

REIMAGINING THERAPEUTIC ANTIBODIES

2019 Wedbush PacGrow Healthcare Conference





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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

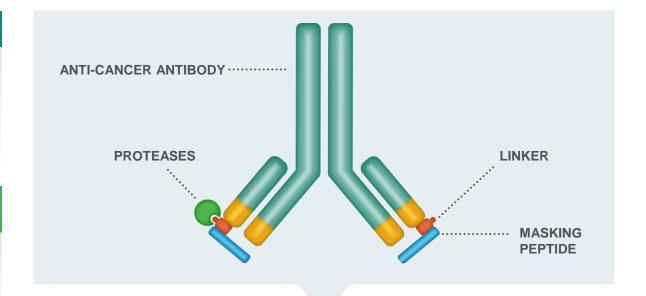
- Powerful, potent modalities; > \$100 billion WW sales 2018
- Potency can be a liability for widely distributed targets
- Major opportunity to improve targeting and localize antibody pharmacology

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

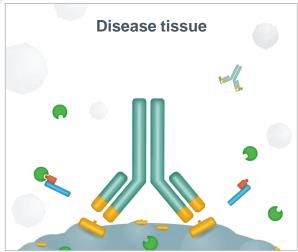
- Maintaining potency
- Reducing side effects
- Enabling new target opportunities

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

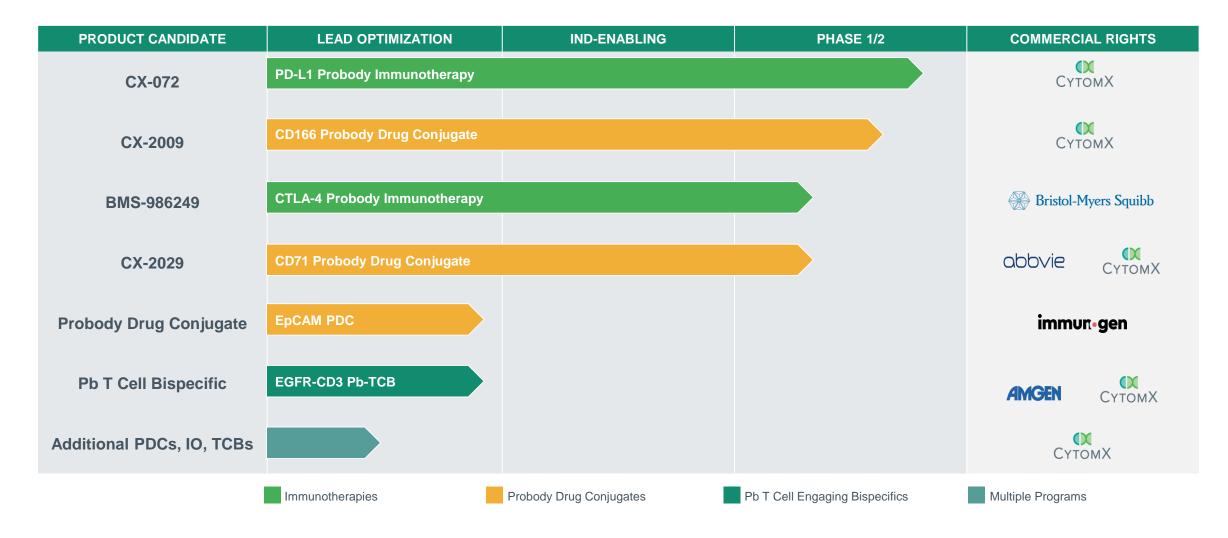








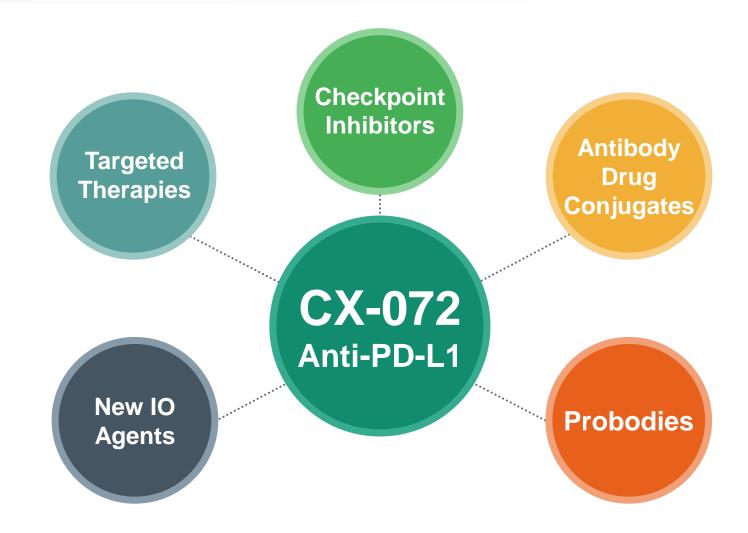
Deep and Differentiated Probody Pipeline





