AACR American Association for Cancer Research®
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10
#AACR24
AACR.ORG/AACR24

IGM-2644, a CD38xCD3 bispecific IgM T cell engager, shows enhanced anti-tumor activity compared to daratumumab in preclinical models of multiple myeloma

Kevin C. Hart, Ph.D.
IGM Biosciences Inc., Mountain View, CA

Kevin C. Hart, Daniel Santos, Keyu Li, Rui Yun, Min Chai, Andras Kabai, Gene Li, Poonam Yakkundi, Roel P. Funke, Yinghui Guan, Thomas Manley, Liqin Liu, Angus M. Sinclair, Albert F. Candia, Bruce Keyt, Maya F. Kotturi

igm biosciences®

Disclosure Information

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

I have the following relevant financial relationships to disclose:

Employee and Stockholder in IGM Biosciences, Inc.

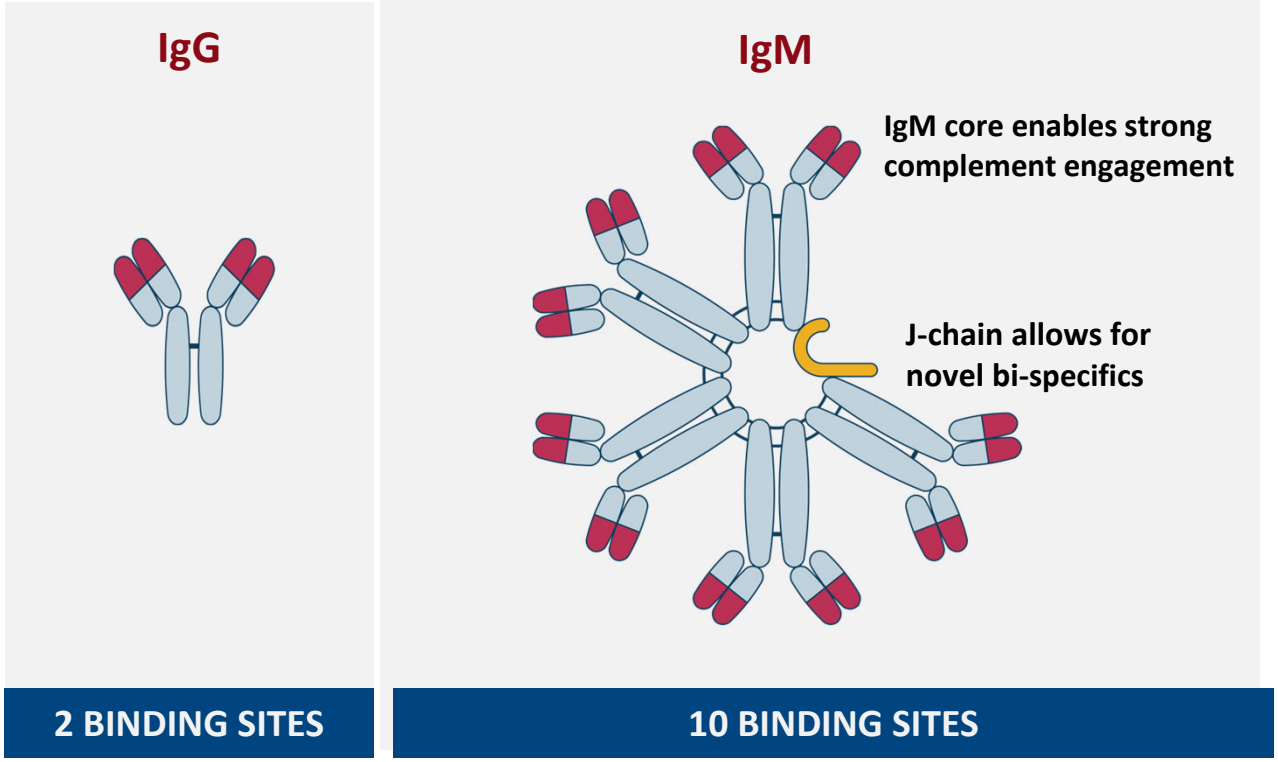
Engineered IgM antibodies have unique structural attributes compared to IgG antibodies

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

Additional binding sites lead to:

- Superior total binding power (avidity)
- Multimerization for agonist applications
- Strong complement engagement

