

## **REIMAGINING THERAPEUTIC ANTIBODIES**

H.C. Wainwright 21<sup>st</sup> Annual Global Investment Conference





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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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## **Company Highlights**

Clinical-stage biopharmaceutical company developing unique cancer treatments with a novel class of antibodies:

> Probody™ Therapeutics

- Leader in field of "conditional activation" of therapeutic antibodies with broad platform technology and discovery engine
- Four drug candidates in the clinic against validated and first in class targets
- CX-072 (anti-PD-L1): an emerging, differentiated centerpiece of combination therapy
- CX-2009 (anti-CD166): first in class potential in many solid tumor types
- Major strategic partnerships: CX-2029 (anti-CD71) with AbbVie, BMS-986249 (anti-CTLA-4) with BMS
- Strong balance sheet; \$349 million at end of Q2



## **Reimagining Therapeutic Antibodies**

#### ANTIBODIES ARE A SUCCESSFUL CLASS OF THERAPEUTICS

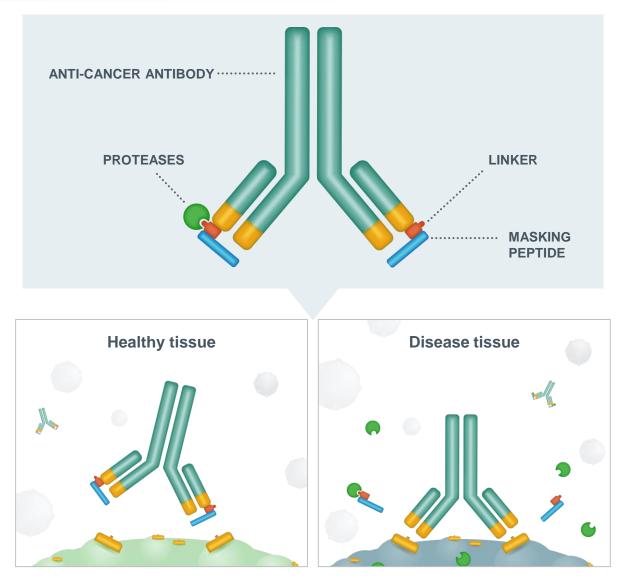
- Powerful, potent modalities; > \$100 billion WW sales 2018
- Potency can be a liability for widely distributed targets
- Major opportunity to improve targeting and localize antibody pharmacology

#### 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 therapeutics, a unique class of localized, antibody prodrugs



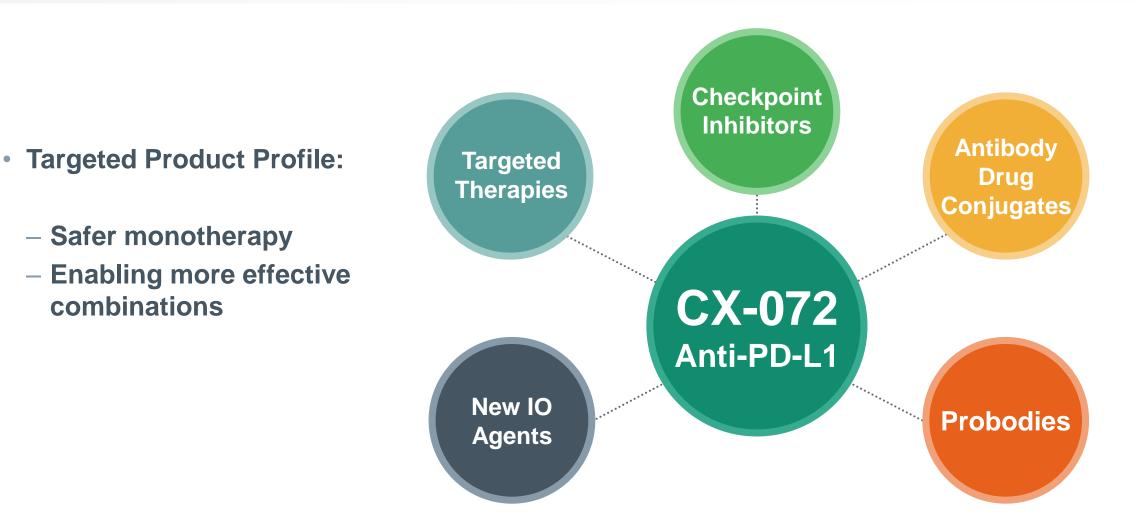


## **Deep and Differentiated Probody Pipeline**

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
BMS-986249	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 Pb-TCB			AMGEN CYTOMX
Additional PDCs, IO, TCBs				СутомХ
	Immunotherapies P	Probody Drug Conjugates	Pb T Cell Engaging Bispecifics	Multiple Programs