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

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







Monotherapy Expansions Underway

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

DOSE ESCALATION COMPLETED

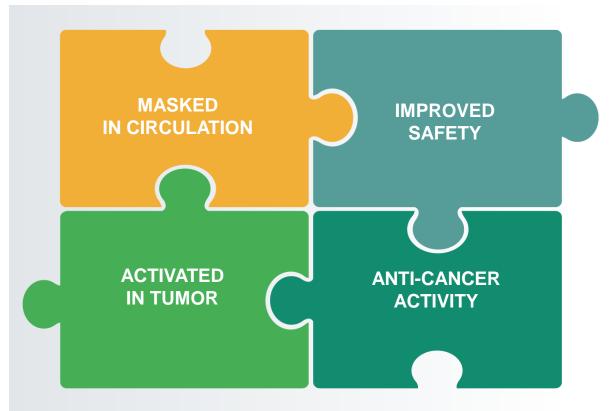
- 0.1 30 mg/kg every 2 weeks
- MTD not reached.
- 10 mg/kg selected for expansion

- Expansions ongoing
- Anti-tumor activity in multiple indications

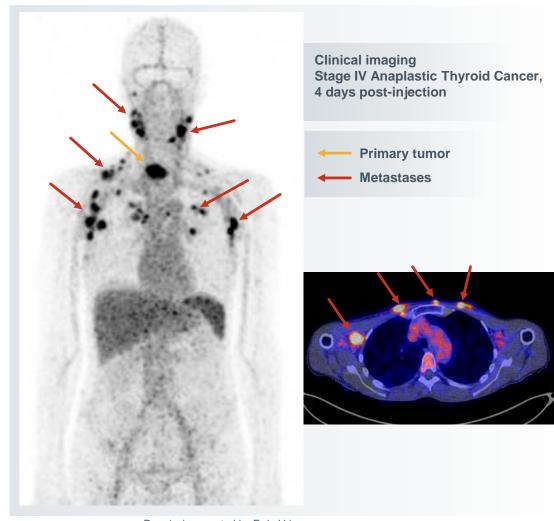


^{*} triple negative breast cancer (TNBC), undifferentiated pleomorphic sarcoma (UPS), cutaneous squamous cell carcinoma (cSCC), squamous cell carcinoma (SCC) and small bowel adenocarcinoma (SBA)

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



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



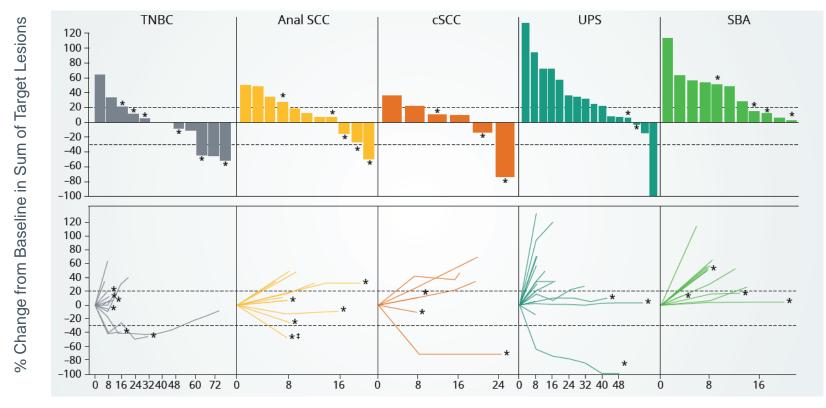
Permission granted by E de Vries





Cohort Expansions: Monotherapy CX-072 is Active 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)

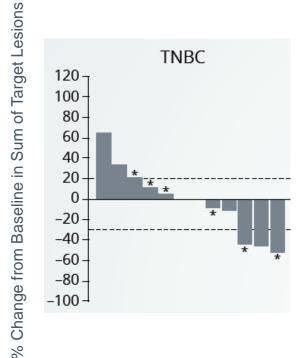
‡ At data cutoff, the patient had unconfirmed partial response that was subsequently confirmed.



