Xencor R&D Strategy Call

September 9, 2024

Today's Agenda

- Overview
- Rationale for bispecific antibodies in autoimmune & inflammatory diseases
- New pipeline programs: B-cell depleting T-cell engagers
  - Plamotamab (CD20 x CD3)
  - XmAb657 (CD19 x CD3)
- New pipeline programs: TL1A portfolio
  - XmAb942 (Xtend™ TL1A)
  - XmAb TL1A x IL-23
- Potential first-in-class T-Cell engagers in solid tumor oncology
  - XmAb819 (ENPP3 x CD3)
  - XmAb808 (B7-H3 x CD28)

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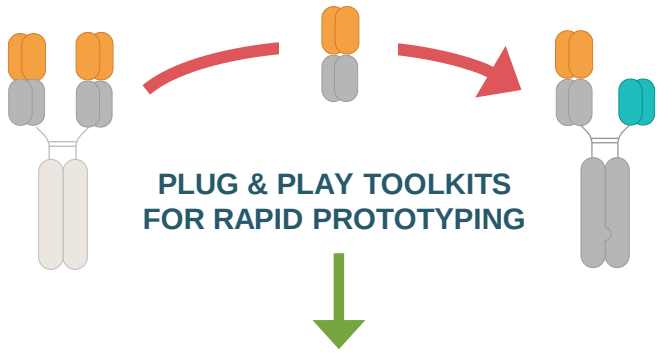
Proven Power of XmAb® Engineering: Proteins By Design®

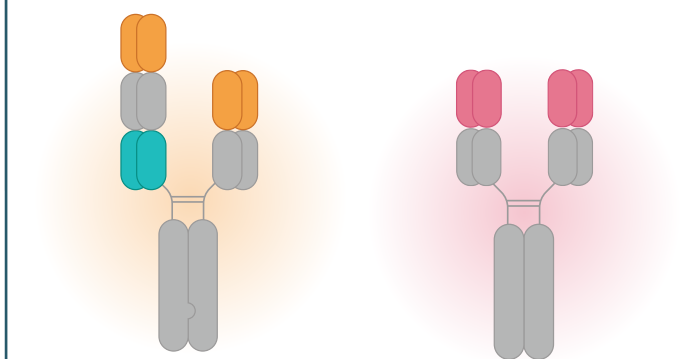
Small changes, big functional impacts

- XmAb Fc Domains augment native immune functions in molecules and/or control their structure, while preserving desired attributes
- XmAb engineered antibodies are designed to solve complex biologic problems
- Strong patent portfolio with over 1,600 patents issued and pending worldwide



Advancing an optimized portfolio of XmAb drug candidates

- **Oncology:** 3 novel TCEs advancing in Phase 1 studies; narrow focus for vudalimab in mCRPC and 1L NSCLC
- **Autoimmune**: Upcoming study initiation plans
  - 4Q'24: XmAb942 (Xtend™ TL1A)
  - 1H'25: Plamotamab (CD20xCD3) in RA
  - 2H'25: XmAb657 (CD19xCD3)



XmAb Bispecific T-cell Engagers (TCEs)

Xtend™ Antibodies with Potential Best-in-class Half-life Extension

Partnerships leverage modular XmAb technology

- More than 15 technology license partnerships greatly broadens scope with little-to-no effort
- Multiple commercialized XmAb antibodies

ULTOMIRIS® **MONJUVI®/MINJUVI®**

COLLABORATION PORTFOLIO INCLUDES

Johnson&Johnson Innovative Medicine · AMGEN · ALEXION AstraZeneca Rare Disease · Incyte · Genentech A Member of the Roche Group · GILEAD · VIR · astellas

Registered trademarks: Ultomiris® (Alexion Pharmaceuticals, Inc.), Monjuvi® & Minjuvi® (Incyte Holdings Corp.)

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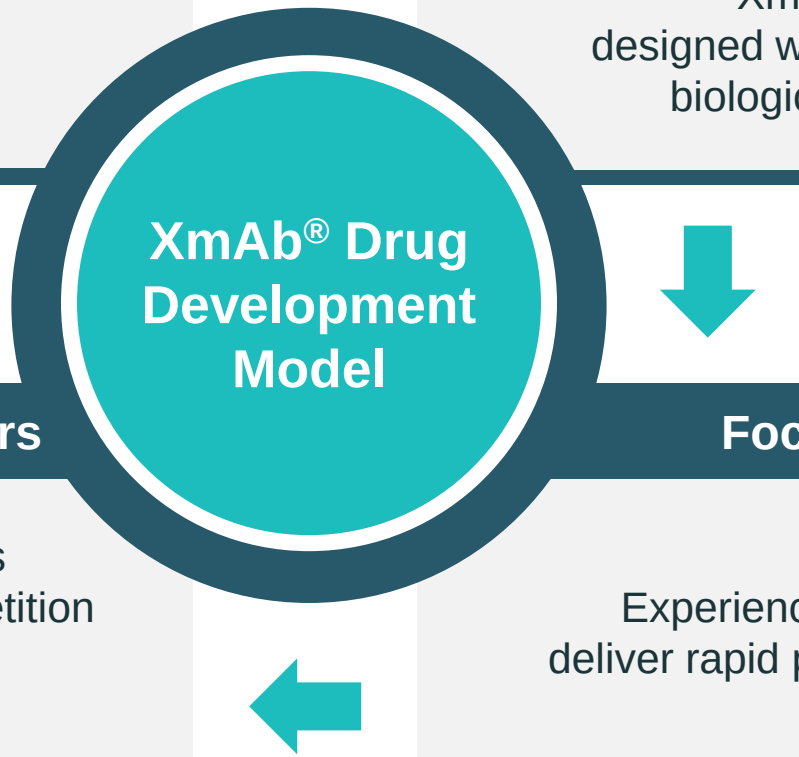
Xencor's Disciplined Drug Development Strategy

Validated Best-in-Class XmAb® Platforms

World-leading protein engineers and proven XmAb® Fc platforms, supported by strong financial position of $585.0* million

Optimally Engineered Novel Drug Candidates

Rapidly prototype and optimize XmAb® drug candidates, designed with purpose to solve complex biological engineering problems



Maximize Outcomes for All Stakeholders

Long-term potential benefit for patients through strict evaluation of data and competition to drive internal advancement towards commercialization or collaboration

Focused Clinical Execution

Experienced drug development team deliver rapid proof-of-concept clinical studies

* As of 6/30/2024. Includes cash, cash equivalents & marketable debt. Updated 8/5/2024.

Next-Gen XmAb® Drug Design in Oncology & Autoimmune Diseases

Pipeline focus on T-cell engagers and bispecific mechanisms

Program	Targets	XmAb® Platforms	Indications	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: T-cell Engagers (CD3 & CD28)								
XmAb819	ENPP3 x CD3	2+1 Bispecific	ccRCC					
XmAb808	B7-H3 x CD28	2+1 Bispecific, Xtend™	Prostate cancer, oncology			+ pembrolizumab		
XmAb541	CLDN6 x CD3	2+1 Bispecific, Xtend	Ovarian cancer, oncology					
XmAb Program	Undisclosed TCE	Bispecific, Xtend	Solid tumor oncology					
Solid Tumor Oncology: T-cell Selective, Dual Checkpoint Inhibitor								
Vudalimab	PD-1 x CTLA-4	Bispecific, Xtend	mCRPC			+/- chemotherapy		
			1L NSCLC			+ chemotherapy		
Immunology Programs								
Plamotamab	CD20 x CD3	Bispecific	Rheumatoid Arthritis				1H'25	
XmAb942	TL1A	Xtend, FcKO	Inflammatory Bowel Diseases (IBD)				4Q'24	
XmAb657	CD19 x CD3	2+1 Bispecific, Xtend	Autoimmune Diseases				2H'25	
XmAb Program	TL1A x IL23	Bispecific, Xtend	Autoimmune Diseases					

ccRCC clear cell renal cell carcinoma **NSCLC** non-small cell lung cancer
mCRPC metastatic castration-resistant prostate cancer **FcKO** Fc knock out

Key: Solid tumors | Immunology | Planned Study Initiation

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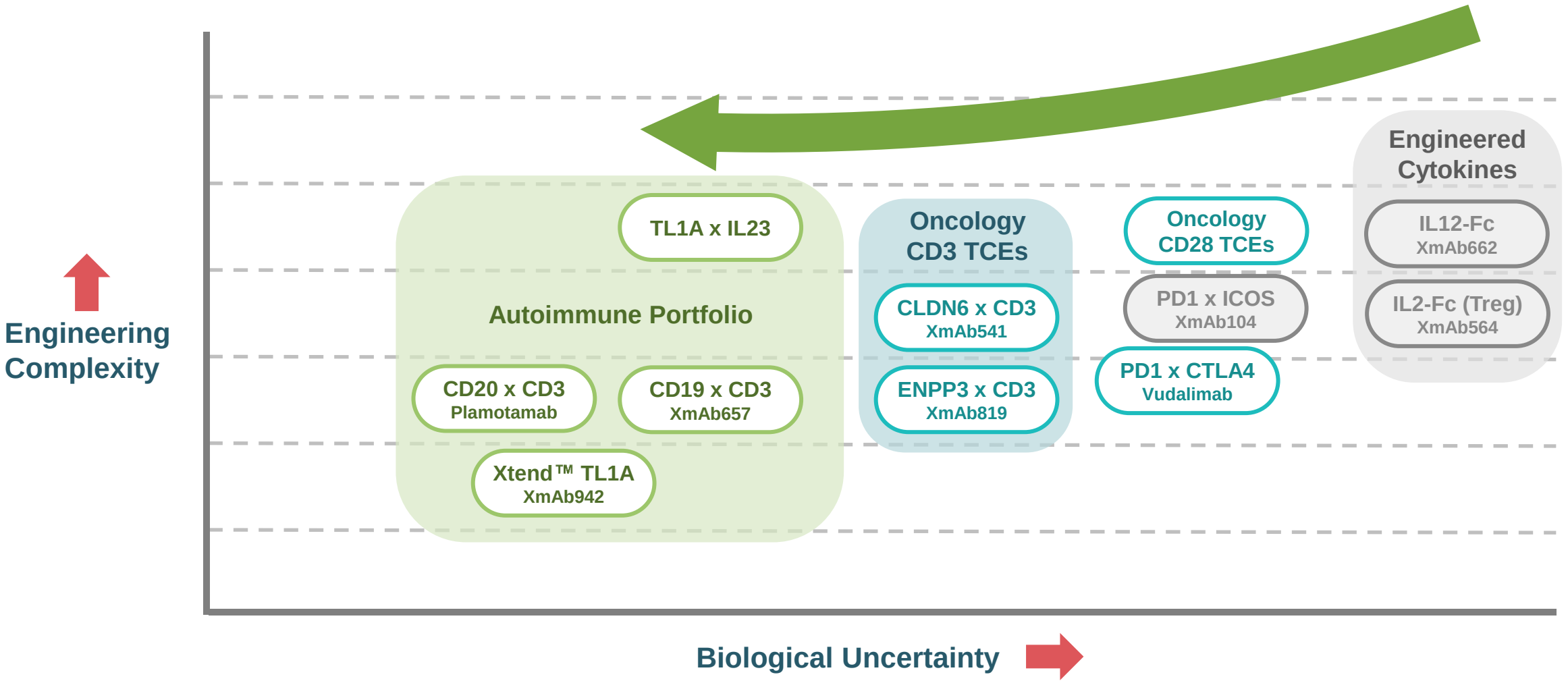
Rebalanced Portfolio Optimized for XmAb® Drug Development

Validated targets across autoimmune disease, leveraging XmAb engineering



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Rationale for bispecific antibodies in autoimmune and inflammatory (A&I) diseases

New Era Emerging for Bispecific Antibody Drug Development in Autoimmune and Inflammatory Diseases

SCIENTIFIC RATIONALE

Multiple related signaling pathways involved in A&I support dual inhibition (BsAbs) and depth of inhibition (TCEs)

PROOF OF CONCEPT

Recent clinical and academic studies have highlighted exciting clinical potential of both mechanisms

REGULATORY

Recent U.S. FDA insight encourages BsAb development[1] beyond oncology

MANUFACTURING

Efficient manufacturing process to produce one drug molecule versus multiple drugs in combination or cellular therapies

DOSING

Avoids complicated clinical dosing algorithms, with dual therapy and/or problematic co-formulation

ACCESS

More favorable formulary access for a single drug product versus multiple drugs used in combination

BsAb bispecific antibody **TCE** T-cell engager **1** "The agency has been encouraging drug development in this area. In 2021, FDA finalized a guidance on BsAb development programs." (U.S. FDA, 2024)

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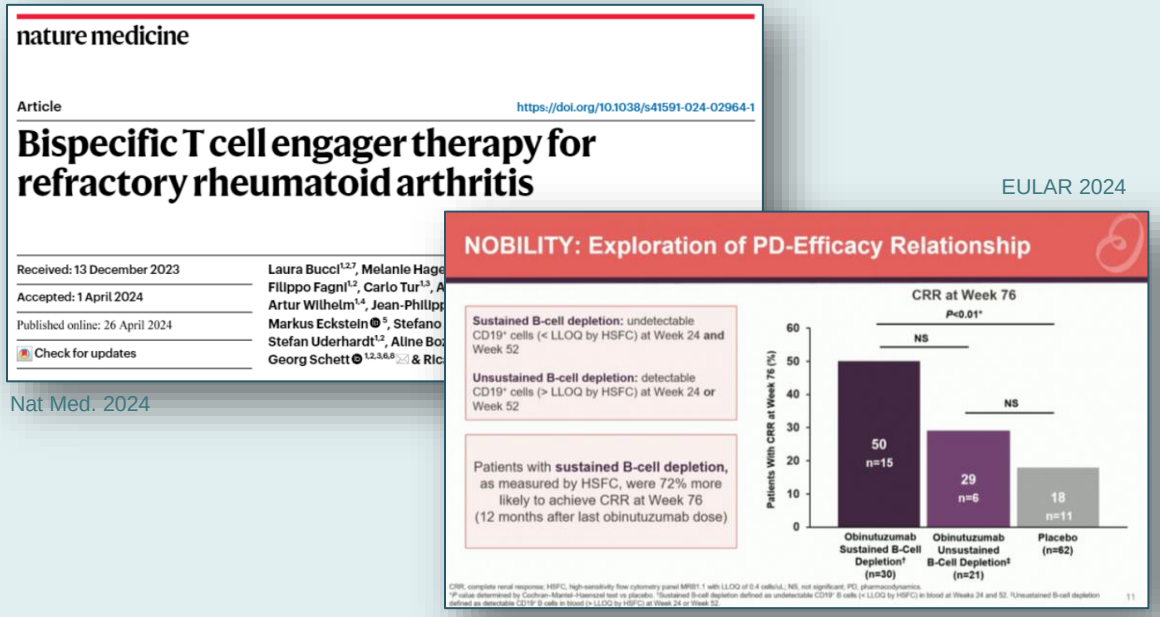
Well Validated Targets and Bispecific Antibody Formats Could Enable New Biology to Create Breakthrough Medicines

Newly published data shows potential for multiple types of bispecific antibodies in autoimmune disease

