Global Leaders in IgM Antibodies

REIMAGINING

antibody medicines

JP Morgan Healthcare Conference

January 12, 2022

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: plans, timelines, and expectations related to our preclinical studies, clinical trials and discovery programs including regarding the availability of data, planned regulatory filings, and the initiation and progress of current and future clinical trials; potential delays and disruptions 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 business strategy and plans; our early stages of clinical drug development; our ability to achieve clinical goals; risks related to the use of 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 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 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, including our unaudited cash and investments balance for the year ended December 31, 2021; 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.

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IGM overview

Global leaders in the development of IgM antibodies for therapeutic use

- **Oncology**
- **Autoimmunity & Inflammation**
- **Infectious Diseases**

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

- Advance product candidates and increase R&D efforts
- Expand manufacturing capabilities
- Expand intellectual property portfolio
- Participate in commercialization if approved

Key facts and figures

- Proprietary IgM antibody technology: 38 patent families
- 145 research, development and manufacturing personnel based in San Francisco Bay Area and Greater Philadelphia Area
- $230 million cash and investments balance, December 31, 2021 (unaudited)

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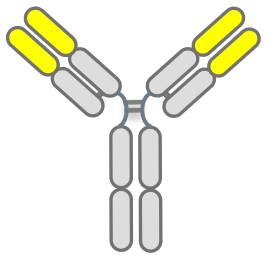
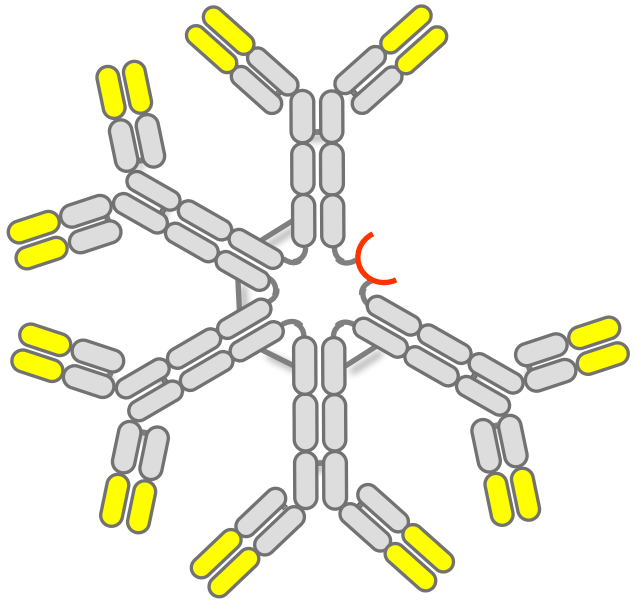
IgM antibodies have unique structural attributes compared to IgG

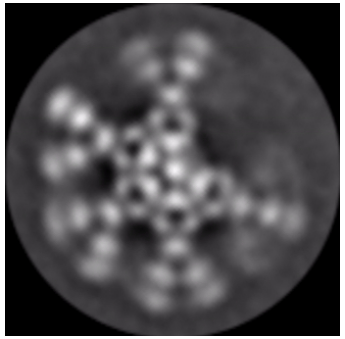
Additional binding sites lead to greatly superior total binding power (avidity)



IgG



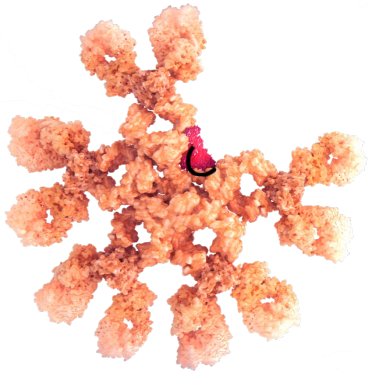
IgM



LEGEND	Target binding domains	Constant domains	Joining chain (J chain)

Leaders in IgM antibody engineering and manufacturing

Protein Engineering



- Conversion of IgGs to IgMs
  - Increased affinity
  - Increased specificity
- Extended half-life IgMs
- Novel bispecific formats

+

Manufacturing

- Wholly-owned GMP facility
- Industry-standard production
- Cost-effective purification

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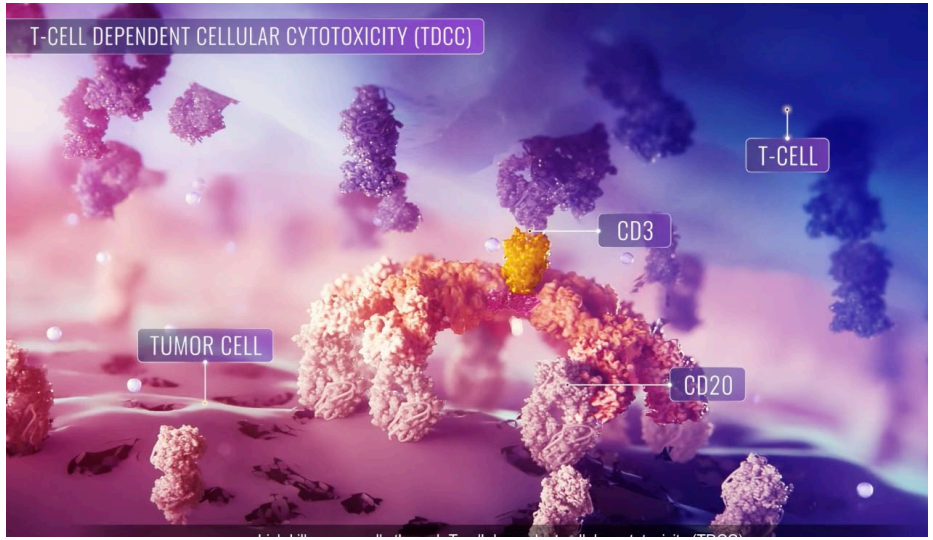
IGM's pipeline: global rights to all programs

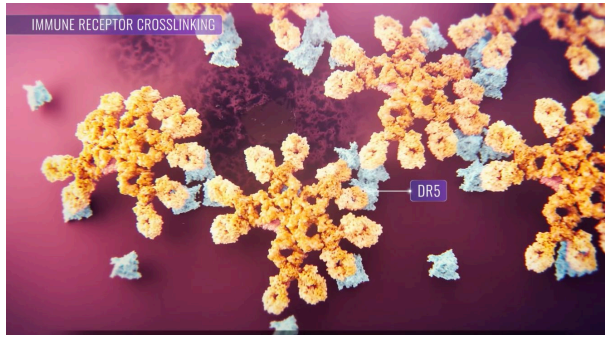
PROGRAM	MODE	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
ONCOLOGY							
IGM-2323 (CD20 x CD3)	T cell Engager	NHL, CLL					
IGM-8444 (DR5)	Receptor Cross-linking Agonist	Solid and Hematologic Malignancies					
IGM-7354 (IL-15 x PD-L1)	Targeted Cytokines	Solid and Hematologic Malignancies					
IGM-2644 (CD38 x CD3)	T cell Engager	Multiple Myeloma					
IGM-2537 (CD123 x CD3)	T cell Engager	AMS, MDS, ALL					
INFECTIOUS DISEASE							
IGM-6268 (SARS-CoV-2)	Target Neutralizer	COVID-19					

Oncology: three distinct mechanisms of action

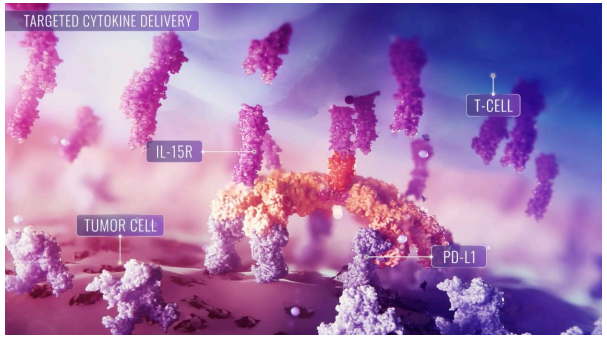
1 Bispecific T cell Engagers
(e.g., CD20 x CD3, CD38 x CD3)



