

Proteins by Design®

XmAb® Antibody & Cytokine Therapeutics



Corporate Overview

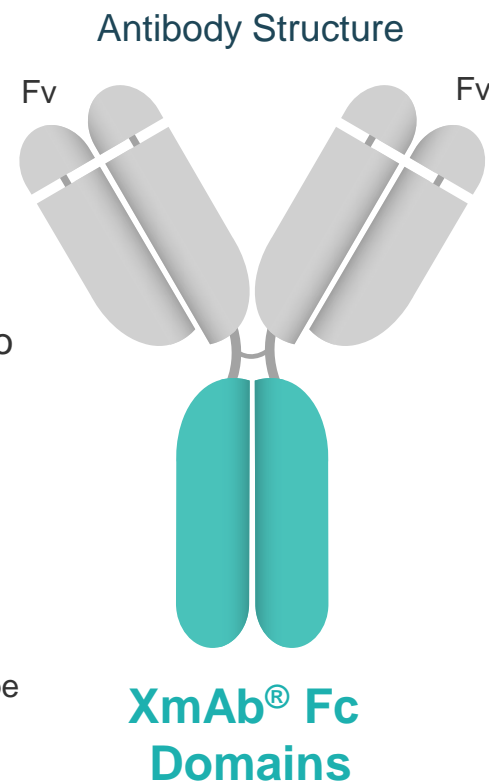
November 2021

Forward-Looking Statements

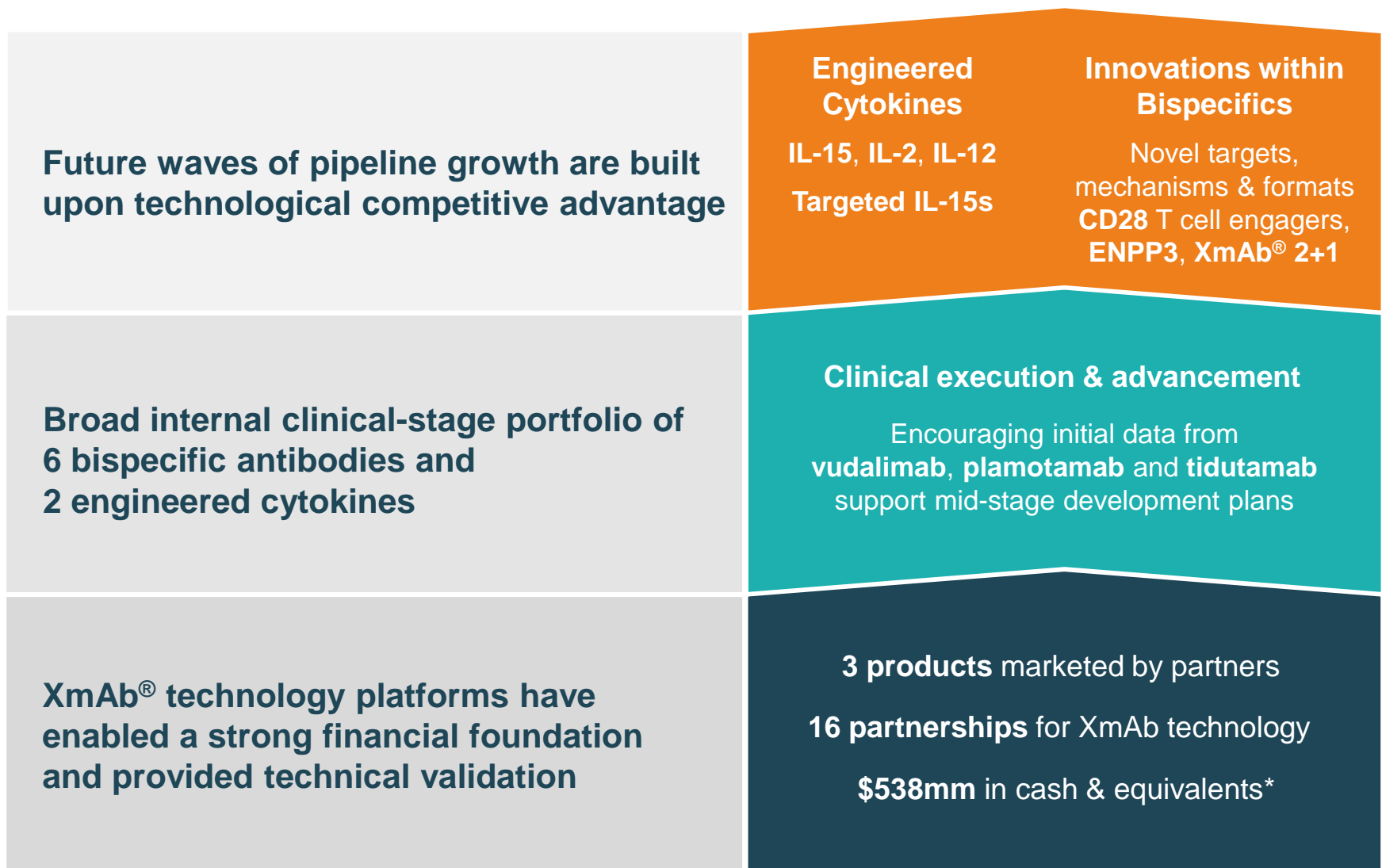
Certain statements contained in this presentation, other than statements of historical fact, may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements regarding Xencor's development plans and timelines; potential regulatory actions; expected use of cash resources; the timing and results of clinical trials; the plans and objectives of management for future operations; and the potential markets for Xencor's product and development candidates. Forward-looking statements are based on the current expectations of management and upon what management believes to be reasonable assumptions based on information currently available to it, and involve numerous risks and uncertainties, many of which are beyond Xencor's control. These risks and uncertainties could cause future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Such risks include, but are not limited to, potential delays in development timelines or negative preclinical or clinical trial results, reliance on third parties for development efforts and changes in the competitive landscape including changes in the standard of care, as well as other risks described in Xencor's filings with the Securities and Exchange Commission (SEC). Xencor expressly disclaims any duty, obligation or undertaking to update or revise any forward-looking statements contained herein to reflect any change in Xencor's expectations with regard thereto of any subsequent change in events, conditions or circumstances on which any such statements are based, except in accordance with applicable securities laws. For all forward-looking statements, we claim the protection of the safe harbor for forward looking statements contained in the Private Securities Litigation Reform Act of 1995.

Xencor: Engineering Antibody Immune Functions to Make Better Drugs

- XmAb® Fc domains: small changes, big functional impacts
 - Augments native immune functions and/or controls structure
 - Preserves half-life, stability and production
 - Over 1,000 issued patents and pending patents worldwide
- Expansive, advancing bispecific antibody and cytokine drug candidate portfolio
 - **8 XmAb bispecific antibodies in Phase 1 or 2 clinical studies**
 - **2 XmAb cytokines in Phase 1 clinical studies**
 - Multiple pre-clinical programs
- Partnership portfolio leverages modular XmAb technology
 - Co-development and extensive commercial rights with Genentech and Janssen
 - Multiple partnerships for technology licenses: little/no effort and greatly broaden scope
- 3 XmAb antibodies commercialized by partners; ongoing revenue generation
 - Monjuvi® (MorphoSys) U.S./EU approvals for relapsed or refractory DLBCL
 - Ultomiris® (Alexion) multiple indications approved U.S., EU, Japan
 - Sotrovimab (Vir/GSK) granted U.S. EUA and global authorizations to treat mild-to-moderate COVID-19



Layers of Value Creation Built on XmAb® Technology



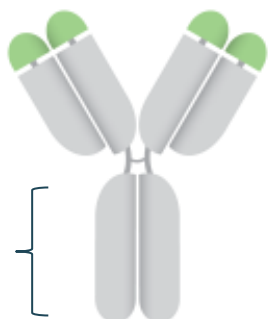
* 9/30/2021

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

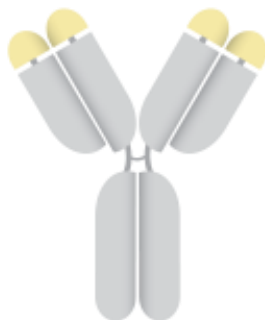
Standard Technology

Fv
focus

Same Fc



Soliris[®]



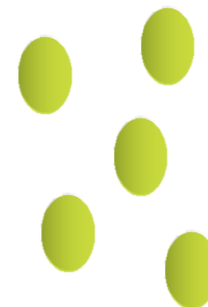
Rituxan[®]



anti-CD19
antibody



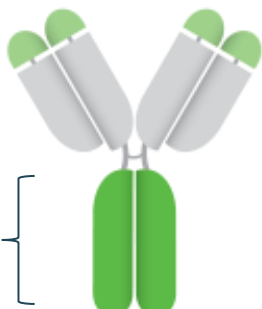
Fv Bispecifics



Cytokines

XmAb Fc Engineering

Xencor Fc
Domains



Ultomiris[®]
(ravulizumab)



Monjuvi[®]
(tafasitamab/XmAb5574)