Highly potent B-cell depletion demonstrated promise for patients with severe rheumatic and inflammatory autoimmune disorders in small academic studies, and depth of B-cell depletion has been linked to better clinical outcomes in larger randomized controlled trials


nature medicine

Article

https://doi.org/10.1038/s41591-024-02964-1

Bispecific T cell engager therapy for refractory rheumatoid arthritis

Received: 13 December 2023

Accepted: 1 April 2024

Published online: 26 April 2024

Check for updates

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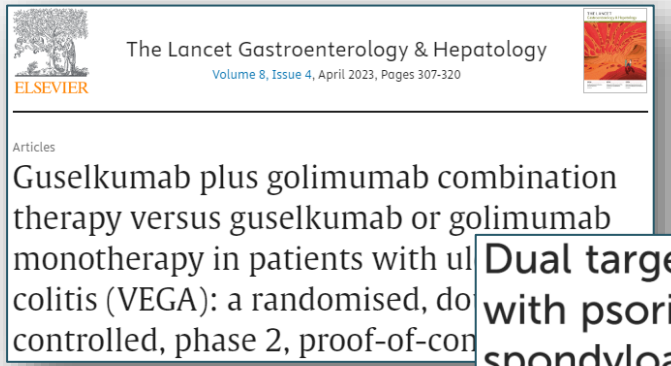
Artur Wilhelm[1,4], Jean-Philipp
Markus Eckstein[5], Stefano
Stefan Uderhardt[1,2], Aline Bo
Georg Schett[1,2,3,6,8] & Ric

Nat Med. 2024

EULAR 2024

Combination therapy using two approved antibodies showed additive efficacy in Phase 2 in colitis (Janssen) and new real-world multicenter studies


The Lancet Gastroenterology & Hepatology

Volume 8, Issue 4, April 2023, Pages 307-320

ELSEVIER

Articles

Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ul
colitis (VEGA): a randomised, do
controlled, phase 2, proof-of-con

Lancet Gastroenterol Hepatol. 2023

Front. Immunol. 2023


Dual targeted therapy in patients with psoriatic arthritis and spondyloarthritis: a real-world multicenter experience from Spain

Cristina Valero-Martínez[1], Judit Font Urgelles[2], Meritxell Sallés[3], Beatriz E. Joven-Ibáñez[4], Alexia de Juanes[4], Julio Ramírez[5], Xavier Juanola[6], Raquel Almodóvar[7], Ana Laiz[8], Mireia Moreno[9], Manel Pujol[10], Emma Beltrán[11], José Antonio Pinto-Tasende[12], Laura Crespí[13], Luis Sala-Icardo[14], Santos Castañeda[1,15] and Rosario García-Vicuña [1,16*]

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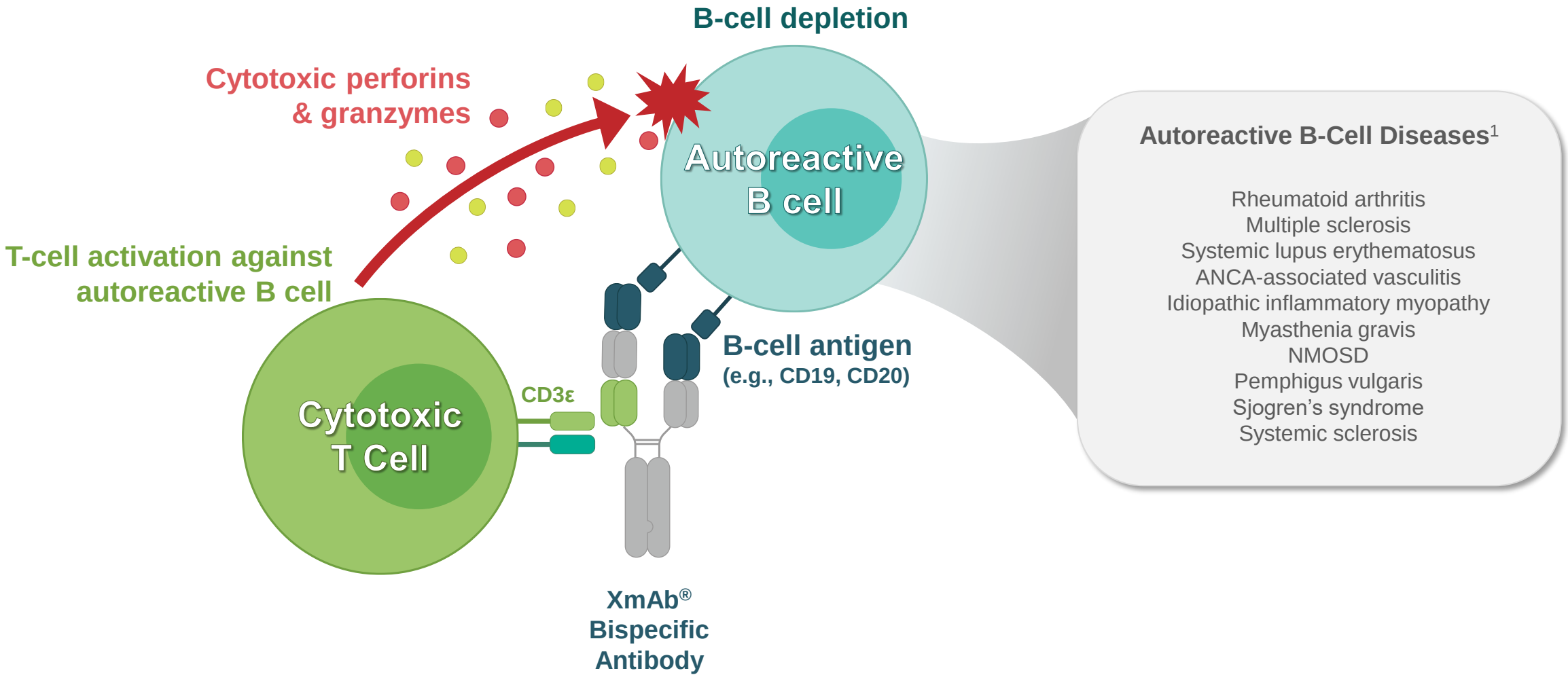
Deep B-Cell Depletion with T-cell Engagers Could Help "Reset" the Immune System for Patients with Autoimmune Disease



1 Schett G, et al. Ann Rheum Dis 2024;0:1-12.

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XmAb® CD20 & CD19 TCEs Can Address Significant Unmet Needs for Autoimmune Disease Responsive to Targeted B-Cell Depletion[1]

~2.2m
Patients with RA in US by 2030[2]

Currently >$20bn in annual disease modifying drug spend for treatment of rheumatoid arthritis within the US[12]

~1.1m
Patients with MS in US by 2030[3]

Ocrevus the market leader in US/EU5 with 24% global patient share, with >$5bn in US sales reported during 2023[12]

>200k
Patients with advanced SLE[4]

BENLYSTA US annual sales of >$1bn with high unmet need remaining for moderate-to-severe SLE[12]

>700k
Patients with other B-cell mediated diseases

B-cell depletion has demonstrated broad benefit across a wide-range of autoimmune diseases:

ANCA-associated vasculitis[5]
Idiopathic inflammatory myopathy[6]
Myasthenia gravis[7]
NMOSD[8]
Pemphigus vulgaris[9]
Sjogren's syndrome[10]
Systemic sclerosis[11]

1 Based on randomized controlled trials with positive primary endpoints (Schett G, et al. Ann Rheum Dis 2024;0:1–12. **2** J Manag Care Spec Pharm. 2018; 24(10):1010-1017. **3** JAMA Neurol. 2023; 80(7):693-701. **4** Arthritis Rheumatol. 2021 Jun; 73(6): 991–996. **5** J Clin Med. 2022;11(9):2573. **6** BMC Musculoskelet Disord. 2012; 13: 103. **7** Front Neurol. 2024; 15:1339167. **8** Mult Scler. 2024; 13524585231224683. **9** JAMA Dermatol. 2019; 155(5): 627-629. **10** Arthritis Care Res (Hoboken). 2017; 69(10):1612-1616. **11** J Manag Care Spec Pharm. 2020 Dec;26(12):1539-1547. **12** GlobalData.

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Rheumatoid Arthritis: Where are we and where do we need to go?

Roy Fleischmann, MD MACR

Adjunct Professor of Medicine
University of Texas Southwestern Medical Center

Medical Director, Metroplex Clinical Research Center
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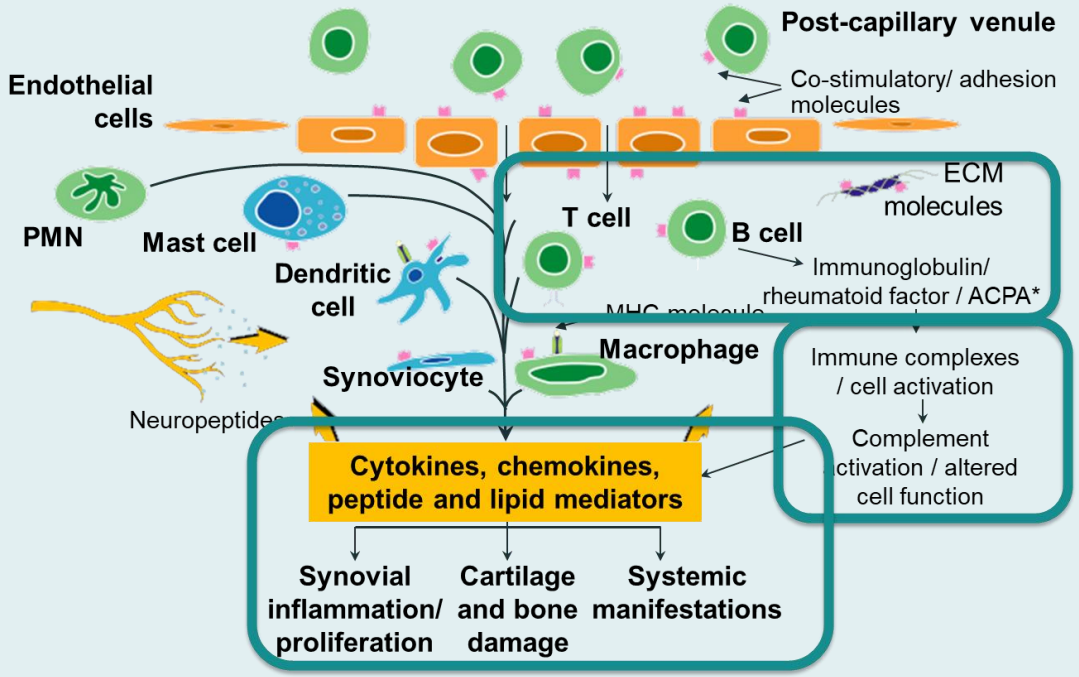
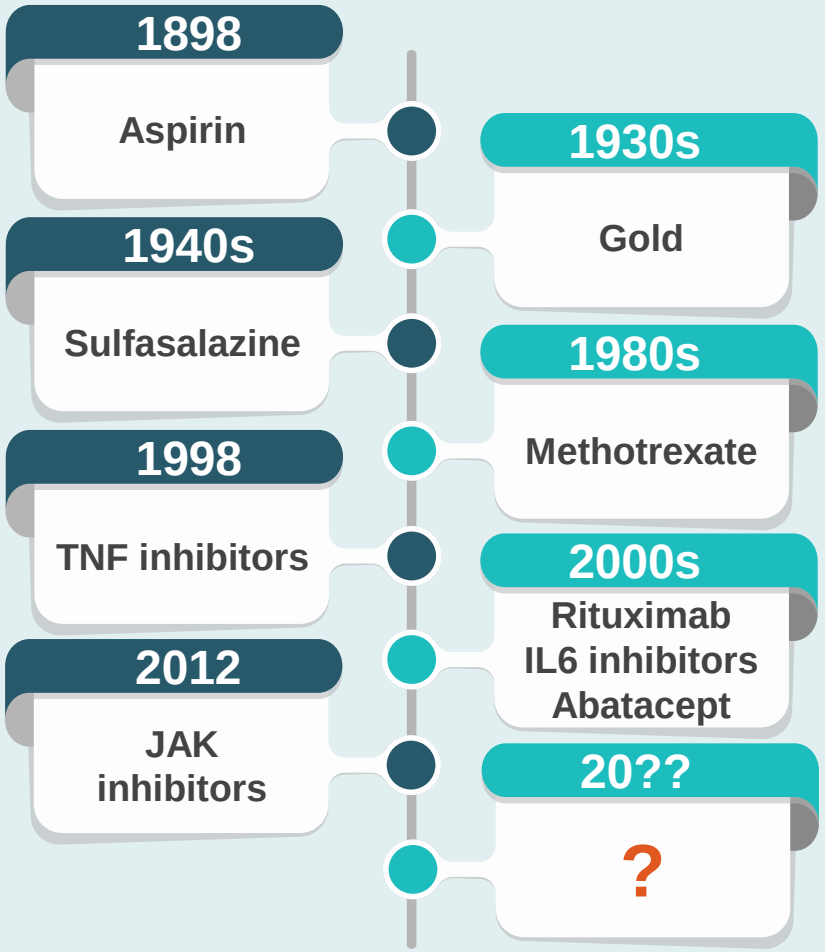
Immunopathogenesis of Rheumatoid Arthritis





New MoA PD-1? New JAK inhibitors?
Molecular Degraders? CAR-Ts?
T-Cell Engagers?

*ACPA = anti-citrullinated protein antibody. Detected as anti-CCP Ab. Citrulline is a post-translational modification of arginine, e.g. at inflammatory sites

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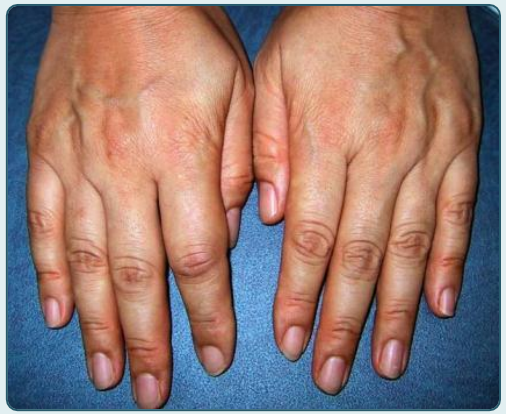
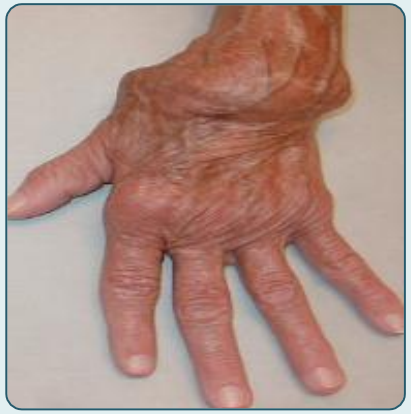
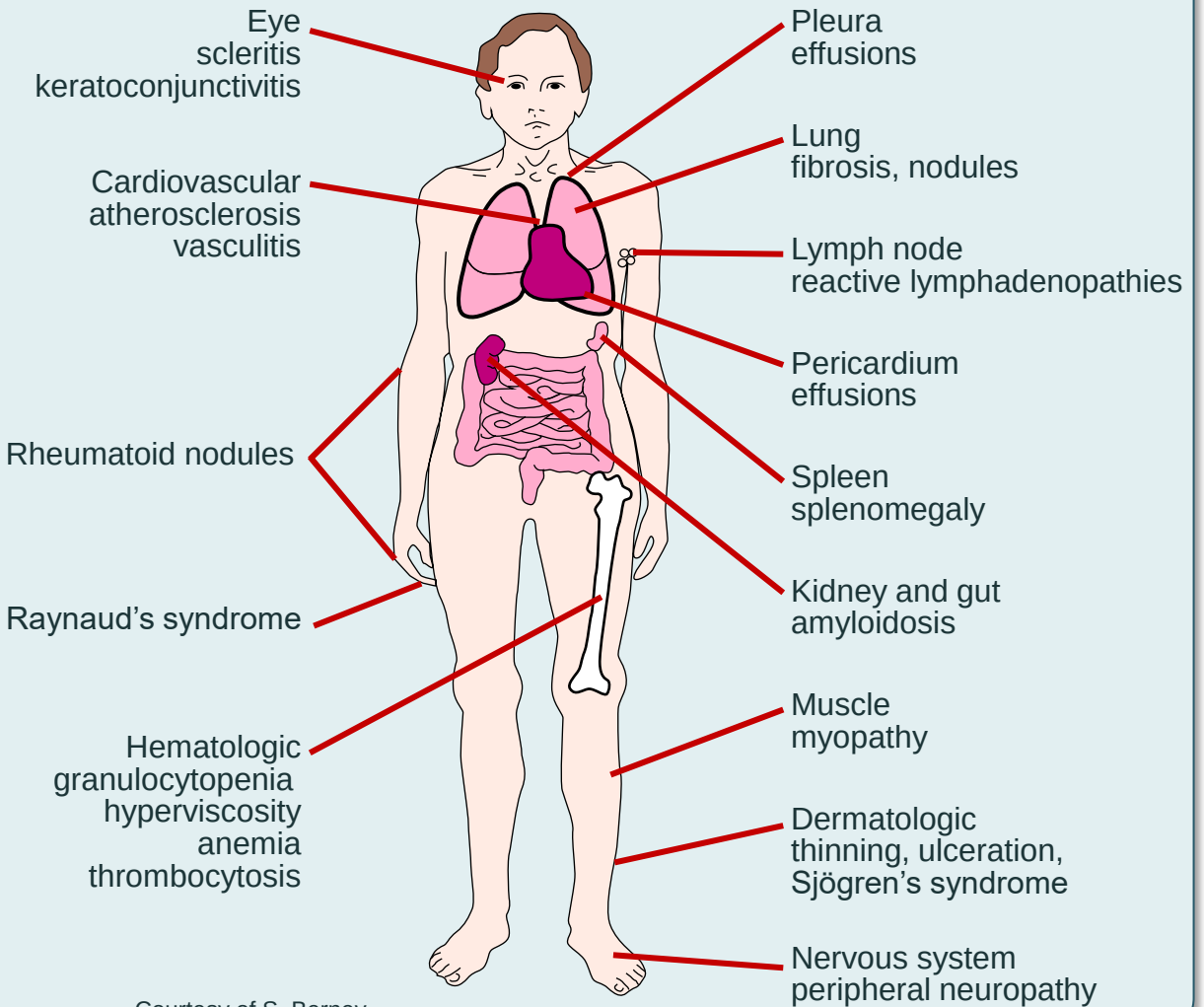
Rheumatoid Arthritis Manifestations