2 Multi-Receptor Agonism
(e.g., DR5, OX40, GITR)



3 Targeted Cytokine Stimulation
(e.g., IL-15)



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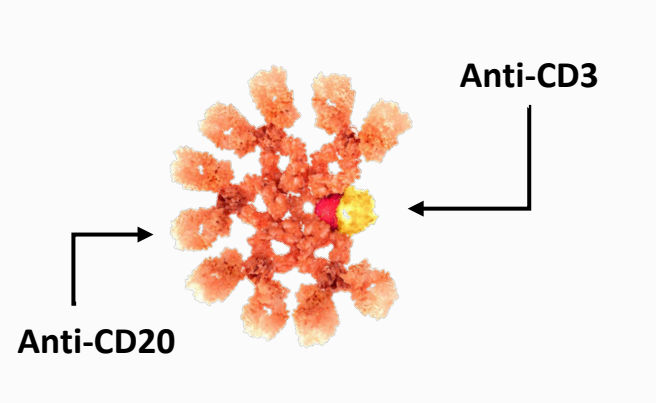
IGM-2323: potential backbone therapy in hematology



Monotherapy in late line NHL

- Optimize dosing and schedule
- Establish POC and launch in 3L+ NHL

Combination therapy in earlier lines

- Explore safety and dosing in combination with approved SOC in NHL
  - Chemotherapy
  - CD19-targeting agents
  - IMiDs
- Define efficacy signals in earlier lines of treatment

Backbone of choice in heme malignancies

- 1L and later line SOC
- Low CD20 B cell malignancies (i.e., CLL)

IGM-2323 Phase 1 safety: low levels of CRS and neutropenia

Titration cohorts (n=28)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
CRS*	3 (11)	1 (4)	1 (4)	0	0
ICANS^	0	0	0	0	0
Neutropenia	1 (4)	0	0	0	0
IRR	3 (11)	3 (11)	1 (4)	0	0

All patients (n=40)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
CRS*	7 (18)	2 (5)	1 (3)	0	0
ICANS^	0	0	0	0	0
Neutropenia	1 (3)	0	1 (3)	1 (3)	0
IRR	3 (8)	7 (18)	2 (5)	0	0

*Cytokine release syndrome graded by ASTCT Consensus Grading (Lee et al. Biol Blood Marrow Transplant 2019)
*Distinction between CRS and IRR were made by the treating investigator
*3 of 5 CRS cases in titration cohorts and 8 of 10 overall occurred in the first cycle
^ICANS: immune effector cell-associated neurotoxicity syndrome

Data cut off: September 10, 2021
Adapted from ASH 2021 , Budde et al, Dec 11, 2021

Phase 1 activity: encouraging response rates at 100 mg dose

DLBCL responses, n (%)	<100 mg (n=2)	100 mg (n=6)	200 mg (n=1)	300 mg (n=3)	600 mg (n=3)	1000 mg (n=1)
ORR	1 (50)	3 (50)	0	0	1 (33)	0
CR	1 (50)	3 (50)	0	0	0	0
PR	0	0	0	0	1 (33)	0

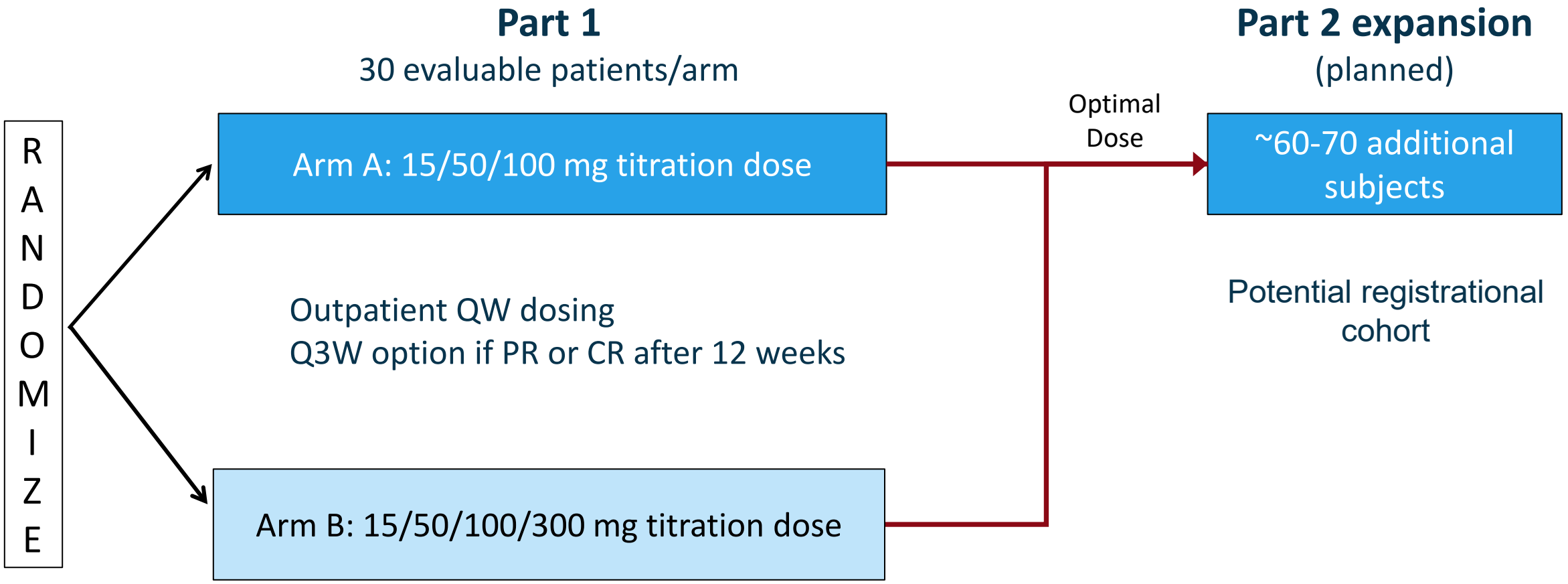
FL responses, n (%)	<100 mg (n=5)	100 mg (n=3)	300 mg (n=3)	600 mg (n=1)	1000 mg (n=2)
ORR	1 (20)	2 (67)	1 (33)	0	0
CR	0	2 (67)	1 (33)	0	0
PR	1 (20)	0	0	0	0

2 of 4 CR patients with tissue biopsies had low CD20 expression at baseline (H-score=15 and 30)

Data cut off: September 10, 2021
Adapted from ASH 2021 , Budde et al, Dec 11, 2021

Phase 2 randomized dose-selection study

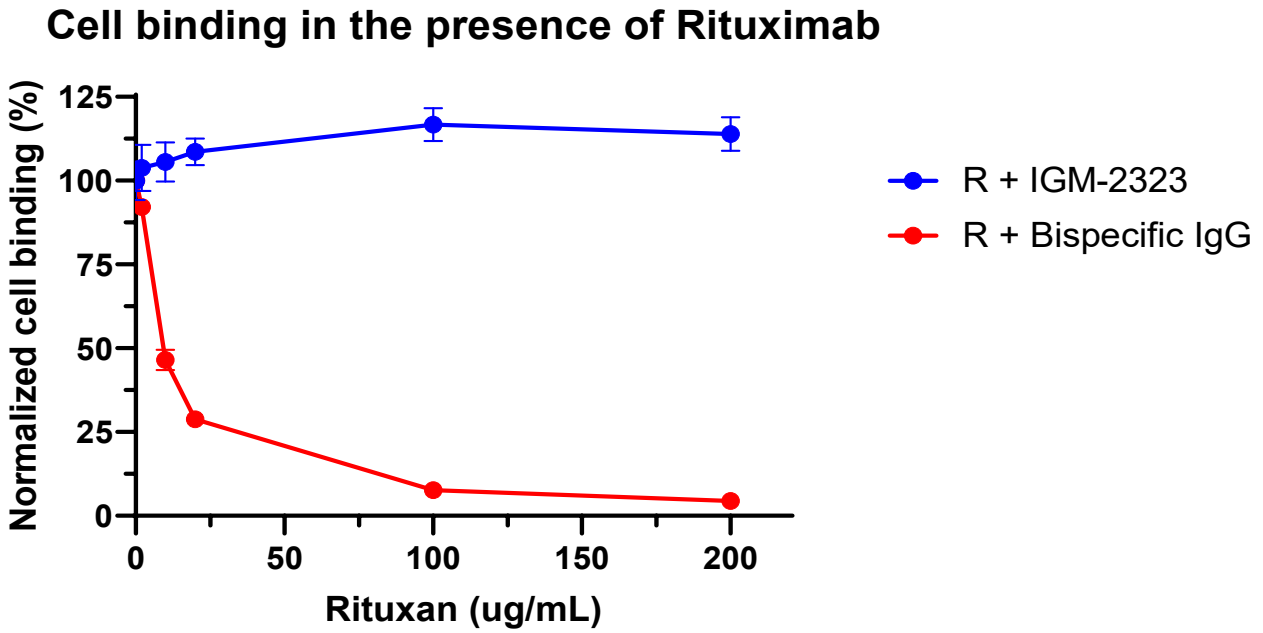
Seamless expansion into a potential registrational cohort



