

Antibodies by Design™

XmAb® Antibody Therapeutics

Corporate Overview

November 2020

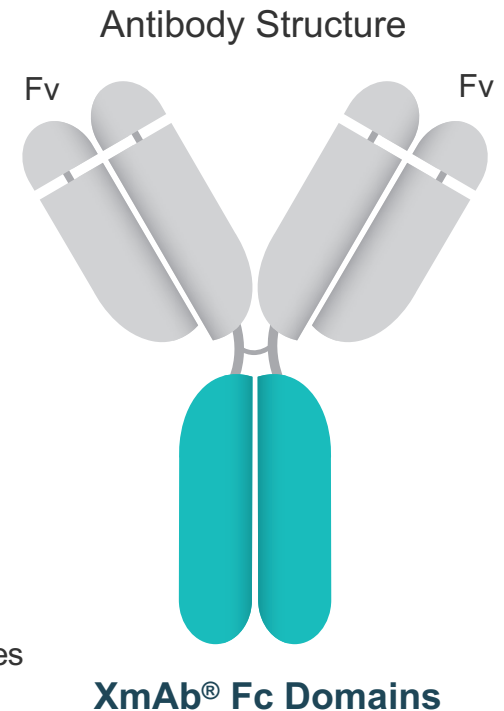


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Xencor: Engineering Antibody Immune Functions to Make Better Drugs

- XmAb® Fc domains: small changes, big functional impacts
 - Augments native immune functions, preserves half-life, stability and production
 - Over 1,000 issued patents and pending patents worldwide
- Expansive bispecific antibody and cytokine oncology pipeline advancing
 - **9 XmAb bispecific antibodies and cytokines in Phase 1 clinical studies**
 - Novartis co-development and ex-U.S. license for XmAb14045 (Phase 1); additional Phase 1 oncology program enrolling patients
 - Amgen's AMG 509 (STEAP1 x CD3) XmAb 2+1 bispecific antibody for prostate cancer, in Phase 1
- Genentech co-development collaboration for novel IL15 cytokines
 - Wide-ranging combination strategy critical to advancing cytokines
 - Retain ability to perform clinical studies with broad spectrum of leading cancer therapies
 - Phase 1 study of XmAb24306 enrolling patients
- XmAb antibodies commercialized, ongoing revenue generation
 - Monjuvi® (MorphoSys) approved in the U.S. for relapsed or refractory DLBCL; co-commercialized in the U.S. by MorphoSys and Incyte; MAA under review by EMA
 - Ultomiris® (Alexion) approved in the U.S., Japan and EU for the treatment of adult patients with PNH and for patients with aHUS; additional indications in clinical testing

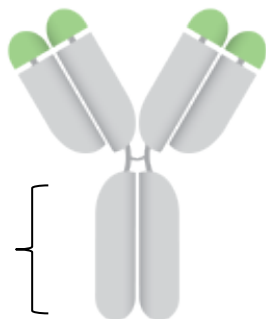


XmAb® Fc Domains Shift Focus of Antibody Drug Discovery by Creating New Axes for Differentiation

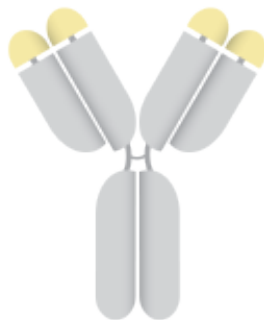
Standard Technology

Fv
focus

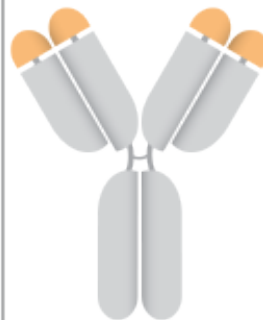
Same Fc



Soliris®



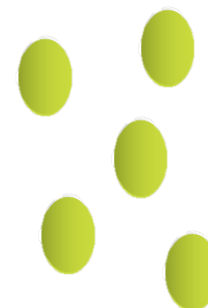
Rituxan®



anti-CD19
antibody



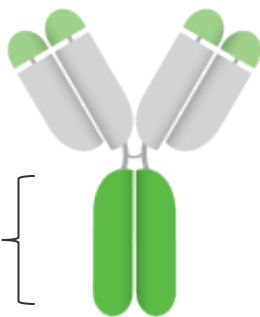
Fv bispecifics



cytokines

XmAb Fc Engineering

Xencor Fc
Domains



Ultomiris®
(ravulizumab)



Monjuvi®
(tafasitamab/XmAb5574)



obexelimab

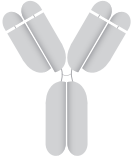
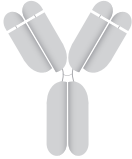
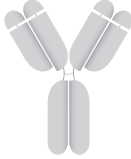
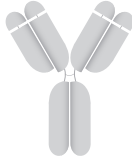





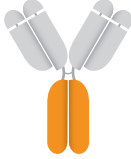
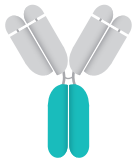



XmAb
bispecifics



XmAb
cytokines















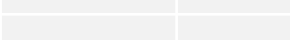

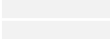
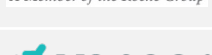
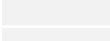
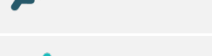
XmAb® Fc Domains Augment Natural Antibody Functions

Natural Fc Function				
	Circulating half-life	Cytotoxicity (immune cell)	Immune regulation Antigen clearance	Stable homodimer structure
Fc Receptor	FcRn	FcγRIIa, FcγRIIIa	FcγRIIb	N/A
Fc Domain Redesigns				
XmAb Enhanced Function				
	Xtend™ Domain Prolonged half-life	Cytotoxic Domain Enhanced cytotoxicity (immune cell)	Immune Inhibitor Domain Immune inhibition Rapid clearance	Bispecific Domain Stable heterodimer structure

Additional Fc domains: stability, complement activation

99.5% identical to natural antibody
Plug-and-play substitution into any antibody














Development Pipeline Focus on XmAb® Bispecific Fc Domains

Program (Targets)	Fc Domain	Primary Indication	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Obexelimab CD19	Immune Inhibitor	IgG4-RD SLE					
Vibecotamab CD123 x CD3	Bispecific	AML					 NOVARTIS *
Plamotamab CD20 x CD3	Bispecific	B-cell malignancy					
Tidutamab SSTR2 x CD3	Bispecific	GEP-NET GIST					
XmAb20717 PD-1 x CTLA-4	Bispecific Xtend	Oncology					
XmAb22841 CTLA-4 x LAG-3	Bispecific Xtend	Oncology					
XmAb23104 PD-1 x ICOS	Bispecific Xtend	Oncology					
XmAb24306 IL15Rβγ (IL15/IL15Rα-Fc)	Bispecific Xtend	Oncology					 A Member of the Roche Group
XmAb27564 IL2R (IL2-Fc)	Bispecific Xtend	Autoimmune					
XmAb30819 ENPP3 x CD3	Bispecific	Renal cell carcinoma					

* Novartis licensed ex-U.S. commercial rights, worldwide co-development

** Co-development with Genentech; 45% P&L share; option to co-promote in U.S.

XmAb® Fc Domains Create Numerous Differentiated Antibodies for Technology Partners

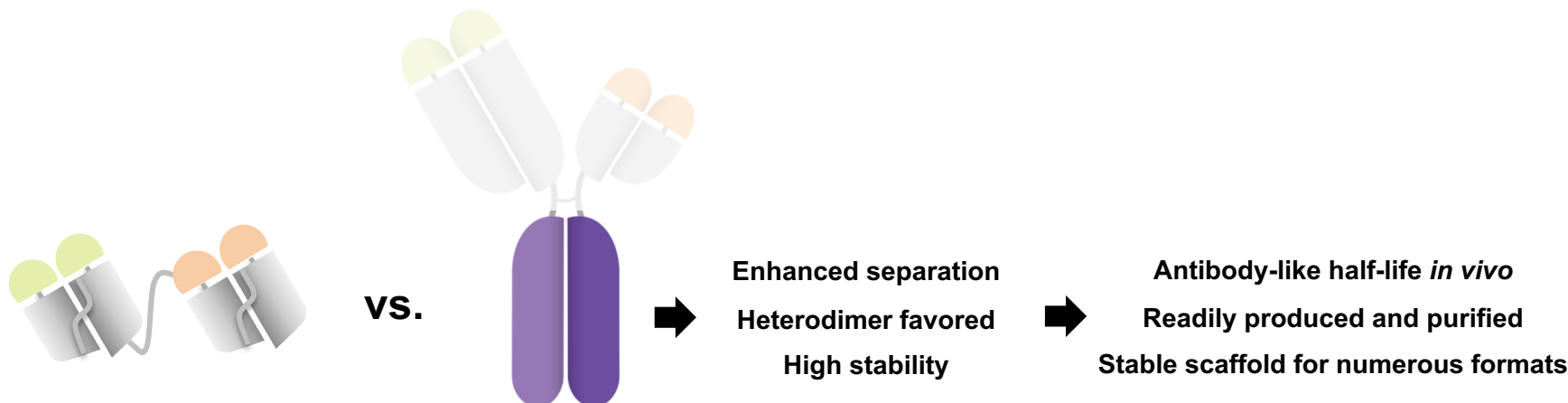
Program	Fc Domain	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Approved	Commercial Rights
Ultomiris®	Xtend™	PNH, aHUS						
Monjuvi® (tafasitamab/XmAb5574)	Cytotoxic	DLBCL	APPROVED IN U.S.; MAA REVIEW (EMA)					 
VIR-7831	Xtend	COVID-19						
AIMab7195 (XmAb7195)	Immune Inhibitor	Food Allergy						
VRC01LS	Xtend	HIV						
AMG 424 CD38 x CD3	Bispecific	Myeloma						
Elipovimab GS-9722	Cytotoxic Xtend	HIV						
VIR-2482	Xtend	Influenza A						
XmAb bispecific	Bispecific	Oncology						
AMG 509 STEAP1 x CD3	2+1 Bispecific	Prostate cancer						
VIR-3434	Xtend	Hepatitis B						
XmAb bispecific	Bispecific	Oncology						