- Systemic, inflammatory polyarthritis that leads to joint destruction, deformity, and loss of function.
- Pathology involves synovial membranes and peri-articular structures of joints, typically resulting in uncontrolled inflammation with pannus formation and clinical symptoms of pain, swelling and stiffness which may lead to irreversible damage and deformity with functional limitation.







Courtesy of S. Berney

ACR Subcommittee on RA Guidelines. Arthritis Rheum. 2002;46:328; Goronzy JJ, Weyand CM. In: Klippel JH, et al, eds. Primer on the Rheumatic Diseases 2001; 12th ed. Atlanta, GA: Arthritis Foundation; 2001. p 209-16. Anderson RJ. ibid. 218; Arnett FC, et al. Arthritis Rheum. 1988;31:315

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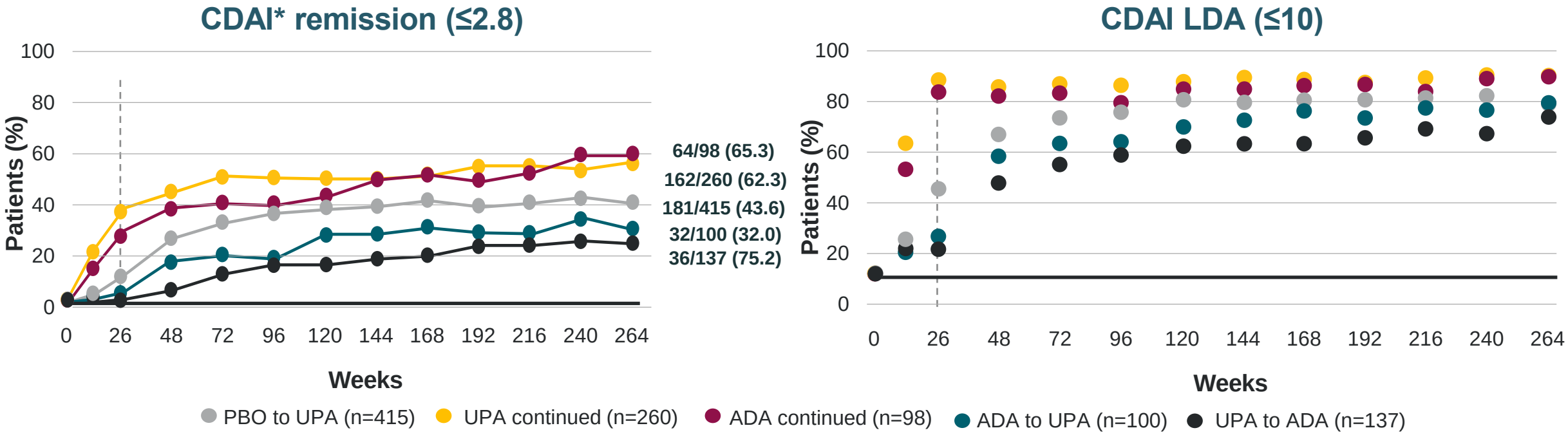
Even with the Most Effective Medications, 40% of RA Patients Do Not Reach Remission Even If They Continue with the Medication (AO)



What degree of disease activity can be reached with effective medications for RA?

SELECT-COMPARE: UPA + MTX vs ADA + MTX. Vertical line at Week 26 indicates the end of the PBO-controlled period. **AO** As Observed **PBO** placebo **UPA** Upadacitinib **ADA** adalimumab **CDAI** Clinical Disease Activity Index **LDA** low disease activity * CDAI remission is a stricter clinical metric than DAS28. Fleischmann R et al. EULAR 2023. Poster POS0849.

Consequences of Inadequately Treated RA

Cardiovascular Disease (CVD)

RA patients have an increased risk of CV events[1,2]. Risk of CVD death 50% higher vs. general population, which correlates with CV risk factors and inflammation[3,4]. DMARDs reduce CV event risk[5,6] if disease activity reduced[7].

Serious Infection (SIE)

RA is associated with a 2-fold increased risk of SIE, thought to be due to defective immune system and comorbidities such as diabetes, pulmonary or renal disease and functional disability[8]. TNFα inhibitors increase the risk 2-fold and glucocorticoids 4-fold.

Venous and Pulmonary Thrombosis

Active RA is associated with a > 2-fold increase in the development of deep venous thrombosis and pulmonary embolus compared to the general population[9].

Lymphoma

Severe disease activity in RA patients is correlated with a 70-fold increased risk of developing malignant lymphomas, particularly diffuse large B cell lymphoma[10].

1 Avina-Zubieta JA, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum 2008;59:1690-7. **2** Solomon DH, et al. Cardiovascular morbidity and mortality in women diagnosed with rheumatoid arthritis. Circulation 2003; 107:1303-7. **3** Del Rincon I, et al. Escalante A. Association between carotid atherosclerosis and markers of inflammation in rheumatoid arthritis patients and healthy subjects. Arthritis Rheum 2002;48:1833-40. **4** Myasoedova E, et al. Lipid paradox in rheumatoid arthritis: the impact of serum lipid measures and systemic inflammation on the risk of cardiovascular disease. Ann Rheum Dis 2011;70:482-7. **5** Micha R, et al. Systematic review and metaanalysis of methotrexate use and risk of cardiovascular disease. Am J Cardiol 2011;108:1362-70. **6** Barnabe C, et al. Systematic review and metaanalysis: anti-tumor necrosis factor a therapy and cardiovascular events in rheumatoid arthritis. Arthritis Care Res (Hoboken) 2011;63:522-9. **7** Solomon DH, et al, Disease Activity in Rheumatoid Arthritis and the Risk of Cardiovascular Events. Arthritis and Rheumatology. Vol. 67, No. 6, June 2015, pp 1449-55. **8** Listing J, et al. Rheumatology, 2013 52(1): 53-61. **9** Choi HK, et al. Ann Rheum Dis 2013;72:1182-87. **10** Baecklund E, et al. Arthritis Rheum 2006;54:692-701.

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Unmet Needs in the Treatment of RA

Current Landscape

- **~ 1,300,000** patients with RA in the US[2]

~15-18% **of patients do not respond adequately or are unable to tolerate the currently approved medications[1]**

- This means that ~ **200,000 - 230,000** patients in the U.S. alone require new therapeutic options
- We do not have the necessary tools to predetermine which patient will have a complete clinical response without adverse events to a specific mechanism or action or specific molecule.

Trends

Survey of 25 rheumatologists[1]: What do they suspect will be the significant changes over the next 5 years in the treatment of RA?

- Convinced that bDMARDs and Jakinibs should be initiated earlier
- Emerging novel MoA offering improved efficacy, safety and tolerability
- Novel B-cell depleting therapies, CAR-T cell therapy, combination biologics, and more targeted, effective treatment options

1 Xencor survey of investigators **2** Helmick and Lawrence et al; Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. Arthritis Rheum. 2008;58(1):15-25

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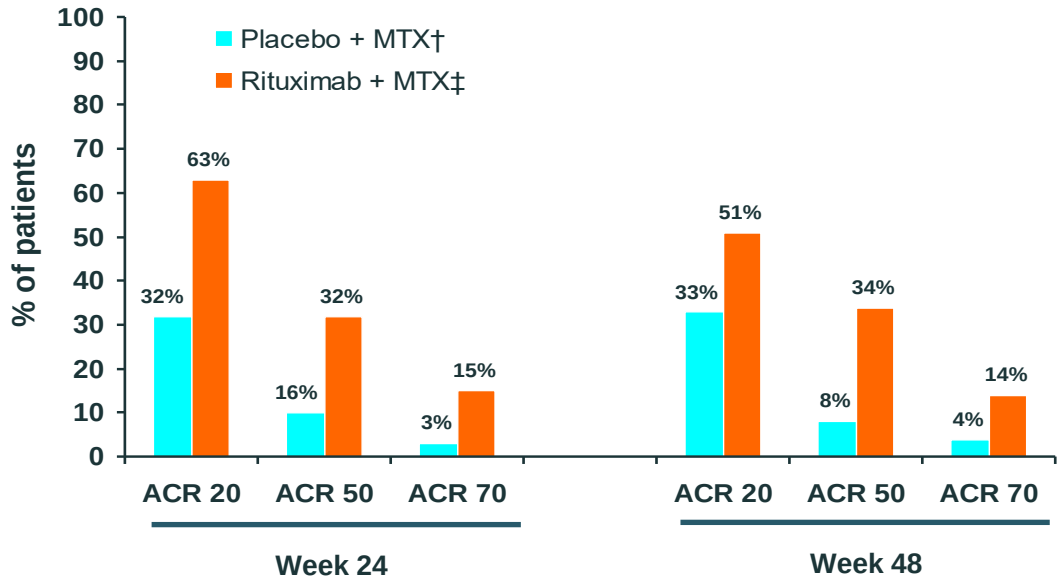
Clinical Experience of Rituximab in RA

A



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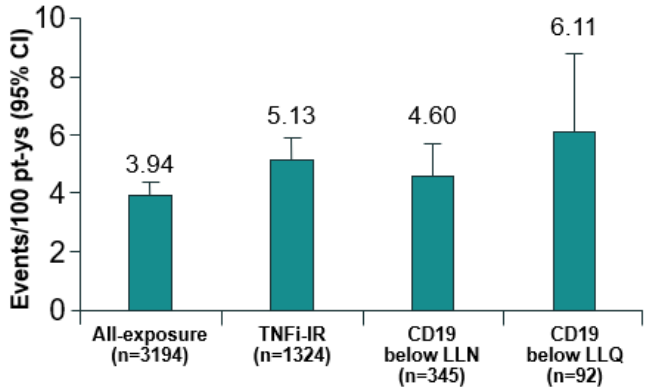

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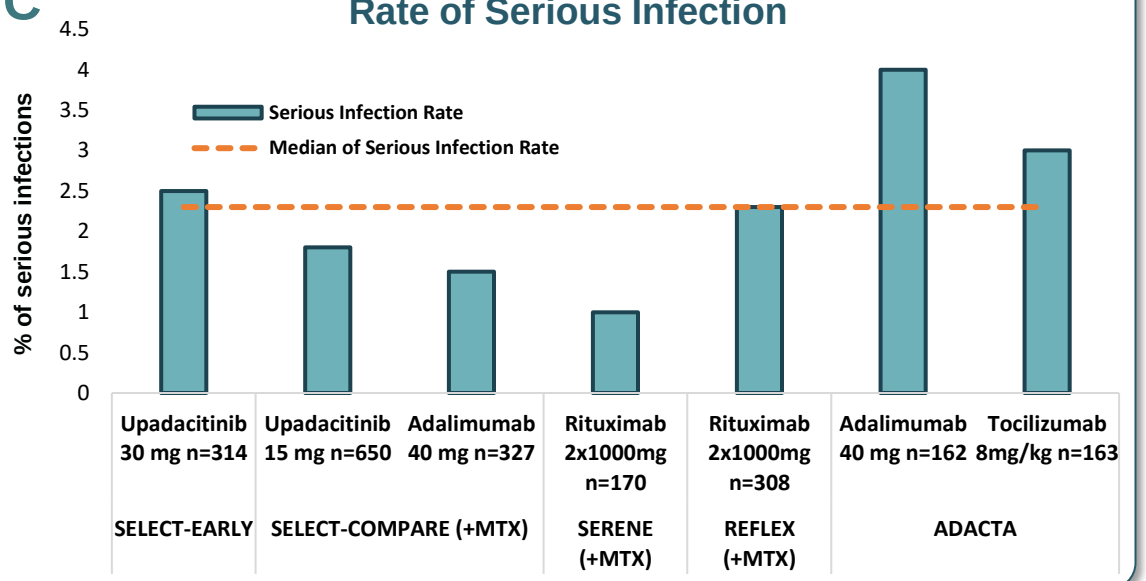

A REFLEX Study; Cohen S, et al. 2006 Arthritis Rheum 54(9): 2793-2806B) TNF-IR: TNF inhibitors Inadequate Responders; **B** Patients with up to 9.5 years of follow-up analyzed ≥2 years after any RTX treatment for limited return (LLN; <80 cells/μL) of CD19 B cells and CD19 cell counts below lower limit of quantification (LLQ; <20 cells/μL). CD19 cell counts were measured from peripheral blood; No measurements from other tissue compartments reported; van Vollenhoven, R.et al. 2015 J. Rheum. 42(10):1761-1766 **C** Cross-trial comparison of serious infection rates (24-week endpoint except for SELECT-COMPARE: 26 weeks).