Obexelimab

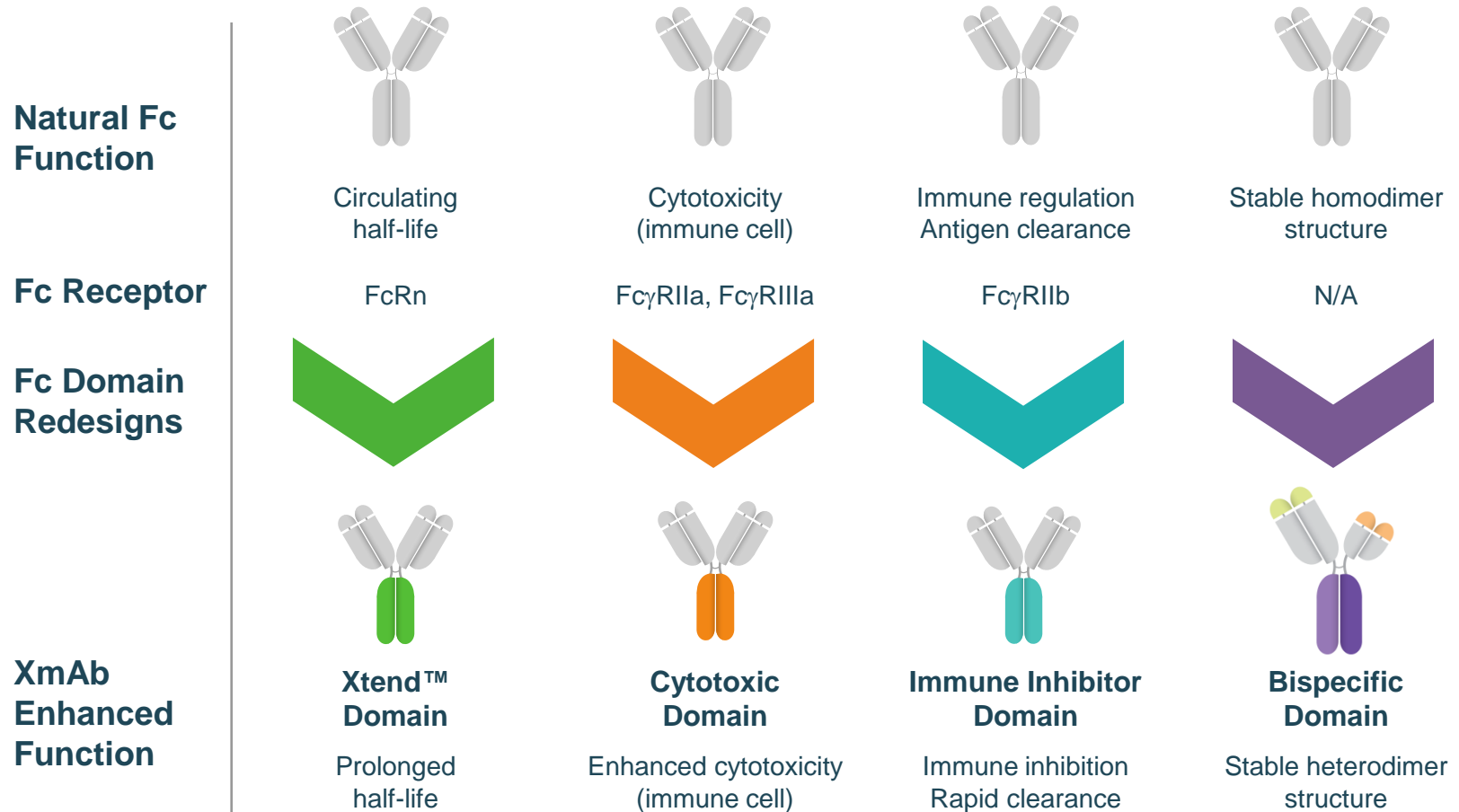


XmAb
Bispecifics



XmAb
Cytokines












XmAb® Fc Domains Augment Natural Antibody Functions



Additional Fc domains: stability, complement activation

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

Development Focus on XmAb® Bispecifics and Cytokines

Program (Targets/Design)	Fc Domain	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Vudalimab (XmAb717) PD-1 x CTLA-4	Bispecific Xtend	mCRPC Gynecologic Tumors					
Tidutamab SSTR2 x CD3	Bispecific	MCC, SCLC			Phase 1b/2		
Plamotamab CD20 x CD3	Bispecific	B-cell malignancies					 ¹
XmAb841 CTLA-4 x LAG-3	Bispecific Xtend	Oncology					
XmAb104 PD-1 x ICOS	Bispecific Xtend	Oncology					
XmAb306 IL15/IL15Rα-Fc	Bispecific Xtend	Oncology					 ² <small>A Member of the Roche Group</small>
XmAb564 IL2-Fc	Bispecific Xtend	Autoimmune					
XmAb968 CD38 x CD3	Bispecific	T-ALL, T-LBL, AML	IST				
XmAb819 ENPP3 x CD3 (2+1)	Bispecific	Renal cell carcinoma					
XmAb808 B7-H3 x CD28	Bispecific Xtend	Prostate cancer, Oncology					
XmAb662 IL12-Fc	Bispecific Xtend	Oncology					


¹ Co-development with Janssen; 20% development cost share; option to co-detail

² Co-development with Genentech; 45% P&L share; option to co-promote in U.S.












Progress Across Portfolio Segments Leading to Value Creating Milestones in 2021/2022

Segment	2020	2021/2022
T Cell Engagers (CD3, CD28)	<ul style="list-style-type: none"> ✓ Entered strategic clinical collaboration with Morphosys and Incyte for plamotamab, tafasitamab combination ✓ Presented initial Phase 1 data of tidutamab in NET ✓ Entered collaboration with Atreca for CD3 BsAbs against novel tumor targets ✓ Entered Janssen CD28 collaboration 	<ul style="list-style-type: none"> ✓ Initiated Phase 1b/2 study of tidutamab for Merkel cell carcinoma and small-cell lung cancer ✓ Entered new Janssen plamotamab/CD28 collaboration ✓ Announce longer follow-up and additional biomarker analysis from Phase 1 of tidutamab in NET ○ ASH: Additional Phase 1 data from plamotamab in NHL ○ Submit IND for XmAb819 for renal cell carcinoma ○ Advance XmAb808 (B7-H3 x CD28) toward 2022 IND
TME Activators	<ul style="list-style-type: none"> ✓ Presented initial Phase 1 data of vudalimab in solid tumors 	<ul style="list-style-type: none"> ✓ Initiated Phase 2 study of vudalimab in mCRPC ○ SITC: Announce maturing Ph1 data from vudalimab in CRPC, RCC and tumors without approved CPIs
Engineered Cytokines	<ul style="list-style-type: none"> ✓ Supported Phase 1 initiation for XmAb306 (Genentech) 	<ul style="list-style-type: none"> ✓ Initiated Phase 1 healthy volunteer study of XmAb564 for autoimmune disease ○ Advance IL-12-Fc cytokine toward 2022 IND
Select Partner Programs	<ul style="list-style-type: none"> ✓ Monjuvi® (tafasitamab) U.S. approval in 2L DLBCL ✓ Expanded Vir license to Xtend for anti-SARS-CoV-2 antibodies ✓ Licensed Xtend and Cytotoxic Fc technologies to Gilead for anti-HIV antibodies ✓ Divested non-core assets: XmAb7195 & others 	<ul style="list-style-type: none"> ✓ U.S. Emergency Use Authorization (EUA) for Vir/GSK's sotrovimab in patients with mild-to-moderate COVID-19 ✓ Licensed Xtend to BMS for anti-SARS-CoV-2 antibodies ✓ Entered academic R&D collaborations with MD Anderson & UCLA to expand XmAb® reach ✓ Minjuvi® (tafasitamab) approved in EU

XmAb® Products Marketed by Partners Provide Three Royalty Streams

XmAb Fc Domain	Medicine	Indications	Commercial Rights/Partners
 <p>Xtend™ Fc Domain</p>	 <p>ULTOMIRIS® (ravulizumab-cwvz) injection for intravenous use 300 mg/3 mL vial</p>	<p>Paroxysmal nocturnal hemoglobinuria (PNH) or atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA)</p>	 <p>ALEXION AstraZeneca Rare Disease</p>
 <p>Sotrovimab</p>	<p>Sotrovimab Injection, 500 mg, for intravenous use</p>	<p>Emergency Use Authorization (EUA) for the Treatment of COVID-19</p>	 <p>VIR gsk</p>
 <p>Cytotoxic Fc Domain</p>	 <p>MONJUVI® tafasitamab-cxix 200mg for injection, for intravenous use</p>	<p>In combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT)</p> <p>Minjuvi® (global)</p>	 <p>morphosys Incyte</p>

XmAb® Fc Domains Create Numerous Differentiated Antibodies for Technology Partners

Selected Programs	Fc Domain	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Ultomiris®	Xtend™	PNH, aHUS						
Monjuvi® (tafasitamab/XmAb5574)	Cytotoxic	DLBCL						
Sotrovimab VIR-7831	Xtend	COVID-19	EMERGENCY USE AUTHORIZATION (FDA)					
VIR-3434	Cytotoxic Xtend	Hepatitis B						
SARS-CoV-2 mAb Duo	Xtend	COVID-19						
AIMab7195	Immune Inhibitor	Food Allergy						
VIR-2482	Xtend	Influenza A						
XmAb bispecific	Bispecific	Oncology						
AMG 509 STEAP1 x CD3	2+1 Bispecific	Prostate cancer						
XmAb bispecific	Bispecific	Oncology						
XmAb bispecific TAA x CD28	Bispecific	Prostate cancer						

Technology licensing expands pipeline with very little opportunity cost

Registered trademarks: Ultomiris® (Alexion Pharmaceuticals, Inc.), Monjuvi® (MorphoSys AG).

