

REIMAGINING THERAPEUTIC ANTIBODIES

Barclays Global Healthcare Conference 2019





MARCH 12, 2019

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Reimagining Therapeutic Antibodies

ANTIBODIES ARE A SUCCESSFUL CLASS OF THERAPEUTICS

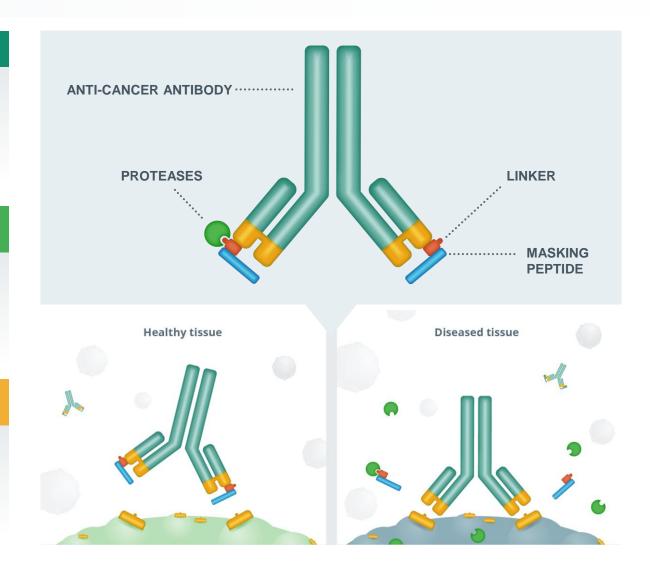
- Powerful, potent modalities; > \$100 billion WW sales 2018
- Potency can be a liability for widely distributed targets
- Major opportunity to improve targeting and localize antibody pharmacology

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

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

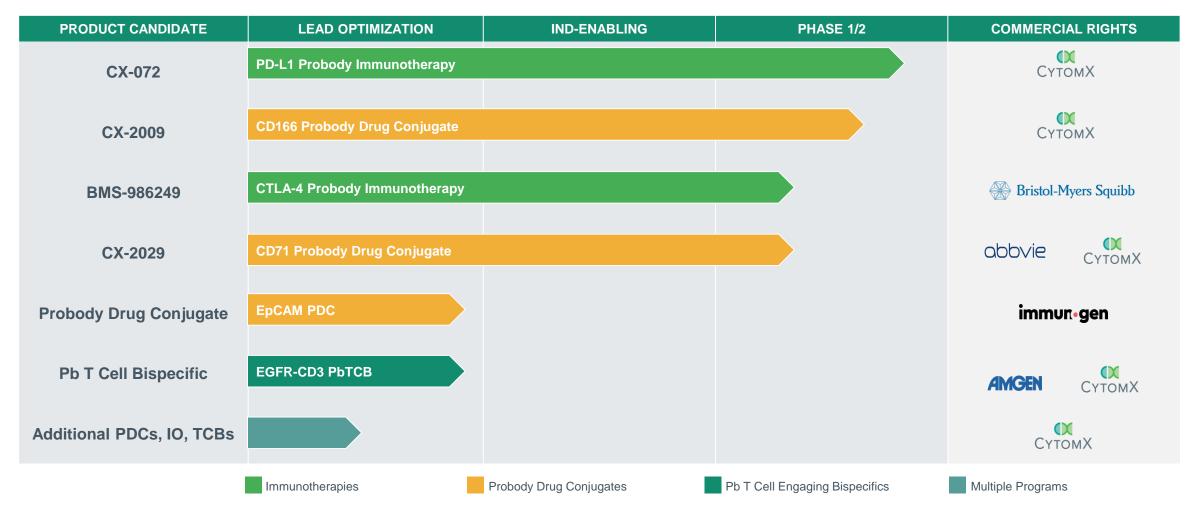
PROBODY PLATFORM BUILT ON A DECADE OF "HIGH SCIENCE" RESEARCH AT CYTOMX

- 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





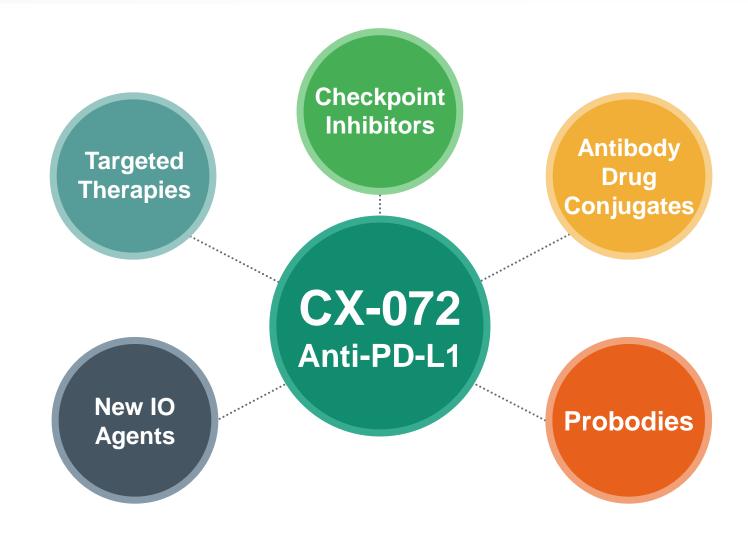






CX-072: Potential as a Differentiated anti-PD-L1 Centerpiece of Cancer Combination Therapy

