



# REIMAGINING THERAPEUTIC ANTIBODIES

Cowen and Company 39<sup>th</sup> Annual Health Care Conference



MARCH 11, 2019

# Forward Looking Statement

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.

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

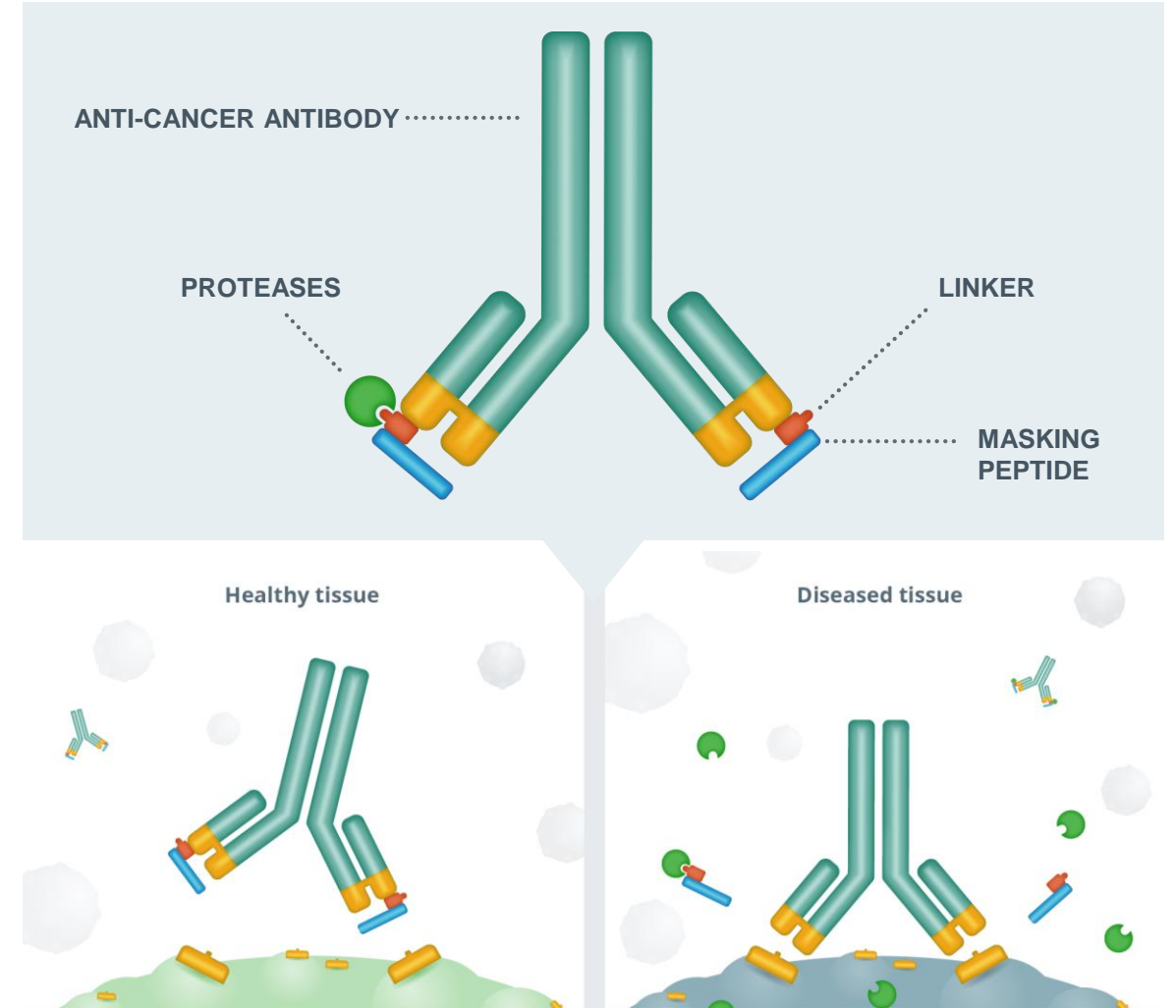
- Powerful, potent modalities; > \$100 billion WW sales 2018
- Potency can be a liability for widely distributed targets
- Major opportunity to improve targeting and localize antibody pharmacology

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

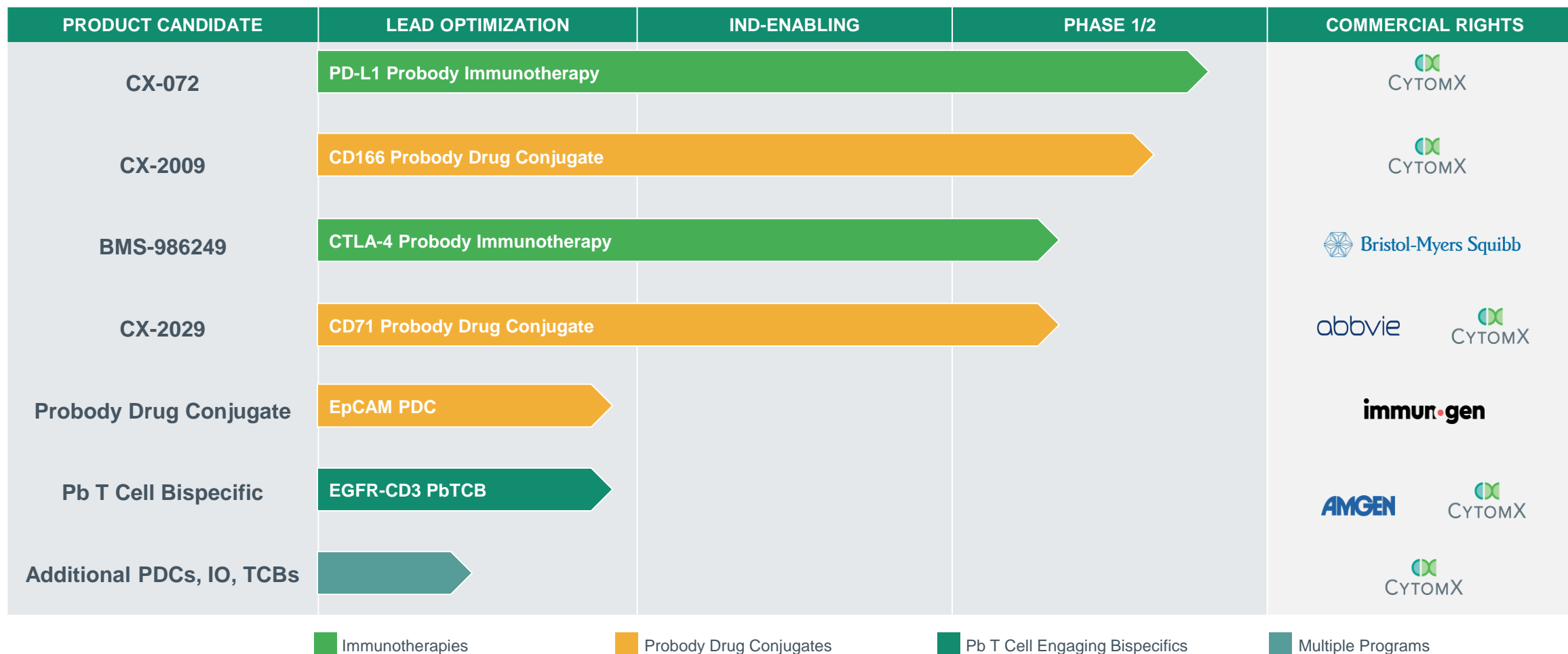
- Maintaining potency
- Reducing side effects
- Enabling new target opportunities

