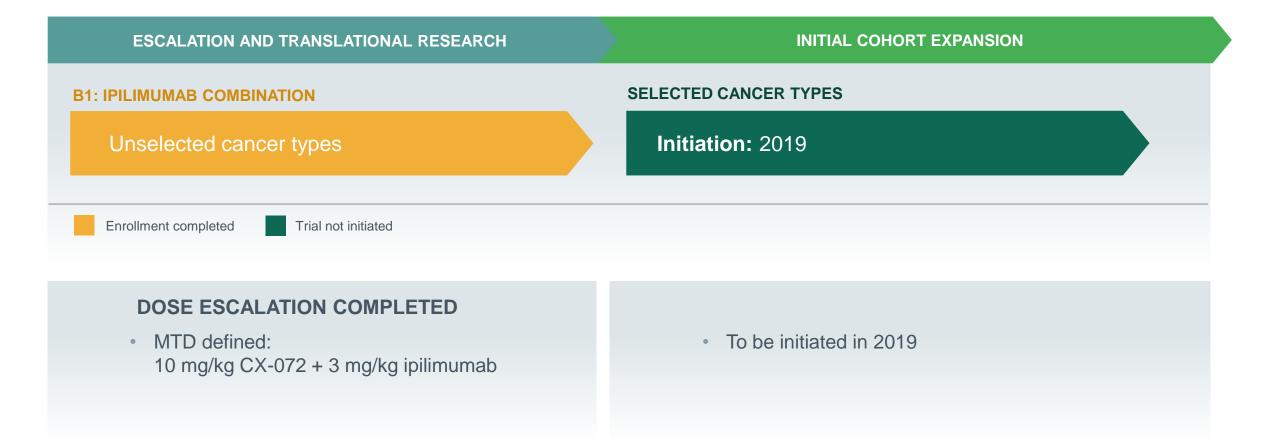
- 64 patients with advanced or unresectable melanoma
- Nivolumab (1 mg/kg) + Ipilimumab (3 mg/kg)
- 38 (59%) Grade 3/4 irAE
- 46 (72%) required steroids
- 36% irAE causing hospitalizations

#### CTLA-4 is the most common target evaluated in combination with PD-1/PD-L1<sup>3</sup>



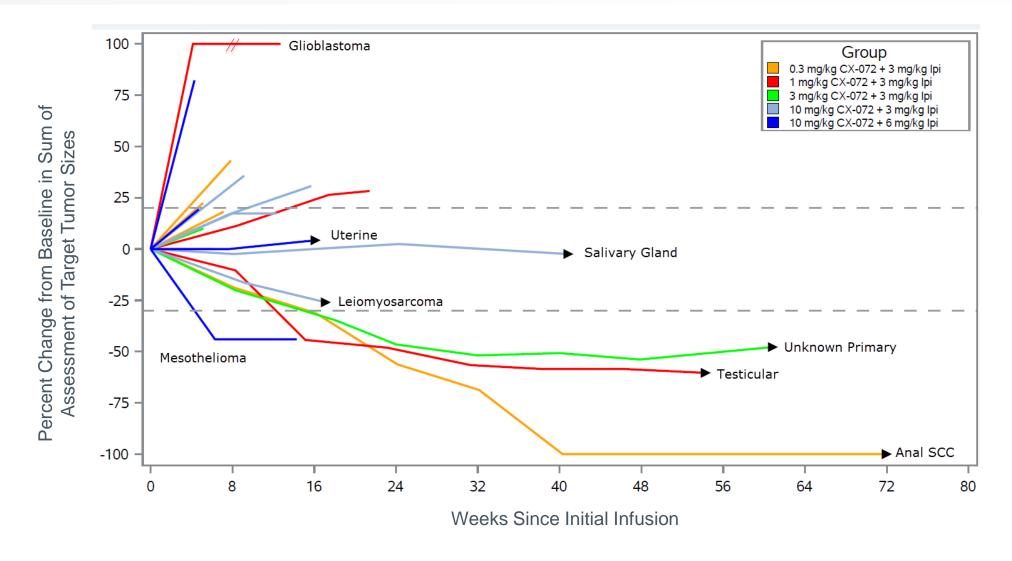
Larkin et al., NEJM, July 2015.
 Shoushtari AN, et al. JAMA Oncol. 2018; 4(1):98-101. doi:101001/jamaoncol.2017.2391
 Tang J, et al. Nature Reviews Drug Discovery. 17, 854–855 (2018)