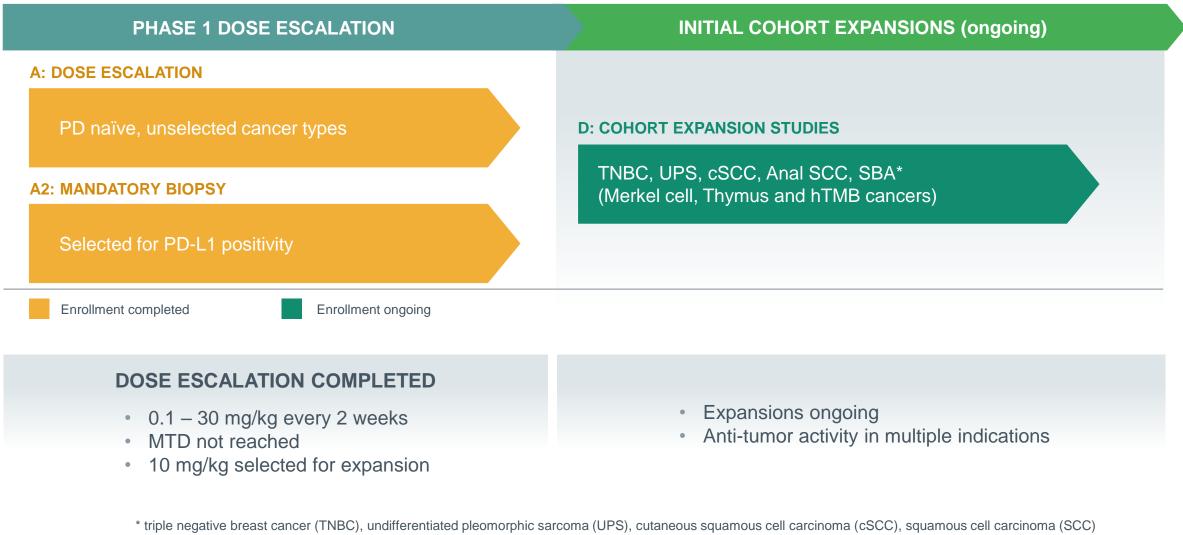


# CX-072: Potential as a Differentiated anti-PD-L1 Centerpiece of Cancer Combination Therapy



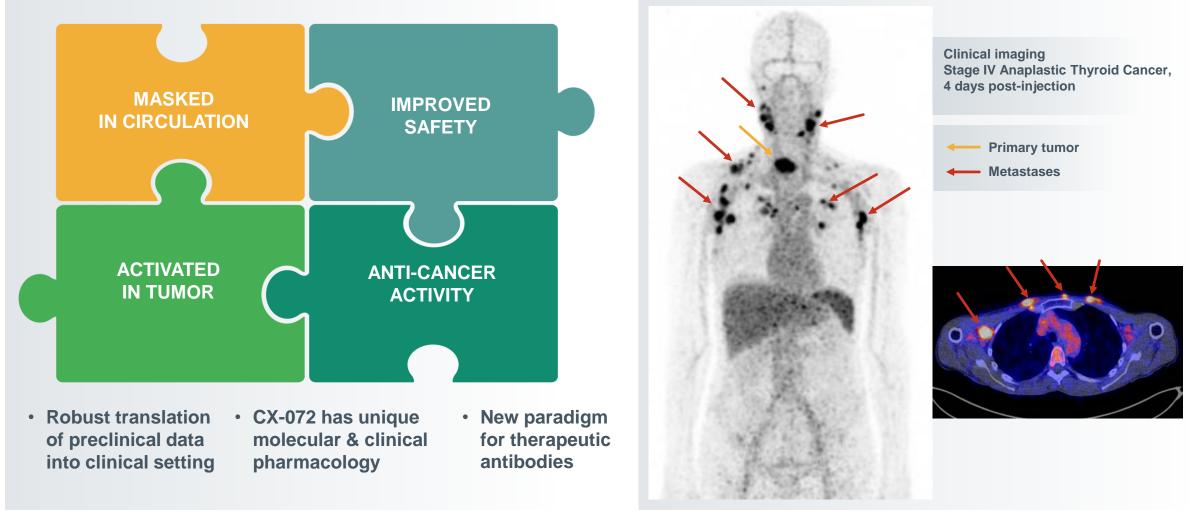






and small bowel adenocarcinoma (SBA)