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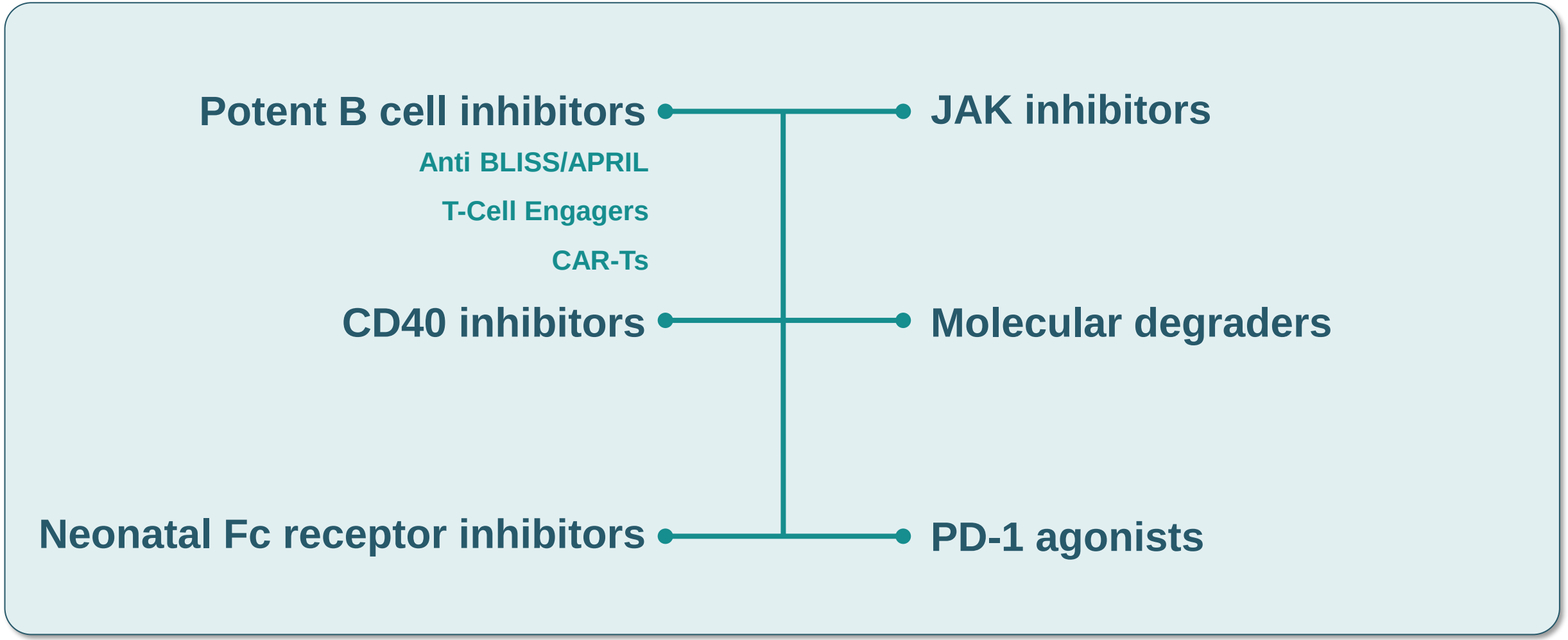
New Therapies on the Horizon in RA



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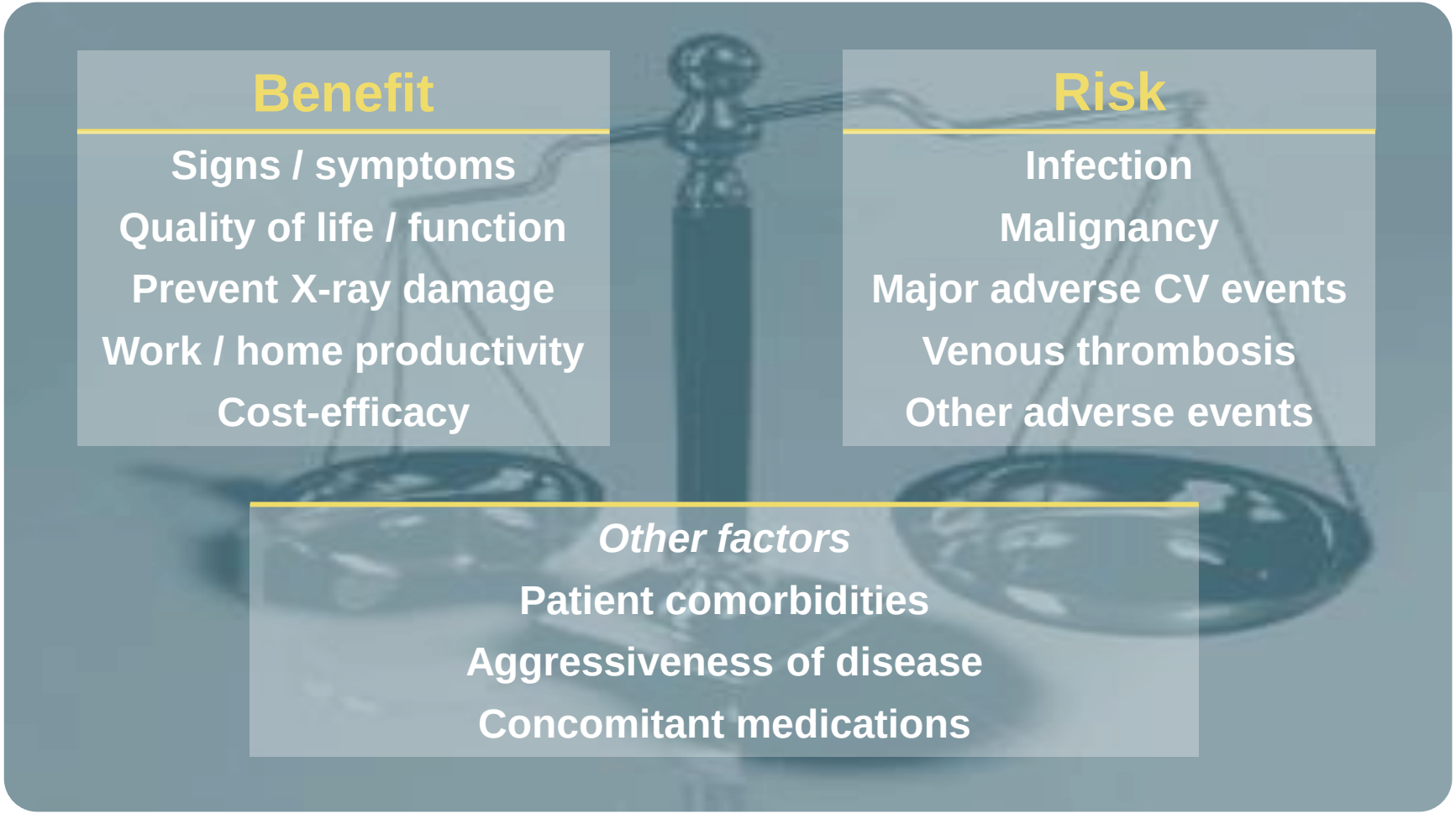
A Highly Effective Medication with a Risk Profile That Can Be Mitigated, Has a Very Favorable Benefit/Risk Profile for Patients with Rheumatoid Arthritis



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New Pipeline Programs:
B-cell Depleting T-cell Engagers

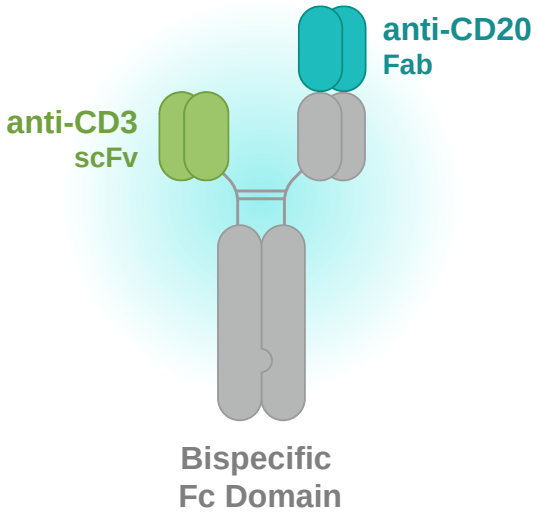
Plamotamab (CD20 x CD3)

XmAb657 (CD19 x CD3)

Plamotamab
Phase 2 Ready, Subcutaneous CD20 x CD3 BsAb

Planned proof-of-concept for the T-cell engager class in autoimmune and inflammatory disease

XmAb® CD20 x CD3 Bispecific Design



- Plamotamab designed in a 1+1 format and selected for extended activity and favorable tolerability observed in NHPs
- Human half-life ~18 days; estimated 80% SC bioavailability
- Robust manufacturing process with high yield and excellent formulation stability data

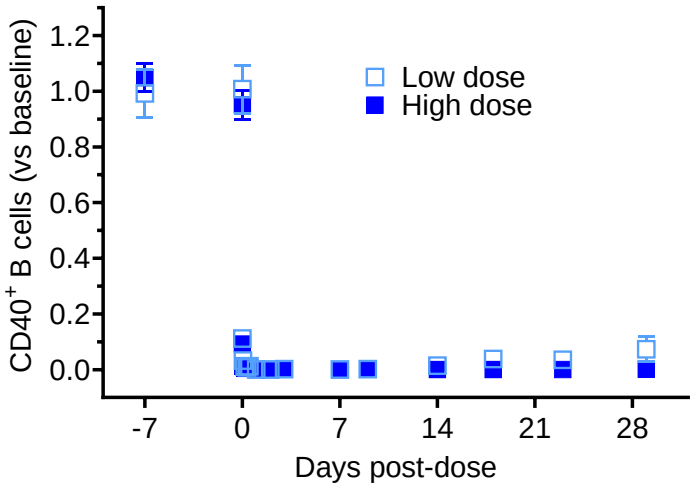
Positioned for Success

- N=154 from dose escalation and expansion cohorts with both IV and SC formulations in B-cell cancers
- Comparable preliminary efficacy data to leading commercial CD20 x CD3 in patients with prior CAR-T
- IV & SC dosing regimens with improved CRS data vs. leading commercial CD20 x CD3[1]
- Existing inventories of drug product and drug substance for seamless integration into the next phase of clinical development

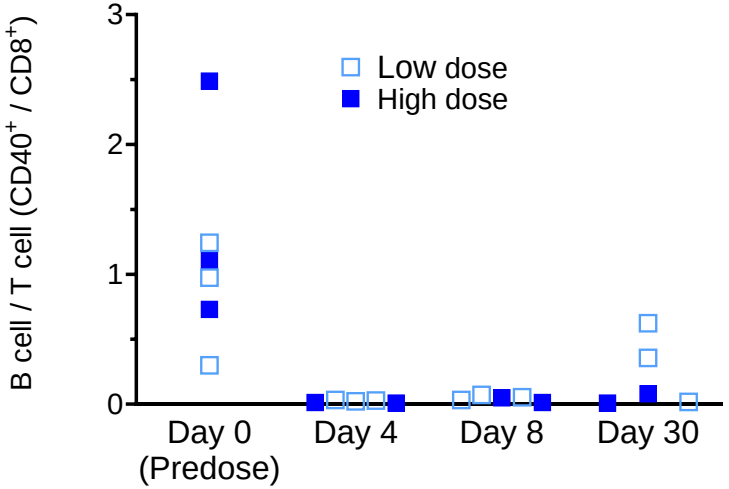
BsAb bispecific antibody **IV** intravenous, **SC** subcutaneous **NHP** non-human primate **CRS** cytokine release syndrome **1** No head-to-head trial has been conducted evaluating plamotamab against other data included herein. Differences exist between clinical trial design, patient populations and the product candidates themselves, and caution should be exercised when comparing data across trials.

Single Dose of Plamotamab in NHPs
Durable B-cell Depletion Observed in Blood and Lymphoid Organs

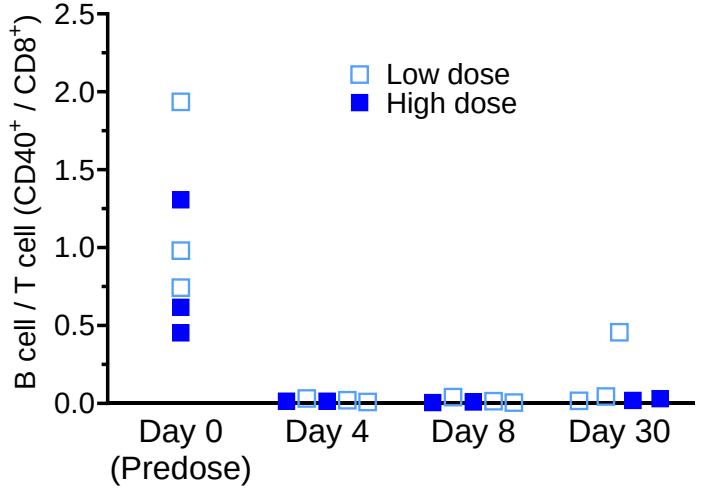
Blood B cells



Bone marrow B cells



Lymph node B cells



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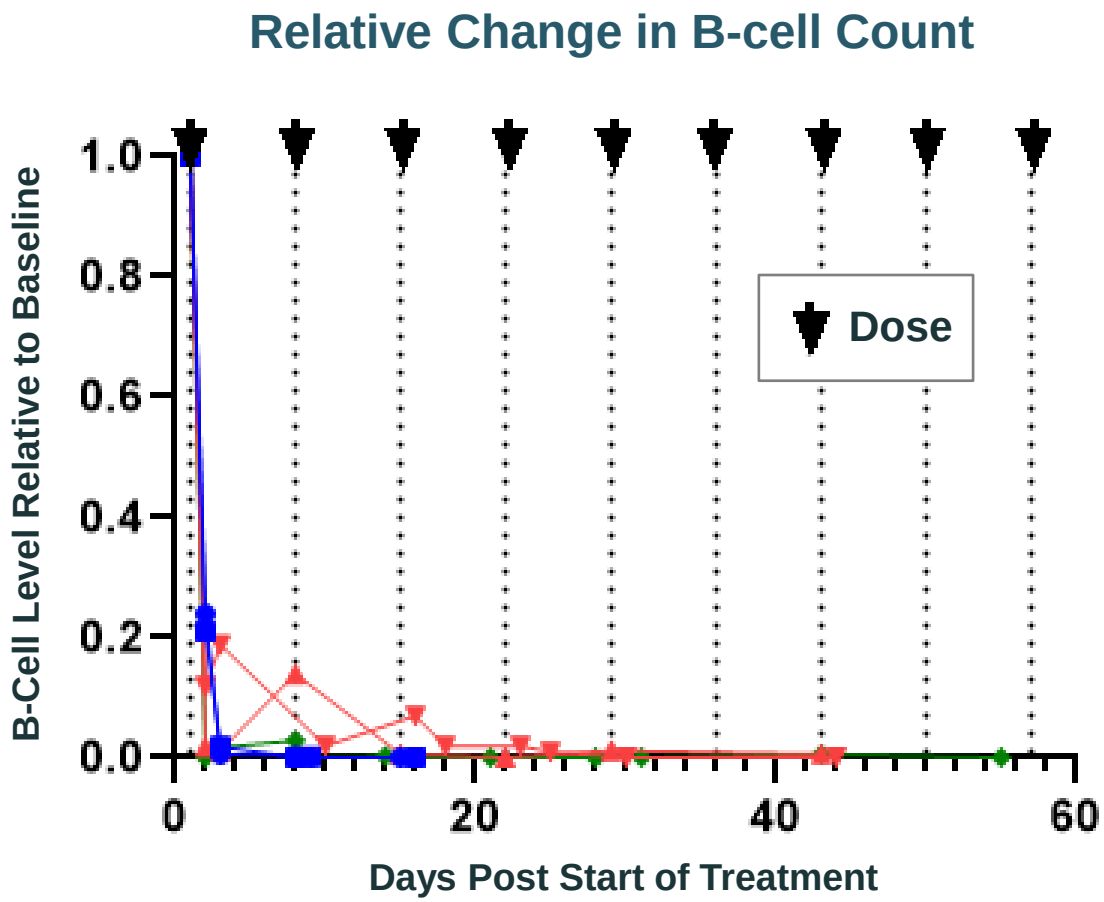
>95-99% Peripheral B-cell Depletion Observed in Lymphoma Patients with IV & SC Plamotamab in Phase 1 Monotherapy Study

- Patients were identified (N=5) that had baseline absolute B-cell count > 30 cells/µL in the blood
- >90% reductions in B-cell count also observed at lower doses



