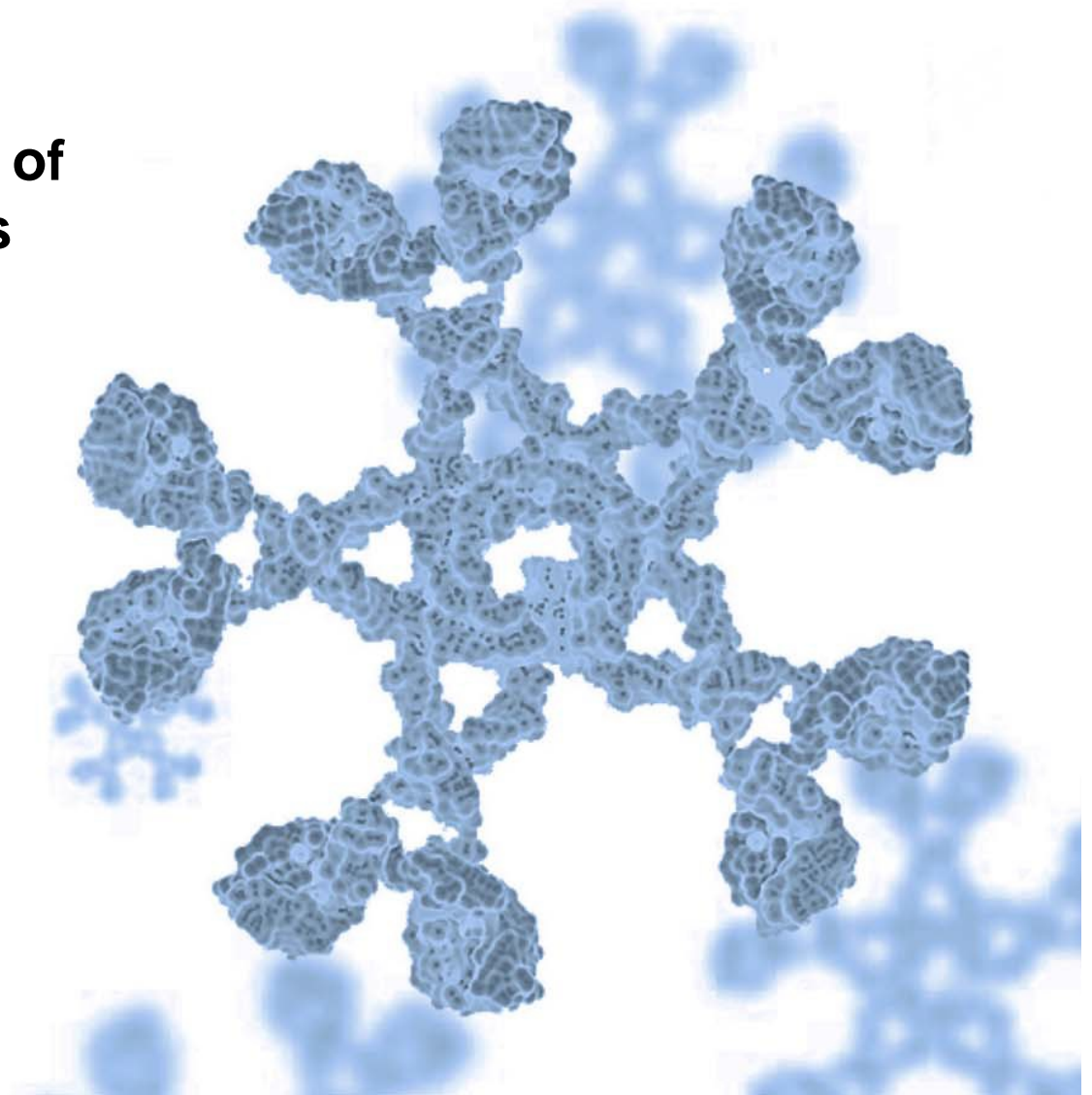




## **Pioneering the Development of Engineered IgM Antibodies**

**October 2020**



# 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 that reflect the current views of IGM Biosciences, Inc. (the “Company,” “we” or “our”) with respect to the Company’s future financial condition, results of operations, business strategy, expectations, milestones and plans. All statements other than statements of historical fact could be deemed forward-looking, including but not limited to statements with words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially” “predict,” “should,” “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: market conditions; the timing of the initiation, progress and results of our preclinical studies, clinical trials and our discovery programs; potential delays and disruption resulting from the COVID-19 pandemic and governmental responses to the pandemic, including any future impacts to our operations, the manufacturing of our product candidates, the progression of our current clinical trials, and enrollment in our current and future clinical trials; our early stages of clinical drug development; risks related to the use of engineered IgM antibodies, which is a novel and unproven therapeutic approach; 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 of our product candidates; 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 commercializing of 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; future strategic arrangements and/or collaborations and the potential benefits of such arrangements; 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 cash equivalents to fund our future operating expenses and capital expenditure requirements; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model, strategic plans for our business and product candidates; the scope of protection we are able to establish and maintain for intellectual property rights, including our IgM platform, product candidates and discovery programs; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; developments relating to our competitors and our industry, including competing product candidates and therapies; and other risks described in the “Risk Factors” section included in our public filings that we have made and will make with the Securities and Exchange Commission (“SEC”). 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. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

We have filed and will file Current Reports on Form 8-K, Quarterly Reports on Form 10-Q and Annual Reports on Form 10-K, and other documents with the SEC. You should read these documents for more complete information about us. You may obtain these documents for free by visiting EDGAR on the SEC website at [www.sec.gov](http://www.sec.gov).

This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. It is currently limited by federal law to investigational use, and no representation is made as to its safety or efficacy for the purposes for which it is being investigated.

# IGM Overview

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Global leaders in the development of engineered IgM antibodies for therapeutic use

## Lead Programs

CD20 x CD3	Non-Hodgkin's Lymphoma	Phase 1 in R/R B cell NHL underway
DR5	Solid and Hem. Malignancies	Phase 1 in solid tumors & NHL underway
IL-15 x PD-L1	Solid and Hem. Malignancies	IND filing: 2021 (anticipated)

Proprietary IgM antibody technology: 27 patent families




Strategy: extend our global leadership in the development of engineered IgM antibodies

- Advance product candidates and increase research and development efforts
- Build and control manufacturing capabilities
- Participate in commercialization if approved
- Expand intellectual property portfolio



\$203.1M Cash and Investments Balance, June 30, 2020

# IGM's Wholly-Owned Oncology Pipeline

## Lead Programs

Mode	Target	Indications	Phase of Development					Worldwide Commercial Rights	Anticipated Milestones
			Discovery	Preclinical	Phase 1	Phase 2	Phase 3		
<b>T cell Engager</b>	IGM-2323 (CD20 x CD3)	NHL, CLL							Initial Phase 1 data for R/R B cell NHL: 2020
<b>Receptor Cross-linking Agonist</b>	IGM-8444 (DR5)	Solid and Hematologic Malignancies							Initial Phase 1 data in solid tumors: 2021
<b>Targeted Cytokines</b>	IGM-7354 (IL-15 x PD-L1)	Solid and Hematologic Malignancies							IND filing: 2021 (anticipated)

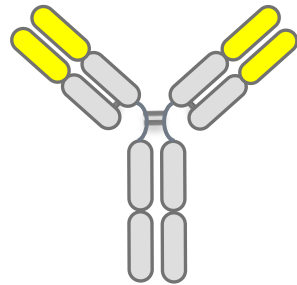
## Research and Discovery Programs

Mode	Target	Indications	Worldwide Commercial Rights
<b>T cell Engagers</b>	CD123 x CD3	Acute Myeloid Leukemia	
	CD38 x CD3	Multiple Myeloma	
	Multiple Targets x CD3	Multiple Solid Tumors	
<b>Receptor Cross-linking Agonists</b>	OX40	Solid and Hematologic Malignancies	
	GITR		

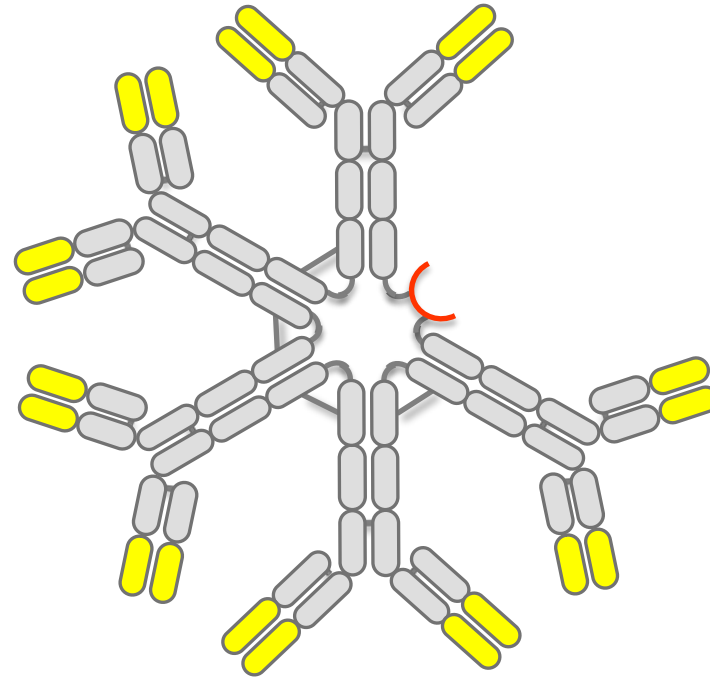
# Why IgM?

