

# Antibodies by Design:

*XmAb<sup>®</sup> Antibody Therapeutics*

*Analyst Day Welcome*

June 28, 2016

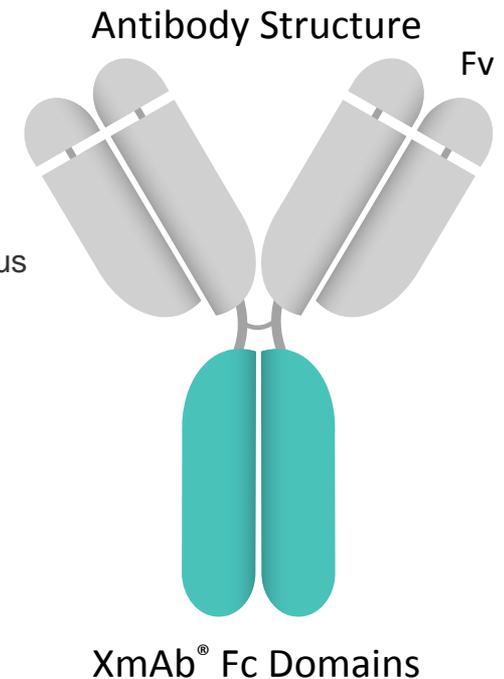


# Forward-Looking Statements

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; 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. 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, preserves half-life, stability and production
  - Over 100 issued and over 150 pending patents worldwide
- Lead internal programs in clinical development
  - **XmAb5871** in Phase 2 in IgG4-Related Disease and Systemic Lupus Erythematosus
  - **XmAb7195** completing Phase 1a, in development for allergic disease
- Expansive bispecific oncology pipeline advancing
  - Planning to initiate clinical trials of **XmAb14045** and **XmAb13676** in 2016
  - Additional bispecific programs planned to start clinical trials in 2017
  - Amgen advancing six XmAb programs in oncology and inflammation
    - \$45M upfront, \$1.7B potential milestones
- Nine XmAb clinical programs ongoing internally or with partners



# XmAb<sup>®</sup> Fc Domains Augment Natural Antibody Functions

**Natural Fc Function**



Immune regulation  
Antigen clearance



Cytotoxicity  
(immune cell)



Circulating  
half-life



Stable homodimer  
structure

**Fc Receptor**

Fc $\gamma$ RIIb

Fc $\gamma$ RIIIa, Fc $\gamma$ RIIIa

FcRn

N/A

**Fc Domain Redesigns**



**XmAb Enhanced Function**



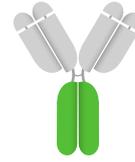
**Immune Inhibitor Domain**

Immune inhibition  
Rapid clearance



**Cytotoxic Domain**

Enhanced cytotoxicity  
(immune cell)



**Xtend Domain**

Prolonged  
half-life



**Bispecific Domain**

Stable heterodimer  
structure

*Additional Fc domains: stability, complement activation*

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

# Agenda

## **Welcome**

*Bassil Dahiyat, Ph.D., CEO*

## **XmAb<sup>®</sup>5871 and XmAb<sup>®</sup>7195 Development Programs**

*Paul Foster, M.D., Chief Medical Officer*

## **XmAb<sup>®</sup> Anti-CD3 Bispecific Platform and Oncology Pipeline Overview**

*John Desjarlais, Ph.D., Chief Scientific Officer  
Paul Foster, M.D., Chief Medical Officer*

## **XmAb<sup>®</sup> Checkpoint Inhibitor Bispecific Platform and Oncology Pipeline Overview**

*John Desjarlais, Ph.D., Chief Scientific Officer  
Paul Foster, M.D., Chief Medical Officer*

## **Hypoxia drives tumor immune suppression and immunotherapy resistance**

*Michael Curran, Ph.D.  
Assistant Professor, Department of Immunology, The University of Texas MD Anderson Cancer Center  
Member, Graduate Faculty, The University of Texas Graduate School of Biomedical Science*

## **Clinical Trial Landscape in NHL: Focus on Immunotherapy**

*Paul Hamlin, M.D.  
Chief, Basking Ridge Medical Oncology Service, Memorial Sloan Kettering Cancer Center*

## **Closing**

*Bassil Dahiyat, Ph.D., CEO*

# Agenda Highlights

- Novartis collaboration
  - Ex-US commercial rights to XmAb14045 and XmAb13676 licensed, 50/50 development cost share worldwide
  - Access to bispecific platform for 4 Novartis programs; Fc platform access
  - \$150M upfront, \$2.41B milestones, royalties
- XmAb5871
  - Review of Phase 2 trials design in IgG4-Related Disease and Systemic Lupus Erythematosus
  - Review of mechanism and Phase 1 and 2a clinical data
  - Plan for XmAb5871 subcutaneous clinical trial in 3Q2016
- XmAb7195
  - Review of Phase 1a clinical data
  - Plan for XmAb7195 subcutaneous clinical trial in 4Q2016
- XmAb oncology bispecifics new programs
  - XmAb18087: SSTR2 x CD3 for neuroendocrine tumors, IND expected 2017
  - XmAb20717: PD-1 x CTLA-4 dual checkpoint inhibitor, IND expected 2017

# Novartis Collaboration for XmAb14045 and XmAb13676 Boosts Development Resources and Retains US Commercial Rights



## Links Novartis' leadership in development and commercialization of oncology drugs with Xencor's XmAb Bispecific programs

- Novartis receives ex – US commercial rights to XmAb14045 and XmAb13676
  - Low double-digit royalties on ex-US sales
- Xencor retains all U.S. commercial rights to XmAb14045 and XmAb13676
- 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 US profit and cost share, co-detail
- Non-exclusive access to Xencor Fc Technologies for 10 programs

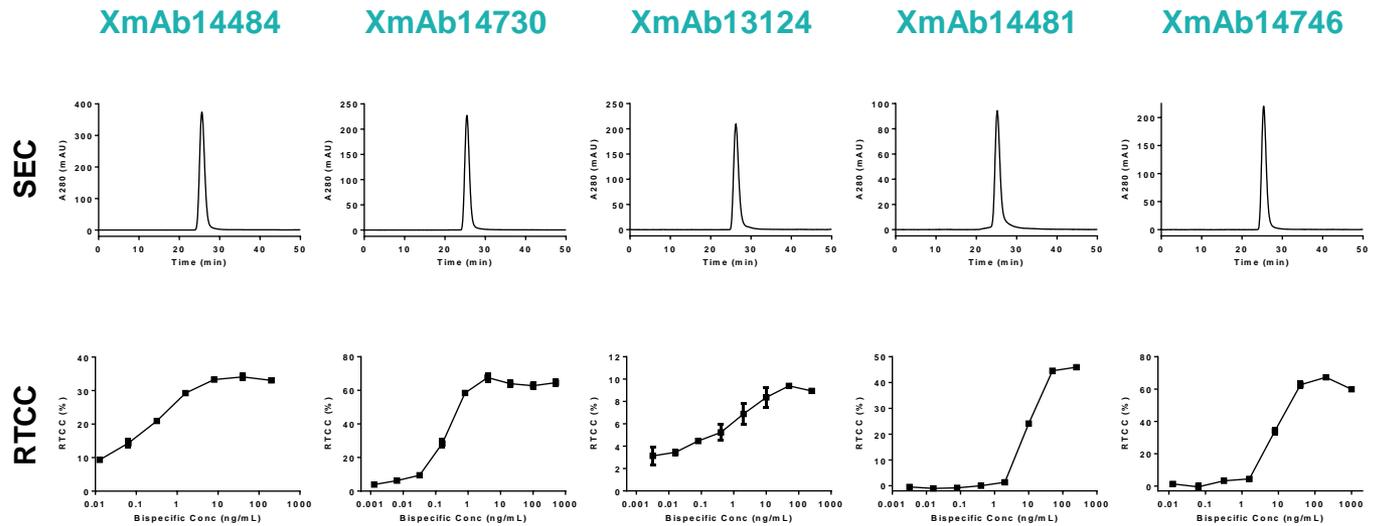
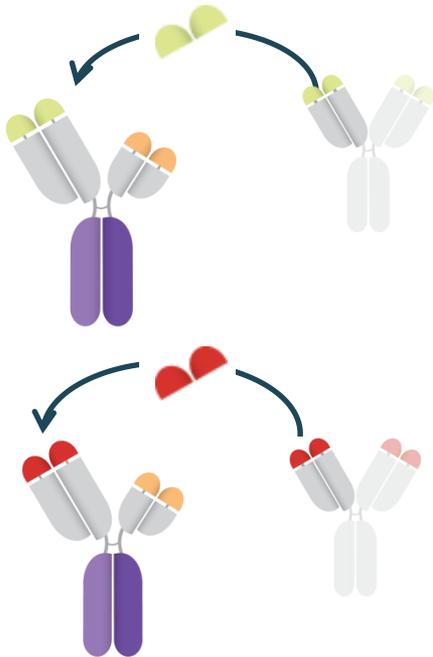
**\$150M upfront, \$2.4B potential milestones, royalties**

# Development Pipeline Focused on Immune Inhibitor and Bispecific Fc Domains

Program (Target)	Fc Domain	Primary Indication	Discovery Lead	Preclinical	Phase 1	Phase 2	Commercial Rights
<b>XmAb5871</b> (CD19)	Immune Inhibitor	IgG4-RD SLE					xencor
<b>XmAb7195</b> (IgE)	Immune Inhibitor	Asthma/ allergy					xencor
<b>XmAb5574/MOR208</b> (CD19)	Cytotoxic	CLL/NHL/ ALL					morphosys
<b>XmAb14045</b> (CD123 x CD3)	Bispecific	AML					xencor*
<b>XmAb13676</b> (CD20 x CD3)	Bispecific	B-cell malignancy					xencor*
<b>XmAb13551</b> (CD38 x CD3)	Bispecific	Myeloma					AMGEN
<b>XmAb18087</b> (SSTR2 x CD3)	Bispecific	Neuroendo- crine tumors					xencor
<b>XmAb20717</b> (PD-1 x CTLA-4)	Bispecific Xtend	Oncology					xencor

\* Novartis licensed ex-US commercial rights, worldwide co-development

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

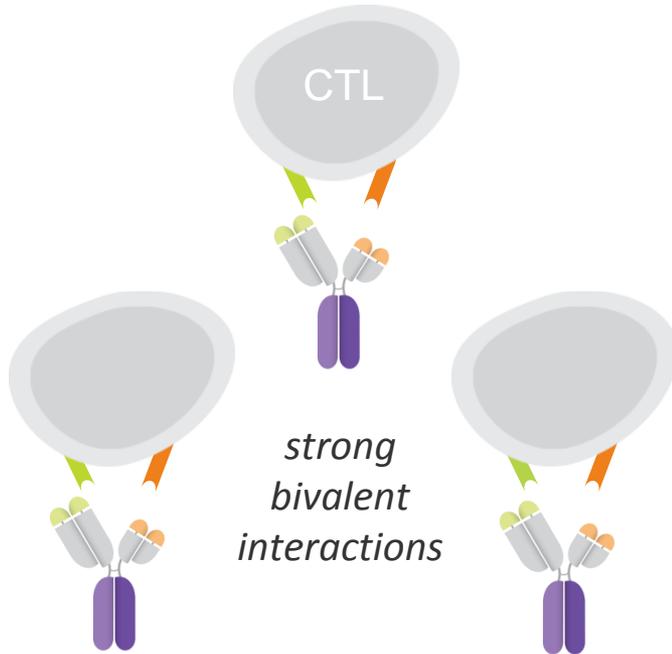


- Portfolio of CD3 bispecific molecules generated and ready for development
- New immuno-oncology programs rapidly prototype different target combinations