- Targeted Product Profile:
 - Safer monotherapy
 - Enabling more effective combinations







Clinical Trial Design Monotherapy

PHASE 1 DOSE ESCALATION

A: DOSE ESCALATION

PD naïve, unselected cancer types

A2: MANDATORY BIOPSY

Selected for PD-L1 positivity

Enrollment completed

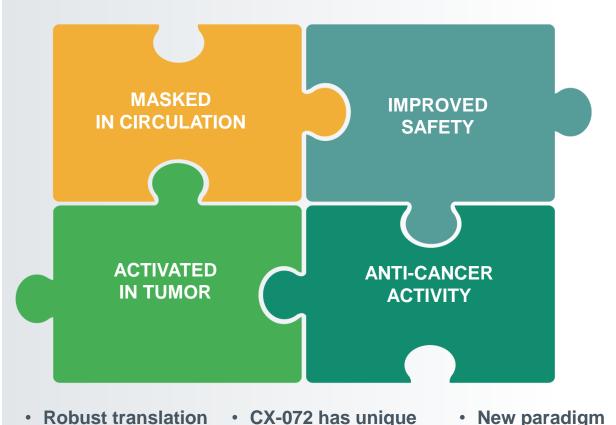
Enrollment ongoing

DOSE ESCALATION COMPLETED

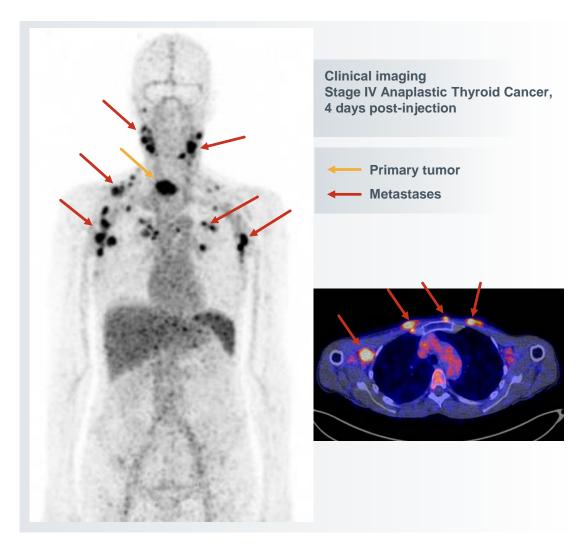
- 0.1 30 mg/kg every 2 weeks
- MTD not reached
- 10 mg/kg selected for expansion



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



- Robust translation of preclinical data into clinical setting
- CX-072 has unique molecular & clinical pharmacology
- New paradigm for therapeutic antibodies

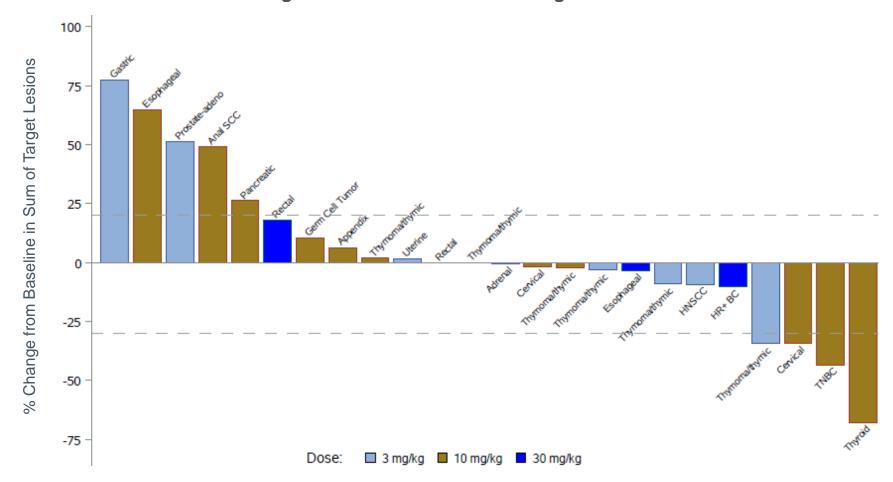






Monotherapy Anti-Cancer Activity at ≥ 3mg/kg from Dose Escalation

Best Percent Change from Baseline in Sum of Target Lesion Measurements







Monotherapy Expansions Underway

PHASE 1 DOSE ESCALATION A: DOSE ESCALATION PD naïve, unselected cancer types A2: MANDATORY BIOPSY Selected for PD-L1 positivity Enrollment completed Enrollment ongoing INITIAL COHORT EXPANSIONS (ongoing) D: COHORT EXPANSION STUDIES TNBC, UPS, cSCC, Anal SCC* (Merkel cell, Small Bowel, Thymus and hTMB cancers)