## Structural comparison of IgG and IgM antibodies

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**IgG**



**IgM**

### LEGEND

 Target binding domains

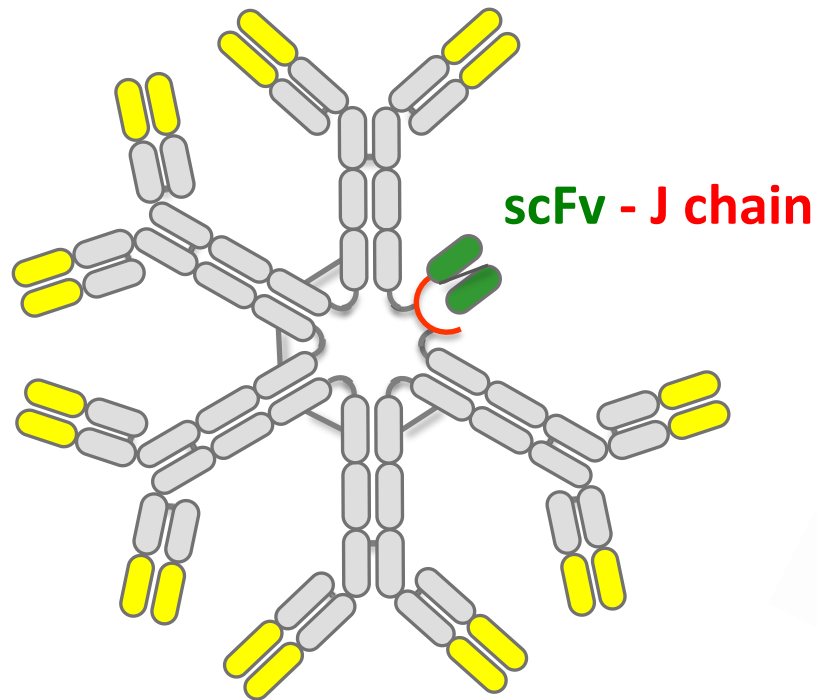
 Constant domains

 Joining chain (J chain)

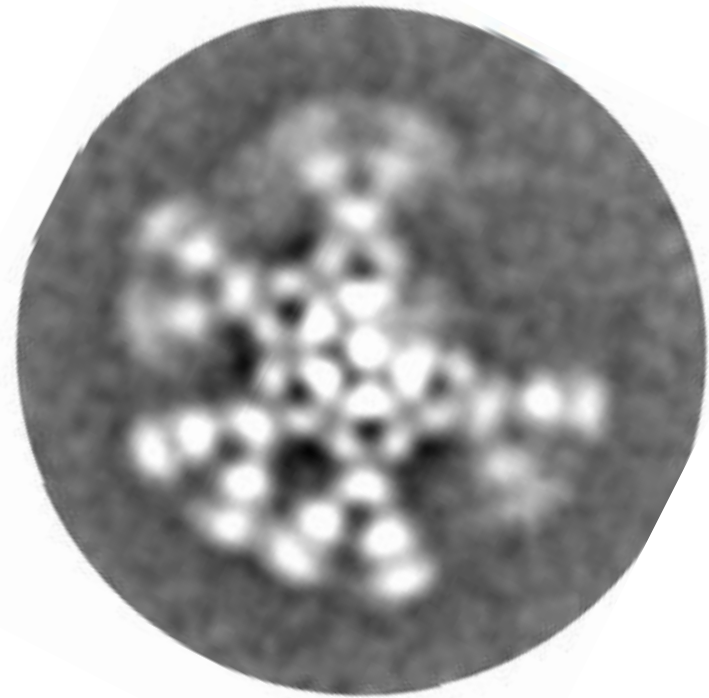
# IgM Asymmetric Bispecific Technology

High avidity, potent T cell dependent cytotoxicity

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CD20 IgM plus  
CD3 on J-chain

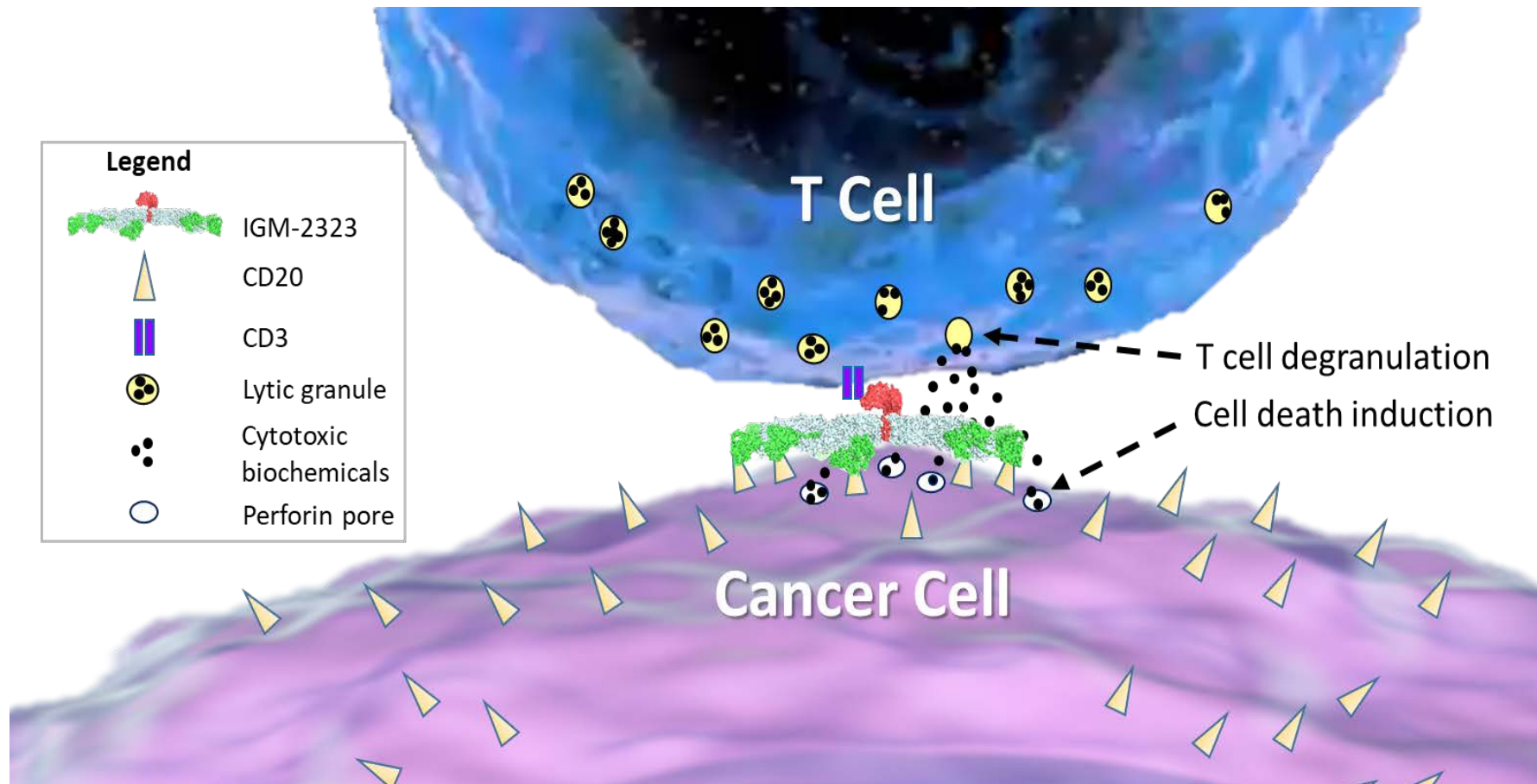




# IGM-2323 Bispecific T Cell Engagement

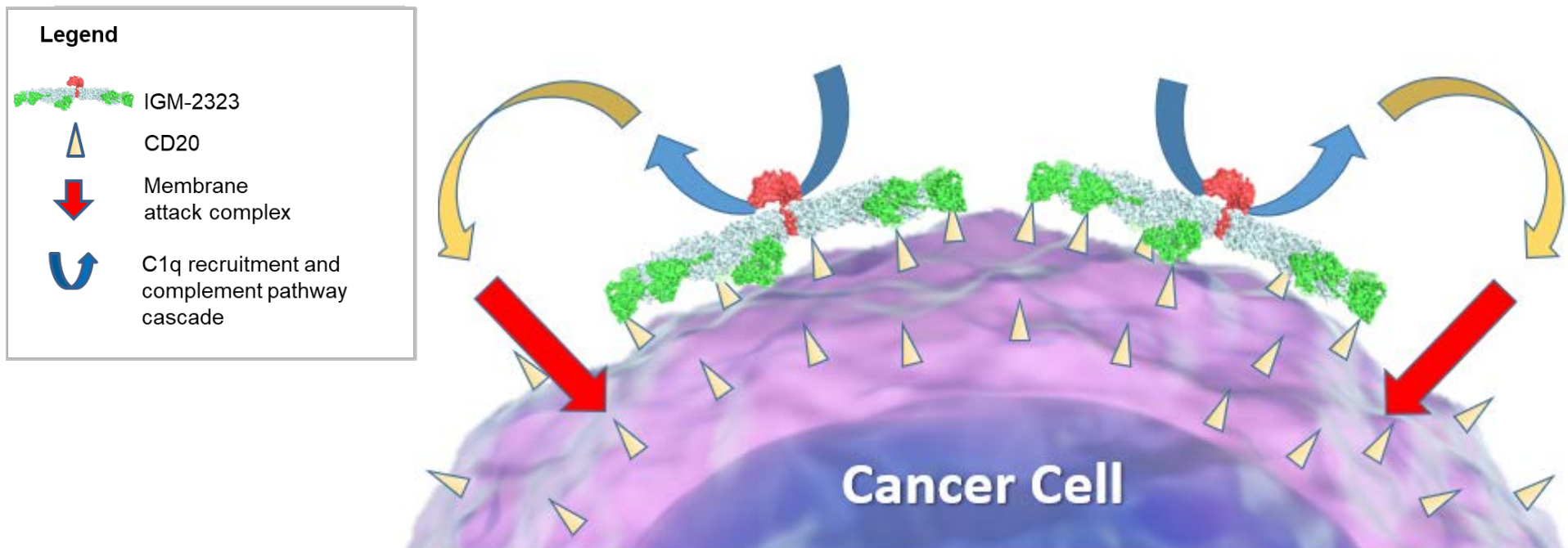
## T cell directed cellular cytotoxicity (TDCC)