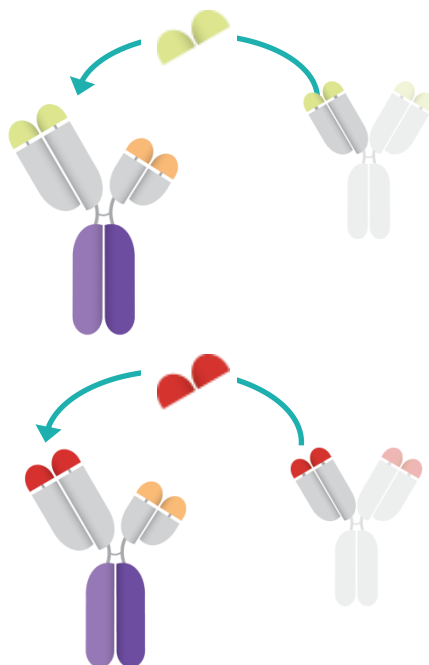
XmAb[®] Bispecific Fc Domain

*Enabling New Classes of Biologics
and Therapeutic Mechanisms of
Action*

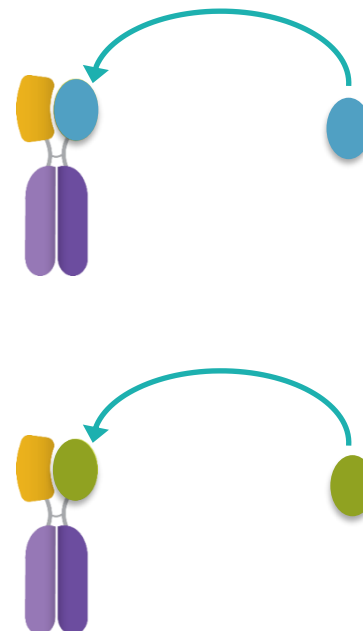


Plug-and-play Fc Domain Enables Rapid Prototyping of Target Combinations and Pipeline Generation

XmAb®
Bispecific
Antibodies



XmAb®
Cytokines



XmAb® Bispecific Fc Domains Retain Beneficial Antibody Properties

Highly stable, modular scaffold

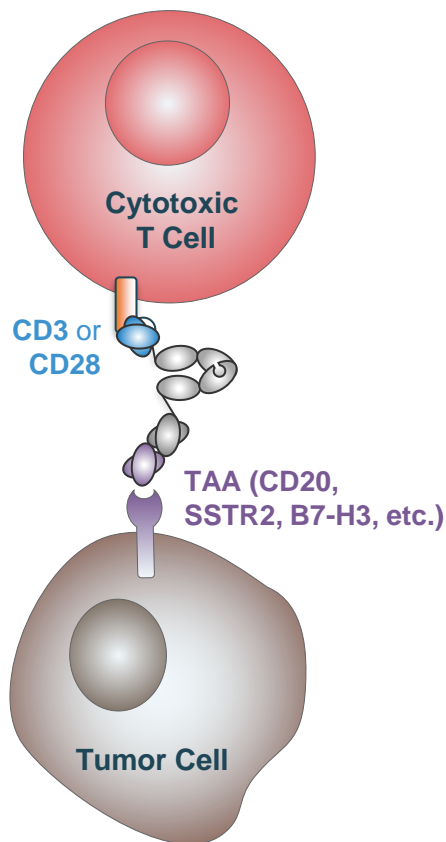
Antibody-like half-life *in vivo*

Compatible with standard manufacturing
and development processes

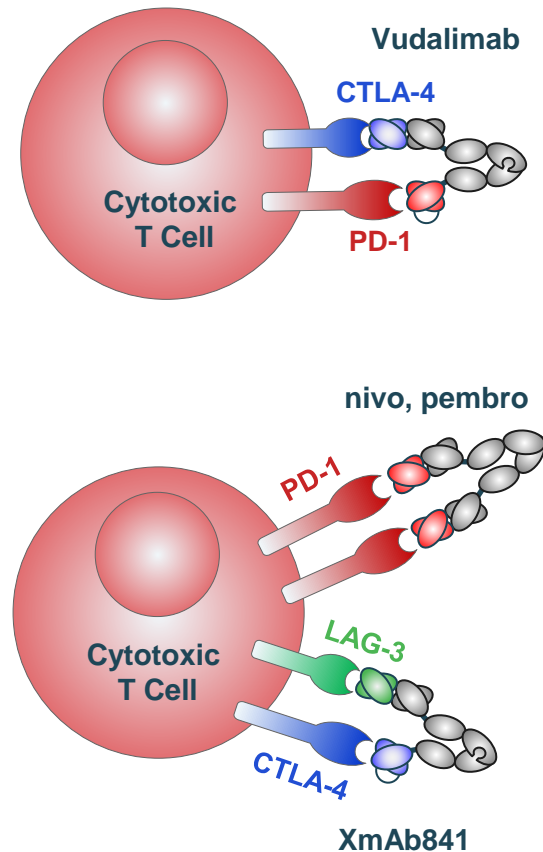
Enable Multiple Classes
of New Biologics

Distinct and Novel Mechanisms-of-Action Enabled By XmAb® Bispecific Domain

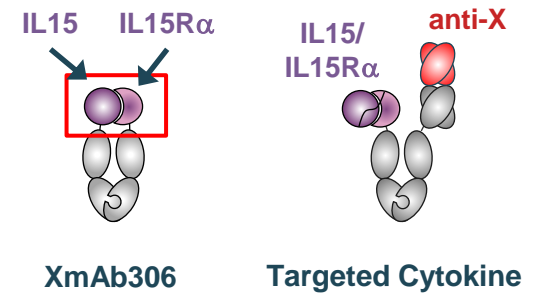
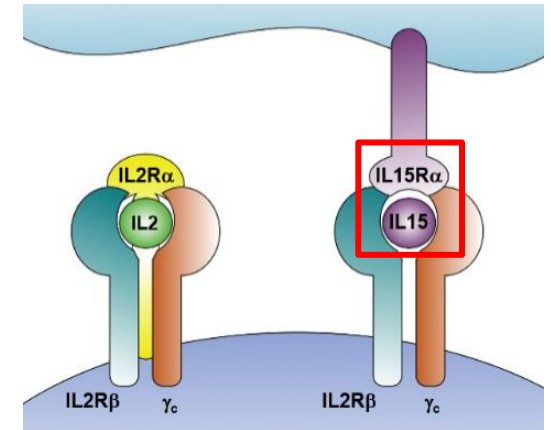
T Cell Engager



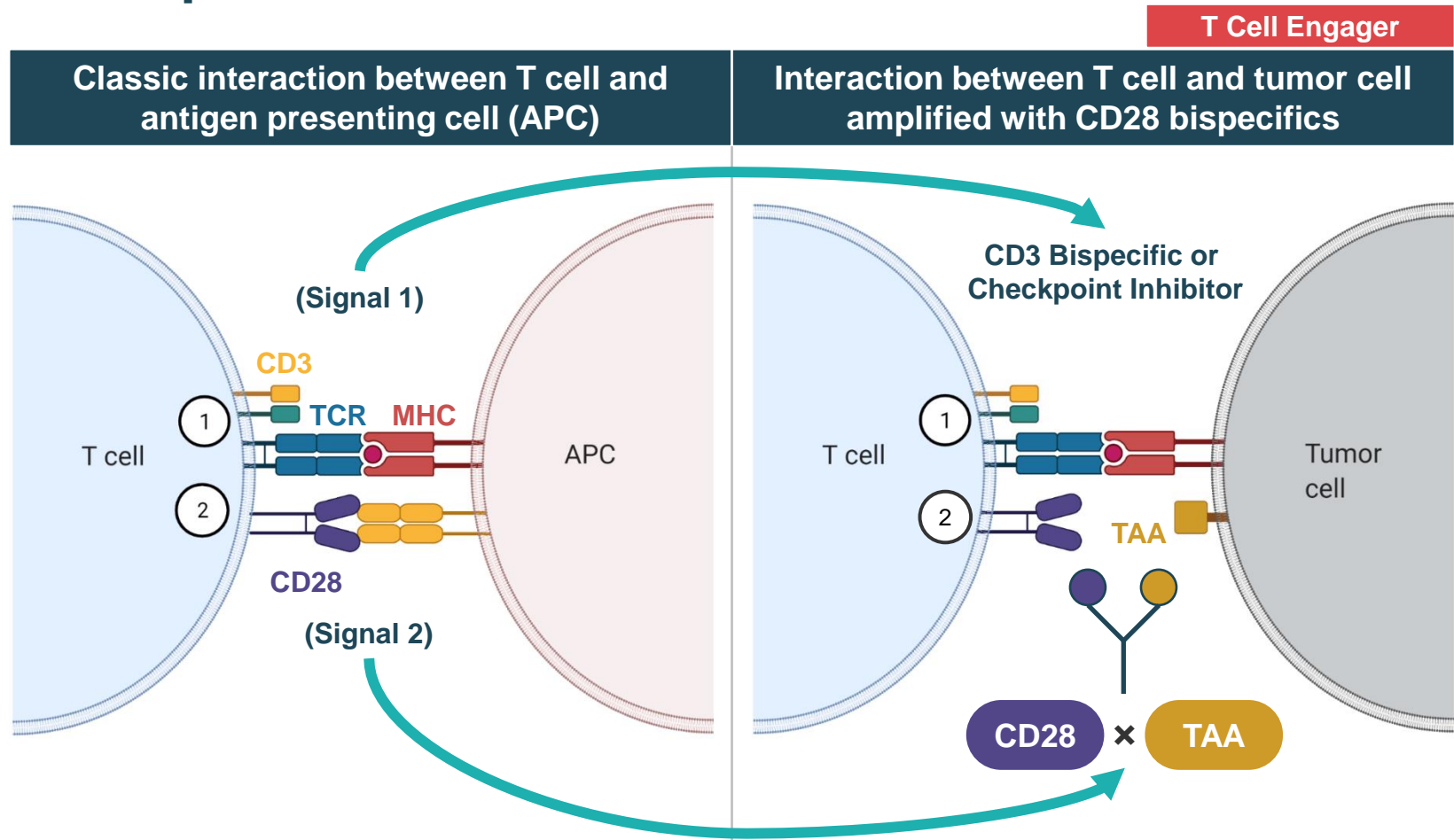
Dual Checkpoint/Co-stim



Cytokine-Fc



XmAb® Bispecific Antibodies Against CD28 Provide Tumor-Specific T Cell Activation Boost



