## Antibodies by Design<sup>™</sup>

XmAb<sup>®</sup> Antibody Therapeutics

Corporate Overview August 2019



## **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

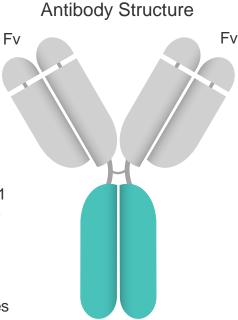
- XmAb<sup>®</sup> Fc domains: small changes, big functional impacts
  - Augments native immune functions, preserves half-life, stability and production
  - Over 500 issued patents and pending patents worldwide
- Expansive bispecific antibody oncology pipeline advancing
  - 7 XmAb bispecific antibodies in Phase 1 clinical studies
  - 2 tumor microenvironment activators entered Phase 1 in Q2 2019
  - Novartis co-development and ex-U.S. license for XmAb14045 (CD123 x CD3), in Phase 1
  - Amgen's AMG 424 in Phase 1 study in myeloma, advancing AMG 509 in prostate cancer
- Genentech co-development collaboration for novel IL15 cytokines
  - Wide-ranging combination strategy critical to advancing cytokines
  - Retained ability to perform clinical studies with broad spectrum of leading cancer therapies
  - IND submission for XmAb24306 in H2 2019
- 14 XmAb clinical programs ongoing internally or with partners, including tafasitamab/MOR208 (Morphosys) in Phase 3 and Ultomiris<sup>®</sup> (Alexion) approved in the U.S., Japan and EU for the treatment of adult patients with PNH