# Xencor Checkpoint Bispecifics: Selective Tumor T-cell Targeting through Bispecific Avidity

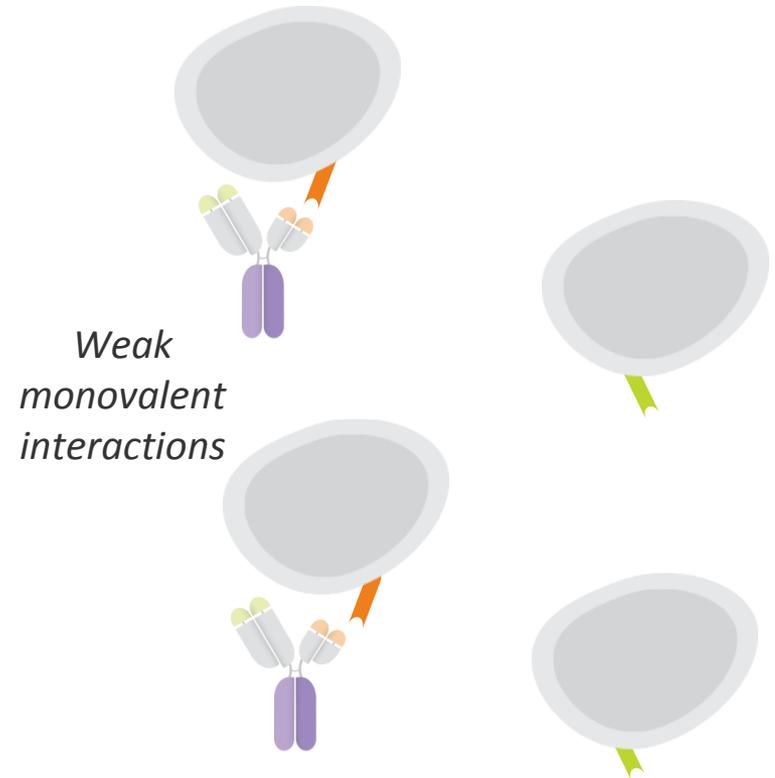
## Tumor Environment:

- Tumor infiltrating lymphocytes (TILs) coexpress multiple checkpoints (Matsuzaki 2010, Fourcade 2012, Gros 2014)
- Bivalent binding increases avidity



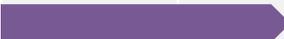
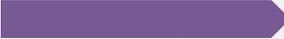
Enhance anti-tumor activity

## Periphery



Avoid peripheral toxicity

# Xencor's Growing Bispecific Oncology Pipeline to Enter Clinical Trials in 2016

Program (Target)	Fc Domain	Primary Indication	Discovery Lead	Preclinical	Phase 1	Commercial Rights
<b>XmAb14045</b> (CD123 x CD3)	Bispecific	AML			(2016)	 xencor*
<b>XmAb13676</b> (CD20 x CD3)	Bispecific	B-cell cancer			(2016/17)	 xencor*
<b>XmAb13551</b> (CD38 x CD3)	Bispecific	Myeloma				 AMGEN
<b>XmAb18087</b> (SSTR2 x CD3)	Bispecific	Oncology				 xencor
<b>XmAb20717</b> (PD1 x CTLA4)	Bispecific/ Xtend	Oncology				 xencor
<b>Undisclosed</b> CI x CI	Bispecific	Oncology				 xencor
<b>Undisclosed</b> (x CD3)	Bispecific	Oncology				 xencor
<b>Undisclosed</b> Immune Modulation	Bispecific	Oncology				 xencor

\* Novartis licensed ex-US commercial rights, worldwide co-development

- CD3 bispecifics to target T cells to tumors, entering clinic in 2016
- SSTR2 x CD3 IND mid-2017, followed by PD1 x CTLA4
- Scalable platform process for GMP manufacturing developed

# XmAb<sup>®</sup>5871

## Development Program

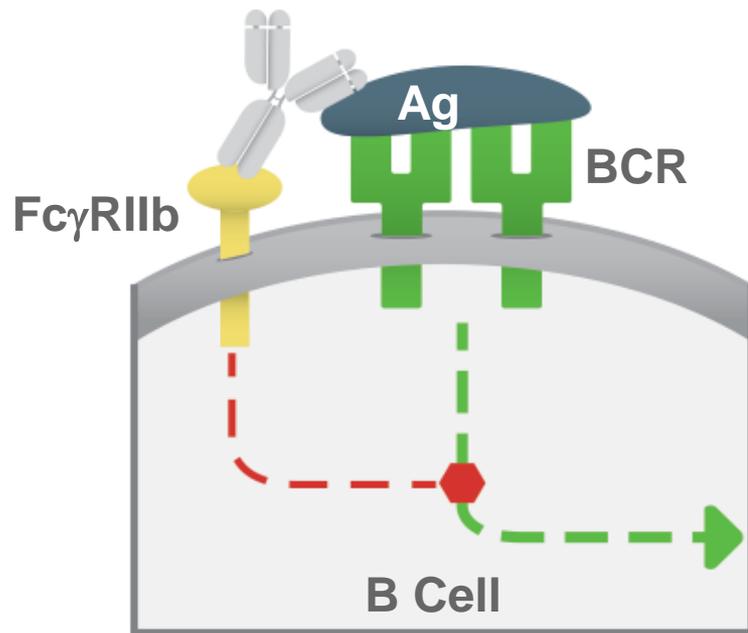
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# XmAb5871 Enhances Natural Regulatory Role of FcγRIIb

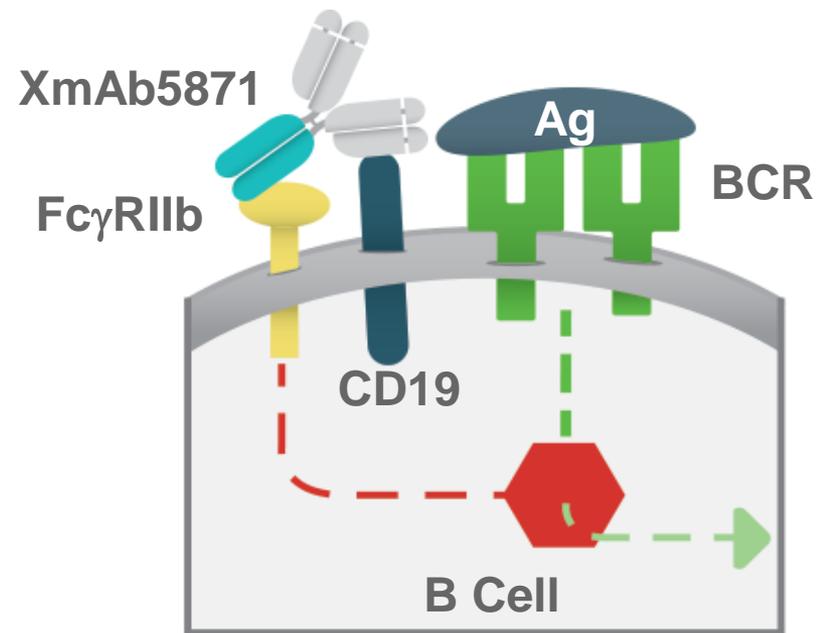
**Natural:**

Ag + αAg Immune Complex



**XmAb5871:**

anti-CD19 with Immune Inhibitor Fc domain



- FcγRIIb inhibitory activity requires bridging to specific co-targets
- Inhibits many activation pathways in both healthy and diseased B cells
- Potent suppression of B-cell responses without destroying B cells

# XmAb5871 Clinical Development - Completed Studies

- Phase 1a FIH SAD study in HV completed in 4Q 2012
- Phase 1b/2a study in patients with RA on stable non-biologic disease modifying anti-rheumatic drug (DMARD) therapy in 3Q 2014

## Design

- Multi-center, randomized, placebo controlled, double-blinded
- Phase 2a portion of trial (27 patients, 2:1 randomized)
- Six bi-weekly IV infusions, 10 mg/kg

## Primary objective of safety and tolerability characterization:

- Generally well tolerated
- Two treatment related SAEs and two placebo treated subjects with SAEs

## Secondary and exploratory efficacy objectives:

Phase 2a Disease Response Assessments at Week 13			
	DAS28 CRP*	ACR70	ACR50
XmAb5871	33%	20%	40%
Placebo	0%	0%	13%

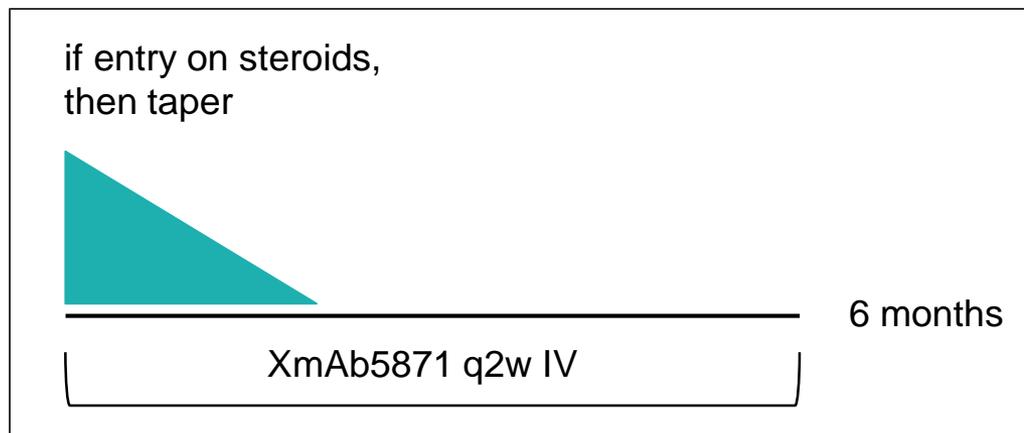
Phase 2a portion of trial: 23 evaluable patients: 15 XmAb5871 treated, 8 placebo treated  
Protocol specified disease response evaluation at Week 13

\* Remission or low disease activity

# XmAb5871 Clinical Development - Ongoing Studies

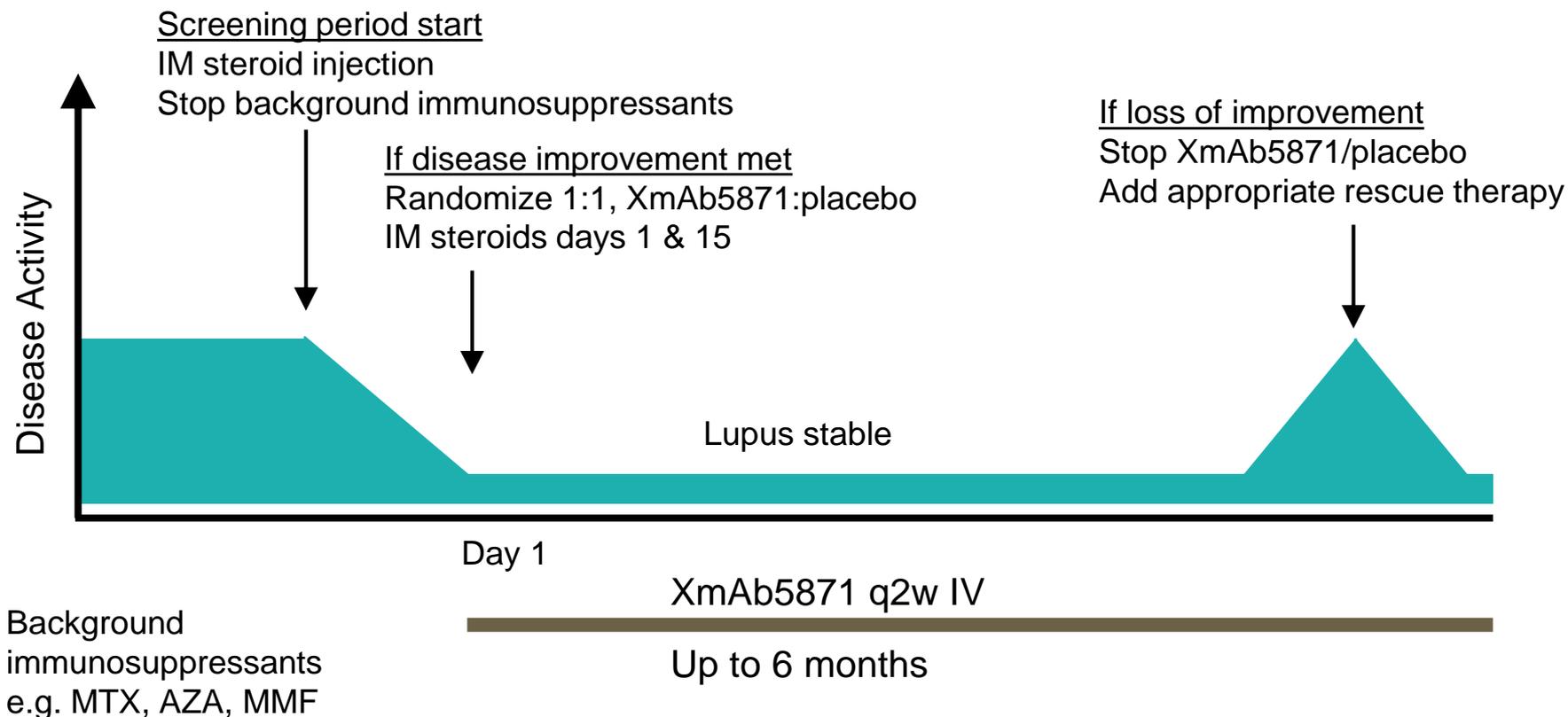
1. Phase 2 open-label, single-arm, single-site (MGH) pilot study in patients with active IgG4-RD (IgG4-RD RI  $\geq 3$ )
  - An immune-mediated condition responsible for fibro-inflammatory lesions that can lead to irreversible damage to virtually any organ
  - No approved therapies; glucocorticosteroids are standard of care
2. Phase 2 randomized double-blind, placebo-controlled study in patients with moderate to severe, non-organ threatening, SLE