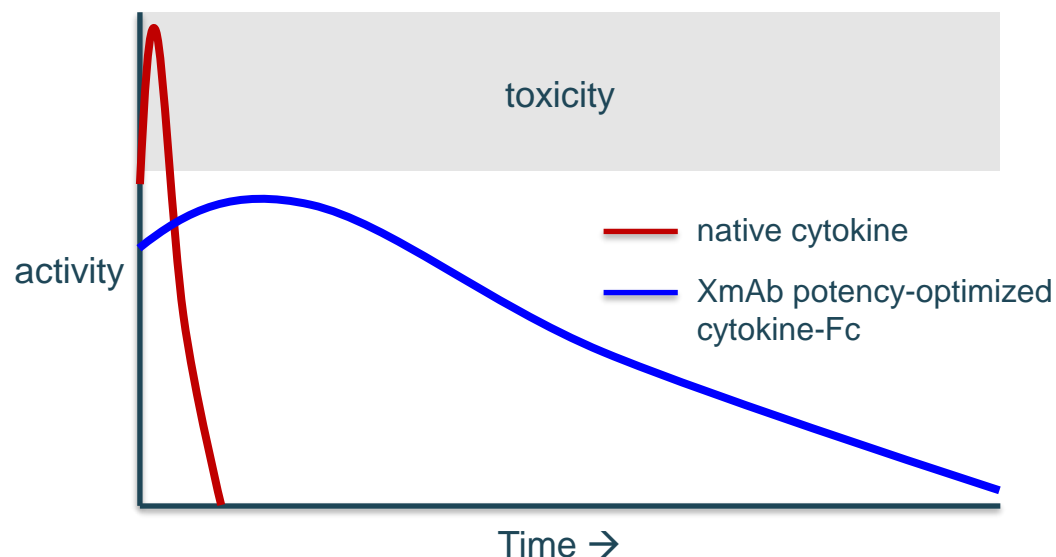
CD28 co-stimulation promotes tumor-specific activation and proliferation

Low affinity, monovalent binding designed to avoid historic safety concerns (superagonism)

XmAb[®] Engineered Cytokines



XmAb® Cytokines: Potency-tuned to Enhance Half-life and Tolerability



Reduced affinity

- Receptor selectivity
- ↑Half-life

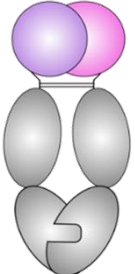
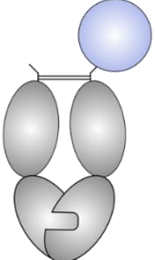
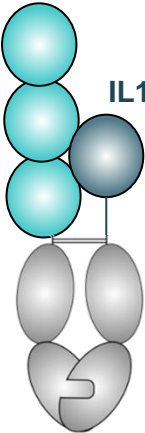
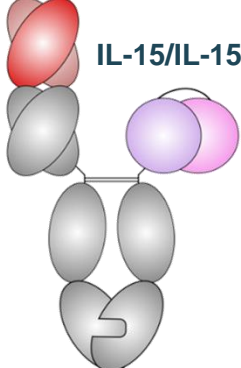
XmAb Fc

- ↑Half-life
- ↑Stability
- Modular
- Enables targeting

Xencor's general approach for creating cytokine therapies

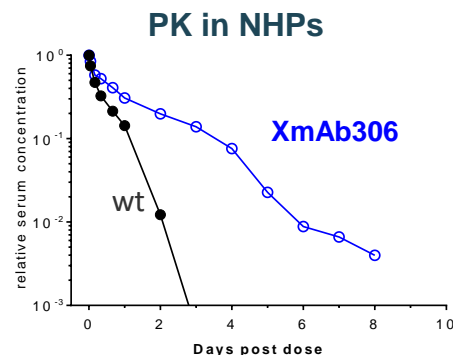
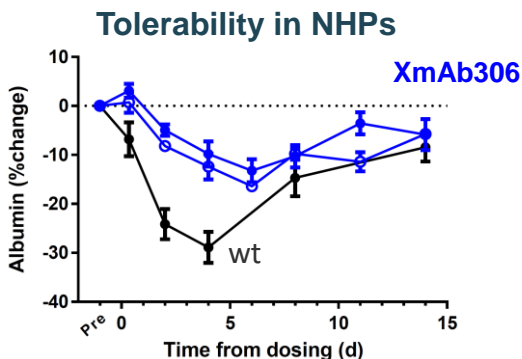
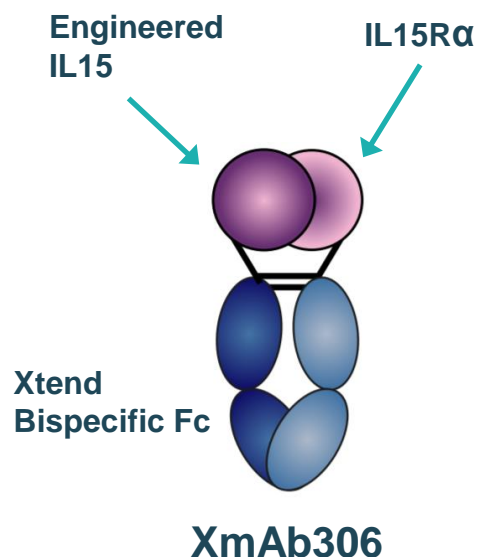
- Overcomes native cytokine short half-life and high toxicity
- Systematically engineering broad portfolio of cytokines

Growing Portfolio of XmAb[®] Cytokines

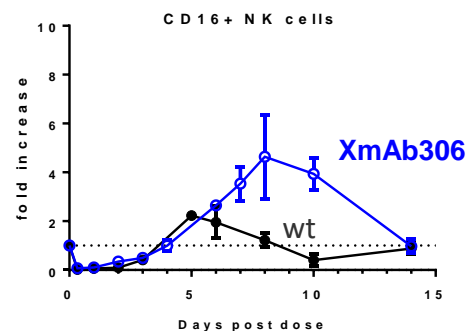
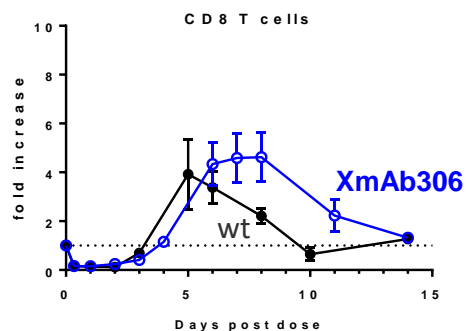
	XmAb306	XmAb564	XmAb662	XmAb Targeted IL-15
Cytokine	IL-15/IL-15R α	IL-2 (Treg selective)	IL12-p35 IL12-p40	anti-X IL-15/IL-15R α
XmAb[®] Bispecific Fc Domain				
Cell Targets	Cytotoxic NK, T cells	Regulatory T cells	IFN γ secreting NK, T cells	Immune marker defined
Indication	Oncology	Autoimmune Disease	Oncology	Oncology
Status	Phase 1 Dose Escalation	Phase 1 Dose Escalation	IND-enabling studies	Preclinical stages

2 clinical-stage XmAb[®] Cytokines, more in IND-enabling and preclinical stages
Engineered to expand select immune cell populations
Designed to be tolerable, active, easy to use

XmAb[®]306: IL-15 with Long Half-life, Improved Tolerability and Extended T and NK Cell Stimulation in NHP Models



In vivo pharmacodynamics



Potential to enhance activity of both NK therapies (Rituxan, Herceptin, allo NK cells, etc.) and T cell therapies (checkpoint inhibitors, cell therapies)

Ongoing Phase 1: monotherapy and combination with atezolizumab (PD-L1) in advanced solid tumors

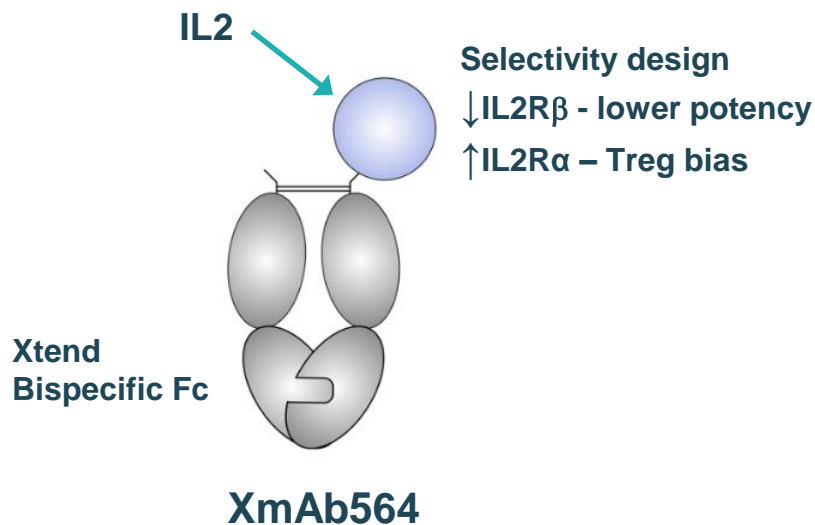
Co-development with Genentech; 45% worldwide P&L share; option to co-promote in U.S.