NOTE: There will be two dose-selection studies: one in DLBCL; the other in FL

Planned combination studies in earlier lines of NHL treatment

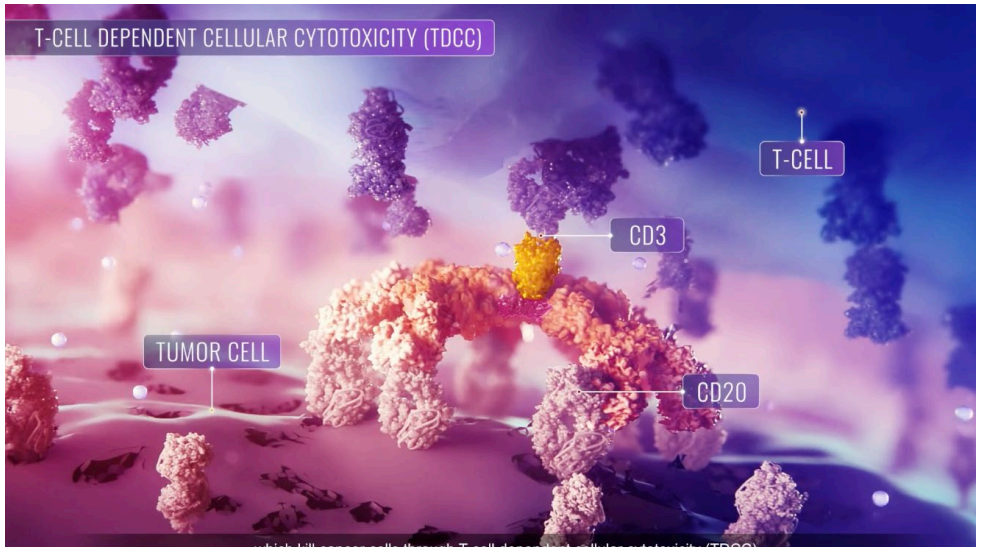
Regimen	
IGM-2323 + Rituximab-GemOx	2L+ DLBCL ASCT ineligible
IGM-2323 + Tafasitamab/Lenalidomide	2L+ DLBCL ASCT ineligible
IGM-2323 + Rituximab/Lenalidomide	2L+ FL



Other combination regimens under consideration:

- iMiDs
- Antibody-drug conjugates
- PI3K inhibitors
- Protein degraders
- BTK inhibitors

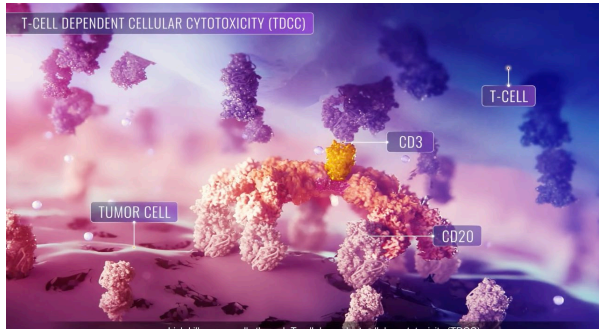
IGM-2323 data supports T cell engager pipeline



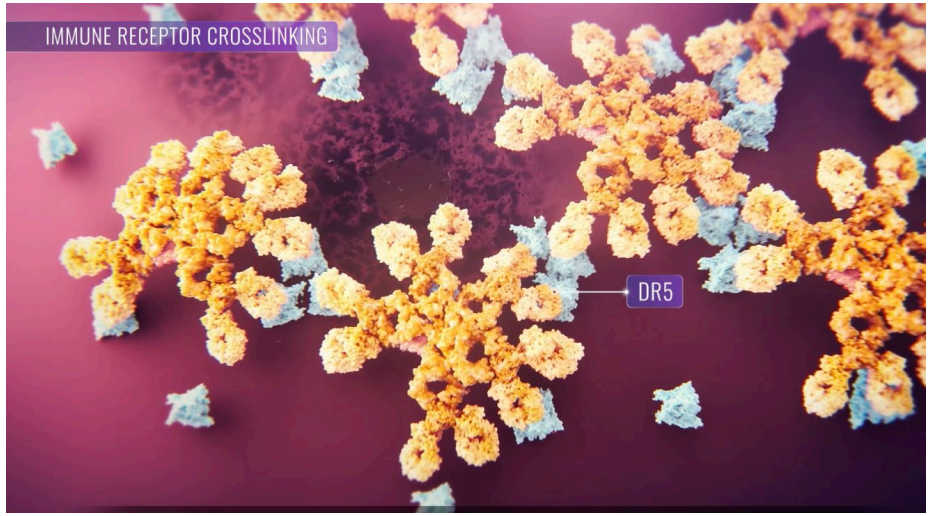
	Indications	Opportunity
IGM-2644 CD38 x CD3	Multiple Myeloma	• ~140K 3L+ MM patients WW
IGM-2537 CD123 x CD3	AML, MDS, ALL	• High unmet need in 1L MDS and R/R AML and ALL • >125K annual WW incidence

Oncology: three distinct mechanisms of action

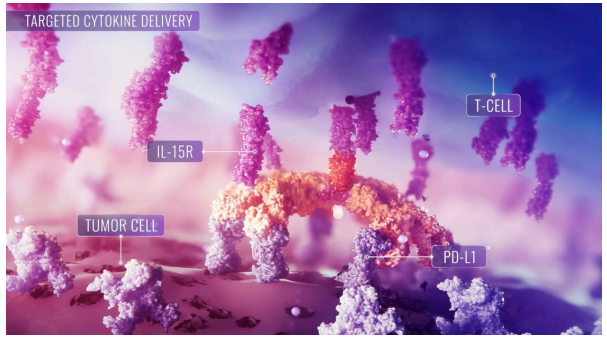
1 Bispecific T cell Engagers
(e.g., CD20 x CD3, CD38 x CD3)