# IgG4-RD Pilot Trial Design To Characterize Activity Of XmAb5871 at Reducing IgG4-RD RI



- **Dose schedule:** IV infusion every 2 weeks for 12 doses (6 months)
- **Number:** Up to 15 patients
- **Primary endpoint:** the proportion of patients at 6 months with an improvement of disease activity score as defined by a decrease of IgG4-RD Responder Index of  $\geq 2$  points from Day 1 pre-dose disease activity score
- Based on design of an open label study of rituximab in IgG4-RD (Carruthers Ann Rheum Dis, 2015)
- Study is enrolling with 1st patient dosed Mar2016. First possible preliminary data report at a medical meeting in 4Q2016

# XmAb5871 SLE Phase 2 Study Design



Randomized, double blinded, placebo controlled

N = ~90 patients, ~20 US sites

Primary objective: ability of XmAb5871 to maintain SLE disease activity improvement

First patient enrolled Mar2016

# XmAb5871 Clinical Development – Planned Studies

## XmAb5871-25: Subcutaneous Bioavailability Study

- **Design:** Phase 1, single-site, open-label, parallel-group, multiple-dose comparison of relative bioavailability and PK of XmAb5871 administered IV versus SC in healthy volunteers
- **Dose schedule:** Q 14 days X 3 doses
- **Number:** 50 subjects
- **Primary endpoint:** Relative bioavailability and PK of SC administration of XmAb5871
- **Expected start:** 3Q2016

# XmAb<sup>®</sup>7195

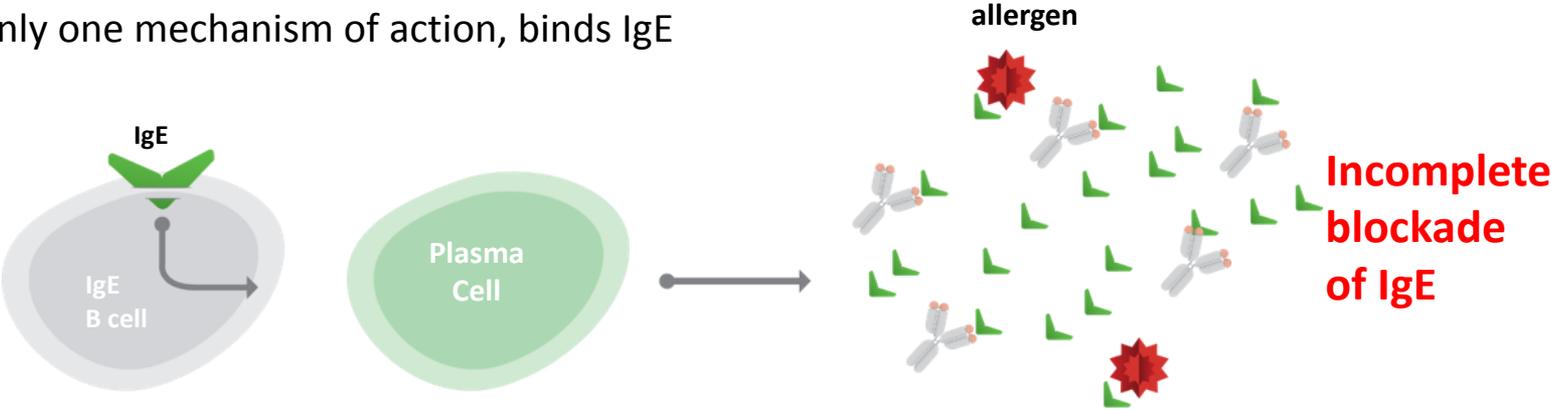
## Development Program

June 28, 2016



# XmAb7195 Multiple Mechanisms of Action

**Xolair:** Only one mechanism of action, binds IgE

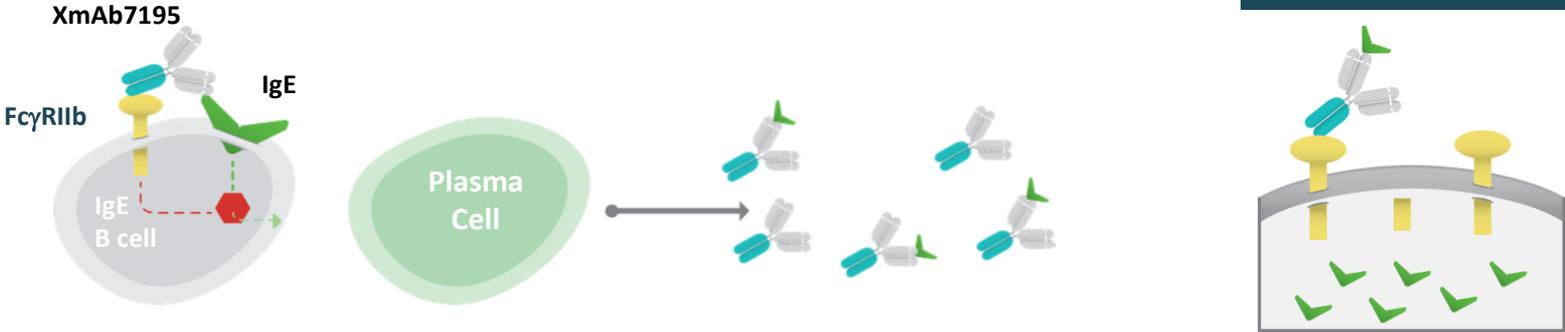


## XmAb7195

**1** Reduces IgE Production

**2** Binds IgE

**3** Sends IgE to liver sinusoidal endothelial cells for destruction



# XmAb7195 Clinical Development - Completed Studies

**XmAb7195-01:** Phase 1 FIH randomized, double-blind, placebo-controlled, ascending dose study of IV administered XmAb7195 in healthy subjects and subjects with a history of atopic disease with elevated serum IgE (300 – 3000 IU/mL inclusive) completed 3Q 2015

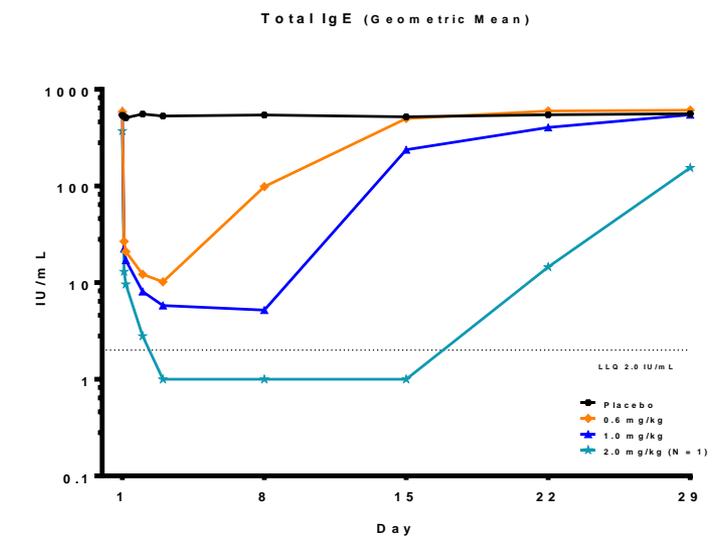
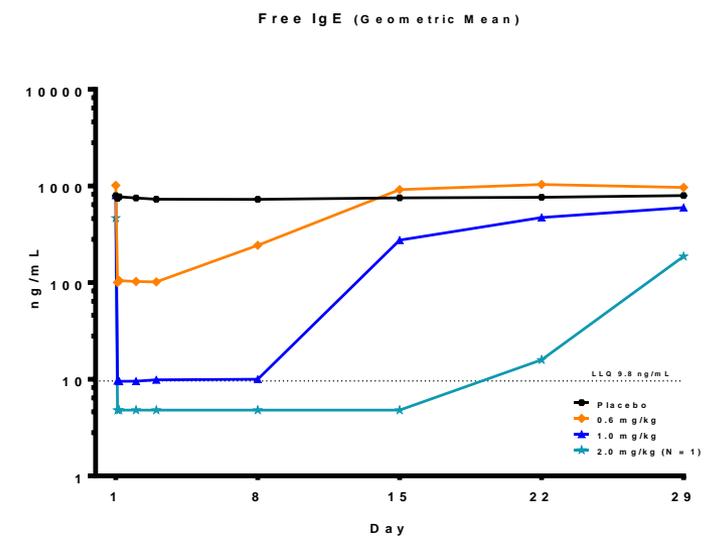
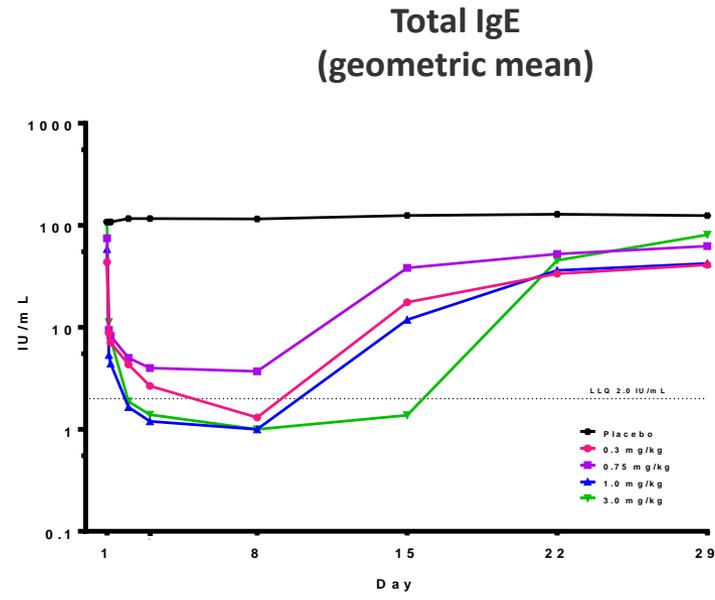
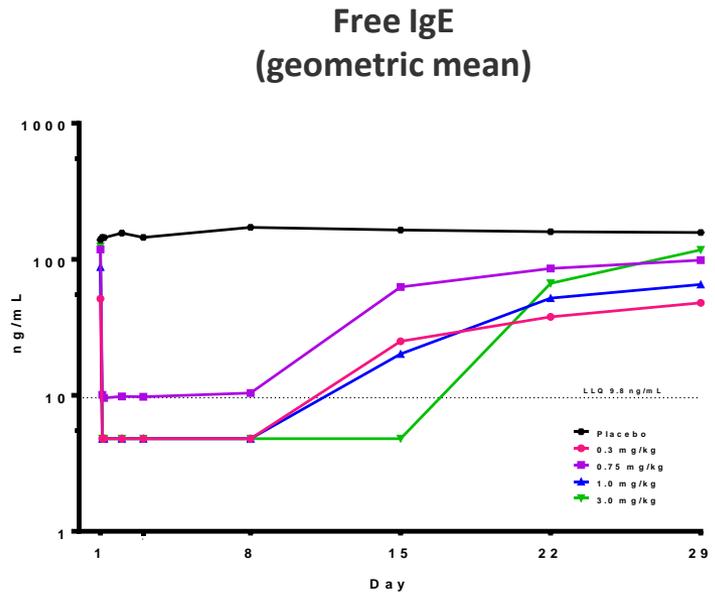
- **Design:** Single IV administration of XmAb7195 or placebo (0.3-3.0 mg/kg in HV; 0.6-2.0 mg/kg in atopic subjects with high IgE). Part 3: Two-dose sequential IV administration of XmAb7195 or placebo on Day 1 and Day 8 (0.3/0.3, 0.3/1.0 mg/kg)
- **Primary endpoint:** To determine the safety and tolerability profile following single-dose IV administration of XmAb7195 and after a priming IV dose followed by an escalating second IV dose of XmAb7195

# XmAb7195-01 Results

- XmAb7195 was generally well tolerated when administered as a single IV infusion with transient, asymptomatic thrombocytopenia occurring at doses  $\geq 2.0$  mg/kg
- One SAE
  - Bronchospasm was reported in an atopic subject with a history of perennial and seasonal allergies experienced severe bronchospasm 25 minutes after the start of the XmAb7195 infusion. The event responded quickly to discontinuation of the infusion and medical intervention
- XmAb7195 induced rapid and extensive depletion of serum free IgE, serum total IgE, basophil surface IgE and basophil Fc $\epsilon$ RI expression levels at all doses tested
- Across all dose levels tested, 93% of healthy adults and 75% of atopic subjects with predose total IgE of  $>300$  IU/ml had reduction of free IgE levels to BLQ ( $<9.59$  ng/ml) following a single dose of XmAb7195