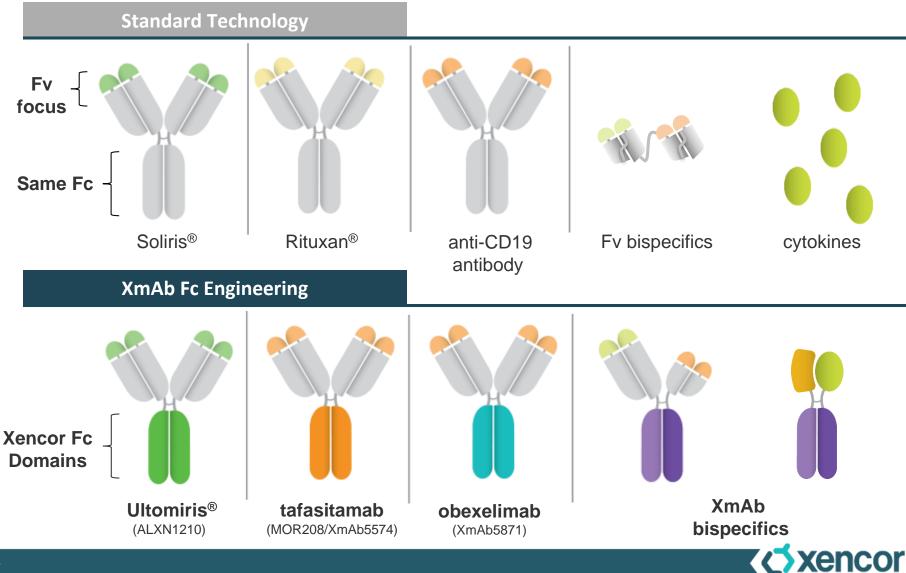
XmAb<sup>®</sup> Fc Domains



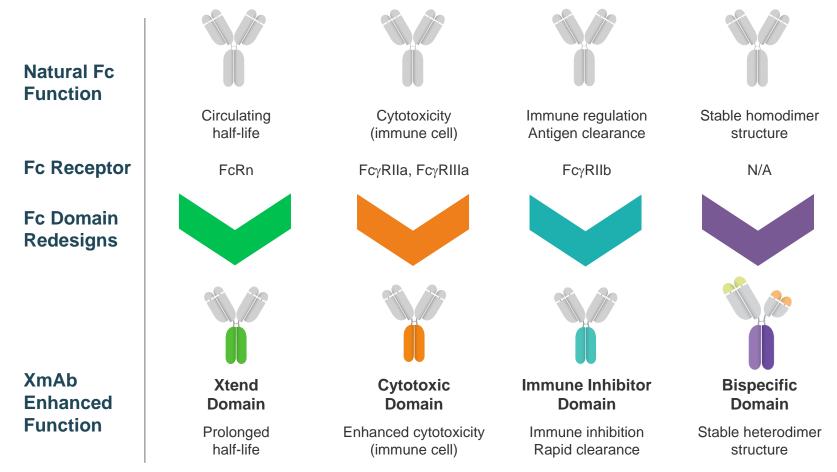




## XmAb<sup>®</sup> Fc Domains Shift Focus of Antibody Drug Discovery by Creating New Axes for Differentiation



# XmAb<sup>®</sup> 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 Pipeline Focused on Bispecific Fc Domains**

<b>Program</b> (Targets)	Fc Domain	Primary Indication	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
<b>obexelimab</b> (XmAb5871) CD19	Immune Inhibitor	lgG4-RD SLE					<b>☆</b> xencor
XmAb7195 IgE	Immune Inhibitor	Asthma/ allergy					<b>☆</b> xencor
XmAb14045 CD123 x CD3	Bispecific	AML					<b>Xencor</b> Novartis*
XmAb13676 CD20 x CD3	Bispecific	B-cell malignancy					<b>☆</b> xencor
XmAb18087 SSTR2 x CD3	Bispecific	GEP-NET GIST					<b>∢</b> xencor
<b>XmAb20717</b> PD-1 x CTLA-4	Bispecific Xtend	Oncology					<b>☆</b> xencor
XmAb22841 CTLA-4 x LAG-3	Bispecific Xtend	Oncology					<b>⊄</b> xencor
XmAb23104 PD-1 x ICOS	Bispecific Xtend	Oncology					<b>¢</b> xencor
<b>XmAb24306</b> IL15Rβγ (IL15/IL15Rα-Fc)	Bispecific Xtend	Oncology					<b>Genentech</b> **

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

\*\* Co-development with Genentech, Xencor option to co-promote in U.S.



## XmAb<sup>®</sup> Fc Domains Have Created Numerous Differentiated Antibodies for Technology Partners

Program	Fc Domain	Primary Indication	Preclinical	Phase 1	Phase 2	Phase 3	Approved	Commercial Rights
Ultomiris <sup>®</sup> (ALXN1210)	Xtend	PNH						ALEXION
<b>Tafasitamab</b> (MOR208/XmAb5574)	Cytotoxic	NHL/CLL						morphosys
Talacotuzumab	Cytotoxic	Leukemia						CSL
BI 836858	Cytotoxic	Oncology						Boehringer Ingelheim
VRC01LS	Xtend	HIV						NIH
AMG424	Bispecific	Myeloma						AMGEN
AMG509	Bispecific	Prostate cancer						AMGEN
XmAb bispecifics x4	Bispecific	Oncology						<b>U</b> NOVARTIS
XmAb bispecific	Bispecific	Oncology						Astellas

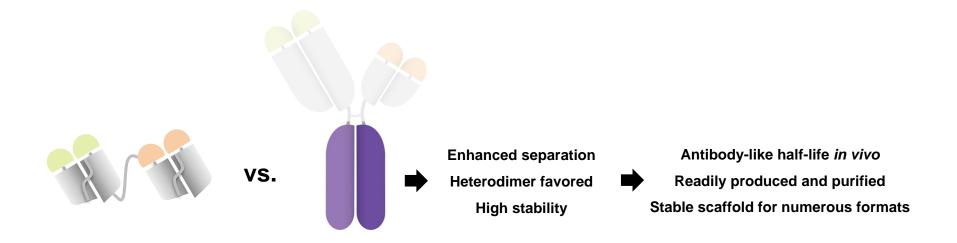
Technology licensing expands pipeline with very little opportunity cost