2 Multi-Receptor Agonism
(e.g., DR5, OX40, GITR)



3 Targeted Cytokine Stimulation
(e.g., IL-15)



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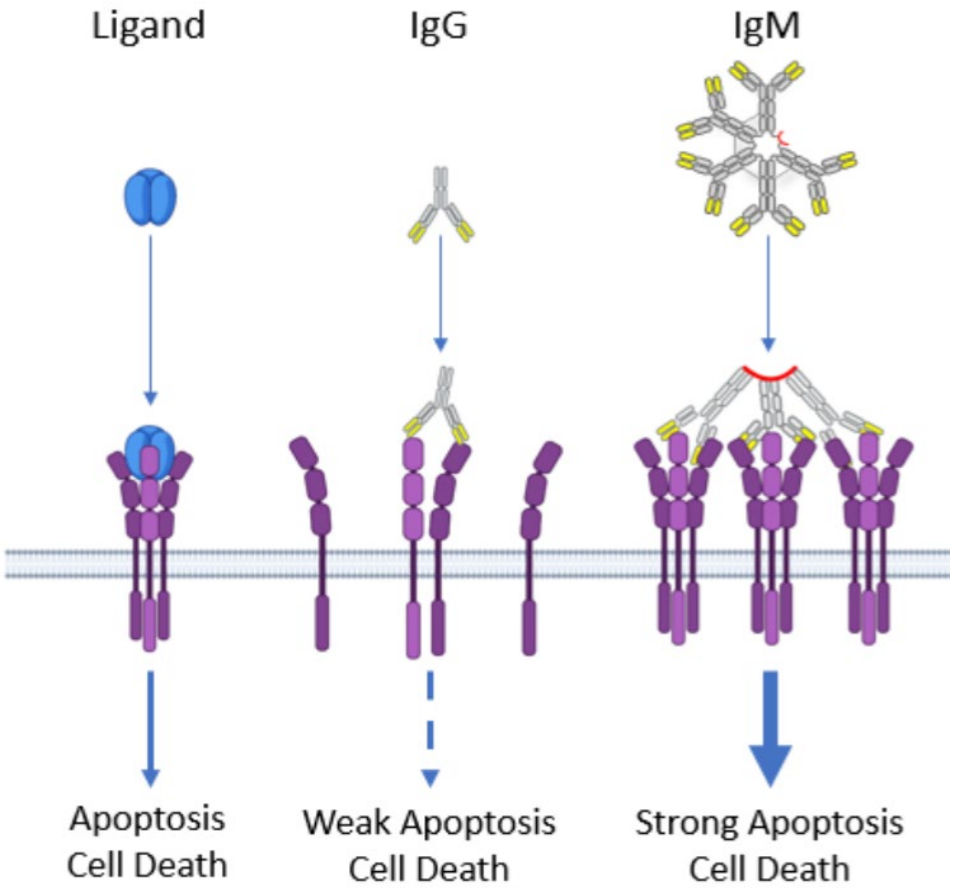
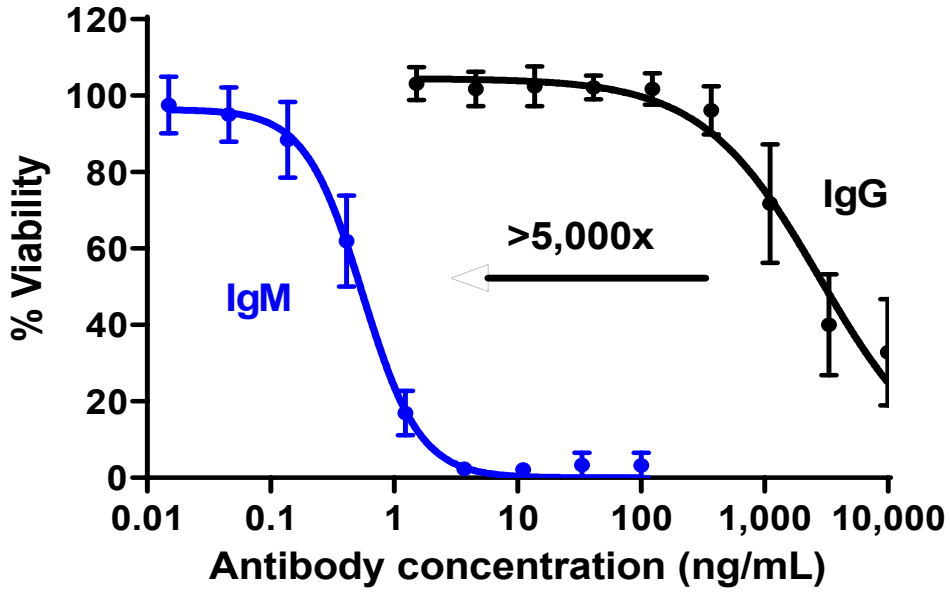
Strong DR5 activation requires multi-receptor agonism

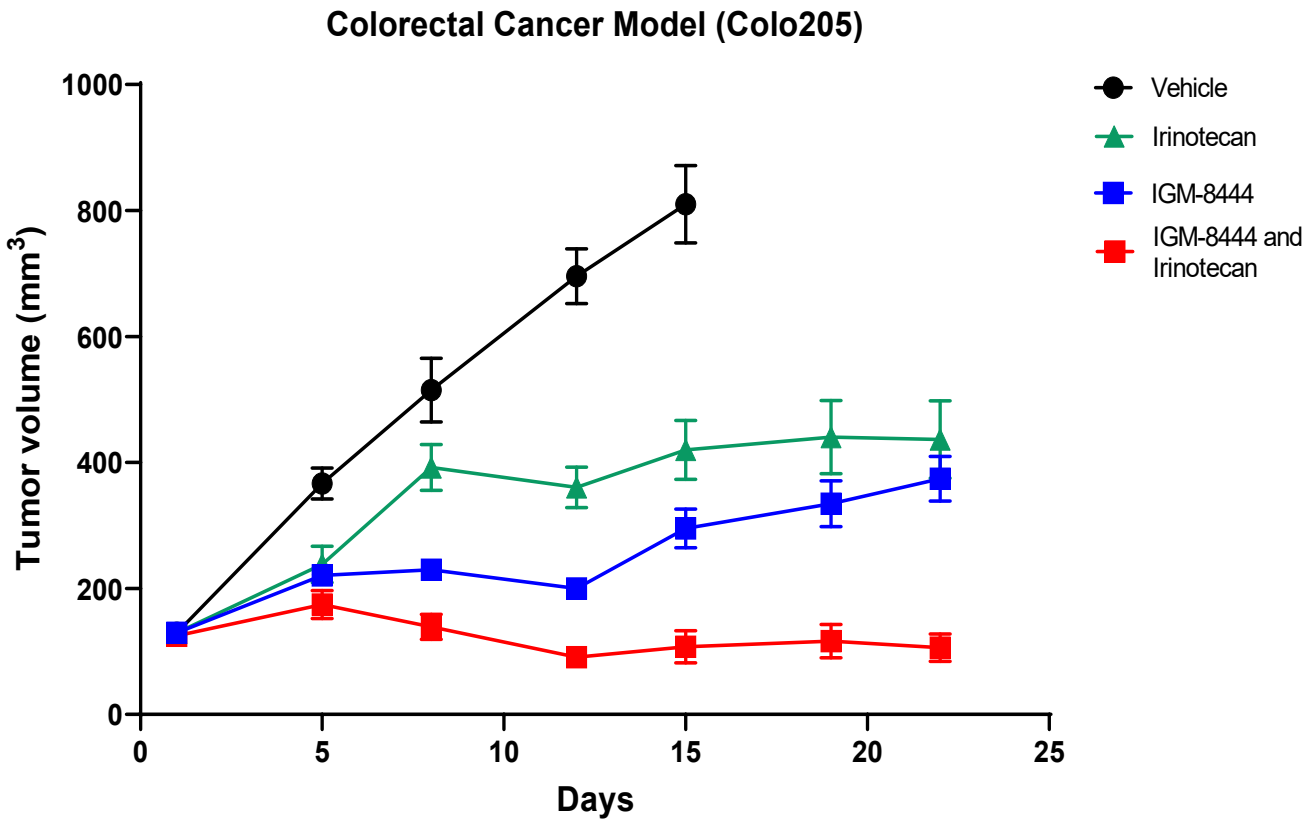
DR5 is highly expressed across many different tumor types



