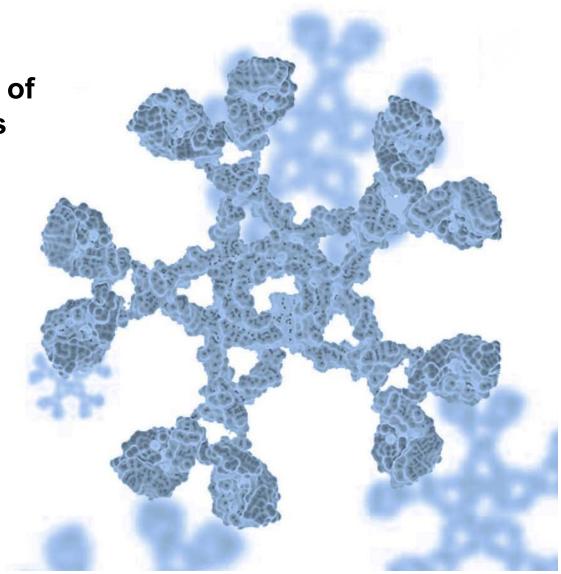


Pioneering the Development of Engineered IgM Antibodies

September 2020



## **Forward-looking Statements**

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.

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**

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 | IND cleared; Phase 1 initiation: 2020 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**

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

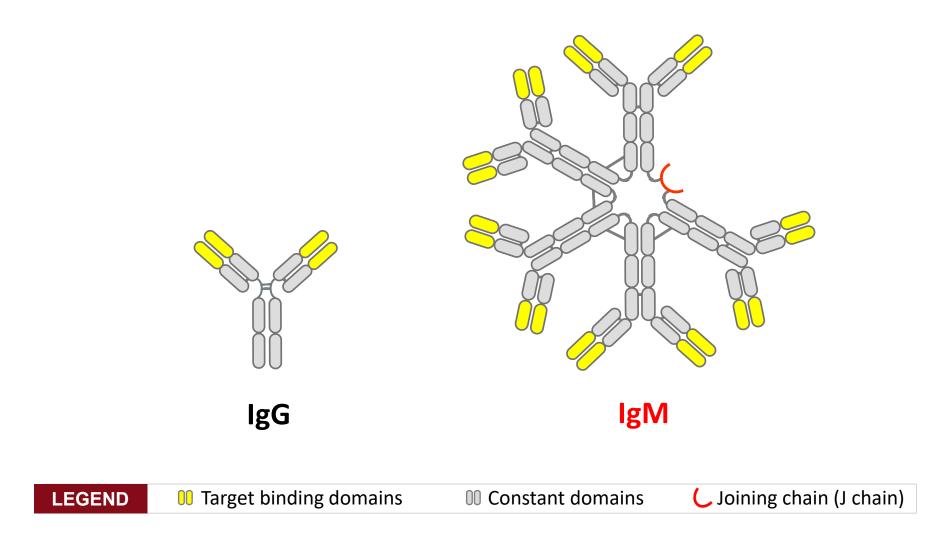
#### **Research and Discovery Programs**

Mode	Target	Indications	Worldwide Commercial Rights	
T cell Engagers	CD123 x CD3	Acute Myeloid Leukemia	<b>#IGM</b> biosciences	
	CD38 x CD3	Multiple Myeloma		
	Multiple Targets x CD3	Multiple Solid Tumors		
Receptor Cross- linking Agonists	OX40	Solid and Hamatalagia Malignanaiaa	€ <sub>w</sub> ₃IGM	
	GITR	Solid and Hematologic Malignancies	<b>biosciences</b>	



## Why IgM?

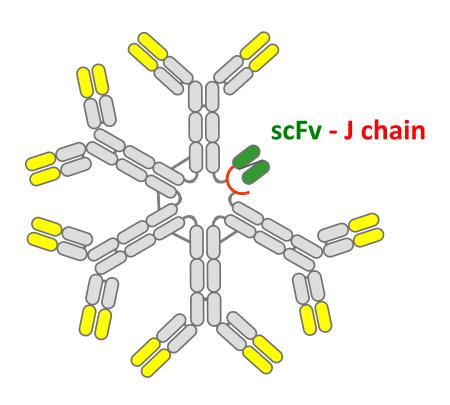
## Structural comparison of IgG and IgM antibodies