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



# Deep and Differentiated Probody Pipeline



*\$436.1M in cash at end of Q4 2018*



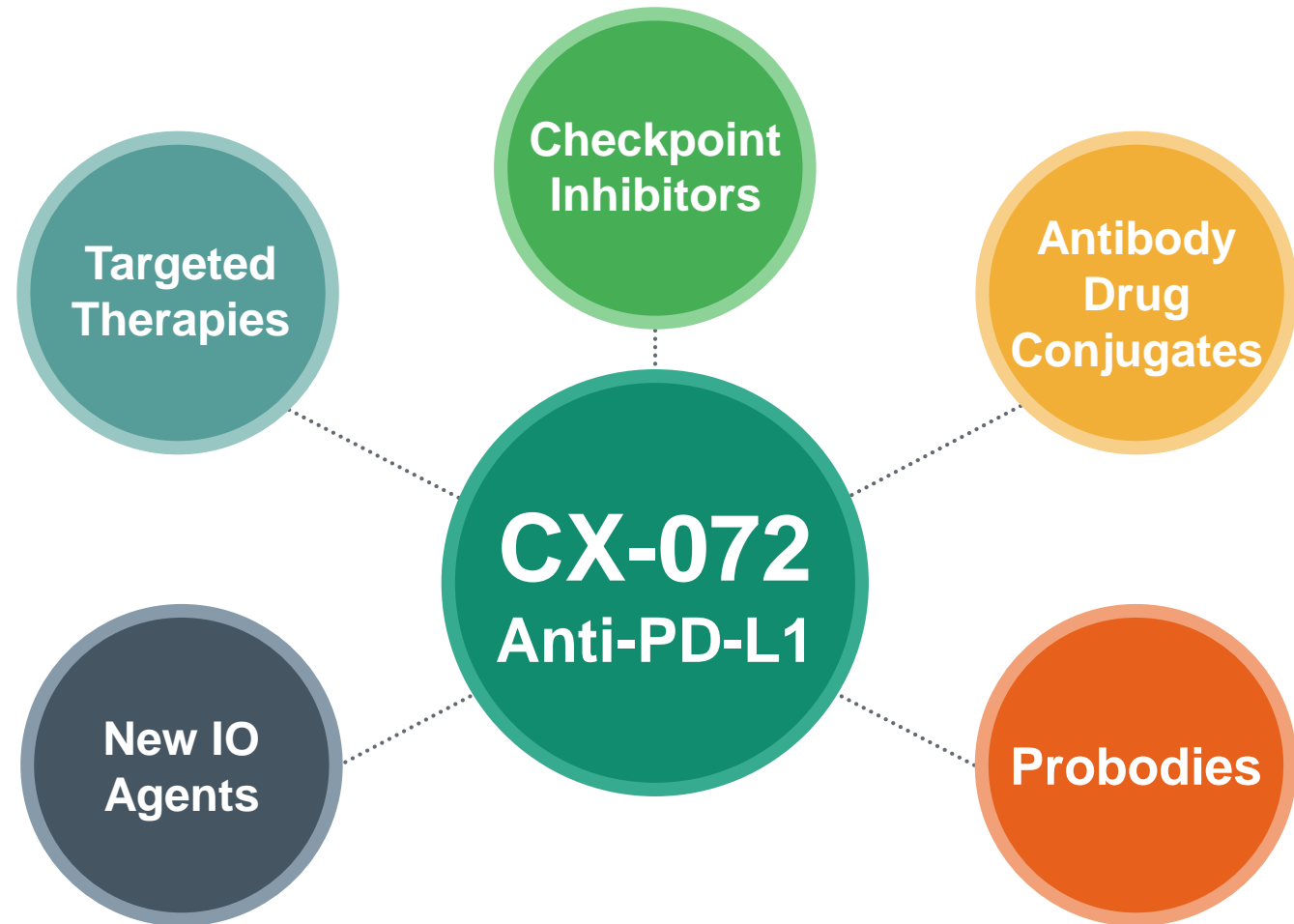
# CX-072

## A Differentiated Anti-PD-L1 Probody Therapeutic



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

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



## PHASE 1 DOSE ESCALATION

### A: DOSE ESCALATION

PD naïve, unselected cancer types

### A2: MANDATORY BIOPSY

Selected for PD-L1 positivity