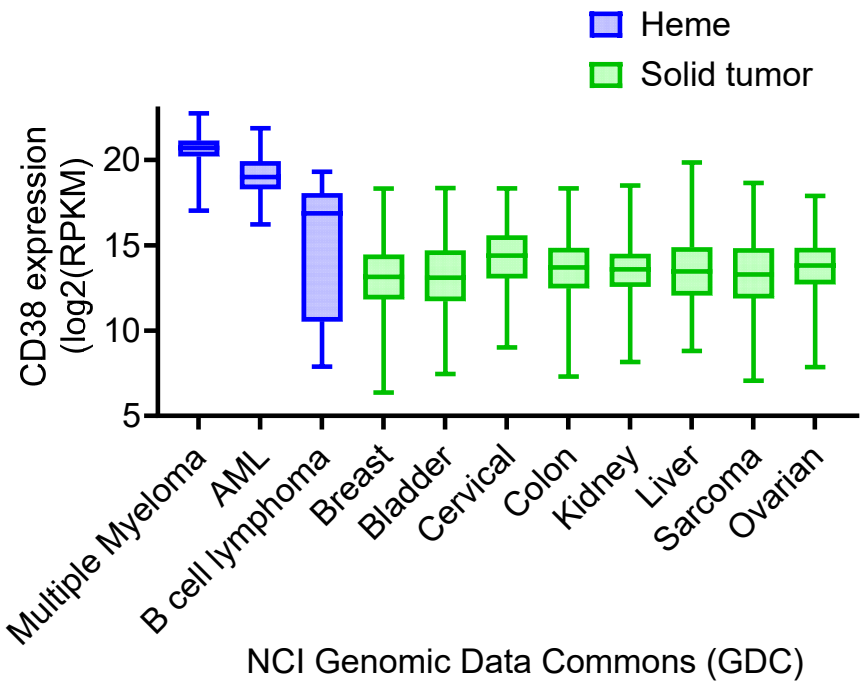
J-chain allows for additional functionality (bispecific and trispecific)



CD38-targeted treatment in multiple myeloma

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

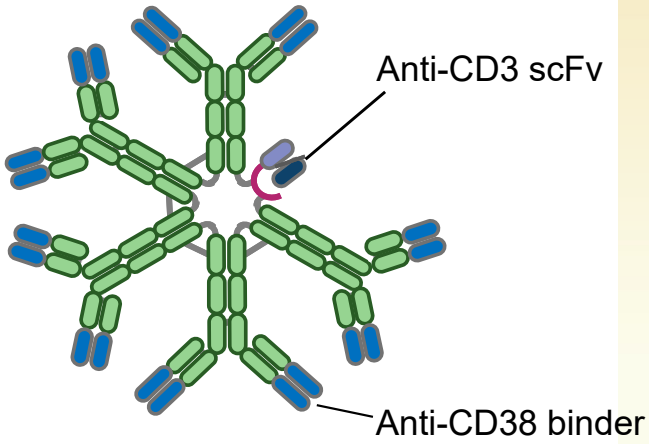
- CD38 is a transmembrane glycoprotein with ecto-enzymatic activity and is highly and uniformly expressed on myeloma cells
- Two therapeutic anti-CD38 IgG antibodies, daratumumab and isatuximab, are FDA-approved, but resistance inevitably develops
- Following treatment, patients have increased risk of infections largely due to immune cell depletion and bone marrow suppression