^{*} 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.



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









^{*} 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.



Preliminary Safety: Monotherapy at 10 mg/kg Low Rates of ≥3 TRAEs and irAEs

	Total (N=72)*
NUMBER (%) OF SUBJECTS EXPERIENCING	
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)

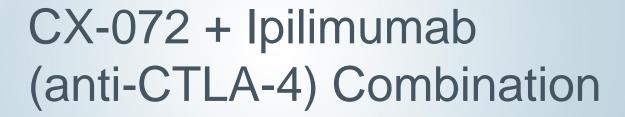
treatment emergent adverse event (TEAE), treatment related adverse event (TRAE) infusion-related reactions (IRR), immune related adverse event (irAE) irAEs are defined as prospectively identified treatment-related AEs that are associated with the use of systemic or topical immunosuppressive agents or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



Data cutoff as of April 5, 2019

11









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

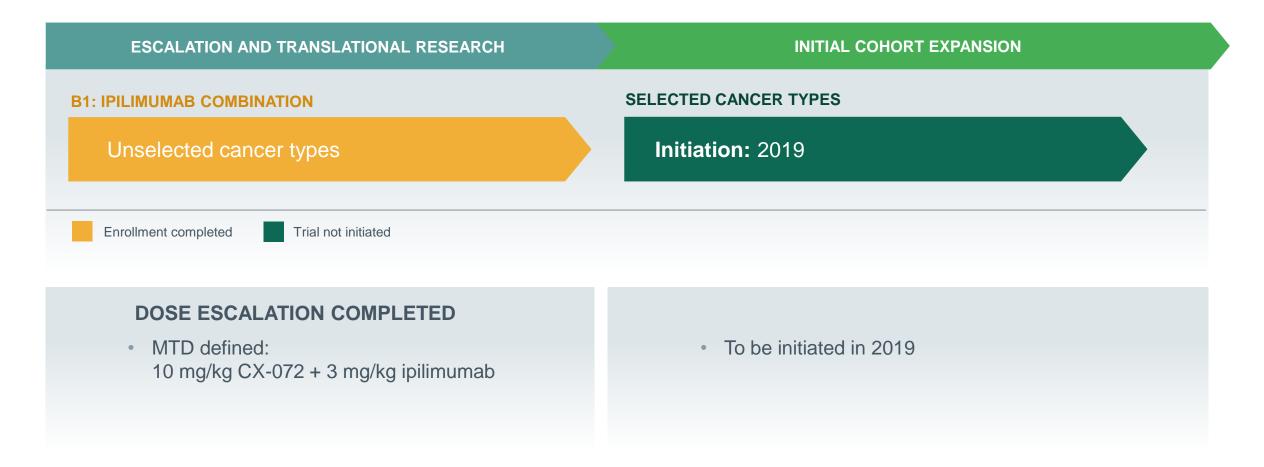
- 64 patients with advanced or unresectable melanoma
- Nivolumab (1 mg/kg) + Ipilimumab (3 mg/kg)
- 38 (59%) Grade 3/4 irAE
- 46 (72%) required steroids
- 36% irAE causing hospitalizations

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)



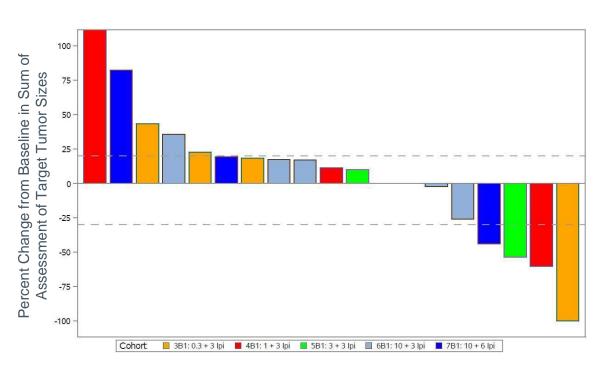
Ipilimumab Combination Dose Escalation Now Complete