CX-072 Phase 1 Dose Escalation Data Support Proof of Concept for Probody Platform and Novel anti-PD-L1 Agent



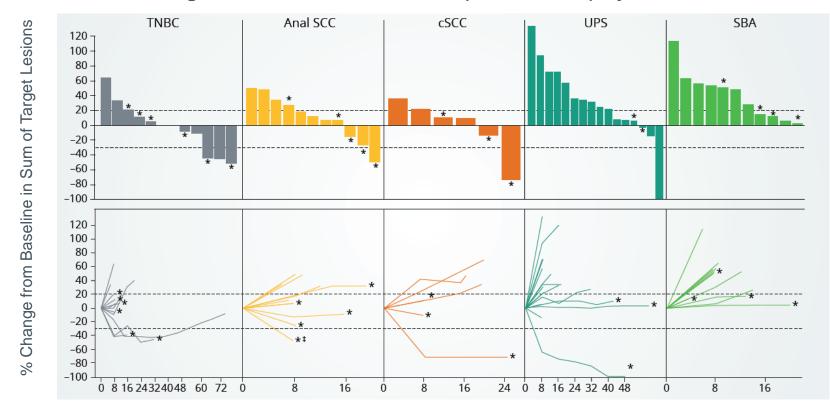
Autio KA et al. Poster 3071. ASCO 2018, Jun 1-5, Chicago, Illinois. Boni V et al. Poster 435P. ESMO 2018, Oct 19-23, Munich, Germany. Lyman SK et al. Poster P87. SITC; 2018 November 7-11, Washington, D.C.



Collaboration with E. G. E. de Vries, University Medical Center Groningen, The Netherlands

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

Percent Change from Baseline in Sum of Target Lesion Measurements (Top Panel) Percent Change in Tumor Burden Over Time (Bottom Panel), by Cancer Classification



Weeks Since Treatment Initiation

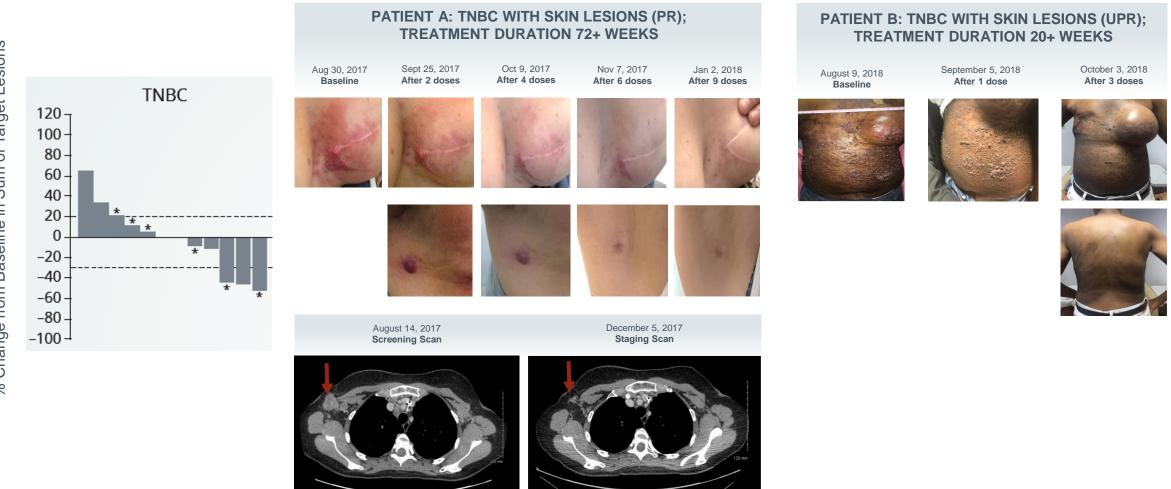
triple negative breast cancer (TNBC), squamous cell carcinoma (SCC), cutaneous squamous cell carcinoma (cSCC), undifferentiated pleomorphic sarcoma (UPS), small bowel adenocarcinoma (SBA)

\* Denotes patient considered to be on treatment, as no end-of-treatment date was listed in database as of data cut-off (April 5, 2019). Evaluable patients include those in the safety population except patients who are ongoing with no post-baseline response assessment as of data cut-off.