## **PROCLAIM**Ipilimumab Combination Dose EscalationCX-072Now Complete





## **PROCLAIM**CX-072 plus Ipilimumab Combination:CX-072Durable Responses Observed





### **PROCLAIM**<br/>CX-072CX-072 plus Ipilimumab Combination: Clinically Manageable<br/>Safety Profile Compares Favorably to Historical Controls\*

	Total (N=27)	10 mg/kg CX-072 +3 mg/kg Ipilimumab (N=8)
NUMBER (%) OF SUBJECTS EXPERIENCING		
TEAE Grade 3+	14 (51.9)	4 (50.0)
Related to CX-072 (TRAE)	7 (25.9)	2 (25.0)
TEAE Leading to CX-072 Discontinuation	1 (3.7)	0
Related to CX-072 (TRAE)	1 (3.7)	0
TEAE Leading to Death	0	0
Related to CX-072 (TRAE)	0	0
IRRs	4 (14.8)	2 (25.0)
Grade 3+	1 (3.7)	1 (12.5)
IRAEs Grade 3+	3 (11.0)	0

\* Larkin et al., NEJM, July 2015.

treatment emergent adverse event (TEAE), treatment related adverse event (TRAE) infusion-related reactions (IRR), immune related adverse event (irAE) irAEs are defined as prospectively identified treatment-related AEs that are associated with the use of systemic or topical immunosuppressive agents or hormonal supplementation



### CX-072: Anti-PD-L1 Probody

SUMMARY	<ul> <li>Emerging product profile consistent with Probody platform vision</li> <li>Single-agent demonstrates anti-cancer activity in multiple tumor types</li> <li>Encouraging and potentially differentiated monotherapy safety profile</li> <li>Enables combination with full dose ipilimumab, leading to deep and durable responses</li> </ul>

#### **NEXT STEPS**

- Completion of monotherapy expansions and potential advancement to registrational study
- Initiation of expansions for ipilimumab combination in select tumor type(s)