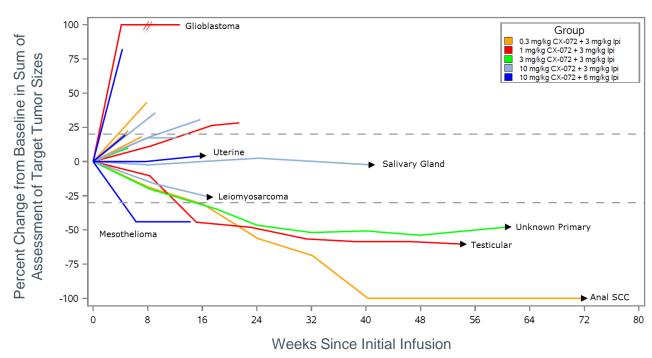




CX-072 plus Ipilimumab Combination: Durable Anti-Cancer Responses Observed







Ipilimumab (ipi); Data cutoff as of February 6, 2019





CX-072 plus Ipilimumab Combination: Clinically Manageable 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



Data cutoff as of February 6, 2019

CX-072: Anti-PD-L1 Probody Therapeutic

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

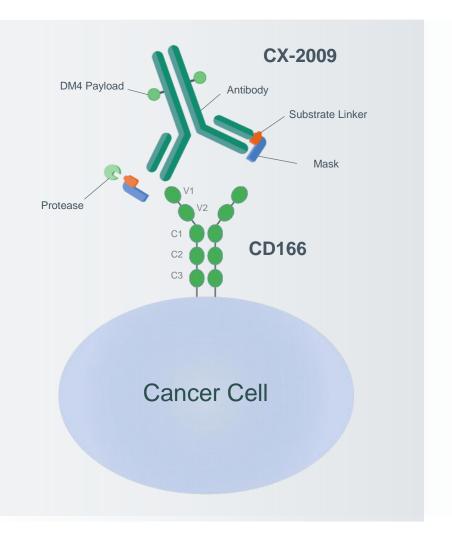
- Completion of monotherapy expansions and potential advancement to registrational study
- Initiation of expansions for ipilimumab combination in select tumor type(s)





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

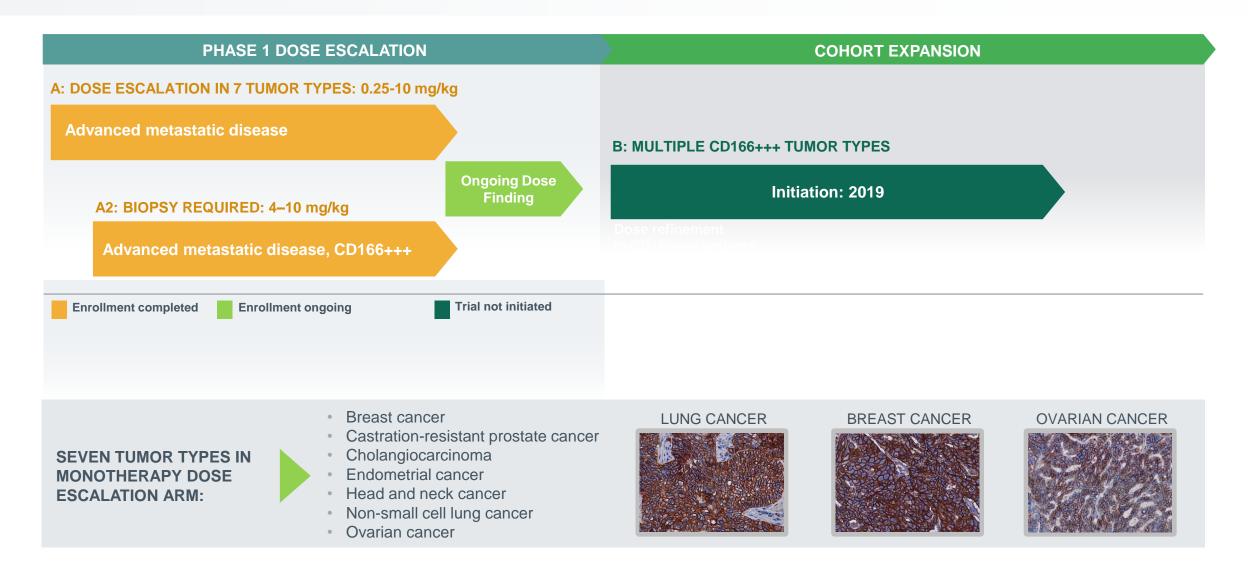
- CD166 is highly expressed in many cancers
 - Including breast, lung, ovarian, head and neck
 - Undruggable with conventional approaches due to normal tissue expression
- Probody platform enables the potential development of this attractive target with CX-2009
 - Masking technology limits binding to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