Technology licensing expands pipeline with very little opportunity cost

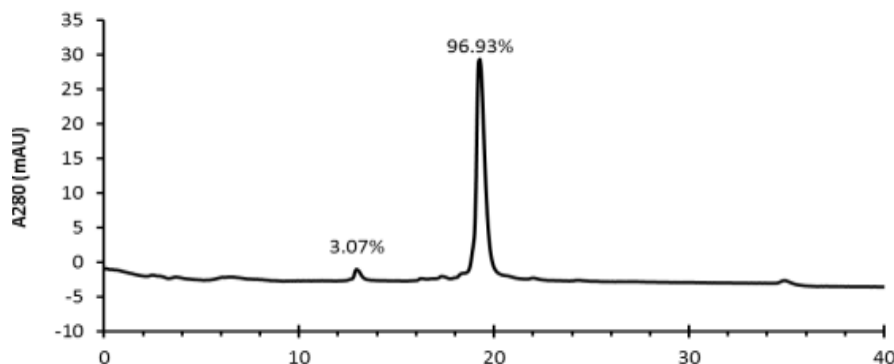
XmAb[®] Bispecific Antibody Programs



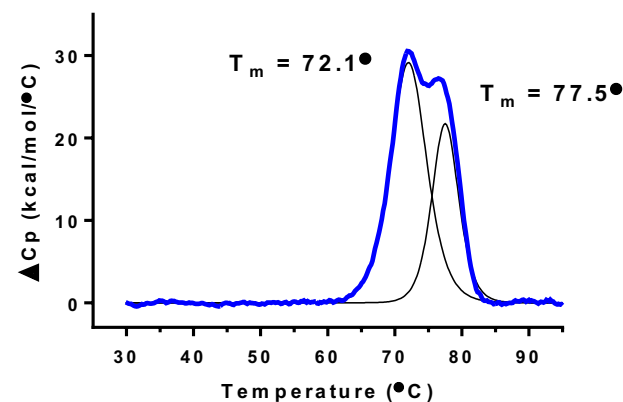
XmAb® Bispecific Fc Domains Retain Beneficial Natural Antibody Properties



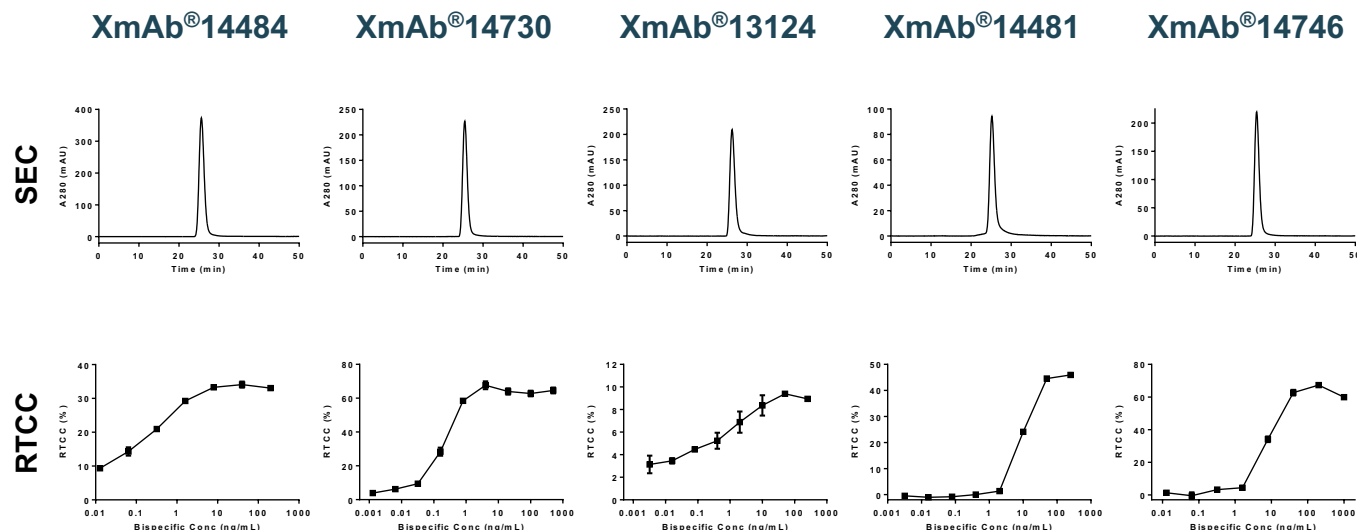
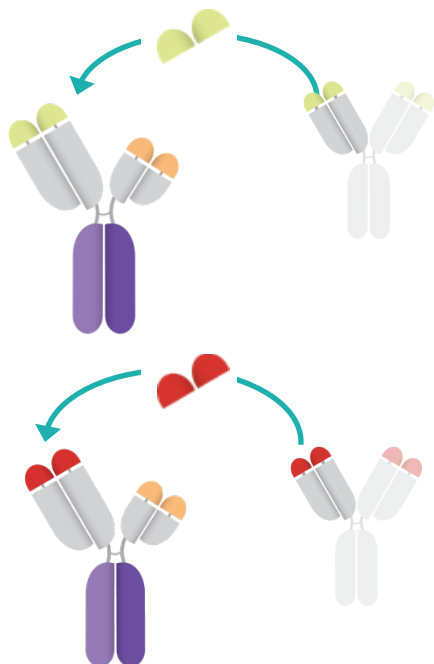
Stable cell line expression of Vibecotamab



Heterodimer Fc domain thermal stability



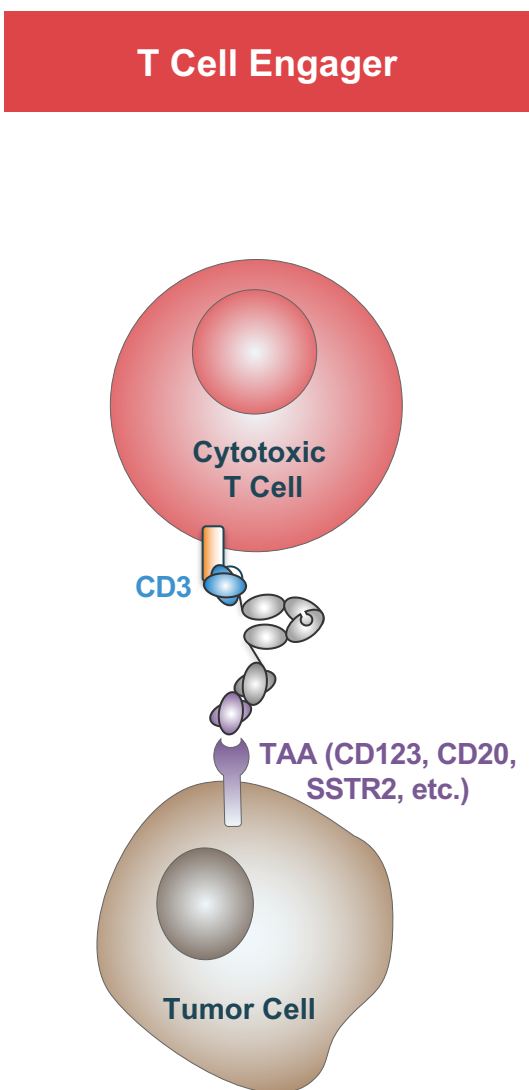
Plug-and-play Fc Domain Enables Rapid Pipeline Generation and Prototyping of Target Combinations



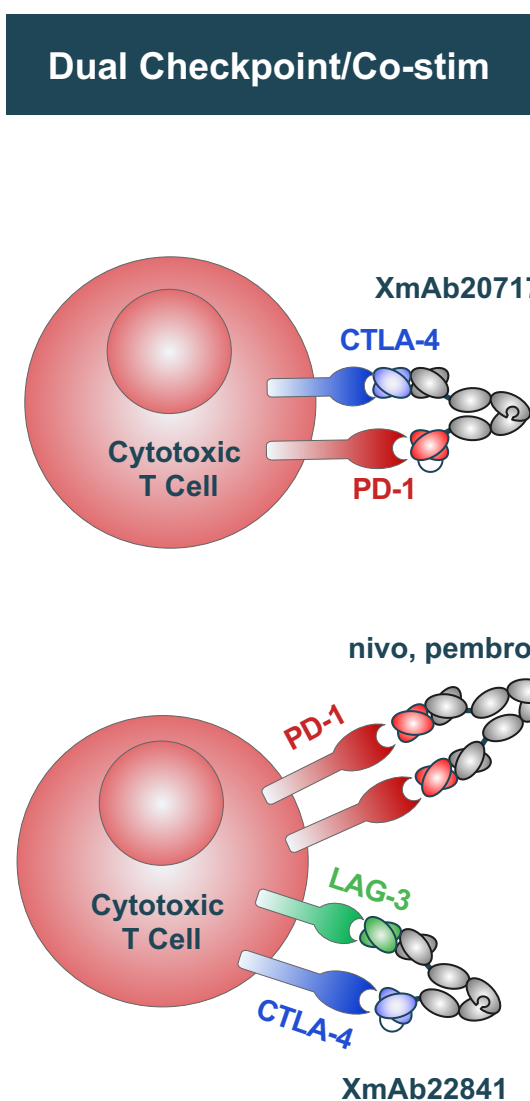
1. CD3 bispecific molecules redirect T cell cytotoxicity (RTCC) against tumors
 - XmAb® 2+1 bispecific antibodies may potentially enhance RTCC of high antigen density tumor tissue versus low antigen density healthy tissue
2. Dual checkpoint/co-stim molecules to activate the tumor microenvironment
3. Engineered cytokine-Fc fusions to expand immune cell populations

The diagram consists of three colored rectangular boxes arranged horizontally, separated by thin vertical lines. The first box is red and contains the text 'T Cell Engager'. The second box is dark blue and contains the text 'Dual Checkpoint/Co-stim'. The third box is yellow and contains the text 'Cytokine-Fc'.