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# IGM-2323 Dual Mechanism of Action

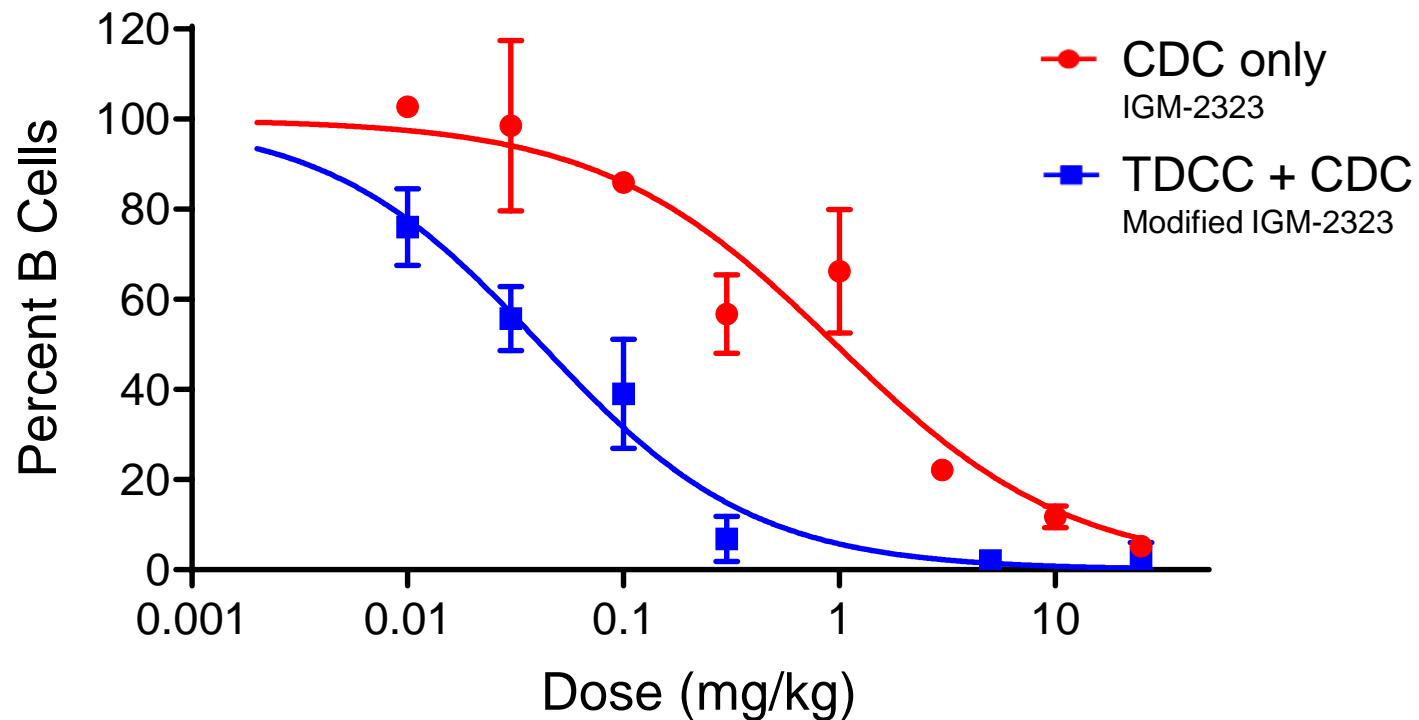
Complement dependent cytotoxicity (CDC)





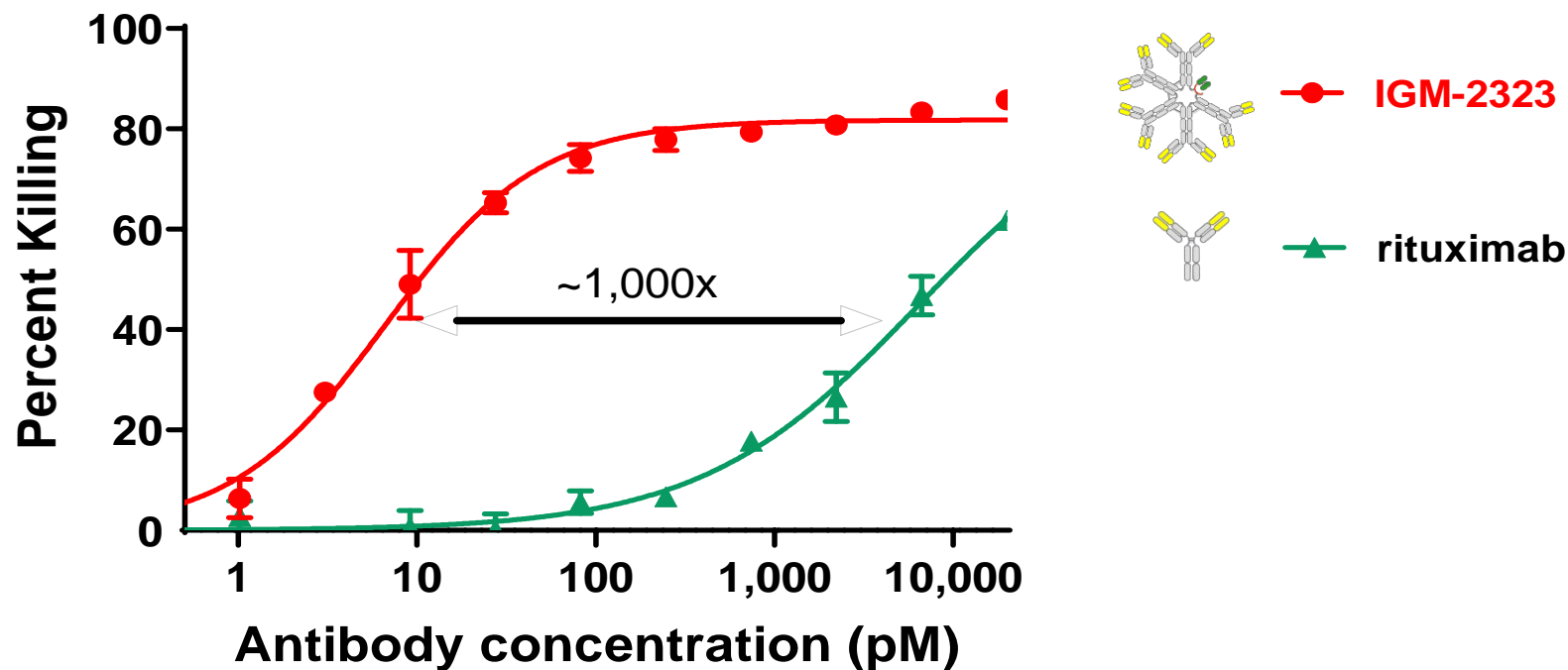
# Dual Mechanisms of Action: TDCC plus CDC

B cell depletion (CD19+) in non-human primate studies  
CDC only versus TDCC + CDC



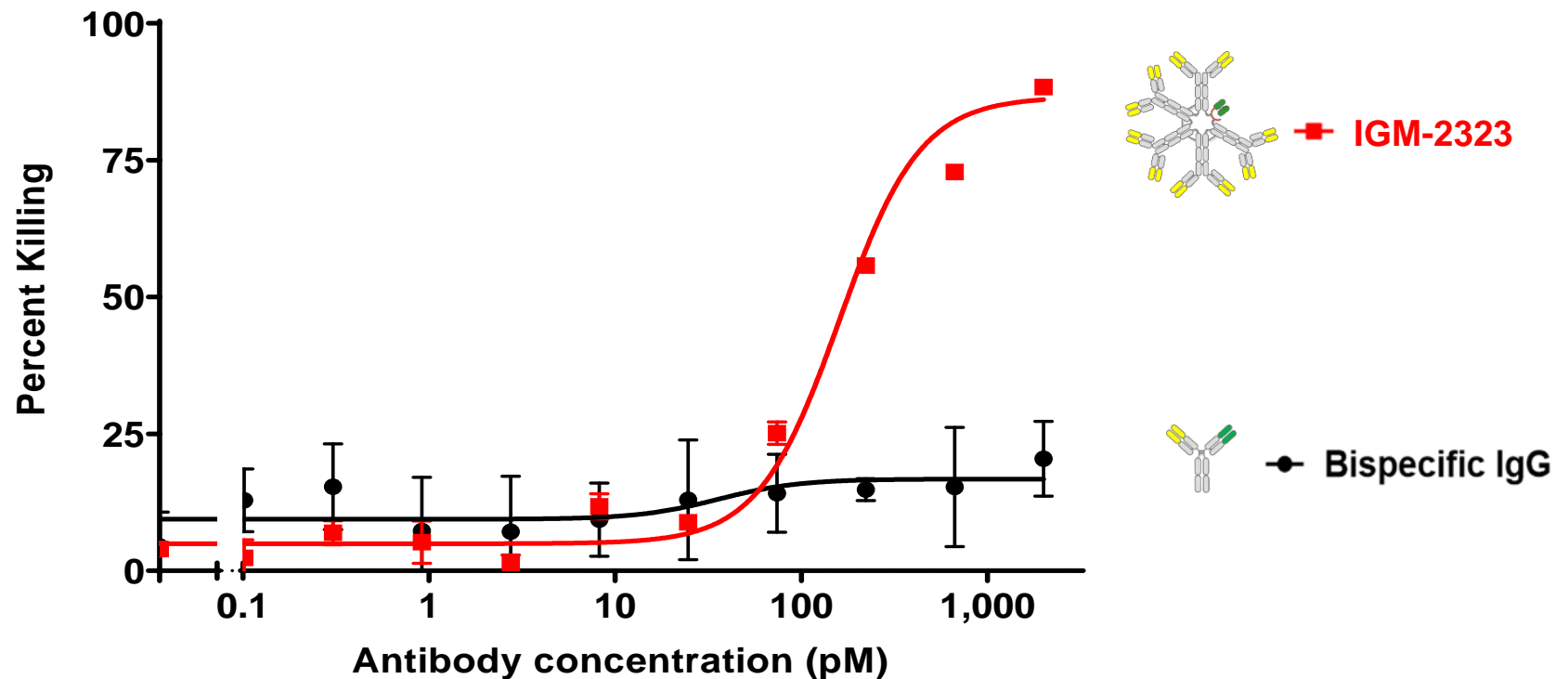
# Superior Killing in Rituximab Resistant Cell Line