DOSE ESCALATION COMPLETED

- 0.1 30 mg/kg every 2 weeks
- MTD not reached.
- 10 mg/kg selected for expansion

- Expansions ongoing
- Anti-tumor activity in multiple indications

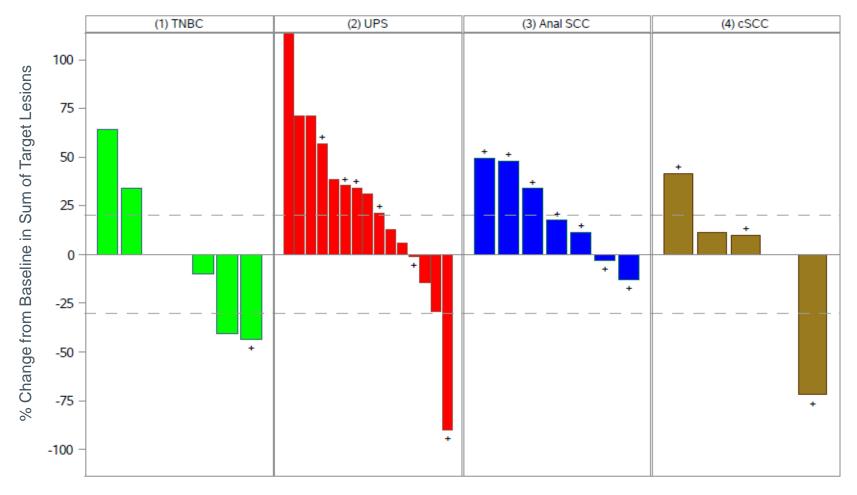


^{*} triple negative breast cancer (TNBC), undifferentiated pleomorphic sarcoma (UPS), cutaneous squamous cell carcinoma (cSCC) and anal squamous cell carcinoma (SCC)



Cohort Expansions: Monotherapy CX-072 is Active in Multiple Tumor Types at 10 mg/kg

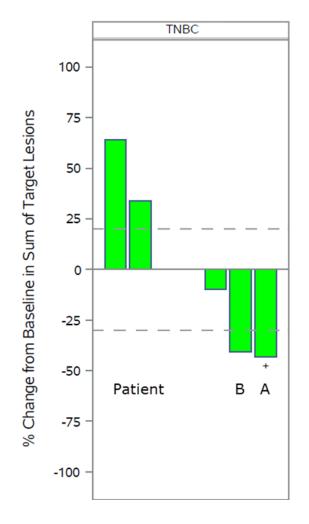
Best Percent Change from Baseline in Sum of Target Lesion Measurements, by Cancer Classification

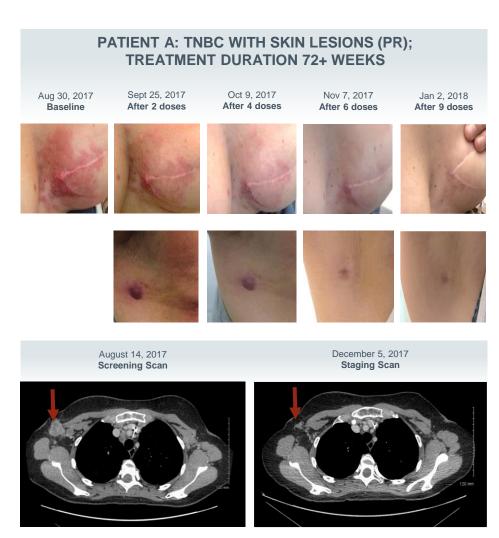






Case Study: Anti-Tumor Activity at 10 mg/kg in TNBC











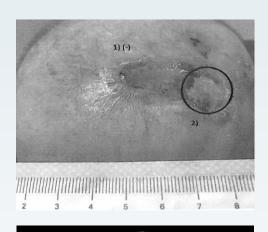
Case Study: Cutaneous Squamous Carcinoma (cSCC) Patient

CUTANEOUS SCC SCALP LESIONS





Baseline Scan 9/21/18





Response Scan 1/25/2019





Preliminary Safety: Monotherapy at 10 mg/kg Limited Grade 3/4 TRAEs and Immune-related AEs