# XmAb7195 reduces free and total IgE in humans

Healthy Subjects



High IgE Subjects  
(300 – 3000 IU/mL);

# XmAb7195 Clinical Development – Planned Studies

## XmAb7195-02: Subcutaneous Bioavailability/MAD Study

- **Design:** Phase 1, open-label, parallel-group, multiple-dose (4 doses) comparison of relative bioavailability and PK of XmAb7195 and a randomized (3:1) double-blinded, placebo-controlled, multiple ascending dose PK and safety study in healthy volunteers and individuals with atopic disease
- **Dose schedule:** Part A: XmAb7195 administration weekly for a total of 4 doses.
- **Number:** Approximately 62 subjects. 30 subjects in Part A; 32 subjects in Part B
- **Primary endpoint:** Relative bioavailability and PK of SC administration of XmAb7195
- **Anticipated start:** 3Q-4Q2016

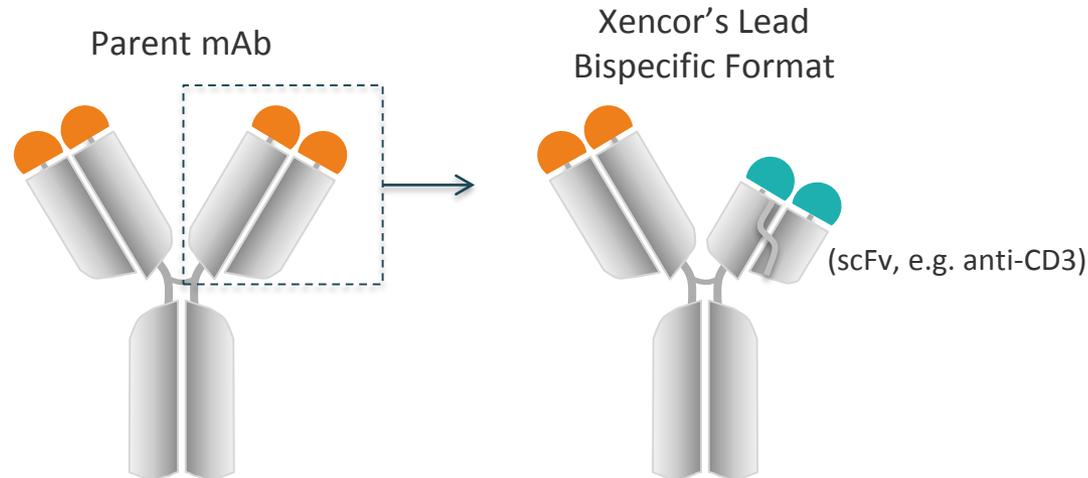
**XmAb<sup>®</sup> Anti-CD3 Bispecific  
Platform and Oncology  
Pipeline Overview**

June 28, 2016

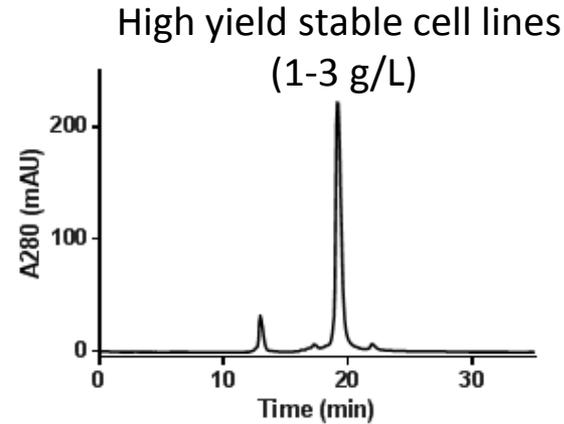
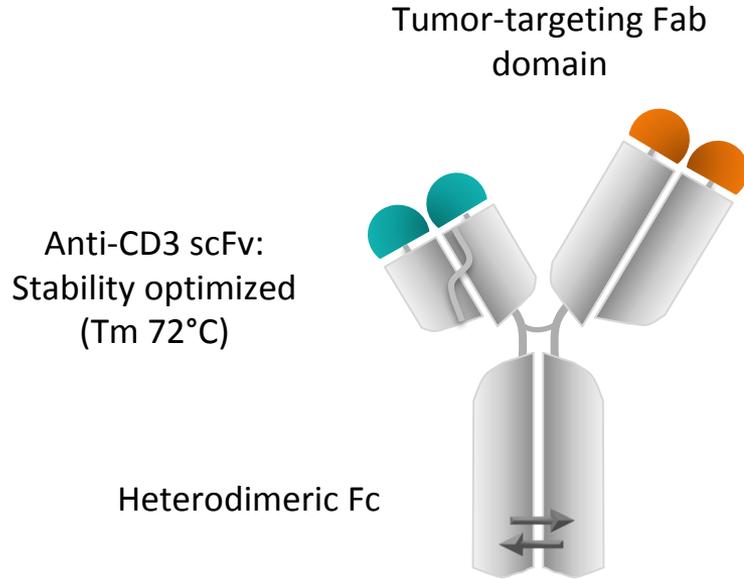


# Bispecific antibodies in immuno-oncology

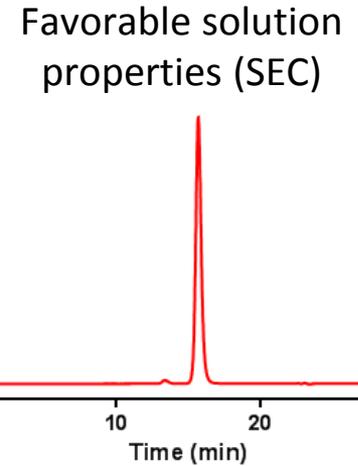
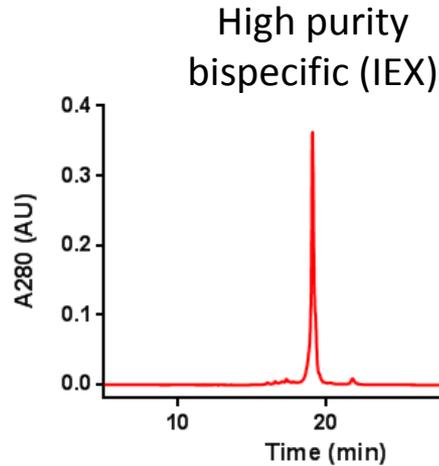
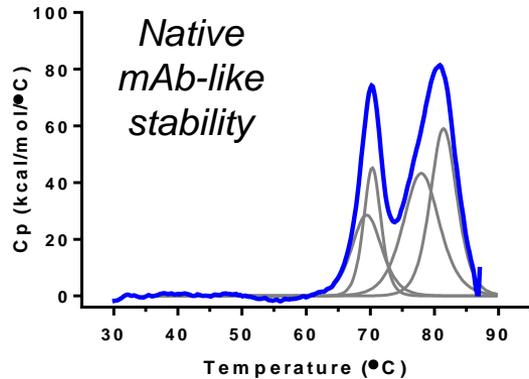
- Tremendous potential across wide range of diseases
- Historically plagued by difficult production
- Xencor bispecifics platform
  - Xencor’s expertise in Fc engineering applied to enable facile production and long half-life
  - Plug-and-play format → rapid lead prototyping & lead generation
  - Potency tuning to maximize therapeutic index



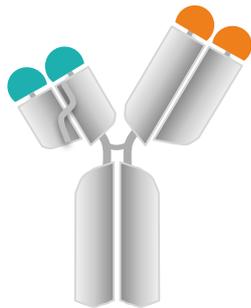
# Plug-and-play scFv-Fab format is stable and well-behaved, and easily purified



*Ion Exchange Chromatography*

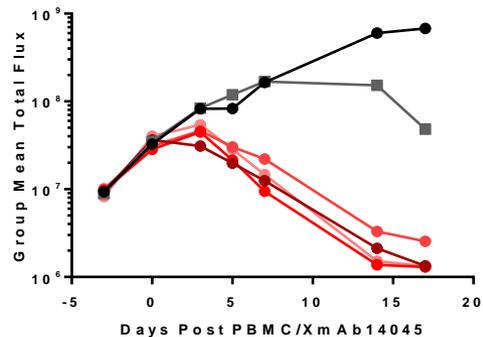


# Xencor Lead Bispecific Programs: T-Cell Engagement with Tuned Potency and mAb-like PK

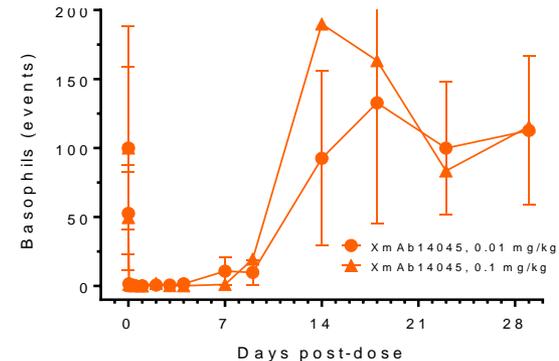


CD3 x CD123  
for AML

Strong anti-tumor activity in mice

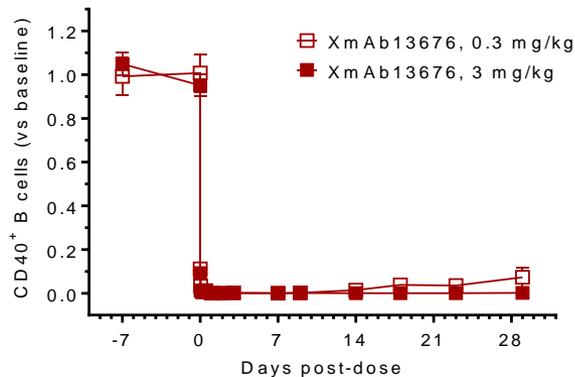


Basophil depletion in monkeys

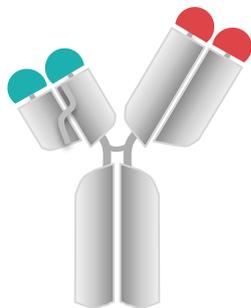
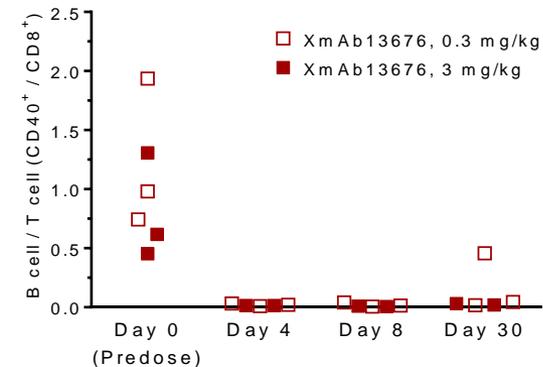


B cell depletion in monkeys

Peripheral B cells



Lymph Node B cells



CD3 x CD20  
for NHL

- Both programs display antibody-like PK in vivo

# Xencor's CD3 bispecifics are easily manufactured at scale

- XmAb14045 (CD123 x CD3):
  - Process and product validated GMP at clinical scale
    - 200L scale (100 L working volume)
    - Standard 3-step purification process
    - 6 month Drug Product stability (1 mg/ml, 5°C):
      - 100% heterodimer by CEX
      - 100% main peak by SEC
- XmAb13676 (CD20 x CD3)
  - Upstream & downstream process identical to XmAb14045
    - 200L scale (100 L working volume)
    - 1 month Drug Product stability (5 mg/ml, 5°C)
      - 100% heterodimer by CEX
      - 100% main peak by SEC

# Plug-and-play platform enables rapid prototyping and lead generation

XmAb14484

XmAb14730

XmAb13124

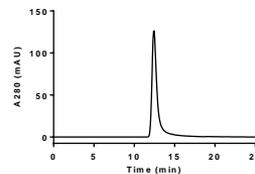
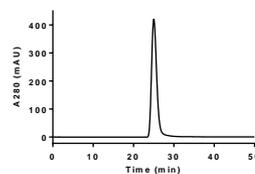
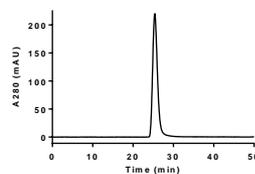
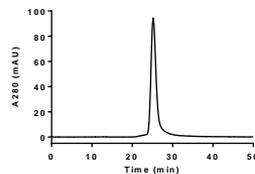
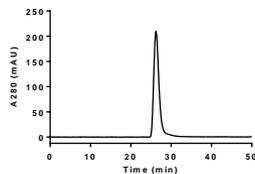
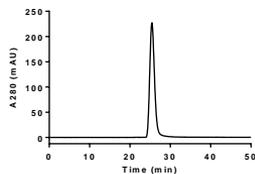
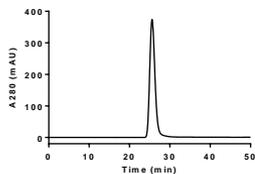
XmAb14481