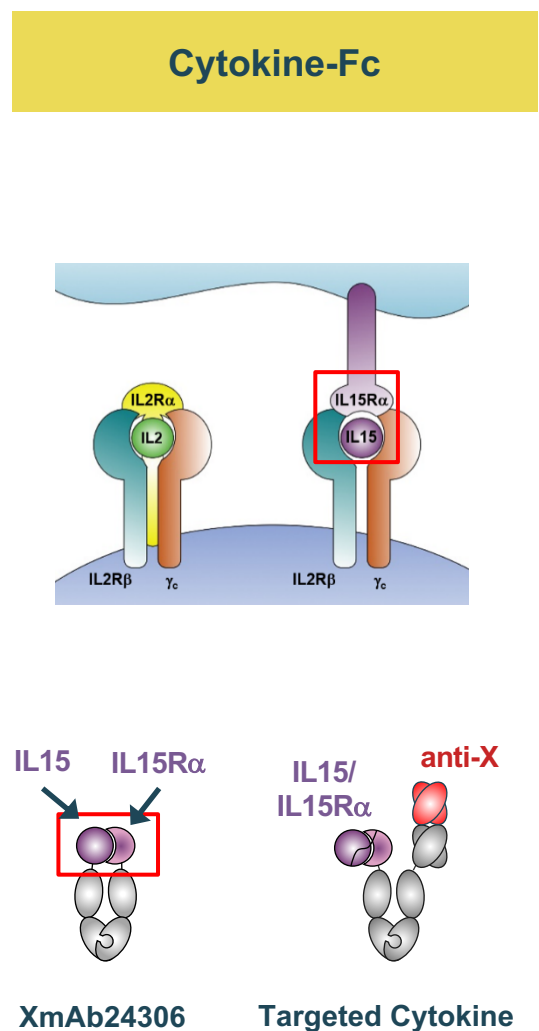
T Cell Engager



Dual Checkpoint/Co-stim

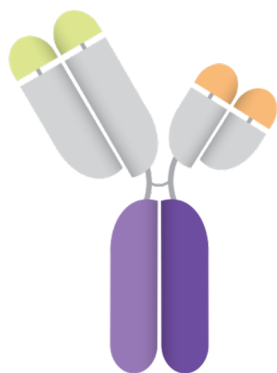


Cytokine-Fc

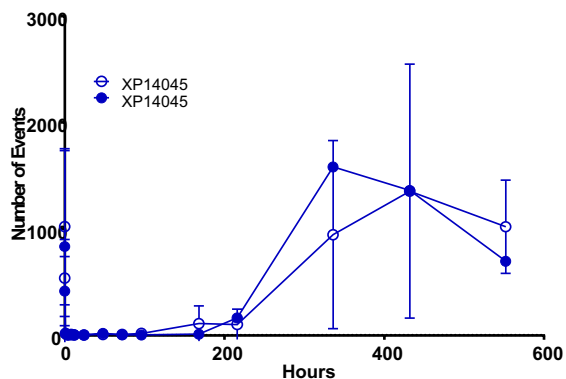


Xencor's Lead Bispecific Programs: CD3 T-Cell Engagement with Tuned Potency and mAb-like PK

Vibecotamab (CD123 x CD3)



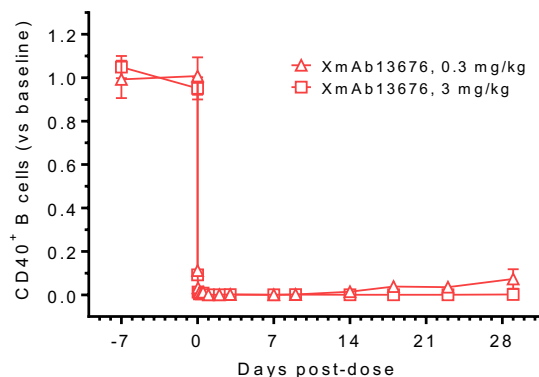
Cynomolgus monkey, single IV bolus
Profound, sustained basophil depletion



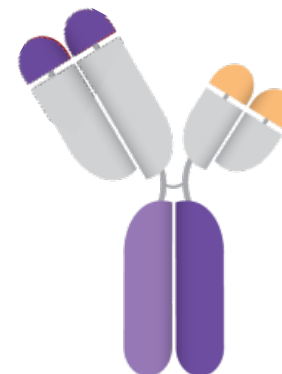
Plamotamab (CD20 x CD3)



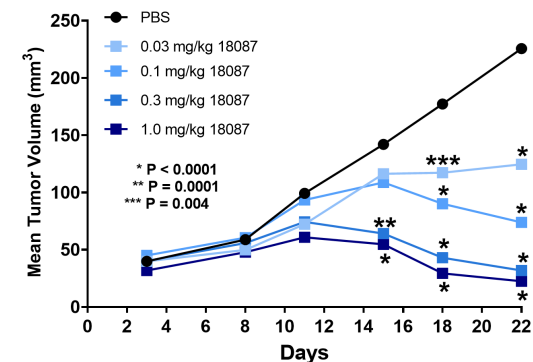
Cynomolgus monkey, single IV bolus
Profound, sustained B-cell depletion



Tidutamab (SSTR2 x CD3)



huPBMC-SCID mouse xenograft
Potent, dose-dependent tumor reduction

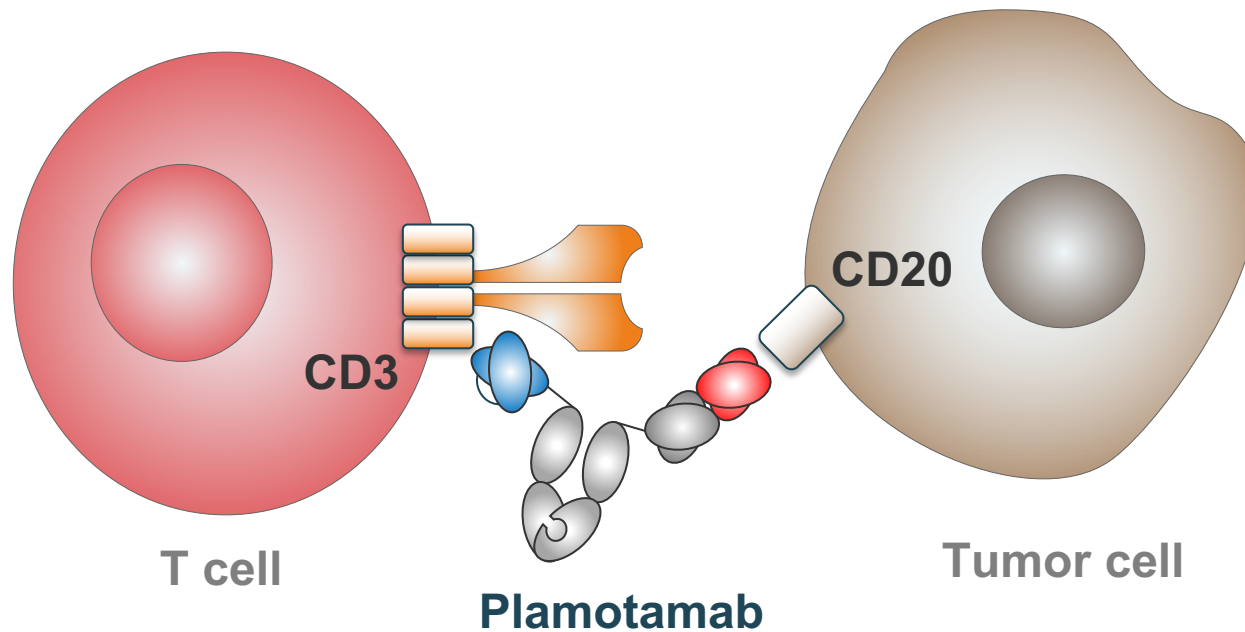


Plamotamab

**Initial Phase 1
Dose Escalation Data
Presented at
ASH 2019**



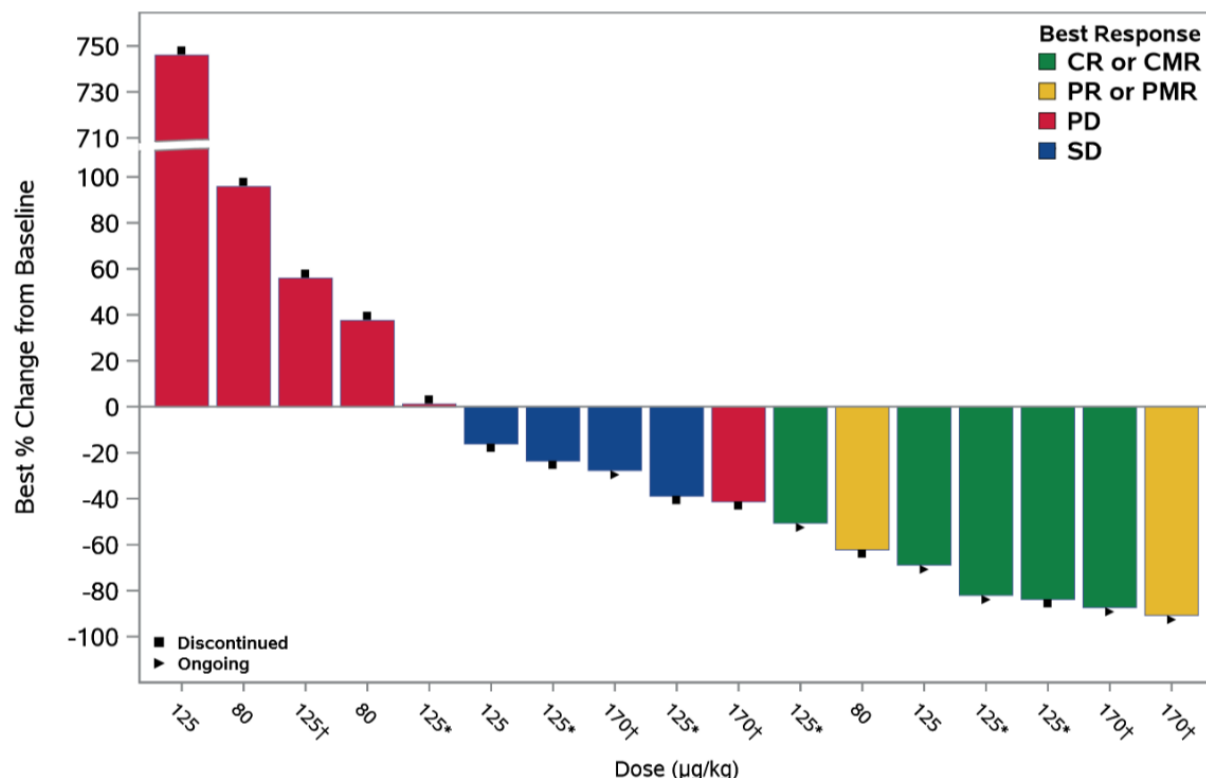
Plamotamab: CD20 x CD3 Bispecific Antibody



