



Global Leaders in IgM Antibodies

REIMAGINING  
antibody medicines™

JP Morgan Healthcare Conference

January 10, 2024



# Forward-looking statements

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This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect the current views of the management of IGM Biosciences, Inc. (the “Company,” “we” or “our”) based on information available to us as of the date hereof. All statements other than statements of historical fact could be deemed forward-looking, including but not limited to statements regarding our future financial performance; our preliminary and unaudited cash and investments balance as of December 31, 2023; our anticipated cash runway; plans, timelines, and expectations related to our preclinical studies, clinical trials, discovery programs and collaboration activities; business plans, strategies, strategic priorities, catalysts and objectives; our ability to obtain regulatory approval; the potential therapeutic benefits and economic value of our product candidates; potential growth opportunities; and our competitive position, industry environment and potential market opportunities. In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially” “predict,” “should,” “target,” “will” or the negative of these terms or other similar expressions. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: plans, timelines, and expectations related to our preclinical studies, clinical trials and our discovery programs including regarding the availability of data, planned regulatory filings, the initiation and progress of current and future clinical trials; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of collaborations with third parties, including the agreement with Sanofi; our early stages of clinical drug development; our ability to achieve clinical goals; risks related to the use of engineered IgM antibodies; our ability to utilize our IgM antibody platform to generate and advance additional product candidates; our ability to advance product candidates into, and successfully complete, clinical trials; our ability to adequately demonstrate sufficient safety and efficacy and reduced toxicity, of our product candidates, either alone or in combination with other compounds; the potential for the results of clinical trials to differ from preclinical, preliminary, initial or expected results; the risk of significant adverse events, toxicities or other undesirable side effects; the timing or likelihood of regulatory filings and approvals; our estimates of the number of patients who suffer from the diseases we are targeting and the number of patients that may enroll in our clinical trials; the ability to commercialize our product candidates, if approved; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved; our ability to accurately forecast future financial results and timelines; our anticipated use of our existing resources, our estimates regarding expenses, future revenue, capital requirements and needs for additional financing and our ability to obtain additional capital; the sufficiency of our existing cash and investments to fund our future operating expenses and capital expenditure requirements; our ability to attract and retain qualified personnel; the impact of our recent strategic refocusing and reduction in our workforce; the implementation of our business model and strategic plans; the scope of our intellectual property protections we are able to establish and maintain; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; developments relating to our competitors and our industry, including competing product candidates and therapies; any potential delays or disruptions resulting from catastrophic events, including epidemics or other outbreaks of infectious diseases; general economic and market conditions including inflation; and other risks described in our public filings with the Securities and Exchange Commission (SEC), including our most recent Quarterly Report on Form 10-Q filed on November 13, 2023. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Additionally, statements that “we believe” and similar statements reflect our management’s beliefs and opinions on the relevant subject. These forward-looking statements are based on information available to us as of the date hereof, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and readers are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason.

This presentation includes information on drug candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. The drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

# IGM Biosciences overview

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Global leaders in the development of IgM antibodies



Wholly-owned, clinical-stage pipeline of medicines in:

- Oncology
- Autoimmune and inflammatory diseases



Worldwide collaboration agreement with Sanofi to develop IgM agonist antibodies against 3 immunology and inflammation targets and 3 oncology targets



Cash and investments of approximately \$338 million\* (unaudited) as of December 31, 2023; expected runway into the second quarter of 2026

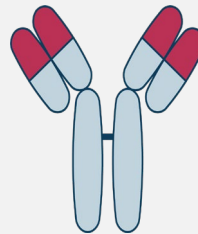
\* Based upon preliminary estimates and information available to the Company as of the date of this presentation

**IgM antibodies  
have unique  
structural attributes  
compared to  
IgG antibodies**

### **Additional binding sites lead to:**

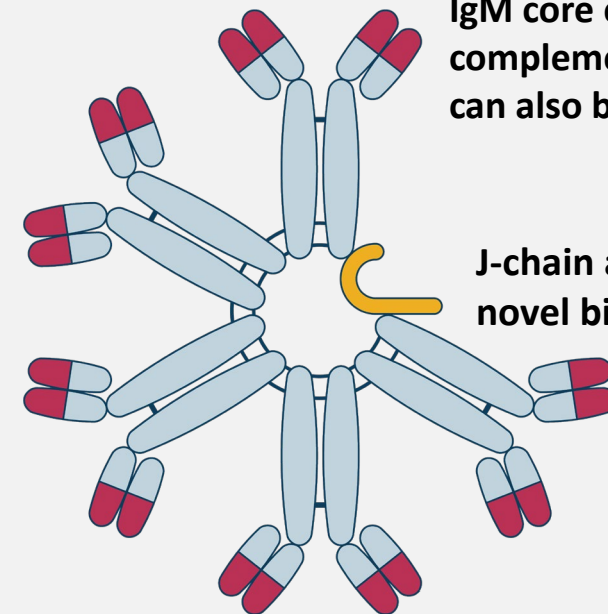
- Superior total binding power (avidity)
- Increased cross-linking of receptors for greater agonism