Enrollment completed



Enrollment ongoing

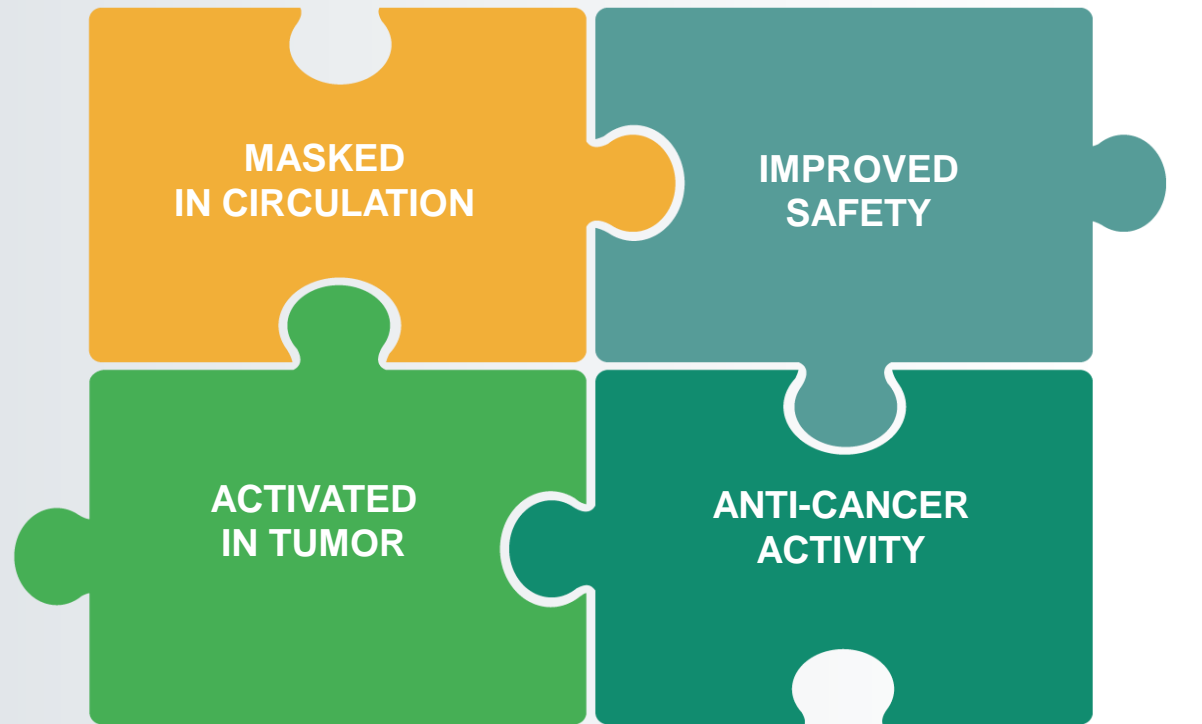
## DOSE ESCALATION COMPLETED

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

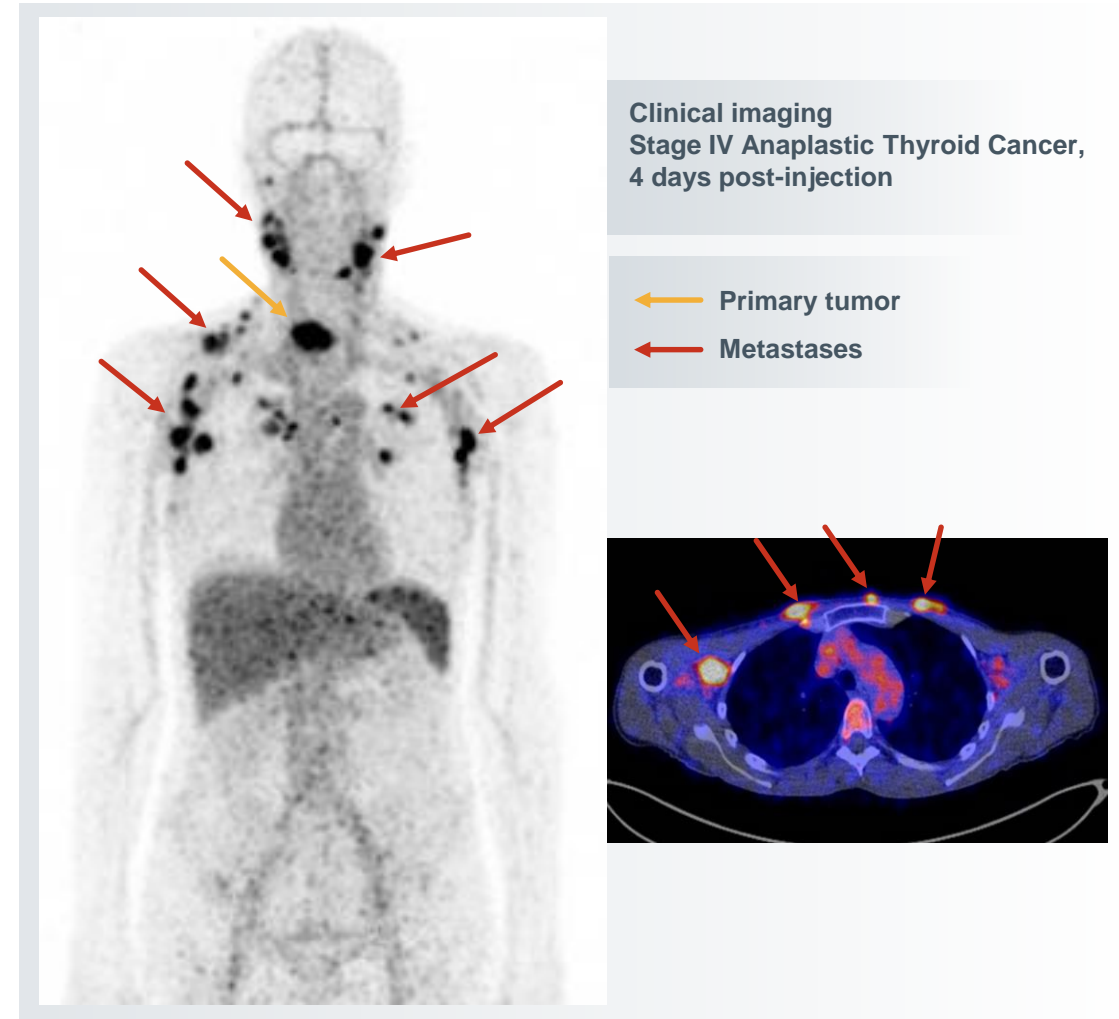


# Clinical and Translational Data Support Probody Platform

## Proof-of-Concept



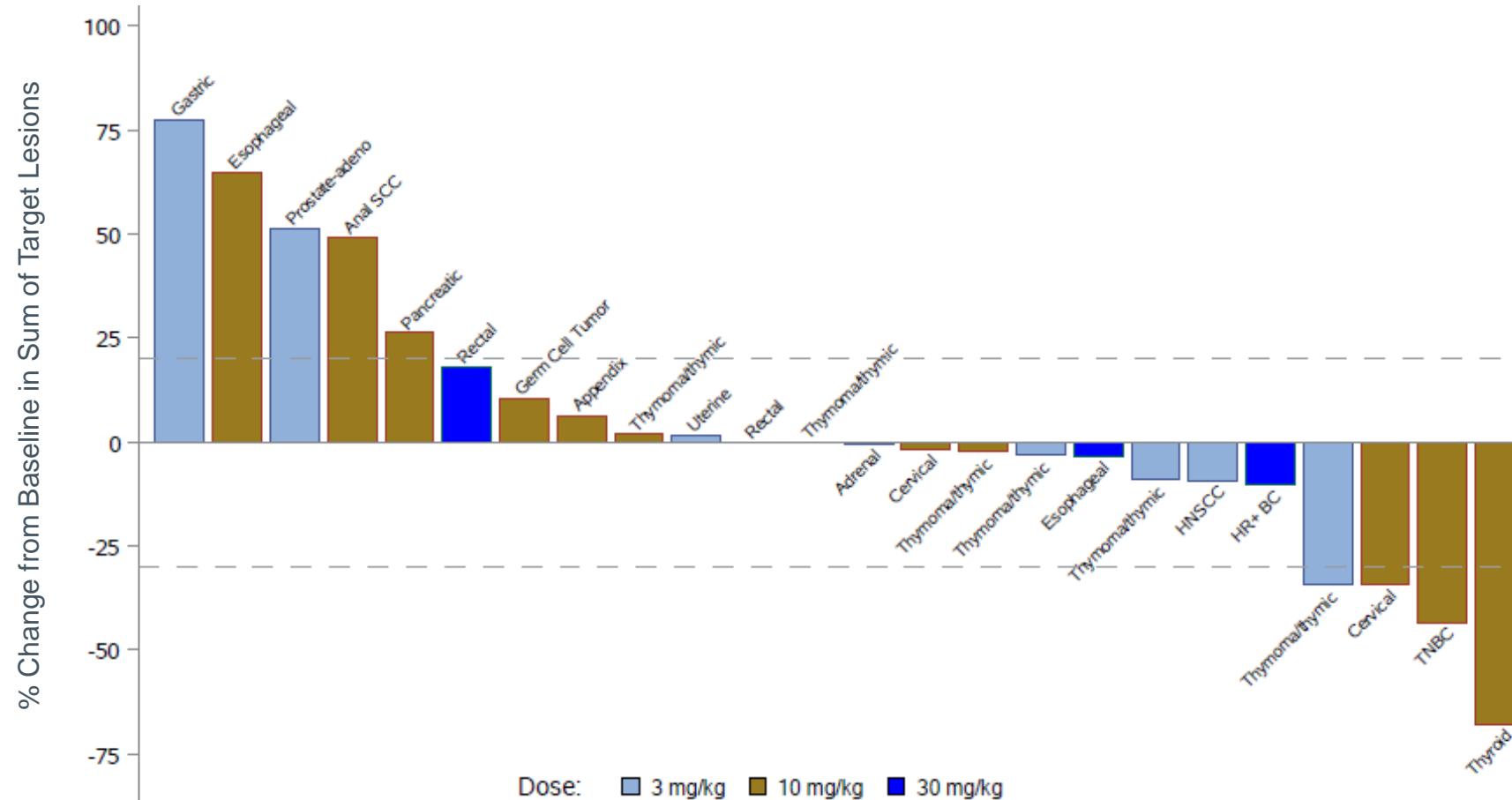
- Robust translation of preclinical data into clinical setting
- CX-072 has unique molecular & clinical pharmacology
- New paradigm for therapeutic antibodies