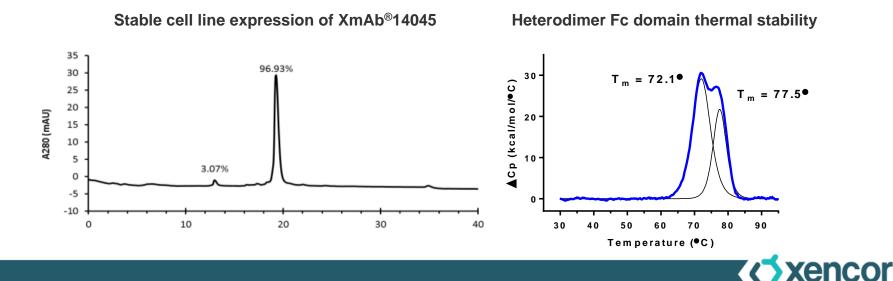


# XmAb<sup>®</sup> Bispecific Fc Programs

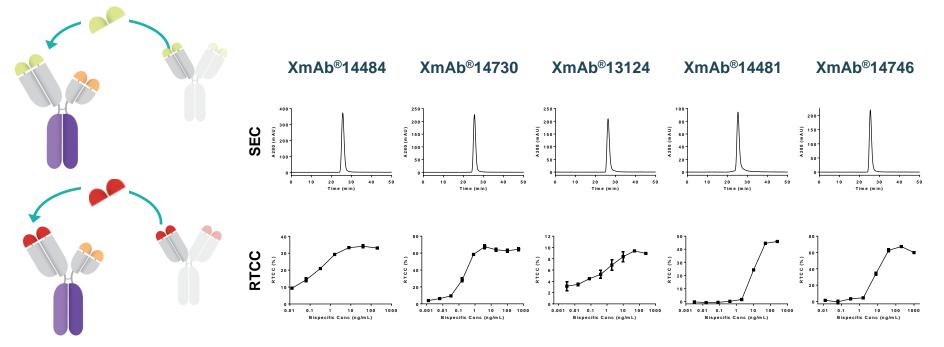


## XmAb<sup>®</sup> Bispecific Fc Domains Retain Beneficial Natural Antibody Properties





# Plug-and-play Fc Domain Enables Rapid Pipeline Generation and Prototyping



- Portfolio of CD3 bispecific molecules generated for development
  - Target T cells against tumors
- New oncology programs rapidly prototype different target combinations

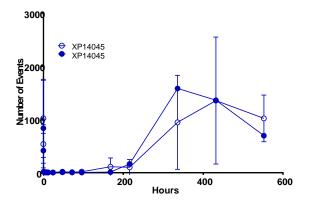


# Xencor Lead Bispecific Programs: T-Cell Engagement with Tuned Potency and mAb-like PK

#### XmAb<sup>®</sup>14045 (CD123 x CD3)



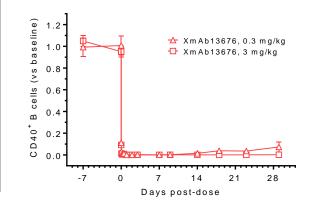
Cynomolgus monkey, single IV bolus Profound, sustained basophil depletion



XmAb<sup>®</sup>13676 (CD20 x CD3)



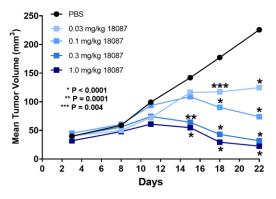
Cynomolgus monkey, single IV bolus Profound, sustained B-cell depletion



#### XmAb<sup>®</sup>18087 (SSTR2 x CD3)

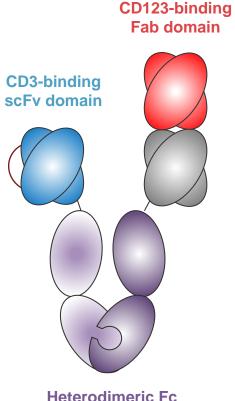


huPBMC-SCID mouse xenograft Potent, dose-dependent tumor reduction





## XmAb<sup>®</sup>14045: CD123 x CD3 Bispecific Antibody – A Full Length mAb to Be Dosed Intermittently



Heterodimeric F domain

### CD123 (IL-3 receptor $\alpha$ subunit)

- Found on early hematopoietic precursor cells and basophils
- Frequently expressed on hematologic malignancies