**IgG**



**2 BINDING SITES**

**IgM**



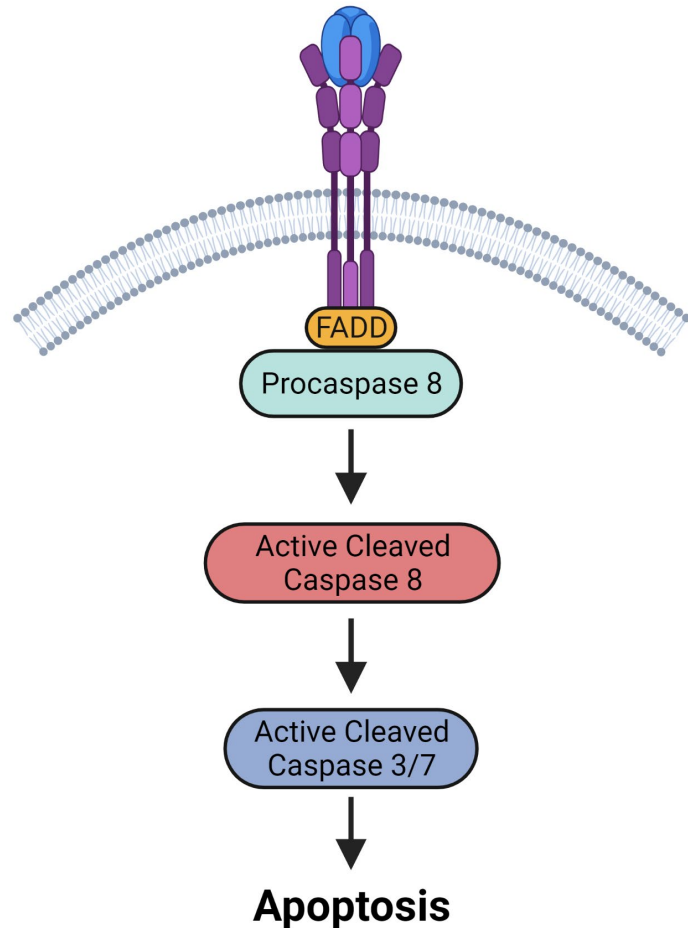
**10 BINDING SITES**

# IGM pipeline

PROGRAM	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Receptor Cross-Linking Agonist						
<b>Aplitabart</b> (DR5)	Colorectal cancer (CRC)					
T Cell Engagers						
<b>Invotamab</b> (CD20 x CD3)	Systemic Lupus Erythematosus (SLE)					
	Rheumatoid Arthritis (RA)					
	Myositis					
<b>IGM-2644</b> (CD38 x CD3)	Autoimmune Disease					
Partnered: 3 Immunology & Inflammation Targets and 3 Oncology Targets						
<b>sanofi</b>	Undisclosed					

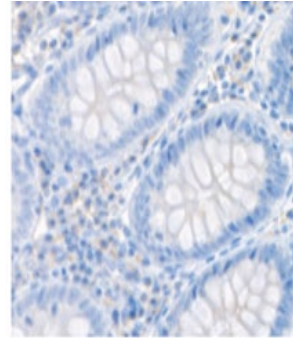


# Death receptor 5 (DR5) is a driver of the extrinsic apoptotic pathway and is overexpressed in multiple tumor types

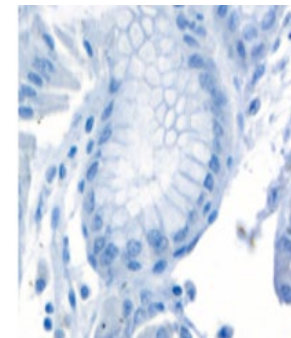


## DR5 Stained Normal Tissues

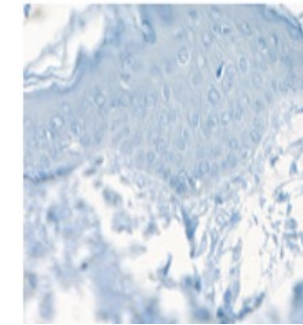
Colon



Stomach

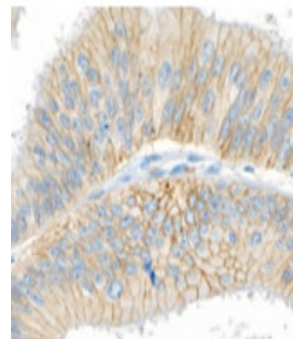


Skin

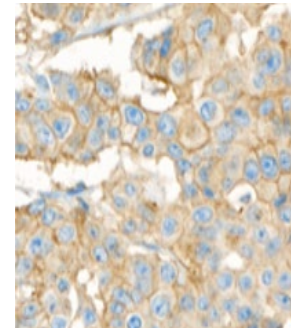


## DR5 Stained Tumor Samples

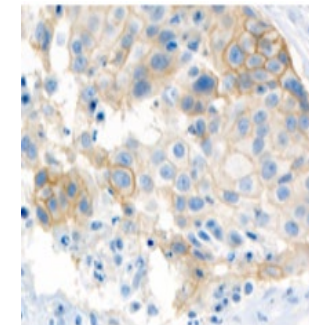
Colon Adenocarcinoma



Gastric Adenocarcinoma



Squamous Cell Carcinoma



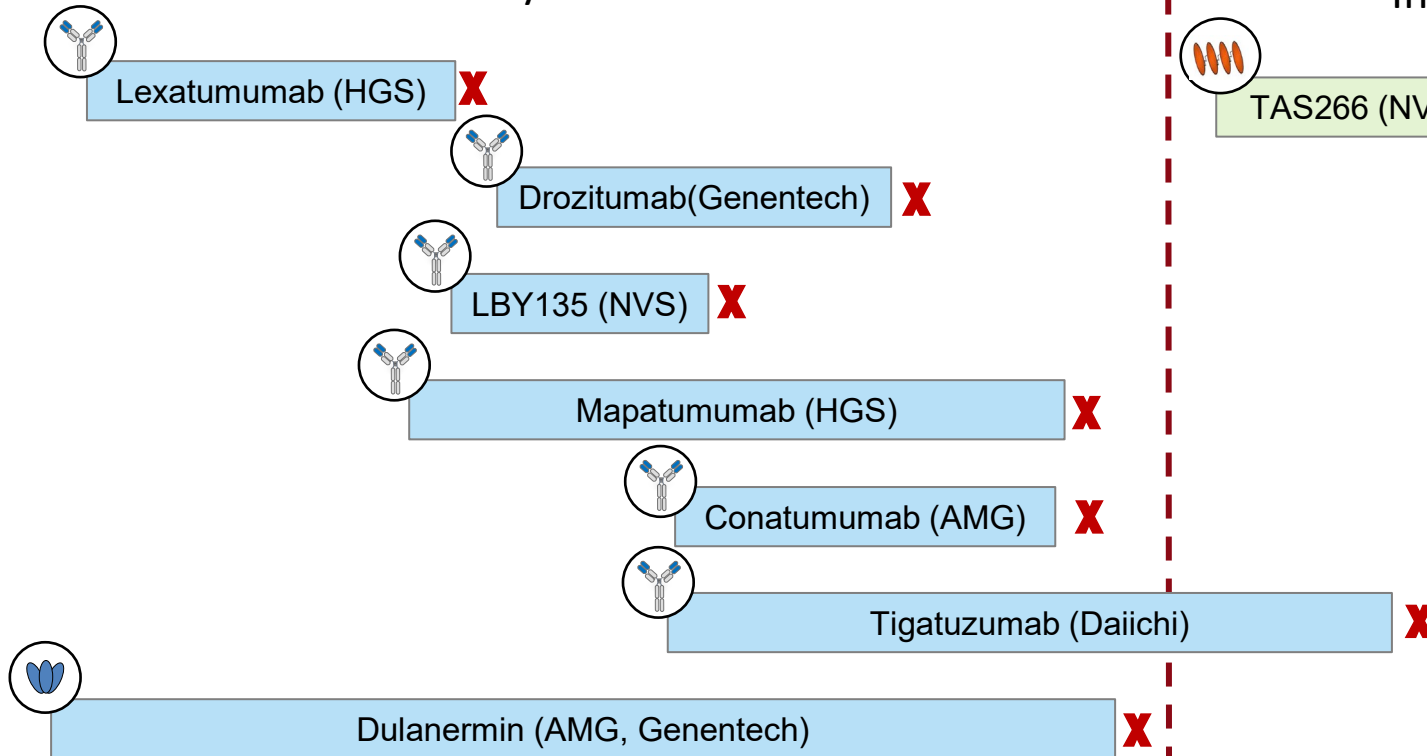
# DR5 has been a therapeutic target for 20 years