XmAb14746

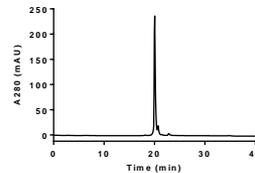
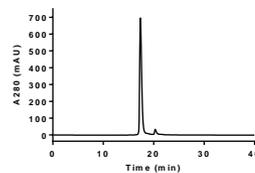
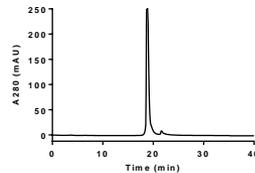
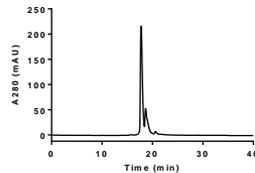
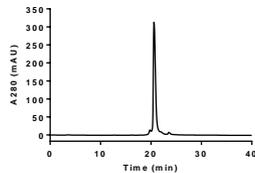
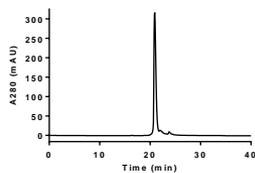
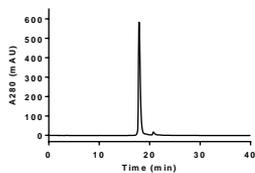
XmAb14455

XmAb18941

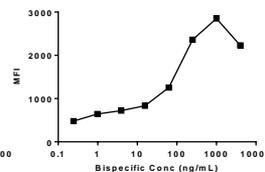
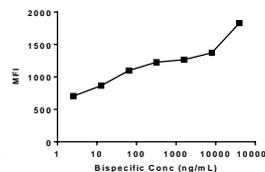
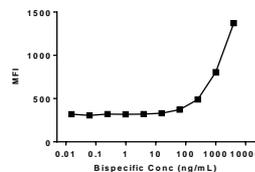
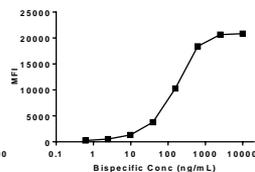
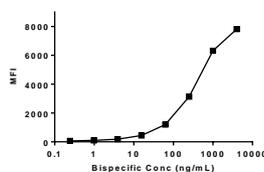
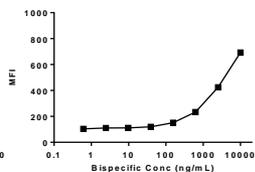
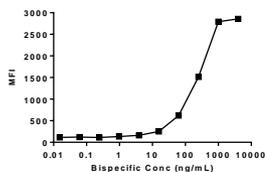
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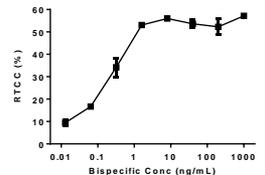
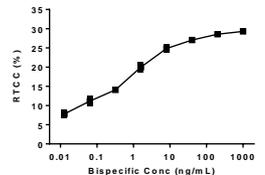
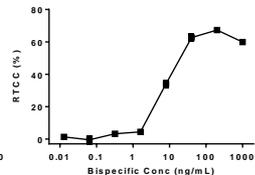
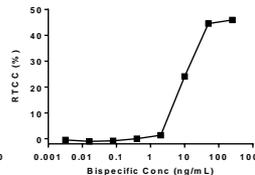
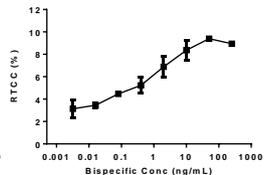
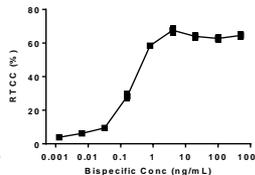
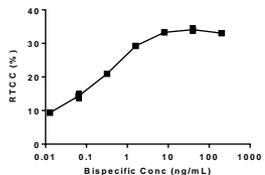
CIEX



Cell Binding



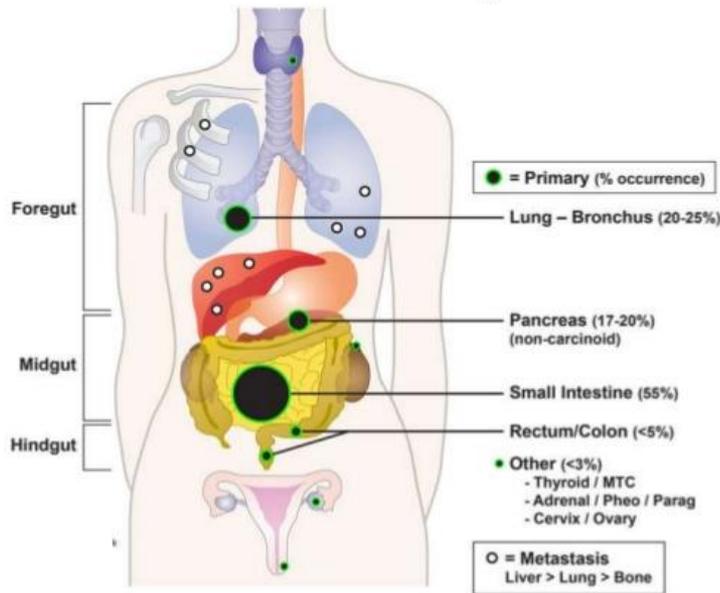
RTCC



*Numerous other CD3 and non-CD3 bispecifics produced*

# SSTR2 x CD3 bispecific antibody for the treatment of neuroendocrine tumors

## Neuroendocrine System



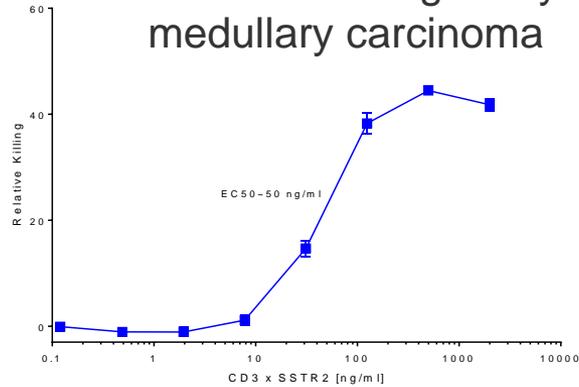
## Disease Overview

- Neuroendocrine tumors (NETs) are relatively rare, slow-growing tumors arising from the neuroendocrine system.
- Neuroendocrine system is formed of cells that produce and release hormones to control a wide range of biological functions
- NETs arise from neuroendocrine cells in a wide range of organs (pancreas, digestive system, respiratory system, thyroid, and pituitary gland)
- Functional tumors often present with symptoms specific to the hormone produced by the tumor
- Unresectable NETs are largely thought to be incurable with 3 – 19 years' survival post-diagnosis
- Current US incidence ~ 18000

SCLC provides expansion opportunity: “SSTR2 is highly expressed in many SCLC tumors ...” J Clin Oncol 34, 2016 (suppl; abstr e20090)

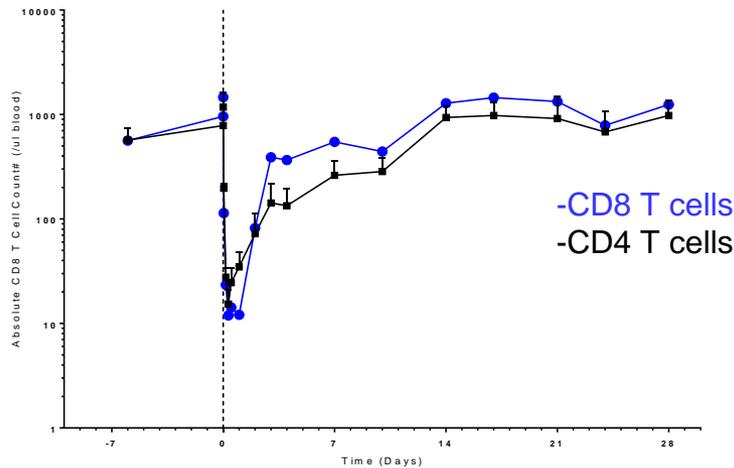
# XmAb18087 (SSTR2 x CD3) bispecific kills NET cells in vitro and activates T cells in monkeys

Potent *in vitro* killing of thyroid medullary carcinoma

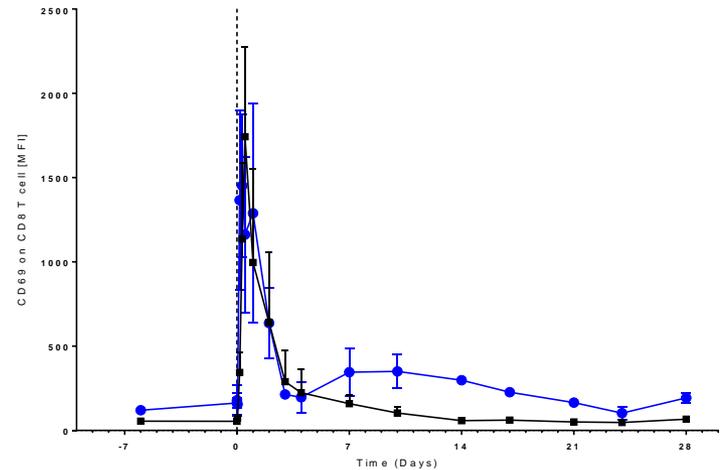


Non-human primate study

T cell redistribution



T cell activation



Target IND filing mid-2017

**XmAb<sup>®</sup>14045**  
**Clinical Development**  
**Program**

June 28, 2016



# XmAb14045 Clinical Development – Planned Studies

## XmAb14045-01

- **Design:** Phase 1, open-label, multiple ascending dose study in patients with CD123 expressing hematologic malignancies
- **Sites:** Up to 8 clinical investigation sites
- **Dose schedule:** XmAb14045 will be administered IV at ascending dose levels. Each cycle will consist of 1 dose per week for 4 weeks (28 days cycle); each patient will receive 2 cycles of therapy. After these 2 cycles, patients will be allowed to continue on therapy as long as there is evidence of clinical benefit
- **Number:** Up to 60 patients
- **Primary endpoint:** Identification of the maximum tolerated dose for first infusion and subsequent infusions and characterization of safety and tolerability
- **Anticipated start:** 3Q-4Q2016

**XmAb<sup>®</sup>13676**  
**Clinical Development**  
**Program**

June 28, 2016



# XmAb13676 Clinical Development – Planned Studies

## XmAb13676-01

- **Design:** Phase 1, open-label, multiple ascending dose study in patients with relapsed or refractory NHL and CLL
- **Sites:** Up to 12 clinical investigation sites
- **Dose schedule:** XmAb13676 will be administered IV over 2 hours at ascending dose levels. Each cycle will consist of 1 dose per week for 4 weeks (28 day cycle); each patient will receive 2 cycles of therapy. After these 2 cycles, patients will be allowed to continue on therapy as long as there is evidence of clinical benefit
- **Number:** Approximately 65 patients
- **Primary endpoint:** Safety and tolerability, maximum tolerated dose determination
- **Anticipated start:** 4Q2016-1Q2017

**XmAb<sup>®</sup> Checkpoint Inhibitor  
Bispecific Platform and  
Oncology Pipeline Overview**

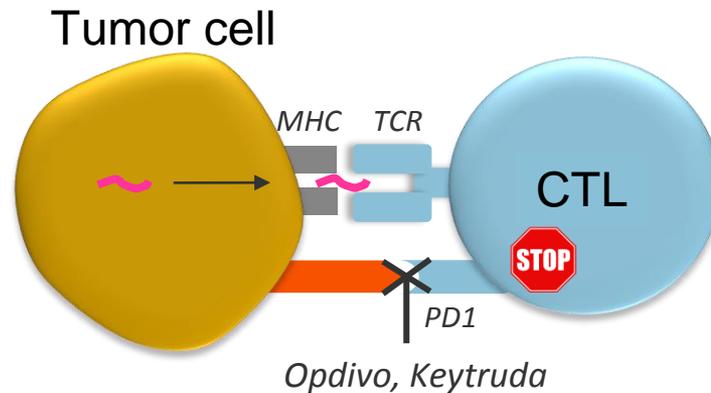
June 28, 2016



# Immuno-Oncology

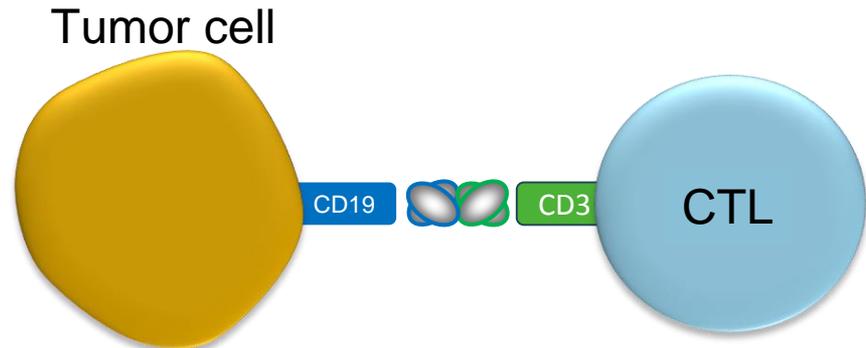
## Natural T cell response

- Targets peptide:MHC complex
- Activated by checkpoint inhibitors



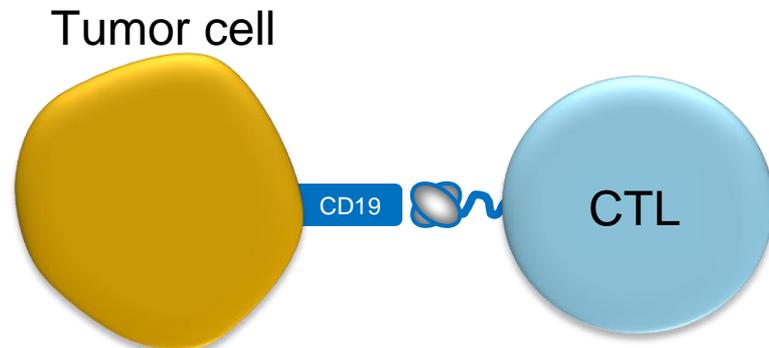
## CD3 bispecifics

- Redirect endogenous T cells
- Target quasi-selective tumor surface markers (CD19, CD38, CD20, etc.)

