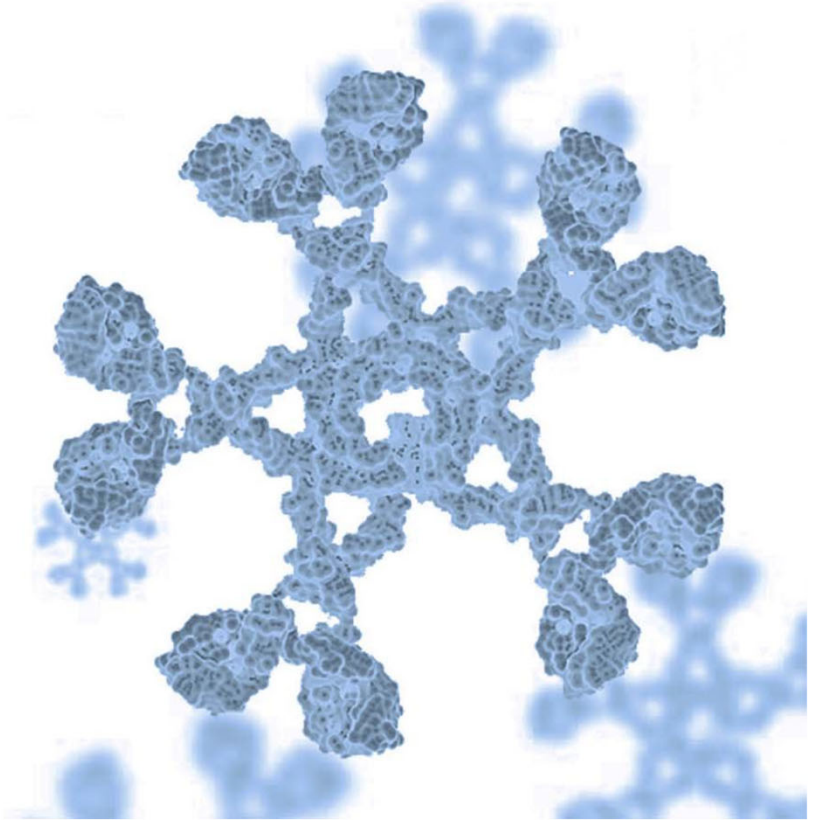
Pioneering the Development of Engineered IgM Antibodies

IGM Corporate Presentation

November 2021



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,” “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: 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 impacts to our operations, the manufacture and supply of our product candidates, the progression of our clinical trials, enrollment and maintenance of patients in our current and future clinical trials and on our collaborations and related efforts; our early stages of clinical drug development; our ability to achieve clinical goals; 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, either alone or in combination with other compounds; the potential for the results of clinical trials to differ from preclinical, preliminary 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; the potential impact of continuing or worsening supply chain constraints; our ability to accurately forecast future financial results and timelines; strategic arrangements, licenses and/or collaborations and the potential benefits of such arrangements; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of our strategic arrangements, licenses and/or collaborations; 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 retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model and 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; general economic and market conditions; and other risks and uncertainties, including those more fully described in the public filings that we have made and will make with the Securities and Exchange Commission (“SEC”), including our Quarterly Report on Form 10-Q filed with the SEC on November 4, 2021. 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. The forward-looking statements in this presentation are based on information available to the Company as of the date hereof and, except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason.

IGM Overview

- Global leaders in the development of engineered IgM antibodies for therapeutic use
- Therapeutic Areas of Focus
  - **Oncology**
  - **Autoimmunity & Inflammation**
  - **Infectious Diseases**
- Proprietary IgM antibody technology: 28 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
- $265.6 Million Cash and Investments Balance, September 30, 2021

IGM's Pipeline

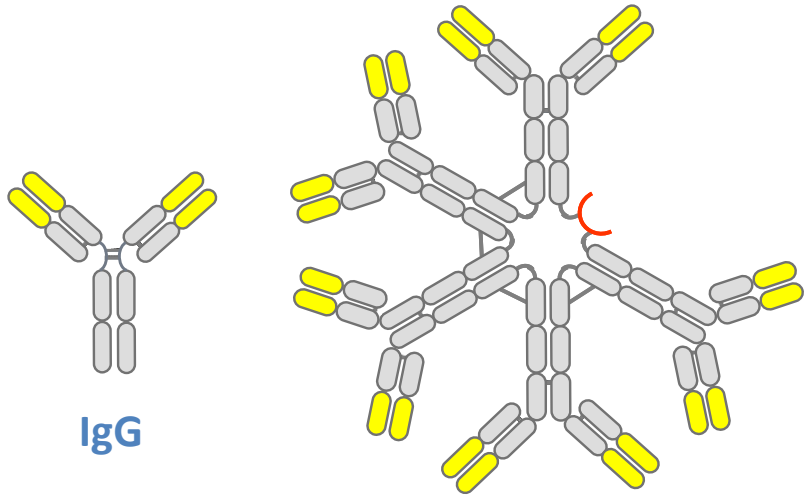
Therapeutic Area	Mode	Target	Indications	Phase of Development					Worldwide Commercial Rights	Anticipated Milestones
				Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3		
Oncology	T cell Engager	IGM-2323 (CD20 x CD3)	NHL, CLL						igm biosciences	Additional Phase 1 data in NHL: ASH 2021
		IGM-2644 (CD38 x CD3)	Multiple Myeloma						igm biosciences	Phase 1 initiation: 2022 (anticipated)
	Receptor Cross-linking Agonist	IGM-8444 (DR5)	Solid and Hematologic Malignancies						igm biosciences	Additional Phase 1 data in solid tumors: 2022
	Targeted Cytokines	IGM-7354 (IL-15 x PD-L1)	Solid and Hematologic Malignancies						igm biosciences	Phase 1 initiation: 2022 (anticipated)
Infectious Disease	Target Neutralizer	IGM-6268 (SARS-CoV-2)	COVID-19						igm biosciences	Phase 1 initiation: Q4 2021 (anticipated)

Research and Discovery Programs	• CD123 x CD3 • Multiple targets x CD3	• OX40 • GITR	• Undisclosed oncology targets • Undisclosed infectious disease targets • Undisclosed autoimmunity and inflammation targets

Why IgM?

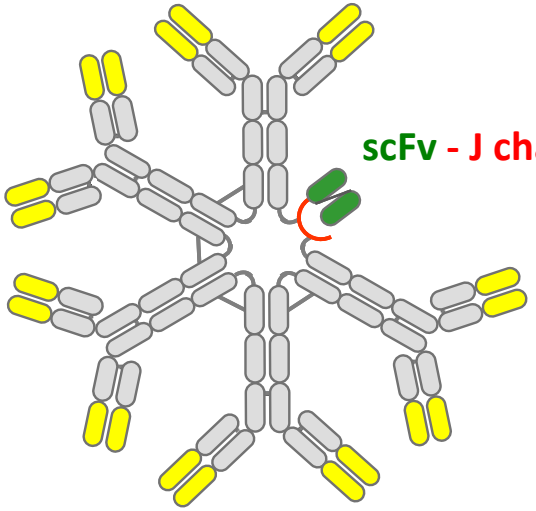
Structural comparison of IgG and IgM antibodies

Greatly superior total binding power (Avidity)