Phase 1 Dose Escalation and Next Steps

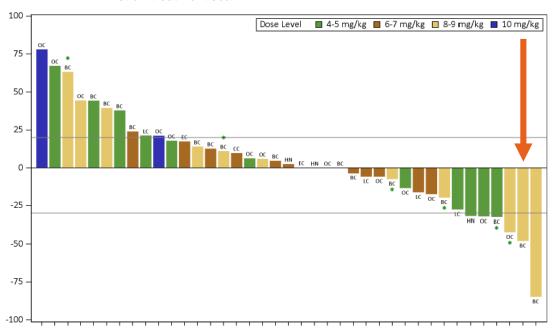






Single Agent Activity for CX-2009 Observed in Phase 1 Dose Escalation

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



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

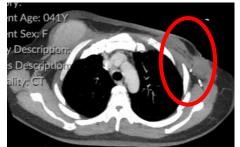
As of February 26, 2019 data snapshot Presented at AACR 2019

July 16, 2018 **BASELINE**

September 11, 2018
3 DOSES

November 12, 2018 **6 DOSES**













New lesion observed. Progression noted

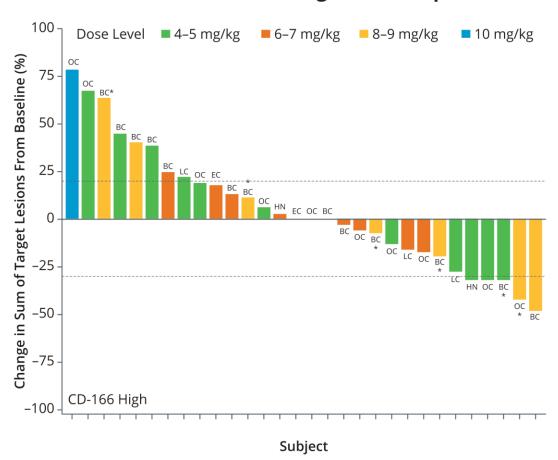
Case Study: Pembrolizumab-refractory TNBC Patient at 8 mg/kg



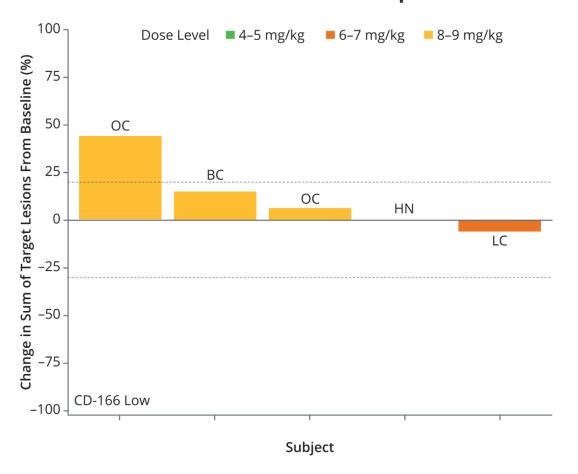


Anti-Cancer Activity Associated with CD166 Expression

Part A and A2 With High CD166 Expression



Part A With Low CD166 Expression

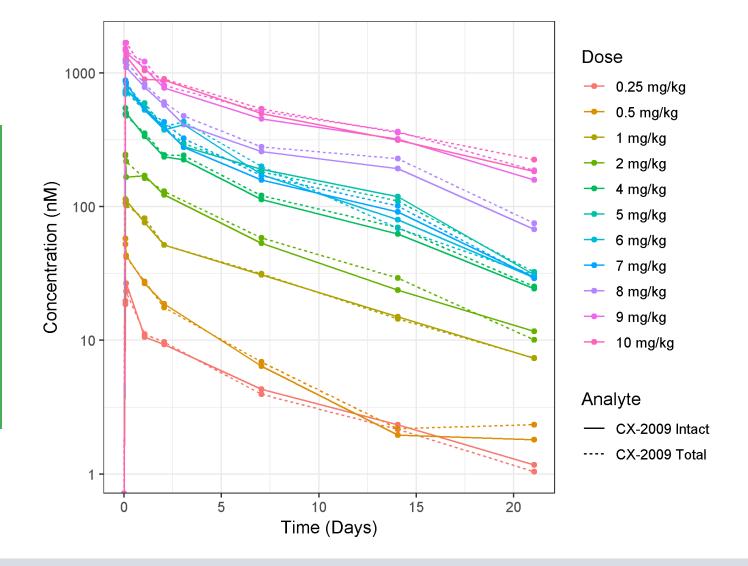






Phase 1 Dose Escalation: CX-2009 Remains Effectively Masked in the Circulation of Cancer Patients