- Potent redirection of T-cell killing toward CD20-expressing cells
- Full-length construct provides improved pharmacokinetics
- “Tunable” binding affinity allows optimization of potency and safety
- No FcγR binding prevents Fc domain-mediated CD3 crosslinking and activation

Encouraging Clinical Activity and Dose Dependent Activity in Initial Dosing Cohorts – r/r DLBCL

DLBCL population with doses at 80 µg/kg or higher (N=18)



CMR: complete metabolic response; PMR: partial metabolic response.

CR: complete response; ORR: objective response rate.

*Includes patients with 125 µg/kg flat dosing and 80/125 µg/kg step-up dosing

† step-up dosing 45/80/125/170 µg/kg.

Safety Population

Overall	
ORR	7/18 (38.9)
CR	5/18 (27.8)
80 µg/kg	
ORR	1/4 (25.0)
CR	0
125 µg/kg*	
ORR	4/10 (40.0)
CR	4/10 (40.0)
170 µg/kg†	
ORR	2/4 (50.0)
CR	1/4 (25.0)

Plamotamab Was Generally Well Tolerated

- Most events were Grade 1 or 2
- 52.8% of patients experienced at least 1 CRS event
 - Of these CRS events, 89% were Grade 1 or 2
 - 5.7% of patients experienced Grade 3 or 4 CRS events
 - Most common symptoms were pyrexia, hypotension, chills, tachycardia and hypertension
- Nervous system disorders occurred in 49.1% of patients
 - Most common were dizziness, headache, paresthesia and lethargy
 - These events were Grade 1 or 2 in severity, except for one Grade 3 headache
 - 1 patient experienced Grade 2 short-term encephalopathy during a CRS event

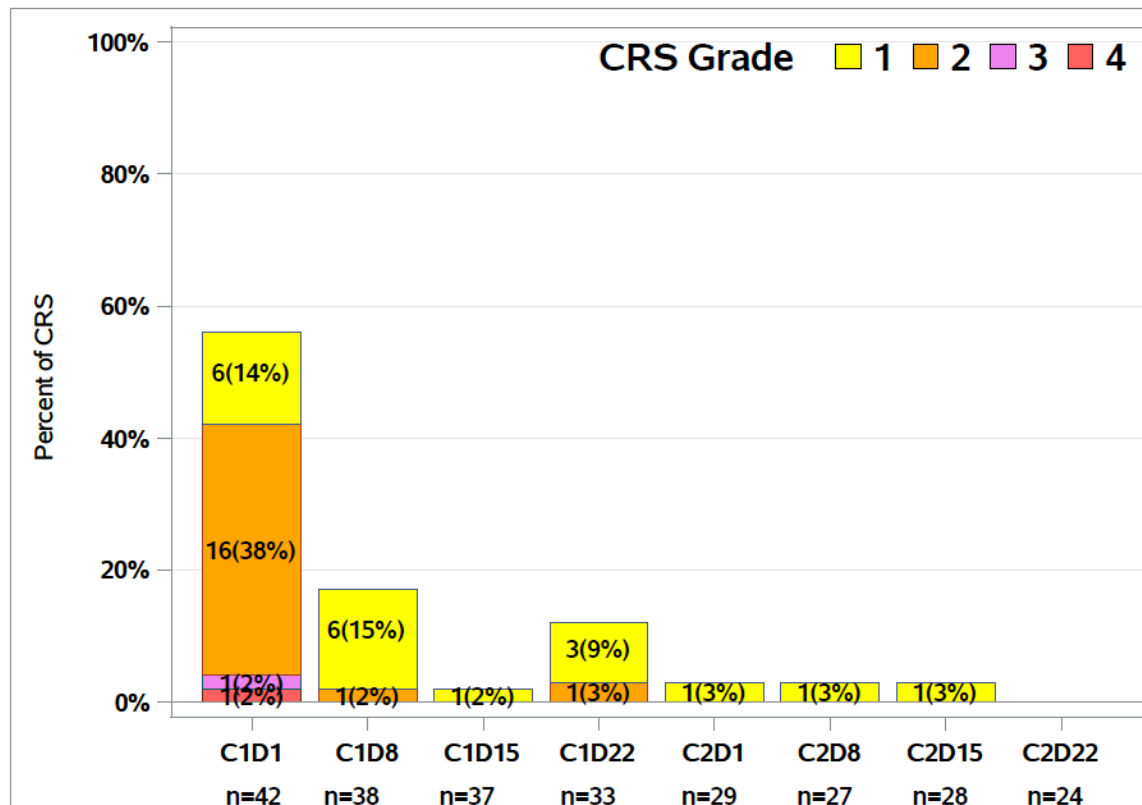
Summary of Treatment-Emergent Adverse Events – Safety Evaluable

Event, n (%)	NHL (N=45)	CLL (N=8)	Overall (N=53)
Any TEAE	45 (100.0)	8 (100.0)	53 (100.0)
Any serious TEAE	24 (53.3)	5 (62.5)	29 (54.7)
Leading to drug withdrawn	4 (8.9)	3 (37.5)	7 (13.2)
Most common TEAEs (≥15)			
Pyrexia	26 (57.8)	3 (37.5)	29 (54.7)
Cytokine release syndrome	25 (55.6)	3 (37.5)	28 (52.8)
Anemia	19 (42.2)	3 (37.5)	22 (41.5)
Diarrhea	12 (26.7)	2 (25.0)	14 (26.4)
Asthenia	10 (22.2)	3 (37.5)	13 (24.5)
Hypotension	12 (26.7)	1 (12.5)	13 (24.5)
Thrombocytopenia	11 (24.4)	2 (25.0)	13 (24.5)
Chills	11 (24.4)	1 (12.5)	12 (22.6)
Cough	10 (22.2)	2 (25.0)	12 (22.6)
Fatigue	8 (17.8)	4 (50.0)	12 (22.6)
Neutropenia	10 (22.2)	2 (25.0)	12 (22.6)
Constipation	10 (22.2)	1 (12.5)	11 (20.8)
Hypokalemia	10 (22.2)	0	10 (18.9)
Edema peripheral	6 (13.3)	4 (50.0)	10 (18.9)
Tachycardia	8 (17.8)	2 (25.0)	10 (18.9)
Dizziness	9 (20.0)	0	9 (17.0)
Dyspnea	7 (15.6)	2 (25.0)	9 (17.0)
Headache	8 (17.8)	1 (12.5)	9 (17.0)
Nausea	7 (15.6)	1 (12.5)	8 (15.1)
Upper respiratory tract infection	7 (15.6)	1 (12.5)	8 (15.1)
Grade ≥3 events, n (%)			
Any TEAE Grade ≥3	31 (68.9)	6 (75.0)	37 (69.8)
Most common TEAEs (≥5%)			
Anemia	11 (24.4)	1 (12.5)	12 (22.6)
Neutropenia	7 (15.6)	1 (12.5)	8 (15.1)
Thrombocytopenia	5 (11.1)	1 (12.5)	6 (11.3)
Lymphopenia	4 (8.9)	1 (12.5)	5 (9.4)
Cytokine release syndrome	2 (4.4)	1 (12.5)	3 (5.7)
Hypokalemia	3 (6.7)	0	3 (5.7)

Note: AEs were graded based on CTCAE version v4.03, except for CRS, which was graded according to the Lee criteria (Blood. 2014;124(2):188-95)

CRS Events More Frequent, Generally Higher Grade on First Treatment

Distribution of CRS Grade by Dosing Visit (NHL, 20 µg/kg and Higher, n=42)