### XmAb14045

- Stimulates targeted T cell-mediated killing of CD123expressing cells, regardless of T cell antigen specificity
- Ablation of Fc gamma receptor binding removes potential for receptor-mediated crosslinking and activation of T cells
- Fc preserves FcRn affinity for antibody-like half-life
- Does not require a continuous infusion
- Efficiently manufactured using standard antibody production methods

## Phase 1 Study in relapsed/refractory AML

Encouraging data, 28% CR/CRi, presented at ASH 2018

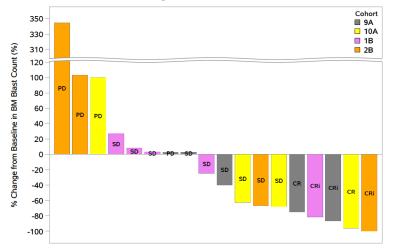


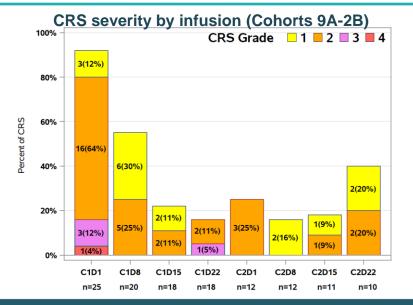
## XmAb14045 Ongoing Phase 1 Study in Relapsed/Refractory AML: Interim Dose-Escalation Data Presented at ASH 2018

#### **Encouraging clinical activity**

- 28% of evaluable patients achieved either complete remission (CR) or CR with incomplete hematologic recovery (CRi) at 2 highest initial doses (1.3 and 2.3 mcg/kg weekly)
- 2 patients with responses bridged to stem cell transplant; additional patient (transplantineligible) has remained in remission for 16+ weeks after discontinuation of therapy
- Dose escalation and dosing optimization continues

#### Percentage change in bone marrow blasts from pretreatment baseline





#### Manageable cytokine release syndrome (CRS)

- Enrolled 66 heavily-pretreated patients
  - Median 3 prior therapies
  - 86% refractory to last therapy
  - 53% categorized as adverse risk (ELN 2017)
- CRS most common toxicity (55%)
  - CRS more severe on first dose
  - 6% experienced Grade 3 or 4 CRS
  - 29% experienced AEs within 24 hours consistent with CRS but not reported as such
- No clear evidence of drug-related myelosuppression



Novartis Collaboration for XmAb<sup>®</sup>14045 Boosts Development Resources and Retains U.S. Commercial Rights



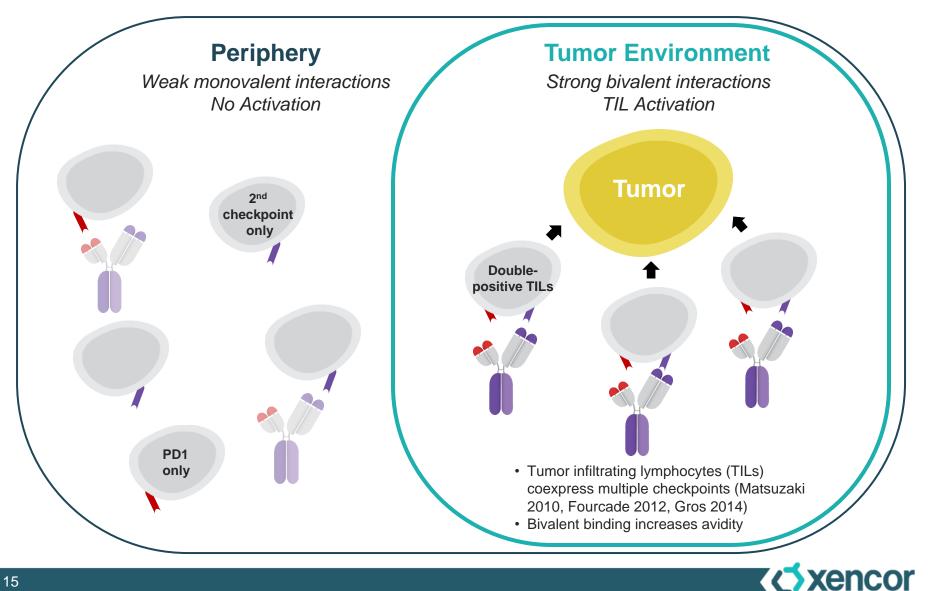
## Links Novartis' leadership in oncology with Xencor's XmAb<sup>®</sup> bispecific programs