Relative killing activity *in vitro* of IGM-2323 and rituximab using a rituximab resistant B cell cancer line



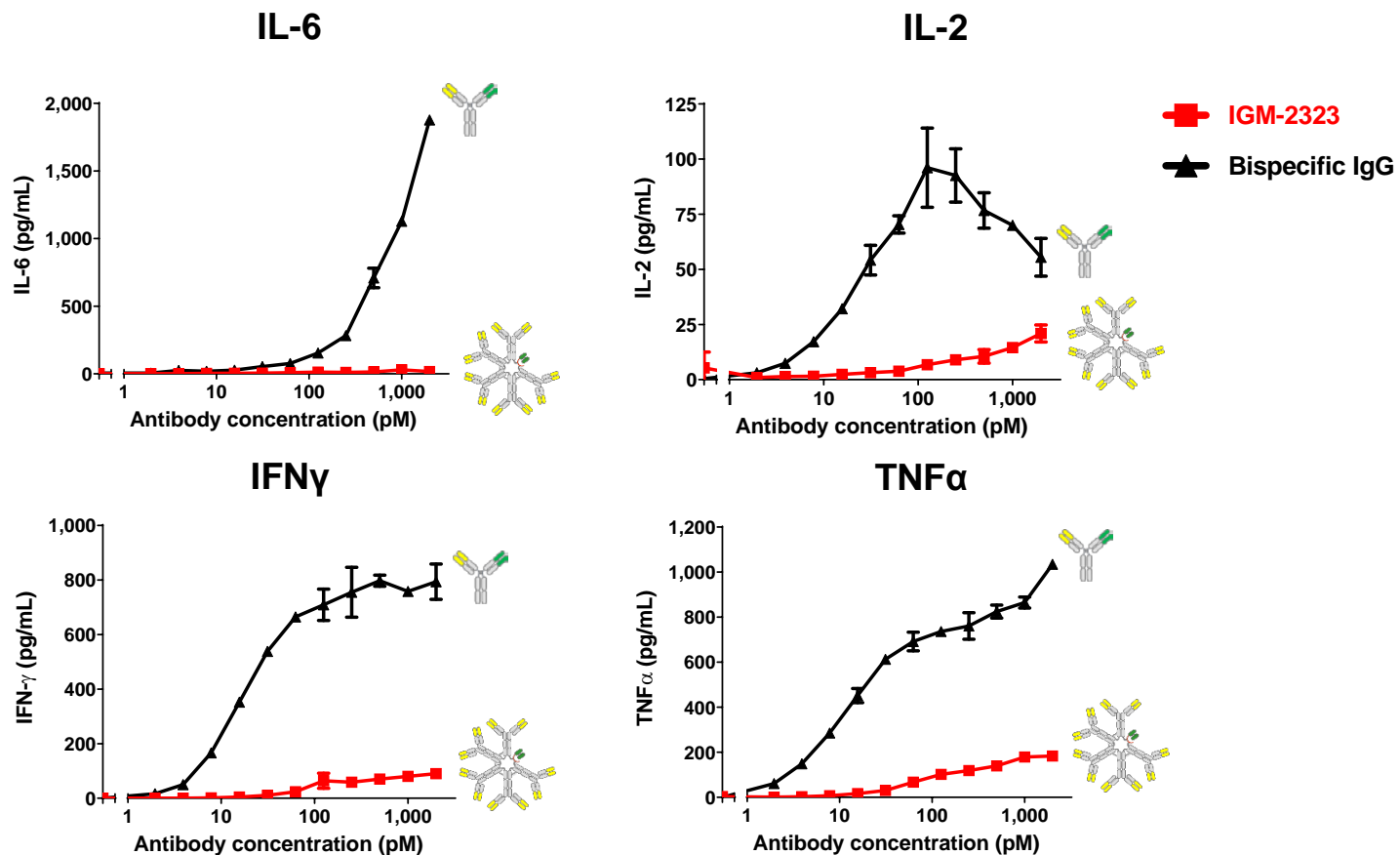
# More Efficient Killing *In Vitro* When T Cells Are Limited in Number

T cell count can be low in certain tumor microenvironments  
One T cell per five cancer cells

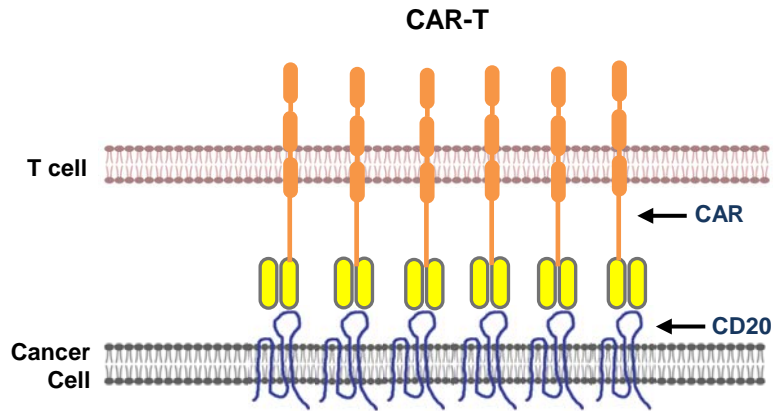


# IgM: Potentially Safer T Cell Directed Bispecific Antibodies

Lower cytokine release profile *in vitro* compared to IgG CD20 x CD3 bispecific antibody

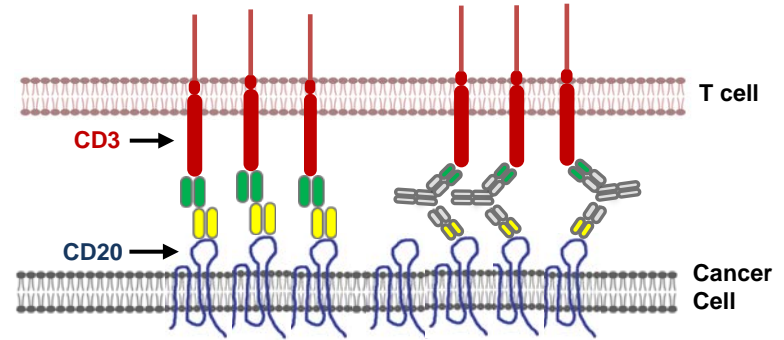


# Immune Synapses

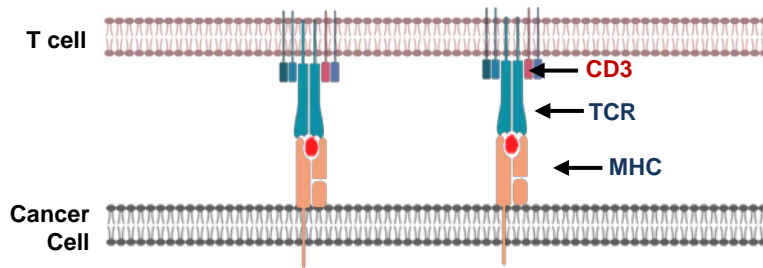


**Bispecific T cell :  
Target Engager  
Single Chain Units**

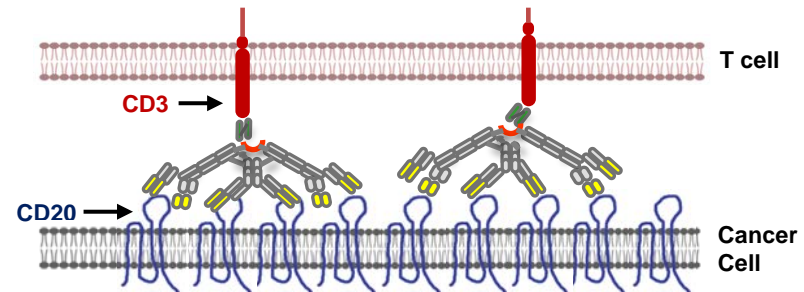
**Bispecific T cell :  
Target Engager IgG**