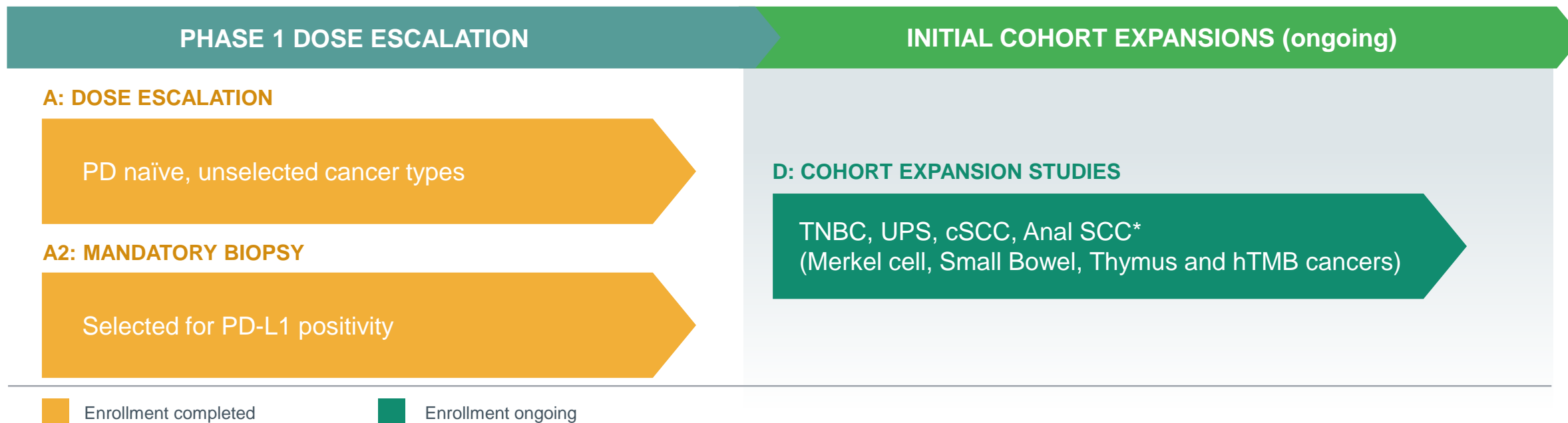




# Monotherapy Anti-Cancer Activity at $\geq 3\text{mg/kg}$ from Dose Escalation

Best Percent Change from Baseline in Sum of Target Lesion Measurements



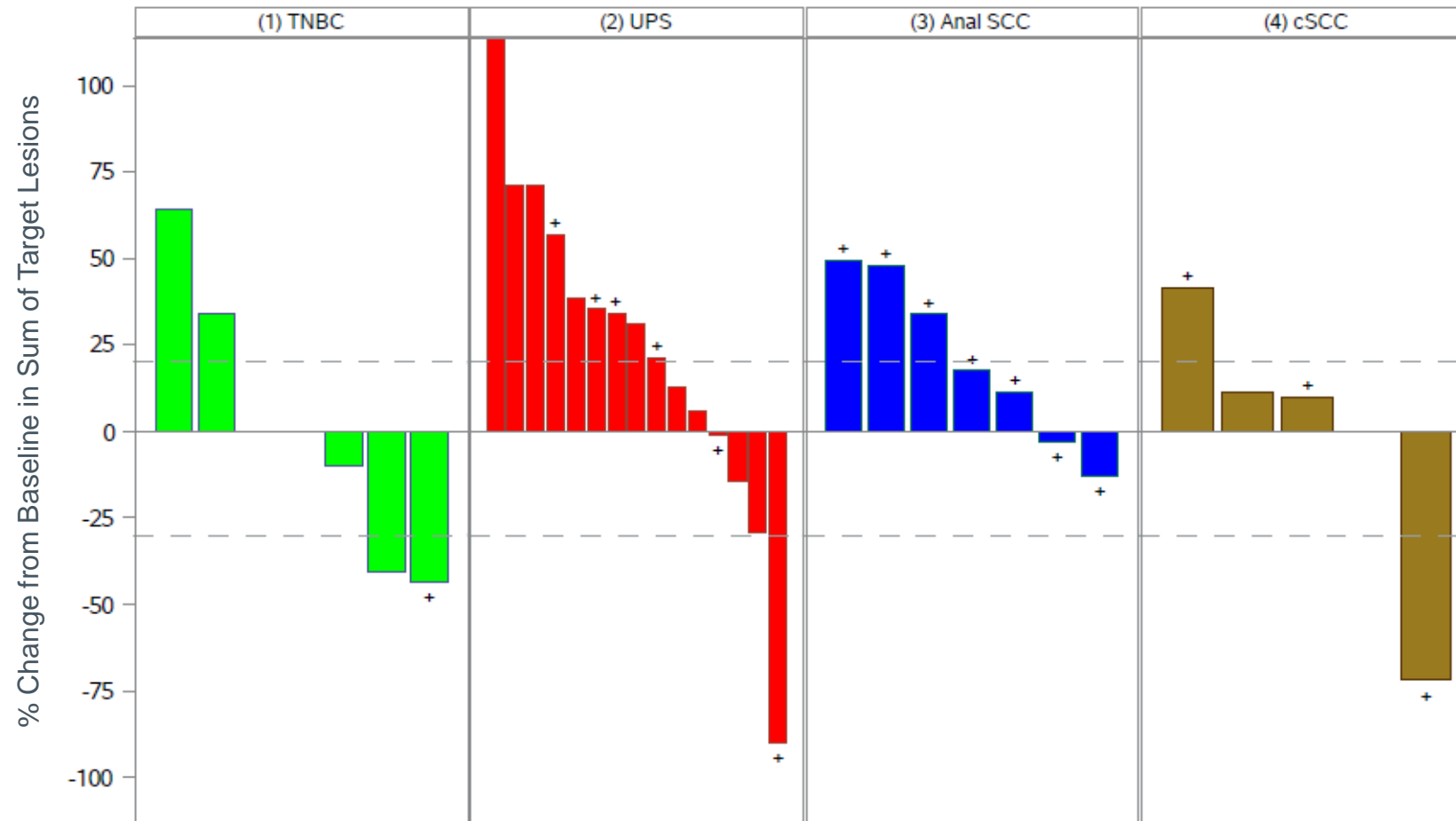


## DOSE ESCALATION COMPLETED

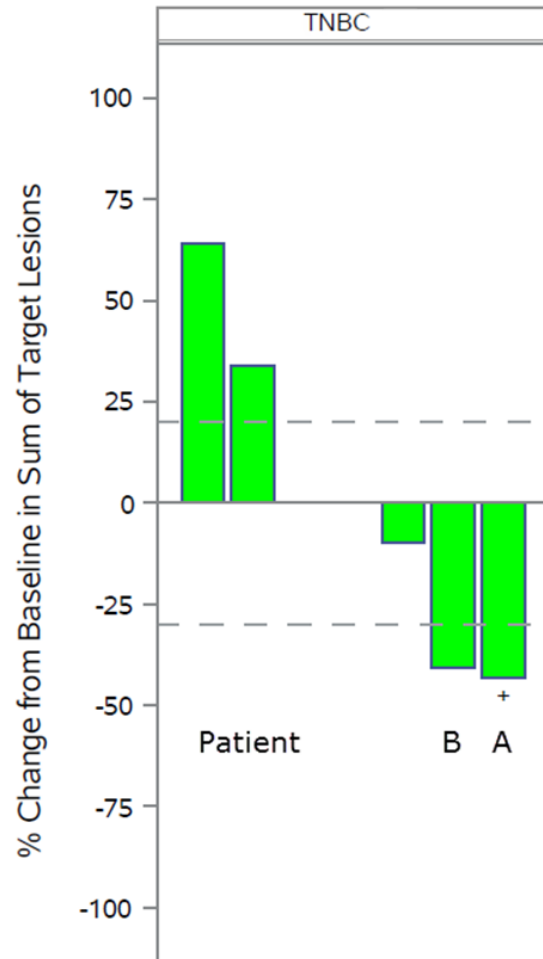
- 0.1 – 30 mg/kg every 2 weeks
- MTD not reached
- 10 mg/kg selected for expansion

- Expansions ongoing
- Anti-tumor activity in multiple indications

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



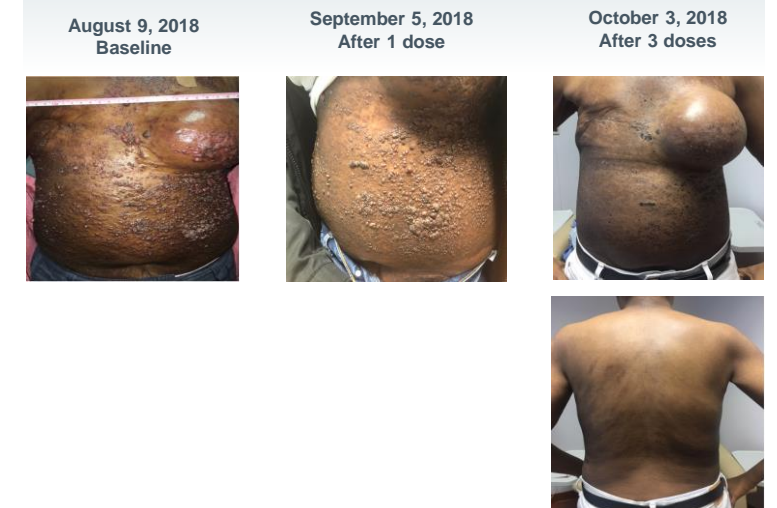
# Case Study: Anti-Tumor Activity at 10 mg/kg in TNBC



**PATIENT A: TNBC WITH SKIN LESIONS (PR);  
TREATMENT DURATION 72+ WEEKS**

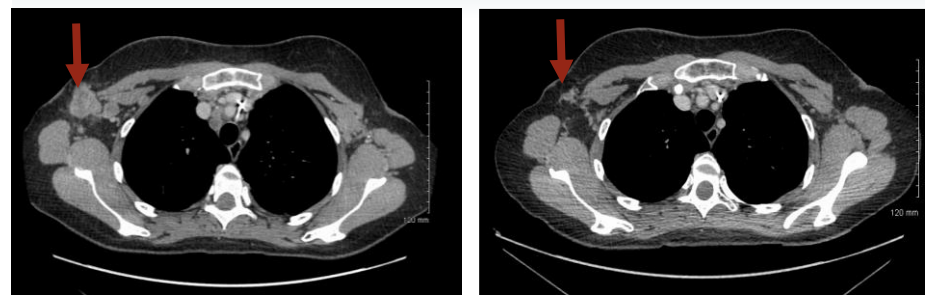


**PATIENT B: TNBC WITH SKIN LESIONS (UPR);  
TREATMENT DURATION 20+ WEEKS**

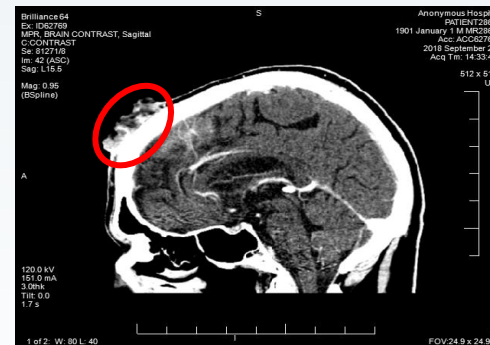
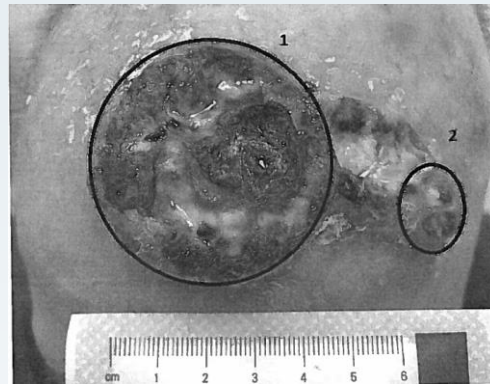