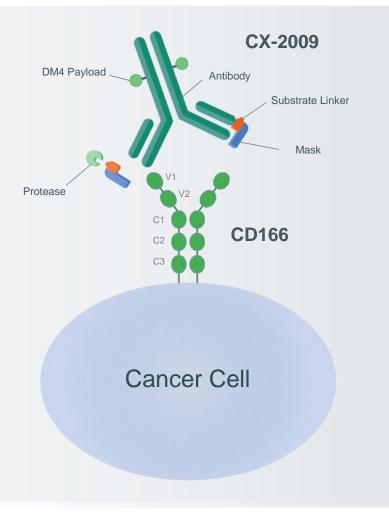


### CX-2009 A Probody Drug Conjugate with First-in-Class Potential



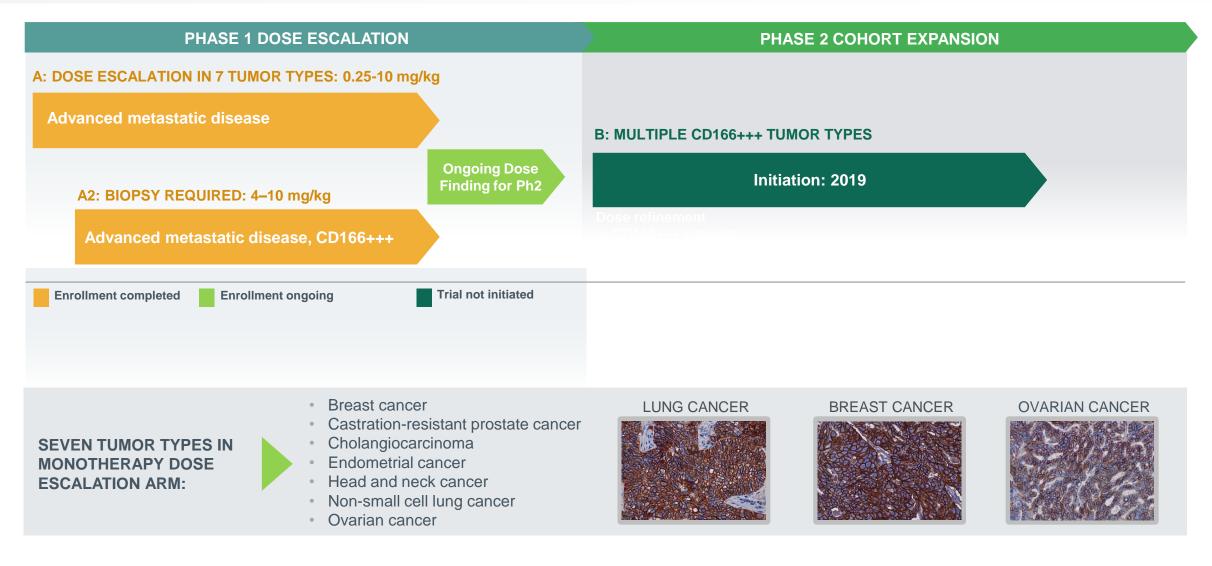
### CX-2009 is an Investigational First-in-Class Anti-CD166 Probody Drug Conjugate with Broad Market Potential

- CD166 is highly expressed in many cancers
  - Including breast, lung, ovarian, head and neck
  - Undruggable with conventional approaches due to normal tissue expression
- Probody platform enables the potential development of this attractive target with CX-2009
  - Masking technology limits binding to normal tissues
  - Potent SPDB-DM4 payload (microtubule inhibitor)





## **PROCLAIM** Phase 1 Dose Escalation and Next Steps

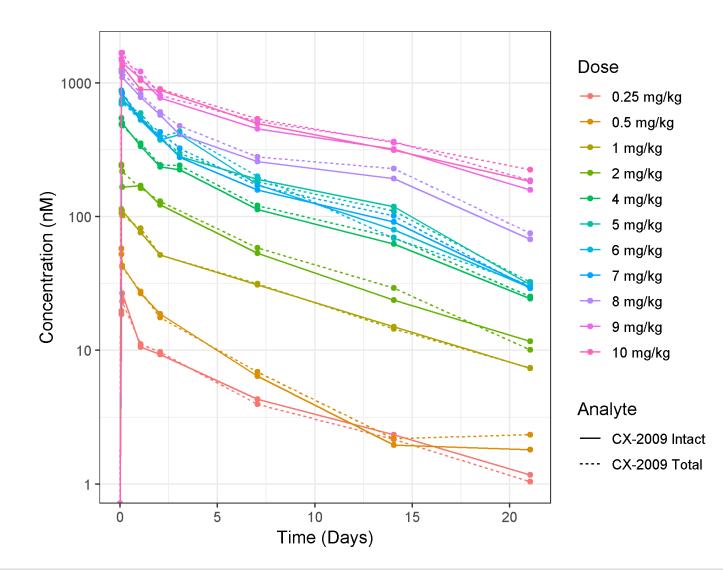




#### PROCLAIM CX-2009

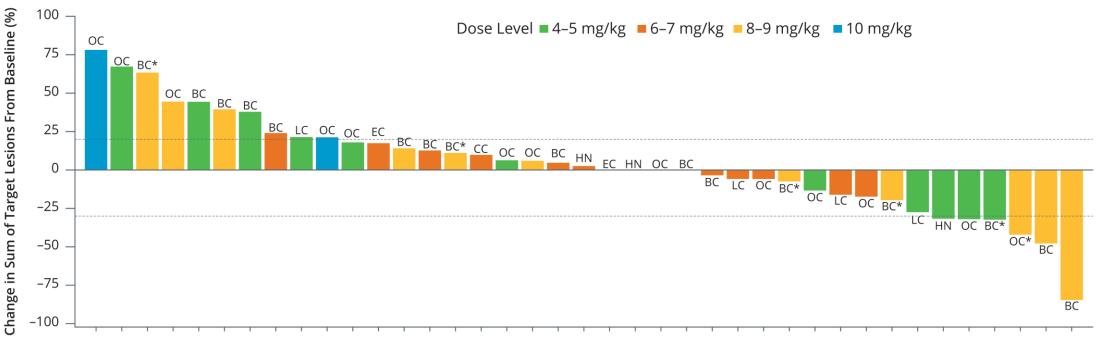
Phase 1 Dose Escalation: CX-2009 Remains Effectively Masked in the Circulation of Cancer Patients