**T cell receptor : MHC Engagement**



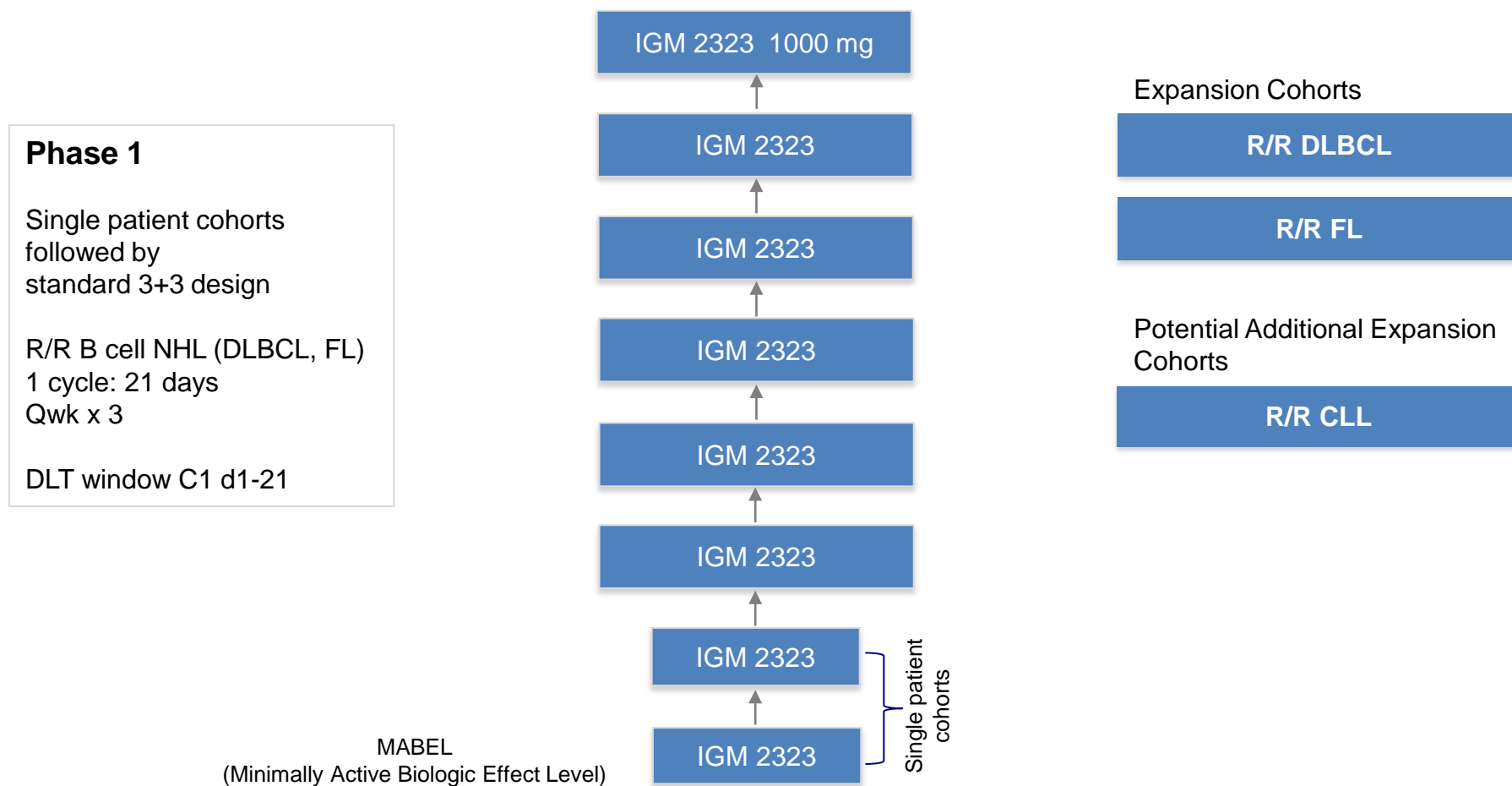
**Bispecific T cell : Target Engager IgM**



CAR-T, Chimeric antigen receptor-T cell  
MHC, Major histocompatibility complex plus peptide  
TCR, T cell receptor

# IGM-2323 Phase 1: Relapsed/Refractory B cell NHL

## Dose escalation schedule

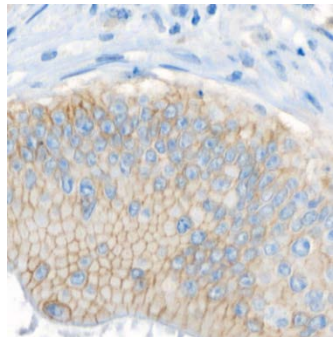




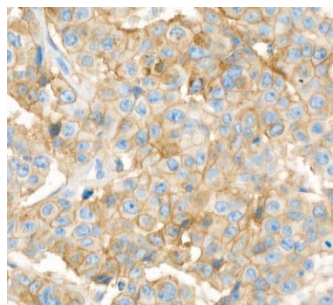
# TNFr Superfamily: Trimerizing Agonists

Examples of TNFr agonism: inducing Death Receptor 5 based cell killing

## DR5 Expression

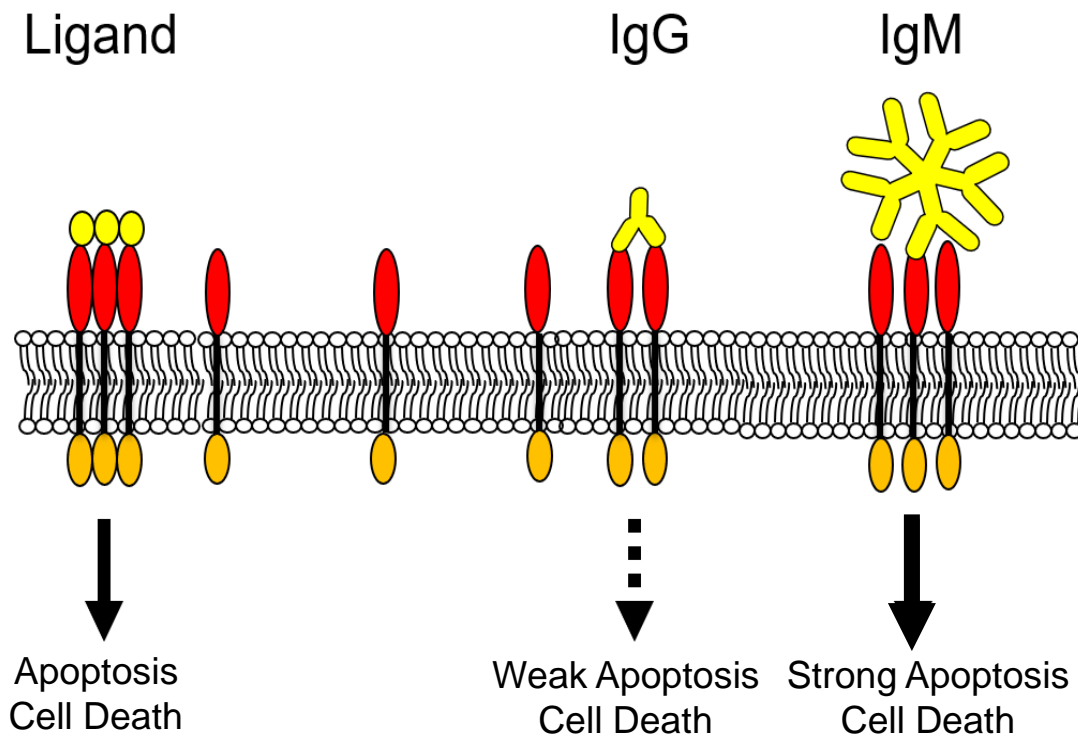


Colon Adenocarcinoma



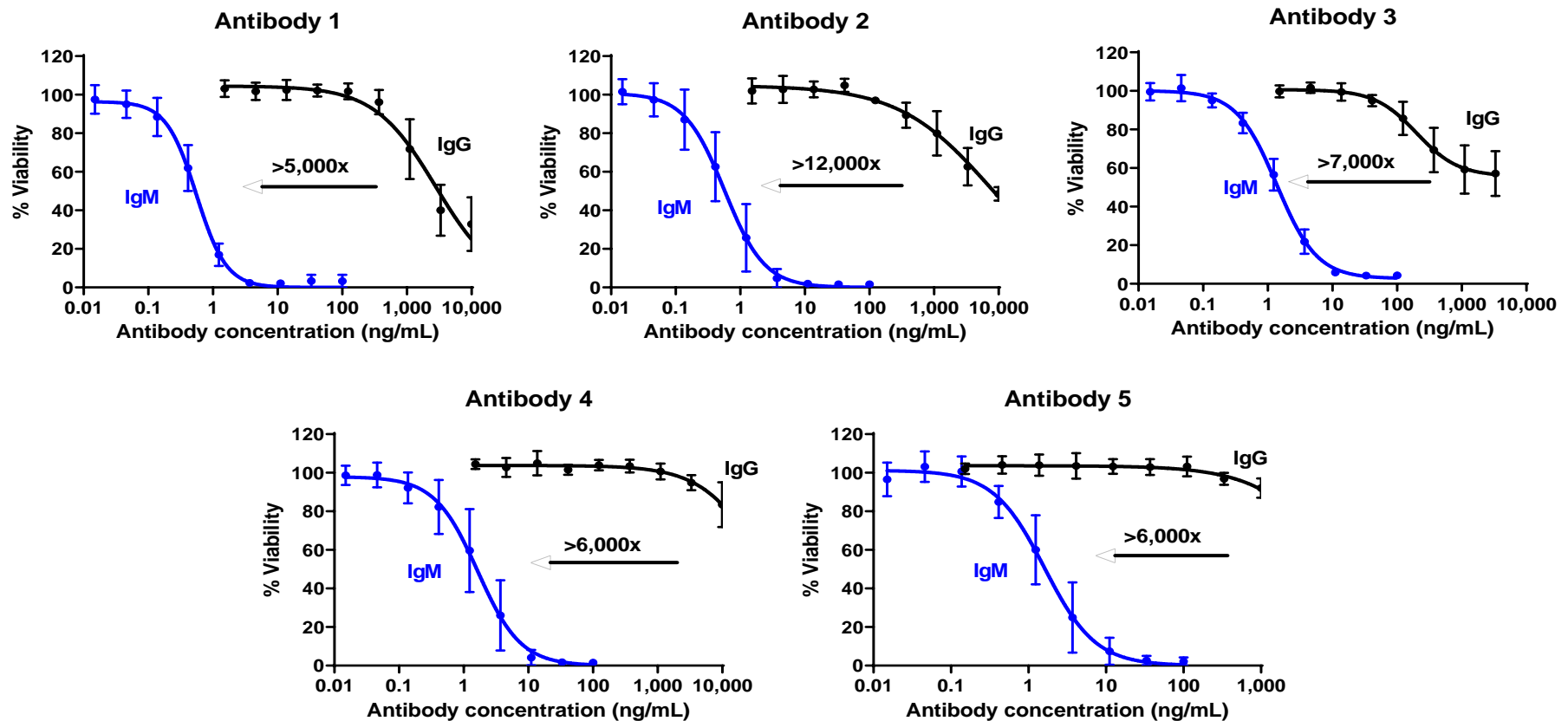
Gastric Adenocarcinoma

Also: pancreatic, lung, breast and prostate tumors, leukemia and lymphoma



# DR5: IgM Superior *In Vitro* to IgG

Cell line killing comparison *in vitro* of IgG and IgM DR5 antibodies with five different binding domains