Limited activity and hepatotoxicity have led to numerous failures

2004 – 2012 – 2024

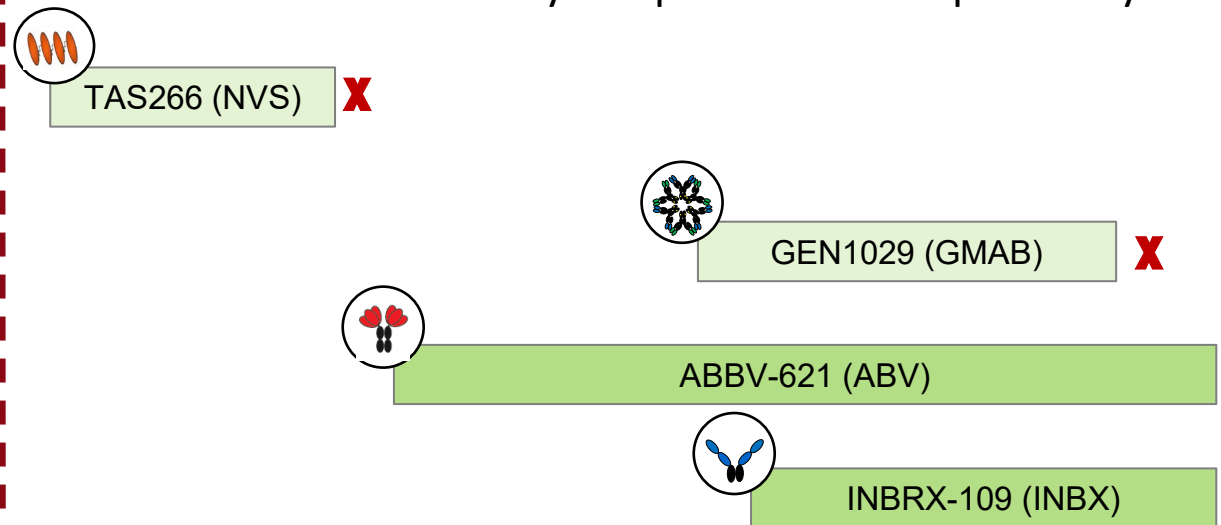
## 1<sup>st</sup> generation bivalent approaches

- TRAIL ligand or IgG DR5 mAbs
- Limited activity



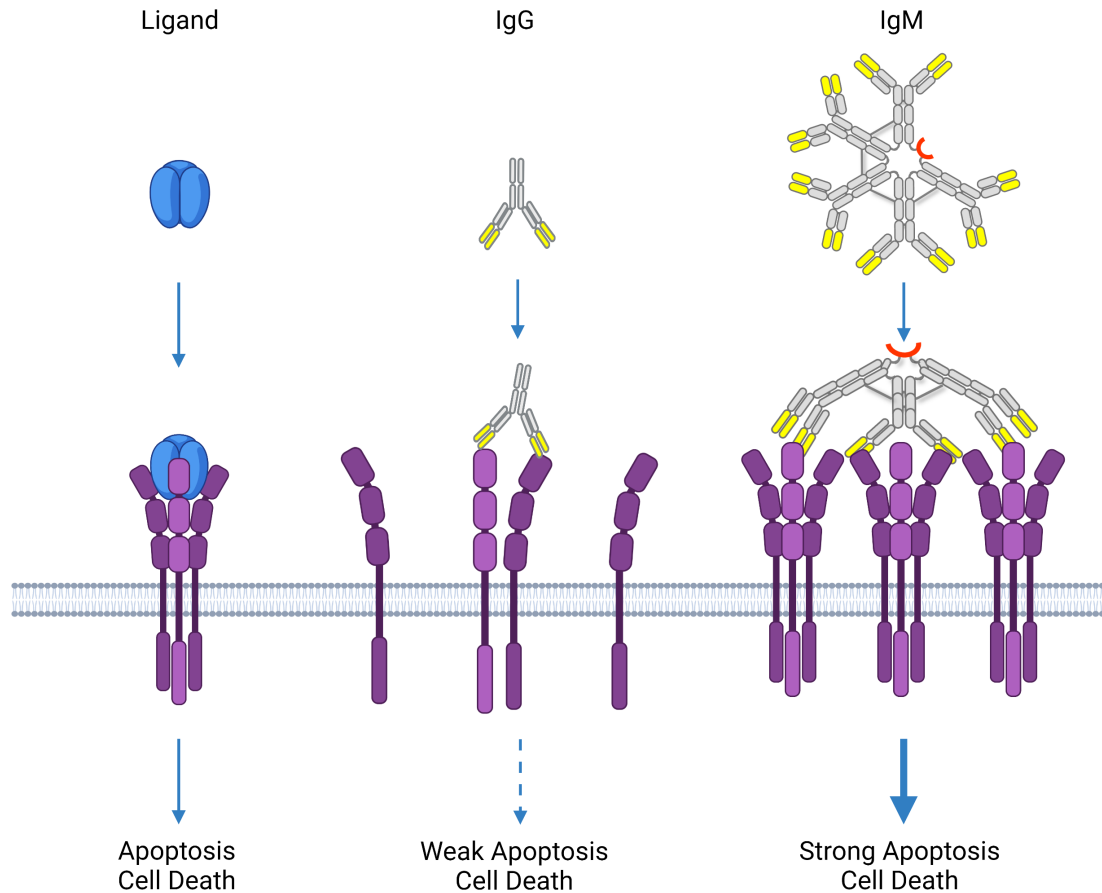
## 2<sup>nd</sup> generation multivalent approaches

- TRAIL ligand or IgG DR5 mAbs
- Increased activity but pronounced hepatotoxicity