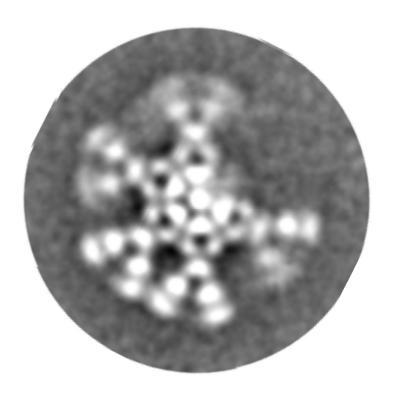


## **IgM Asymmetric Bispecific Technology**

High avidity, potent T cell dependent cytotoxicity



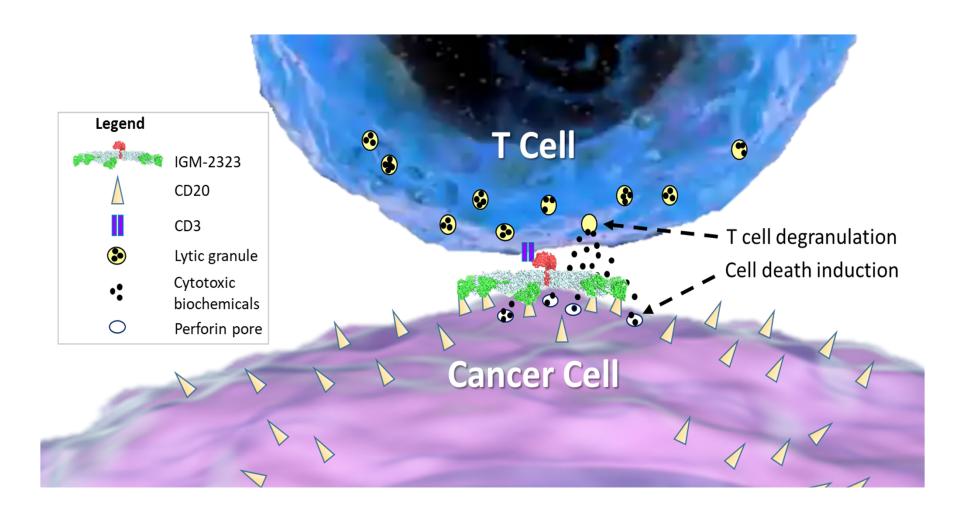
CD20 IgM plus CD3 on J-chain





## **IGM-2323** Bispecific T Cell Engagement

T cell directed cellular cytotoxicity (TDCC)

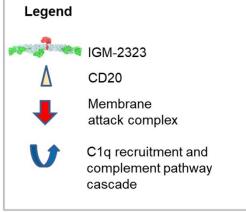


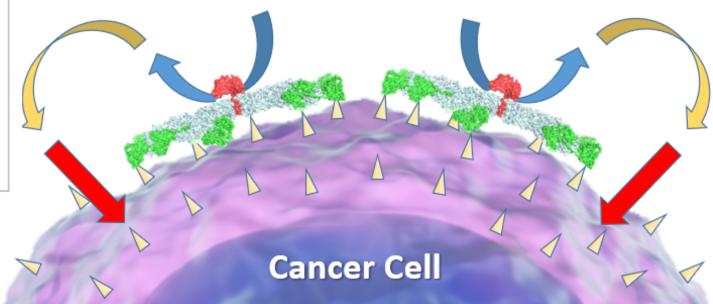


## **IGM-2323 Dual Mechanism of Action**

Complement dependent cytotoxicity (CDC)