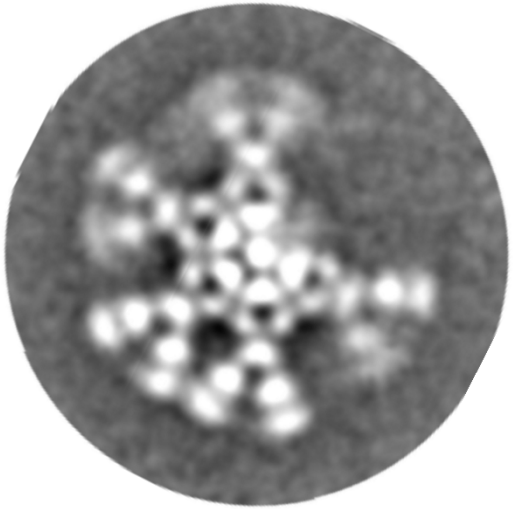


IgM Asymmetric Bispecific Technology

High avidity, potent T cell dependent cytotoxicity

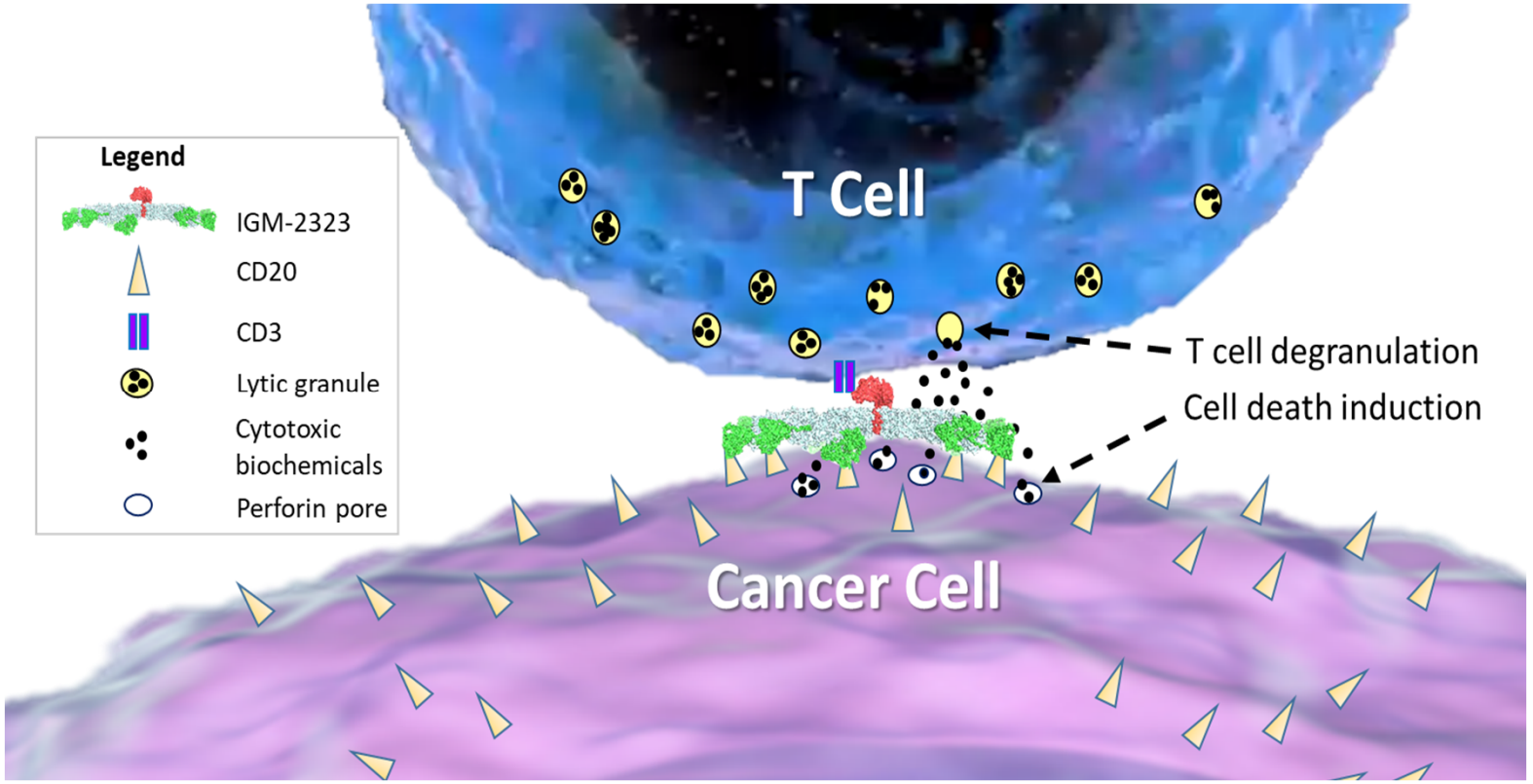


CD20 IgM plus
CD3 on J-chain



IGM-2323 Bispecific T Cell Engagement

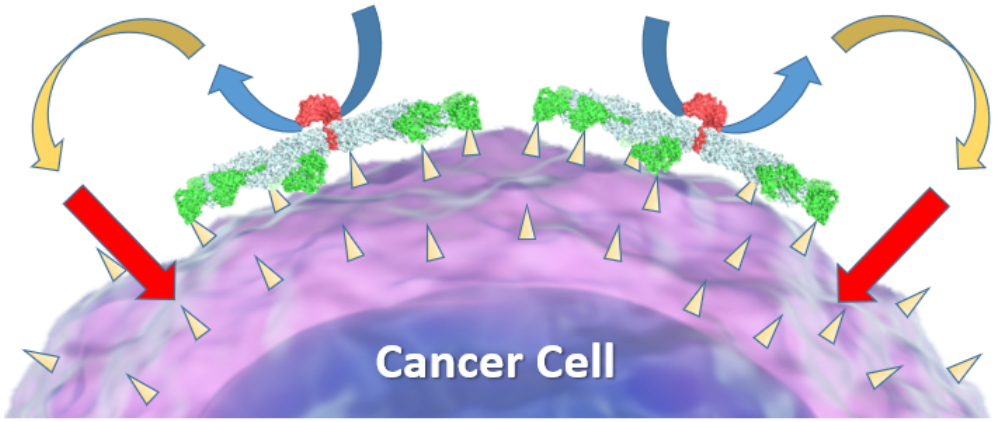
T cell directed cellular cytotoxicity (TDCC)

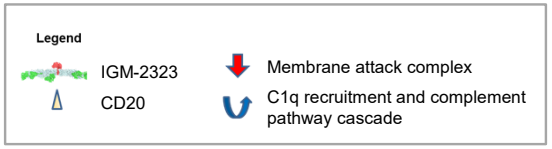


IGM-2323 Dual Mechanism of Action

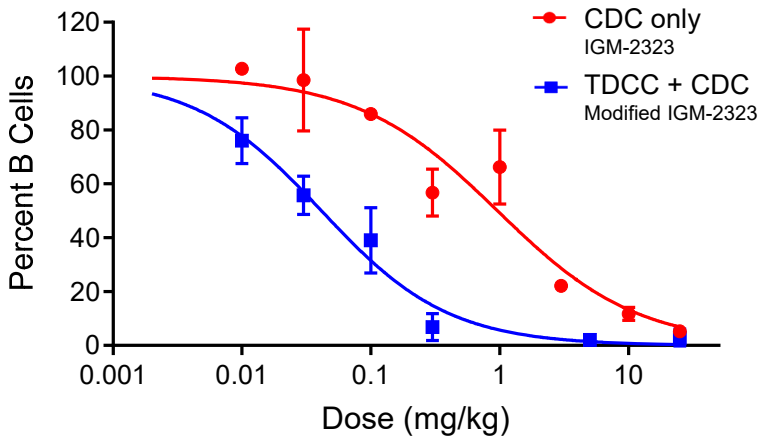
Complement dependent cytotoxicity (CDC)

Complement cascade





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



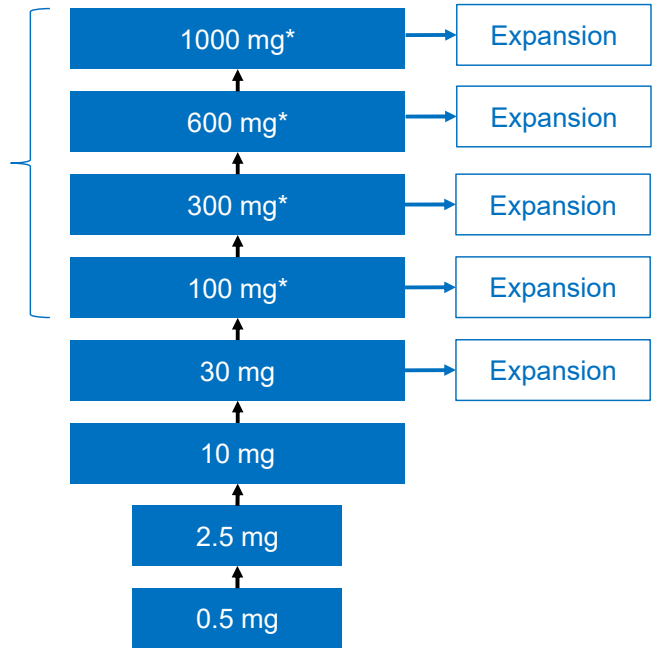
IGM-2323 Phase I Dose Escalation Clinical Trial

- **Relapsed/Refractory B cell NHL**
- **Primary objectives**
  - ❑ Safety and tolerability
  - ❑ R2PD and schedule
  - ❑ Maximum Tolerated Dose
- **Study design**
  - IV weekly therapy: 1 cycle = 21 days
  - Tumor assessment at 6,12,24 weeks
  - First 2 cohorts single patient, followed by 3+3 design
- **Status as of November 2021** 1000 mg dose escalation cohort cleared. No dose limiting toxicities.