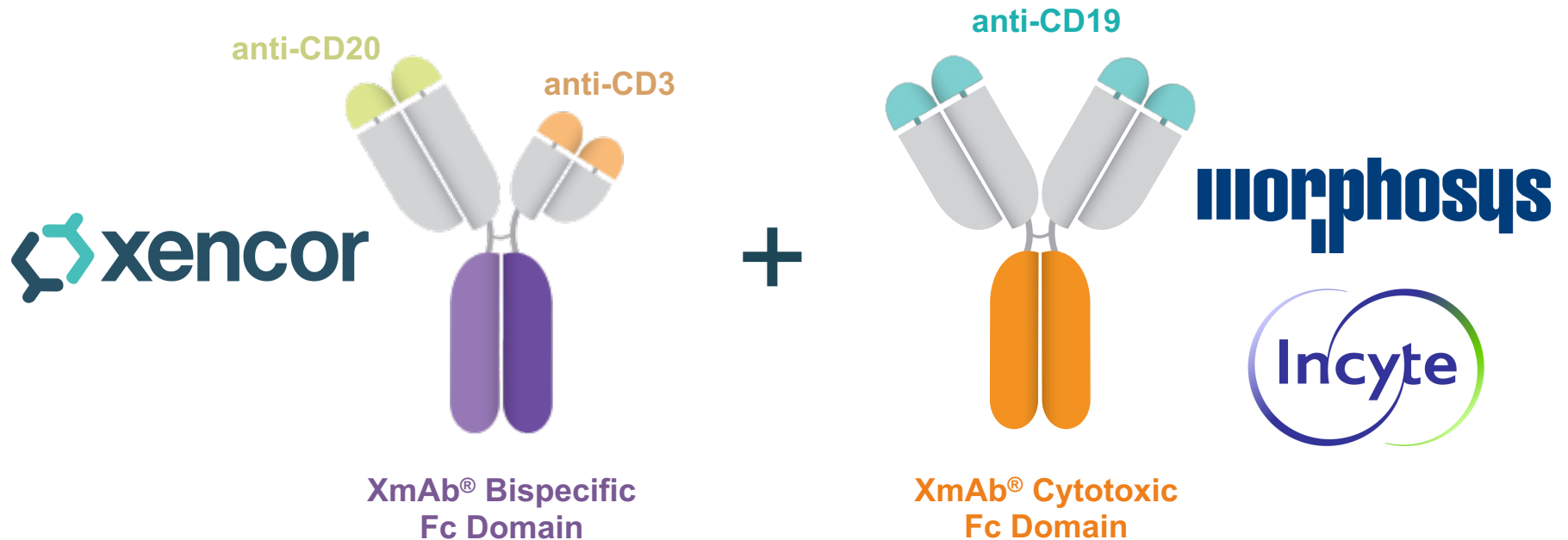
1. Adverse Events with preferred term Cytokine Release Syndrome (CRS) are used in the analysis. For multiple CRS events for a subject at a dosing visit, the record with maximum CRS grade was used in the analysis.
2. The denominator for percentages are the number of subjects (n) dosed at each visit.
3. Includes all NHL subjects who have had a dose of at least 20 µg/kg of XmAb13676

Plamotamab is Generally Well Tolerated with Encouraging Signs of Clinical Activity in Early Dosing

- Plamotamab was generally well tolerated
 - CRS, an AE associated with this class of agents, was observed in 52.8% of patients
 - Most CRS events occurred with the first dose of plamotamab and were Grade 1 and 2 by the Lee criteria
 - There were no Grade 3 or 4 CRS events once step-up dosing was implemented
 - Nervous system disorders were generally mild and did not lead to discontinuation of treatment
- Plamotamab demonstrated clinical activity in DLBCL at doses of 80 µg/kg and higher in a dose-dependent manner
- Additional responses have been observed in Waldenström macroglobulinemia and Richter transformation of CLL, both CRs and both at 20 µg/kg; and in follicular lymphoma at step-up dosing to 170 µg/kg, also a CR (1/5 patients treated at $\geq 80\mu\text{g/kg}$)
- PK was dose proportional
- Dose escalation and schedule optimization are ongoing

Global Collaboration with MorphoSys and Incyte to Combine Plamotamab, Tafasitamab in Multiple Studies

- Phase 1/2 study to evaluate the combination of tafasitamab, plamotamab and lenalidomide in patients with relapsed or refractory DLBCL; Phase 1b studies also planned in 1L DLBCL, r/r FL
 - MorphoSys and Incyte will provide tafasitamab
 - Xencor will sponsor and fund the studies



Tidutamab

**Initial Phase 1
Dose Escalation Data
Presented at
NANETS 2020**



Tidutamab: SSTR2 x CD3 Bispecific Antibody

- Tidutamab directs T-cell mediated cytotoxicity to SSTR2+ cells
- SSTR2 is highly overexpressed in neuroendocrine tumors (NET) and several other tumor types, including GIST, Merkel cell carcinoma and small cell lung cancers

Ongoing Phase 1 study in patients with NET and GIST

- Dosing in the study includes a lower priming dose, followed by a higher repeated dose on subsequent dosing days
- Reported initial data for NET cohorts at the NANETS 2020 (n=27)
 - Patients were a median of 61 years old and received a median of 4 prior disease-specific systemic therapies
 - Initial lesion location: pancreas (56%), intestinal (15%), pulmonary (15%), other GEP-NET (7%), unknown (7%)
 - 56% received prior receptor radionuclide therapy

Tidutamab Generally Well Tolerated at the Expansion Dose

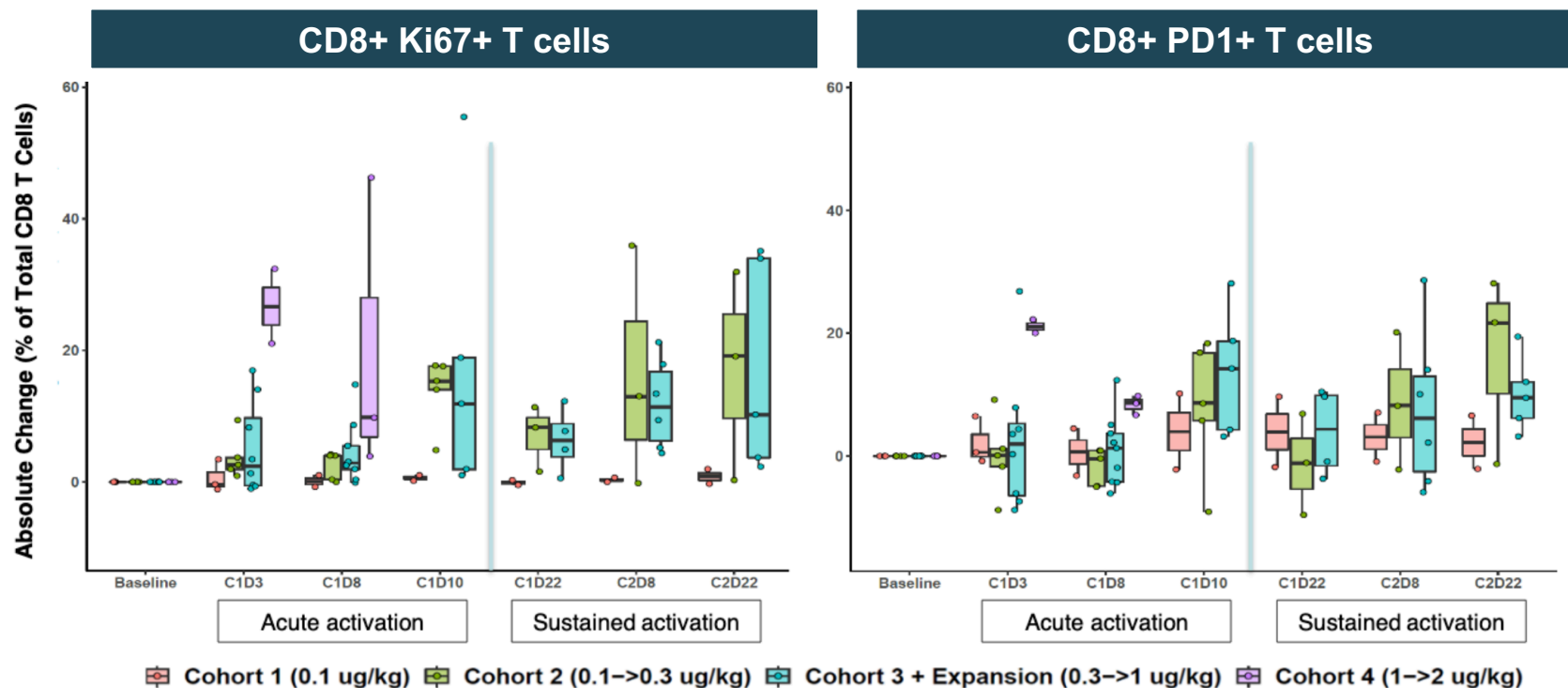
Treatment-Related Grade 3/4 Adverse Events by Dose Level (µg/kg, n≥2)					
Event, n (%)	0.1 → 0.1 (n=5)	0.1 → 0.3 (n=5)	0.3 → 1.0 (n=12)	1.0 → 2.0 (n=5)	Overall (n=27)
Any	4 (80)	3 (60)	7 (58)	3 (60)	17 (63)
Lymphopenia/lymphocyte count decreased	4 (80)	3 (60)	3 (25)	1 (20)	11 (41)
GGT increased	1 (20)	1 (20)	3 (25)	-	5 (19)
Vomiting	-	-	2 (17)	3 (60)*	5 (19)
ALT/AST increased	1 (20)	1 (20)	2 (17)	1 (20)	5 (19)
Nausea	-	-	1 (8)	3 (60)*	4 (15)
Diarrhea	-	-	2 (17)	1 (20)	3 (11)
Hypophosphatemia	-	-	2 (17)	1 (20)	3 (11)
Anemia	-	1 (20)	1 (8)	-	2 (7)
Fatigue	-	-	-	2 (40)	2 (7)
Lipase increased	1 (20)	1 (20)	-	-	2 (7)

* DLT – May be related to engagement of SSTR2 in the GI tract

**Recommended
Expansion Dose**

Cytokine Release Syndrome Restricted to Grades 1, 2 and Limited to First 2 Doses					
CRS, n (%)	0.1 → 0.1	0.1 → 0.3	0.3 → 1.0	1.0 → 2.0	Overall
Grade 1	-	2 (40)	4 (33)	-	6 (22)
Grade 2	-	1 (20)	2 (17)	2 (40)	5 (19)

Tidutamab Induces Acute and Sustained T-Cell Activation and Proliferation in Peripheral Blood



CD8-positive effector T cells showed a dose-dependent increase in proliferation (Ki67) and activation (PD-1) markers that began within 48 hours of the first dose and persisted at least seven weeks, as measured at cycle 2, day 22