### Complement cascade

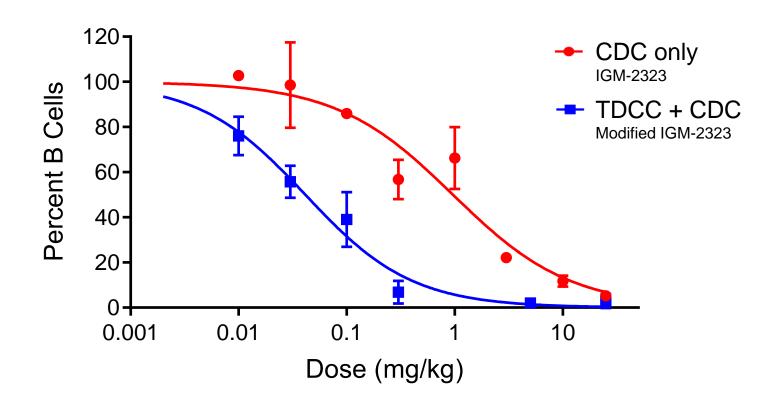






## **Dual Mechanisms of Action: TDCC plus CDC**

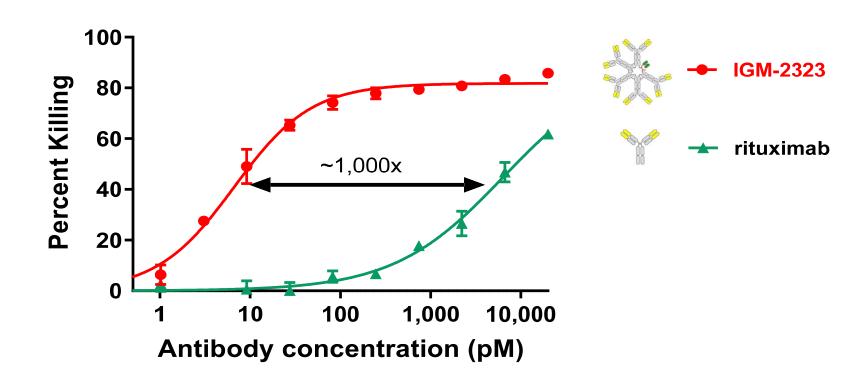
B cell depletion (CD19+) in non-human primate studies CDC only versus TDCC + CDC





## Superior Killing in Rituximab Resistant Cell Line

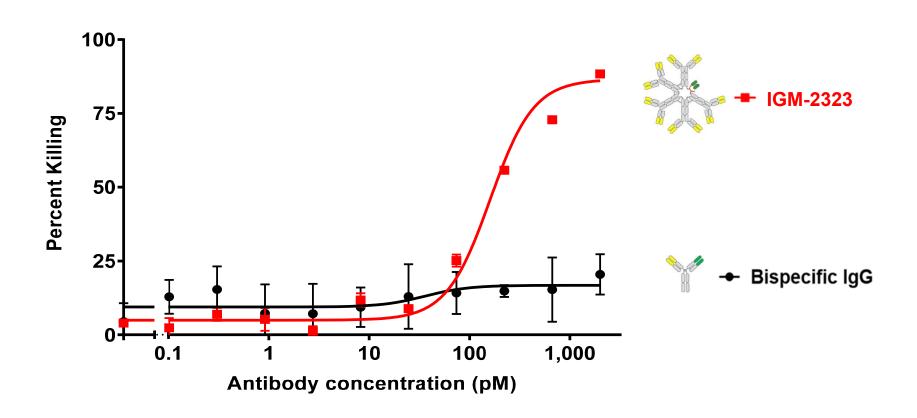
Relative killing activity *in vitro* of IGM-2323 and rituximab using a rituximab resistant B cell cancer line





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

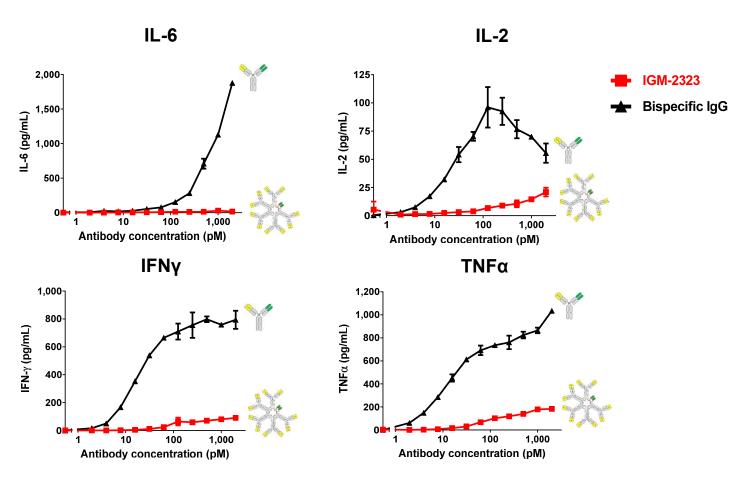
T cell count can be low in certain tumor microenvironments
One T cell per five cancer cells