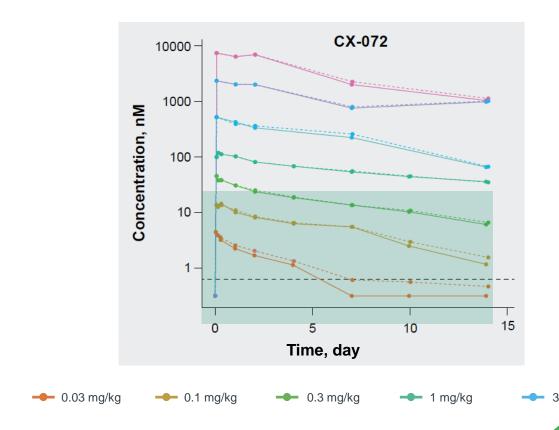
	Total (N=50)*
NUMBER (%) OF SUBJECTS EXPERIENCING	
TEAE Grade 3+	21 (42.0)
Related to CX-072 (TRAE)	2 (4.0)
TEAE Leading to CX-072 Discontinuation	1 (2.0)
Related to CX-072 (TRAE)	0
TEAE Leading to Death	1 (2.0)
Related to CX-072 (TRAE)	0
IRRs	3 (6.0)
Grade 3+	0
IRAEs Grade 3+	2 (4.0)

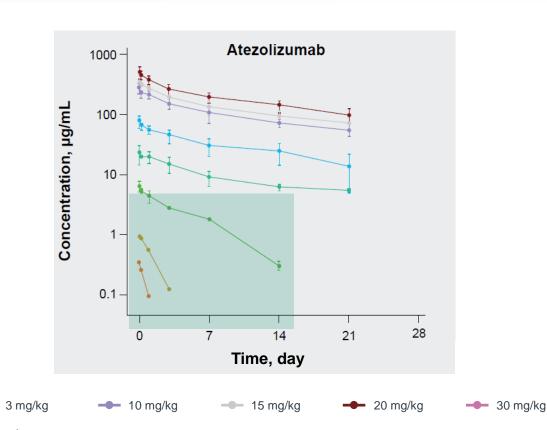
^{*} triple negative breast cancer (TNBC), undifferentiated pleomorphic sarcoma (UPS), cutaneous squamous cell carcinoma (cSCC) and anal squamous cell carcinoma (SCC) patients treatment emergent adverse event (TEAE), treatment related adverse event (TRAE) infusion-related reactions (IRR), immune related adverse event (irAE) irAEs are defined as prospectively identified treatment-related AEs that are associated with the use of systemic or topical immunosuppressive agents or hormonal supplementation





Phase 1 Dose Escalation: CX-072 Remains Effectively Masked in the Circulation of Cancer Patients

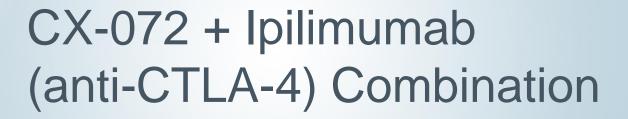




- Single-dose CX-072 PK data and PK modelling suggest that CX-072 circulates predominantly as the intact prodrug species
- Clearance is minimally influenced by target mediated drug disposition











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

CHECKMATE 67: COMBINATION TOXICITIES

	Nivolumab Mono	Ipilimumab 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 PROGRAM²

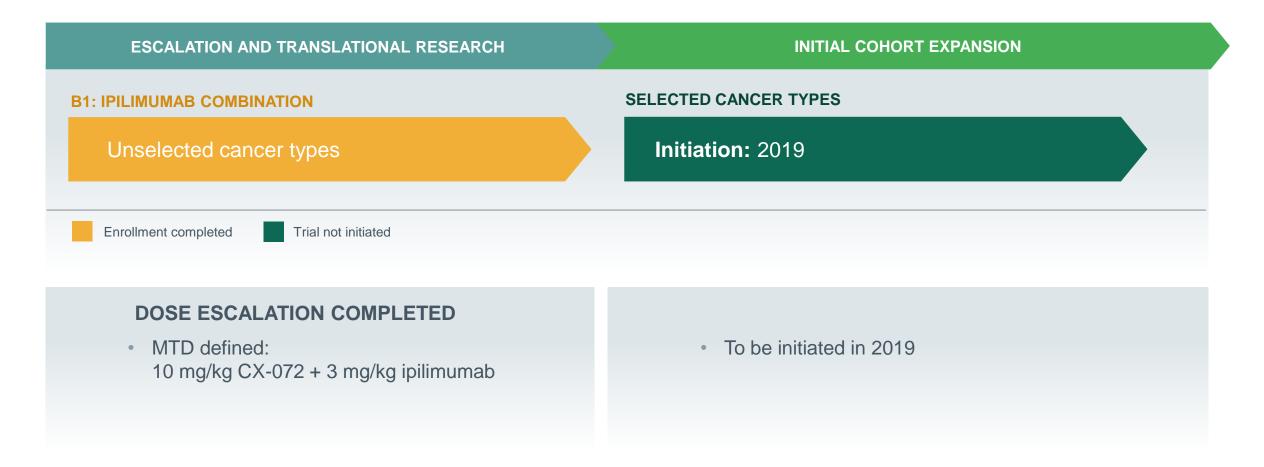
- 64 patients with advanced or unresectable melanoma
- Nivolumab (1 mg/kg) + Ipilimumab (3 mg/kg)
- 38 (59%) Grade 3/4 irAE
- 46 (72%) required steroids
- 36% irAE causing hospitalizations