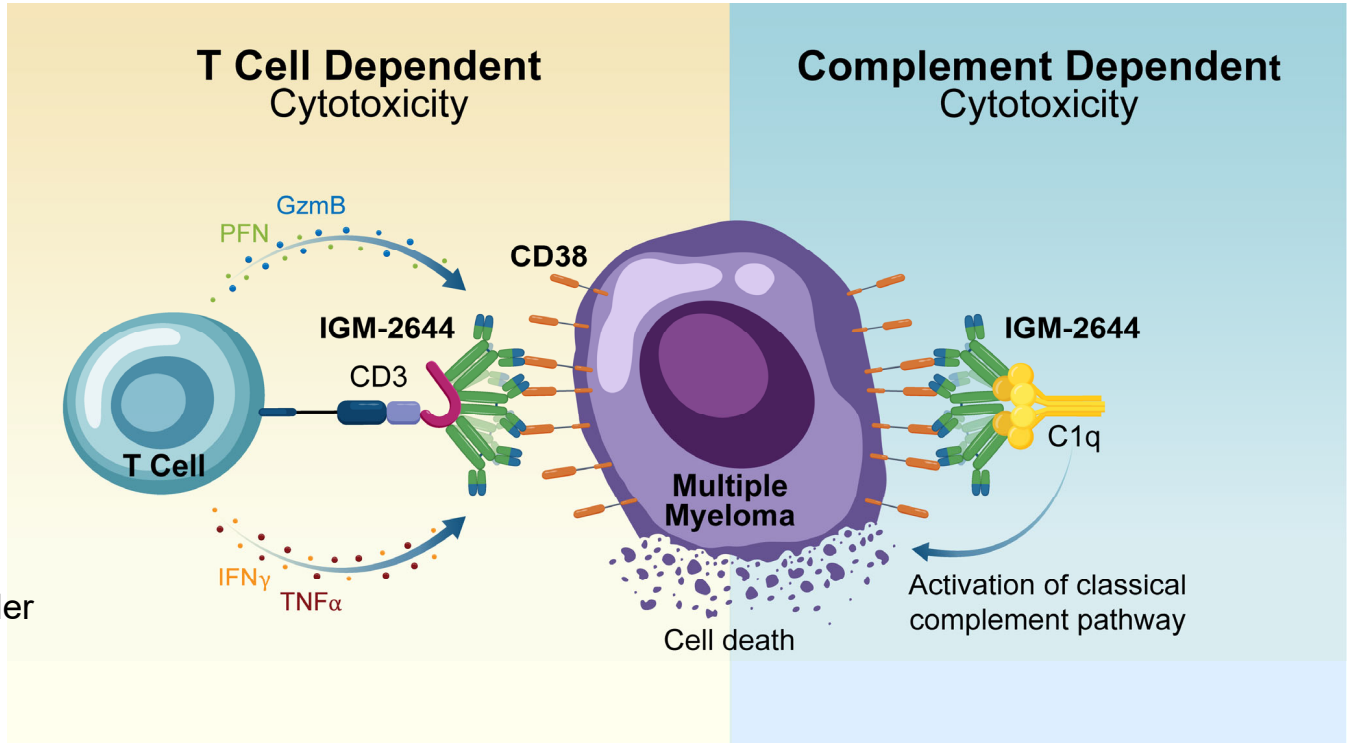


IGM-2644, an engineered CD38xCD3 bispecific IgM T cell engager, has dual mechanisms of tumor killing

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

IGM-2644

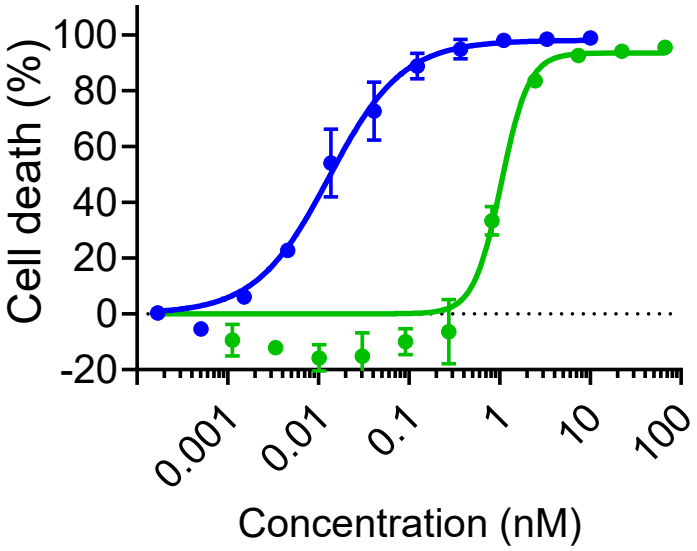




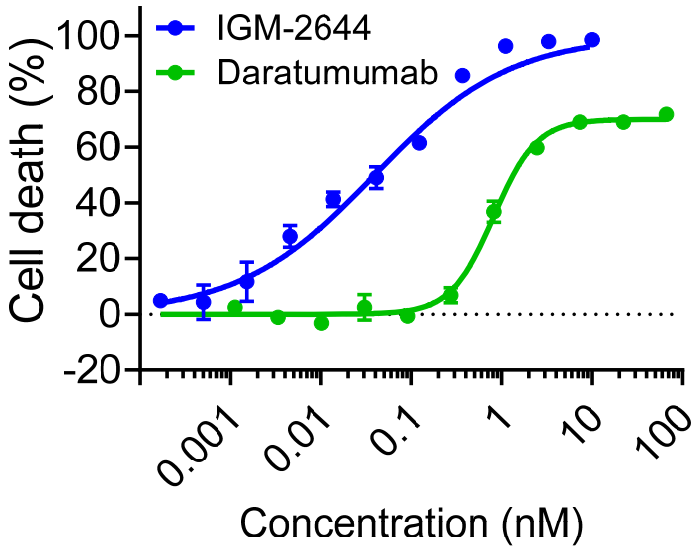
IGM-2644 demonstrates superior complement-dependent cytotoxicity to daratumumab *in vitro*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

Human myeloma cell line LP-1 ($CD38^{high}$ expression)