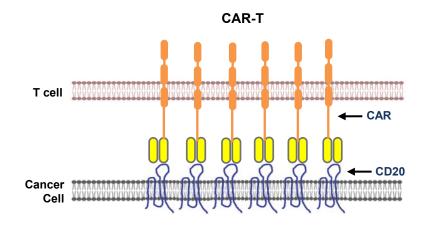
## IgM: Potentially Safer T Cell Directed Bispecific Antibodies

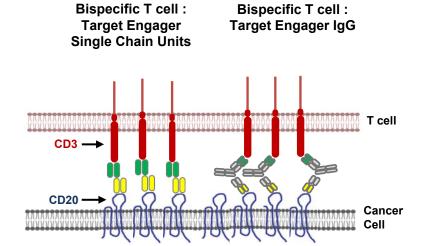
Lower cytokine release profile *in vitro* compared to IgG CD20 x CD3 bispecific antibody



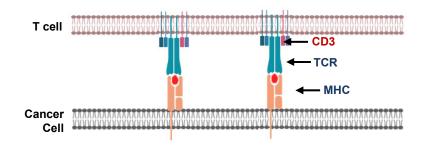


## **Immune Synapses**

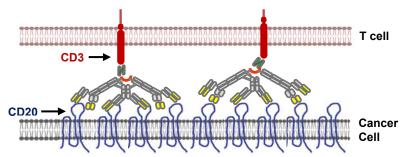




#### T cell receptor : MHC Engagement



#### 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

## Phase 1

Single patient cohorts followed by standard 3+3 design

R/R B cell NHL (DLBCL, FL) 1 cycle: 21 days Qwk x 3

DLT window C1 d1-21



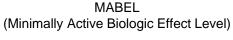
**Expansion Cohorts** 

R/R DLBCL

R/R FL

Potential Additional Expansion Cohorts

R/R CLL

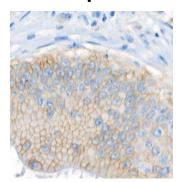




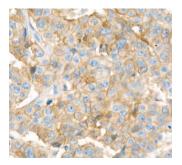
## **TNFr Superfamily: Trimerizing Agonists**