Key Takeaways from Ongoing Phase 1 Study in NET

Inform New Study in Merkel Cell Carcinoma and SCLC

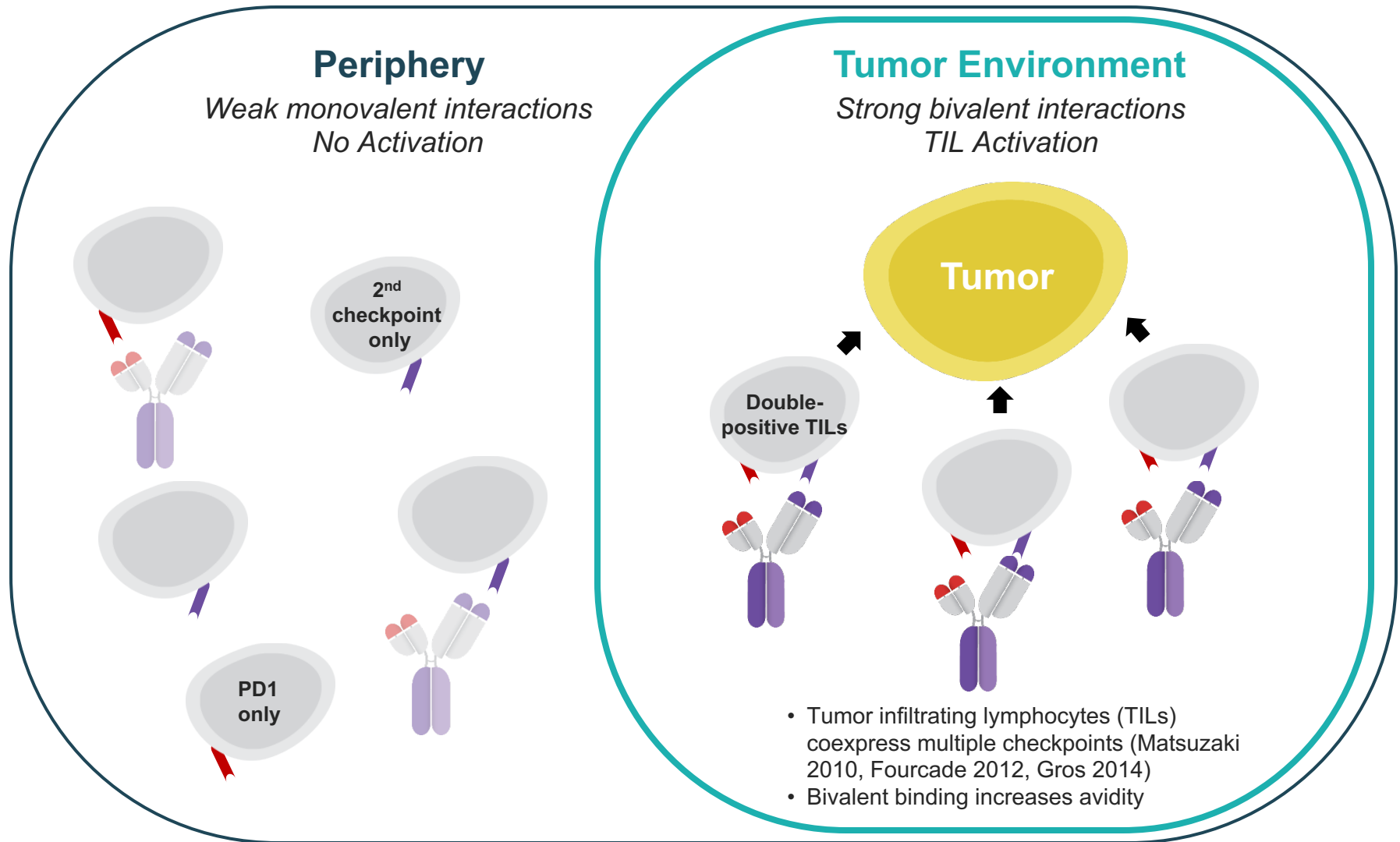
- Tidutamab was associated with stable disease in 43% of patients across dose levels
 - Longer follow-up required to evaluate PFS and clinical utility in NET
- Well tolerated at the identified recommended dose
 - Low rate and grade of cytokine release syndrome (Grade 1 or 2 only)
- Sustained activation of cytotoxic T cells and engagement of SSTR2 support tidutamab's mechanism of action
- Dose-proportional PK and half-life (~4 days) support weekly dosing

New study in Merkel cell carcinoma and small cell lung cancer, SSTR2-expressing tumor types known to be responsive to immunotherapy, to start in 2021, subject to COVID-19 impact

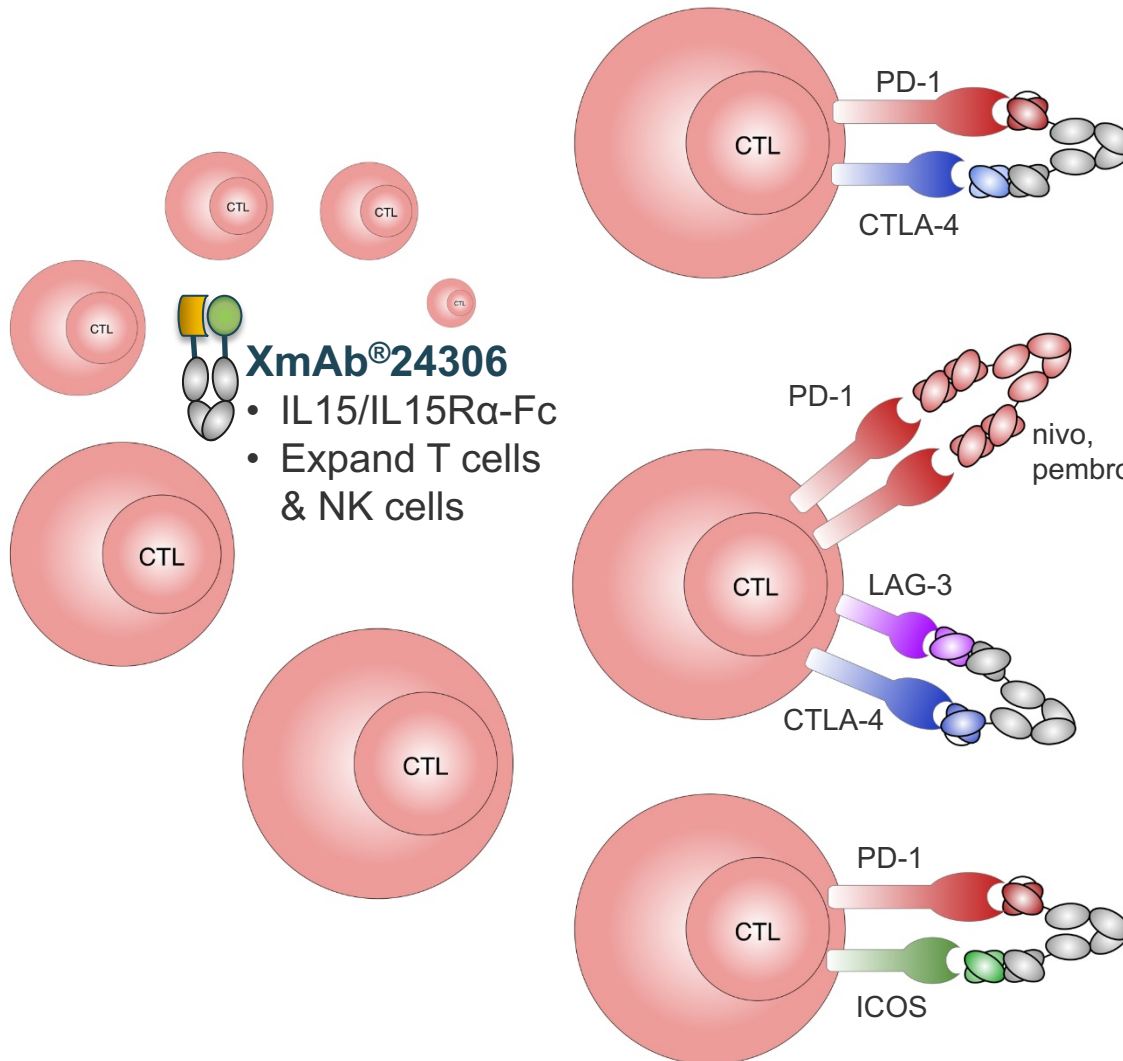
**TME Activating
Bispecific Antibodies
Engineered Cytokines**



Xencor's Dual Checkpoint/Co-Stim Bispecifics are Designed to Promote Tumor-Selective T Cell Targeting



Distinct and Novel Mechanisms-of-Action Define Xencor's Growing Oncology Pipeline



XmAb®20717

- PD-1 x CTLA-4 bispecific
- Two most validated checkpoint receptors
- Phase 1 dose-escalation and expansion ongoing