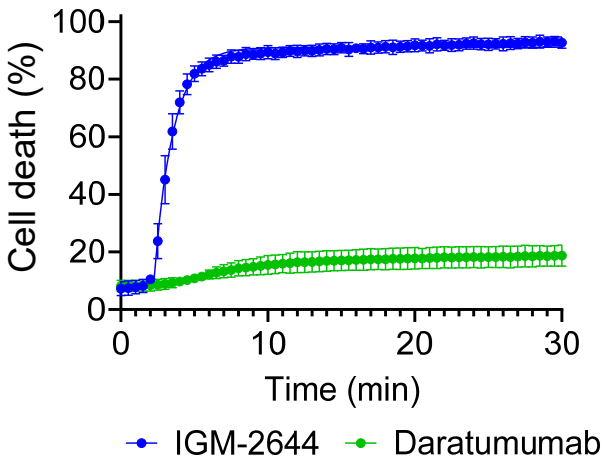
Human B lymphoma cell line Ramos ($CD38^{medium}$ expression)

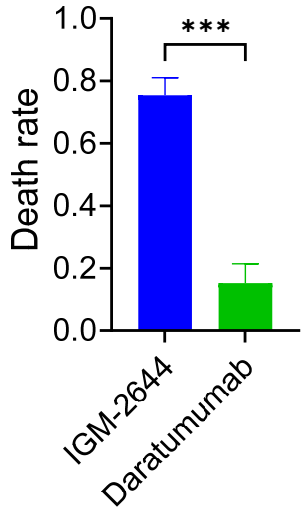


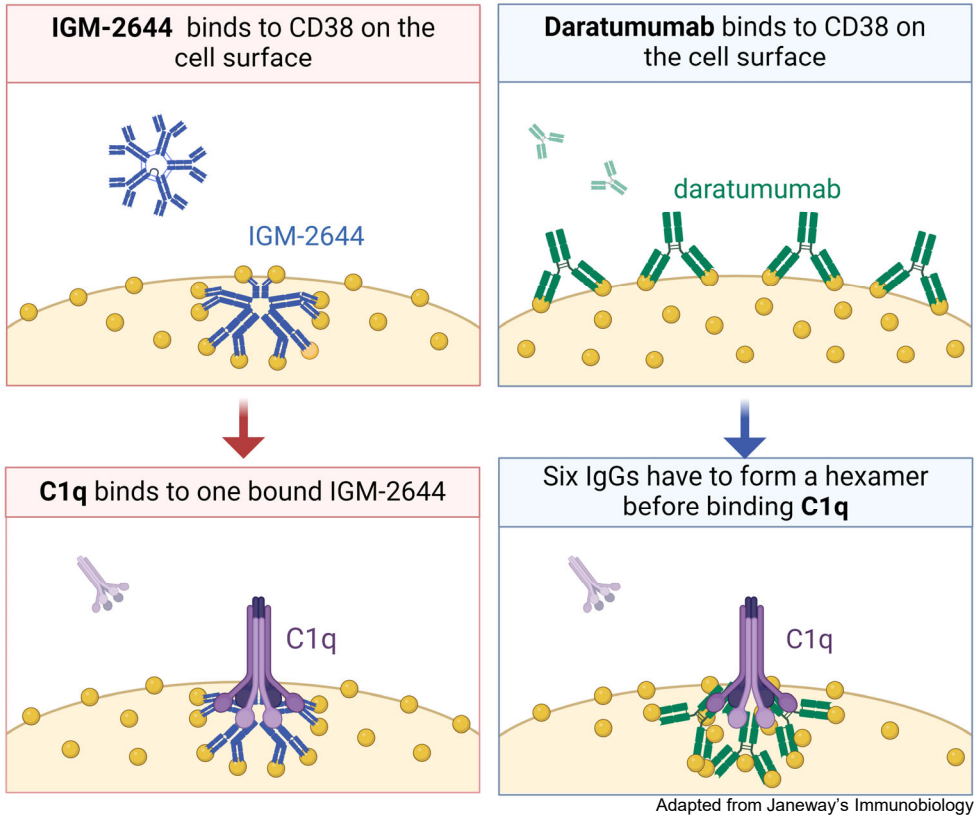
4 hour incubation with antibodies, 10% normal human serum as source of complement

IGM-2644 demonstrates superior CDC to daratumumab by live-cell imaging *in vitro*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24