- Novartis receives ex-U.S. commercial rights to XmAb14045
  - \$325M in milestones, including \$90M in development milestones
  - Low double-digit royalties on ex-U.S. sales
- Xencor retains all U.S. commercial rights to XmAb14045
- Worldwide 50/50 development collaboration and cost share
- Research collaboration for XmAb Bispecific Technology in 4 Novartis programs
  - Novartis starting antibodies plugged into XmAb bispecific constructs, Xencor provides molecular engineering; mid single-digit royalties
  - Xencor has opt-in right to one Novartis program for U.S. profit and cost share, co-detail
- Non-exclusive access to Xencor Fc technologies for 10 programs

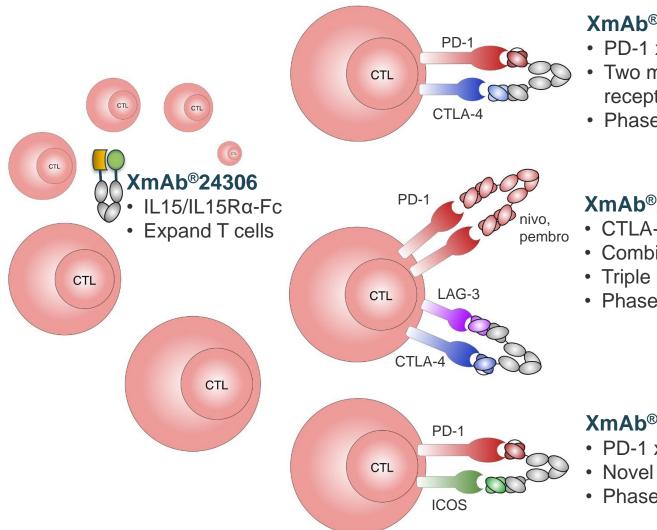
## \$150M upfront, \$2.1B total potential milestones, royalties



## 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<sup>®</sup>20717

- PD-1 x CTLA-4 bispecific
- Two most validated checkpoint receptors
- Phase 1 study initiated July 2018

#### XmAb<sup>®</sup>22841

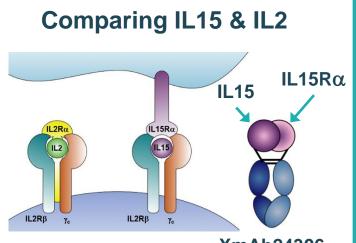
- CTLA-4 x LAG-3 bispecific
- Combinable with anti-PD1
- Triple checkpoint blockade
- Phase 1 study initiated May 2019

#### XmAb<sup>®</sup>23104

- PD-1 x ICOS bispecific
- Novel checkpoint x co-stim pairing
- Phase 1 study initiated May 2019



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



#### XmAb24306

- 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<sup>™</sup> for longer half-life





### 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 preclinical IL15 cytokine XmAb24306
- \$120M upfront and up to \$160M in XmAb24306 development milestone payments; up to \$180M for each new IL15 program
- IND application for XmAb24306 planned H2 2019



# Xencor's Expanding Bispecific Oncology Pipeline

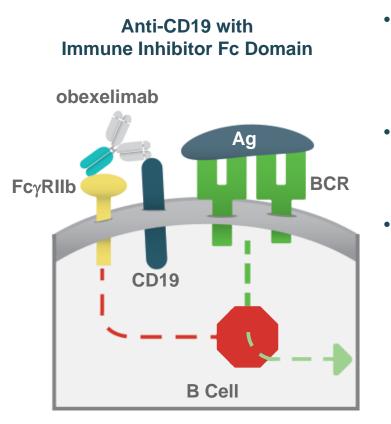




# obexelimab (XmAb®5871)



# Obexelimab Inhibits Multiple Pathways of B Cells Without Killing B Cells



**FcγRIIb binding up by ~400x** 

Potent suppression of B-cell responses without destroying B cells

- Phase 2 trials in IgG4-Related Disease and SLE
  - Final data on IgG4-RD presented at the American College of Rheumatology (ACR) Meeting in Nov. 2017
  - Topline data from SLE presented at ACR in Oct. 2018
- B-cell inhibition: proven for autoimmune disease
  - B-cell depletion (e.g., Rituxan) RA, MS, others off-label
  - B-cell growth inhibition (Benlysta) Lupus
- Current limitations of B-cell targeting antibodies
  - Tradeoff of potency against long-term B-cell ablation
  - No simple subcutaneous delivery