August 14, 2017  
Screening Scan

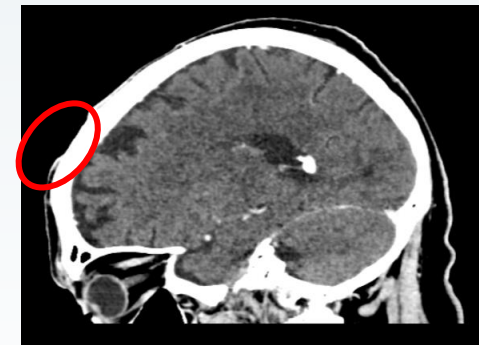
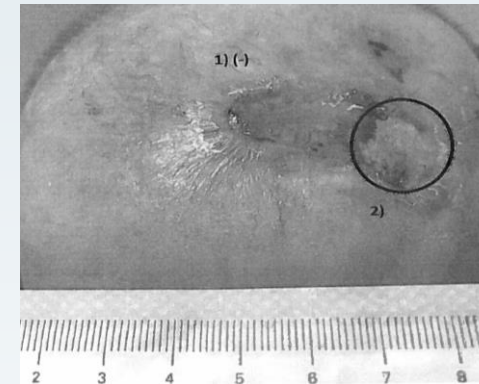
December 5, 2017  
Staging Scan



## CUTANEOUS SCC SCALP LESIONS



**Baseline Scan**  
**9/21/18**

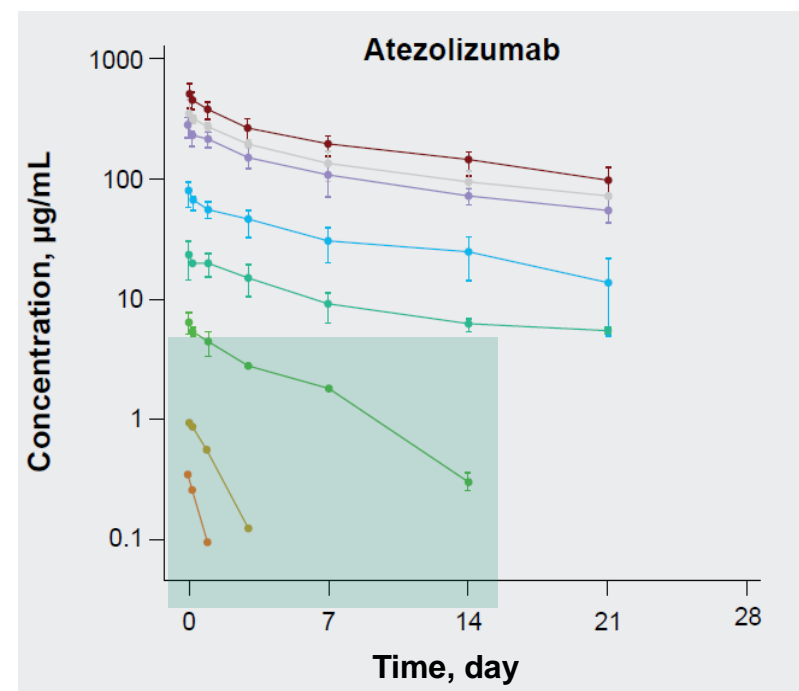
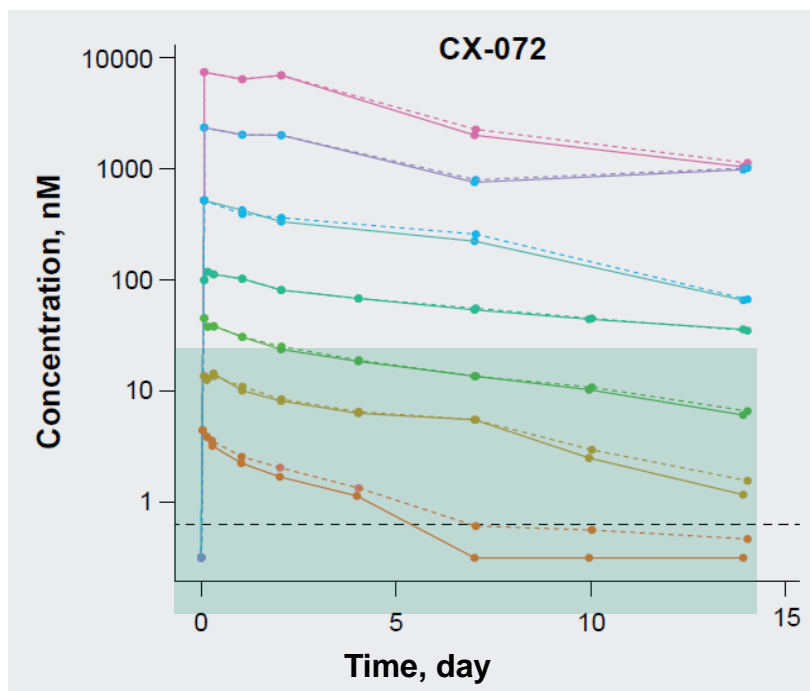


**Response Scan**  
**1/25/2019**

# 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



—●— 0.03 mg/kg   
 —●— 0.1 mg/kg   
 —●— 0.3 mg/kg   
 —●— 1 mg/kg   
 —●— 3 mg/kg   
 —●— 10 mg/kg   
 —●— 15 mg/kg   
 —●— 20 mg/kg   
 —●— 30 mg/kg

- 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





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



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

## CHECKMATE 67: COMBINATION TOXICITIES

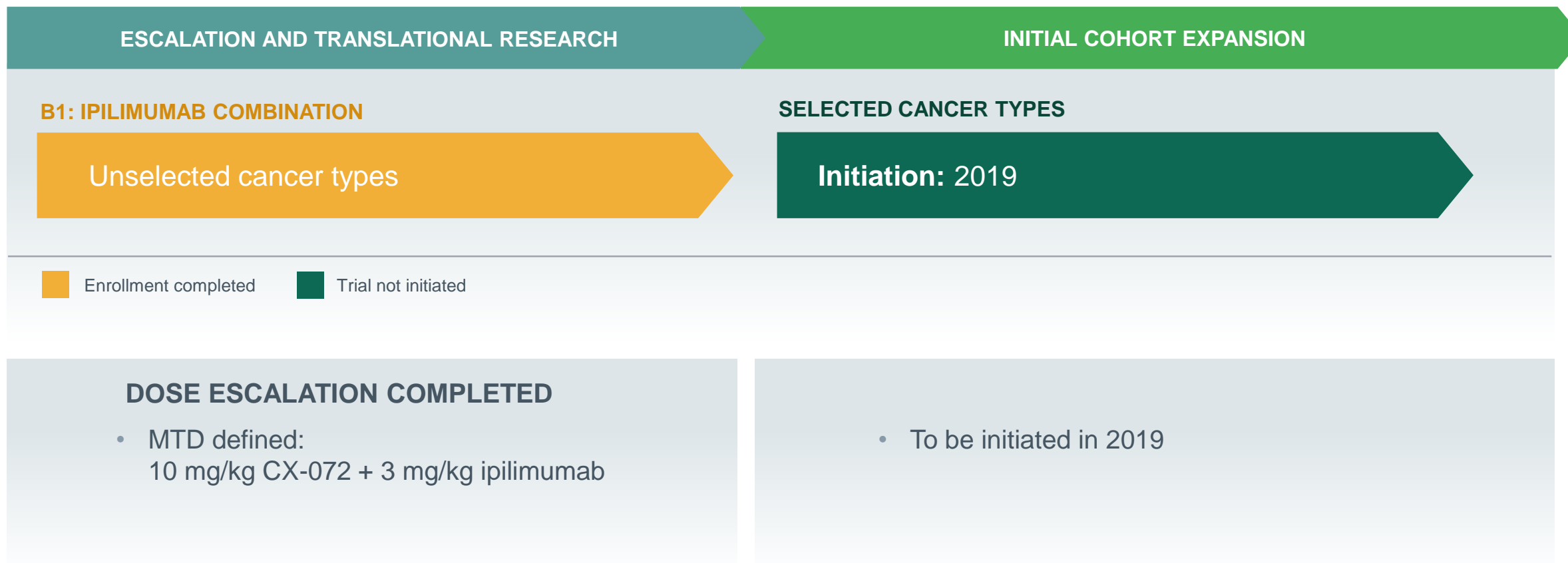
	Nivolumab Mono melanoma	Ipilimumab Mono melanoma	Nivo + Ipi Combo <sup>1</sup> melanoma
	3mg/kg every 2 weeks	3mg/kg every 3 weeks	nivo 1mg/kg + ipi 3mg/kg every 3 weeks
ORR	44%	19%	58%
Treatment related Grade 3/4 AEs	16%	27%	55%
Discontinued Drug	8%	15%	36%