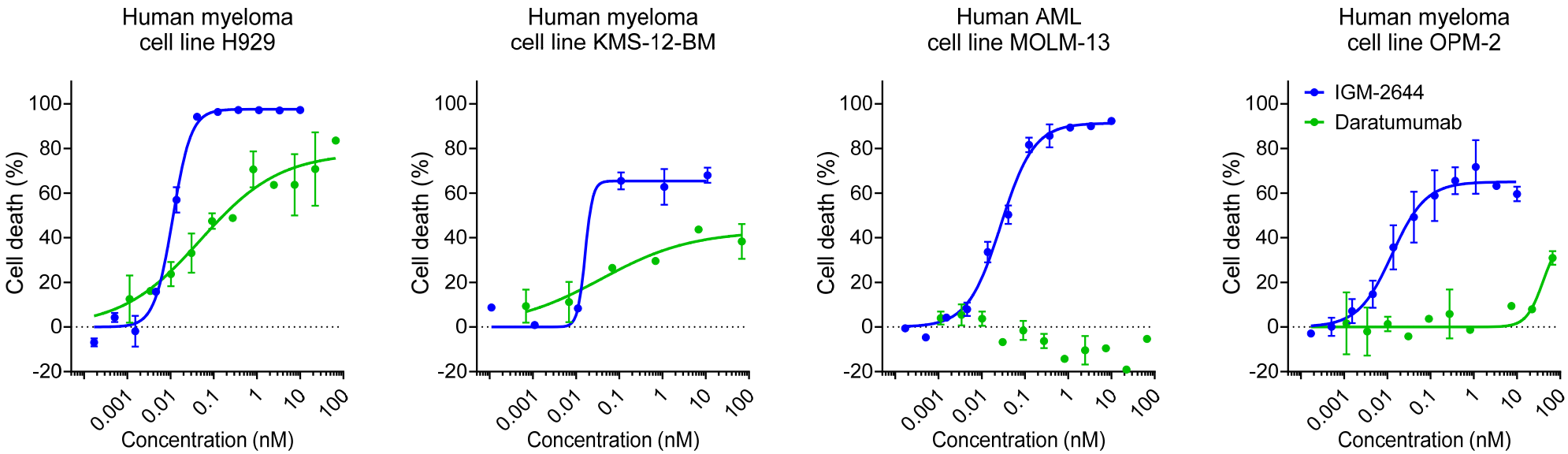


Human Raji B lymphoma cell line (CD38^{medium} expressing), 10% normal human serum, 1 µg/mL mAb

IGM-2644 has greater cellular-dependent cytotoxicity across a range of CD38 expression *in vitro*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