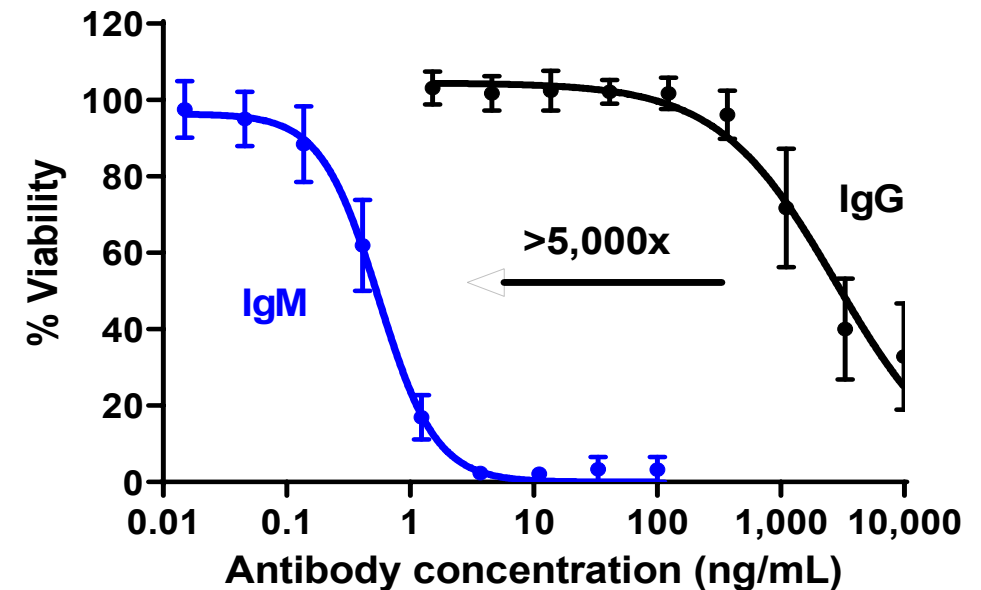


X Discontinued Program

# IgM antibodies can cross-link multiple DR5 receptors potentially leading to increased apoptotic signaling and potency

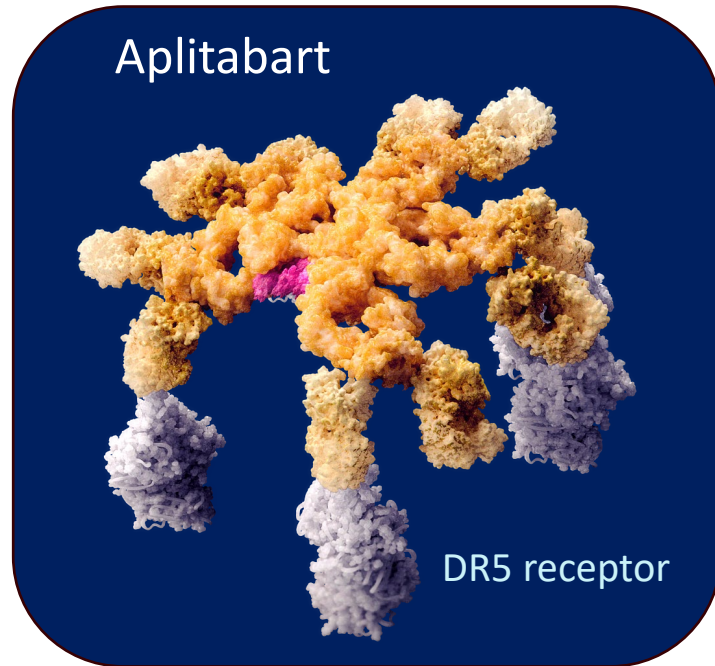


*In vitro* apoptosis comparing IgG and IgM DR5 antibodies using the same binding domain

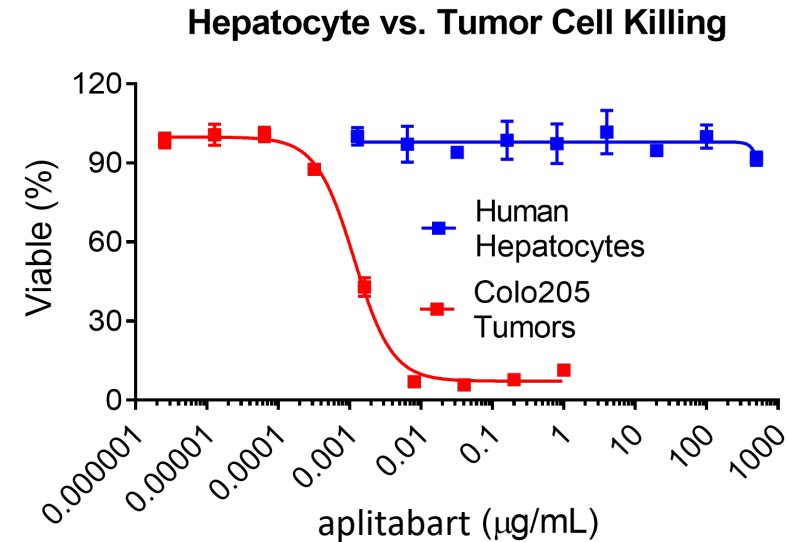




# Aplitabart: a multimeric DR5 agonist designed to optimize therapeutic index



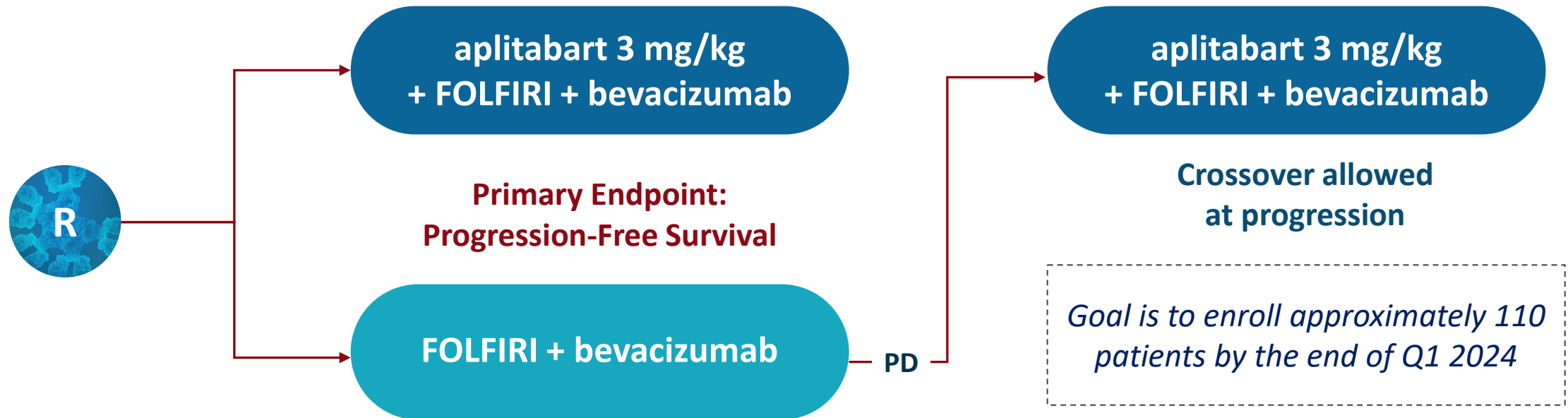
Pentameric structure enables cross linking of DR5 receptors creating stronger apoptotic signal