XmAb®22841

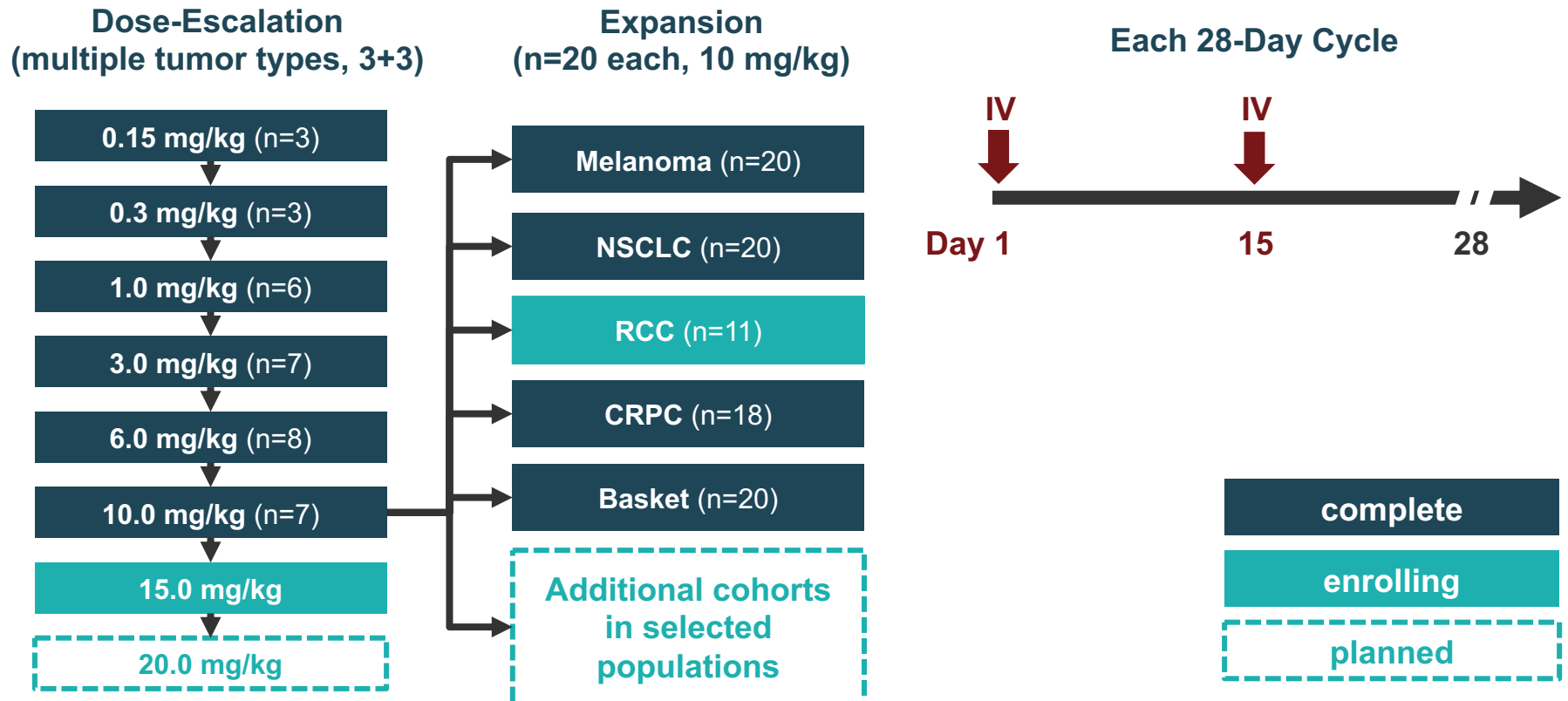
- CTLA-4 x LAG-3 bispecific
- Combinable with anti-PD1
- Triple checkpoint blockade
- Phase 1 dose-escalation ongoing

XmAb®23104

- PD-1 x ICOS bispecific
- Novel checkpoint x co-stim pairing
- Phase 1 dose-escalation ongoing

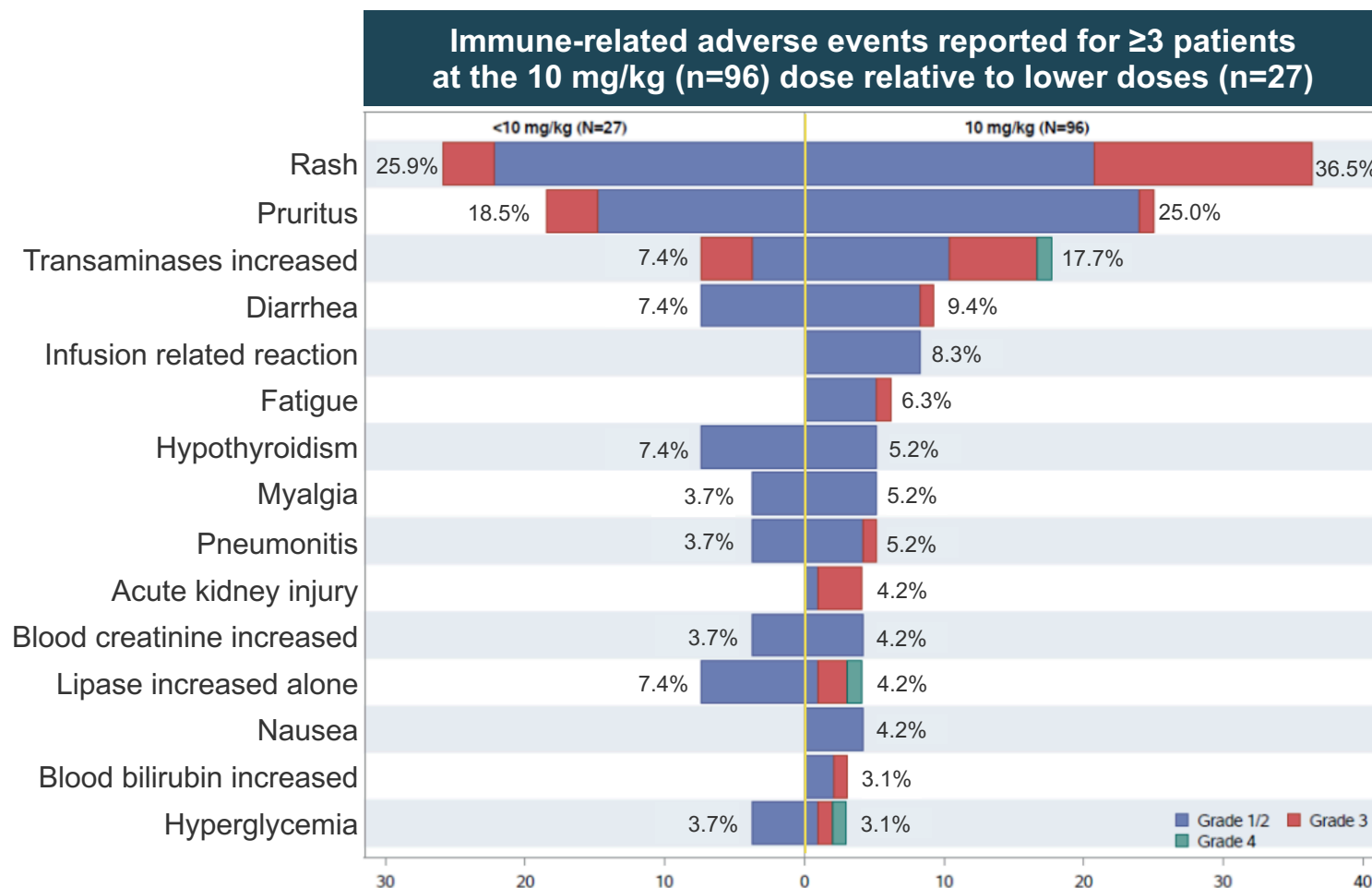
XmAb[®]20717 (PD-1 x CTLA-4) Phase 1 Study Design and Plans

- Purpose: Evaluate the safety and tolerability of XmAb20717 and to establish a recommended dose or MTD for further investigation
- Secondary objectives: Assess PK, PD and preliminary anti-tumor activity



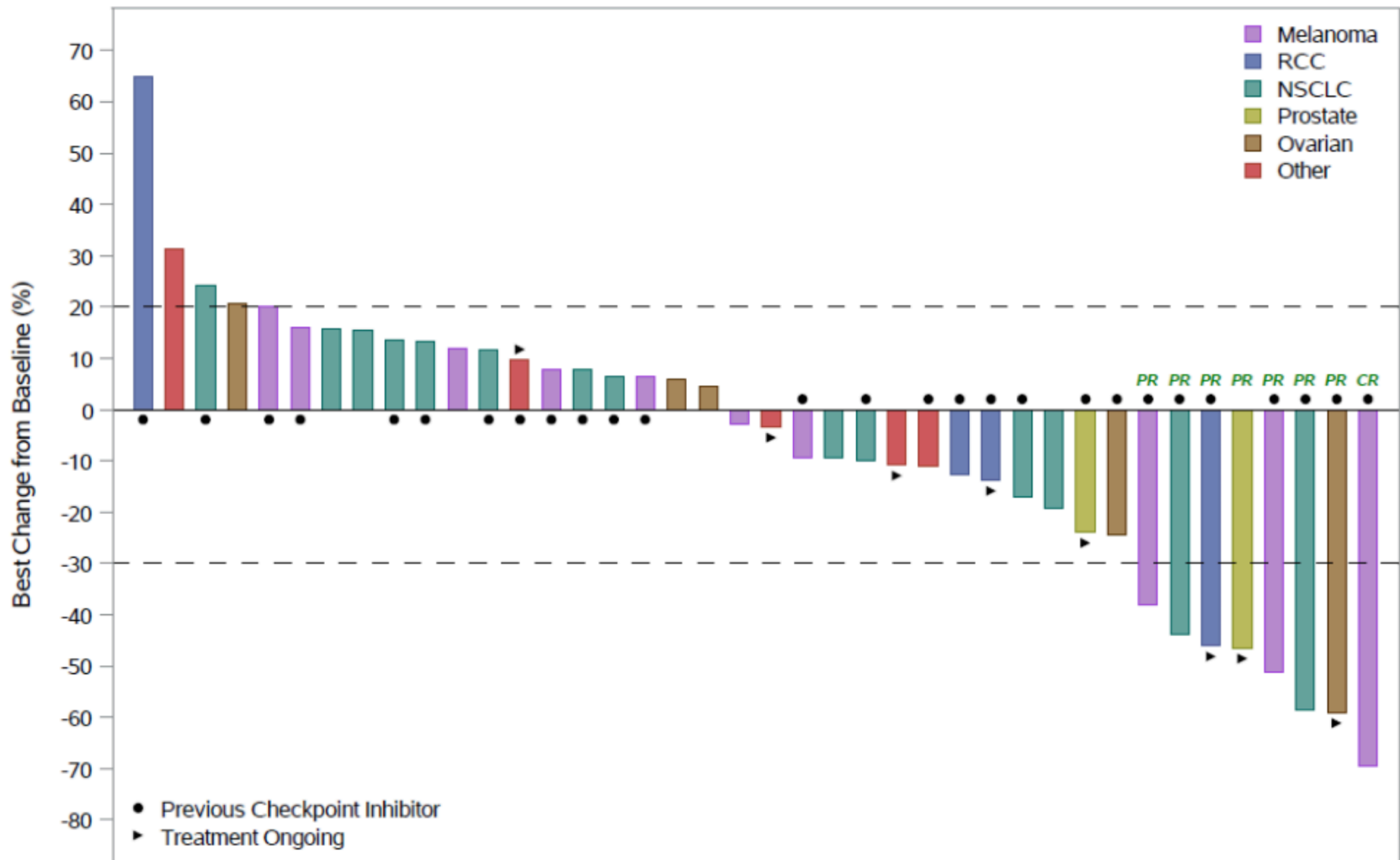
Data cut: September 30, 2020

XmAb®20717 Was Generally Well Tolerated; Most Common Adverse Events Were Immune Related