CTLA-4 is the most common target evaluated in combination with PD-1/PD-L13

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



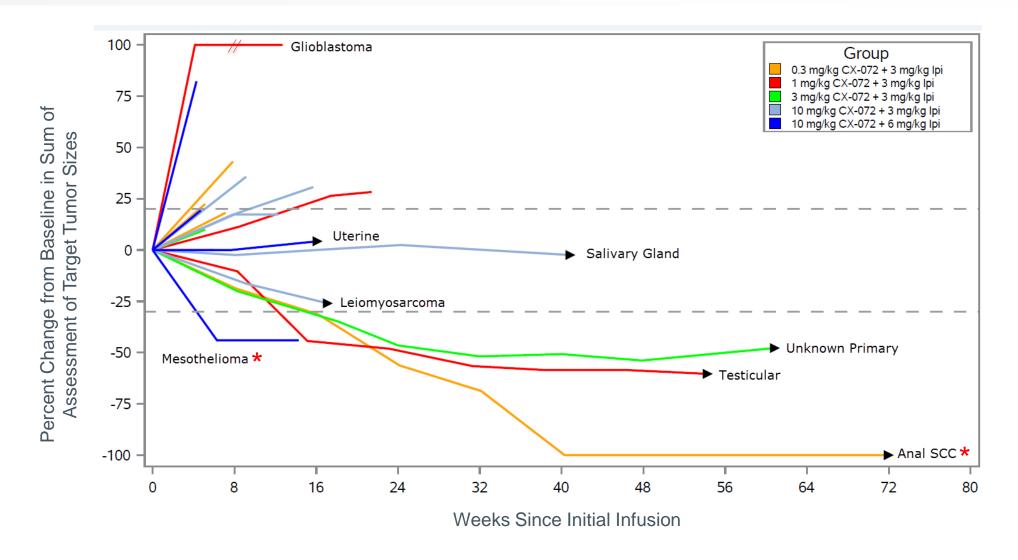
Ipilimumab Combination Dose Escalation Now Complete







CX-072 plus Ipilimumab Combination: Durable Responses Observed







CX-072 plus Ipilimumab Combination: Clinically Manageable 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