#### **Obexelimab Target Product Profile**

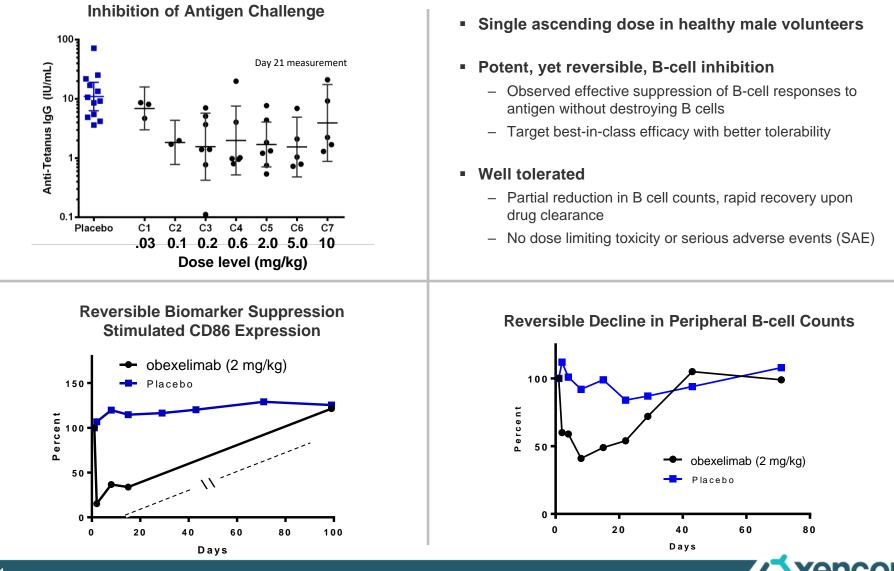
Monoclonal antibody that inhibits B-cell function to treat autoimmune diseases

No long-term immune suppression

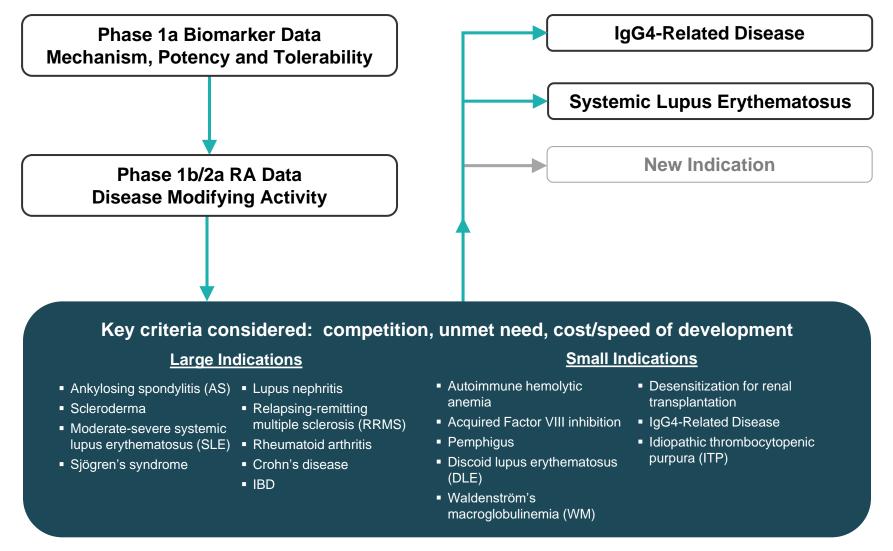
Subcutaneous injection, every other week