XmAb[®]306 Promotes High Levels of Sustained NK Cell Expansion in Ongoing Phase 1 Dose-Escalation Study

Encouraging preliminary data announced in November 2021

- Consistent and robust dose-dependent NK cell expansion and accumulation upon repeat dosing has been observed for multiple NK cell subsets, including mature NK cells. Significant NK cell expansion and accumulation was observed beginning in lower dose cohorts, and at higher dosing cohorts NK cell expansion has reached 40- to 100-fold higher levels than baseline and has been sustained for weeks throughout dosing.
- Unconfirmed RECIST responses have been observed in multiple tumor types, including in a patient treated with XmAb306 monotherapy.
- The study has reached dose levels that promote T cell activity, and evidence of peripheral effector T cell proliferation has been observed.
- Generally well tolerated as both a monotherapy and in combination with atezolizumab. No DLTs or treatment-related SAEs have been observed to date. Dose escalation continues for both monotherapy and in combination with atezolizumab.
- XmAb306 has a multi-day circulating half-life, which is consistent with its reduced-potency design and data generated in preclinical studies.
- Additional studies of XmAb306 in combination with other agents are being planned.

XmAb[®]564: IL-2 with Long Half-life, Improved Tolerability and Selectivity for Treg Activation in NHP Models



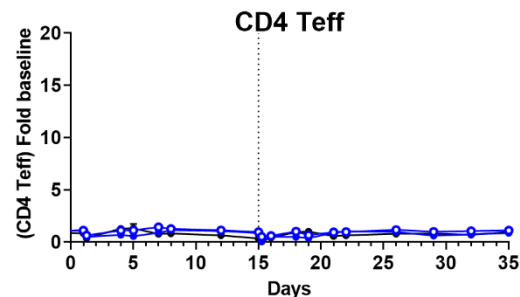
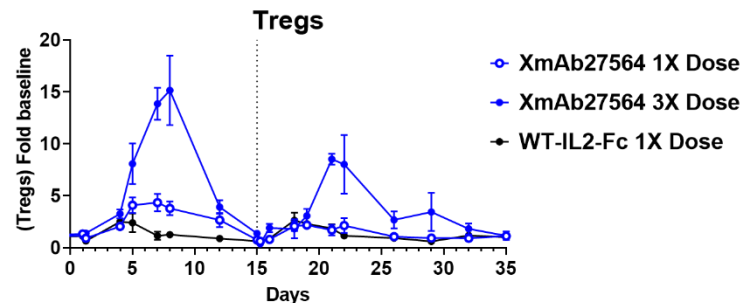
Monovalent design to avoid undesired activation

On-going Phase 1:

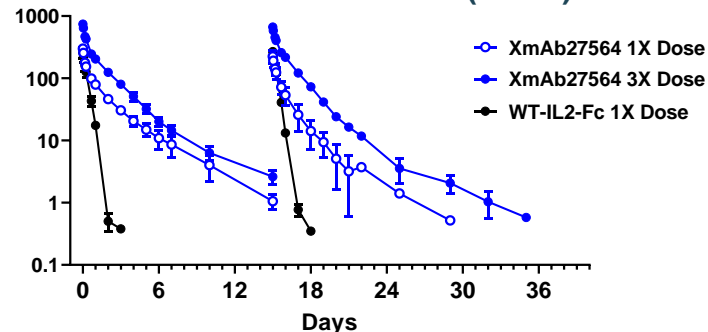
- Single ascending dose trial in healthy volunteers
- Subcutaneous delivery
- Assessing PK, safety, biomarkers of activity (Treg vs. T effectors)

Treg amplification has potential in numerous autoimmune diseases – use of native IL-2 limited by toxicity and poor selectivity

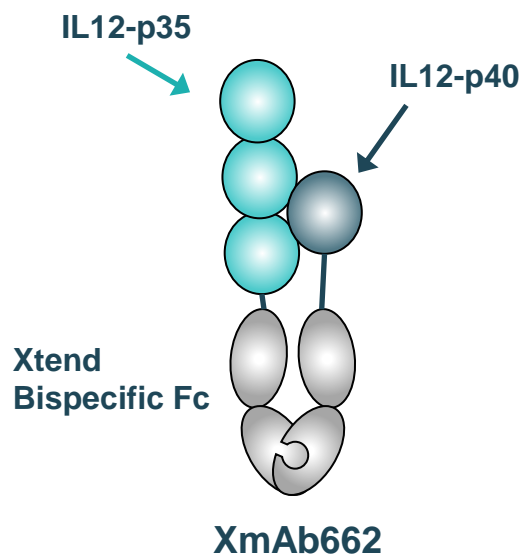
In vivo pharmacodynamics (NHPs)



Pharmacokinetics (NHPs)



XmAb[®]662: IL-12 with Long Half-life, Improved Tolerability and Potent Immune Stimulation



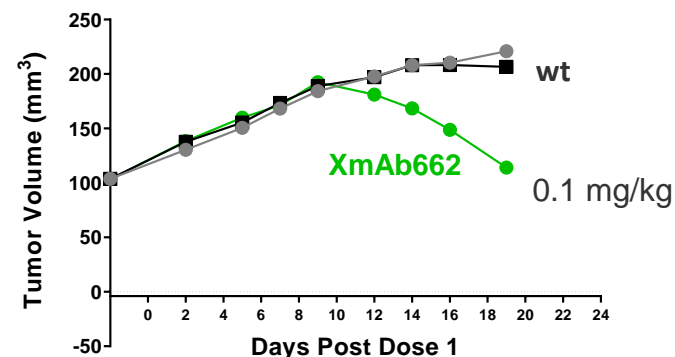
IND planned in 2022, IND-enabling studies ongoing

Highly immune stimulating – IFN γ secretion, activation of NK and CD8 T cells

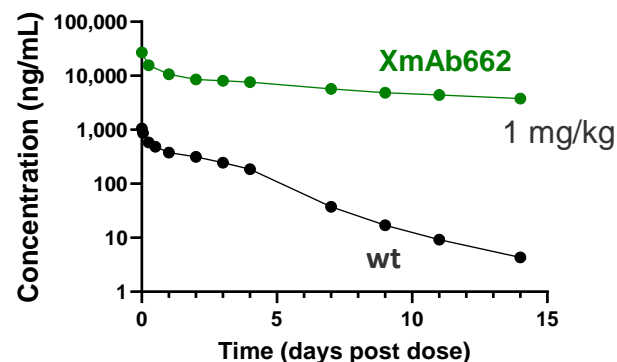
Gradual activity build up for potential improved tolerability

Native IL-12 therapy active in multiple tumor types, but toxic

Strong anti-tumor activity (mice)



Superior PK (NHPs)