Data cutoff as of February 6, 2019

CX-072 Anti-PD-L1 Probody

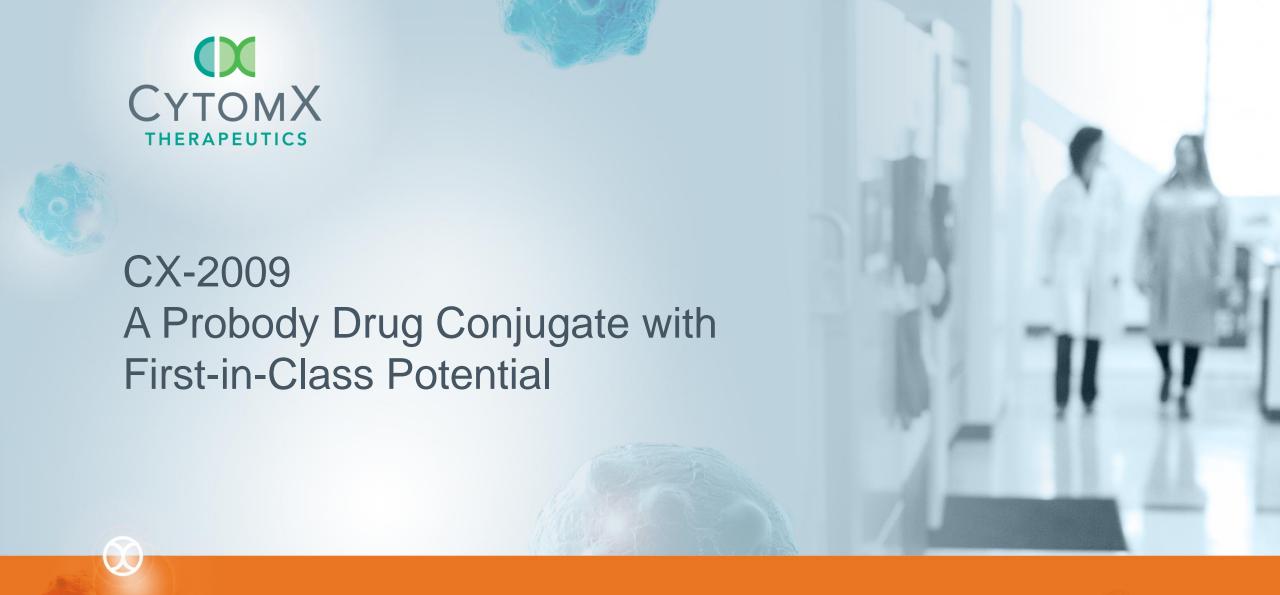
Summary

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

Next Steps

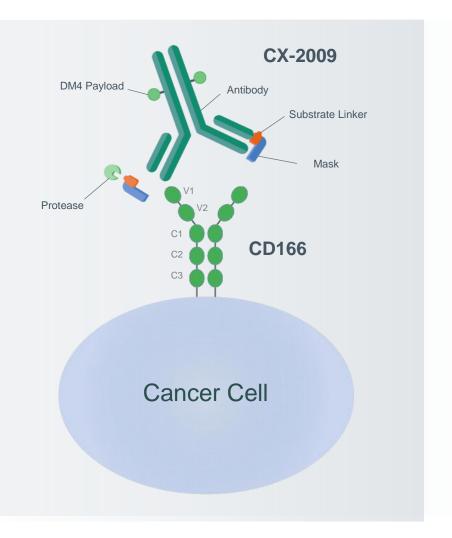
- Completion of monotherapy expansions and potential advancement to registrational study
- Initiation of expansions for ipilimumab combination in select tumor type(s)





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

- CD-166 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)







Phase 1 Dose Escalation

A: DOSE ESCALATION IN 7 TUMOR TYPES: 0.25-10 mg/kg

Advanced metastatic disease

A2: BIOPSY REQUIRED: 4-10 mg/kg

Advanced metastatic disease, CD166+++

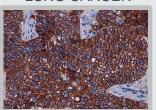
Enrollment completed

SEVEN TUMOR TYPES IN MONOTHERAPY DOSE ESCALATION ARM:

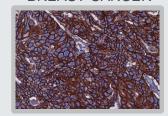


- Breast cancer
- · Castration-resistant prostate cancer
- Cholangiocarcinoma
- Endometrial cancer
- Head and neck cancer
- Non-small cell lung cancer
- Ovarian cancer

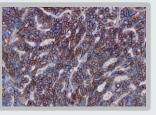
LUNG CANCER



BREAST CANCER



OVARIAN CANCER





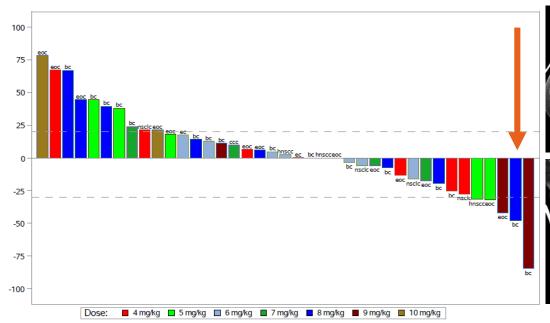


Single Agent Activity for CX-2009 Observed in Phase 1 Dose Escalation

July 16, 2018 BASELINE

September 11, 2018 3 DOSES

November 12, 2018 6 DOSES















New lesion observed. Progression noted

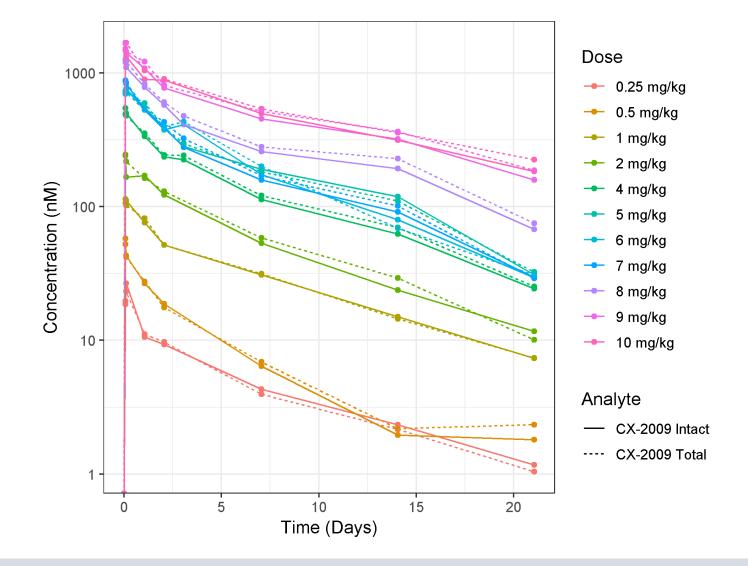
Case Study: Pembrolizumab-refractory TNBC Patient at 8 mg/kg