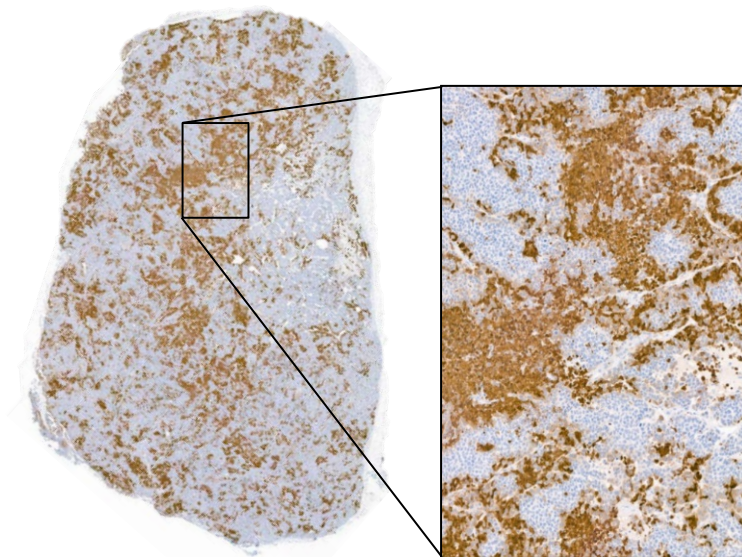
# Anti-DR5 IgM Antibodies Penetrate Tumors and Rapidly Induce Apoptosis After a Single Dose

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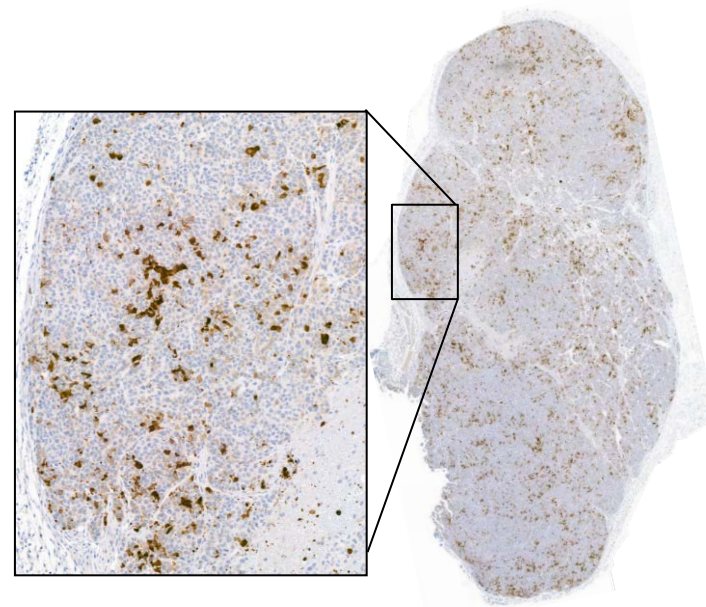
## Cleaved Caspase-3 at 1 hour