Phase 1 Monotherapy Study of Plamotamab

Heavily Pre-Treated Population with High Rates of Prior CAR-T

DLBCL + HGBCL Patient Characteristics

Characteristics		RD (IV) (n = 35)	SC all cohorts (n = 20)
Age, median (range)		69 (36-86)	67 (27-90)
Baseline ECOG	0, n (%)	13 (37.1)	7 (35.0)
	1	19 (54.3)	13 (65.0)
	2	3 (8.6)	0
Bulky disease at study entry, n (%)			
> 6 cm		10 (28.6)	5 (25.0)
> 10 cm		5 (14.3)	0
Median number of prior systemic therapies		**4.0 (2-11)**	**4.0 (2-10)**
Refractory to last therapy, n (%)		**25 (71.4)**	**10 (50.0)**
Prior transplantation, n (%)		**3 (8.6)**	**4 (20.0)**
Prior CAR-T, n (%)		**21 (60.0)**	**17 (85.0)**

RD (IV) recommended IV dose **DLBCL** diffuse large B-cell lymphoma **HGBCL** high-grade B-cell lymphoma **ECOG** Eastern Cooperative Oncology Group

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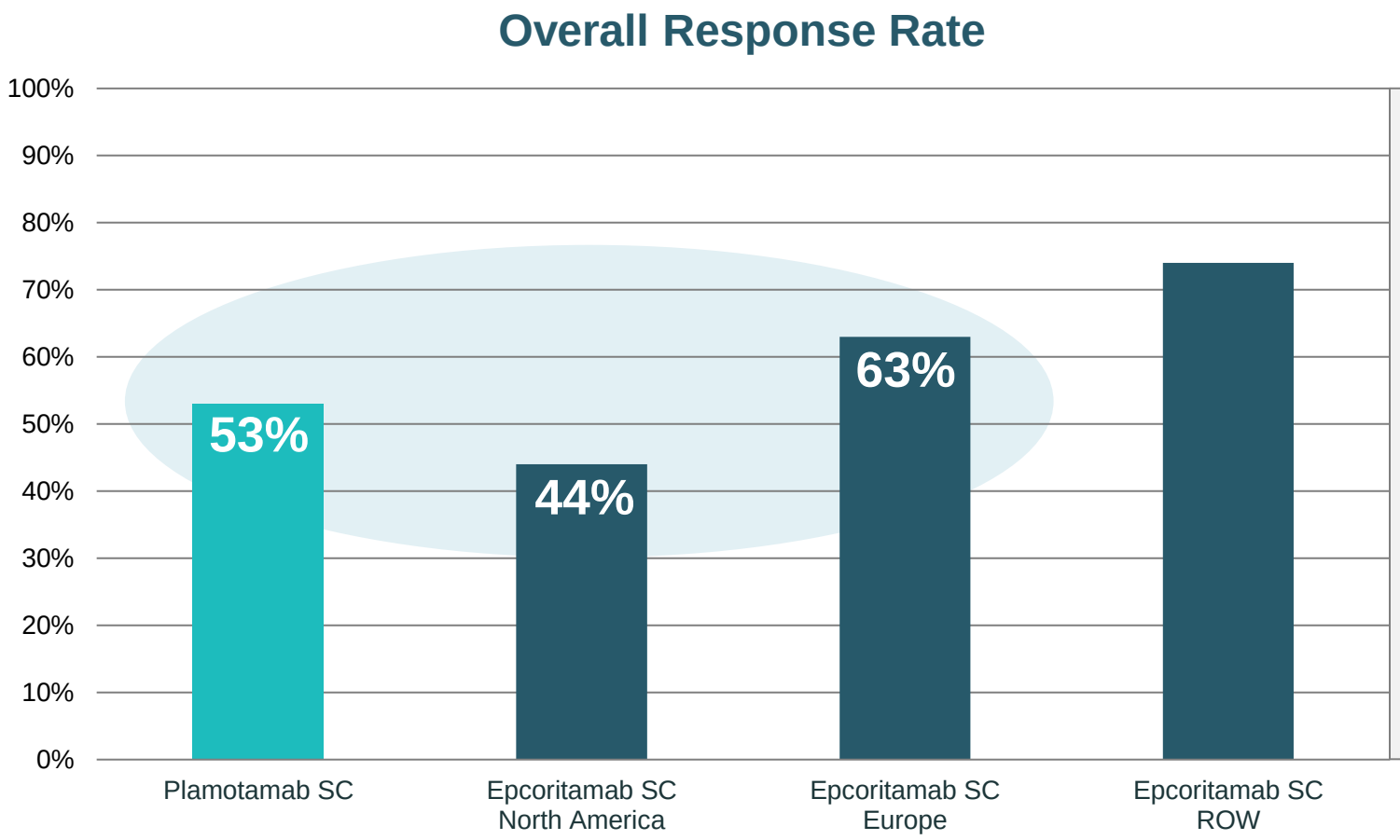
Plamotamab ORR Compared to Commercial CD20 x CD3[1]

Regional differences in lymphoma prior therapy markedly impact outcomes



Phase 1/2 expansion cohort of epcoritamab reported high variance in overall response rates (ORR) associated by treatment geography, with a significantly lower 44% ORR reported for North America due to high utilization of CAR-T (noted by study investigators), as compared to 62.7% ORR in Europe and 73.5% ORR in the rest of the world (ROW).[2]

Note: Plamotamab geographic enrollment distribution for the subcutaneous (SC) dosing cohort (n=17): 76.5% North America and 23.5% Europe.

1 No head-to-head clinical trial has been conducted evaluating plamotamab against epcoritamab. Differences exist between trial design and patient populations, and caution should be exercised when comparing data across unrelated trials. **2** Thieblemont and Lugtenburg et al.; J Clin Oncol 41:2238-2247.

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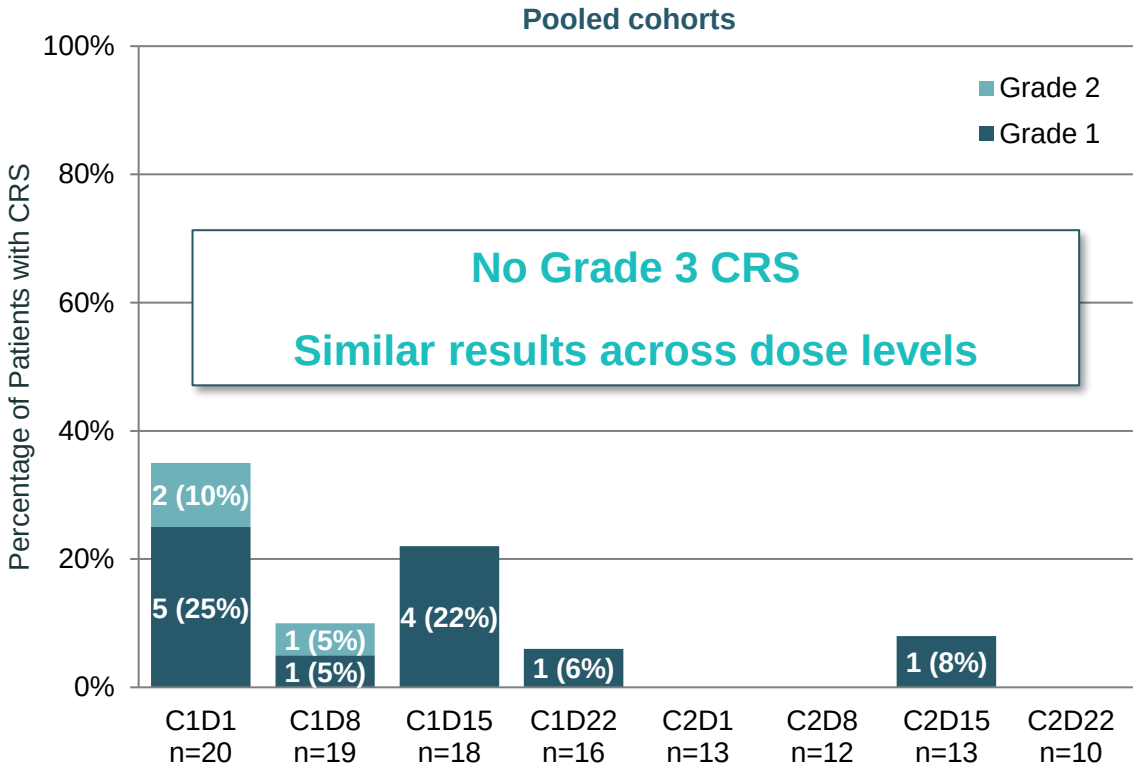
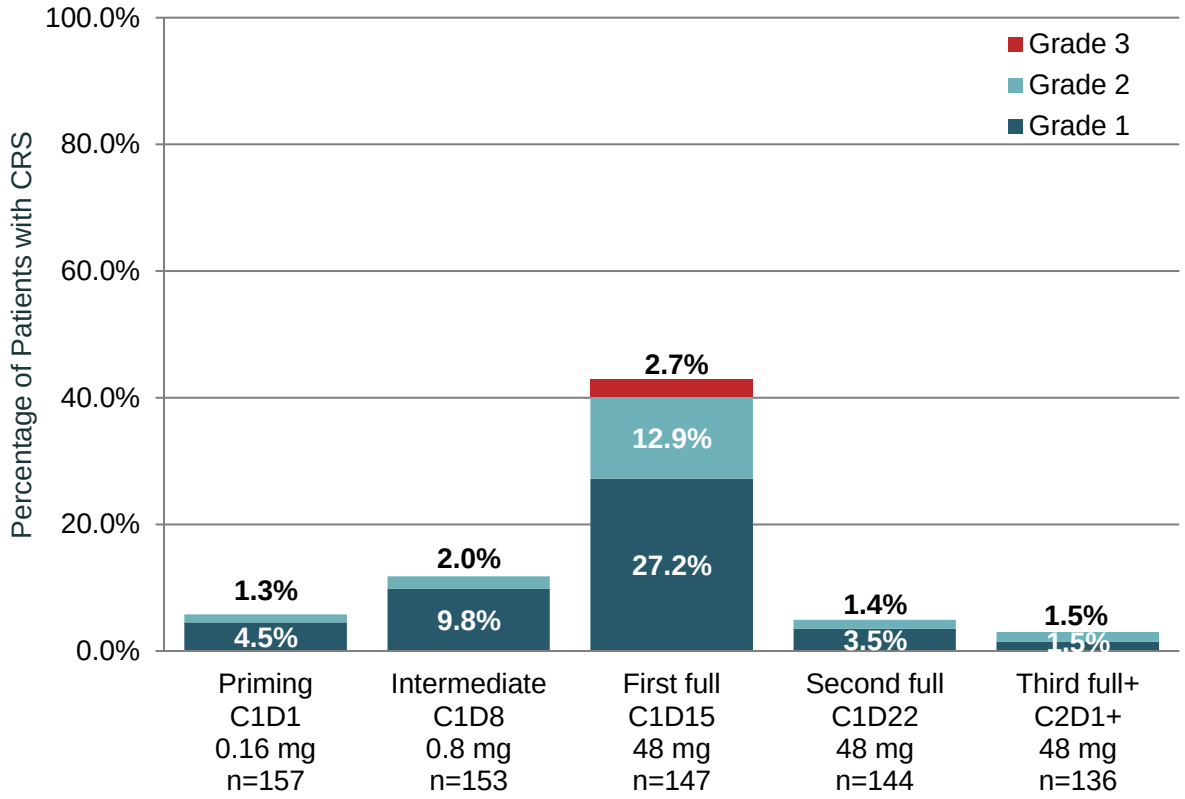
No Grade 3 CRS and Lower Grade CRS Observed, Compared to Commercial CD20 x CD3[1]

Plamotamab SC CRS



Epcoritamab SC CRS[2]



Summary of CRS at Recommended IV Dose regimen: < 50% incidence overall, no Grade 3, Cycle 1 limited

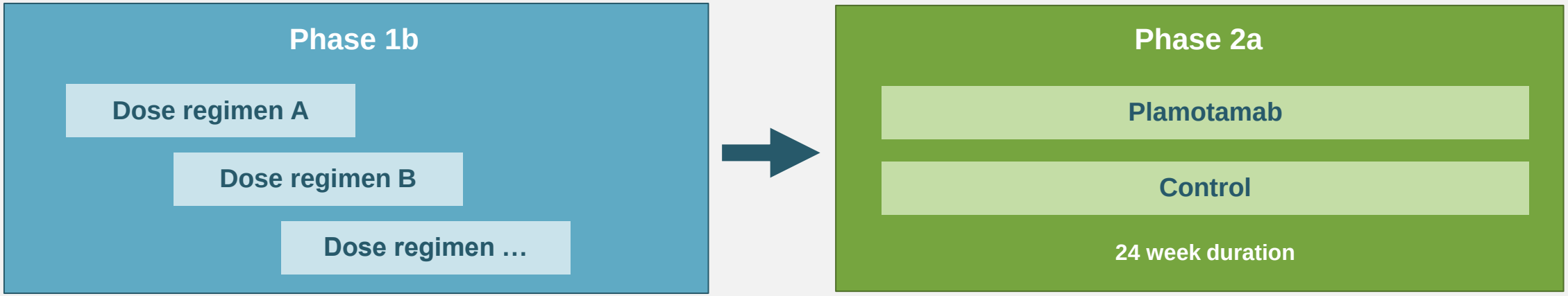
1 No head-to-head clinical trial has been conducted evaluating plamotamab against epcoritamab. Differences exist between trial design and patient populations, and caution should be exercised when comparing data across unrelated trials. **2** Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial; Thieblemont and Lugtenburg et al.; J Clin Oncol 41:2238-2247. Data cutoff: January 31, 2022.

Plamotamab: Plan for Phase 1b/2a Rheumatoid Arthritis Study Start

Maximal efficiency to clinical proof of concept in multi-drug resistant rheumatoid arthritis (MDR-RA)

Phase 1b/2a Study Initiation Planned for 1H'25

Single 1b/2a study for seamless transition to randomized proof-of-concept trial



- Quickly refine priming/step-up dosing regimens used in lymphoma studies
- Assess SC and IV routes, and pre-medication regimen including corticosteroids, to be run in parallel on a staggered start
- Assess safety, biomarkers, initial efficacy in RA patients

- Advance selected dosing regimen into placebo-controlled trial in MDR-RA patients
- Single-cycle dosing in line with other B-cell depleting agents
- 24-week efficacy endpoint with interim efficacy analysis at week 12 with paired biomarker assessment

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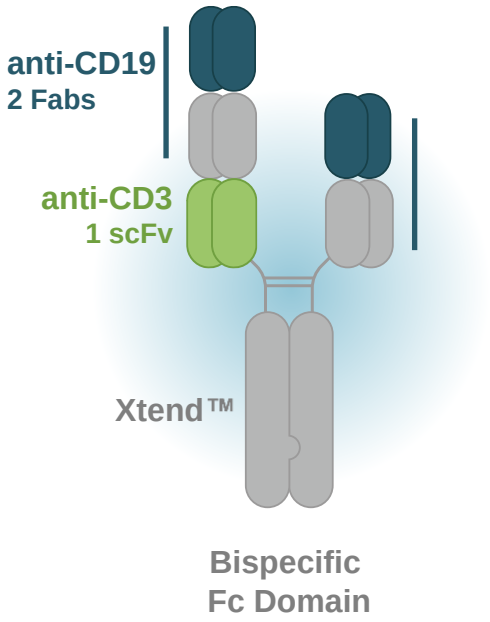
XmAb657
CD19 x CD3 Optimized for Autoimmune Disease