IGM-2323 Dose Escalation Schedule

Titration Dosing

Escalates from starting dose to sustained maximum dose indicated.



MABEL
(Minimally Active Biologic Effect Level)

* Represents maximum dose in each cohort

IGM-2323 Recent Program Updates

- **Data from IGM-2323 Phase 1 trial selected for oral presentation at 2021 ASH Annual Meeting and Exposition [Saturday, December 11, 2021, at 1:15 p.m. ET]**

- **ASH abstract released November 4, 2021[1]:**
  - 29 patients enrolled as of April 30 data cut-off: 12 at 5 fixed dose levels and 17 at 5 dose titration levels
    - No dose limiting toxicities (DLTs) and no neurotoxicity adverse events (AEs)
    - No patients discontinued due to an AE
    - 6 patients experienced cytokine release syndrome, primarily Grade 1
  - Of the 11 evaluable patients treated in the titration dose cohorts, 5 responses including 3 complete responses and 2 partial responses

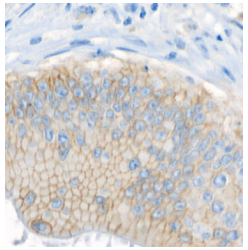
- **IGM announced plans to initiate potentially registrational Phase 2 studies**
  - Will test doses of 100 mg and 300 mg in separate, randomized, 'pick the winner' Phase 2 studies
  - 30 patients at each dose level
  - One Phase 2 study in Diffuse Large B-cell Lymphoma and one Phase 2 study in Follicular Lymphoma