<sup>‡</sup> At data cutoff, the patient had unconfirmed partial response that was subsequently confirmed.



#### Case Studies: PROCLAIM Anti-Tumor Activity at 10 mg/kg in TNBC CX-072





\* Denotes patient considered to be on treatment, as no end-of-treatment date was listed in database as of data cut-off (April 5, 2019). Evaluable patients include those in the safety population except patients who are ongoing with no post-baseline response assessment as of data cut-off.

## PROCLAIM<br/>CX-072Preliminary Safety: Monotherapy at 10 mg/kgLow Rates of ≥3 TRAEs and irAEs

	Total (N=72)*
NUMBER (%) OF SUBJECTS EXPERIENCING	3
TEAE Grade 3+	35 (49.0)
Related to CX-072 (TRAE)	4 (6.0)
TEAE Leading to CX-072 Discontinuation	2 (3.0)
Related to CX-072 (TRAE)	0
TEAE Leading to Death	1 (1.0)
Related to CX-072 (TRAE)	0
IRRs	4 (6.0)
Grade 3+	0
IRAEs Grade 3+	2 (3.0)

\* triple negative breast cancer (TNBC), squamous cell carcinoma (SCC), cutaneous squamous cell carcinoma (cSCC), undifferentiated pleomorphic sarcoma (UPS), small bowel adenocarcinoma (SBA)

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 + Ipilimumab (anti-CTLA-4) Combination

CYTOMX THERAPEUTICS

Sydnia

CYTOMX

Erwan

## 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>

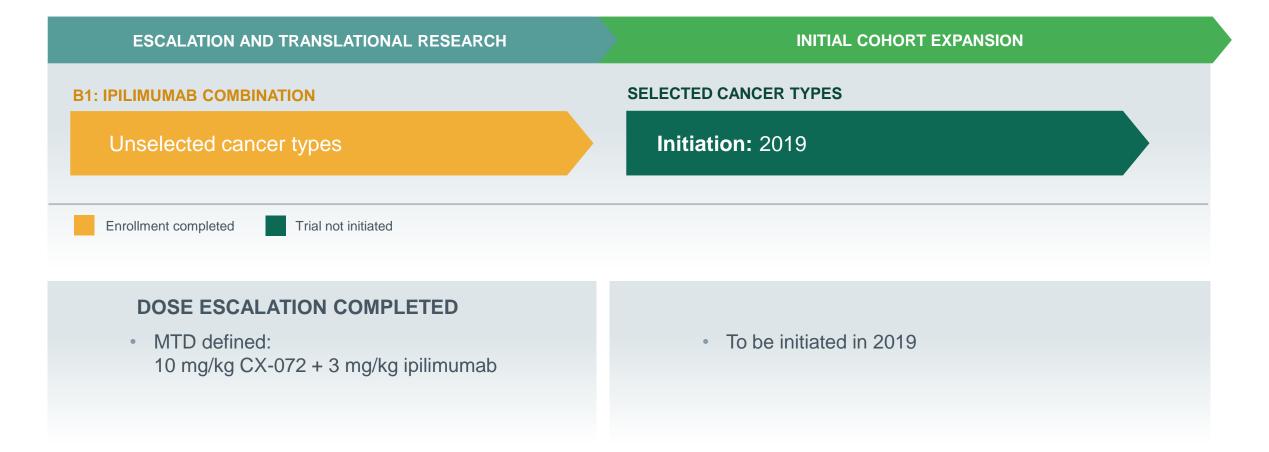
- 64 patients with advanced or unresectable melanoma
- Nivolumab (1 mg/kg) + Ipilimumab (3 mg/kg)
- 38 (59%) Grade 3/4 irAE
- 46 (72%) required steroids
- 36% irAE causing hospitalizations