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

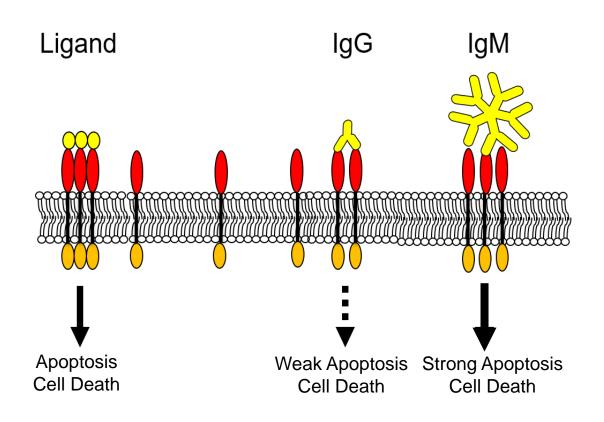
#### **DR5 Expression**



Colon Adenocarcinoma



Gastric Adenocarcinoma

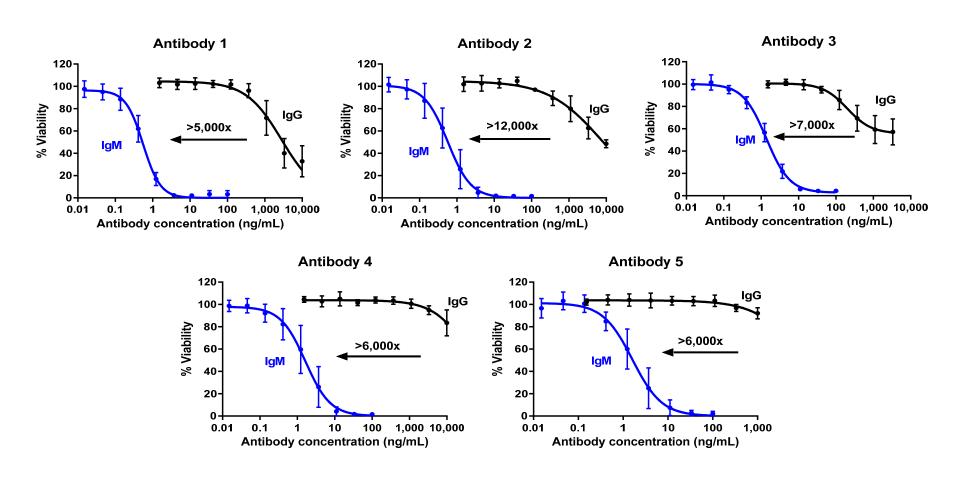


Also: pancreatic, lung, breast and prostate tumors, leukemia and lymphoma



## DR5: IgM Superior In Vitro to IgG

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

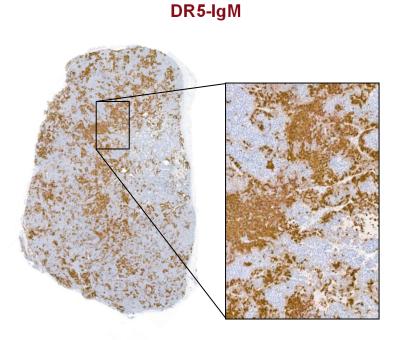


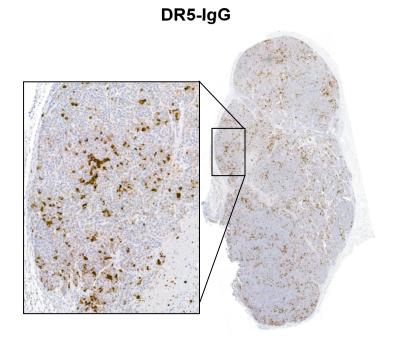