[1] Data cut-off = April 30, 2021

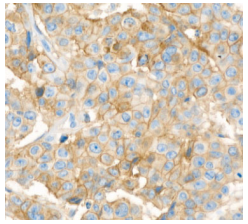
TNFr Superfamily: Trimerizing Agonists

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

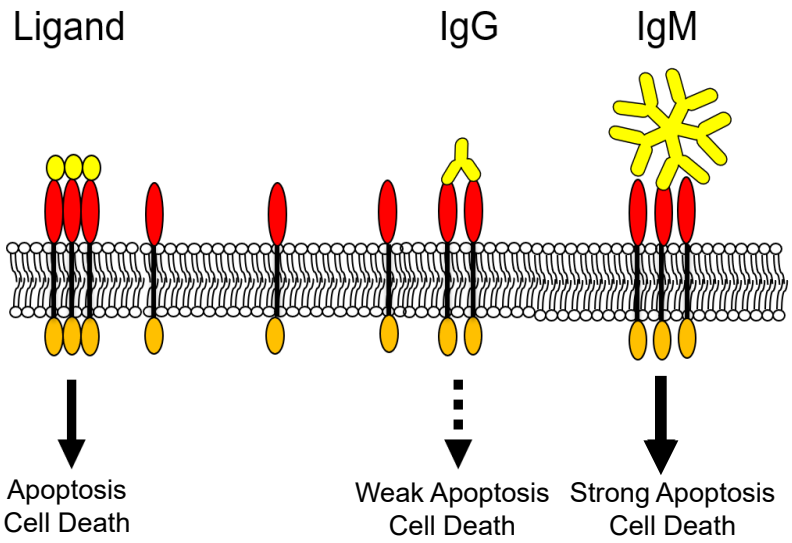
DR5 Expression



Colon Adenocarcinoma



Gastric Adenocarcinoma

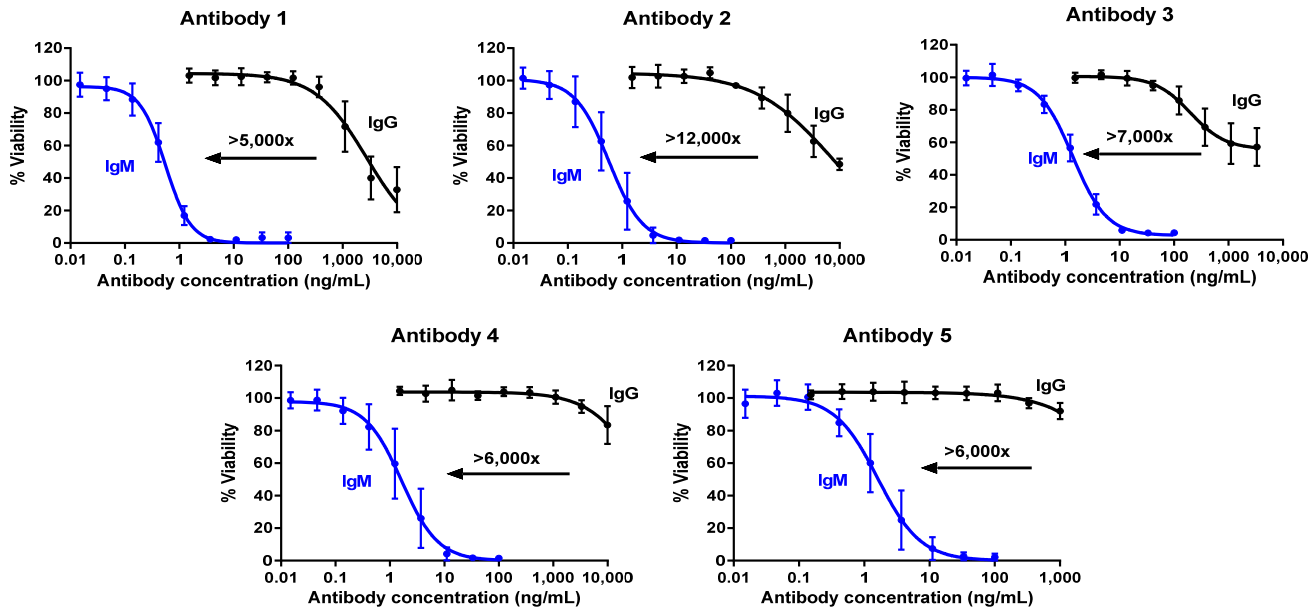


Also: pancreatic, lung, breast and prostate tumors, leukemia and lymphoma

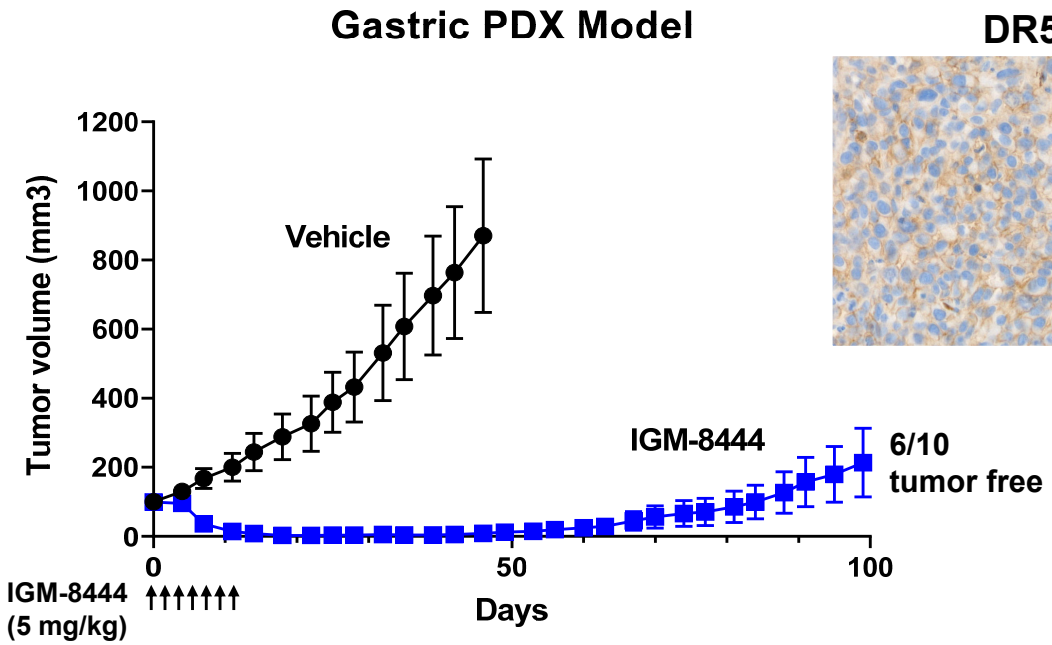
TNFr: tumor necrosis factor receptor

DR5: IgM Superior *In Vitro* to IgG

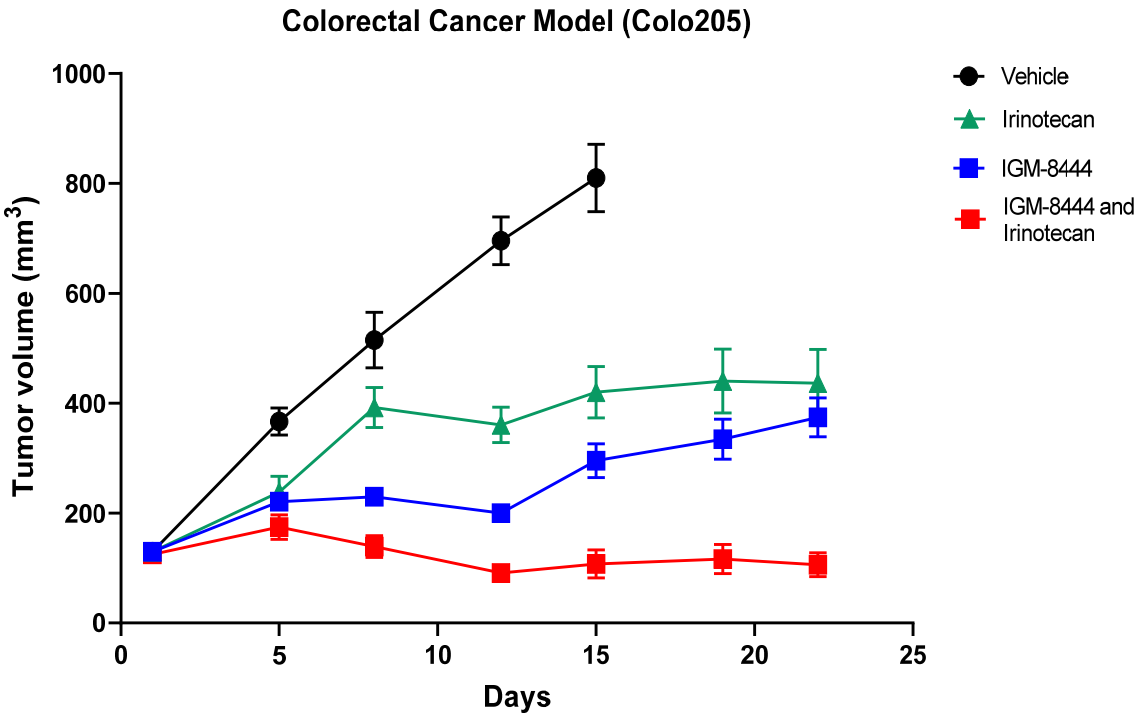
Cell line killing comparison *in vitro* of IgG and IgM DR5 antibodies with five different binding domains



DR5: IGM-8444 *In Vivo* Mouse Xenograft Study



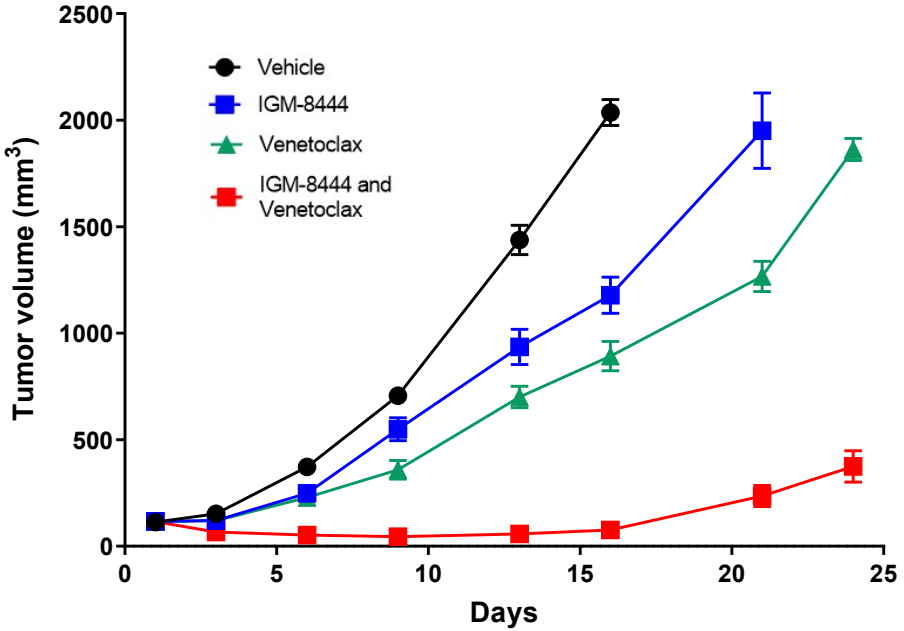
DR5: IGM-8444 *In Vivo* Combination with Irinotecan



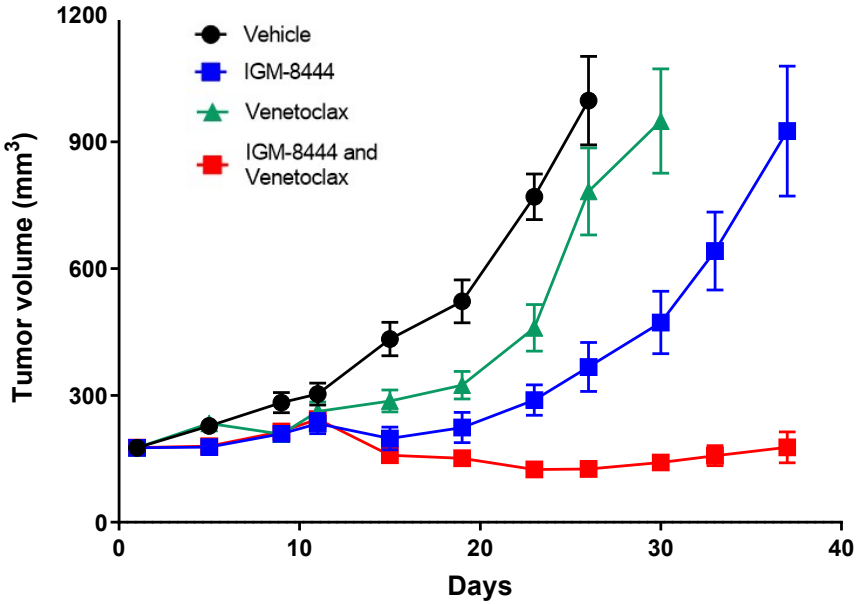
IGM-8444 (5 mg/kg Q2D x 7); Irinotecan (100 mg/kg QW x 3)

DR5: IGM-8444 *In Vivo* Combination with Venetoclax

Non-Hodgkin's Lymphoma Model (DOHH-2)