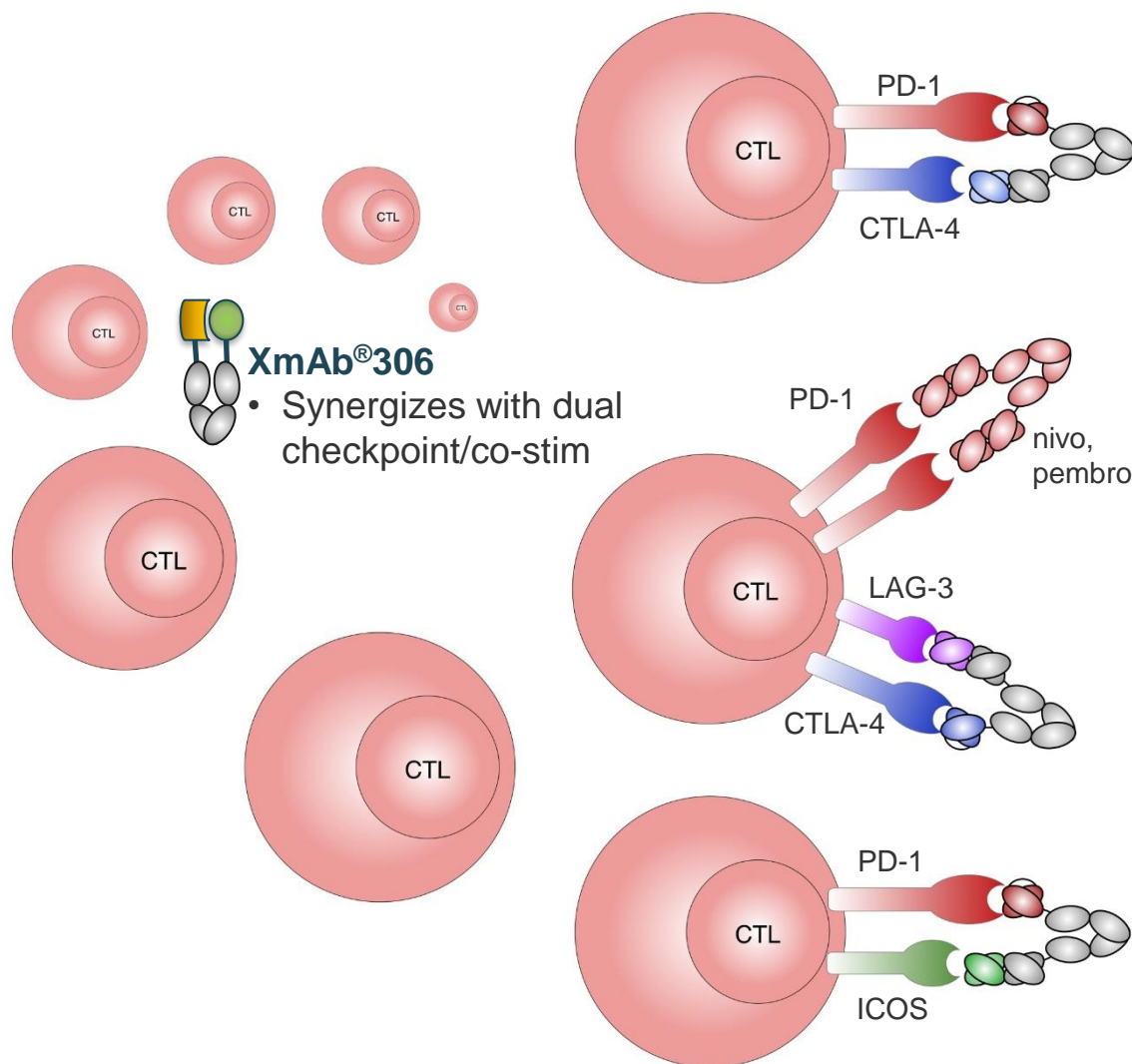


XmAb[®] Bispecific Antibodies

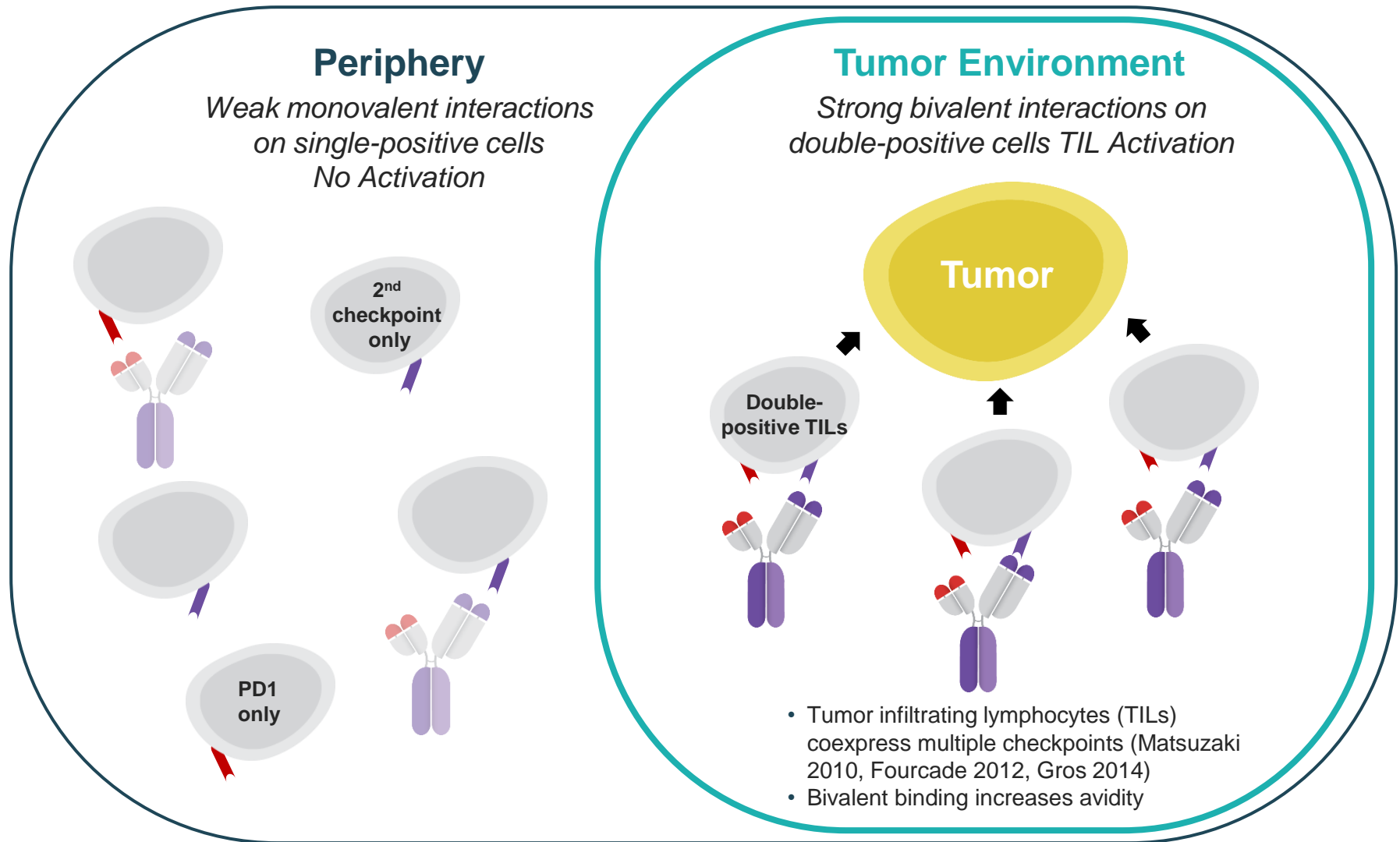
Tumor Microenvironment Activators



XmAb® Bispecific Checkpoint Inhibitors Have Distinct Mechanisms to Stimulate the Tumor Microenvironment



XmAb® Dual Checkpoint/Co-Stim Bispecifics are Designed to Promote Tumor-Selective T Cell Targeting



Vudalimab: Selective PD-1 x CTLA-4 Inhibition to Enable Dual Checkpoint Inhibition in Broad Range of Indications

Phase 2 metastatic castration resistant prostate cancer (mCRPC) started Q3 2021

- Patients stratified by molecular subtype
- Combination or monotherapy, depending on subtype

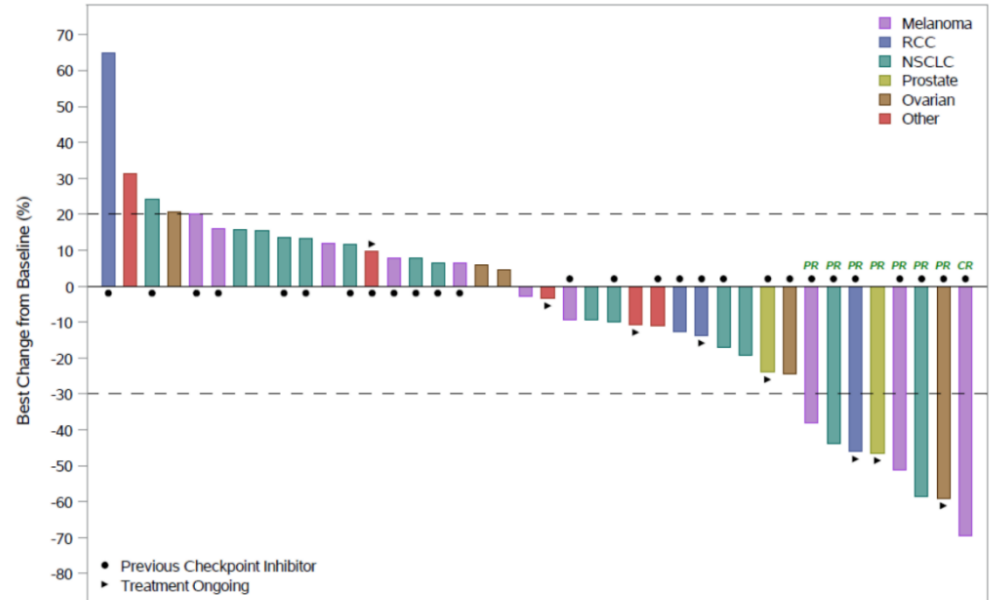
mCRPC rationale

- Initial data from vudalimab Phase 1 study
- Limited checkpoint inhibitor competition
- High unmet need
- CTLA-4 blockade historically associated with increased response rates

Expect phase 2 start in additional indications early 2022

Data update at SITC 2021

- Mature expansion cohort data from mCRPC, renal cell carcinoma and basket cohort



Interim data Phase 1 expansion cohorts SITC Nov 2020

Activity in multiple tumor types in patients with prior treatment with checkpoint inhibitors

Generally well tolerated throughout expansion cohorts, most common adverse events were immune-related rash and transaminase elevations

Lower rates of some types of immunotherapy-related adverse events, including colitis, than are typically seen with CTLA-4 blockade

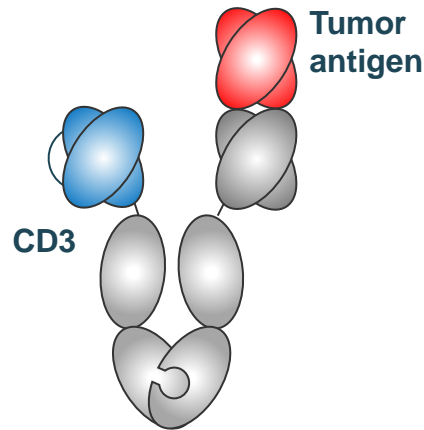
XmAb[®] Bispecific Antibodies

CD3 and CD28 T Cell Engagers



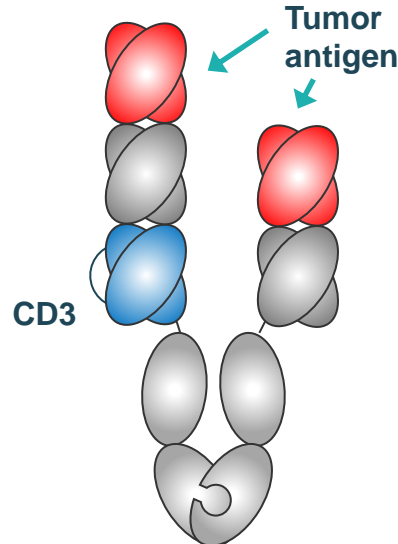
XmAb® T Cell Engagers Use Multiple Formats and Affinity Designs to Customize for Each Tumor Target