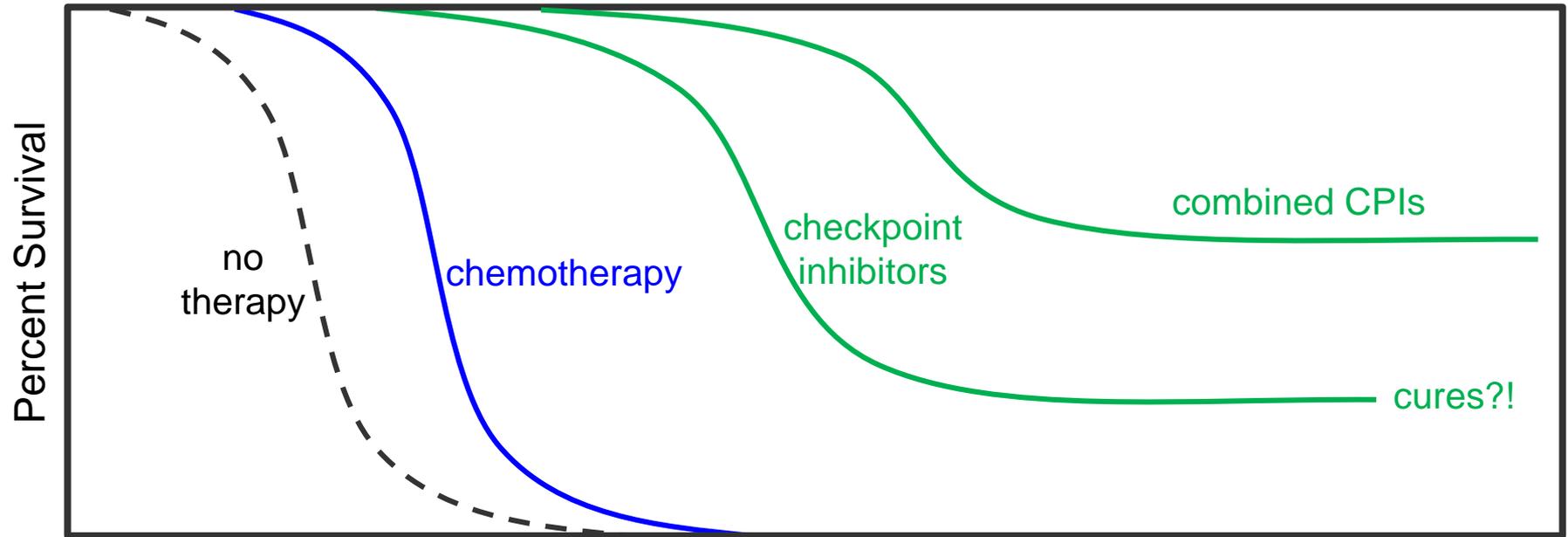


## CAR-T

- Engineered T cells
- Target quasi-selective tumor surface markers



# Checkpoint inhibitors are changing the cancer treatment landscape dramatically



BUT, combinations synergistic in efficacy and toxicity (and cost)

Response rates:

Monotherapies : ~10-30%

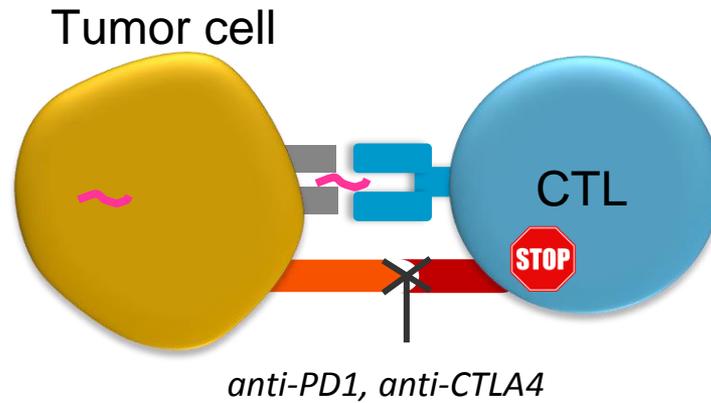
Combinations: ~40-60%

Grade 3/4 Adverse Events

Monotherapies: ~10-20%

Combinations: ~30-60%

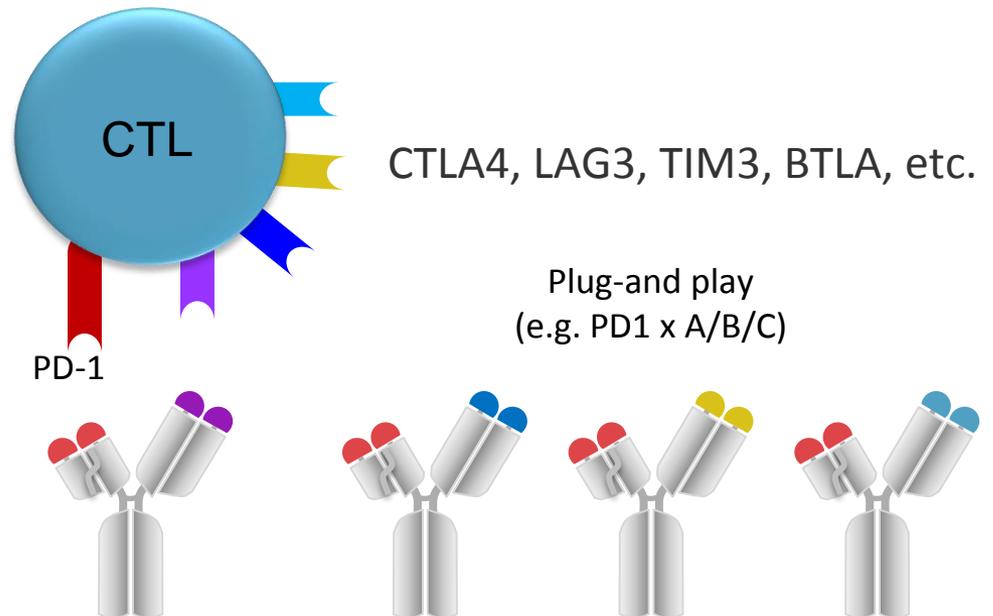
# Bispecific checkpoint inhibitors can improve on combinations



Tumor T cells typically co-express multiple checkpoints  
(Matsuzaki 2010, Fourcade 2012, Gros 2014)

## Why Bispecifics?

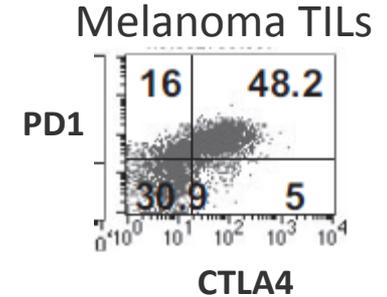
- Reduced costs
- Improved selectivity & safety



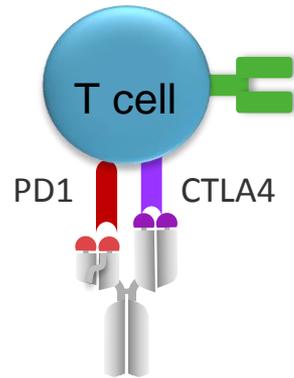
# Checkpoint bispecific hypothesis: target tumor-reactive TILs preferentially

Tumor Environment:

- TILs coexpress multiple checkpoints: Matsuzaki 2010, Fourcade 2012, Gros 2014, Ahmadzadeh 2009
- Bivalent binding increases avidity



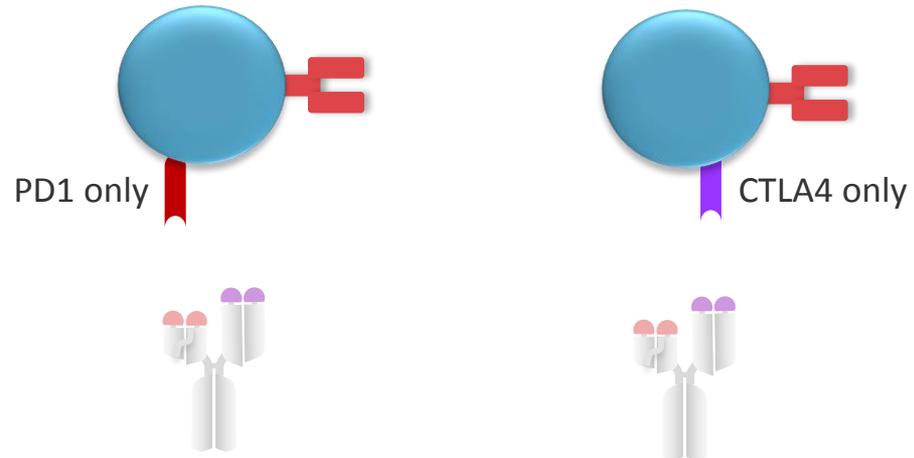
*Tumor-reactive*



- Strong interactions
- TIL activation

*Enhance anti-tumor activity*

*Non-tumor reactive*

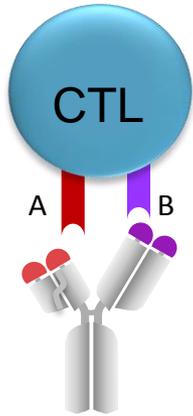


- Weak interactions
- No activation

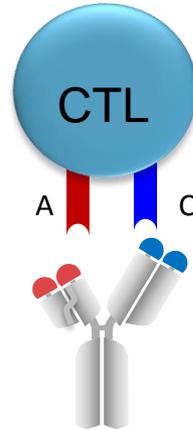
*Avoid peripheral toxicity*

# Exploring numerous hypotheses in checkpoint bispecifics

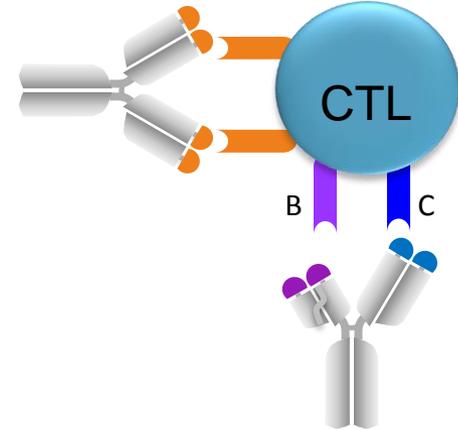
Lead 1: PD1 x CTLA4



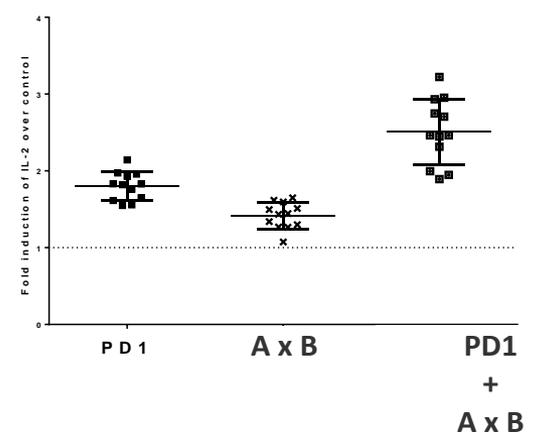
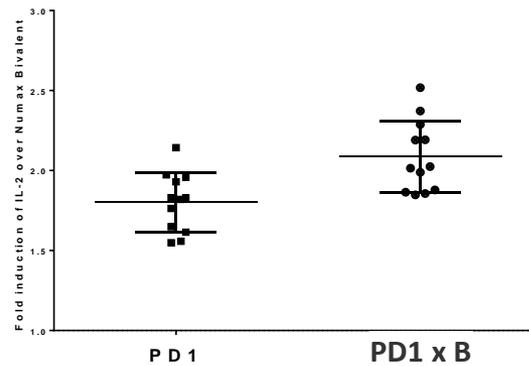
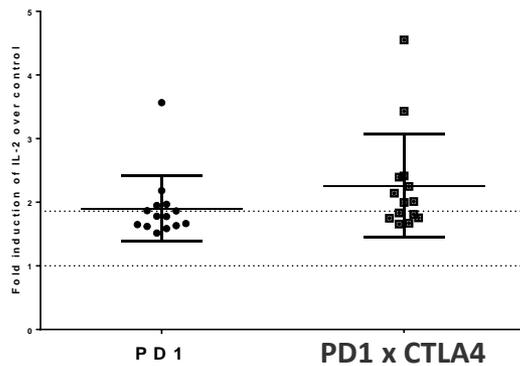
Lead 2: PD1 x B