Colo205 Tumors

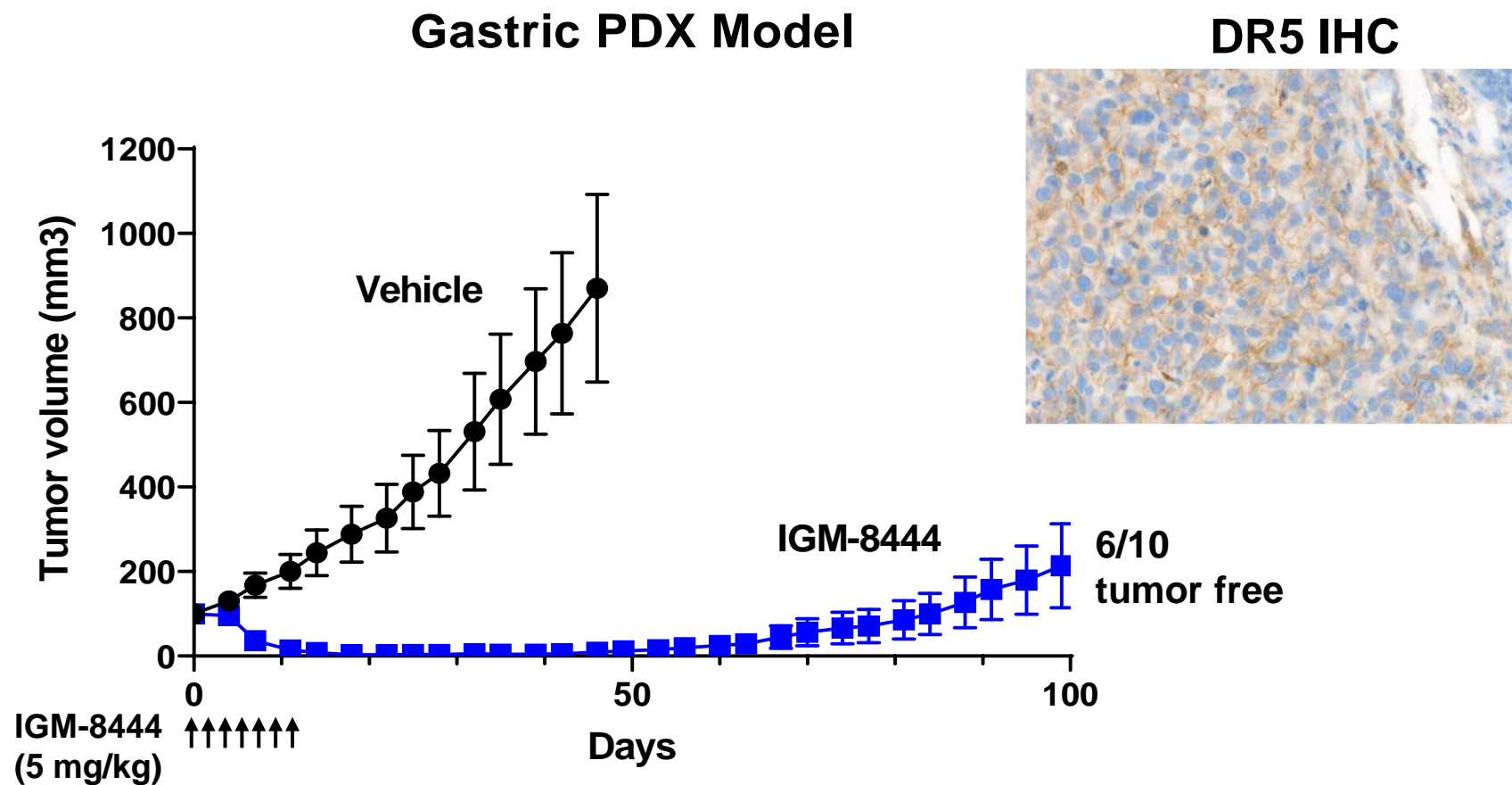
DR5-IgM



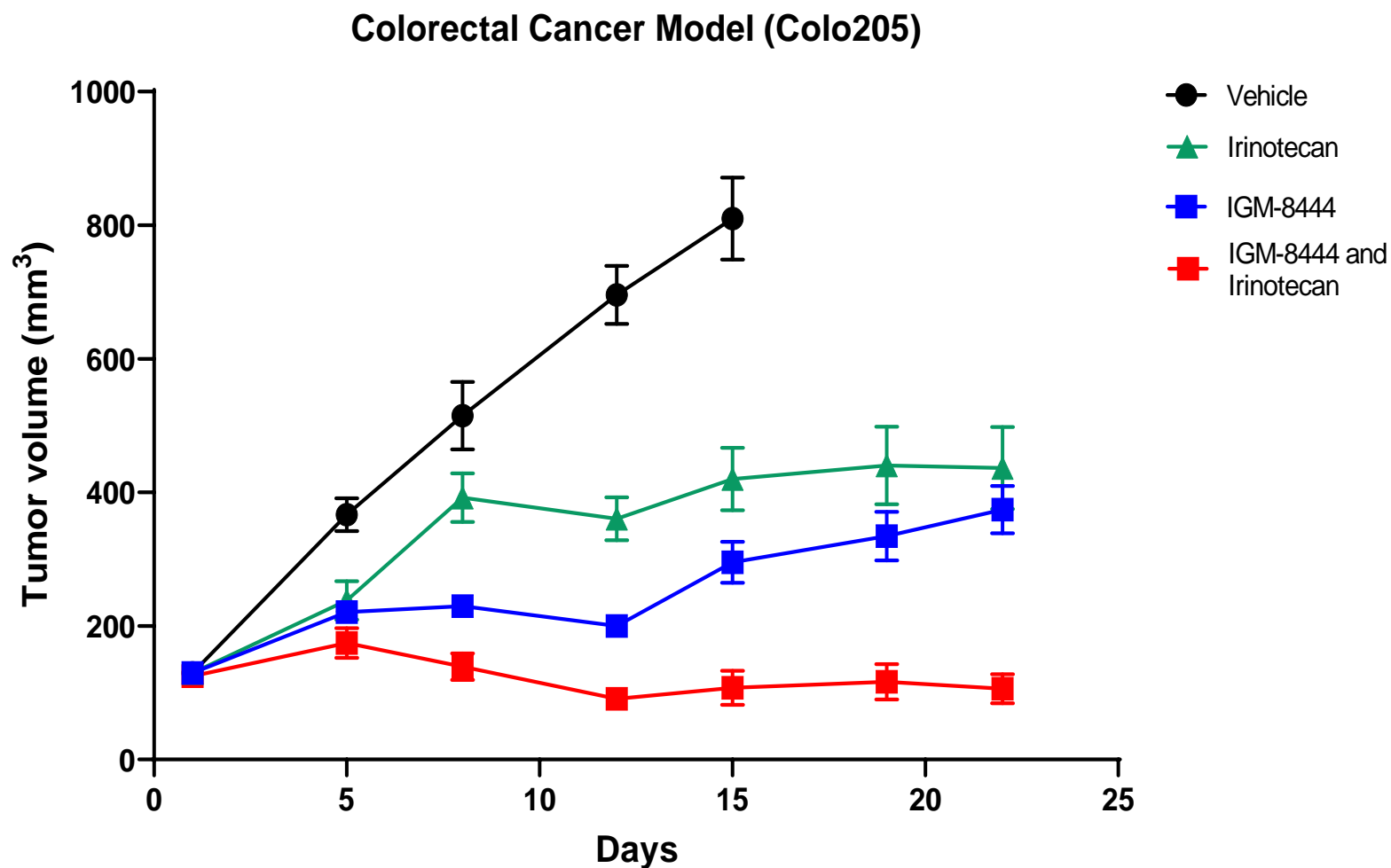
DR5-IgG



## DR5: IGM-8444 *In Vivo* mouse xenograft study

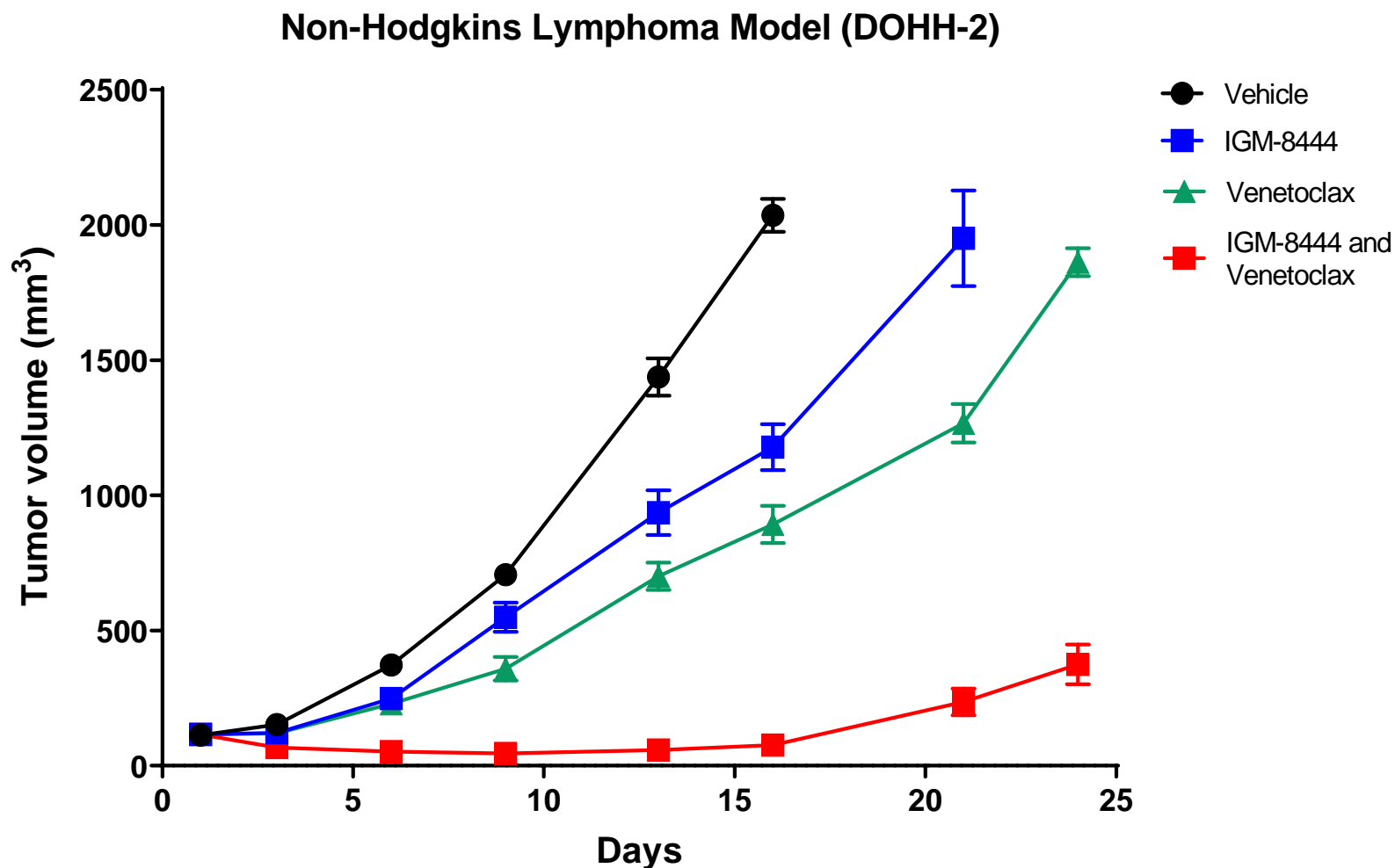


## DR5: IGM-8444 *In Vivo* combination with Irinotecan



IGM-8444 (5 mg/kg Q2D x 7); Irinotecan (100 mg/kg QW x 3)

## DR5: IGM-8444 *In Vivo* combination with Venetoclax



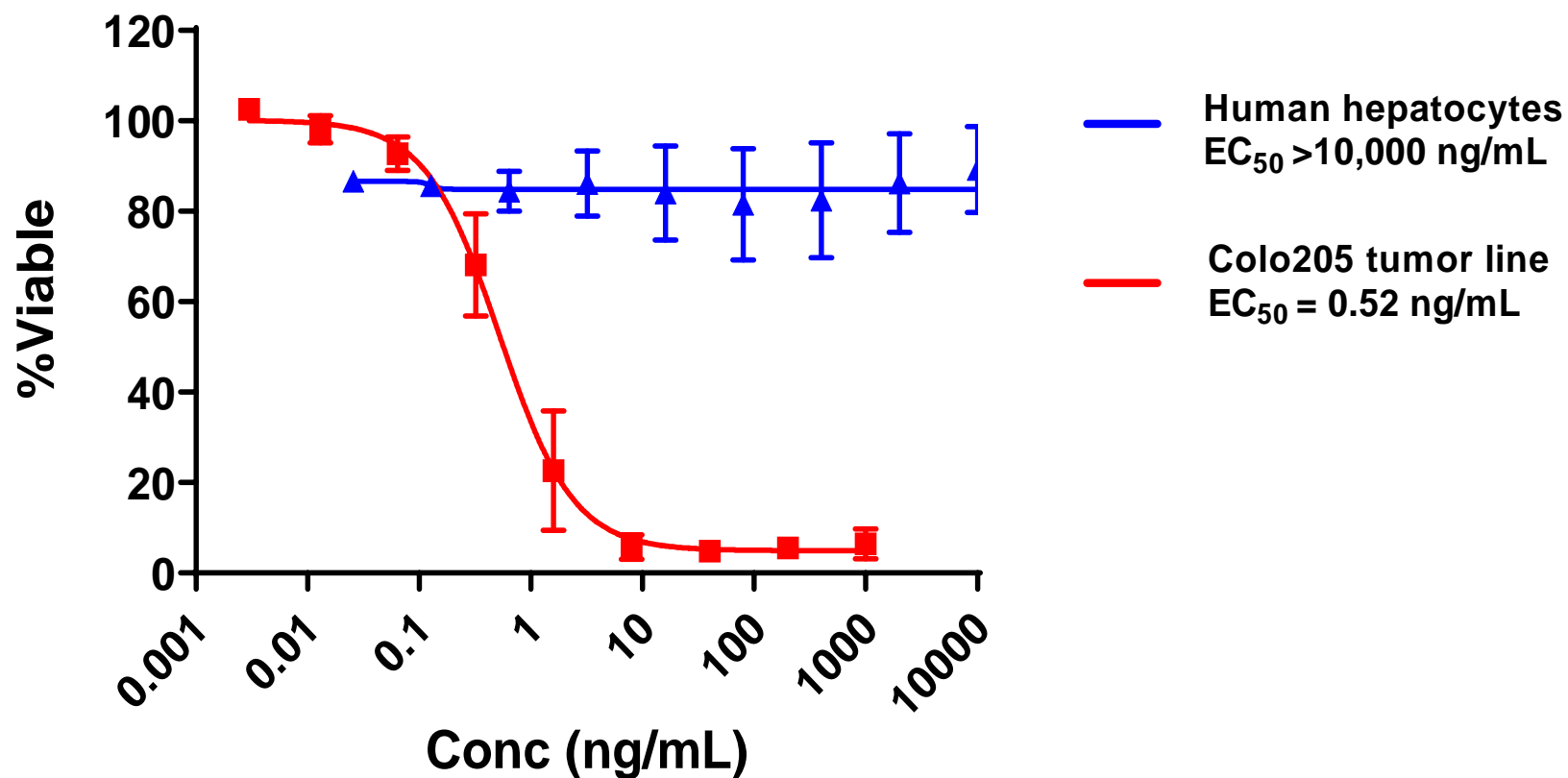
IGM-8444 (5 mg/kg Q2D x 11); Venetoclax (100 mg/kg QD x 21)