- Potent *in vitro* killing of tumor cells
- Preclinical assays showed no cytotoxicity to hepatocytes across dose range

Affinity, avidity, clustering, DR5 epitope, multimerizing kinetics and exposure all contribute to optimization

# Ongoing randomized 2L metastatic colorectal cancer clinical trial intended to quantify additional benefit of aplitabart



## Population

- 2L mCRC, all molecular subtypes including KRAS mutant
- Prior FOLFIRI treatment excluded
- Global trial

## Trial Design

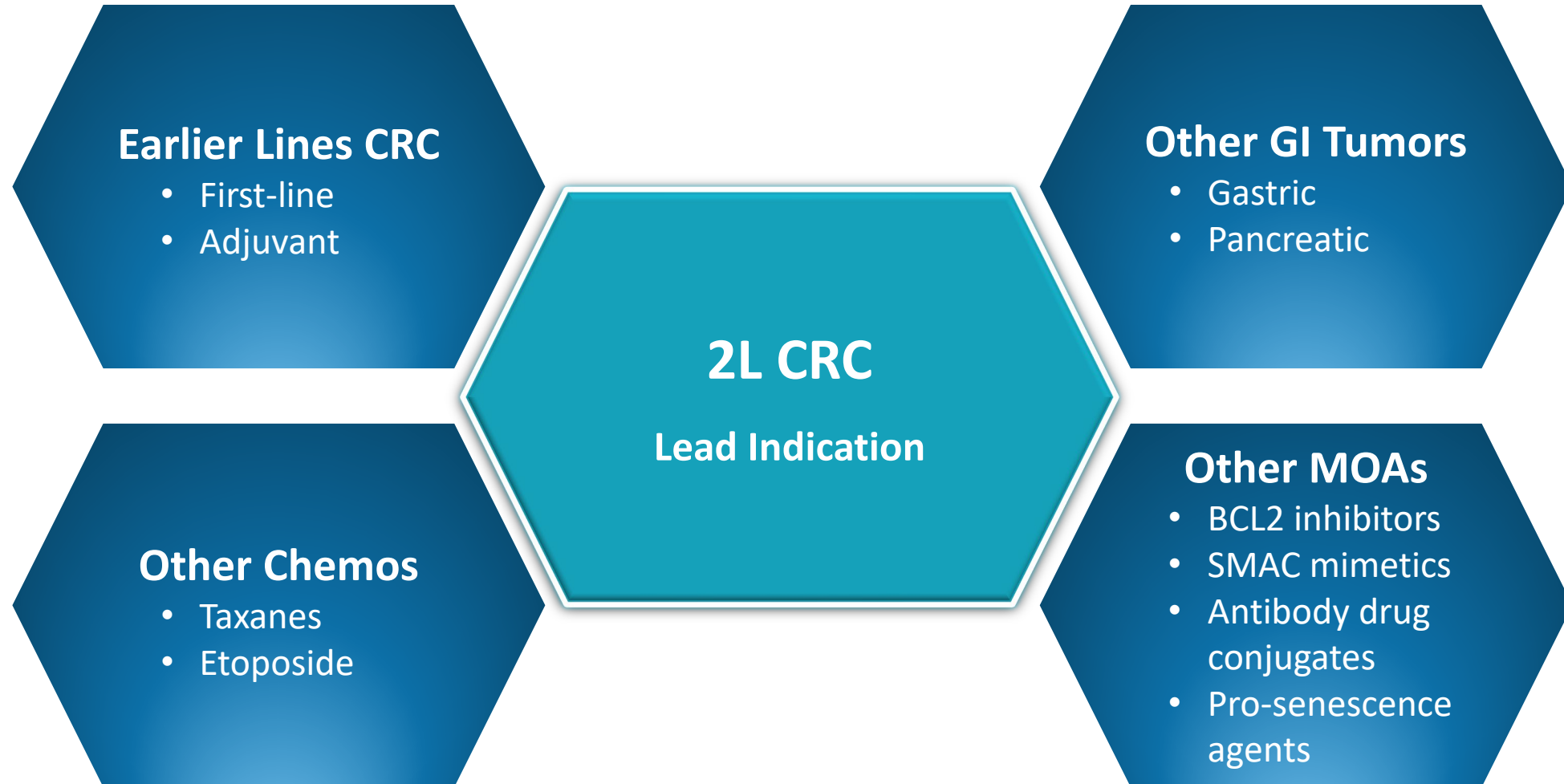
- N=110, 1:1 randomization
- Primary endpoint: PFS
- Secondary endpoints: ORR, OS, safety
- Blinded independent radiographic review