XmAb® 1+1



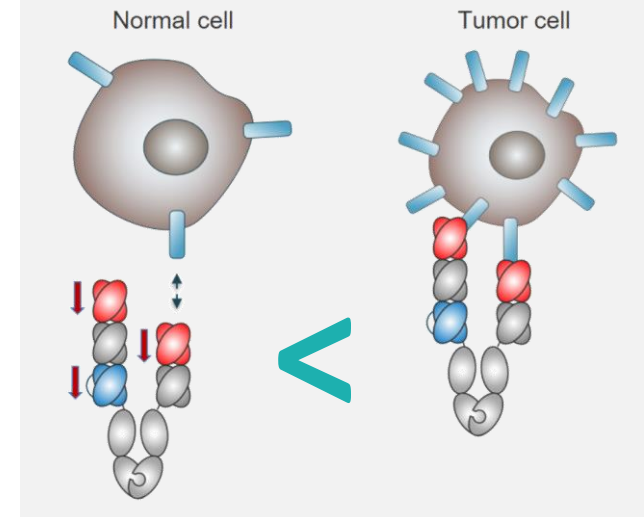
- 6 clinical programs
- Multiple preclinical

XmAb® 2+1



- AMG 509
- XmAb819

Tuned 2+1 Format = Selective Reactivity

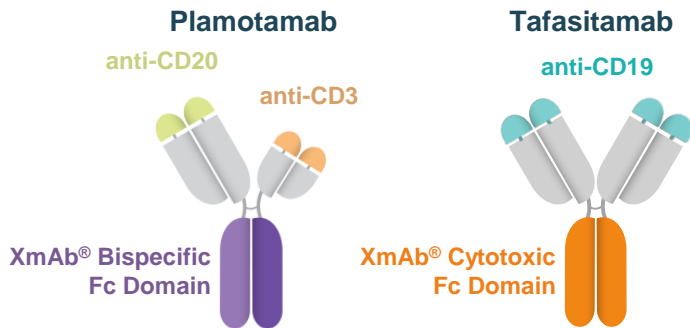


CD3 affinity tuned for reduction of cytokine release syndrome and off-tumor cell killing
Tumor antigen binding affinity tuned for tumor expression density and to match format

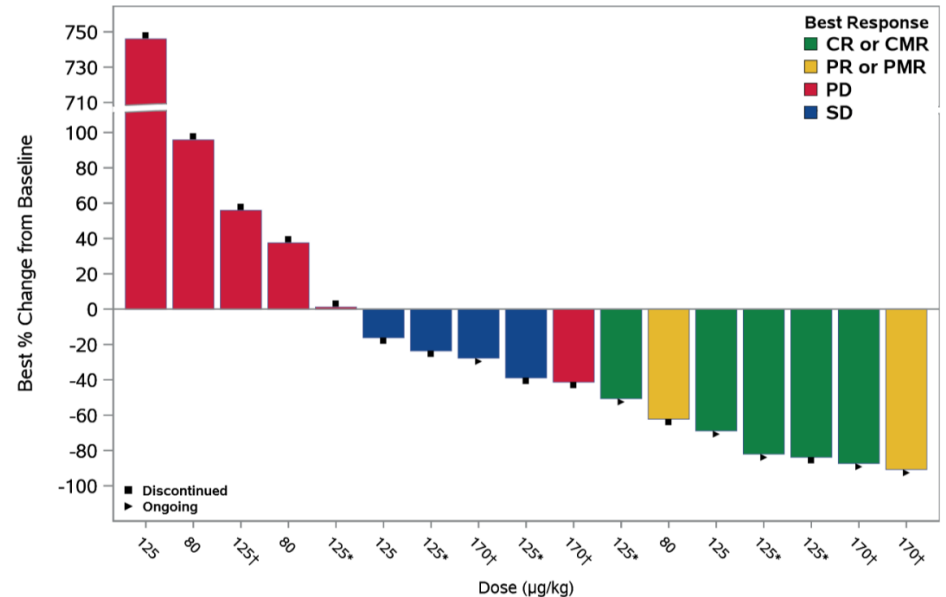
Plamotamab: Leading the Creation of Highly Active, Chemo-free Antibody Combinations in Lymphoma

Phase 2 in relapsed/refractory diffuse large B-cell lymphoma (DLBCL) start planned late 2021/early 2022

Unique chemo-free combination with tafasitamab (Monjuvi®) and lenalidomide; Phase 1b studies also planned in frontline DLBCL, r/r follicular lymphoma



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



Interim data Phase 1 ASH 2019

Janssen worldwide collaboration to develop plamotamab and novel CD28 bispecifics in B-cell cancers, October 2021

Phase 1 data update at ASH 2021

50 mg flat dosing every two weeks after step-up dosing for Phase 2 study

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 follicular lymphoma, Waldenström macroglobulinemia and Richter transformation of CLL

Generally well tolerated, most CRS events occurred with the first dose of plamotamab and were Grade 1 and 2 by the Lee criteria

Xencor & Janssen to Advance Plamotamab & Novel B-cell Targeted, Tumor-selective, CD28 Bispecific Antibodies

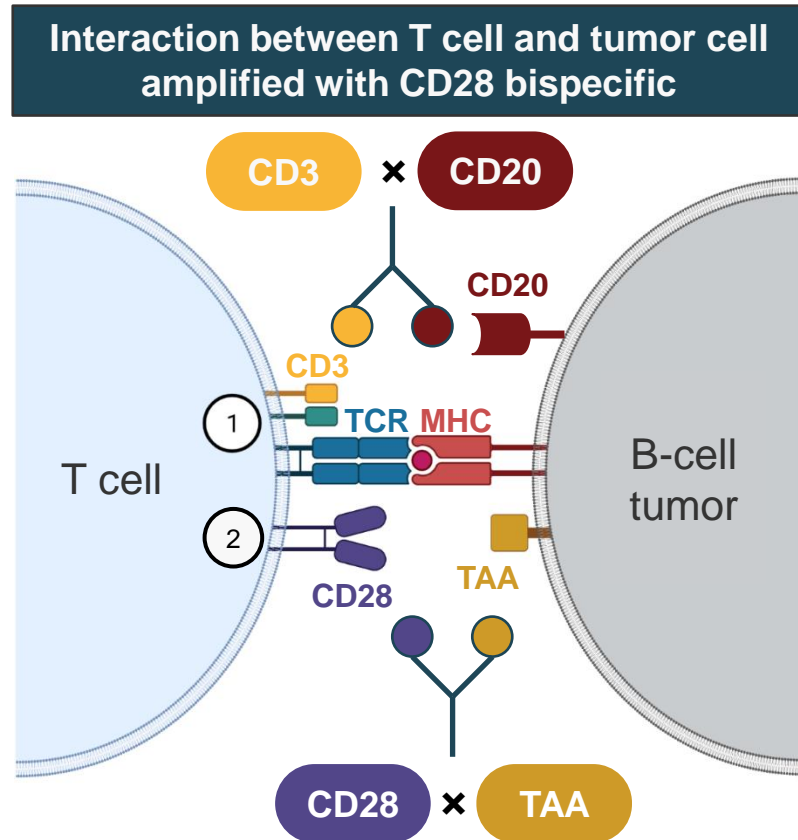
Global collaboration and license agreement with Janssen expands the scope of the plamotamab program and provides additional differentiated and potentially highly active chemo-free approach, announced Oct. 2021

Two-year research collaboration to create novel XmAb® CD28 bispecific antibodies targeted against certain B cell targets

- Potential to amplify the activity of plamotamab and other CD3 bispecifics with targeted, tumor-selective co-stimulation

Janssen receives worldwide license to plamotamab and certain B cell x CD28 bispecifics

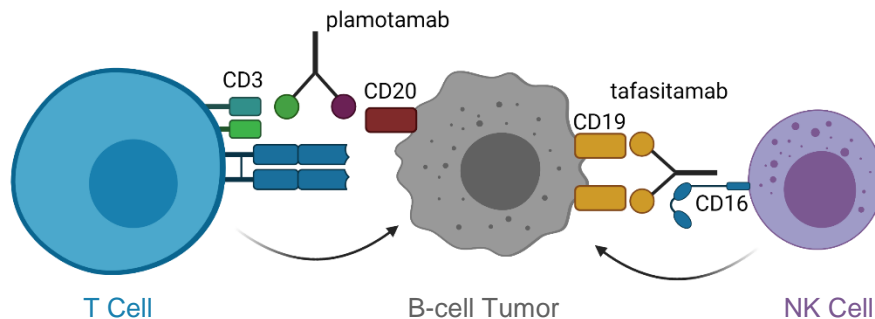
- \$100m upfront payment; \$25m equity investment
- Plamotamab: \$517.5m in plamotamab milestones; mid-teen to low-twenties royalties; Xencor 20% development cost-sharing; option for 30% co-detail
- CD28 bispecifics: \$670m in CD28 milestones; high-single to low-double digit royalty; Xencor option to fund 15% of development costs for increased royalties; option for 30% co-detail