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



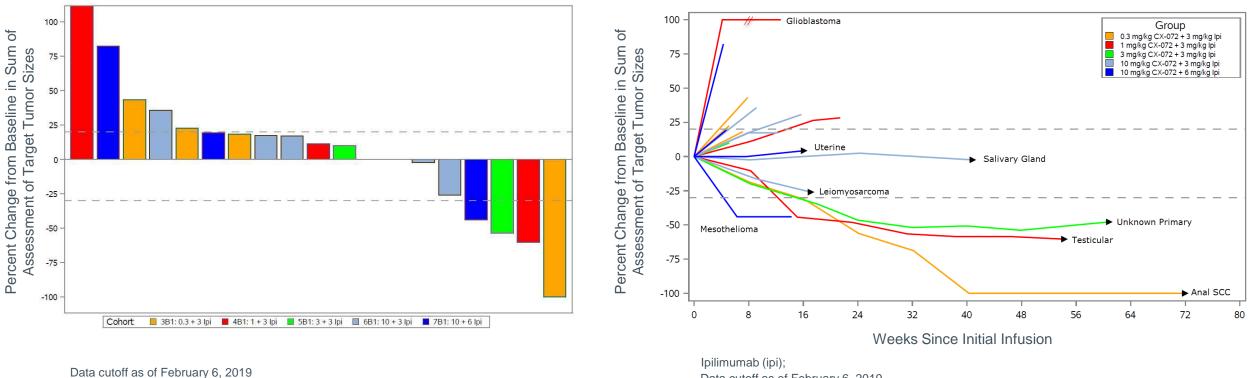
Larkin et al., NEJM, July 2015.
 Shoushtari AN, et al. JAMA Oncol. 2018; 4(1):98-101. doi:101001/jamaoncol.2017.2391
 Tang J, et al. Nature Reviews Drug Discovery. 17, 854–855 (2018)

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





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



Data cutoff as of February 6, 2019



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

	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 Therapeutic

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)



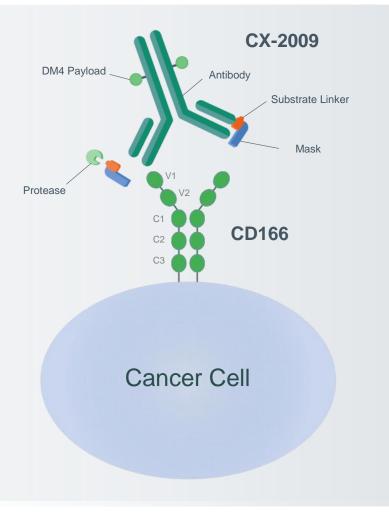


## CX-2009 A Probody Drug Conjugate with First-in-Class Potential



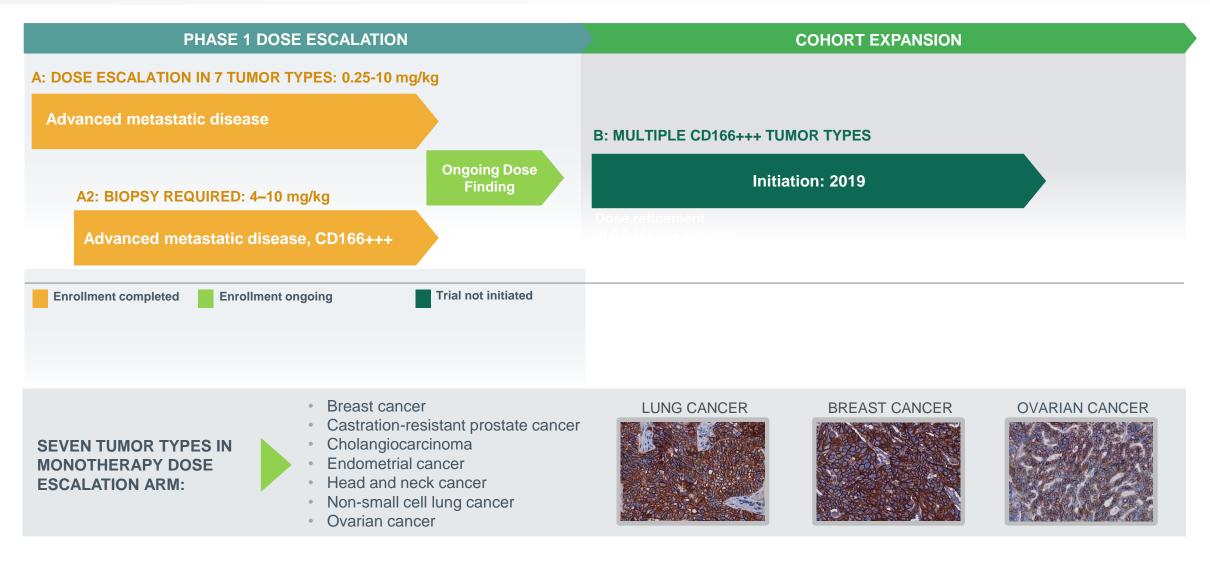
## CX-2009 is an Investigational First-in-Class Anti-CD166 Probody Drug Conjugate with Broad Market Potential