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

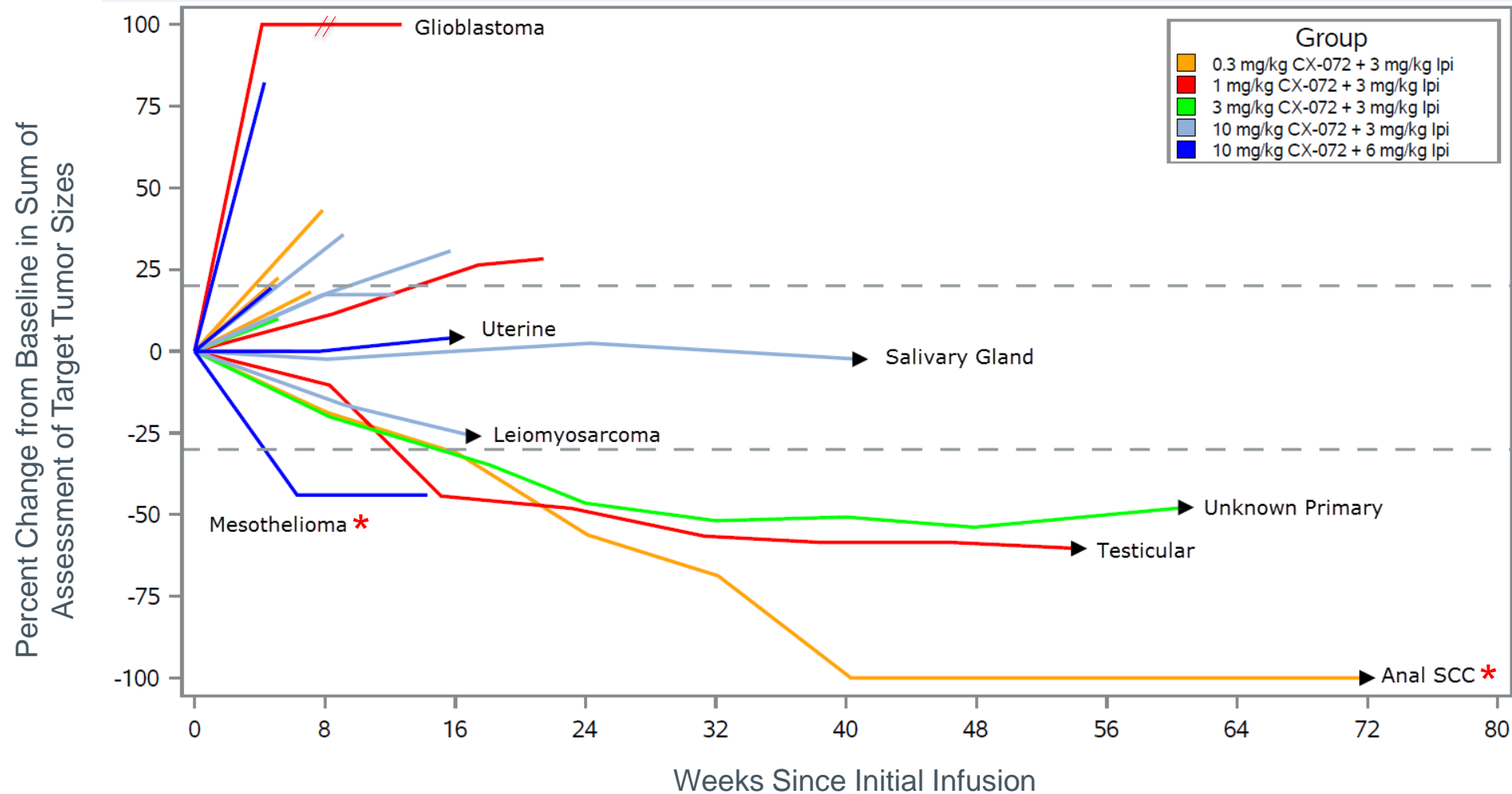
- 64 patients with advanced or unresectable melanoma
- Nivolumab (1 mg/kg) + Ipilimumab (3 mg/kg)
- 38 (59%) Grade 3/4 irAE
- 46 (72%) required steroids
- 36% irAE causing hospitalizations

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

# 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)
<b>NUMBER (%) OF SUBJECTS EXPERIENCING</b>		
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

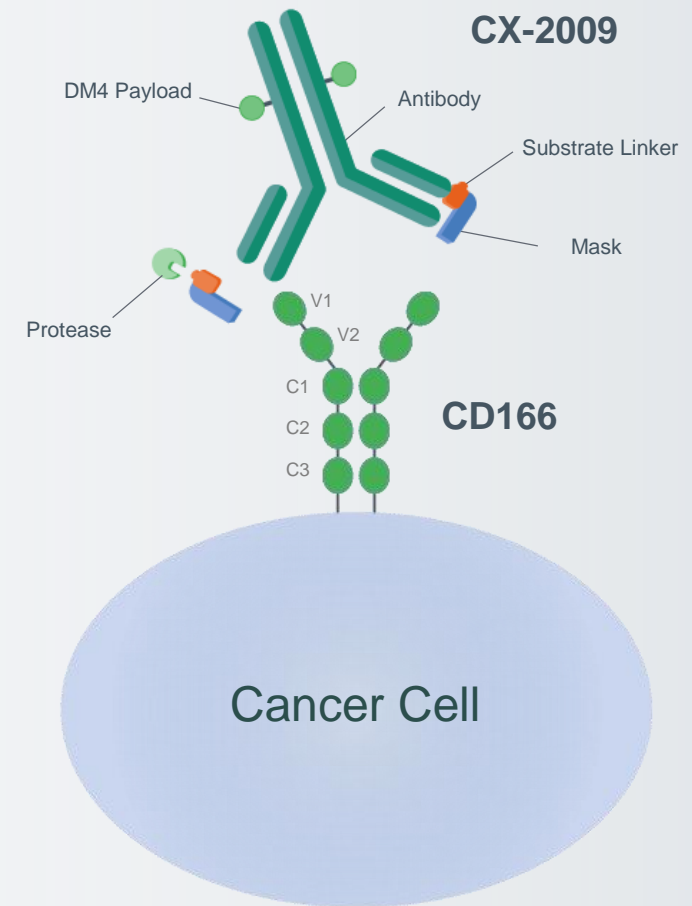
## A Probody Drug Conjugate with First-in-Class Potential





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

- 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)



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

**Advanced metastatic disease**

**A2: BIOPSY REQUIRED: 4–10 mg/kg**

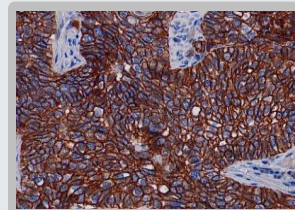
**Advanced metastatic disease, CD166+++**