Differentiated Chemo-free Combination Strategy to Develop Plamotamab in Lymphoma

Plamotamab + Tafasitamab

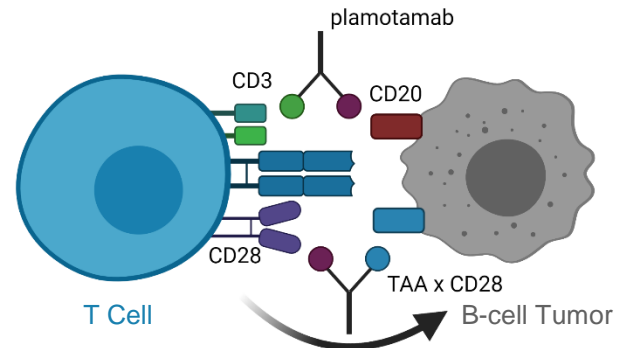
- Targets two different highly expressed B-cell antigens, CD19 and CD20, to potentially avoid resistance due to antigen loss
- Recruits distinct and complementary cytotoxic immune cells, T cells and Natural Killer cells, against tumor cells



Two Complementary Anti-Tumor Mechanisms

Plamotamab + B Cell x CD28 Bispecific

- Novel mechanism to amplify T-cell cytotoxicity by binding CD28 to activate co-stimulation pathways in a targeted, tumor-selective manner
- Offers additional level of control over CD3 bispecific T-cell activation, offering potentially reduced toxicity and higher tumor killing



Amplified T-cell Cytotoxicity

Tidutamab: SSTR2 x CD3 Antibody in Solid Tumor Indications with High Unmet Need

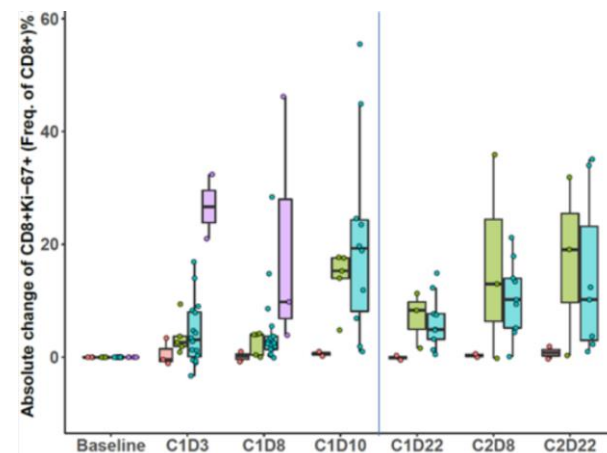
Phase 1b/2 study initiated 3Q2021 in small cell lung cancer (SCLC) and Merkel cell carcinoma (MCC)

- SSTR2-expressing tumor types known to be responsive to immunotherapy

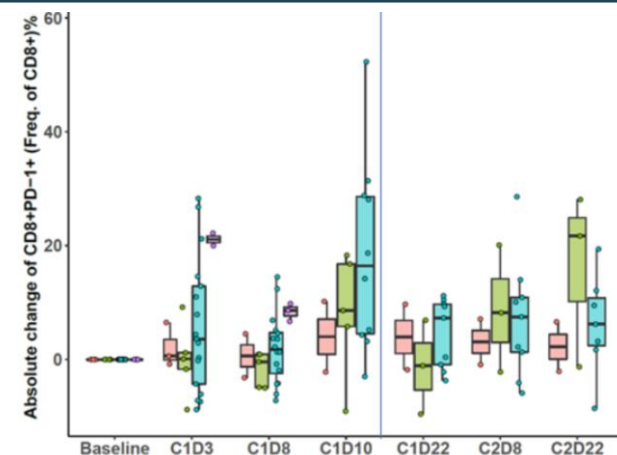
Phase 1 data update in neuroendocrine tumors (NET) presented at NANETS, October 2021

- 21 patients in dose-escalation, 20 patients in expansion
- Heavily pre-treated: 50% received prior radionuclide
- Stable disease in 27%
- Generally well tolerated; CRS observed in 41% of patients, nearly all Grade 1/2
- CD8+ effector T cells showed a dose-dependent and persistent increase in proliferation activity marker Ki67
- Higher baseline intratumoral PD-L1 expression and increases on treatment were associated with a shorter time on study

Acute & Sustained T Cell Proliferation



Acute & Sustained T Cell Activation



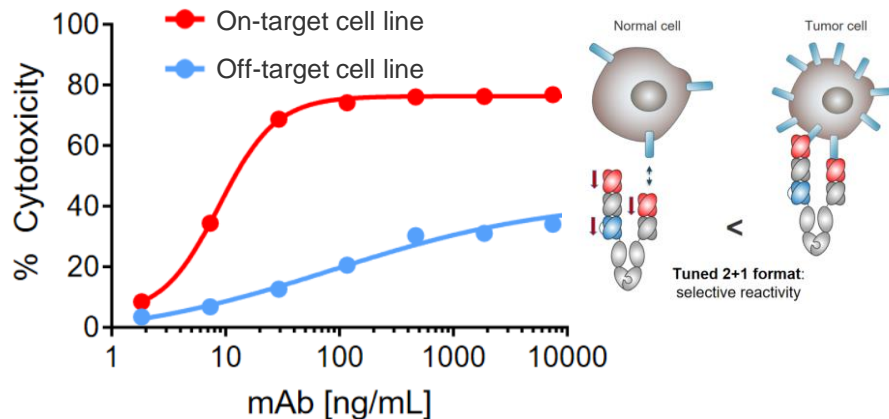
■ Cohort 1 (0.1 ug/kg) ■ Cohort 2 (0.1-0.3 ug/kg)

■ Cohort 3 + Expansion (0.3-1 ug/kg) ■ Cohort 4 (1-2 ug/kg)

Novel Tumor Targets and Immune Activation Differentiate Next Clinical Bispecific Antibodies (e.g., ENPP3, CD28)

XmAb819 (ENPP3 x CD3)

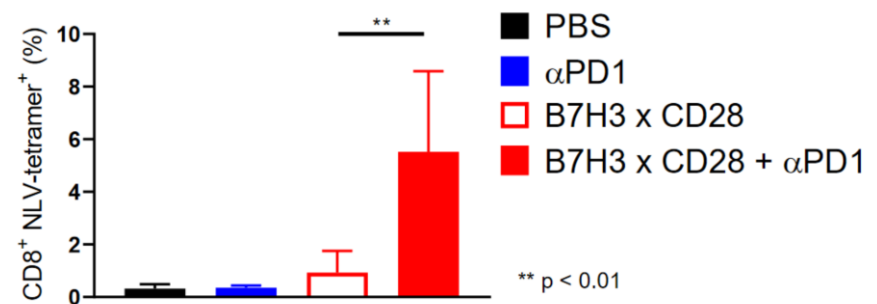
Selective T cell directed cytotoxicity



- Renal cell tumor antigen ENPP3 also expressed at low levels on normal tissue
- Multi-valent XmAb 2+1 format for selective high-density ENPP3 binding
- Reduced potency CD3 binding to improve rates/severity of cytokine release syndrome
- IND submission planned in 2021

XmAb808 (B7-H3 x CD28)

Enhanced, selective T cell activation through CD28



- Tumor-specific boost to T cells (Signal 2)
- B7-H3 enables potentially broad solid tumor use; high expression in prostate cancer
- IND submission planned in 2022

Janssen collaboration for CD28 bispecific antibody against an undisclosed prostate target opens access to prostate-cancer franchise for clinical combinations

Layers of Value Creation Built on XmAb® Technology

2021/2022 Milestones

Technological Competitive Advantage Creates Future Pipeline Growth

Engineered
Cytokines

Tumor-selective
CD28 Bispecific
Antibodies

Multi-valent
Formats

Clinical Execution & Advancement

Encouraging initial data from
vudalimab, **plamotamab** and **tidutamab**
support mid-stage development plans

Strong Financial Foundation & Technical Validation

3 products marketed by partners

16 partnerships for XmAb technology

\$538mm in cash & equivalents*

- ✓ Initiated Phase 1 healthy volunteer study of XmAb564 for autoimmune disease
- Submit IND for XmAb819 for renal cell carcinoma
- Advance XmAb808 (B7-H3 x CD28) toward 2022 IND
- Advance IL-12-Fc cytokine toward 2022 IND
- ✓ Entered new Janssen plamotamab/CD28 collaboration
- ✓ Initiated Phase 2 study of vudalimab in mCRPC
- ✓ Initiated Phase 1b/2 study of tidutamab in Merkel cell carcinoma & SCLC
- ✓ Announce longer follow-up and additional biomarker analysis from Phase 1 of tidutamab in NET
- SITC: Announce maturing Ph1 data from vudalimab in CRPC, RCC and tumors without approved CPIs
- ASH: Announce additional Phase 1 data from plamotamab in NHL
- ✓ U.S. Emergency Use Authorization (EUA) for Vir/GSK's sotrovimab in patients with mild-to-moderate COVID-19
- ✓ Licensed Xtend to BMS for anti-SARS-CoV-2 antibodies
- ✓ Entered academic R&D collaborations with MD Anderson & UCLA to expand XmAb reach
- ✓ Minjuvi® (tafasitamab) approved in EU

* 9/30/2021

Proteins by Design®

XmAb® Antibody & Cytokine Therapeutics



Corporate Overview

November 2021