 Single-dose CX-2009 PK data suggest that CX-2009 circulates predominantly as the intact prodrug species





## **PROCLAIM**Single Agent Activity for CX-2009 Observed inCX-2009Phase 1 Dose Escalation



Patient

\*Denotes patient considered to be on treatment, as no end-of-treatment date listed in database as of data cut-off date.

<sup>a</sup> CX-2009 4- to 10-mg/kg dose levels; response-evaluable population with post-baseline disease assessments.

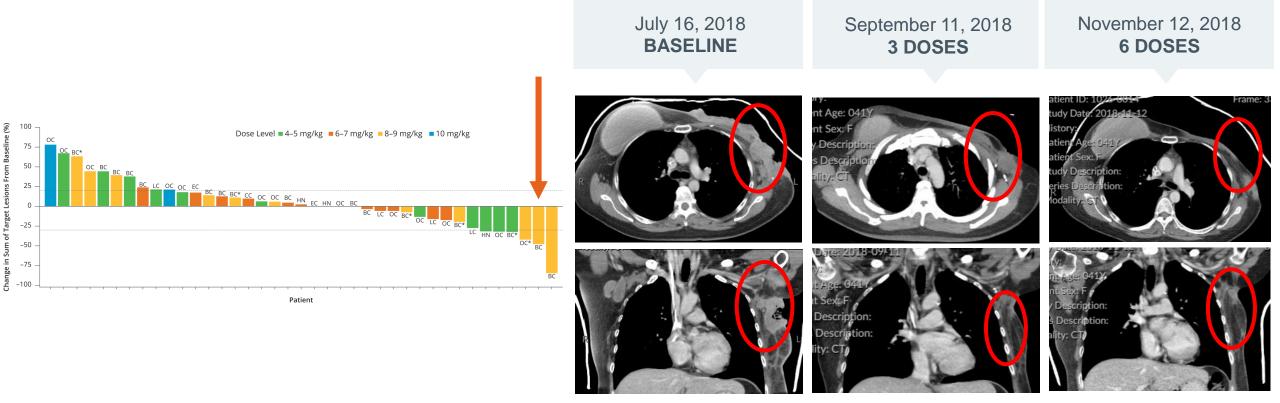
Patients (n=9) who are evaluable for efficacy but are not presented in the figure as the magnitude of tumor burden change was not in the database at the time of data cut-off. Patients (n=2) with non-measurable disease at baseline who are evaluable for efficacy are not included in the figure. Patients (n=3) with one evaluable post-baseline tumor scan <7 weeks from treatment start assessed as stable disease will be considered to have best overall response of not evaluable.

BC=breast carcinoma; LC=non-small cell lung carcinoma; OC=epithelial ovarian carcinoma; EC=endometrial carcinoma; HN=head and neck squamous cell carcinoma; CC=cholangiocarcinoma.

- 15/39 (38%) achieved tumor shrinkage
- 29/39 (74%) achieved stable disease or better at the time of the first on-treatment scan



## **PROCLAIM**Single Agent Activity for CX-2009 Observed in<br/>Phase 1 Dose Escalation



New lesion observed. Progression noted.