Rational XmAb® Design



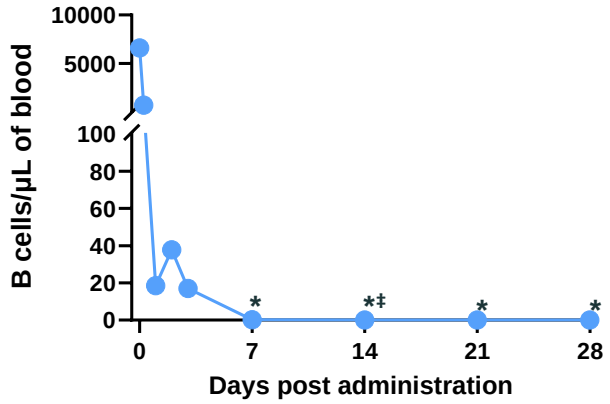
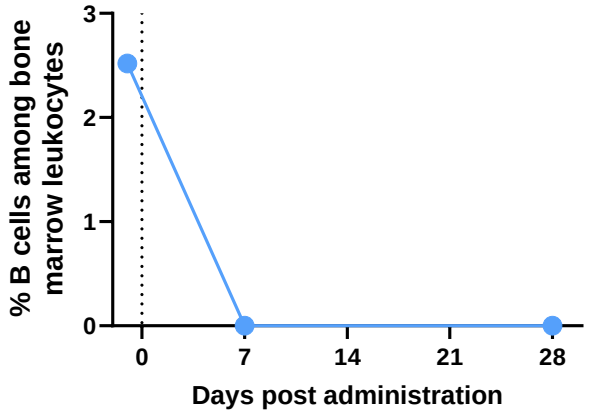
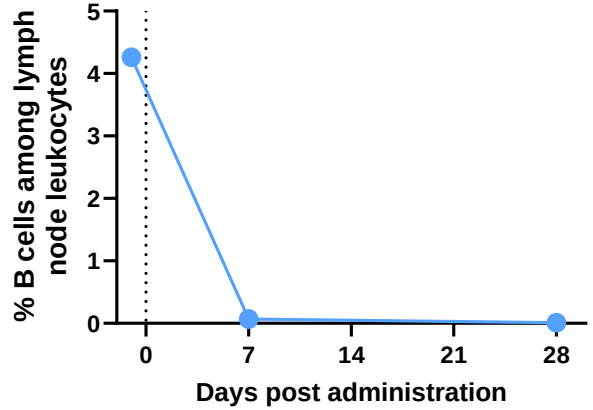
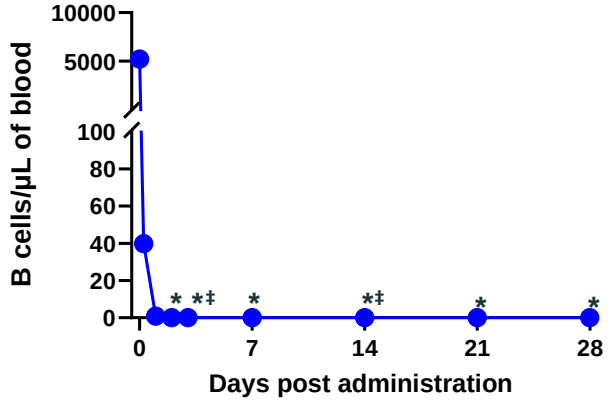
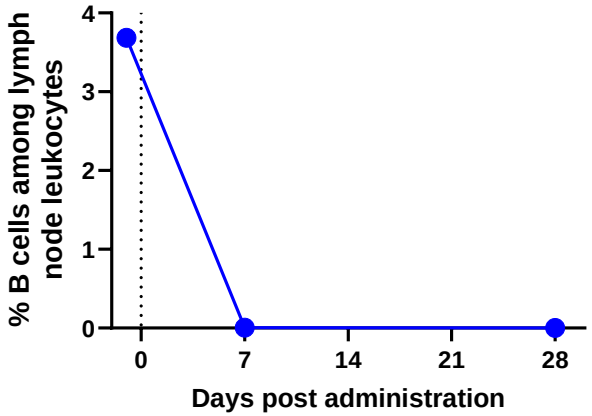
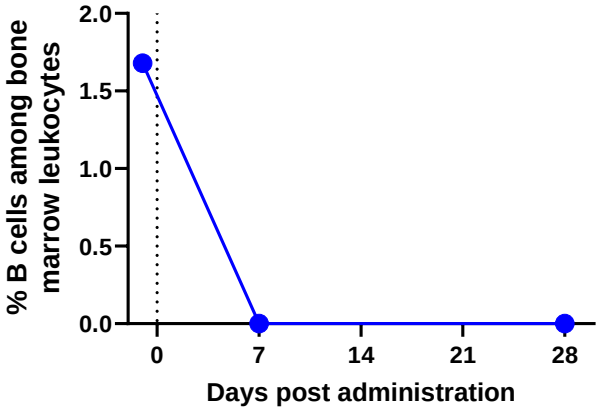
- High affinity and stability anti-CD19 binder
  - Bivalent to efficiently target B cells expressing very low levels of CD19 (e.g., plasma cells and plasmablasts)
- Affinity-tuned and highly stable anti-CD3 binder
- Uses Xencor's clinically validated 2+1 format
- Heterodimeric Fc domain engineered to abrogate effector function and improve half-life
- Xtend™ Fc for long half life

Positioned for Success

Ongoing NHP studies have shown effective B-cell depletion with single dose

- Broad opportunity set of disease indications supports multiple development pathways for success
- EULAR 2024 and subsequent updates of CD19 CAR-T clinical data highlighted potential issues with CAR-T approach on efficacy and safety
- Rational design of XmAb657 supports best-in-class potential for clinical outcomes
- **Current timeline to FIH study in 2H'25 puts Xencor on-track to be a leading CD19 x CD3 program within autoimmune disease**

Single Dose of XmAb657 in NHPs
Deep B-cell Depletion Sustained for at Least 28 Days

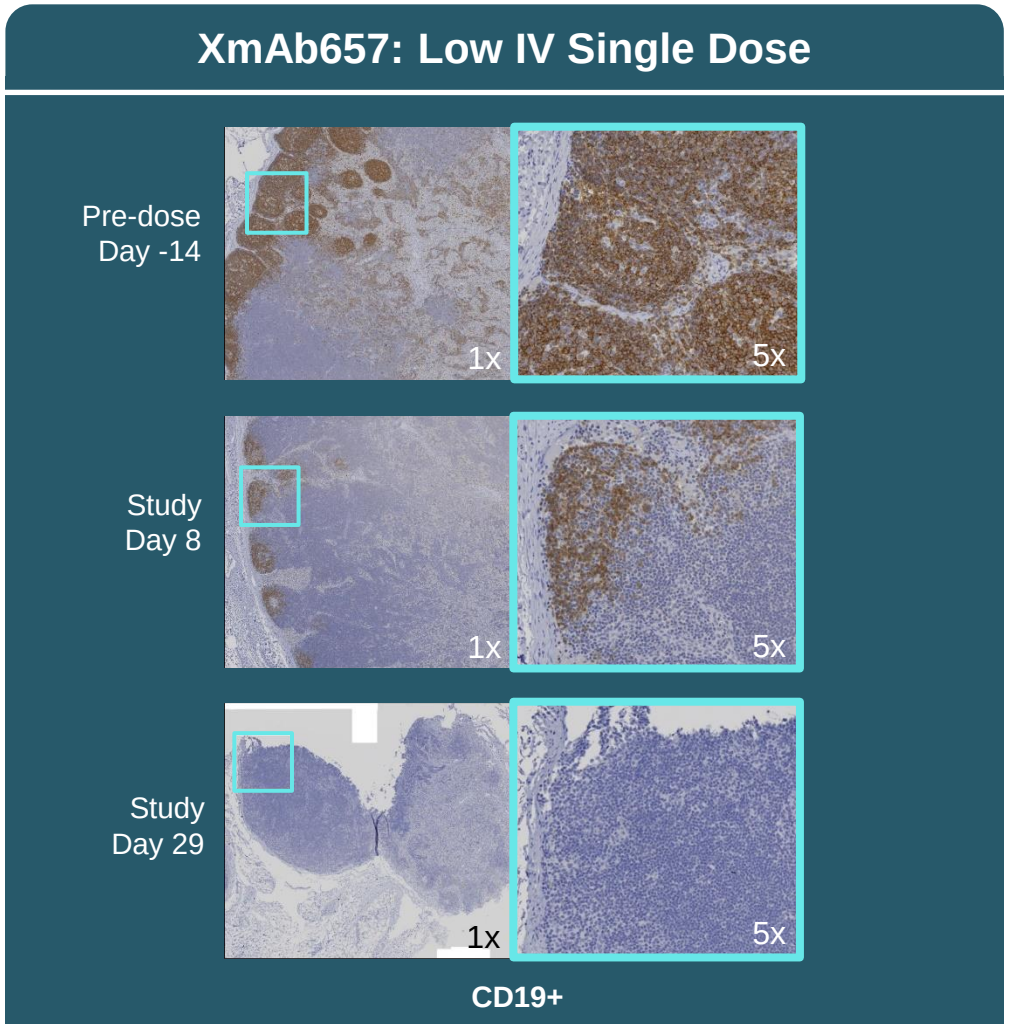
	Peripheral blood	Bone marrow	Lymph nodes
XmAb 657 Single IV Dose (low)			
XmAb657 Single IV Dose (high)			

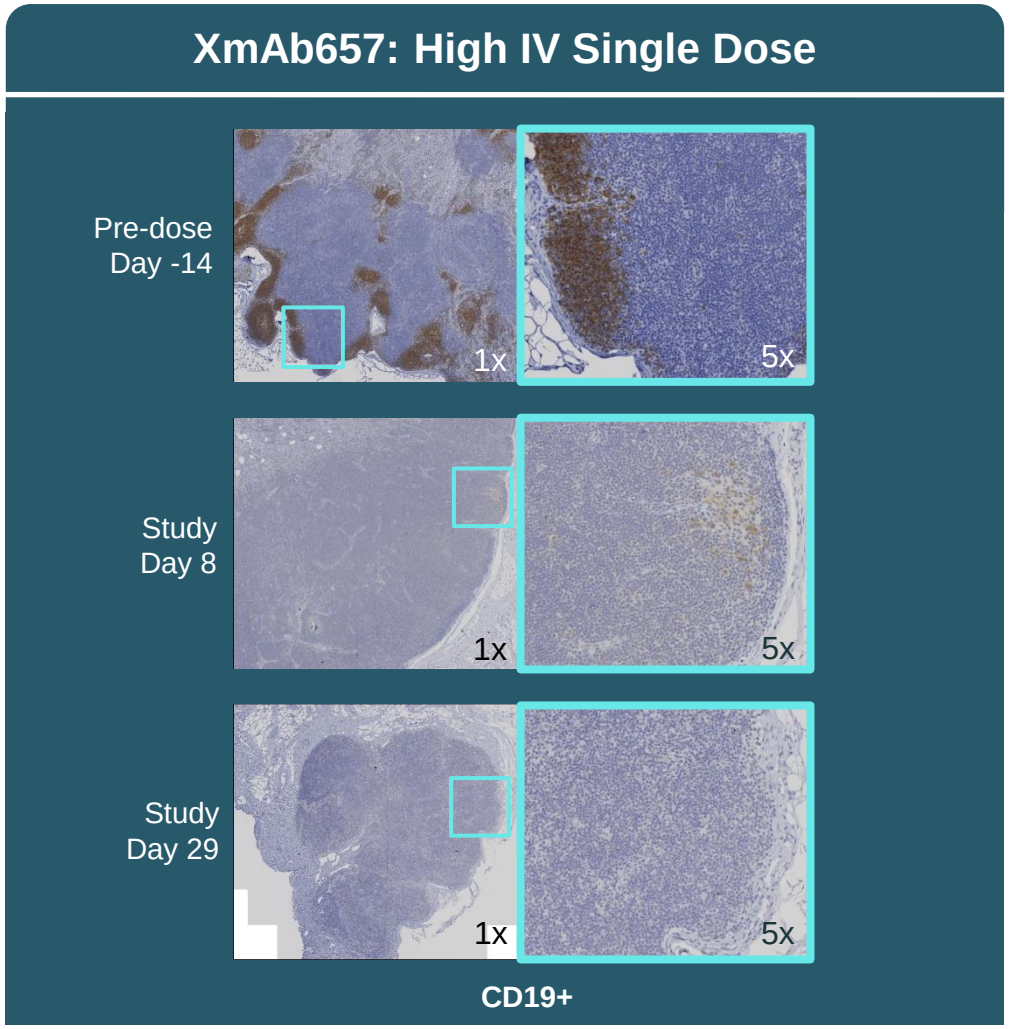
*peripheral B cells <1 B cell per µL;
‡this data point is zero B cells per µL

B cells were gated as CD45+CD2-/lowCD20+CD4-CD8a-CD159a-

xencor

Deep B-Cell Depletion in Lymph Nodes in NHPs Confirmed by CD19+ IHC

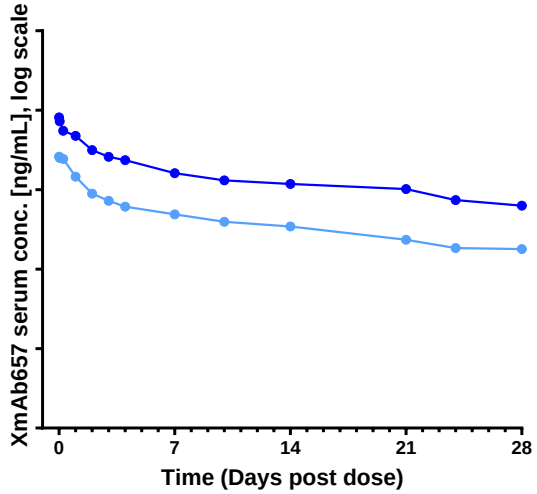




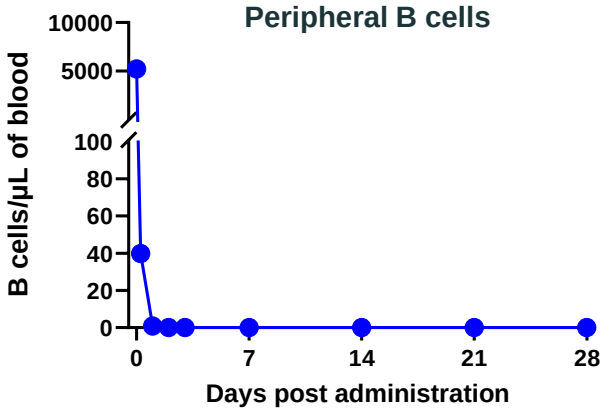
CD19 IHC reagent antibody non-interfering with XmAb657

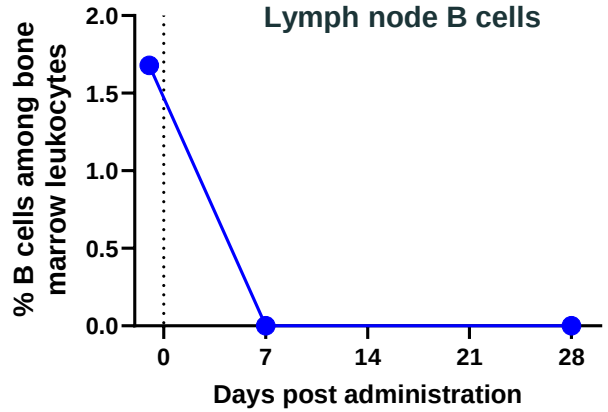
XmAb657: Rationally Designed for Autoimmune Disease
FIH Planned 2H'25

- Has been observed to demonstrate deep and durable B-cell depletion in NHPs, enabled by potentially best-in-class pharmacokinetics
- Has been well tolerated in NHP with no clinical signs of CRS
- GMP production campaign initiated
- Further plans to investigate subcutaneous dosing and priming
- **First-in-human study planned to initiate in 2H'25**



Long half life with Xtend™ Fc technology (~15 days in NHP) has potential for durable B-cell depletion





New Pipeline Programs: TL1A Portfolio

XmAb942 (Xtend™ TL1A)