# **Anti-DR5 IgM Antibodies Penetrate Tumors and Rapidly Induce Apoptosis After a Single Dose**

### **Cleaved Caspase-3 at 1 hour**

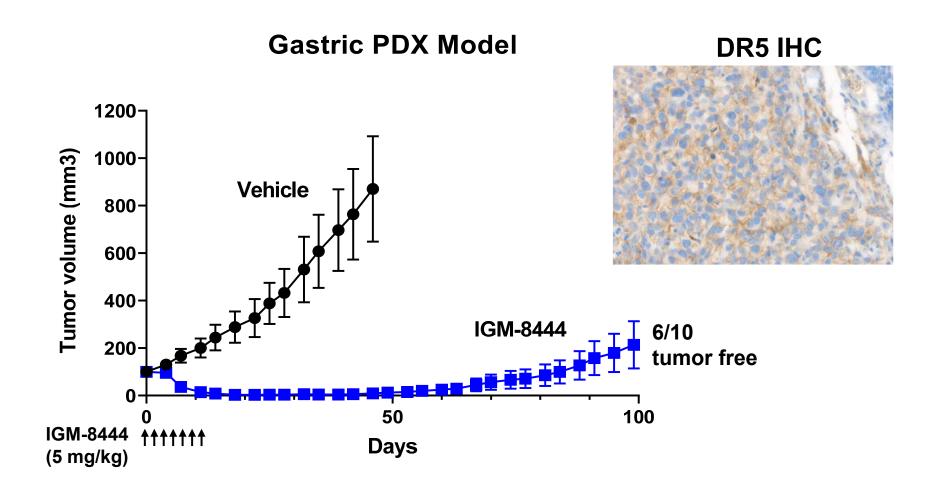
**Colo205 Tumors** 





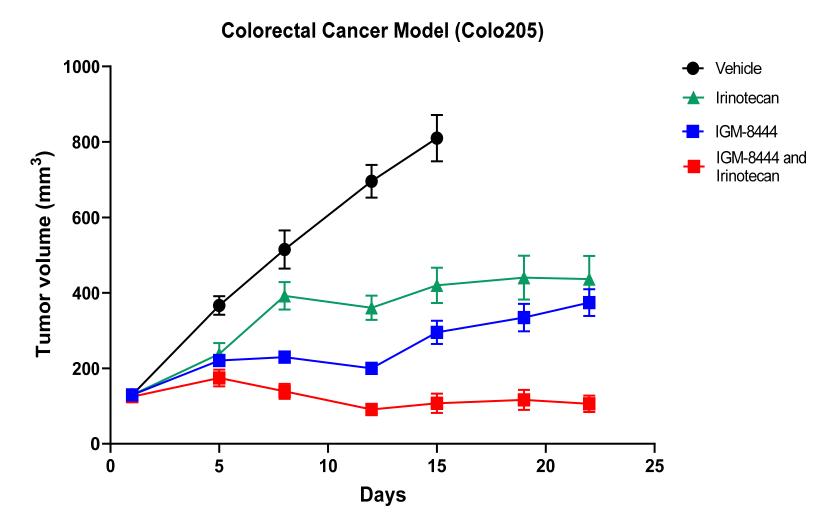


## DR5: IGM-8444 In Vivo mouse xenograft study





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

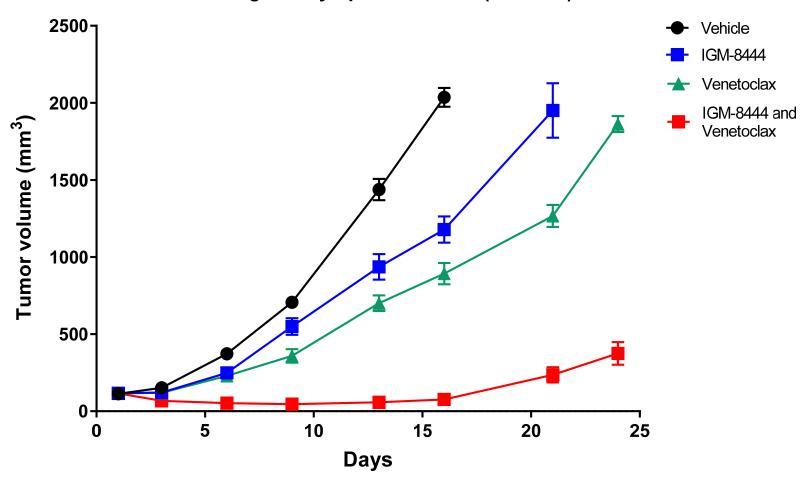


IGM-8444 (5 mg/kg Q2D x 7); Irinotecan (100 mg/kg QW x 3)



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



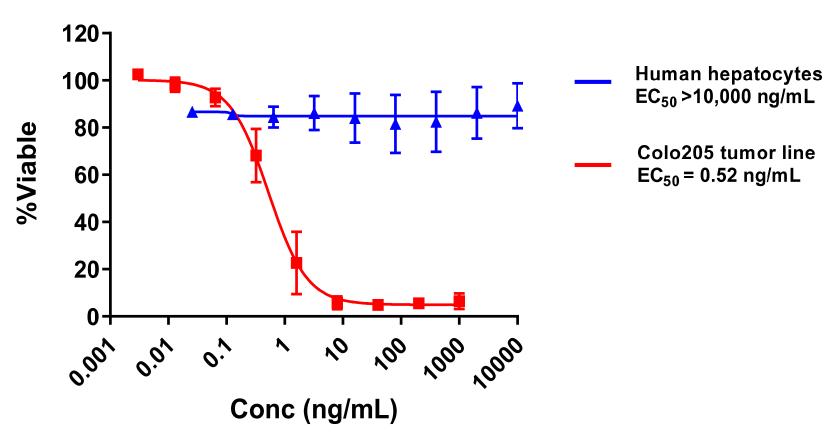


IGM-8444 (5 mg/kg Q2D x 11); Venetoclax (100 mg/kg QD x 21)