# Obexelimab Phase 1a Data Show Potent and Reversible B-cell Inhibition



## **Obexelimab B-cell Inhibition Profile Presents Opportunity Across Numerous Indications**



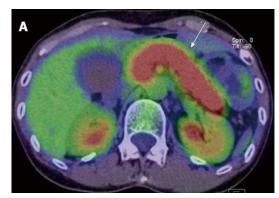


# IgG4-RD Fibro-inflammatory Activity Causes Progressive Organ Damage, with No Approved Therapies

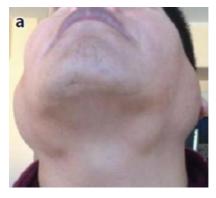
- Multi-organ disease with a common histopathology
  - Dense lymphoplasmacytic infiltrate
    - IgG4+ plasma cells
    - T cells
  - Storiform fibrosis
  - Obliterative phlebitis
  - More than one organ involved in majority
- Patients present with tissue infiltration, damage and pseudo-tumors
  - Pancreas: pancreatitis, pancreatic insufficiency, diabetes, pain
  - Eye: vision loss, proptosis
  - Biliary tree: cirrhosis, cholangitis, pain
  - Submandibular glands: difficulty swallowing, pain

#### Awareness growing; still underdiagnosed

- ~ 40,000 patients in the United States
- No approved therapies; steroids are SOC
- IgG4-RD Responder Index (RI)
  - Assessed in multi-specialty international validation study
  - RI found to be a valid measure of disease activity, regardless of the manifestation or specialist (Wallace Arthritis Care Res 2018)



**PET/CT** pancreatic swelling (arrow)



Submandibular swelling



Proptosis

Mahajan Annu Rev Pathol 2014

Murakami World J Clinical Oncol 2011

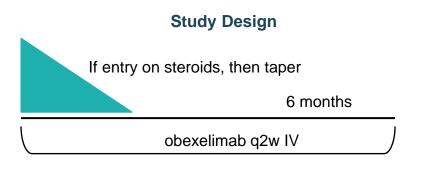
Xencor physician survey

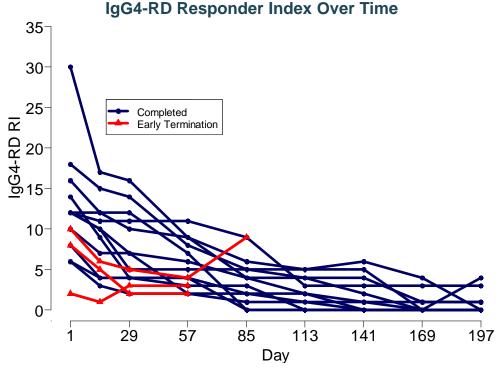


# Data from IgG4-RD Phase 2 Study Show Promising Activity

# Obexelimab was well tolerated and showed promising activity in IgG4-RD

- Phase 2 primary objective: to evaluate the effect on the IgG4-RD Responder Index (RI) in patients with active IgG4-RD (proportion of patients with improvement in IgG4-RI at 6 mos
- Corticosteroids were tapered and discontinued in all five patients that were on corticosteroids at first obexelimab dose
- Most frequent AEs were GI infusion-related symptoms
- Plasmablasts decreased by about 70-80%, while B cells decreased by 40-55%, both within 2 weeks
- 14 of 15 patients achieved a decrease of ≥ 5 in the IgG4-RD RI. Initial response to therapy occurred quickly, most within two weeks of first dose
- 12 patients (80%) completed the study. All 12 achieved the primary endpoint of a decrease of IgG4-RD RI of ≥ 2 at Day 169
- Remission (IgG4-RD RI of 0 and no corticosteroids after month 2) was attained in 8 patients at Day 169; 4 others achieved an RI ≤ 4