## Stratification Factors

- Liver metastases
- KRAS status

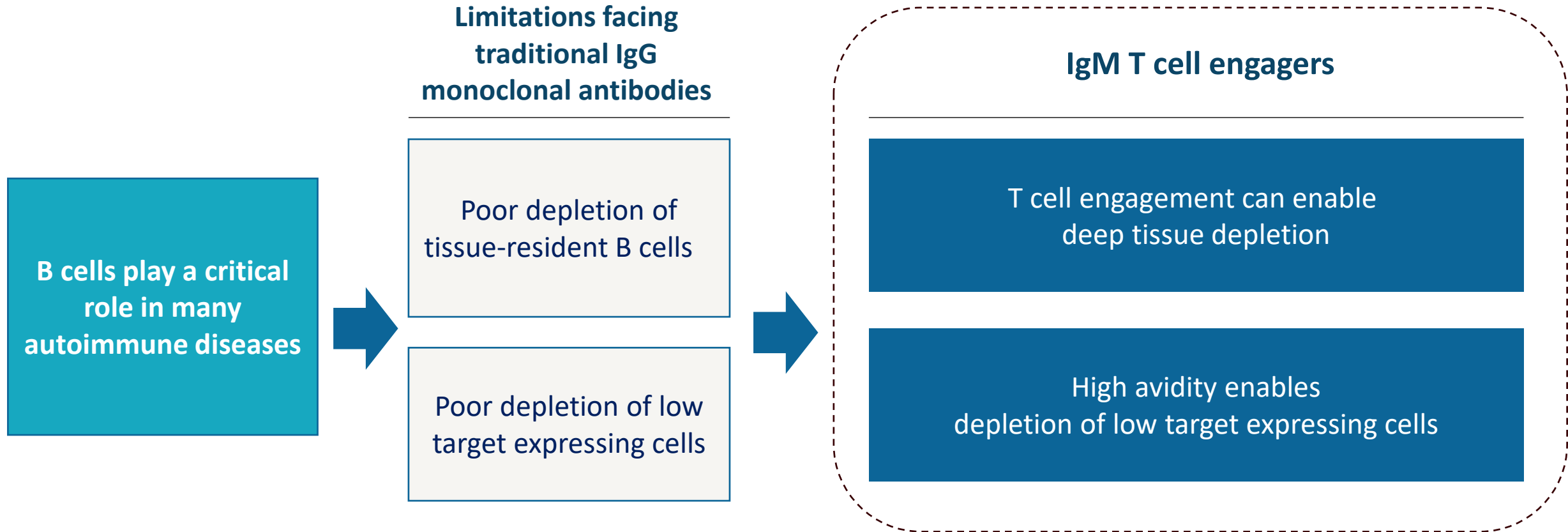
# Future development opportunities

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# IgM-based T cell engagers in autoimmunity

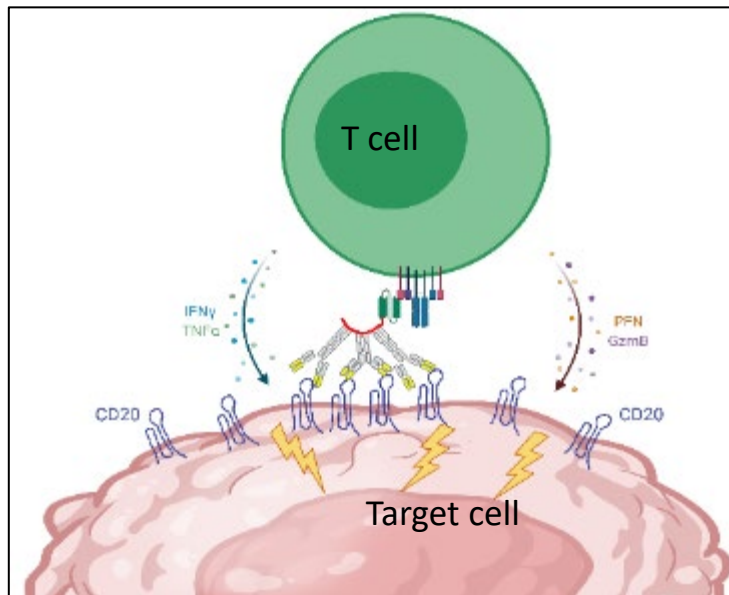
Potential to treat autoimmune diseases via deep B cell depletion



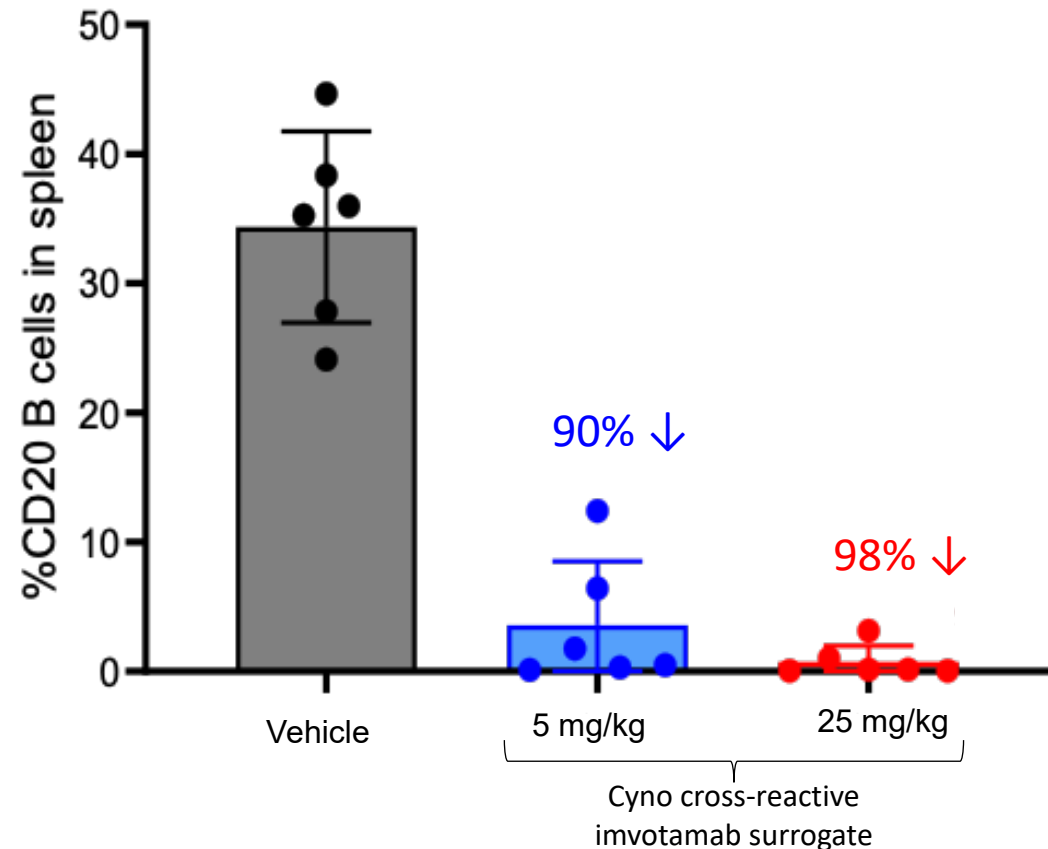
A safe, effective and accessible approach to utilize T cells to drive deep B cell depletion could address a broad range of B cell mediated autoimmune diseases

# IgM-based T cell engagers can deplete tissue resident B cells

IgM-based TCEs do not require local availability of NK cells, unlike ADCC-dependent antibodies