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







Most Frequent Grade 3/4 Treatment-Related Adverse Events

	< 4mg/kg (N=10)	4-5 mg/kg (N=19)	6-7 mg/kg (N=18)	8-9 mg/kg (N=21)	10 mg/kg (N=8)
TOTAL SUBJECTS WITH GRADE 3-4 TRAEs	0	4 (21.1)	4 (22.2)	11 (52.4)	4 (50)
EYE DISORDERS*	0	1 (5.3)	0	5 (23.8)	1 (12.5)
METABOLISM AND NUTRITION DISORDERS	0	0	2 (11.1)	2 (9.5)	0
LIVER FUNCTION TESTS	0	0	0	1 (4.8)	3 (37.5)
GASTROINTESTINAL DISORDERS	0	0	1 (5.6)	2 (9.5)	1 (12.5)
NERVOUS SYSTEM DISORDERS	0	1 (5.3)	2 (11.1)	0	0

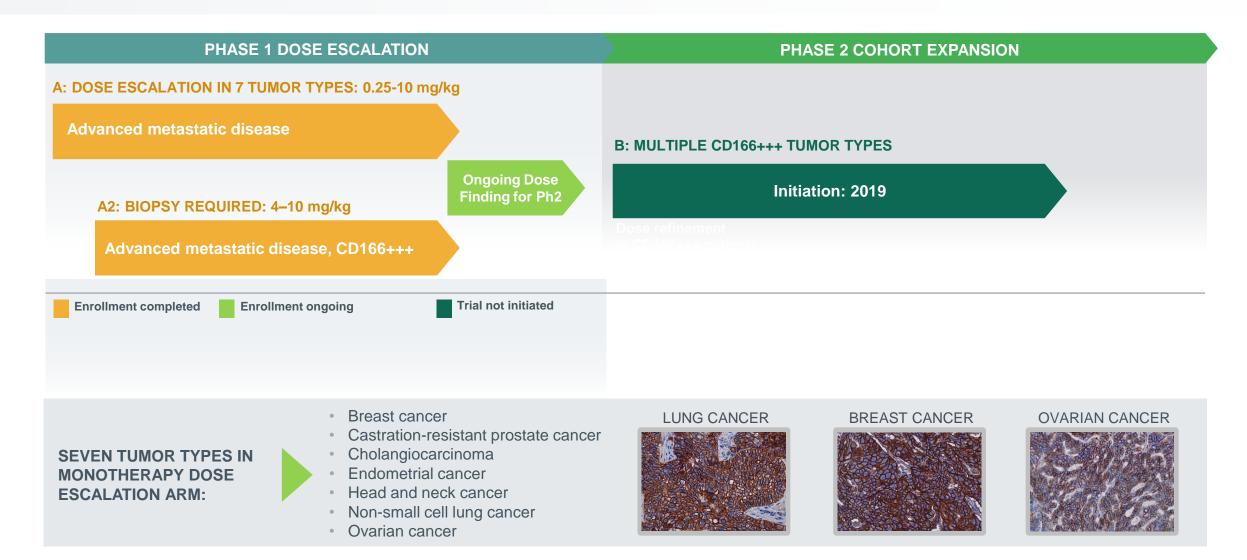
Grade 3/4 Treatment Related Adverse Events Observed in ≥ 2 Patients