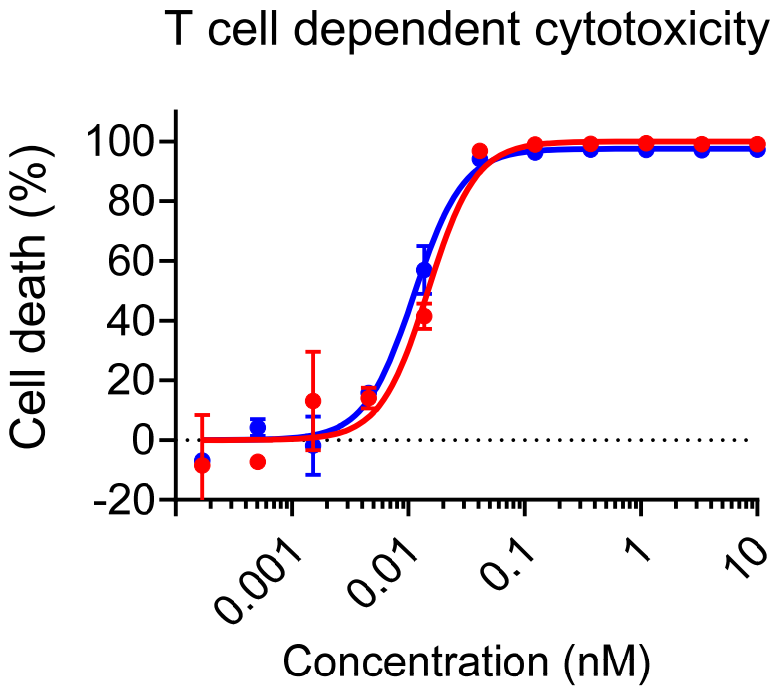
CD38 Expression Level

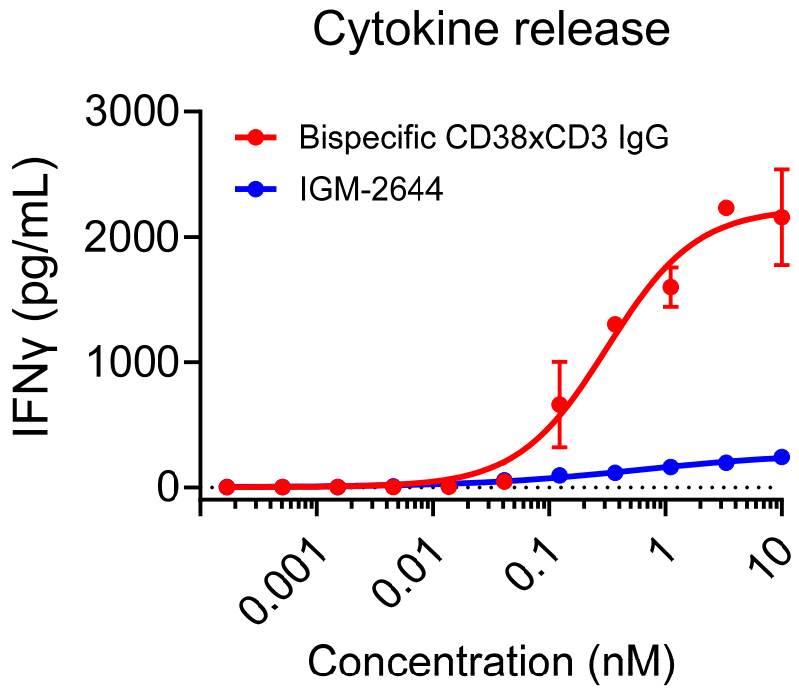


72 hour incubation, 10:1 effector to target ratio (PBMCs : tumor cell line)

IGM-2644 has comparable killing with minimal cytokine release relative to a CD38xCD3 bispecific IgG *in vitro*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24



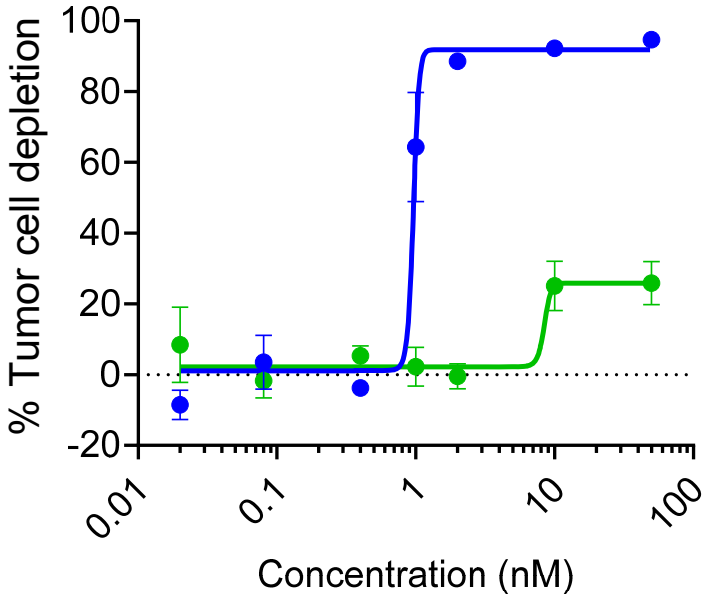


Human H929 myeloma cell line (CD38^{high} expressing), 72 hour incubation, 10:1 effector to target ratio

IGM-2644 depletes tumor cells in relapsed/refractory multiple myeloma patient samples *ex vivo*

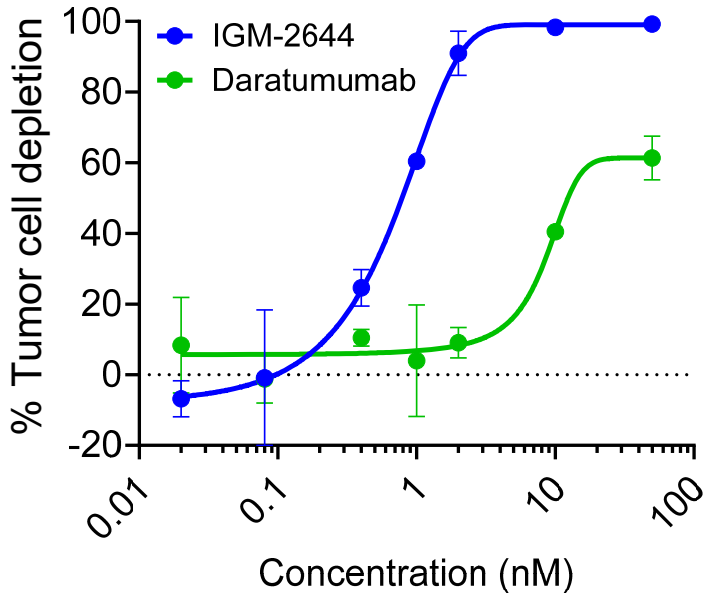
AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

r/r MM BMMC Donor #1



Daratumumab resistant (7 months post-daratumumab and 1 month post talquetamab (anti-GPRC5DxCD3 bsIgG)