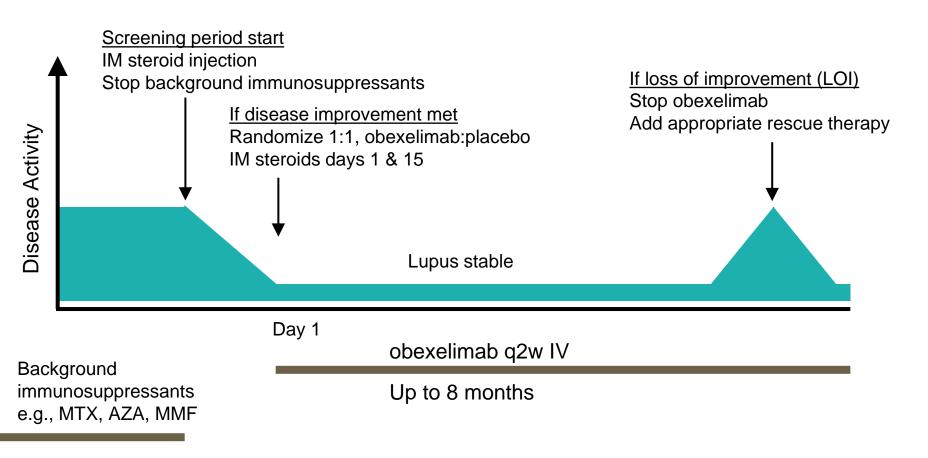






ACR Meeting, November 2017

# **Obexelimab Lupus (SLE) Phase 2 Study Design**



Primary objective: ability of obexelimab to maintain SLE disease activity improvement

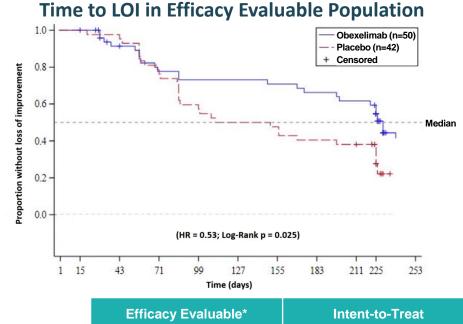
Randomized, double-blinded, placebo-controlled

N = 104 patients, 20 U.S. sites, topline data at ACR meeting in October 2018



## **Obexelimab Shows Disease Modifying Activity in Randomized Phase 2 Study in SLE**

- Positive trend in primary endpoint, proportion of patients without loss of improvement (LOI) at Day 225, not statistically significant
  - LOI: SLEDAI increase ≥4 points or new BILAG A or B score AND physician intent to treat with rescue medication
- Met pre-defined secondary endpoint, time to LOI, 76% improvement in median time to LOI (p=0.025)
- Obexelimab well-tolerated and safety profile is consistent with prior studies
  - Most common AEs were transient, infusion-related
  - No opportunistic infections or deaths reported
  - Low incidence of major organ flares



	Efficacy E	valuable*	Intent-to-Treat			
	<b>Obexelimab</b> (n=50)	Placebo (n=42)	<b>Obexelimab</b> (n=52)	Placebo (n=52)		
% Response (Day 225)	42.0%	28.6%	40.4%	23.1%		
	p = (	0.18	p = 0.06			
Median time to LOI (days)	230	131	230	156		
	HR = 0.53	p = 0.025	HR = 0.59, p = 0.06			
Time on treatm	ent (months, m	<b>6.9</b> [0-7.4]	<b>3.6</b> [0-7.0]			
Number of infu	sions (median)	<b>15</b> [1-16]	<b>8.5</b> [1-16]			

\* Excludes 12 patient discontinuations for reasons other than LOI or toxicity



# 2019/2020 Milestones and Goals

#### **Trial Initiations / IND Submissions**

Initiate Phase 1 study of XmAb23104 (PD-1 x ICOS) in advanced solid tumors



Initiate Phase 1 study of XmAb22841 (CTLA-4 x LAG-3) in advanced solid tumors

Support Genentech's IND for **XmAb24306** (IL15/IL15R $\alpha$ -Fc targeting IL15R $\beta\gamma$ )

#### **Initial Phase 1 Data Readouts**

XmAb13676 (CD20 x CD3) in B cell malignancies (2H2019)

XmAb18087 (SSTR2 x CD3) in NET and GIST (1H2020)

XmAb20717 (PD-1 x CTLA-4) in multiple solid tumor types(1H2020)

\$626.1 million in cash at June 30, 2019 Runway beyond 2024