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

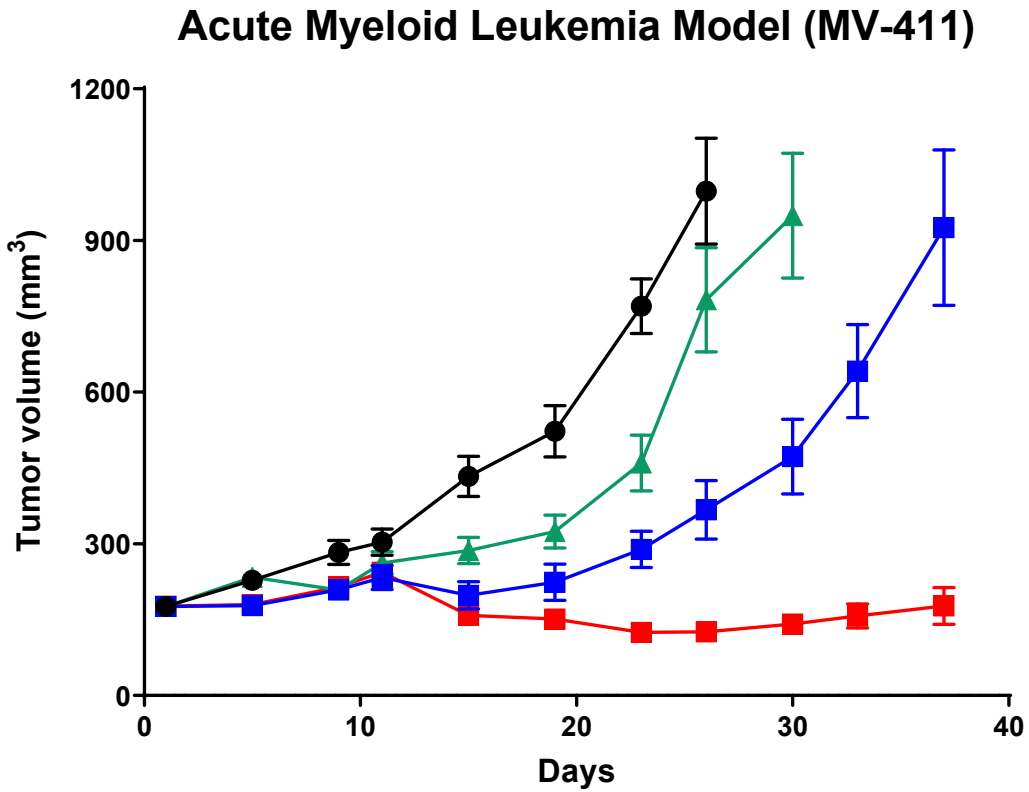


Increased *in vivo* activity seen in combination with irinotecan



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

Synergistic activity seen with IGM-8444 and Bcl-2 inhibitors

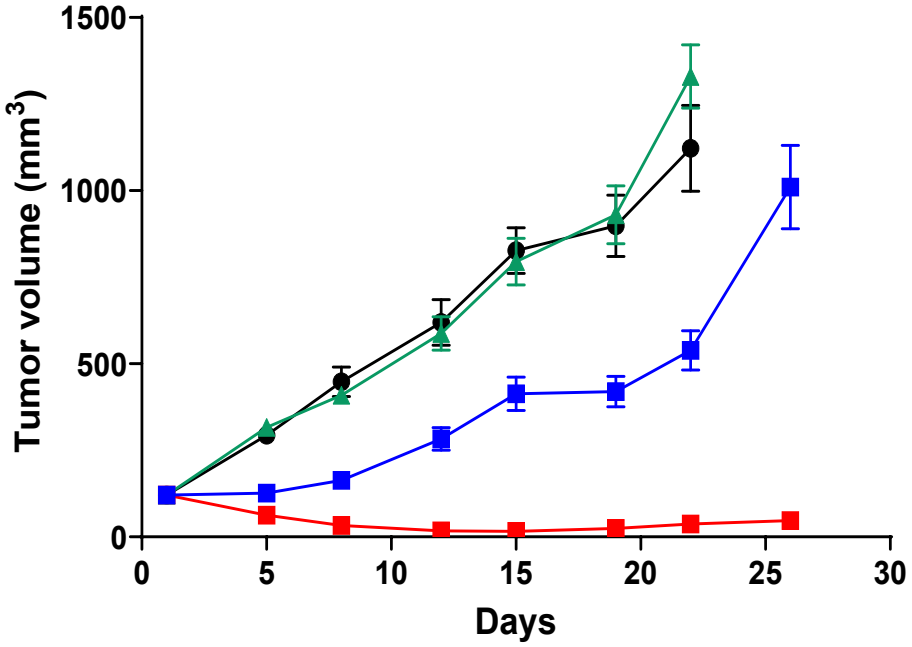


IGM-8444 (5 mg/kg Q2D x 11);
Venetoclax (100 mg/kg QD x 21)

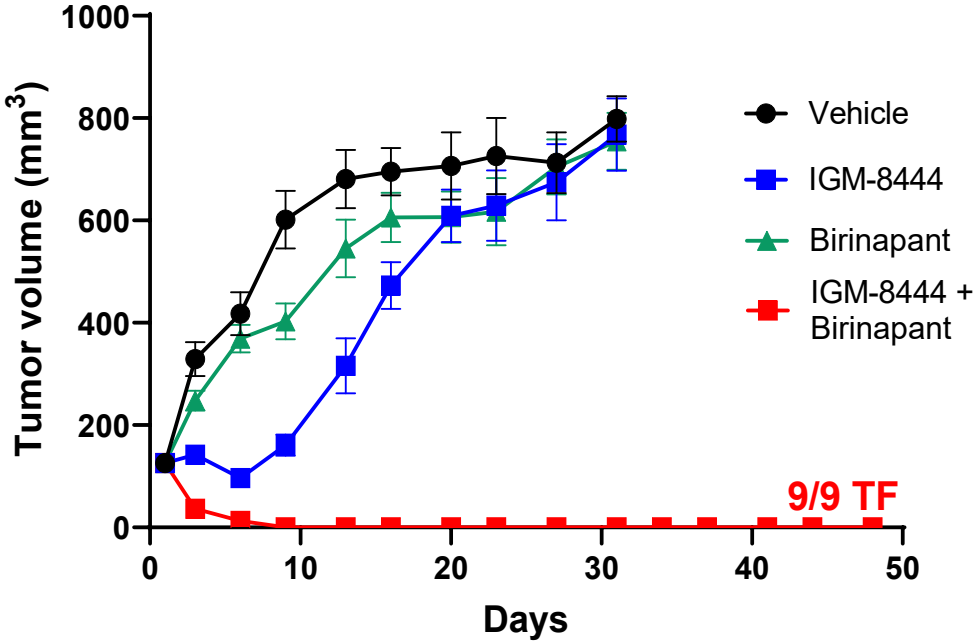
DR5: extrinsic apoptotic pathway
Bcl-2: intrinsic apoptotic pathway

Synergistic activity seen with IGM-8444 and birinapant

Triple Negative Breast Cancer Model
(MDA-MB-231)



Fibrosarcoma Cancer Model
(HT1080)



DR5: extrinsic apoptotic pathway
Birinapant: intrinsic apoptotic pathway

Phase 1 monotherapy and combination studies

Monotherapy Cohort

IGM- 8444

- Standard 3+3 design
- Dosing q2week
- All cohorts cleared
- No DLTs

Ongoing Combination Cohorts

IGM-8444 + FOLFIRI	• 2nd dose cohort cleared No DLTs observed to date
IGM-8444 + Venetoclax	• 1st cohort open
IGM-8444 + Birinapant	• 1st patient dosed Q421

IGM-8444 Phase 1 dose escalation clinical trial updates

38

patients treated with IGM-8444 as of 1/7/2022

13

patients remain on treatment

0

discontinuations for drug related safety reasons

No maximum tolerated dose defined nor any clinically significant liver toxicity

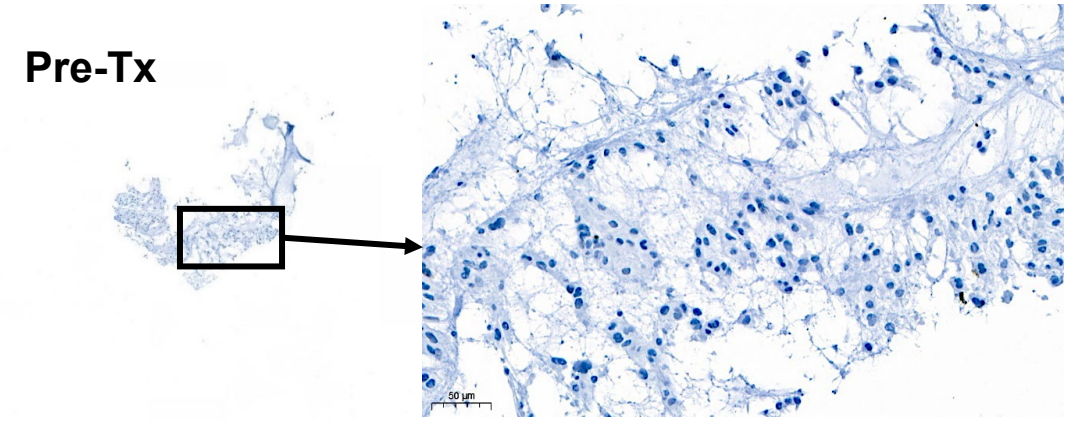
Signs of biological activity consistent with the activation of DR5 by a DR5 agonist