- 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)



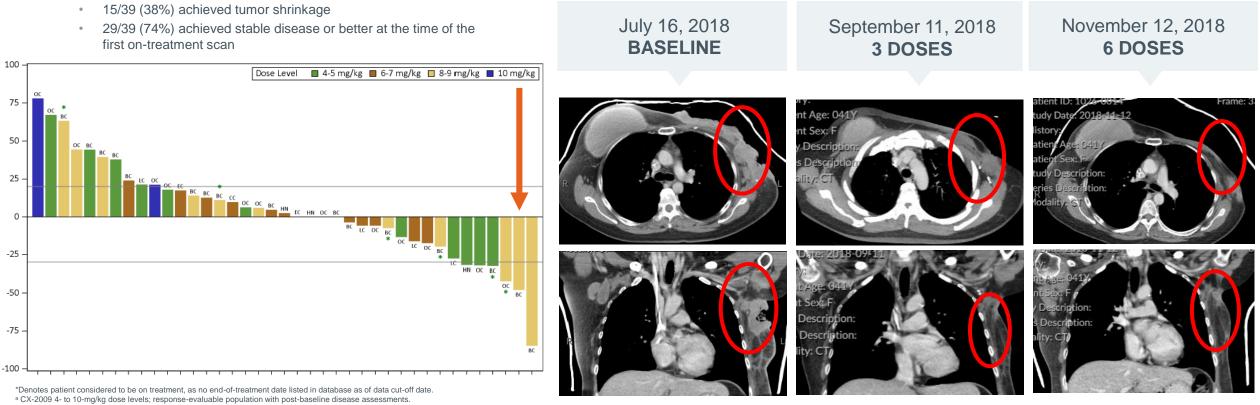








## **PROCLAIM**Single Agent Activity for CX-2009 Observed in<br/>Phase 1 Dose Escalation



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 as the magnitude of tumor total cut-off. Patients (n=2) with non-measurable disease at baseline who are evaluable for efficacy are not included in the figure as the magnitude of tumor total cut-off. Patients (n=2) with non-measurable disease at baseline who are evaluable for efficacy are not included in the figure as the magnitude of tumor total cut-off. Patients (n=2) with non-measurable disease at baseline who are evaluable for efficacy are not included in the figure as the magnitude of total cut-off.

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.

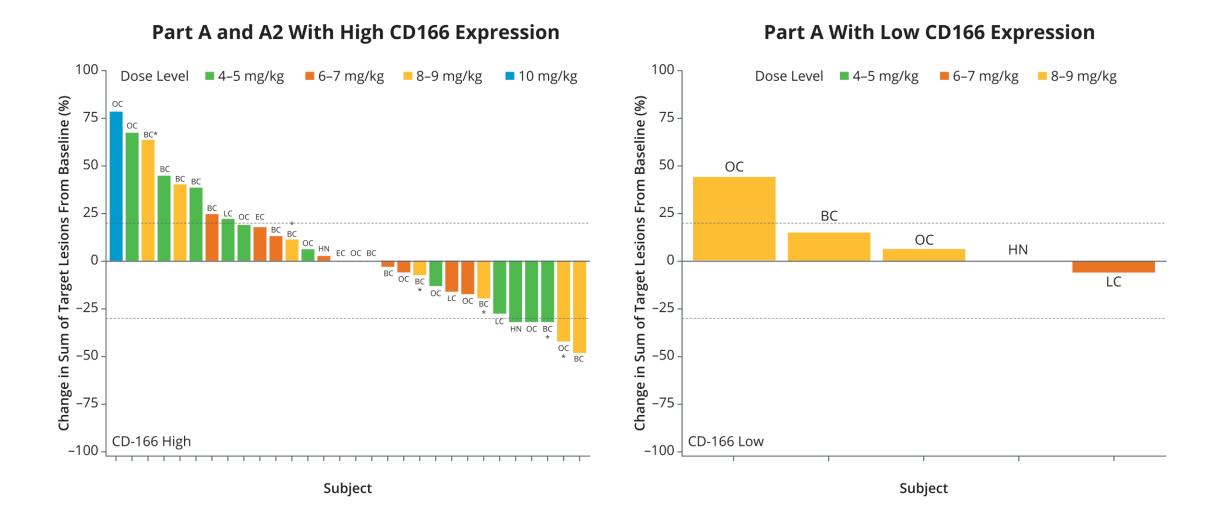
As of February 26, 2019 data snapshot Presented at AACR 2019 New lesion observed. Progression noted.