r/r MM BMMC Donor #2



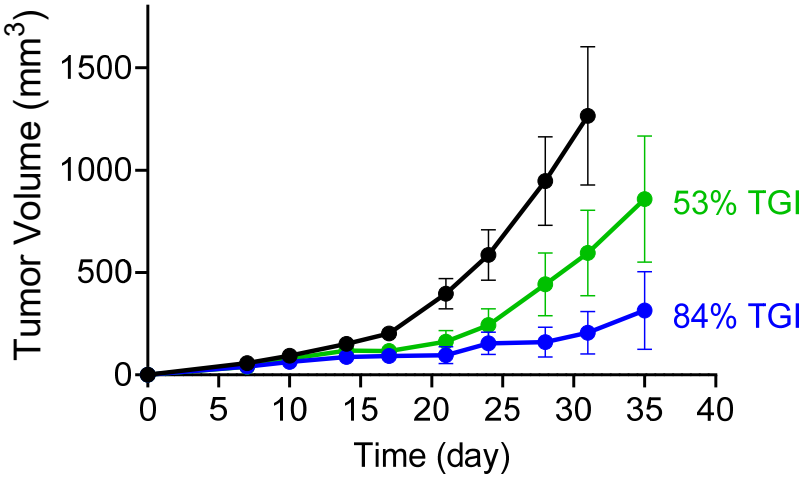
Post carfilzomib, lenalidomide, and dexamethasone

5 day incubation

IGM-2644 shows increased anti-tumor activity and TILs in humanized xenograft tumor models compared to daratumumab *in vivo*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

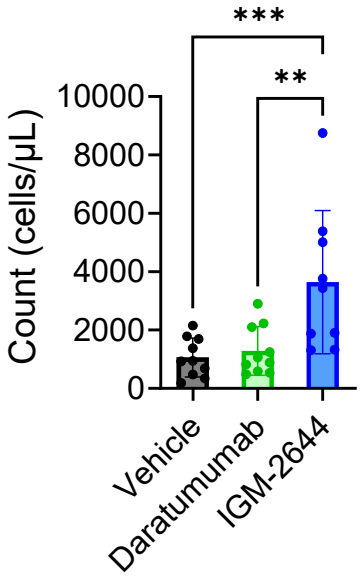
Human myeloma
KMS-12-BM xenograft
(CD38$^{low\text{-}med}$ expression)



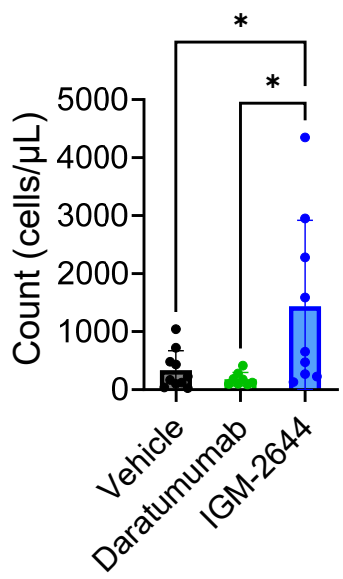
Vehicle
IGM-2644 (10 mg/kg): q2d x 12
daratumumab (10 mg/kg): qw x 3