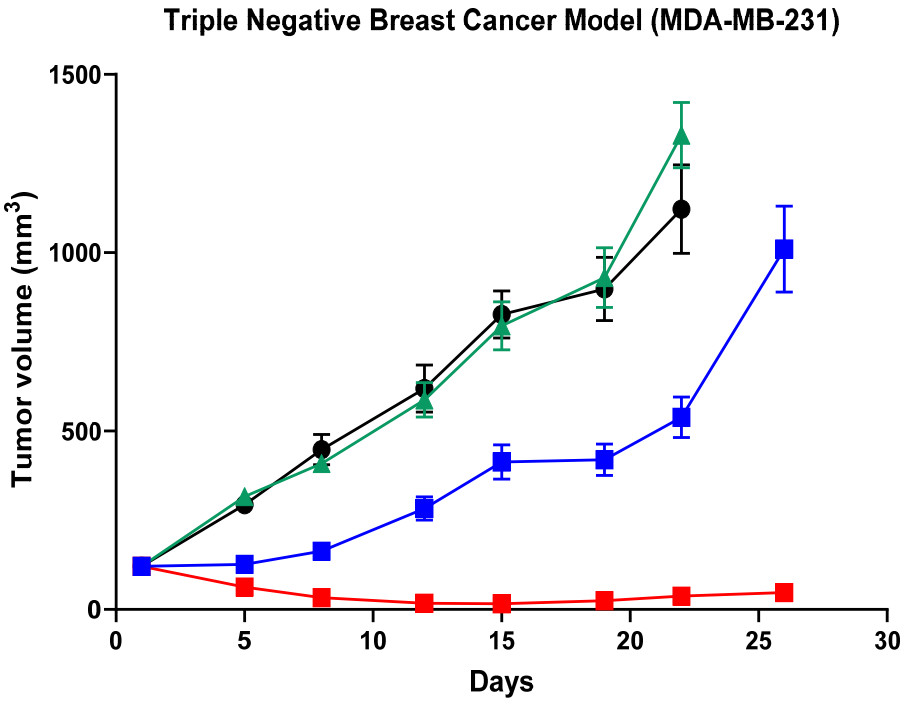


Acute Myeloid Leukemia Model (MV-411)



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

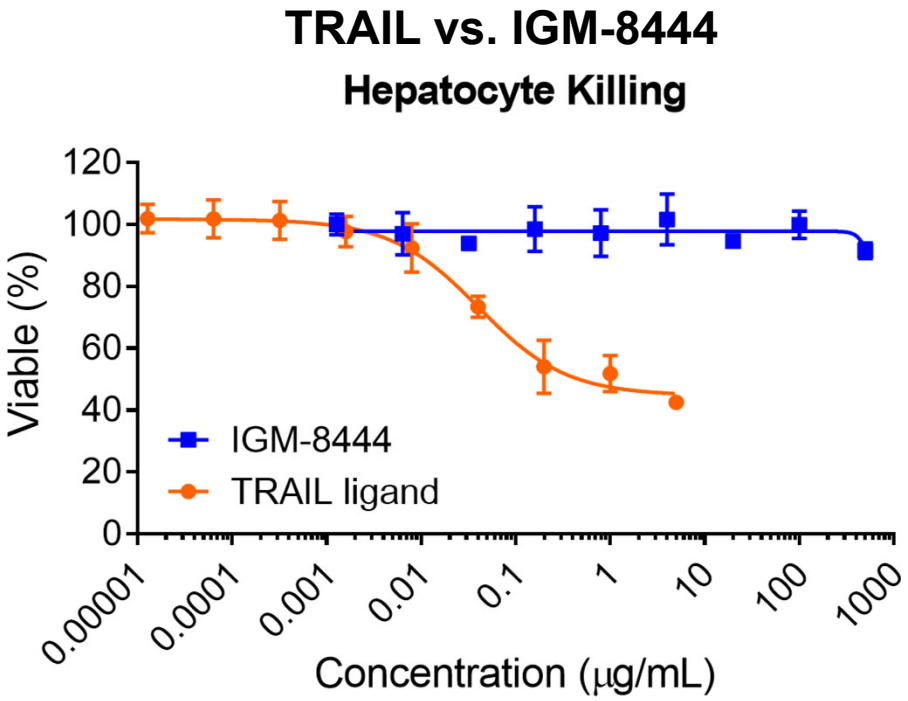
DR5: IGM-8444 *In Vivo* Combination with Birinapant

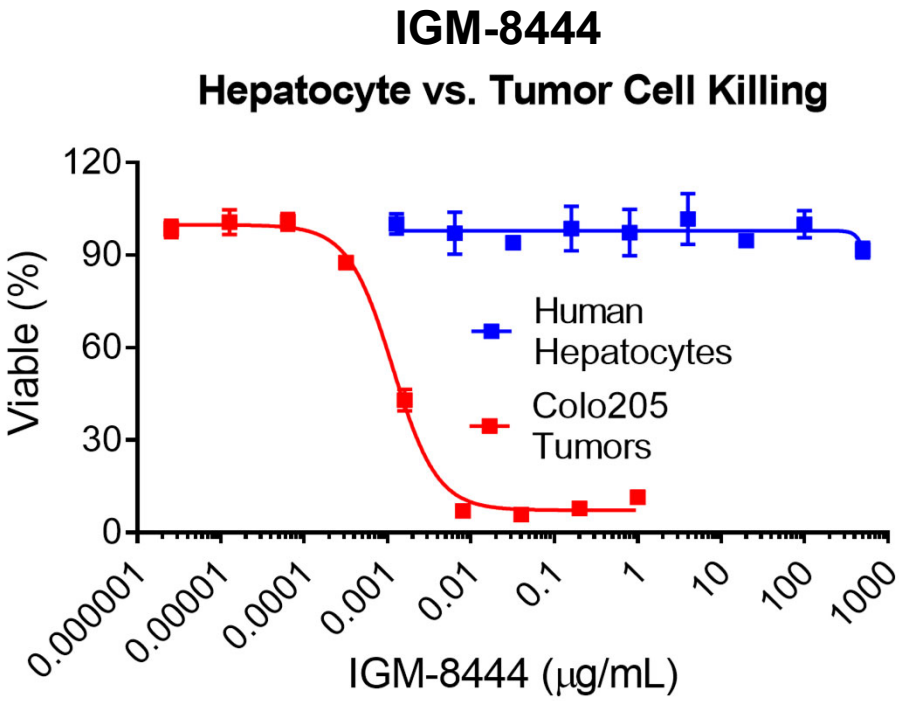


- Birinapant is a SMAC mimetic designed to inhibit IAPs
- IGM acquired exclusive worldwide development and commercial rights from Medivir in 2021

IGM-8444 (5 mg/kg Q2D x 11); Birinapant (2.5 mg/kg Q3D x 7)

IGM-8444 Designed to Optimize Cancer Cell Killing With Minimal Hepatocyte Toxicity



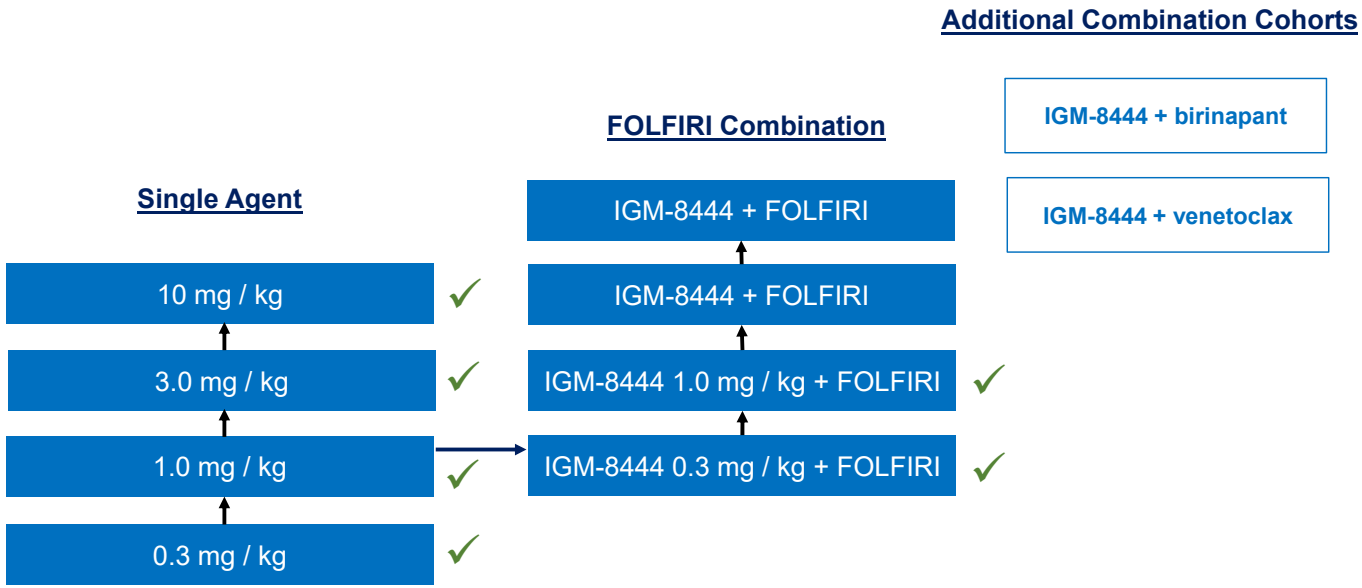


Affinity, avidity, clustering, DR5 epitope, multimerizing kinetics and exposure all contribute to optimization