Case Study: Pembrolizumab-refractory TNBC Patient at 8 mg/kg



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

гомХ

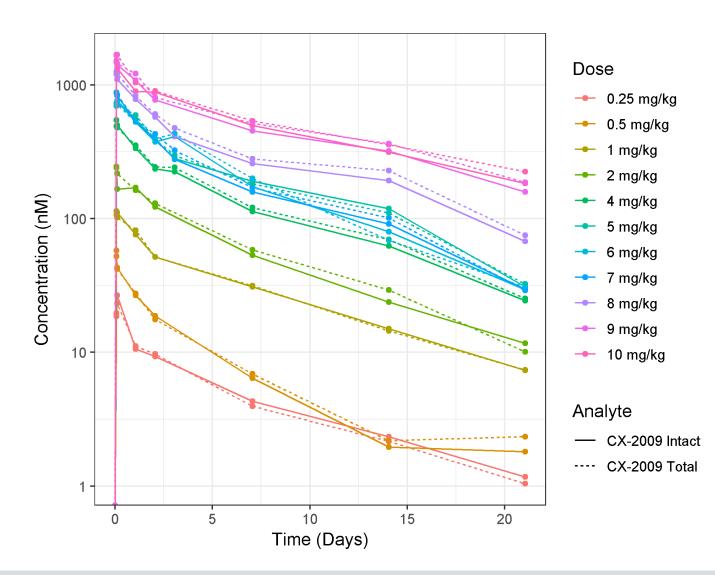




### PROCLAIM CX-2009

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
- Consistent with prior findings for CX-072





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

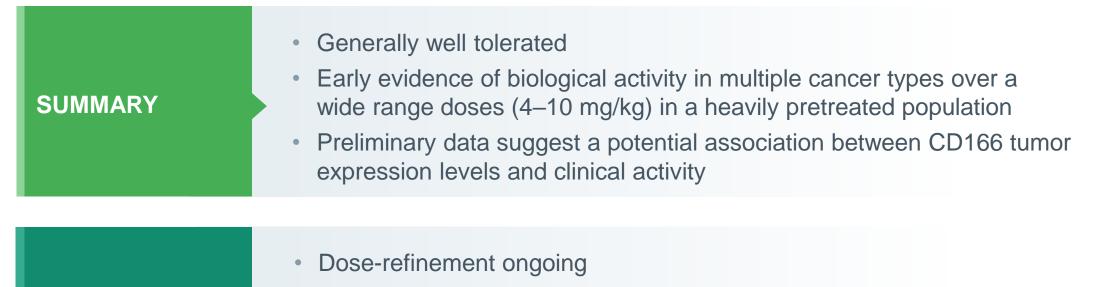
	< 4mg/kg (N=10)	4-5 mg/kg (N=19)	6-7 mg/kg (N=18)	8-9 mg/kg (N=23)	10 mg/kg (N=8)	All Cohorts
KERATITIS*	0	1 (5)	0	4 (17) <sup>a</sup>	1 (13)	6 (8)
INCREASED AST	0	0	0	1 (4)	3 (38)	4 (5)
INCREASED ALT	0	0	0	1 (4)	2 (25)	3 (4)
NAUSEA	0	0	1 (6)	2 (9)	1 (13)	4 (5)
HYPONATREMIA	0	0	2 (11)	1 (4)	0	3 (4)
ANEMIA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



**NEXT STEPS** 

## Major Alliances Broaden Our Pipeline of Probody Therapeutics



- Multi-target collaboration
- CTLA-4 Probody Tx entering
   Ph.2
- \$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

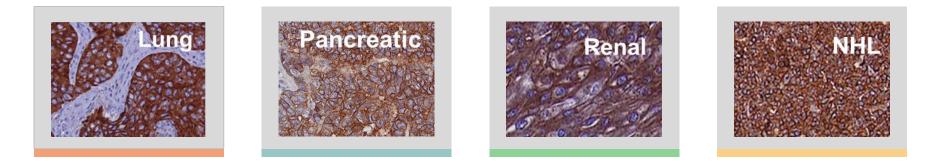
- IND for CX-2029 cleared in May 2018
- \$75 million earned to date
- Up to \$1B in potential milestones