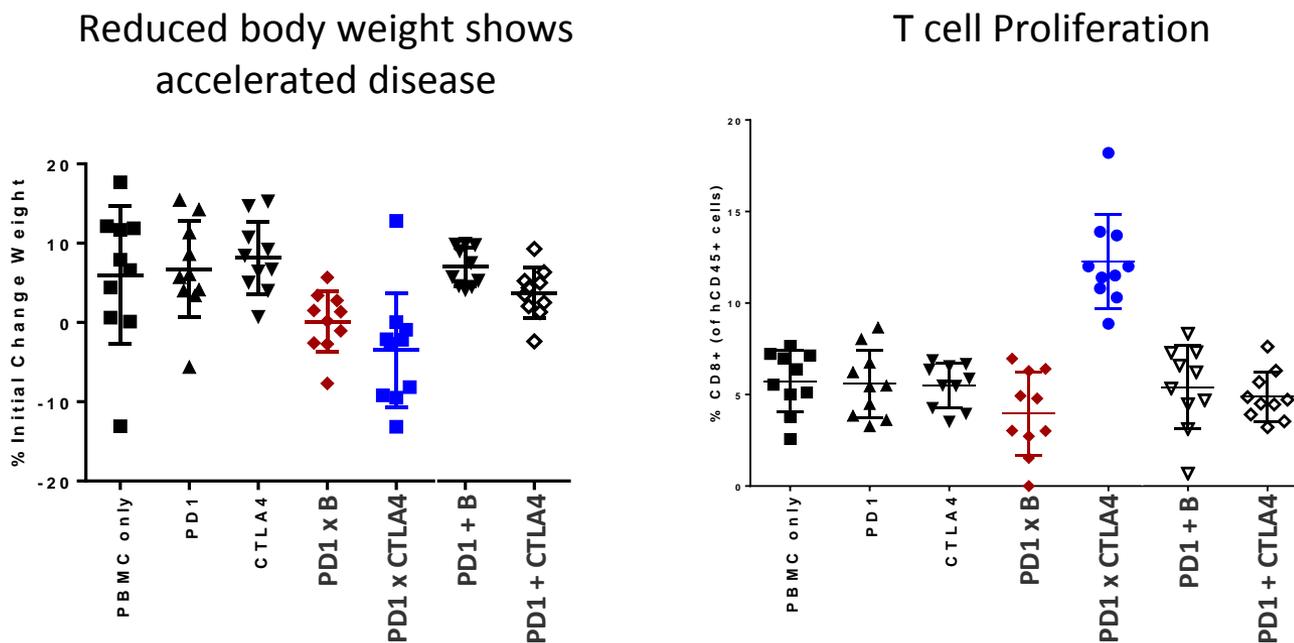
Lead 3: A x B  
(combine with anti-PD1)



In vitro SEB stimulation assays (multiple donors), IL2 production



# In vivo model for checkpoint blockade: acceleration of GVHD with prototype bispecifics

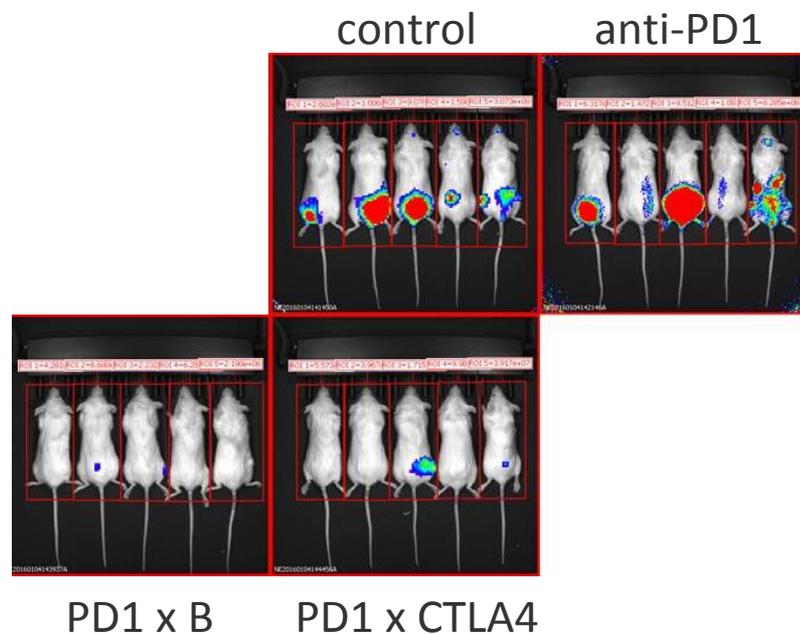
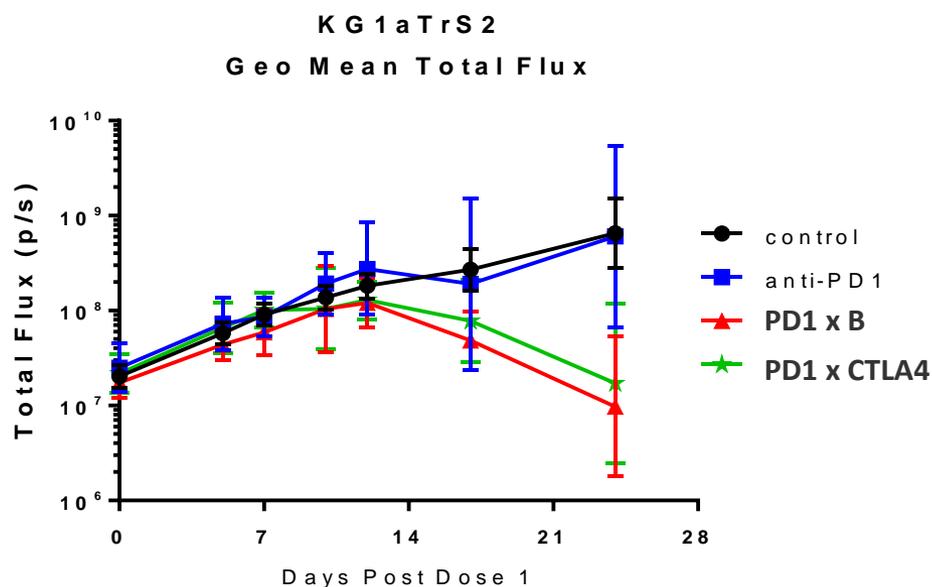


## Summary:

- **Bispecifics accelerate disease relative to combinations**
- New biology emerges with bispecific checkpoint blockade
- Bispecifics have complex biological differences compared to each other
- Bispecifics different from combinations!

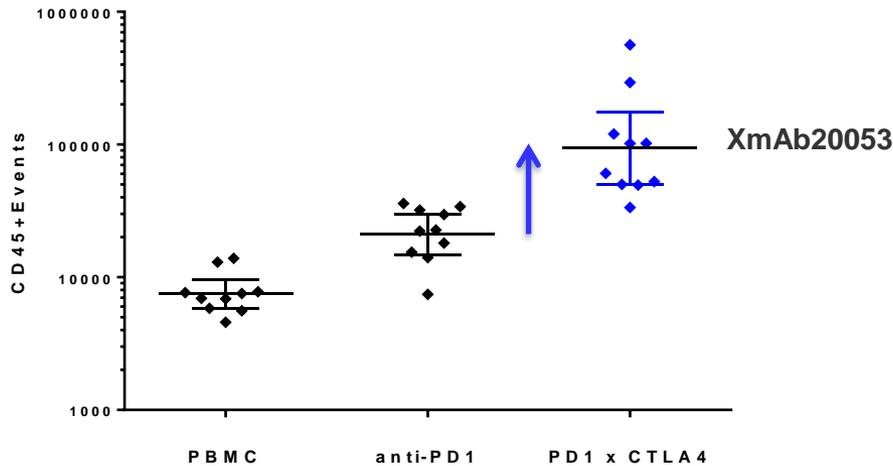
# Checkpoint bispecific prototypes have superior anti-tumor activity in a pilot xenograft study