- Single-dose CX-2009
 PK data suggest that
 CX-2009 circulates
 predominantly as
 the intact prodrug
 species
- Consistent with prior findings for CX-072







Most Common 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=23)	10 mg/kg (N=8)	All Cohorts
KERATITIS*	0	1 (5)	0	4 (17)ª	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 ≥ 2 Patients



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

^a Including one patient with Grade 4 Keratitis

CX-2009: CD166 Probody Drug Conjugate

SUMMARY

- Generally well tolerated
- Early evidence of biological activity in multiple cancer types over a wide range doses (4–10 mg/kg) in a heavily pretreated population
- Preliminary data suggest a potential association between CD166 tumor expression levels and clinical activity

NEXT STEPS

- Dose-refinement ongoing
- Addition of mandatory prophylactic measures to manage ocular toxicity and potentially prolong duration of treatment
- Plans for expansion under development



Major Alliances Broaden Our Pipeline of Probody Therapeutics



abbvie



- 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

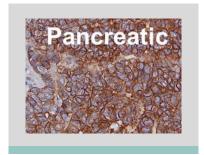
- CD71 (CX-2029) +
 2 additional targets
- Co-development,
 co-commercialization, and
 profit split on CX-2029
- IND for CX-2029 cleared in May 2018
- \$75 million earned to date
- Up to \$1B in potential milestones

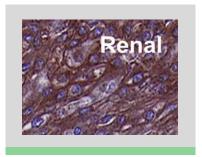
- EGFR-TCB + 3 additional targets
- Co-development, profit split on EGFR-TCB
- \$1.4B in potential development, regulatory & commercial milestones
- \$60M earned to date
- CytomX receives rights to one Amgen preclinical TCB
- ~\$400 million to date from pharma partnering
- Two partnered assets advanced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



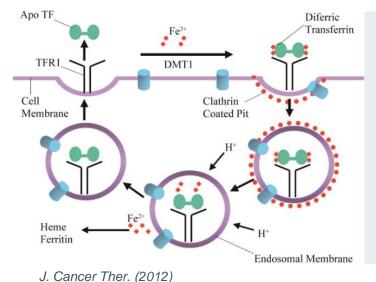
CD71 is a High Potential Target for a Probody Drug Conjugate







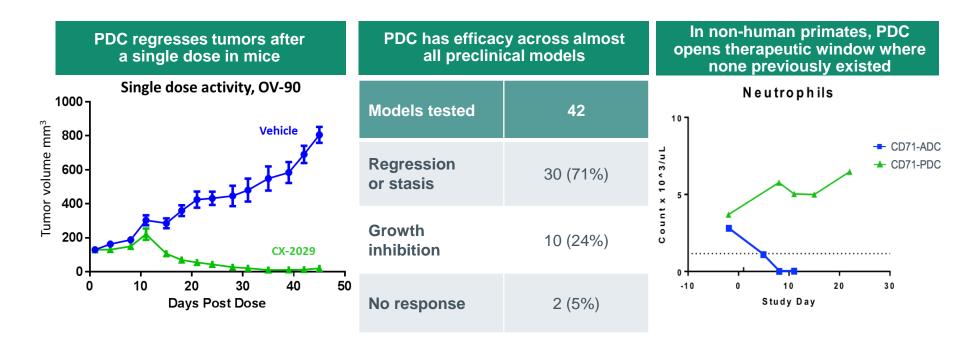




- Ubiquitously expressed on dividing, normal and malignant cells
- Mediates iron uptake required for cell division
- Professional internalizing protein: often used as a positive control in ADC experiments
- Expression in normal dividing cells prohibits development of a traditional ADC