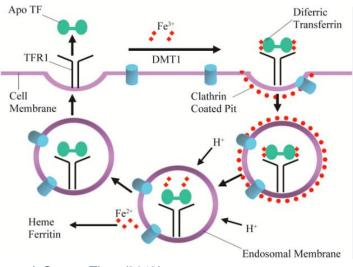


- EGFR-TCB + 3 additional targets
- Co-development, profit split on EGFR-TCB
- \$1.4B in potential development, regulatory & commercial milestones
- \$60M earned to date
- CytomX receives rights to one Amgen preclinical TCB
- ~\$400 million to date from pharma partnering
- Two partnered assets advanced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



## CD71 is a High Potential Target for a Probody Drug Conjugate





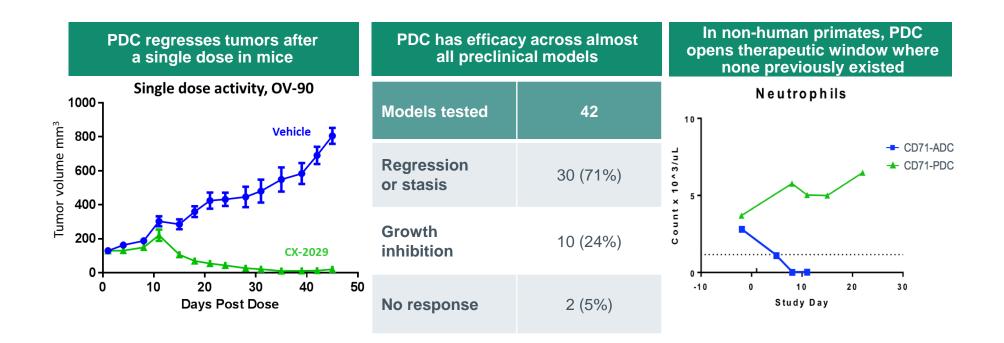
J. Cancer Ther. (2012)

- Ubiquitously expressed on dividing, normal and malignant cells
- Mediates iron uptake required for cell division
- Professional internalizing protein: often used as a positive control in ADC experiments
- Expression in normal dividing cells prohibits development of a traditional ADC





# Probody Platform Has the Potential to Enable CD71 as a Drug Conjugate Target



Partnered with AbbVie: Co-development rights and profit split; \$25M milestone to CytomX received July 2018; Enrolling Phase 1/2 Trial

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PROCLAIM-CX-2029: CD71-Directed PDC Exploratory Studies in 2018-2019 Drive Expansion Studies in 2019-2020

EXPLORATORY	EXPANSION			
A: DOSE ESCALATION Initiation: Q2 2018 Inclusion: Solid Tumors, Lymphoma Data Presentation: TBA Initiation: 2019 Inclusion: Solid Tumors, Lymphoma Data Presentation: TBA	<b>C: COHORT EXPANSION(S)</b> Initiation: TBD Inclusion: Solid Tumors, Lymphoma Data Presentation: TBA			
Enrollment ongoing Trial not initiated				
CytomX and AbbVie are co-developing a PDC against CD71, with CytomX leading pre-clinical and early clinical development				

abbvie



## Deep and Differentiated Probody Pipeline

PRODUCT CANDIDATE	LEAD OPTIMIZATION	IND-ENABLING	PHASE 1/2	COMMERCIAL RIGHTS
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Additional PDCs, IO, TCBs				СутомХ
	Immunotherapies	Probody Drug Conjugates	Pb T Cell Engaging Bispecifics	Multiple Programs



## 2019 Achievements and Upcoming Milestones

### **Wholly-Owned Clinical Programs**

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

- ✓ Part D monotherapy expansion data
- ✓ Additional Ipilimumab combination data

### 2H 2019

- Monotherapy next steps
- YERVOY<sup>®</sup> (ipilimumab) combination next steps
- ZELBORAF<sup>®</sup> (vemurafenib) combination

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

- ✓ Phase 1 dose escalation
- Initiation of dose-finding mTPI phase

#### 2H 2019

 Dose selection and indication(s) for cohort expansion

### **Partnered Clinical Programs**

#### **BMS** Alliance

 Ongoing BMS-986249 Phase 1 Study (anti-CTLA-4)

### 2H 2019

Randomized Phase 2 Study (www.ClinicalTrials.gov)

#### **AbbVie Alliance**

- Progression of CX-2029 (anti-CD71)
   Phase 1 dose escalation by CytomX
- Selection of 2<sup>nd</sup> target under Discovery Collaboration