huPBMC model with KG1a established tumors

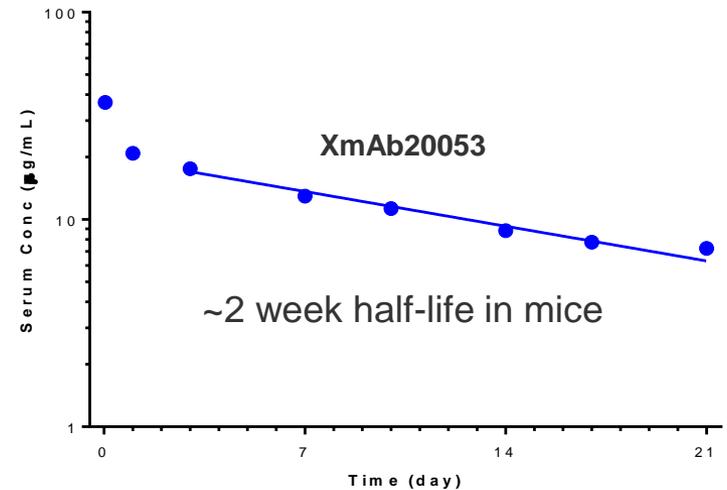


# Selected PD1 x CTLA4 candidate bispecific has superior activity to nivolumab in vivo, and long half-life

Mouse model (huPBMC-NSG):  
superior T cell activation



Antibody-like PK in Mice

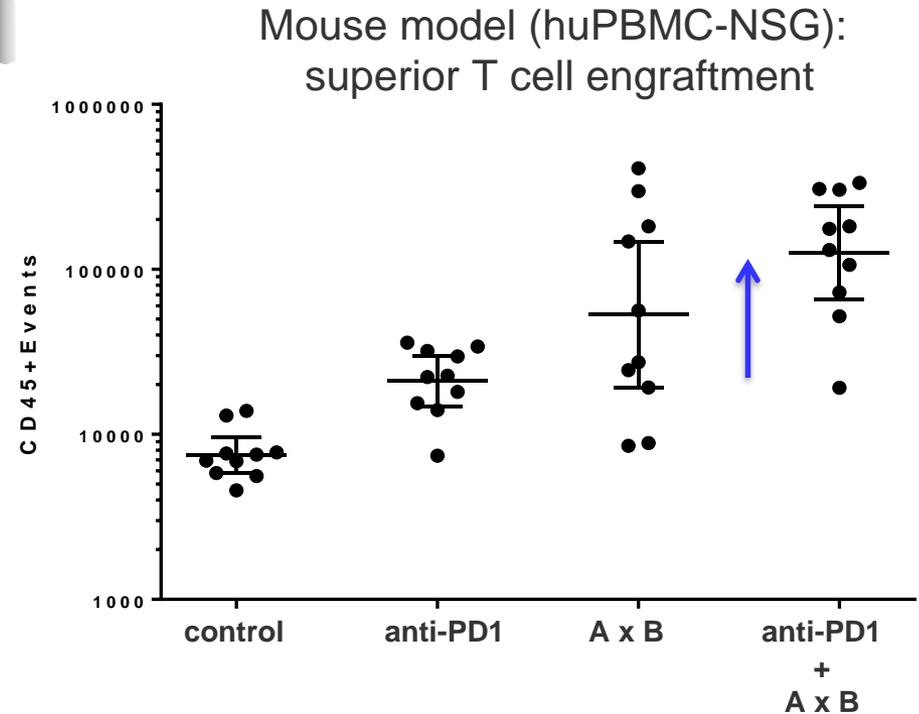
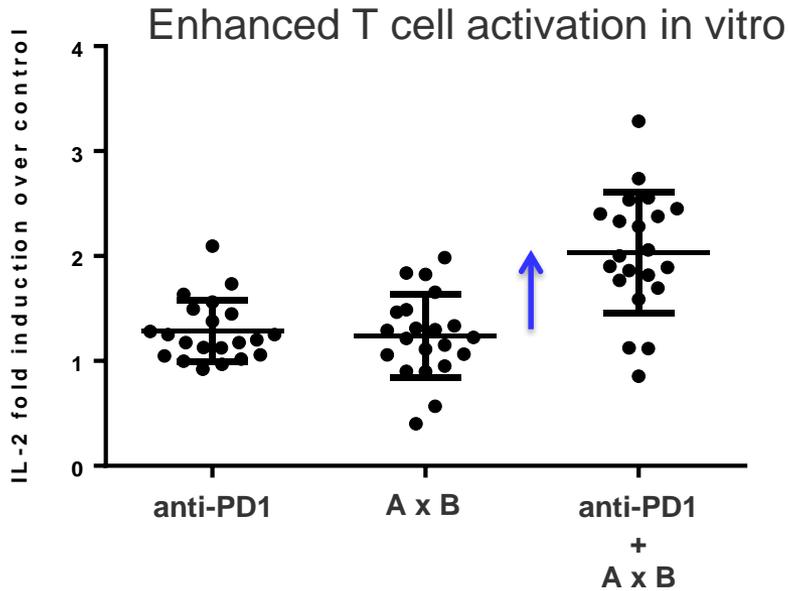
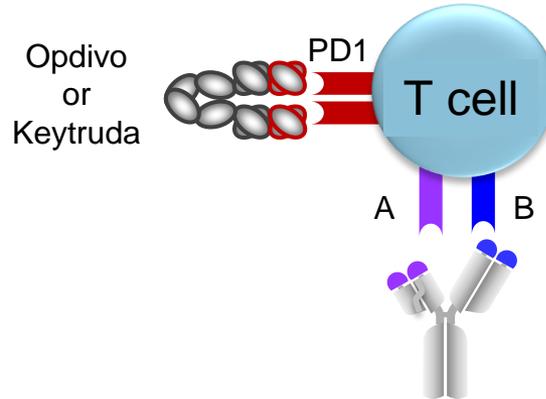


Two candidates:

- XmAb20053
- XmAb20717 (Xtend version)
- Stable cell lines in progress
- Projected IND filing late 2017

# A x B bispecific combines with anti-PD1 for additional T cell activation (lead optimization in progress)

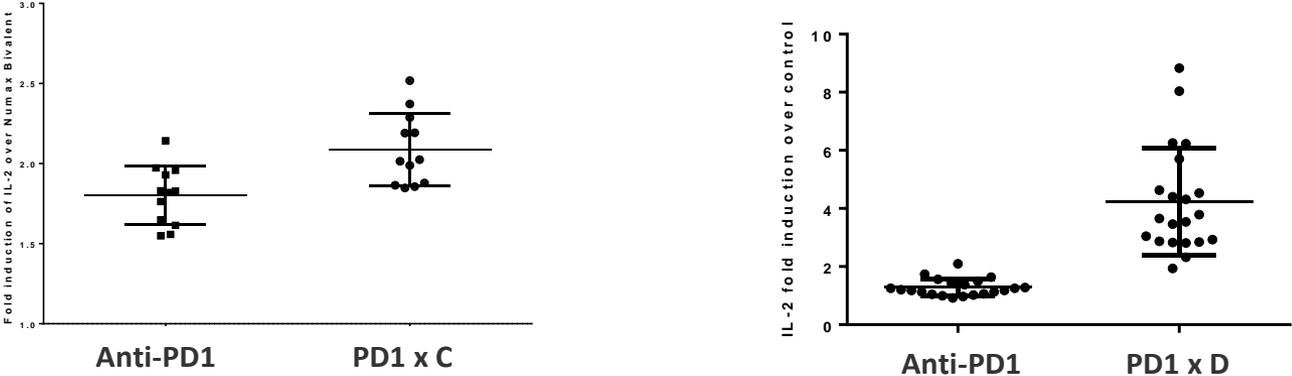
Triple checkpoint blockade



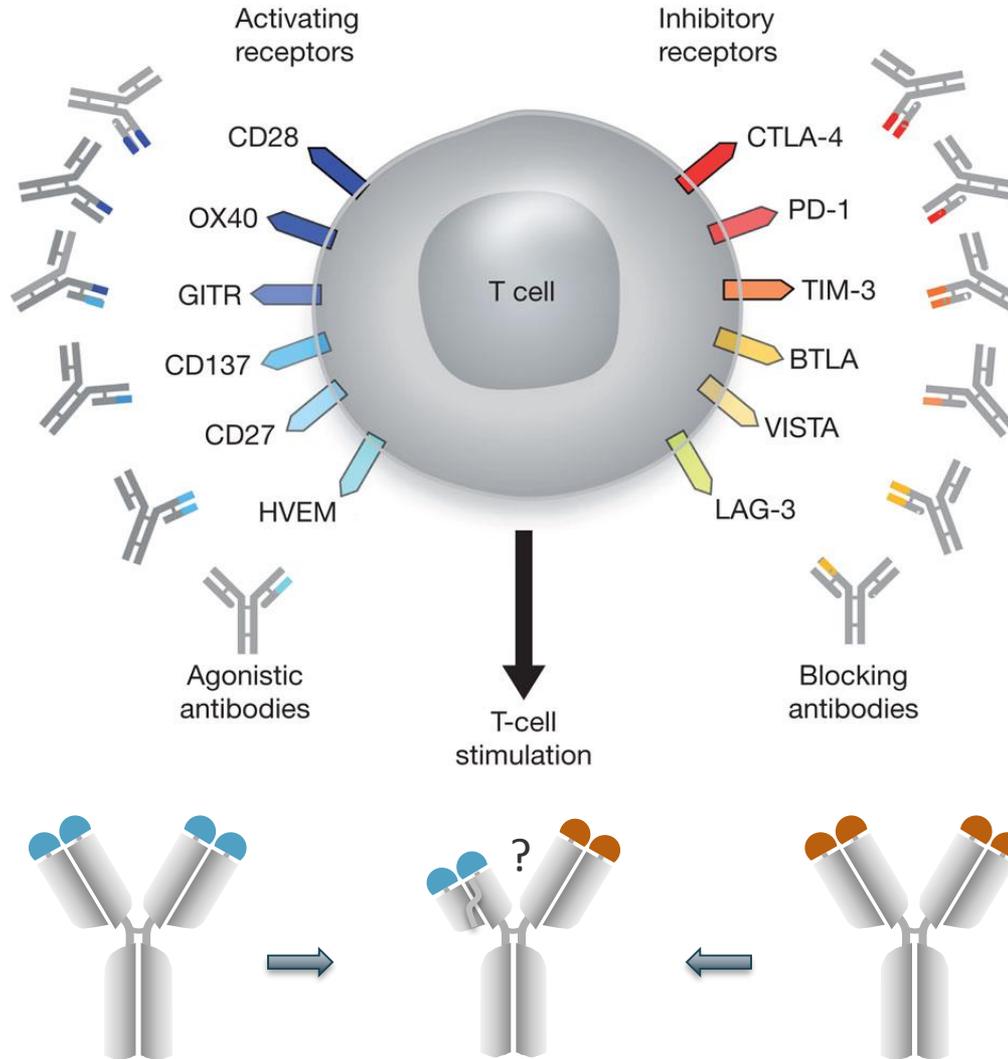
# Additional bispecific checkpoint combinations in lead optimization or screening



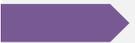
In vitro SEB stimulation assays (multiple donors), IL2 production



# Can checkpoint blockade and costimulation be productively combined in a bispecific antibody?



# Xencor's Growing Bispecific Oncology Pipeline to Enter Clinical Trials in 2016

Program (Target)	Fc Domain	Primary Indication	Discovery Lead	Preclinical	Phase 1	Commercial Rights
<b>XmAb14045</b> (CD123 x CD3)	Bispecific	AML			(2016)	 *
<b>XmAb13676</b> (CD20 x CD3)	Bispecific	B-cell cancer			(2016/17)	 *
<b>XmAb13551</b> (CD38 x CD3)	Bispecific	Myeloma				
<b>XmAb18087</b> (SSTR2 x CD3)	Bispecific	Oncology				
<b>XmAb20717</b> (PD1 x CTLA4)	Bispecific/ Xtend	Oncology				
<b>Undisclosed</b> CI x CI	Bispecific	Oncology				
<b>Undisclosed</b> (x CD3)	Bispecific	Oncology				
<b>Undisclosed</b> Immune Modulation	Bispecific	Oncology				

\* Novartis licensed ex-US commercial rights, worldwide co-development

- CD3 bispecifics to target T cells to tumors, entering clinic in 2016
- SSTR2 x CD3 IND mid-2017, followed by PD1 x CTLA4
- Scalable platform process for GMP manufacturing developed

# Antibodies by Design:

*XmAb<sup>®</sup> Antibody Therapeutics*

*Analyst Day Closing*

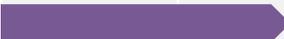
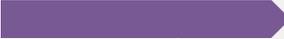
June 28, 2016



# Agenda Highlights

- Novartis collaboration
  - Ex-US commercial rights to XmAb14045 and XmAb13676 licensed, 50/50 development cost share worldwide
  - Access to bispecific platform for 4 Novartis programs; Fc platform access
  - \$150M upfront, \$2.41B milestones, royalties
- XmAb5871
  - Review of Phase 2 trials design in IgG4-Related Disease and Systemic Lupus Erythematosus
  - Review of mechanism and Phase 1 and 2a clinical data
  - Plan for XmAb5871 subcutaneous clinical trial in 3Q2016
- XmAb7195
  - Review of Phase 1a clinical data
  - Plan for XmAb7195 subcutaneous clinical trial in 4Q2016
- XmAb oncology bispecifics new programs
  - XmAb18087: SSTR2 x CD3 for neuroendocrine tumors, IND expected 2017
  - XmAb20717: PD-1 x CTLA-4 dual checkpoint inhibitor, IND expected 2017

# Xencor's Growing Bispecific Oncology Pipeline to Enter Clinical Trials in 2016

Program (Target)	Fc Domain	Primary Indication	Discovery Lead	Preclinical	Phase 1	Commercial Rights
<b>XmAb14045</b> (CD123 x CD3)	Bispecific	AML			(2016)	 xencor*
<b>XmAb13676</b> (CD20 x CD3)	Bispecific	B-cell cancer			(2016/17)	 xencor*
<b>XmAb13551</b> (CD38 x CD3)	Bispecific	Myeloma				 AMGEN
<b>XmAb18087</b> (SSTR2 x CD3)	Bispecific	Oncology				 xencor
<b>XmAb20717</b> (PD1 x CTLA4)	Bispecific/ Xtend	Oncology				 xencor
<b>Undisclosed</b> CI x CI	Bispecific	Oncology				 xencor
<b>Undisclosed</b> (x CD3)	Bispecific	Oncology				 xencor
<b>Undisclosed</b> Immune Modulation	Bispecific	Oncology				 xencor

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- CD3 bispecifics to target T cells to tumors, entering clinic in 2016
- SSTR2 x CD3 IND mid-2017, followed by PD1 x CTLA4
- Scalable platform process for GMP manufacturing developed

# Milestones and Goals 2015-2016

2015	
✓	XmAb7195 Phase 1a healthy volunteer IgE reduction data
✓	XmAb5871 Phase 1b/2a data in RA
✓	XmAb14045, anti-CD123 x CD3 GMP production
✓	XmAb13676, anti-CD20 x CD3 GMP production
	Additional partner milestones
✓	<ul style="list-style-type: none"> <li>• <i>Amgen research collaboration</i></li> </ul>
✓	<ul style="list-style-type: none"> <li>• <i>Janssen/CSL Phase 2</i></li> </ul>

2016	
✓	XmAb5871 clinical trial start IgG4-Related Disease
✓	XmAb5871 clinical trial start in SLE
✓	XmAb7195 Phase 1a complete data,
	XmAb7195 Phase 1 subcutaneous trial start
	XmAb14045 Phase 1 start in AML
	XmAb13676 Phase 1 start in B-cell cancer

Cash at March 31, 2016 \$178.7 million; \$150M upfront payment from Novartis