Data as of 1/07/2022

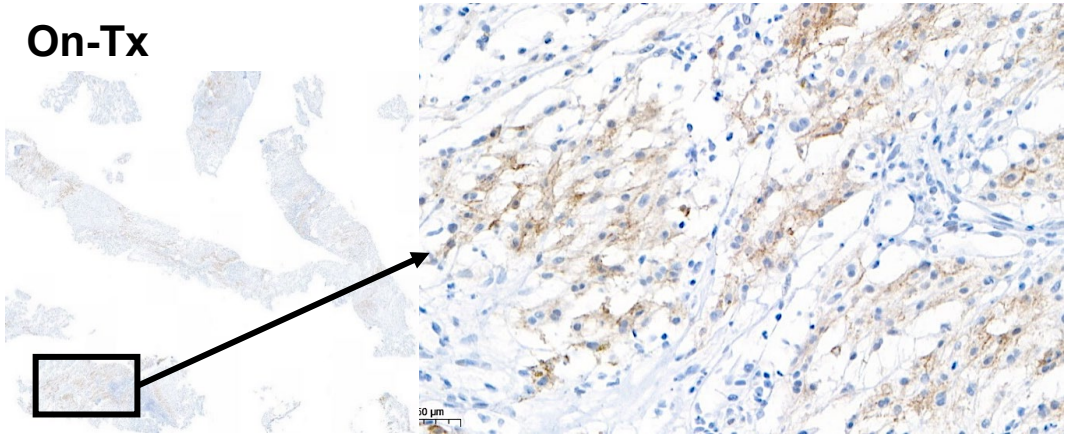
Indications of DR5 activation: cleaved caspase 3 (brown)

102-012 (9A) Chordoma, 3 mg/kg

Pre-Tx

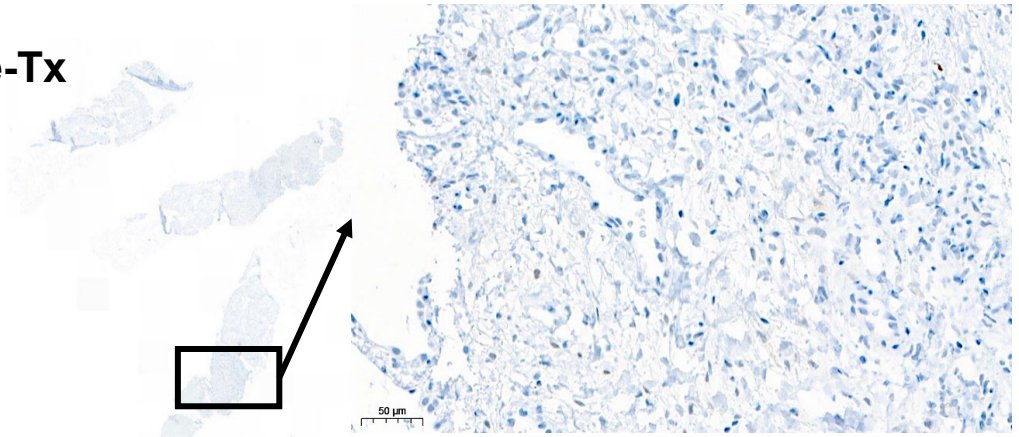


On-Tx

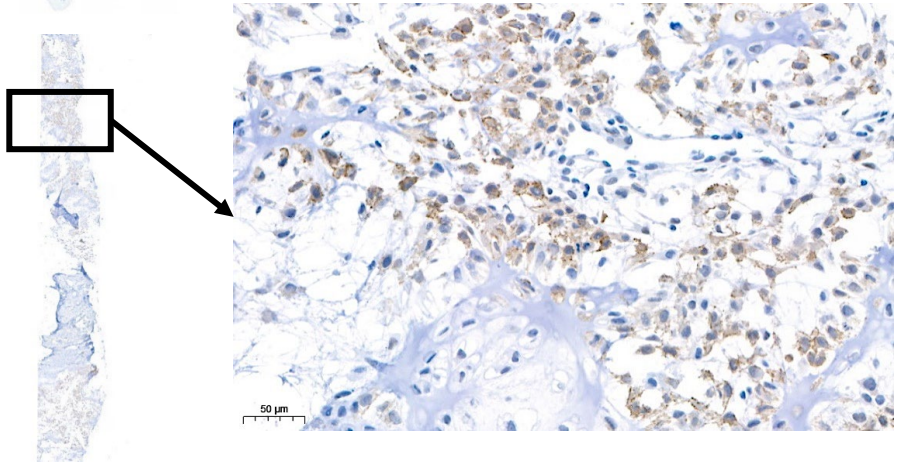


105-023 (17A), Chondrosarcoma, 10 mg/kg

Pre-Tx

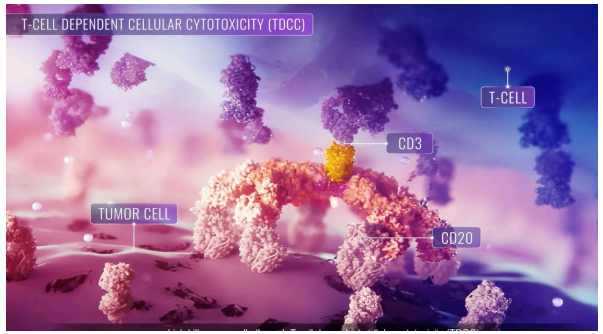


On-Tx



Oncology: three distinct mechanisms of action

1 Bispecific T cell Engagers
(e.g., CD20xCD3, CD38xCD3)



2 Multi-Receptor Agonism
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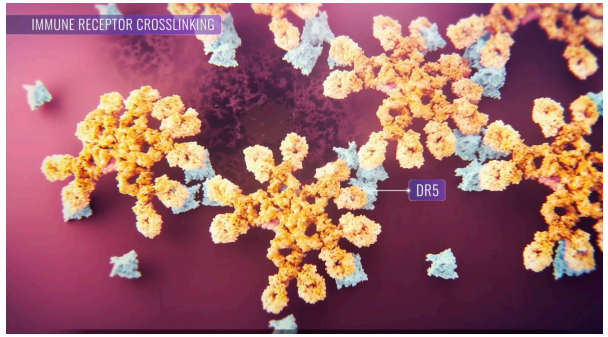
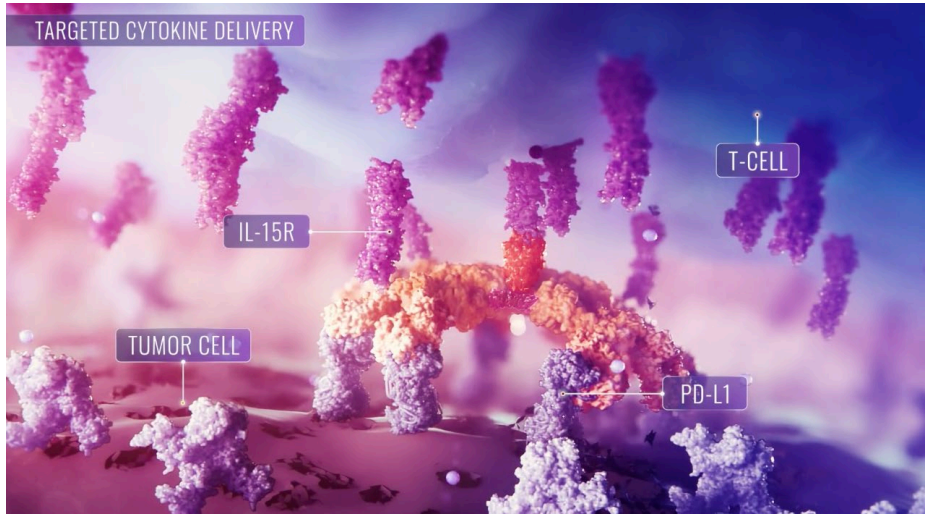
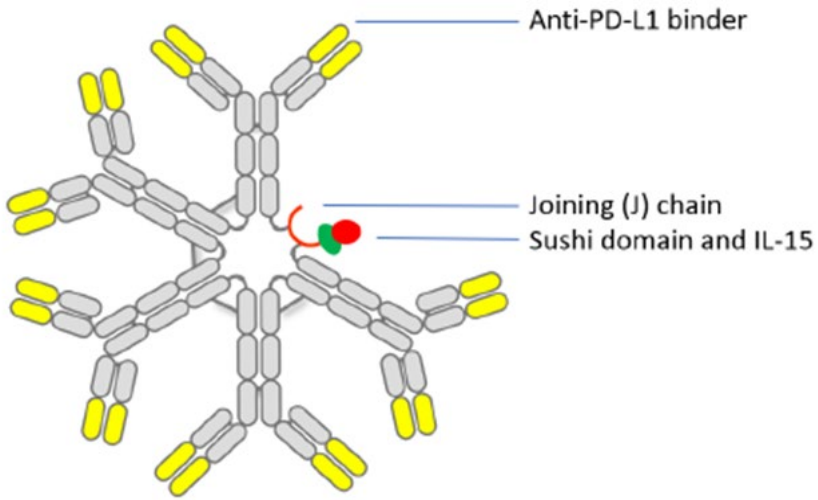