## DR5: IGM-8444 In Vitro therapeutic window

## In Vitro Cytotoxicity





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

#### Dose escalation schedule

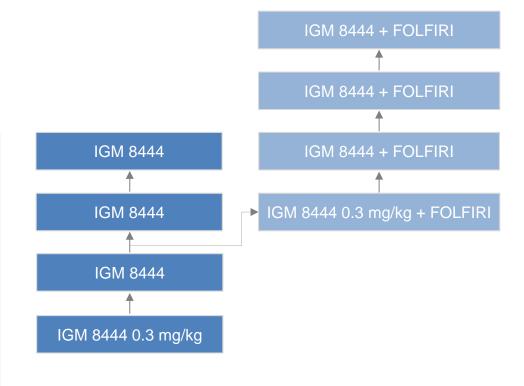
#### Phase 1

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

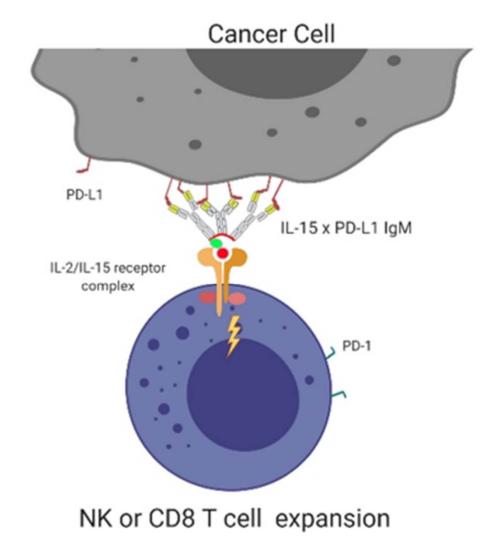
1L/2L CRC
IGM-8444 + FOLFIRI + Avastin

Potential Additional Expansion Cohorts

IGM-8444 + Targeted therapies

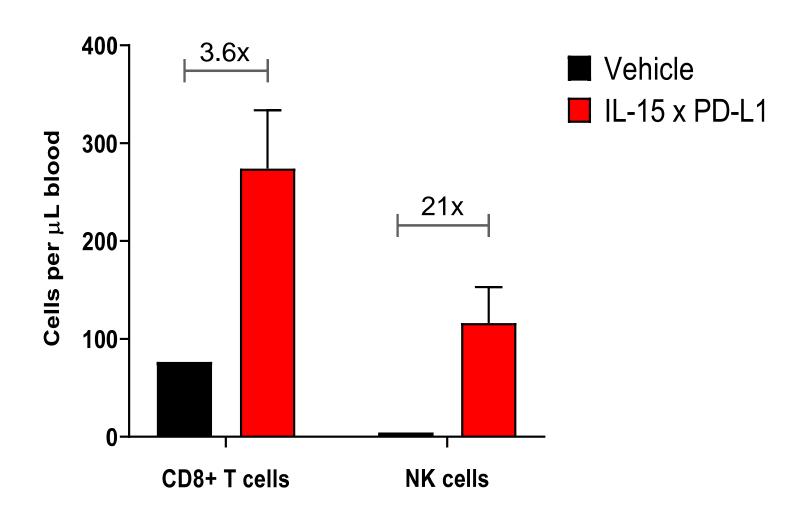


## IL-15 delivered by high avidity PD-L1 IgM antibody





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





## **Leadership Team**



**FRED M. SCHWARZER** *Chief Executive Officer* 



//> HESK'A



ELIZABETH HAANES, PhD VP, Intellectual Property





**SUZETTE TAUBER** *VP, Human Resources* 







BRUCE KEYT, PhD
Chief Scientific Officer
Genentech

MILLENNIUM



ANGUS SINCLAIR, PhD

VP, Immuno-Oncology

Northern
Biologics





**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* **FivePrime** 





MISBAH TAHIR
Chief Financial Officer
Dermira
AMGEN



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





MARVIN PETERSON, PhD VP, Process Sciences & Manufacturing



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# **Thank You**