^{*} Ocular prophylaxis not mandated in Phase 1 Dose Escalation



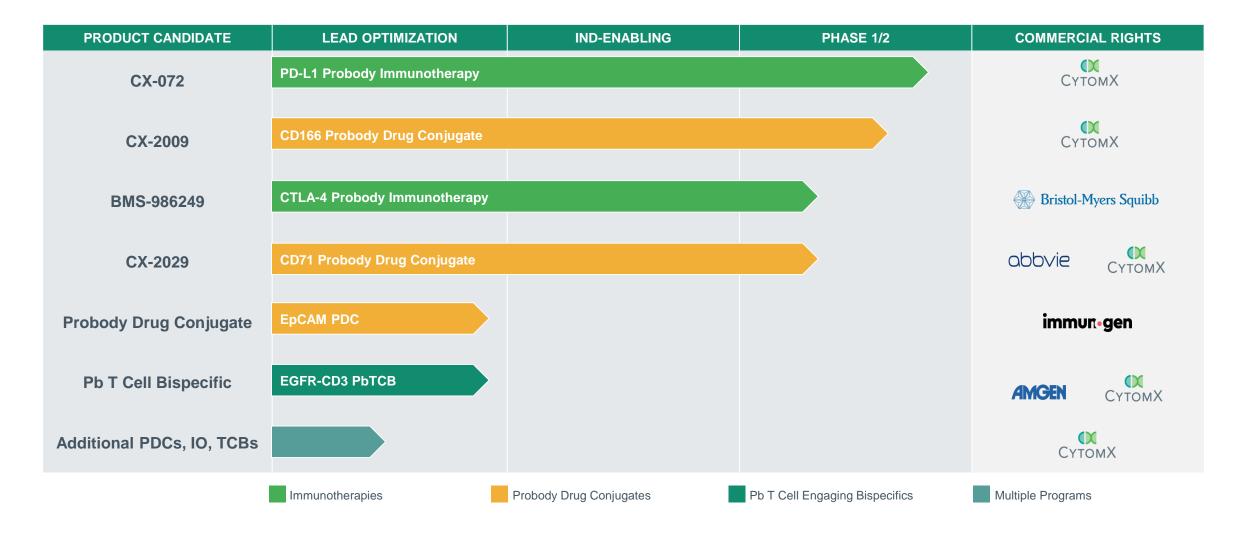
Data cutoff as of February 6, 2019

PROCLAIM Next Steps





Deep and Differentiated Probody Pipeline





Major Alliances Broaden Our Pipeline of Probody Therapeutics



abbvie



- 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
- 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



Upcoming Milestones



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

Updates 2019:
 Monotherapy Expansion
 Data, Zelboraf®
 Combination Data,
 Ipilimumab Combination
 Next Steps

PROCLAIM-CX-2009 (CD166 PDC)

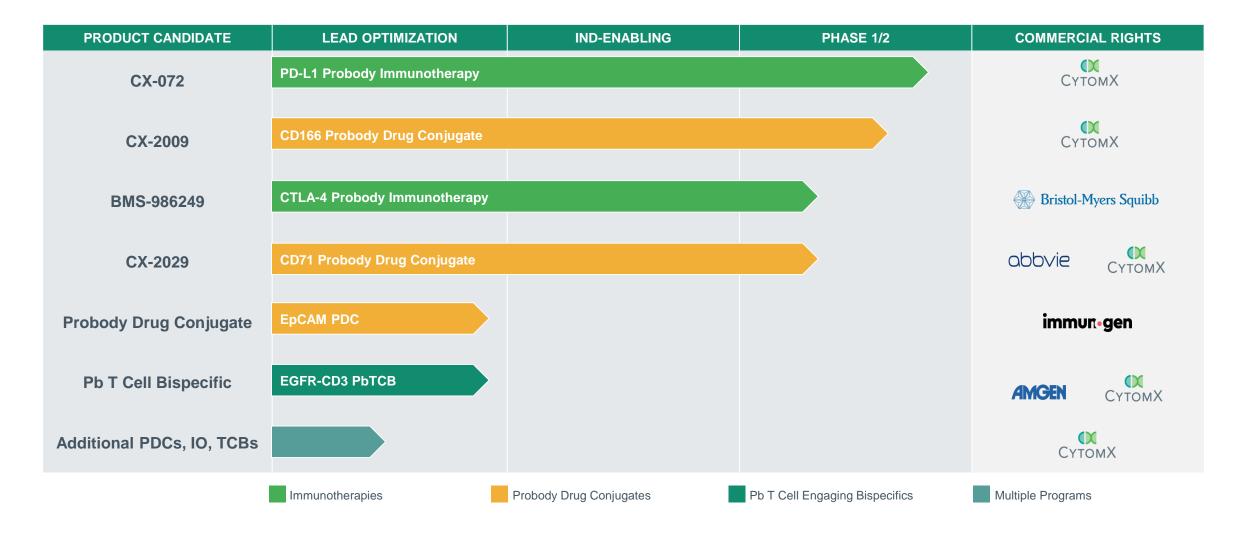
 Update 2019: Additional safety and efficacy readout from Parts A and A2, Cohort Expansions Open

BMS-986249 (CTLA-4 Probody Tx)

 BMS Anticipates Data Disclosures in 2019

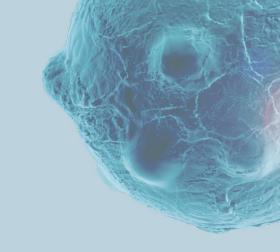


Deep and Differentiated Probody Pipeline









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