3 Targeted Cytokine Stimulation
(e.g., IL-15)



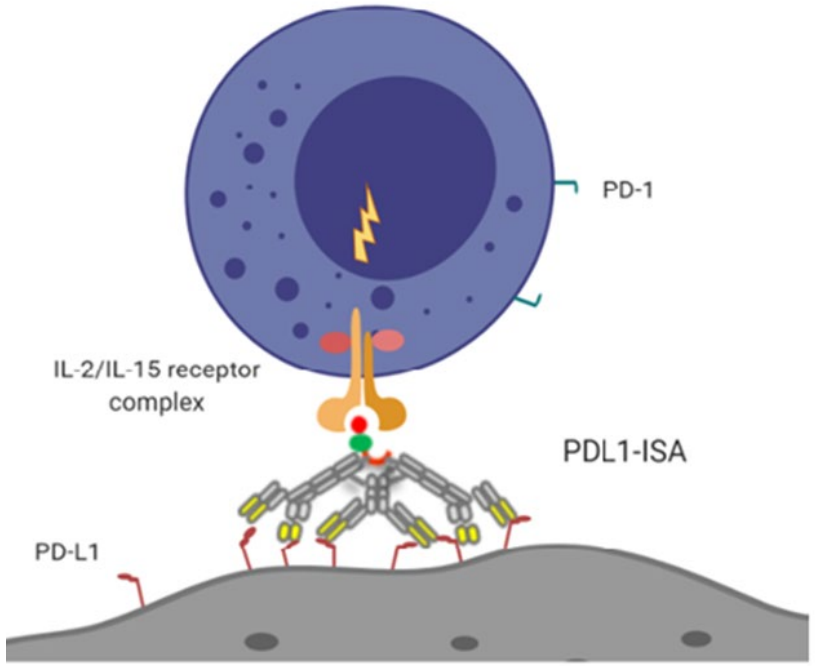
IGM-7354: targeted IL-15 delivery via PD-L1 expressing cells

IGM - 7354



IL-15 x anti-PDL1 IgM

NK or CD8 T cell expansion

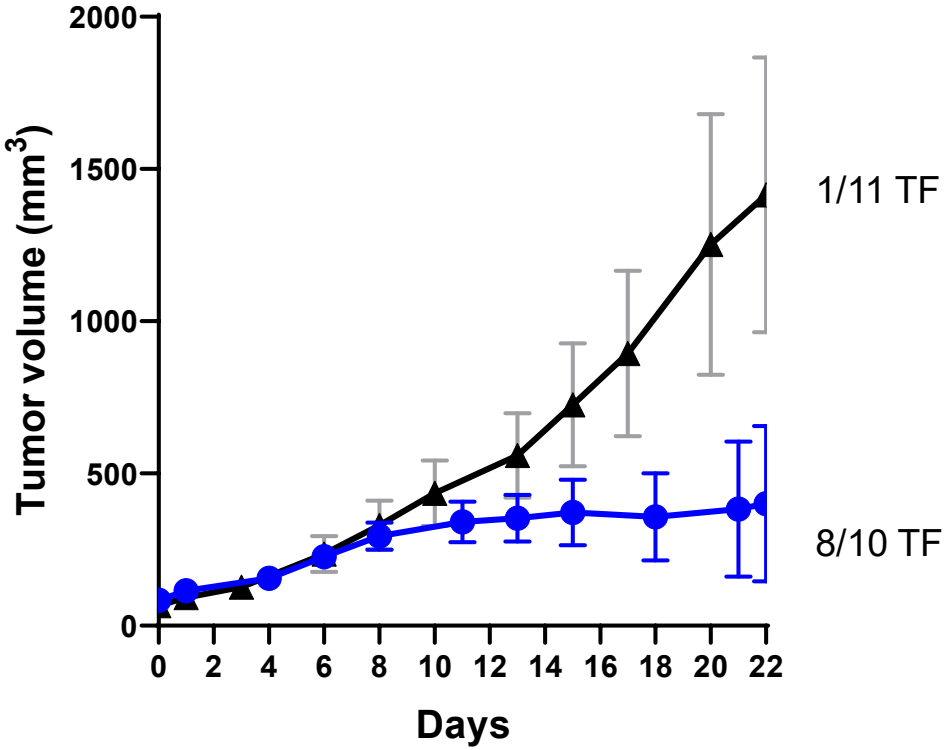


Tumor and/or Antigen Presenting Cell

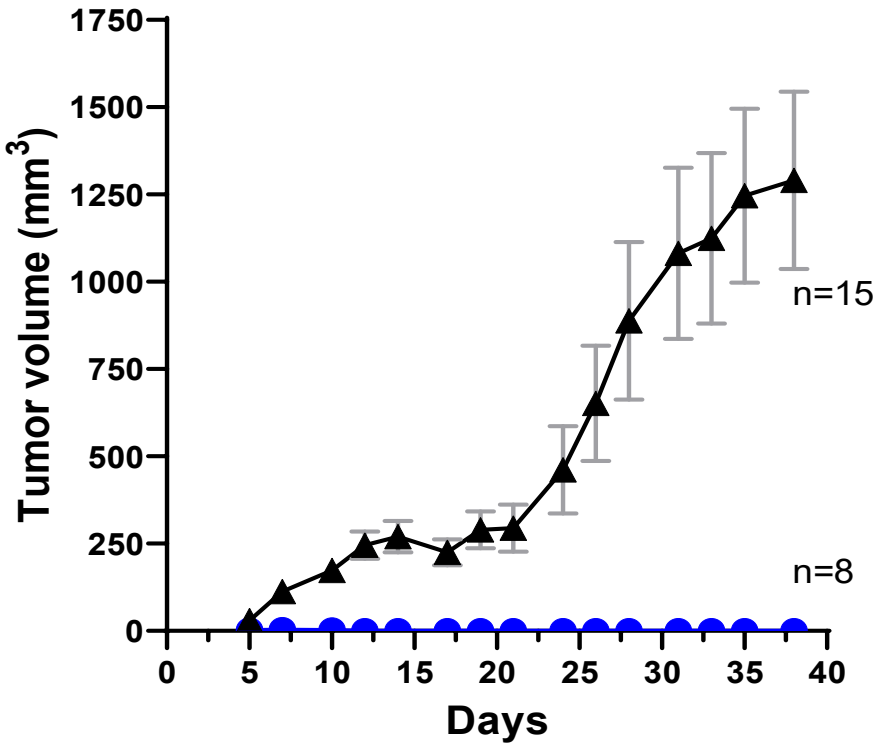
- IGM-7354 presents IL-15 to CD8 and NK cells
- Targeted delivery may increase efficacy and reduce toxicity
- Phase 1 initiation 2022 (anticipated)

IGM-7354: *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

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
Received: 23 February 2021
Accepted: 26 May 2021
Published online: 3 June 2021