**Enrollment completed**

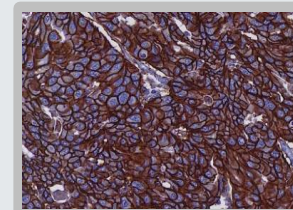
**SEVEN TUMOR TYPES IN  
MONOTHERAPY DOSE  
ESCALATION ARM:**

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

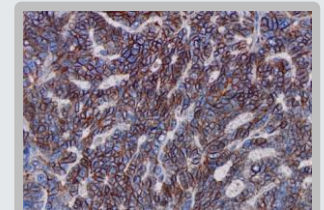
**LUNG CANCER**



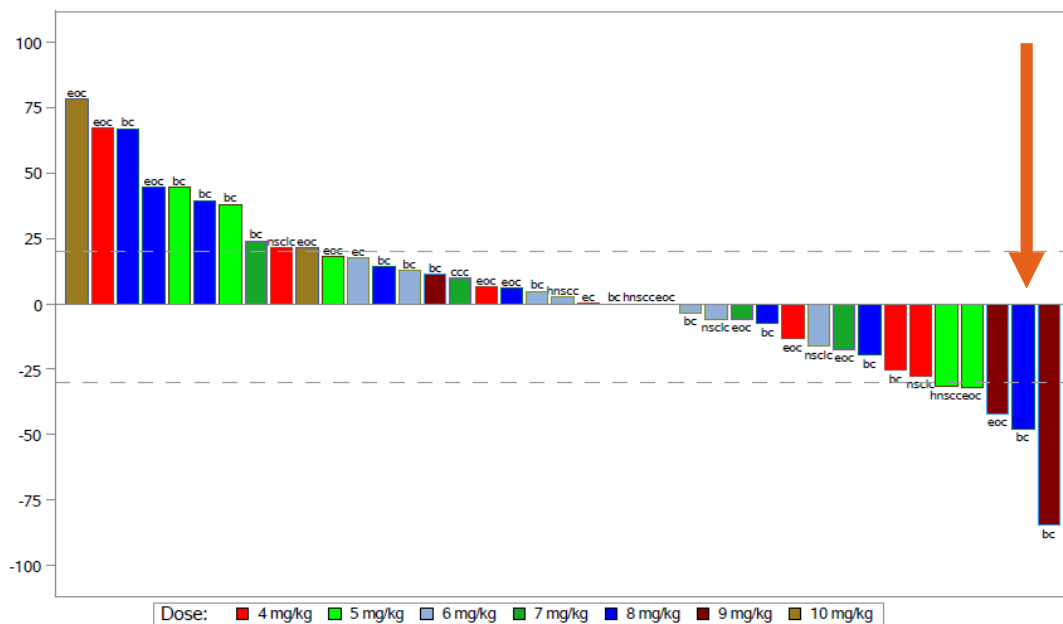
**BREAST CANCER**



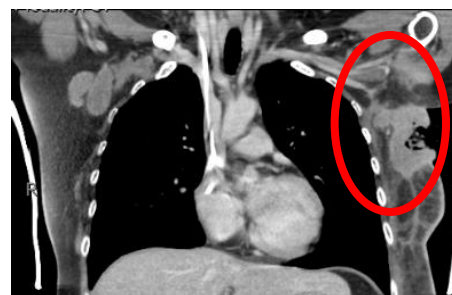
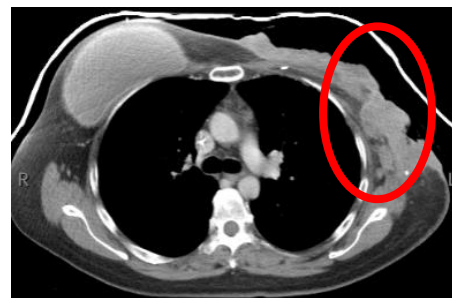
**OVARIAN CANCER**



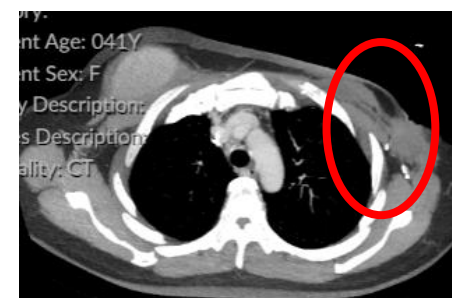
# Single Agent Activity for CX-2009 Observed in Phase 1 Dose Escalation



July 16, 2018  
BASELINE



September 11, 2018  
3 DOSES



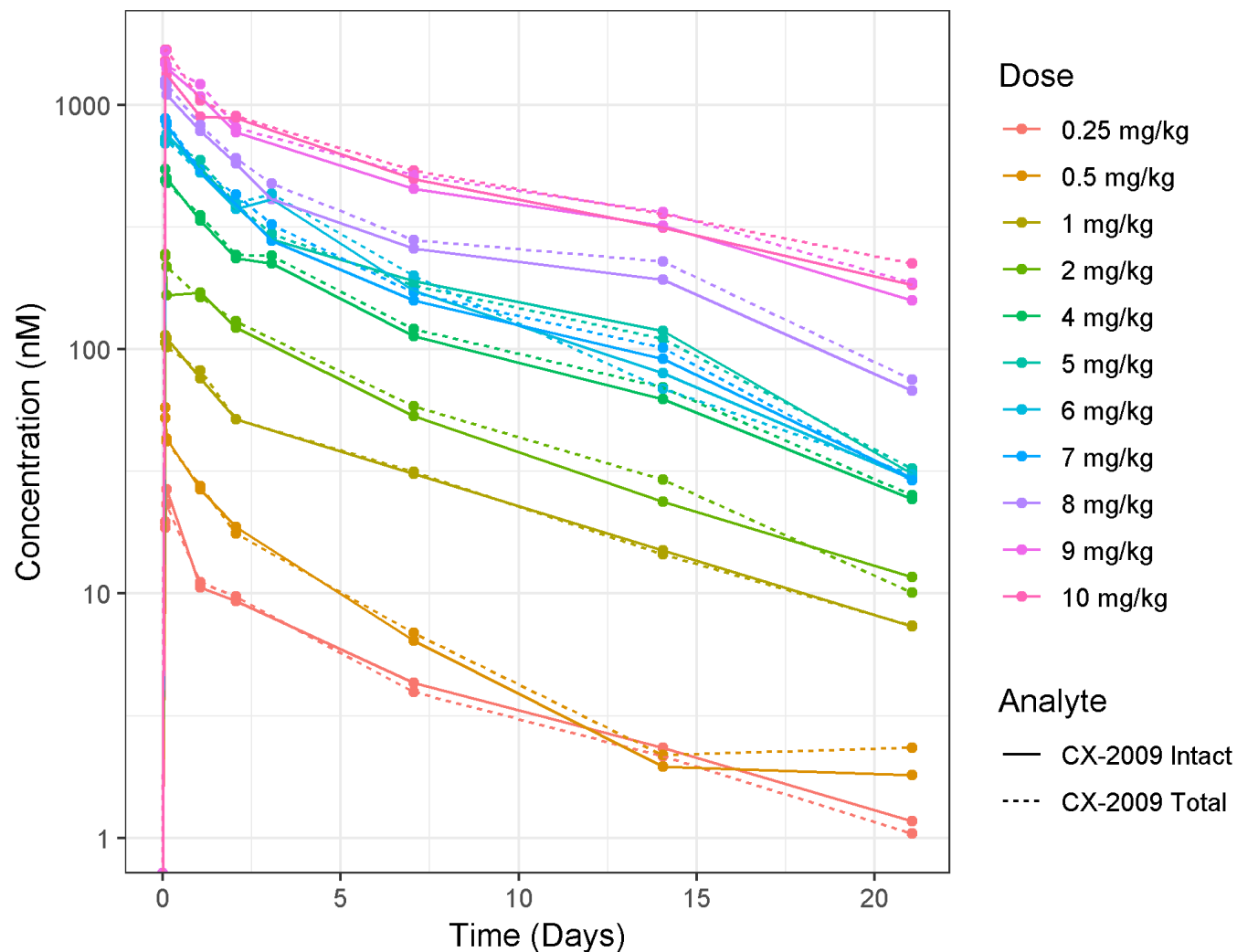
November 12, 2018  
6 DOSES



New lesion observed. Progression noted.