XmAb TLA1 x IL-23

Inflammatory Bowel Disease (IBD) is a Devastating Disease with Significant Unmet Medical Need

~3m
Estimated diagnoses in the US[1]

Two common forms:
Crohn's disease
Ulcerative colitis

Economic burden estimated at $5.4B in 2023[2]

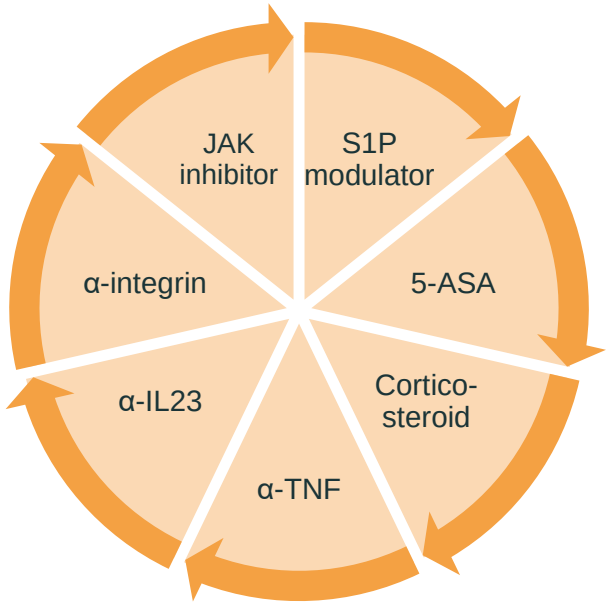
Significant Health Burden

- Impaired quality of life
- Lower life expectancy
- Surgeries, hospitalization
- Increased risk for intestinal resection
- Increased risk for colorectal cancer

Severe Symptoms of IBD

- Fatigue
- Fever
- Reduced appetite
- Mental health

Current Standards of Care are Lacking



Patients cycle through suboptimal treatments

- **Suboptimal efficacy:** ~10-20% disease remission[3]
- **Adverse events:** Infection, malignancy, thromboembolism, cardiac
- **Burdensome regimens:** poor patient compliance

1 Clarivate **2** GlobalData **3** Prescient whitepaper

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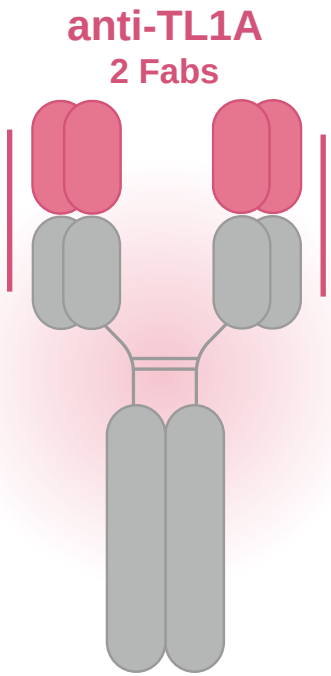
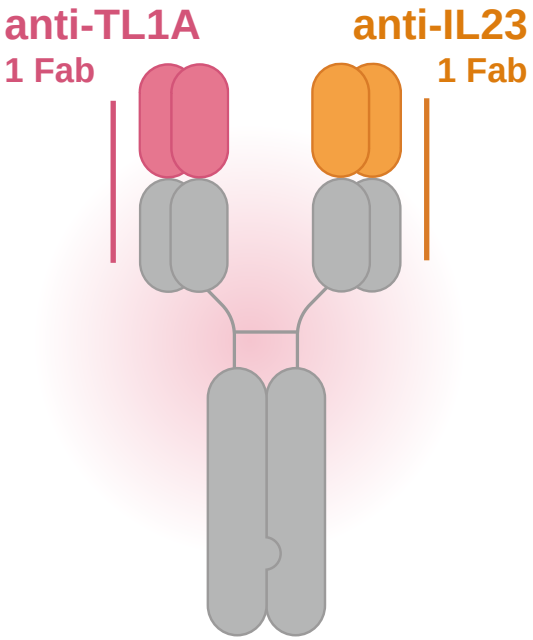
Development of XmAb942 and XmAb TL1A x IL-23 for IBD

XmAb942 Design



Xtend™ + FcKO

XmAb TL1A x IL-23 Design

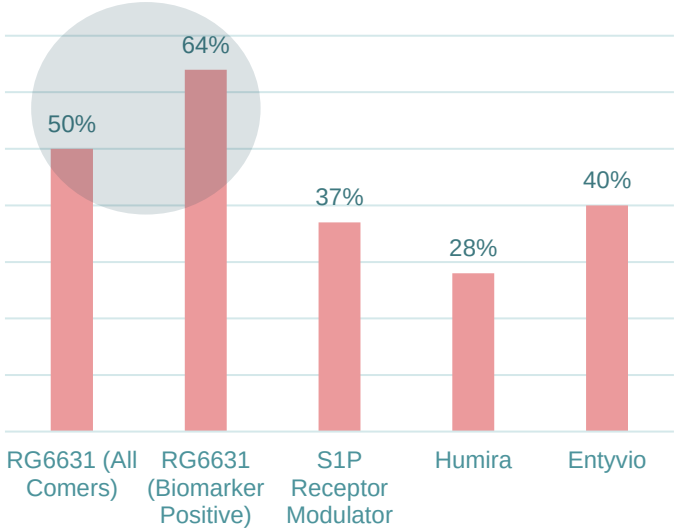


Bispecific
Fc Domain

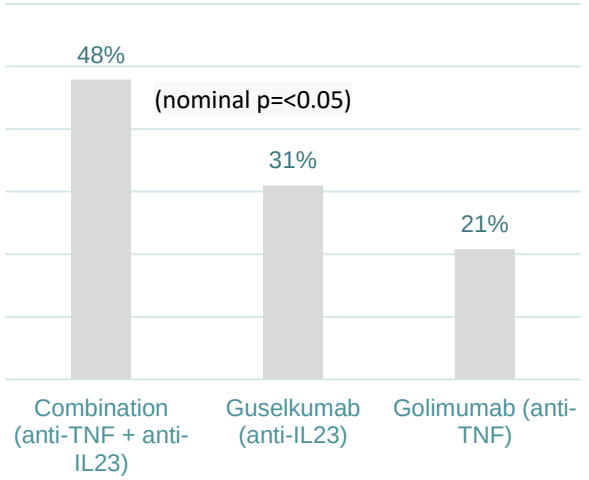
Phase 2 TL1A Studies and VEGA Study Support Strategy

- Building upon proof-of-concept studies with TL1A targeted therapy and combination therapies for the treatment of Ulcerative Colitis (UC) and Crohn's Disease (CD)
  - Validated best-in-class Xtend™ half-life extension in XmAb942
  - First-in-class potential of TL1A x IL-23 to target dual pathway inhibition

RG6631 Phase 2 TUSCANY (Roche TL1A)
(cross UC study comparison of Endoscopic Improvement)[1]



VEGA Ph2a
(Clinical Remission of UC at Week 38)[2]

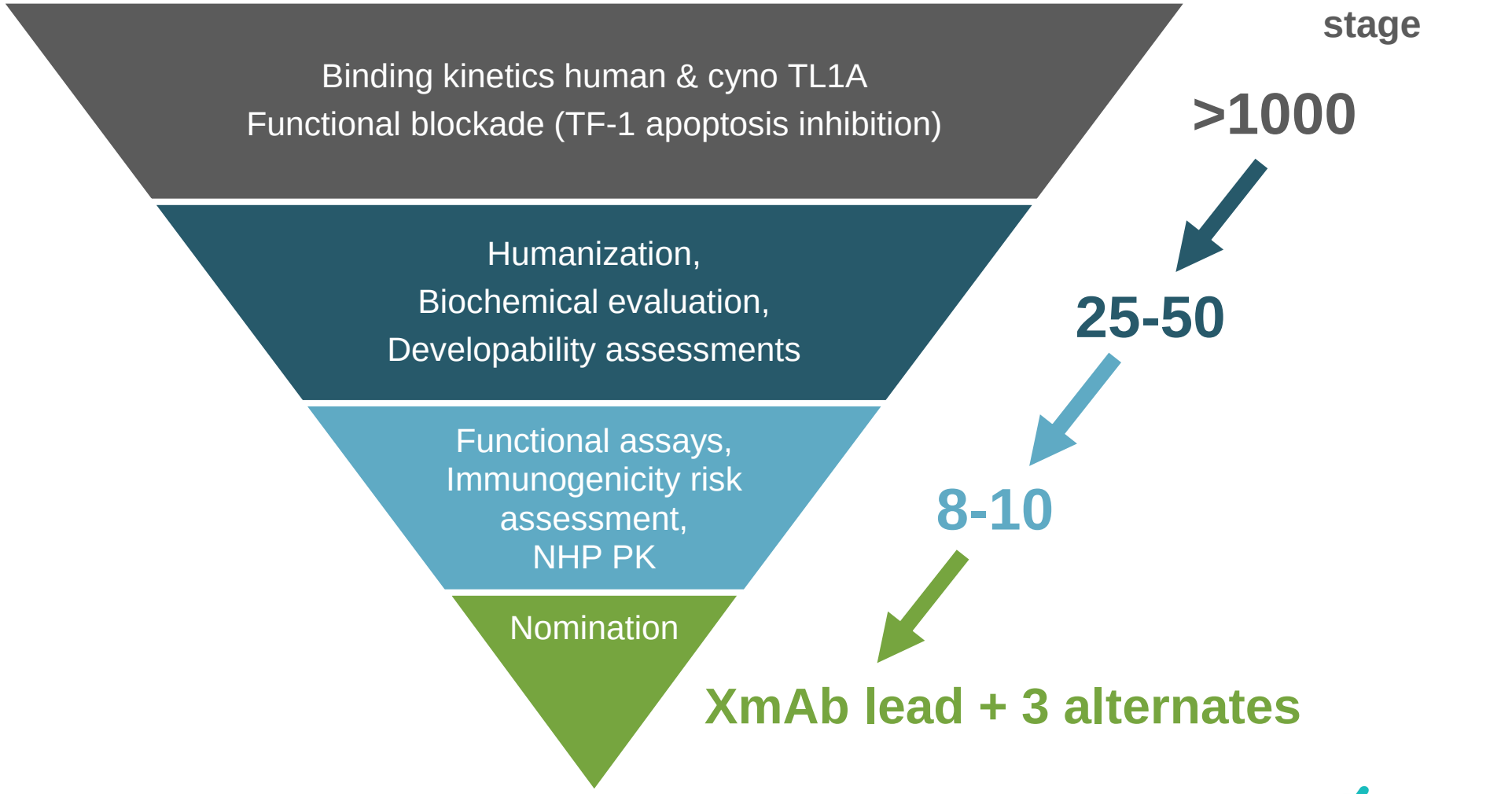


1 Sourced from Roivant presentation of TUSCANY, Entyvio (anti-integrin) and Humira (anti-TNF) data from VARSITY P3 study, S1P receptor modulator data from ELEVATE 52 P3 study
2 Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA); Feagan and Shao et al.; The Lancet G&H; Feb 2023

Discovery Campaign for Anti-TL1A Generation

Design of lead and backups in less than 6 months

Recombinant human TL1A immunization of mice and rats
Single B-cell antibody discovery



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Xtend™ Fc: Validated Half-Life Extension (HLE) Technology Enabling Potential Best-in-Class Anti-TL1A

Clinically validated with significantly improved half-life and dose frequency

- Ultomiris half-life extended >4x as compared to Soliris; maintenance dose frequency reduced by 4X[1]
- VRC01LS half-life extended >4X as compared to parental (71 days vs 15 days)[2]

Similar safety and immunogenicity risk as parental antibodies in studied antibodies using Xtend Fc domains[3,4,5]

Antibody thermostability maintained in studied antibodies using Xtend Fc domains[6,7]

Superior or comparable to other HLE technologies (e.g., YTE) across multiple studies and parameters[6,7,8]

Typical HLE scaling from cyno to human is ~3.5x[9]

Clinical Half-Life and Maintenance Dosing Ultomiris vs. Soliris[10]

Product	Half-life (days)[11]	Dosing Interval[1,12]
Ultomiris (with Xtend™)	**49.7-64.3**	**Q8W**
Soliris	11.33-12.1	Q2W

Proprietary Xtend™ Fc Domain has been incorporated into ≥ 21 molecules that have been tested in clinical studies

Xtend is commonly referred to as 'LS' in academic literature

1 Ultomiris & Soliris drug labels **2** Ledgerwood Clin Exp Imm 2015 **3** Lee et al. Blood 2019 **4** Gaudinski et al. PLOS Med 2018 **5** Vu et al. J Neurol 2023 **6** Ko et al. Exp Mol Med 2022 **7** Internal Data **8** Ko et al. Nature Letter 2014 **9** Haraya & Tachibana. BioDrugs (2023) 37:99–108 **10** Data adapted from FDA and EMA drug labels **11** Reported Half-life across approved indications **12** Maintenance dosing interval in adults

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XmAb942: Novel High-Affinity Anti-TL1A mAb Designed for Extended Half-Life, Under Development for the Treatment of IBD

- XmAb942 utilizes Xtend™ Fc domain technology with potentially class-leading potency
- Half-life in non-human primate studies >22 days supports Q8W to Q12W dosing in humans
- High concentration formulation for subcutaneous dosing
- **First-in-human clinical studies to begin 4Q'24**

Discovery & characterization of XmAb942 accepted for presentation during UEG Week on Tues., Oct. 15

Company	Program[1]	Potent	SC Dosing	Q8-12W Dosing	Half-life extension	Low Immunogenicity
Xencor	XmAb942	✓	✓	✓	✓	✓ Predicted
Merck (Prometheus)[2,3]	MK-7240	✗	✓	✗	✗	✓
Roche (Roivant)[4,5]	RG-6631	✓	✓	✗	✗	✗
Sanofi (Teva)[6]	TEV-48574	✓	✓	✗	✗	TBD

1 No head-to-head trial has been conducted evaluating XmAb942 against other data included herein. Differences exist between clinical trial design, patient populations and the product candidates themselves, and caution should be exercised when comparing data across trials **2** PRA023 Progress Update (Prometheus presentation) **3** Feagan et al. The Anti-TL1A Antibody PRA023 Demonstrated Proof-of-Concept in Crohn's Disease: Phase 2a APOLLO-CD Study Results (DOP87) Abstract citation ID: jjac190.0127 **4** Banfield et al. Br J Clin Pharmacol. 2020;86:812–824 **5** Clarke et al. mAbs. 2018;10:4, 664-677 **6** Danese et al. Clin Gastroenterology and Hepatology. 2021;19:11, 2324-32.e6