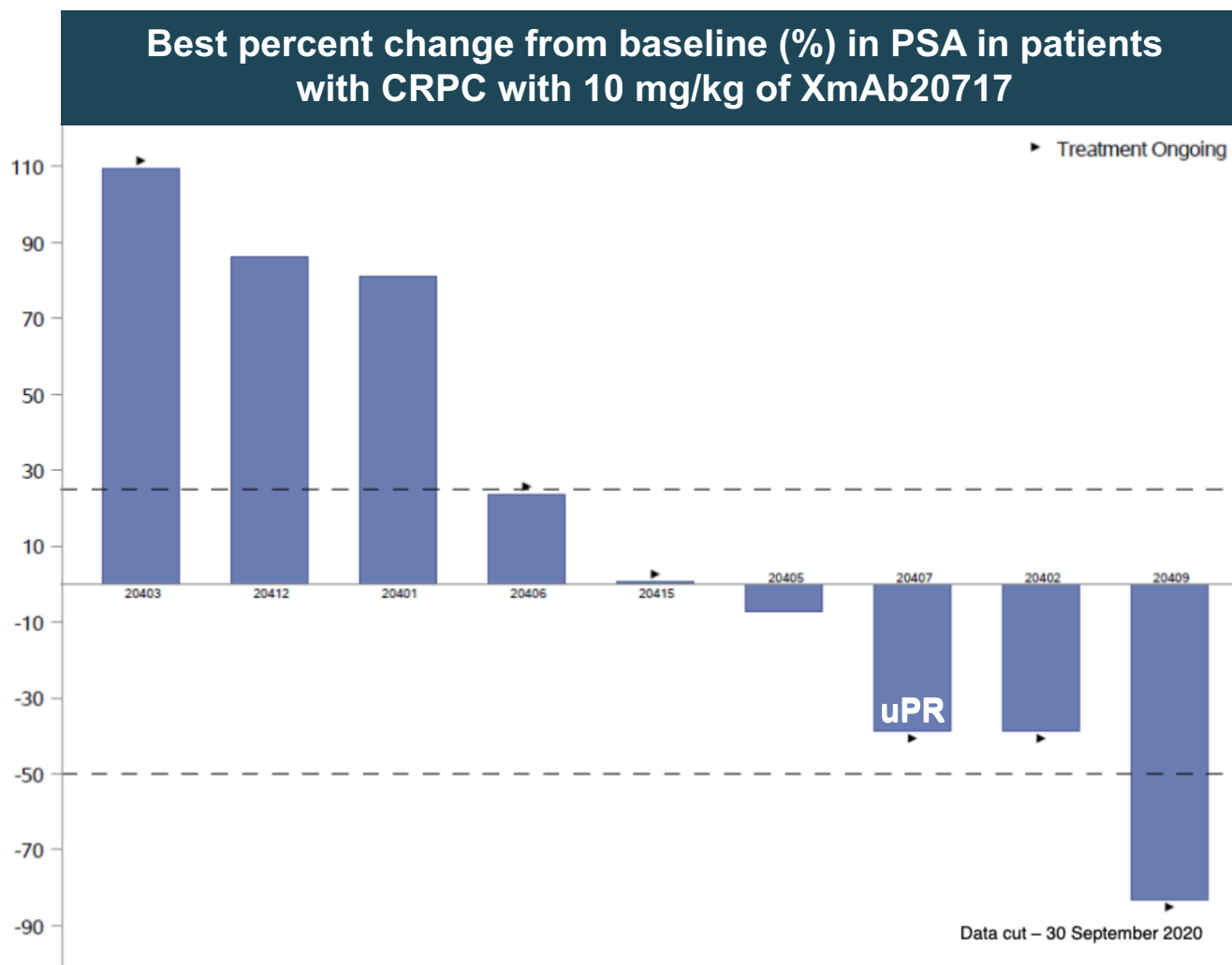
Immune-mediated pancreatitis (Grade 5) was reported for one patient with RCC, whose cancer had already metastasized to the pancreas at baseline and progressed on study. Grade 5 myocarditis and respiratory failure were reported for a patient with NSCLC who had a history of significant cardiac events, including atrial fibrillation and the insertion of a dual-chamber pacemaker.

Clinical Activity Across Multiple Tumor Types in Patients Who Had Previously Been Treated With a Checkpoint Inhibitor

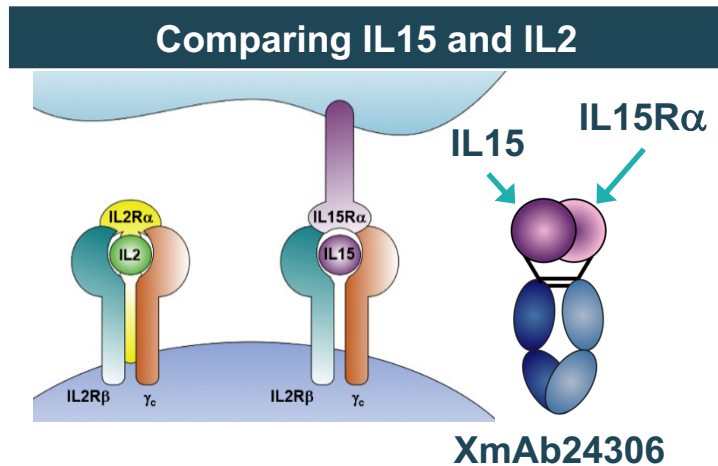


The median duration of response was 119 days at the time of the data cut off, and 24 patients remained on treatment.

Encouraging Reductions in PSA, PR in 1/4 Evaluable Patients; New Phase 1b Study of XmAb20717 in mCRPC to Start in 2021



Genentech Collaboration Boosts Development Resources for Novel IL15 Cytokine Combinations for Oncology



- IL15 is a highly active immune signaling protein that stimulates tumor killing NK cells and CD8+ T cells
- IL2 and IL15 share IL2Rβγ receptor interactions, but IL-15 avoids biased T reg activation
- Xencor's IL15 cytokines are built on a heterodimeric Fc domain and have potency tuned to improve therapeutic index, and incorporate Xtend™ for longer half-life

























Genentech
A Member of the Roche Group



Extensive clinical strategy to explore numerous combinations with Genentech's leading oncology portfolio

- Two-year research collaboration for IL15 programs
- Xencor retains ability to perform clinical studies, subject to requirements
- Xencor shares in 45% worldwide P&L and development costs; co-promotion option in U.S.
- Genentech receives worldwide commercial license to lead IL15 cytokine XmAb24306
- \$120M upfront and up to \$160M in XmAb24306 development milestone payments; up to \$180M for each new IL15 program
- XmAb24306 in Phase 1 study

Xencor's Expanding Bispecific Oncology Pipeline

Program	Targets	Primary Indication	Preclinical	Phase 1	Phase 2	Commercial Rights
Vibecotamab	CD123 x CD3	AML				
Plamotamab	CD20 x CD3	B-cell cancer				
Tidutamab	SSTR2 x CD3	GEP-NET/GIST				
XmAb20717	PD-1 x CTLA-4	Oncology				
AMG 424	CD38 x CD3	Myeloma				
XmAb22841	CTLA-4 x LAG-3	Oncology				
XmAb23104	PD-1 x ICOS	Oncology				
XmAb	Undisclosed	Oncology				
XmAb24306	IL15R β γ (IL15/IL15Ra-Fc)	Oncology				 <small>A Member of the Roche Group</small>
AMG 509	STEAP1 x CD3 (2+1)	Prostate cancer				
XmAb	Undisclosed	Oncology				
XmAb30819	ENPP3 x CD3 (2+1)	Prostate cancer				

T Cell Engager

Dual Checkpoint/Co-stim

Cytokine-Fc

2020/2021 Priorities for Internal Programs and Progress with Partners

Advance Internal Portfolio of Novel Bispecific Antibodies and Cytokines

- ✓ Supported Genentech's initiation of Phase 1 study for **XmAb24306** (IL15/IL15R α -Fc targeting IL15R $\beta\gamma$)
 - ✓ Presented initial data from Phase 1 study of **XmAb20717** (PD-1 x CTLA-4) in solid tumors
 - ✓ Presented data on multiple preclinical bispecific antibodies (e.g., **B7-H3 x CD28**) & **IL-12-Fc** cytokine
 - ✓ Present initial data from Phase 1 study of **tidutamab** (SSTR2 x CD3) in NET
- 2021, subject to COVID-19 impact: initiate additional clinical studies of **vibecotamab**, **plamotamab**, **tidutamab** and **XmAb20717**; initiate first-in-human studies of **XmAb27564** (IL-2-Fc) in healthy volunteers and **XmAb30819** (ENPP3 x CD3) in renal cell carcinoma

Progress with Partnered Programs

- ✓ Licensed anti-IgE antibody **XmAb7195** (now AIMab7195) to Aimmune Therapeutics
 - ✓ Licensed Xtend™ and Cytotoxic Fc technologies to Gilead for anti-HIV antibody **elipovimab**
 - ✓ Expanded Vir Biotechnology license for Xtend™; **VIR-7831** & **VIR-7832** for SARS-CoV-2/COVID-19
 - ✓ Entered collaboration with Atreca for CD3 bispecific antibodies against novel tumor targets
 - ✓ FDA approval for MorphoSys' Monjuvi® (tafasitamab-cxix) in second-line DLBCL
- 2 XmAb bispecific antibodies in Phase 1 clinical studies from Amgen and Novartis

\$582.9 million in cash at September 30, 2020; Runway into 2024*

* Last updated: November 5, 2020

Antibodies by Design™

XmAb® Antibody Therapeutics

Corporate Overview

November 2020