## DR5: IGM-8444 *In Vitro* therapeutic window

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### In Vitro Cytotoxicity



# IGM-8444 Phase 1: All-comers Solid Tumors and Heme

## Dose escalation schedule

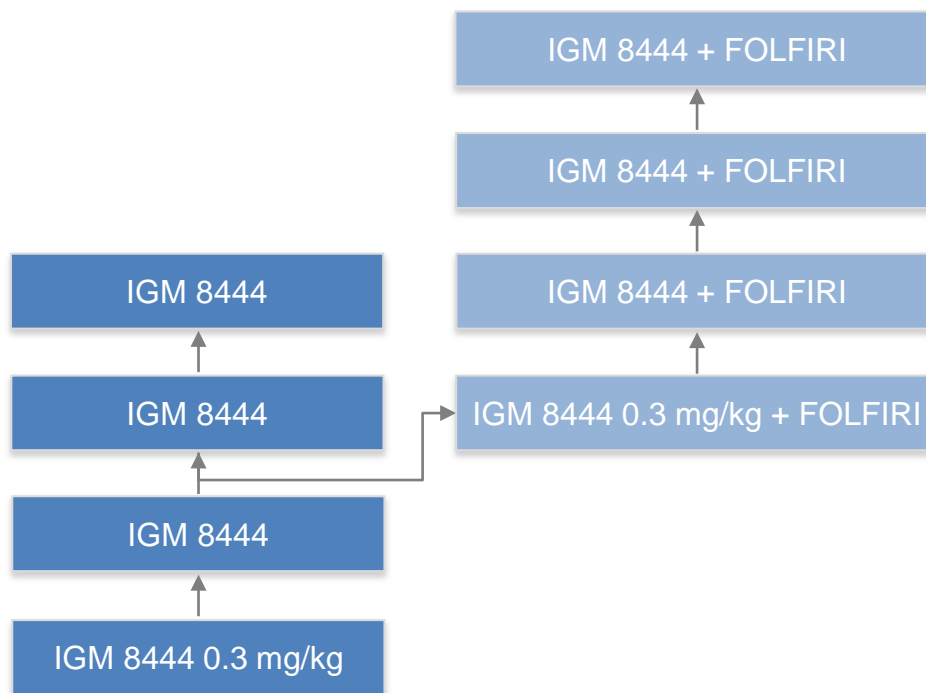
### Phase 1

Standard 3+3 design

All-comers solid tumor escalation as monotherapy and in combination with chemotherapy

Dosing q2week (with flexibility to test additional schedules)

DLT window d1-28 (Cycle 1)



### Single Agent Expansion Cohorts

#### Solid Tumor

including Colorectal, Lung, Gastric Cancer, Other

#### Hematologic Malignancies

including NHL

### Combination Expansion Cohorts

#### 1L/2L CRC

IGM-8444 + FOLFIRI

#### 1L/2L CRC

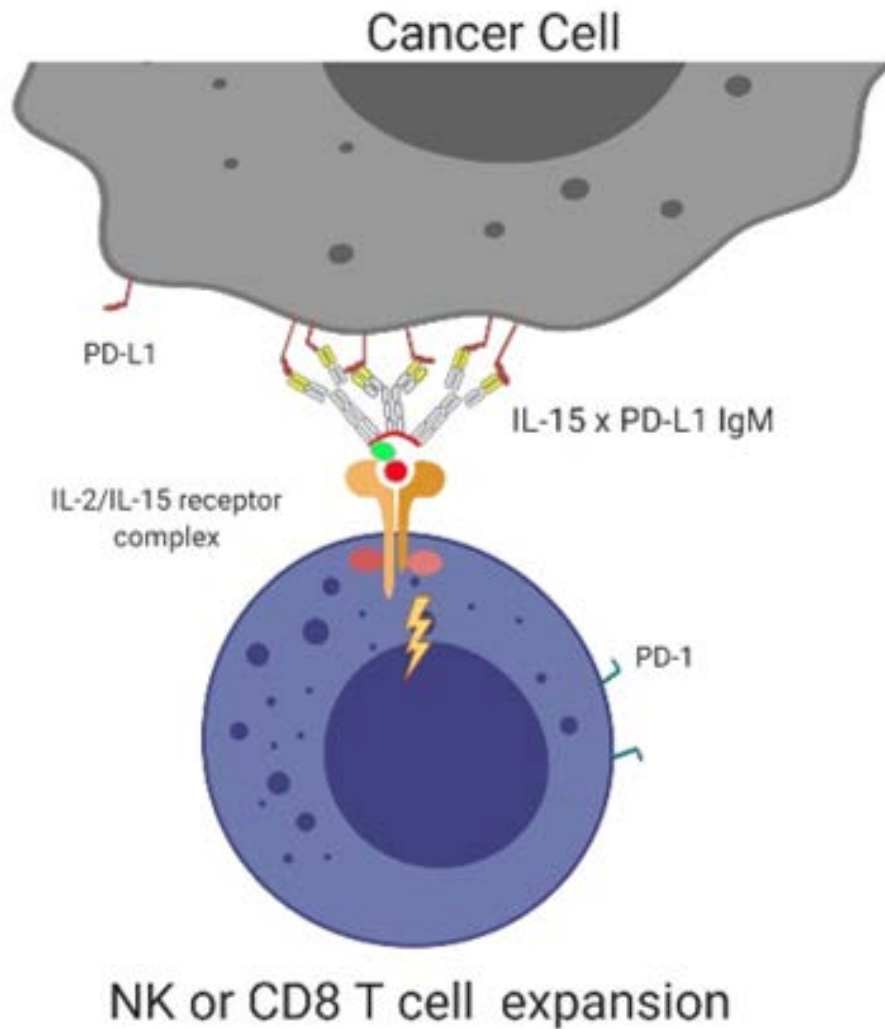
IGM-8444 + FOLFIRI + Avastin

### Potential Additional Expansion Cohorts

IGM-8444 + Targeted therapies

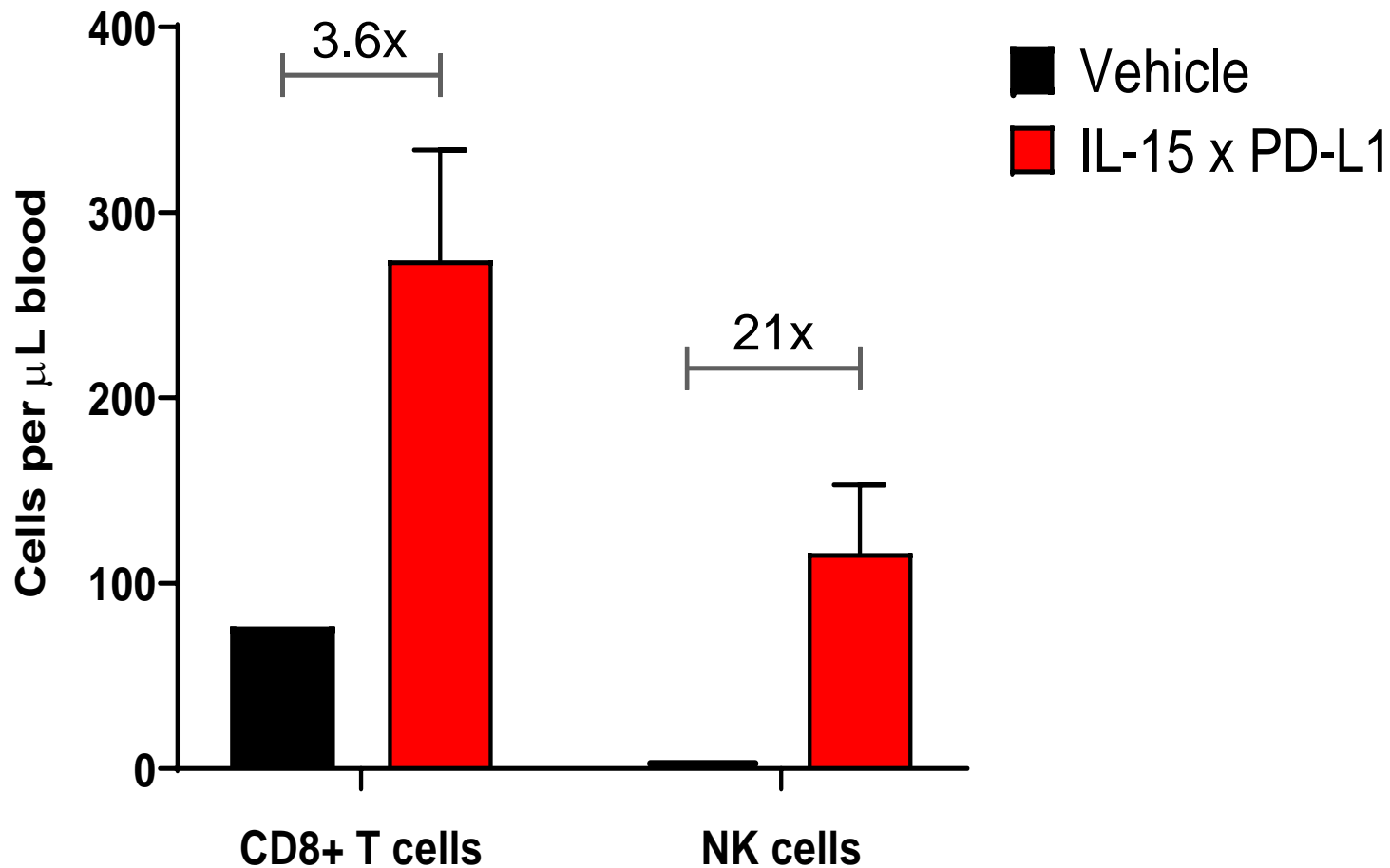
# IL-15 delivered by high avidity PD-L1 IgM antibody

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## IL-15 x PD-L1: IGM-7354 induces NK and CD8 T cell expansion in humanized mice

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# Leadership Team



**FRED M. SCHWARZER**  
Chief Executive Officer



**ELIZABETH HAANES, PhD**  
VP, Intellectual Property



**SUZETTE TAUBER**  
VP, Human Resources



**BRUCE KEYT, PhD**  
Chief Scientific Officer



**ANGUS SINCLAIR, PhD**  
VP, Immuno-Oncology



**STEVE CARROLL, PhD**  
VP, Preclinical Sciences



**DANIEL S. CHEN, MD, PhD**  
Chief Medical Officer



**WAYNE GODFREY, MD**  
VP, Clinical Development



**KATHY MILLER, PhD**  
VP, Antibody Discovery



**MISBAH TAHIR**  
Chief Financial Officer



**ERIC HUMKE, MD, PhD**  
VP, Clinical Development



**MARVIN PETERSON, PhD**  
VP, Process Sciences  
& Manufacturing



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\$203.1M Cash and Investments Balance, June 30, 2020





**Thank You**