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

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

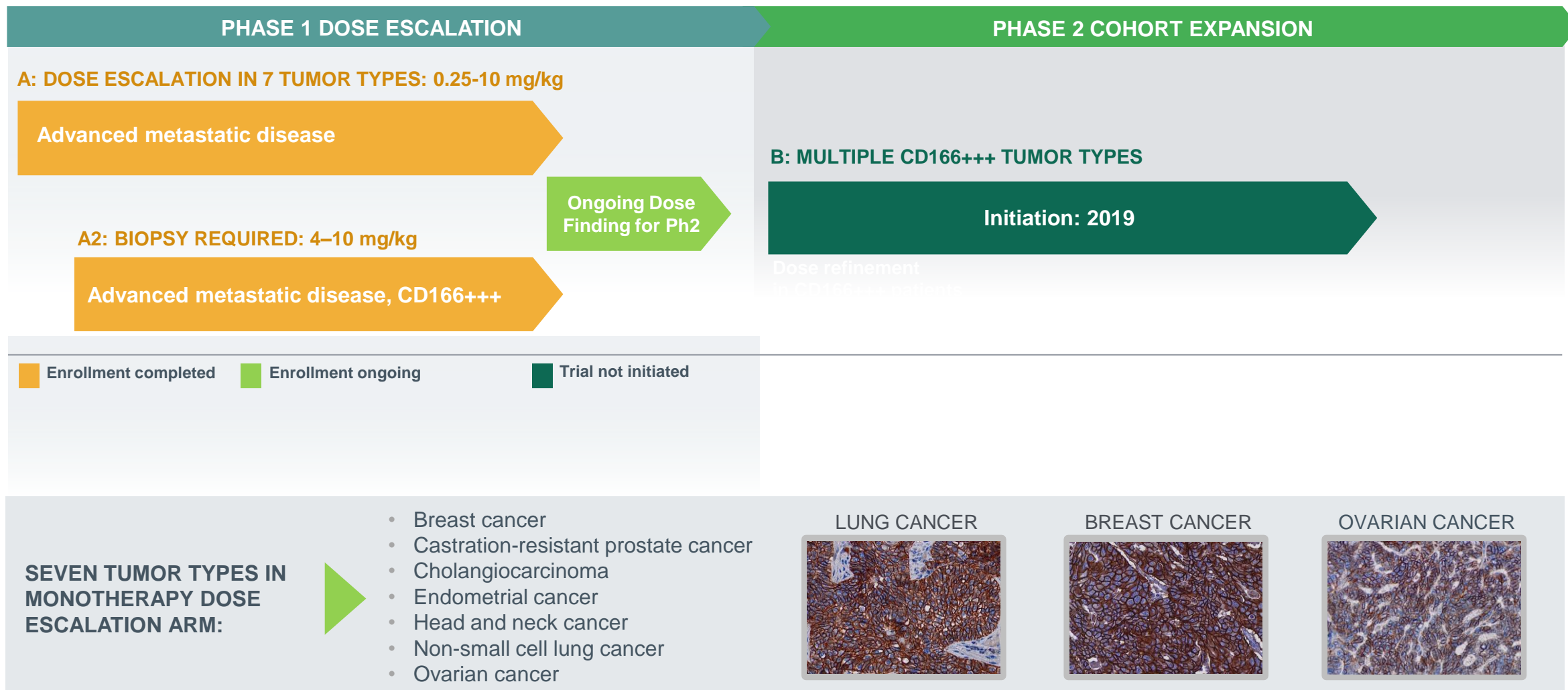


# Most Frequent Grade 3/4 Treatment-Related Adverse Events

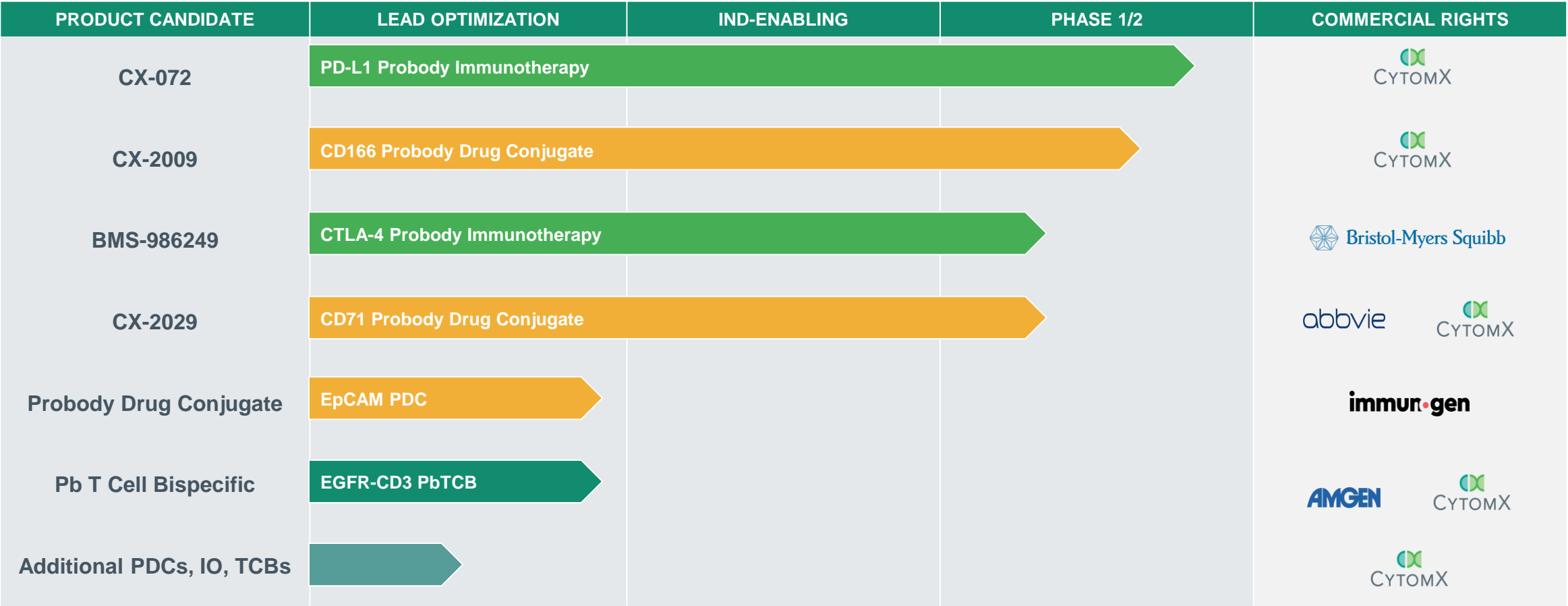
	< 4mg/kg (N=10)	4-5 mg/kg (N=19)	6-7 mg/kg (N=18)	8-9 mg/kg (N=21)	10 mg/kg (N=8)
<b>TOTAL SUBJECTS WITH GRADE 3-4 TRAEs</b>	0	4 (21.1)	4 (22.2)	11 (52.4)	4 (50)
<b>EYE DISORDERS*</b>	0	1 (5.3)	0	5 (23.8)	1 (12.5)
<b>METABOLISM AND NUTRITION DISORDERS</b>	0	0	2 (11.1)	2 (9.5)	0
<b>LIVER FUNCTION TESTS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



# Deep and Differentiated Probody Pipeline



 Immunotherapies

 Probody Drug Conjugates

 Pb T Cell Engaging Bispecifics

 Multiple Programs



# 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
- 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

**PROCLAIM**  
CX-2009

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

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

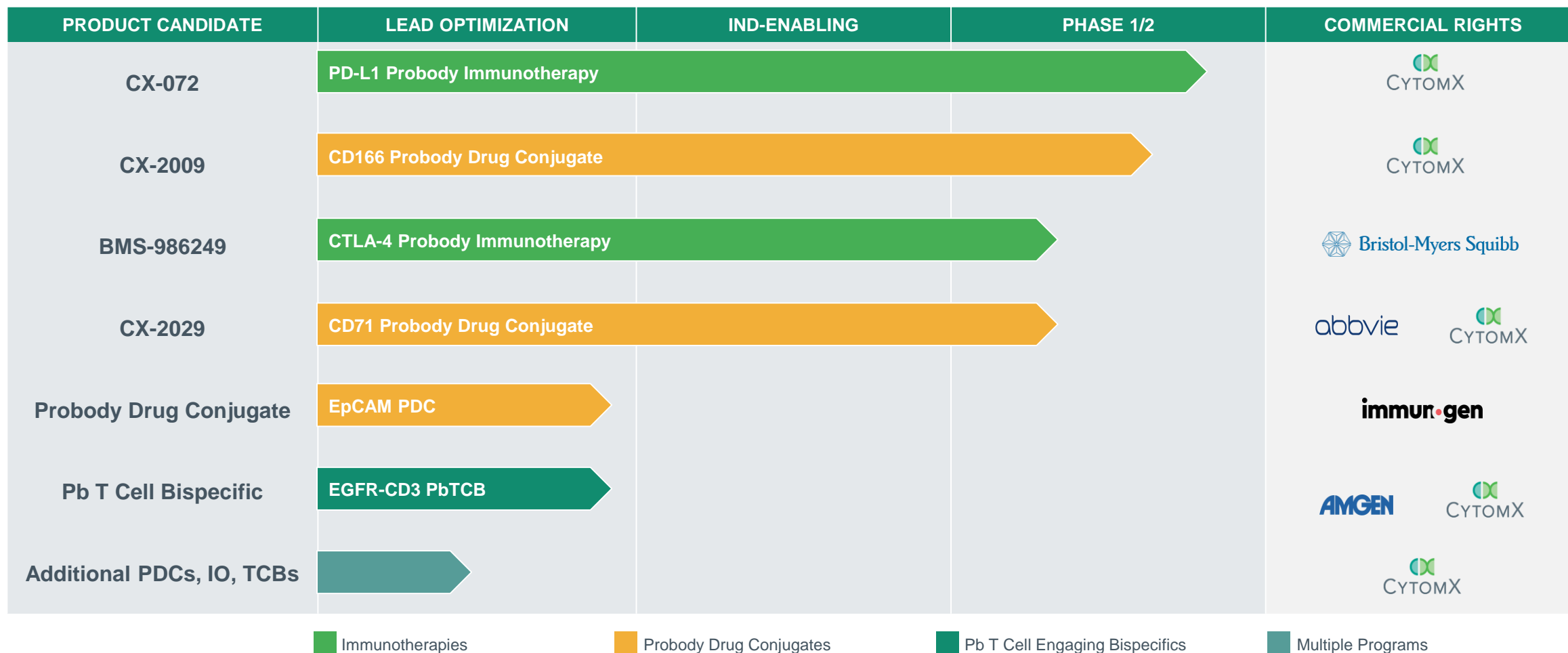
## **PROCLAIM-CX-2009 (CD166 PDC)**

- 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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