As of February 26, 2019 data snapshot Presented at AACR 2019 Case Study: Pembrolizumab-refractory TNBC Patient at 8 mg/kg



## **PROCLAIM**Anti-Cancer Activity Associated withCX-2009CD166 Expression

гомХ





# PROCLAIM Most Common Grade 3/4 Treatment-Related CX-2009 Adverse Events

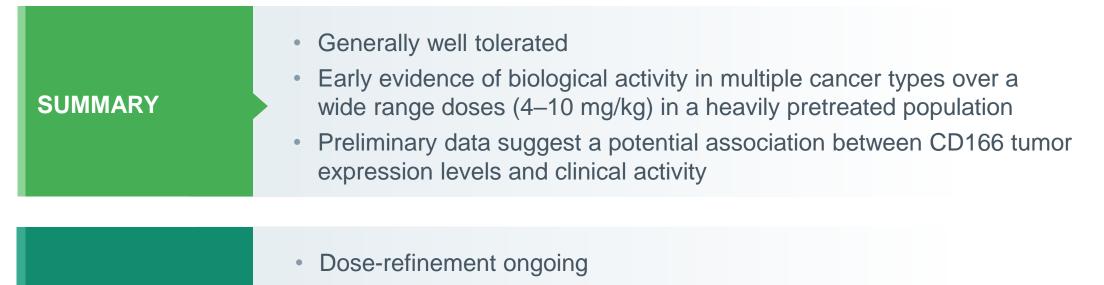
	< 4mg/kg (N=10)	4-5 mg/kg (N=19)	6-7 mg/kg (N=18)	8-9 mg/kg (N=23)	10 mg/kg (N=8)	All Cohorts
KERATITIS*	0	1 (5)	0	4 (17) <sup>a</sup>	1 (13)	6 (8)
INCREASED AST	0	0	0	1 (4)	3 (38)	4 (5)
INCREASED ALT	0	0	0	1 (4)	2 (25)	3 (4)
NAUSEA	0	0	1 (6)	2 (9)	1 (13)	4 (5)
HYPONATREMIA	0	0	2 (11)	1 (4)	0	3 (4)
ANEMIA	0	1 (5)	1 (6)	0	0	2 (3)
FATIGUE	0	1 (5)	0	0	1 (13)	2 (3)
PERIPHERAL SENSORY NEUROPATHY	0	1 (5)	1 (6)	0	0	2 (3)
VOMITING	0	0	1 (6)	1 (4)	0	2 (3)

Grade 3/4 Treatment Related Adverse Events Observed in  $\geq$  2 Patients

- \* Ocular prophylaxis not mandated in Phase 1 Dose Escalation
- <sup>a</sup> Including one patient with Grade 4 Keratitis



### CX-2009: CD166 Probody Drug Conjugate



 Addition of mandatory prophylactic measures to manage ocular toxicity and potentially prolong duration of treatment

• Plans for Phase 2 expansion under development



**NEXT STEPS** 

### Major Alliances Broaden Our Pipeline of Probody Therapeutics



#### • Multi-target collaboration

- CTLA-4 Probody Tx in Ph.1
- \$287 million earned to date
- >\$4 billion in potential milestones, tiered royalties up to low-double digits
- CD71 (CX-2029) +
  2 additional targets
- Co-development, co-commercialization, and profit split on CX-2029

abbvie

- IND on CX-2029 cleared in May 2018
- \$65 million earned to date
- Up to \$1B in potential milestones



- EGFR-TCB + 3 additional targets
- Co-development, profit split on EGFR-TCB
- \$1.4B in potential development, regulatory & commercial milestones
- \$60M earned to date
- CytomX receives rights to one Amgen preclinical TCB
- ~\$400 million to date from pharma partnering
- Two partnered assets in the clinic



### Deep and Differentiated Probody Pipeline

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	Immunotherapies	Probody Drug Conjugates	Pb T Cell Engaging Bispecifics	Multiple Programs



### 2019 Milestones



#### PROCLAIM-CX-072 (PD-L1 Probody Tx)

- ASCO 2019: Additional Monotherapy Expansion Data
- Ipilimumab Combination Next Steps
- Zelboraf<sup>®</sup> Combination Update

#### PROCLAIM-CX-2009 (CD166 PDC)

- Ongoing Dose Ranging
- Phase 2 Strategy

#### BMS-986249 (CTLA-4 Probody Tx)

 BMS Anticipates Data Disclosures in 2019





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