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]✉

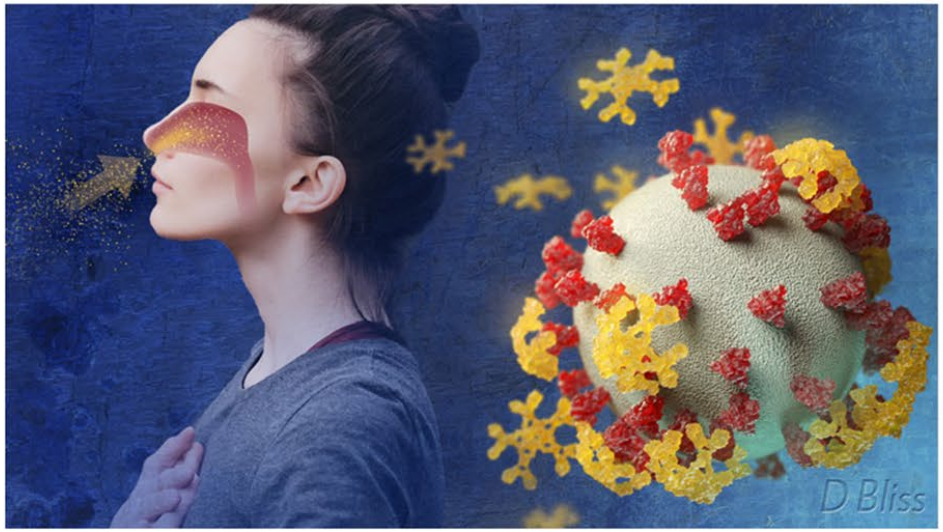
Resistance represents a major challenge for antibody-based therapy for coronavirus disease 2019 (COVID-19)[1–4]. Here we engineered an immunoglobulin M (IgM) neutralizing antibody (IgM-14) to overcome the resistance encountered by IgG-based therapeutics. IgM-14 is >230-fold more potent than its parental 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

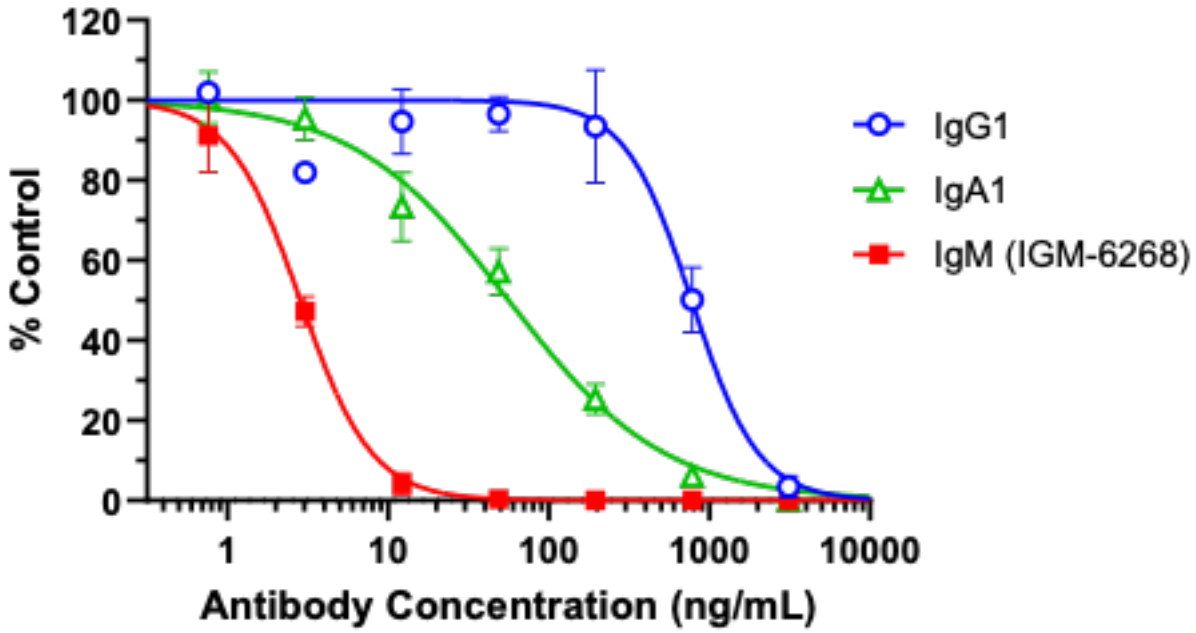


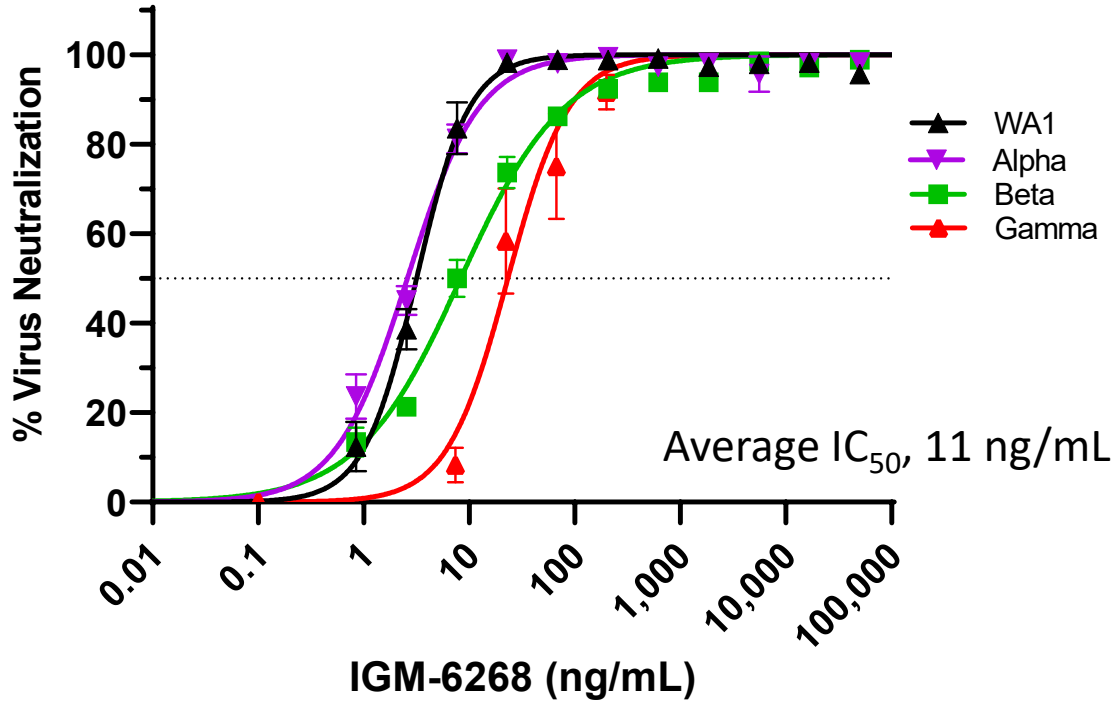
There are now several monoclonal antibodies, identical copies of a therapeutic antibody produced in large numbers, that are authorized for the treatment of COVID-19. But in the ongoing effort to beat this terrible pandemic, there's plenty of room for continued improvements in treating

igm biosciences™

IgM antibodies show increased neutralization potency *in vitro*

- Significantly improved potency in SARS-CoV-2 neutralization assay when converted from IgG
- Improved *in vitro* neutralization potency across tested variants relative to corresponding IgG





Modified from Ku 2021b, *Nature*

IGM-6268 is designed to be self-administered at home

- Our approach – intranasal spray
  - Targets upper respiratory tract (nasal cavity, mouth, throat)
  - No needles required
- In mouse models of COVID-19, intranasal IGM-6268
  - **Prevents** infection at low doses
  - **Treats** infection by reducing viral load in the lungs
- Current EUA-approved antibodies (all IgG) are administered by infusion or injection
  - Limited access since a hospital or clinic visit is required
  - 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

Phase 1 Dose Escalation Trial Initiated Q4 2021: First Dose Cohort Cleared

Multiple catalysts anticipated in 2022

Anticipated

Clinical Advancement	**IGM-2323** (CD20 x CD3) ❑ Phase 2 initial data **IGM-8444** (DR5) ❑ Phase 1 initial combination data **IGM-6268** (SARS-CoV-2) ❑ Phase 1 initial data
Pipeline Expansion	**IGM-7354** (IL-15 x PD-L1) ❑ Phase 1 initiation **IGM-2644** (CD38 x CD3) ❑ Phase 1 initiation