IGM-8444 Phase I Dose Escalation Clinical Trial

- **All-comers solid tumor escalation as monotherapy and in combination with chemotherapy**
- **Study design**
  - Standard 3+3 design
  - Dosing q2week (with flexibility to test additional schedules)
  - DLT window d1-28 (Cycle 1)
- **Status as of November 2021**
  - Single agent every two weeks: All cohorts cleared. No DLTs
  - FOLFIRI combination: 2nd dose cohort cleared. No DLTs
  - Birinapant combination: 1st patient dosed

IGM-8444 Dose Escalation Schedule



IGM-8444 Recent Clinical Trial Updates

- **No acute or chronic clinically significant liver toxicity or clinically significant anti-drug antibodies observed to date[1]**

- **32 patients treated with IGM-8444[1]**
  - 11 remain on treatment
  - 7 patients have been on treatment for 5 or more months without showing signs of any chronic toxicities to date
  - No patient has discontinued treatment for drug related safety reasons

- **Signs of biological activity consistent with the activation of DR5 by a DR5 agonist have been observed in some patients, both in circulating biomarkers and histological tumor samples[1]**

- **First patient dosed in combination with birinapant**
  - Birinapant is a small molecule SMAC mimetic that binds to and degrades Inhibitors of Apoptosis Proteins (IAPs) which can lead to cell death (apoptosis) in tumor cells
  - January 2021 – IGM received an exclusive, global license to develop and commercialize birinapant from Medivir AB

[1] As of Nov. 4, 2021

IGM-6268 Preclinical Results in Nature and NIH Director's Blog

Article

Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants

https://doi.org/10.1038/s41586-021-03673-2
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Zhiqiang Ku[1,6], Xuping Xie[2,6], Paul R. Hinton[3,6], Xinli Liu[4,6], Xiaohua Ye[1], Antonio E. Muruato[2], Dean C. Ng[3], Sujit Biswas[4], Jing Zou[2], Yang Liu[2], Deepal Pandya[3], Vineet D. Menachery[5], Sachi Rahman[3], Yu-An Cao[3], Hui Deng[1], Wei Xiong[1], Kevin B. Carlin[3], Junquan Liu[1], Hang Su[1], Elizabeth J. Haanes[3], Bruce A. Keyt[3]✉, Ningyan Zhang[1]✉, Stephen F. Carroll[3]✉, Pei-Yong Shi[2]✉ & Zhiqiang An[1]✉

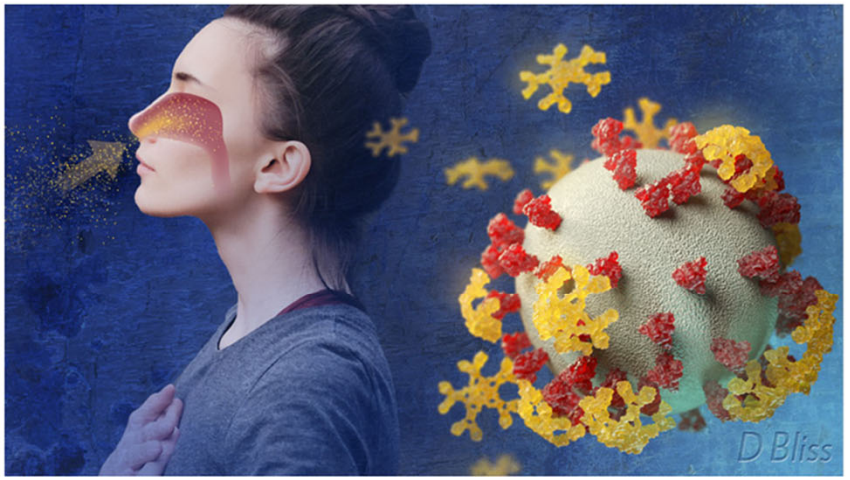
Resistance represents a major challenge for antibody-based therapy for coronavirus disease 2019 (COVID-19)[1–4]. Here we engineered an immunoglobulin M (IgM) neutralizing antibody (IgM-14) to overcome the resistance encountered by IgG-based therapeutics. IgM-14 is >230-fold more potent than its parental IgG-14 in neutralizing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). IgM-14 potently neutralizes the resistant virus raised by its corresponding IgG-14, the newly emerged

Ku, Z. et al. Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants. *Nature*

NIH Director's Blog

Could a Nasal Spray of Designer Antibodies Help to Beat COVID-19?

Posted on June 15th, 2021 by Dr. Francis Collins



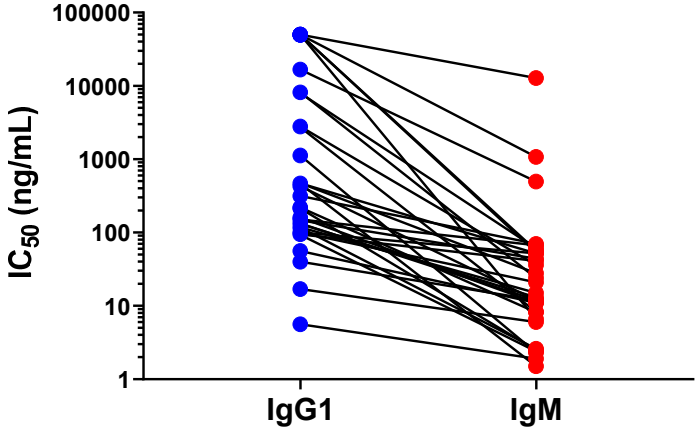
There are now several monoclonal antibodies, identical copies of a therapeutic antibody produced in large numbers, that are authorized for the treatment of COVID-19. But in the ongoing effort to beat this terrible pandemic, there's plenty of room for continued improvements in treating

IgMs Consistently Show Improved *In Vitro* Neutralization Potency

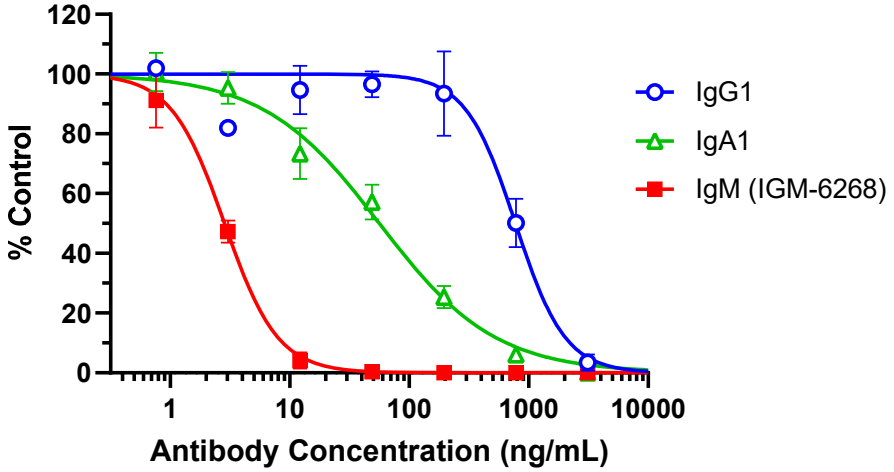
Most IgMs substantially more potent than IgGs