abbvie

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



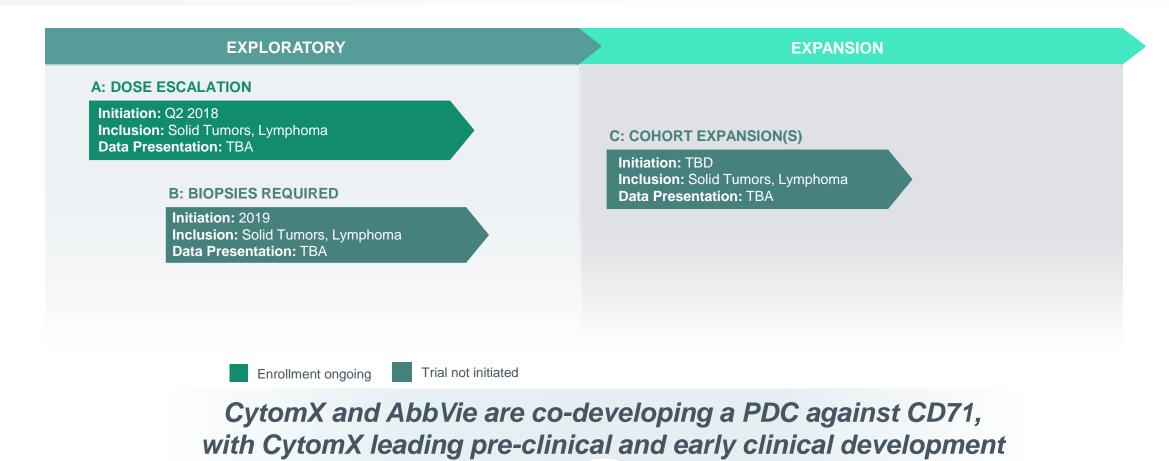
Partnered with AbbVie: Co-development rights and profit split; \$25M milestone to CytomX received July 2018; Enrolling Phase 1/2 Trial







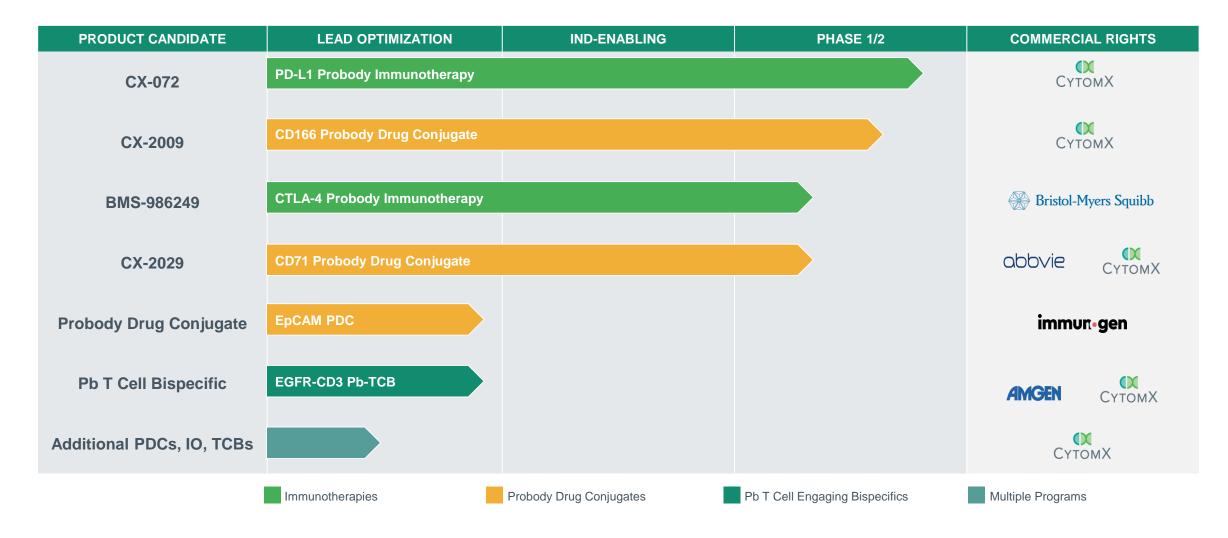
PROCLAIM-CX-2029: CD71-Directed PDC Exploratory Studies in 2018-2019 Drive Expansion Studies in 2019-2020



abbyie



Deep and Differentiated Probody Pipeline





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® (ipilimumab) combination next steps
- ZELBORAF® (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

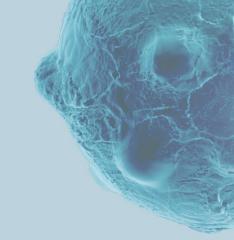
 Randomized Phase 2 Study (www.ClinicalTrials.gov)

AbbVie Alliance

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







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AUGUST 13, 2019