Deep depletion of CD20+ cells within spleen tissue (cyno)\*

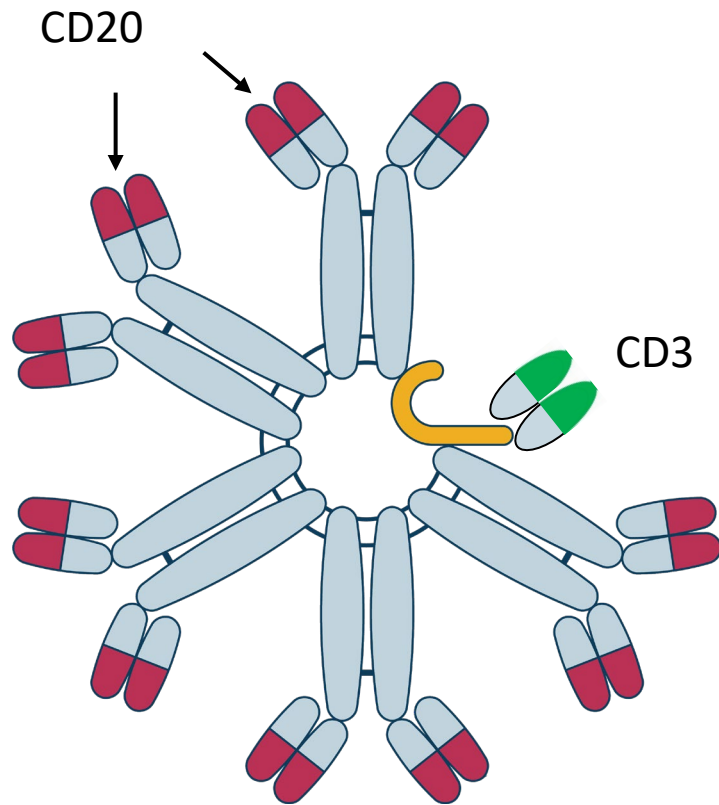




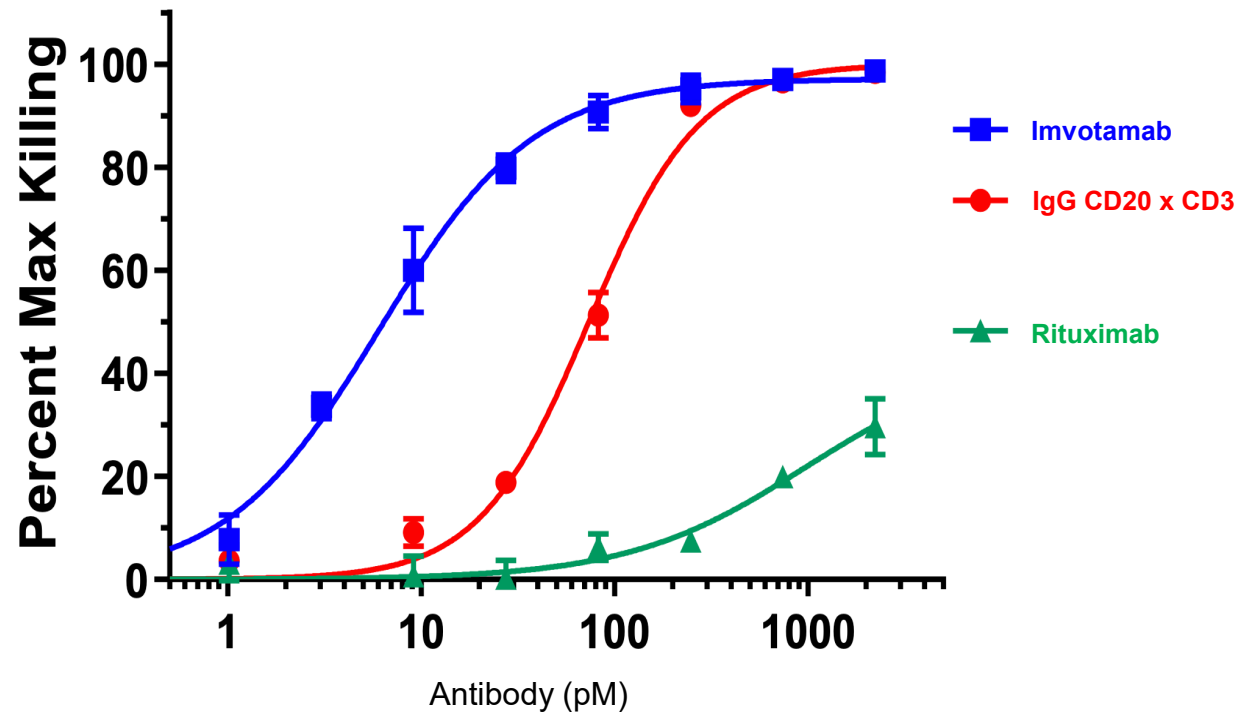
# IgM-based T cell engagers in autoimmunity

High avidity enables depletion of low CD20 target expressing cells

10 high affinity CDRs generate high avidity



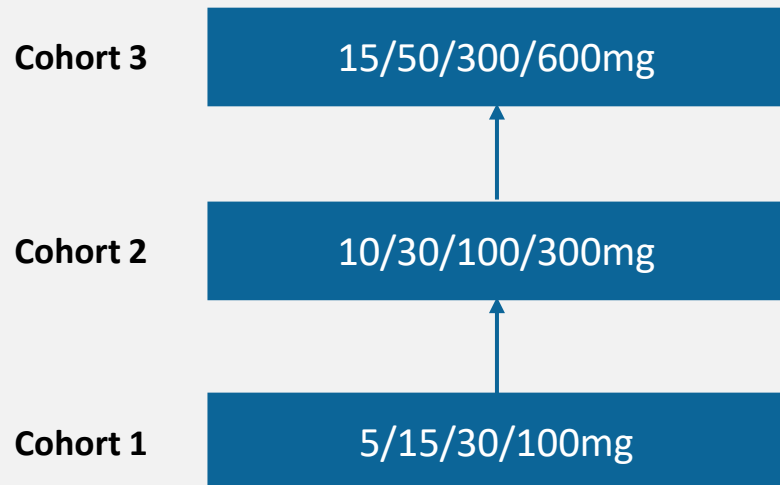
Killing of low CD20 expressing cells (in vitro)