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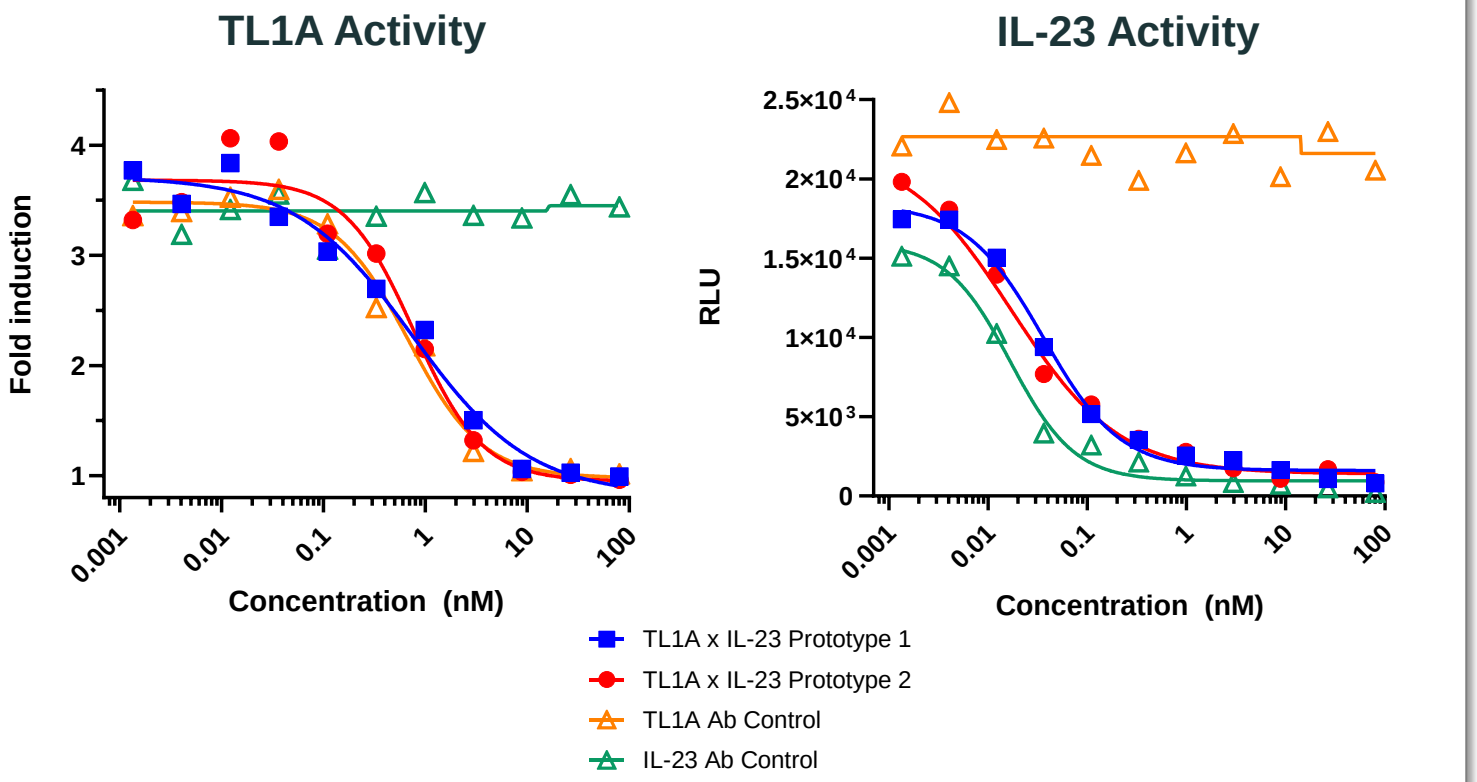
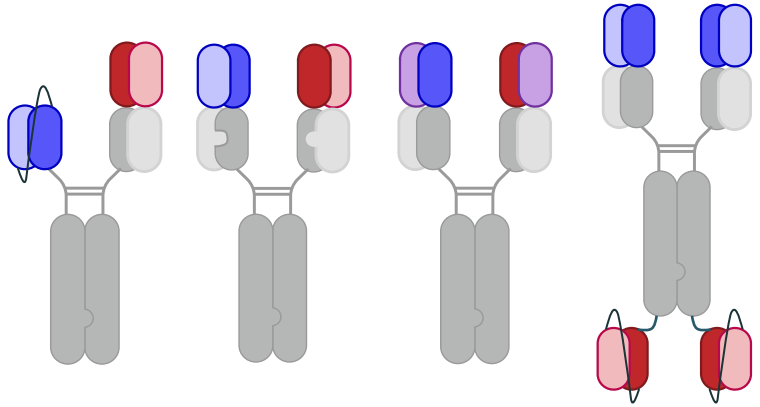
XmAb® TL1A x IL-23 to Have First-in-Class Potential First-in-Human Study Planned in 2026

Prototype TL1A x IL-23p19 bispecifics are functionally active on both axes



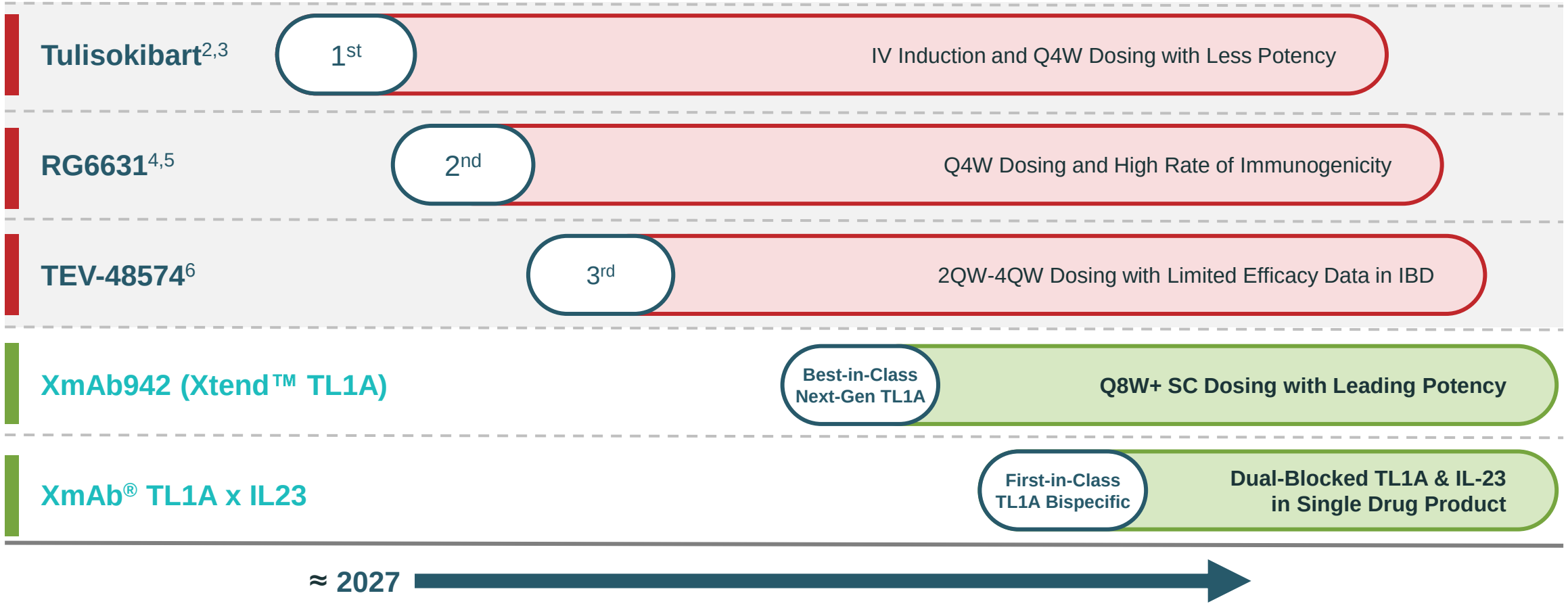
XmAb protein engineering allows for a range of stable molecular structures



- Rapidly prototype in multiple formats
- Optimize and tune for biological activity

Xencor Positioned for Best-in-Class TL1A Portfolio in $23bn+ Global IBD Market[1]

Potential Commercializations for First-Gen Programs and XmAb® TL1A Portfolio



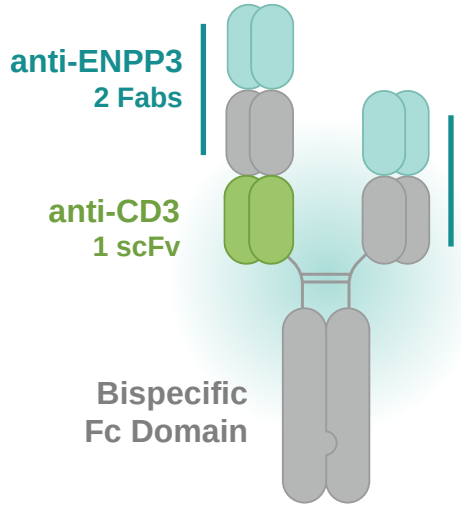
Timelines are illustrative only and subject to FDA approvals **1** Estimate of US, UK, Spain, Japan, Italy, Germany, France and Canada market size in 2030 (GlobalData) **2** PRA023 Progress Update (Prometheus presentation) **3** Feagan et al. The Anti-TL1A Antibody PRA023 Demonstrated Proof-of-Concept in Crohn's Disease: Phase 2a APOLLO-CD Study Results (DOP87) Abstract citation ID: jjac190.0127 **4** Banfield et al. Br J Clin Pharmacol. 2020;86:812–824 **5** Clarke et al. mAbs. 2018;10:4, 664-677 **6** Danese et al. Clin Gastroenterology and Hepatology. 2021;19:11, 2324-32.e6

Potential First-in-Class T-Cell Engagers in Solid Tumor Oncology

XmAb® T-Cell Engager Programs Designed to Address Unmet Need with Potential Across Multiple Tumor Types

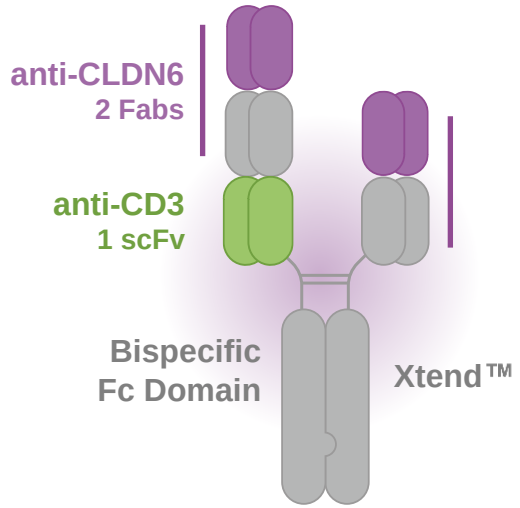
XmAb819 (ENPP3 x CD3)

- Engineered for greater selectivity for ENPP3-expressing tumor cells compared to normal cells, which also express ENPP3 at lower levels
- In development for patients with relapsed/ refractory clear cell RCC (ccRCC), which has nearly uniformly high ENPP3 expression
- Dose-escalation ongoing



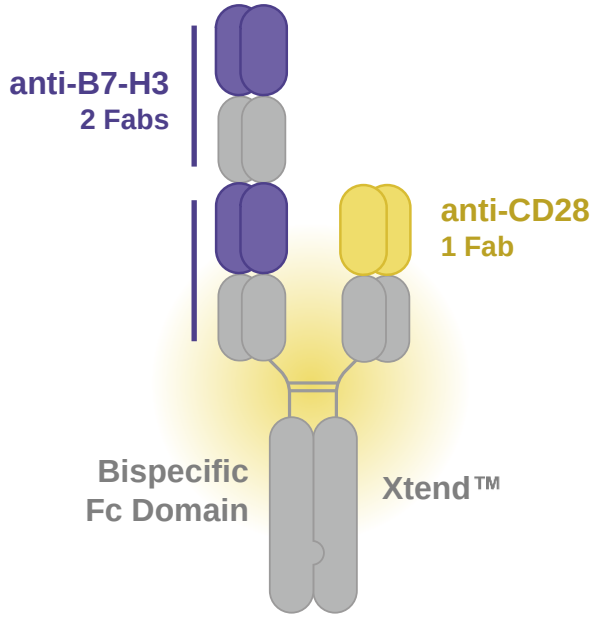
XmAb541 (CLDN6 x CD3)

- Engineered for CLDN6 selectivity over similar CLDN9, CLDN3 and CLDN4
- In development for patients with CLDN6+ tumors, including ovarian cancer
- Dose-escalation ongoing



XmAb808 (B7-H3 x CD28)

- Engineered to provide tumor-selective co-stimulation only when bound to tumor cells
- Combination with anti-PD1 (pembrolizumab)
- In development for patients with solid tumors
- Dose-escalation ongoing



XmAb819 Status Update[1]: Encouraging Initial Data in Ongoing Dose Escalation in ccRCC

>$2bn
peak sales potential in ccRCC[2]

XmAb819

Potential first-in-class ENPP3 x CD3

Dose escalation on-track with RECIST responses in recent dose cohorts

XmAb819 remains on-track to reach target dose levels by year-end

Observed in escalation:

- Clear initial evidence of anti-tumor activity, including RECIST responses, in recent cohorts
- Duration of treatment for several patients in earlier dose cohorts has extended beyond one year
- Cytokine release syndrome (CRS) manageable
- No MTD reached; tolerability from recent dose cohorts continues to support dose escalation

- Investigators remain highly engaged, and enrollment into new dose cohorts has been rapid
- Intravenous and subcutaneous cohorts continue dose escalation in parallel
- Evaluation of expansion into additional tumor types is ongoing
- **Clinical update and first dose expansion cohort expected to start during 1H'25**

1 Update provided 09-Sep-2024, based on 30-Aug-2024 data cutoff **2** Based upon internal Xencor projections of non-risk adjusted peak sales **ccRCC** clear cell renal cell carcinoma **MTD** maximum tolerated dose

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XmAb808 Status Update[1]: Continued Progress in Dose Escalation

>$3bn
peak sales potential[2]

XmAb808

Potential first-in-class B7-H3 x CD28

Dose escalation on-track with PSA reductions observed for patients with mCRPC during monotherapy run-in period

XmAb808 remains on-track to reach target dose levels by year-end

Observed in escalation:

- Tolerability from recent dose cohorts remains supportive of continued combination with per label dosing of pembrolizumab
- Safety data have supported adding cohorts with Day 1 start for dosing the combination of XmAb808 and pembrolizumab, along with cohorts that use a four-week XmAb808 monotherapy run-in period
- Dose-escalation cohorts continue to enroll patients with multiple tumor types, majority with mCRPC
- For the subgroup of mCRPC patients, biologic activity of XmAb808 has been observed with PSA declines during the four-week monotherapy run-in period, but higher doses are expected to be needed to trigger more meaningful clinical activity
- **Clinical update and dose expansion expected to start during 1H'25**

1 Update provided 09-Sep-2024, based on 16-Aug-2024 data cutoff **2** Based upon internal Xencor projections of non-risk adjusted peak sales **mCRPC** metastatic castration-resistant prostate cancer

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Guidance for Progress Across XmAb® Portfolio Programs in 2024

XmAb Drug Candidate		2024 Priority
Solid Tumors: T-Cell Engagers (CD3 & CD28)		
XmAb819	ENPP3 x CD3	Advance dose escalation toward target dose levels in 2024
XmAb808	B7-H3 x CD28	Advance dose escalation toward target dose levels in 2024
XmAb541	CLDN6 x CD3	Dose first patient during 1H 2024, enroll Phase 1 study ✓
Immunology		
XmAb942	Xtend™ TL1A	Present preclinical data during UEG Week 2024 on October 15
		Initiate first-in-human Phase 1 study in Q4 2024
Plamotamab	CD20 x CD3	Define clinical development plan ✓
XmAb657	CD19 x CD3	GMP campaign and IND preparation ✓

Potential Inflection Points for Xencor's Clinical Portfolio in 2025

XmAb Drug Candidate		Indication	1H'25	2H'25
Oncology Portfolio				
XmAb819	ENPP3 x CD3	ccRCC	**Initiation of dose expansion**	
XmAb808	B7-H3 x CD28	Solid tumor	**Initiation of dose expansion**	
XmAb541	CLDN6 x CD3	Ovarian+		**Advance toward target dose levels**
Vudalimab	PD-1 x CTLA-4	mCRPC	**Mono & combo cohort expansion readout**	
		NSCLC	**Evaluate chemo combination safety**	
Immunology Portfolio				
XmAb942	Xtend™ TL1A	IBD+	**SAD readout**	**MAD readout and Phase 2 start**
Plamotamab	CD20 x CD3	Rheumatoid arthritis	**Initiate Phase 1/2 study**	
XmAb657	CD19 x CD3	Autoimmune		**Initiate FIH study**

SAD Single ascending dose **MAD** multiple ascending dose **FIH** first-in-human

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Xencor R&D Strategy Call

September 9, 2024