- More than 50 IgGs converted into >150 IgA1, IgA2 and IgM mAbs
- Most antibodies tested show significantly improved potency in SARS-CoV-2 neutralization assay when converted from IgG to IgM
- Some exhibit exceptional potency (IGM-6268 IC_{50} ~ 2 ng/mL, ~ 2 pM)

IgMs Show Superior Neutralization Activity to IgGs

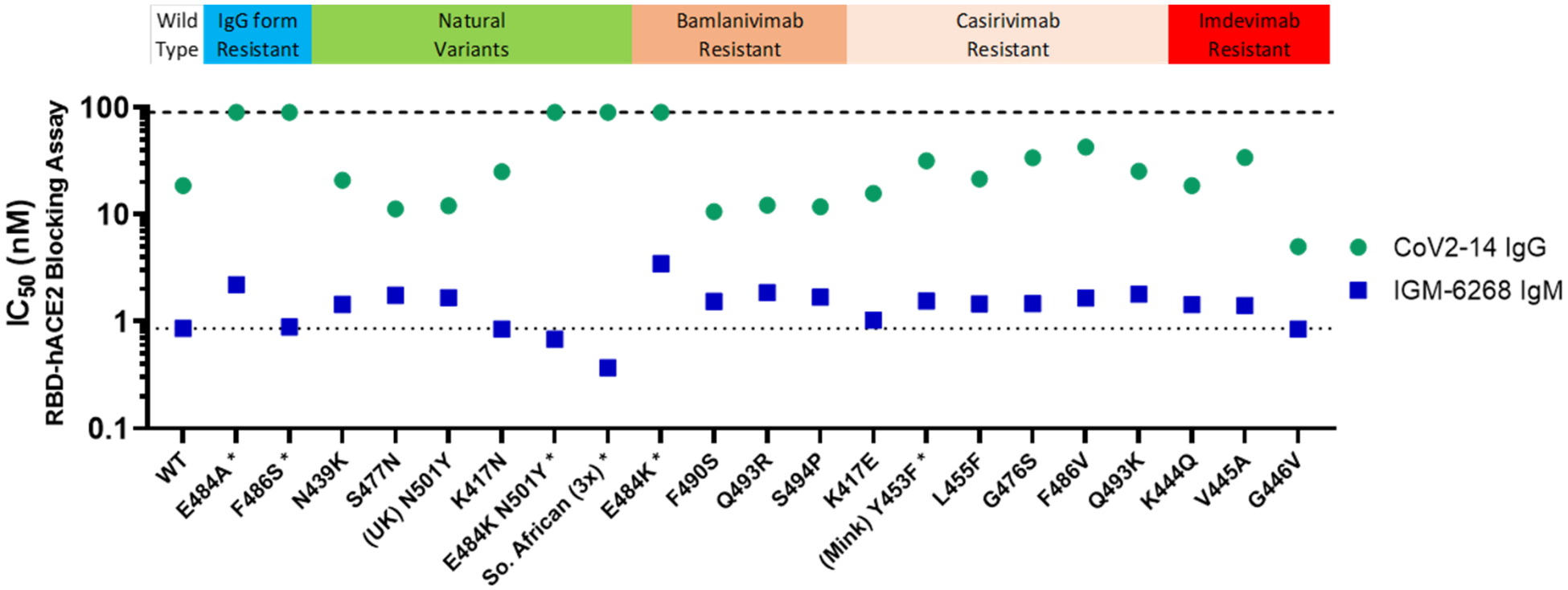


IGM-6268, IgA1 Have Superior Potency to IgG1



IGM-6268 Retains Activity Against SARS-CoV-2 Variant RBDs

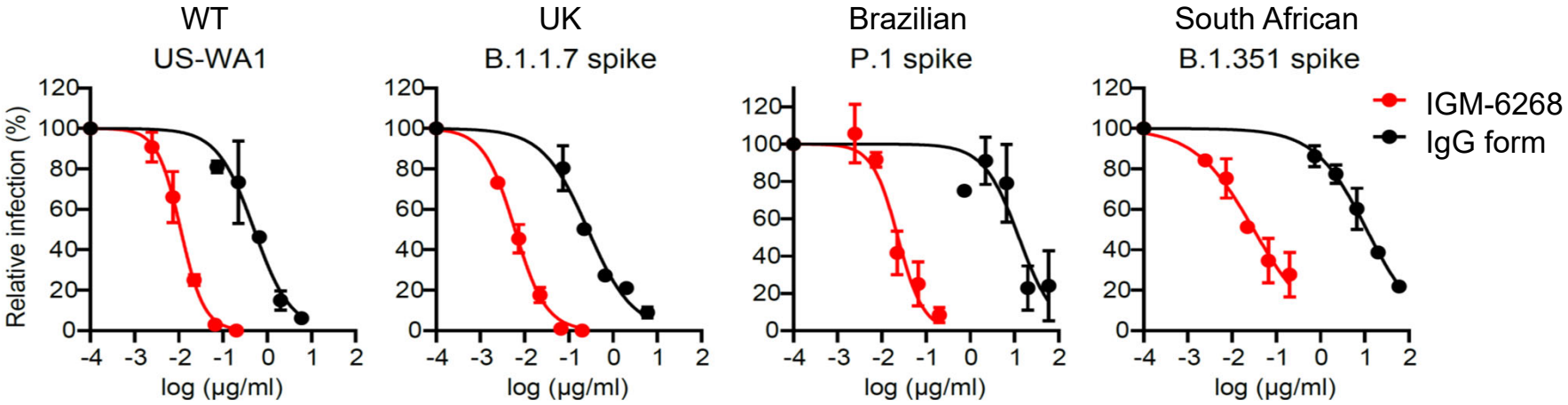
Natural and escape variants – *in vitro* RBD-hACE2 blocking assay



Modified from Ku, Z. et al. Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants. *Nature*

IGM-6268 Potently Neutralizes Escape & Emerging CoV-2 Variants

In vitro studies include Alpha, Beta and Gamma VoCs, IgG escape mutants



	$PRNT_{50}$ (μg/ml)			
	US-WA1	B.1.1.7 spike	P.1 spike	B.1.351 spike
IgM	0.011	0.006	0.023	0.031
IgG	0.51	0.27	12.59	11.06
Fold	47	45	547	374

Ku, Z. et al. Nasal delivery of an IgM offers broad protection from SARS-CoV-2 variants. *Nature*

IGM-6268 Is Designed to Be Self Administered at Home

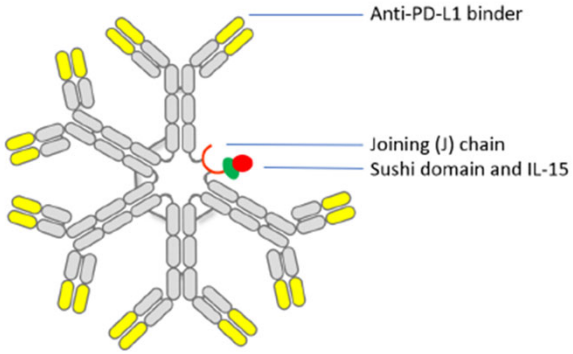
- Our Approach – Intranasal Spray
  - Targets upper respiratory tract (nasal cavity, mouth, throat)
  - 10x to 100x less IGM-6268 is required to neutralize SARS-CoV-2 *in vitro* relative to the EUA-approved IgGs
  - No needles required
- In mouse models of COVID-19, intranasal IGM-6268
  - **Prevents** infection at very low doses
  - **Treats** infection by reducing viral load in the lungs
- Current EUA-approved antibodies (all IgG) are administered by intravenous (IV) infusion
  - Limited access since a hospital or clinic visit is required
  - Very limited window of time to administer
  - Requires high dosage levels and resultant high cost of goods