# Ongoing invotamab (CD20 x CD3) Phase 1b clinical trials explore potential for deep B cell depletion

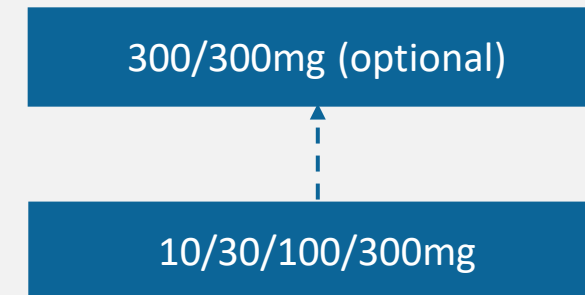
## SLE and RA

- 4 weekly escalating doses of invotamab
- 52-week follow-up
- **Systemic Lupus Erythematosus (SLE)**
  - Single arm, open label (N = 18)
  - Actively enrolling
- **Rheumatoid Arthritis (RA)**
  - Placebo controlled, double blinded (N = 24)
  - Actively enrolling



## Idiopathic Inflammatory Myopathies (Myositis)

- 4 weekly escalating doses of invotamab; 2 additional doses optional
- 52-week follow-up
- Single arm, open label (N = 5-10)
- Initiating Q1 2024



# Invotamab (CD20 x CD3) experience in NHL

Clinical evidence of B cell depletion in tissue and favorable safety profile

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## Favorable Efficacy Signals

Complete responses observed across all major non-Hodgkin lymphoma subtypes (DLBCL, FL, MCL, MZL)



**Invotamab demonstrated ability to effectively deplete B cells, even rapidly growing lymphoma cells**

## Favorable Safety Signals

Controlled physiologic stimulation of T cells resulted in relatively low levels of cytokine release syndrome

No reports of immune effector cell-associated neurotoxicity syndrome (ICANS)

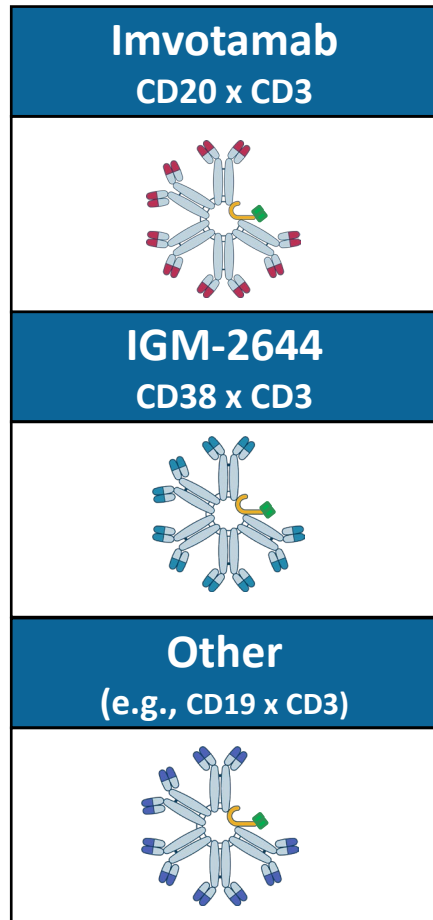


**Invotamab has shown an advantageous safety profile including CRS among CD20 x CD3 T cell engagers**

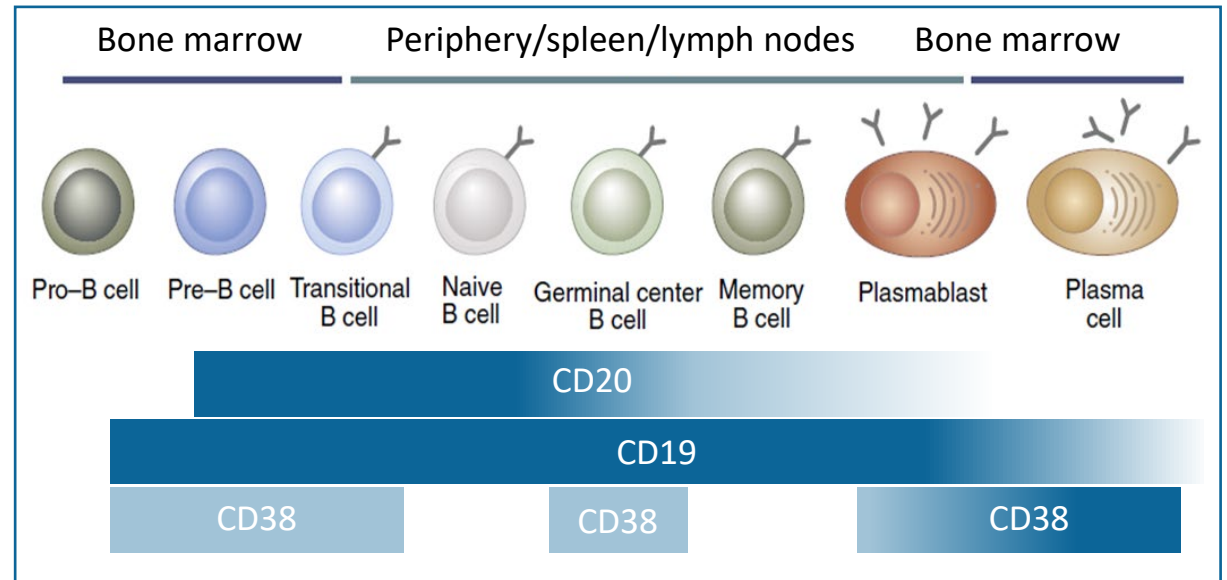
# Portfolio of IgM T cell engagers

Opportunity to explore range of targets across B cell lineage

## Broad Platform of Molecules



## Target Expression across B Cell Lineage



# Broad range of autoimmune diseases may benefit from deeper B cell depletion



**Multiple Sclerosis**

**Myasthenia Gravis**

**Neuromyelitis  
Optica**

**Demyelinating  
Polyneuropathy**



**Rheumatoid  
Arthritis**

**Systemic Lupus  
Erythematosus**

**Sjogren's**

**Myositis**



**Lupus nephritis**

**IgA nephropathy**

**ANCA vasculitis**



**Idiopathic  
thrombocytopenia  
purpura**

**Autoimmune  
Hemolytic Anemia**

**Anti-phospholipid  
Syndrome**



**Pemphigus Vulgaris**

**Alopecia Areata**



# Sanofi/IGM multi-target collaboration agreement

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Global research collaboration to leverage proprietary IgM antibody technology platform to create, develop and potentially commercialize agonists against three oncology targets and three autoimmunity and inflammation targets

- Financial Terms**
- \$150M upfront payment from Sanofi received
  - Equity investment in April 2022 follow-on public offering
  - Potentially \$6B+ in preclinical, clinical, regulatory and commercial milestone payments
  - Sanofi responsible for worldwide commercialization

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