Phase 1 Trial:
Mucosal Atomizer

Expected Commercial:
Nasal Spray Pump

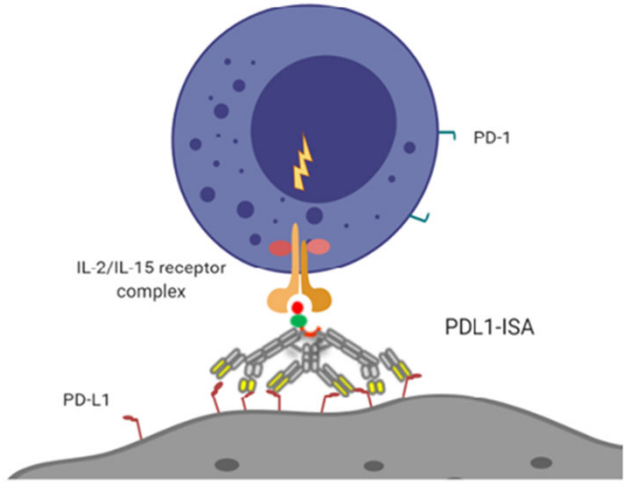
Targeting IL-15 Delivery to PD-L1 Expressing Tumors with an IgM

Targets and blocks PD-L1 on tumor cells and APCs, inhibits PD-1 signaling (avoids immune suppression) and delivers active IL-15 to tumor infiltrating lymphocytes



IL-15 x anti-PDL1 IgM

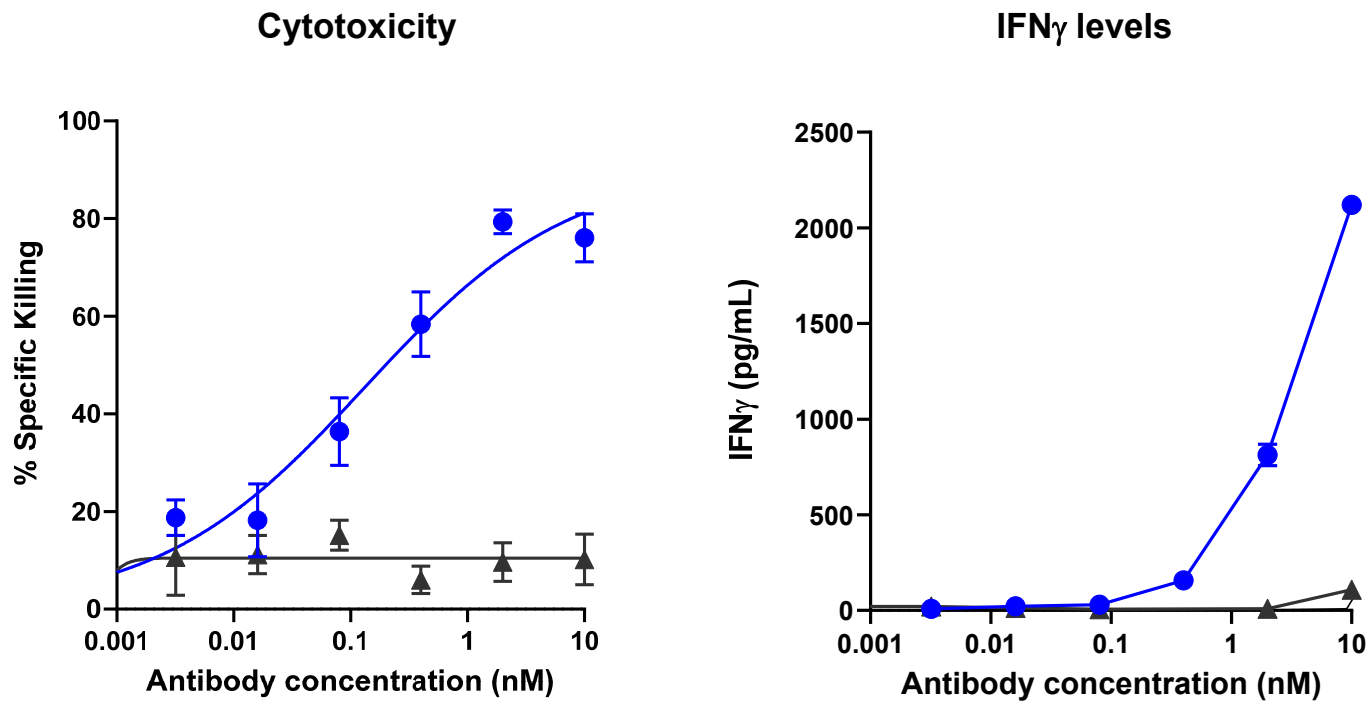
NK or CD8 T cell expansion



Tumor and/or Antigen Presenting Cell

APC: antigen presenting cell

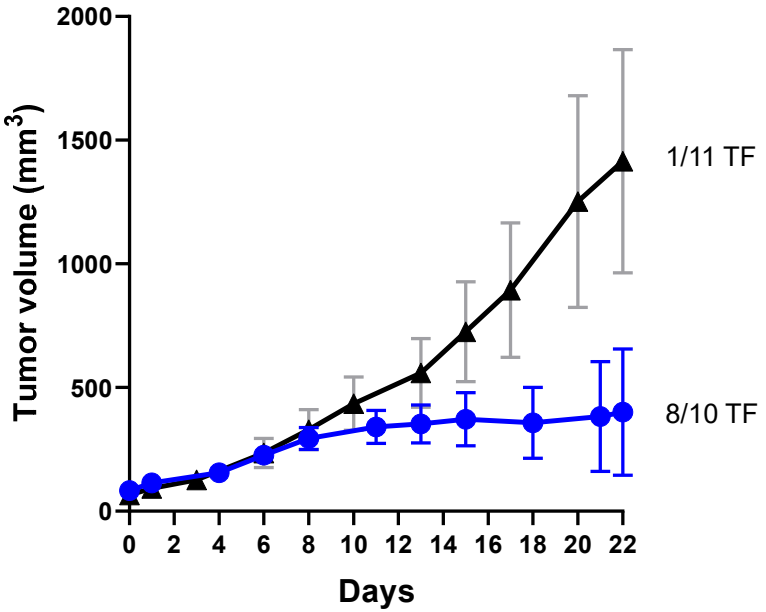
IGM-7354: IL-15 x PD-L1 *In Vitro* CD8 T cell Induced Tumor Cytotoxicity



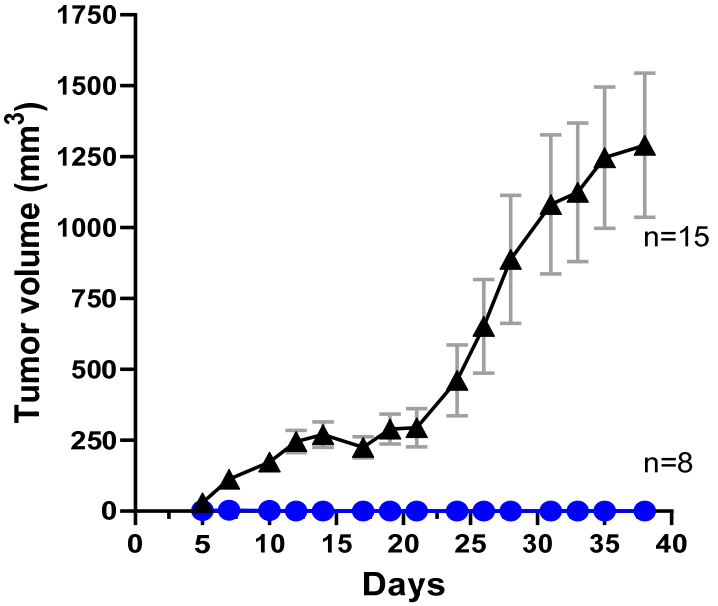
IL-15 x PD-L1 IgM; PD-L1 IgM

IGM-7354: IL-15 x PD-L1 *In Vivo* Efficacy and Immune Memory

Initial treatment of CT26 tumor



CT26 tumor rechallenge



Vehicle; IL-15 x PD-L1 IgM dosed Q2Dx3 at 5 mg/kg

Multiple Catalysts Anticipated Through 2022

	Anticipated
IGM-2323	❑ Presentation of Phase 1 clinical data at ASH 2021 ❑ Phase 2 initiation
IGM-8444	❑ Presentation of Phase 1 clinical data, including initial efficacy data ❑ Phase 1 initiation in combination with venetoclax
IGM-6268	❑ Phase 1 initiation
IGM-7354	❑ File IND; Phase 1 initiation
IGM-2644	❑ File IND; Phase 1 initiation
Manufacturing Capabilities	❑ Operations at newly-constructed GMP manufacturing facility