Human B lymphoma Raji xenograft

Human CD3+ TILs



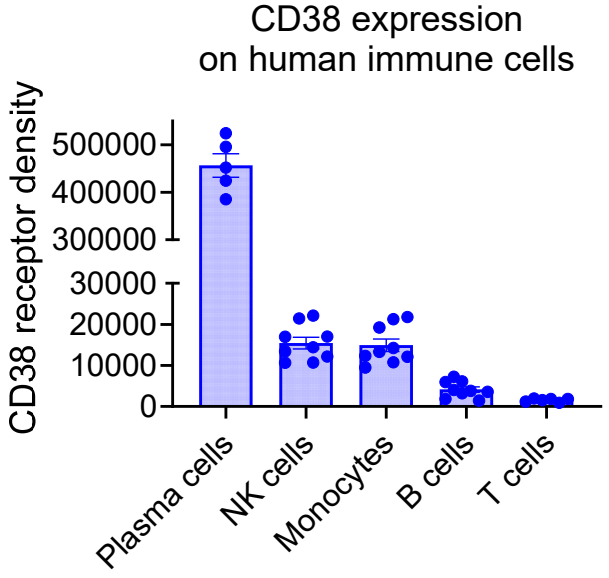
Human CD8+GrB+ TILs

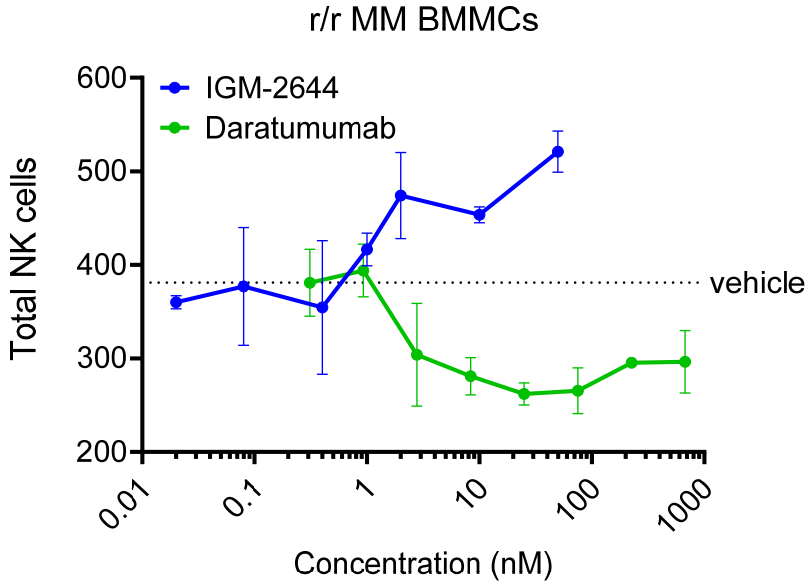


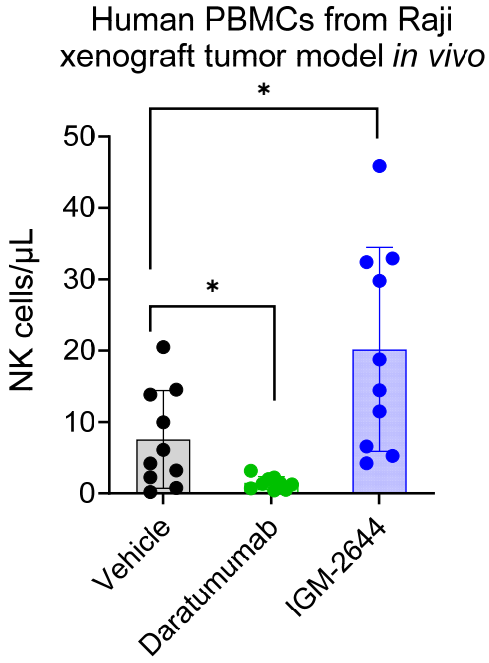
Vehicle
IGM-2644 (10 mg/kg): q2d x 6
daratumumab (10 mg/kg): q5d x 3

NK cell fratricide is detected following treatment with daratumumab, but not with IGM-2644, *ex vivo* & *in vivo*

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24





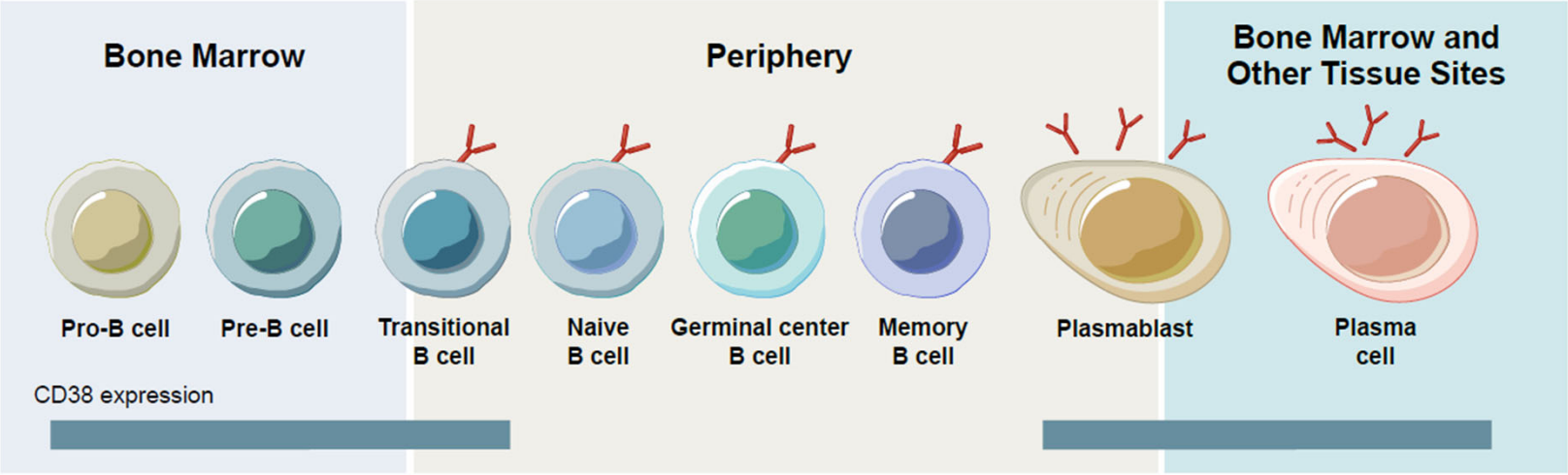


Forward Looking Strategy

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24

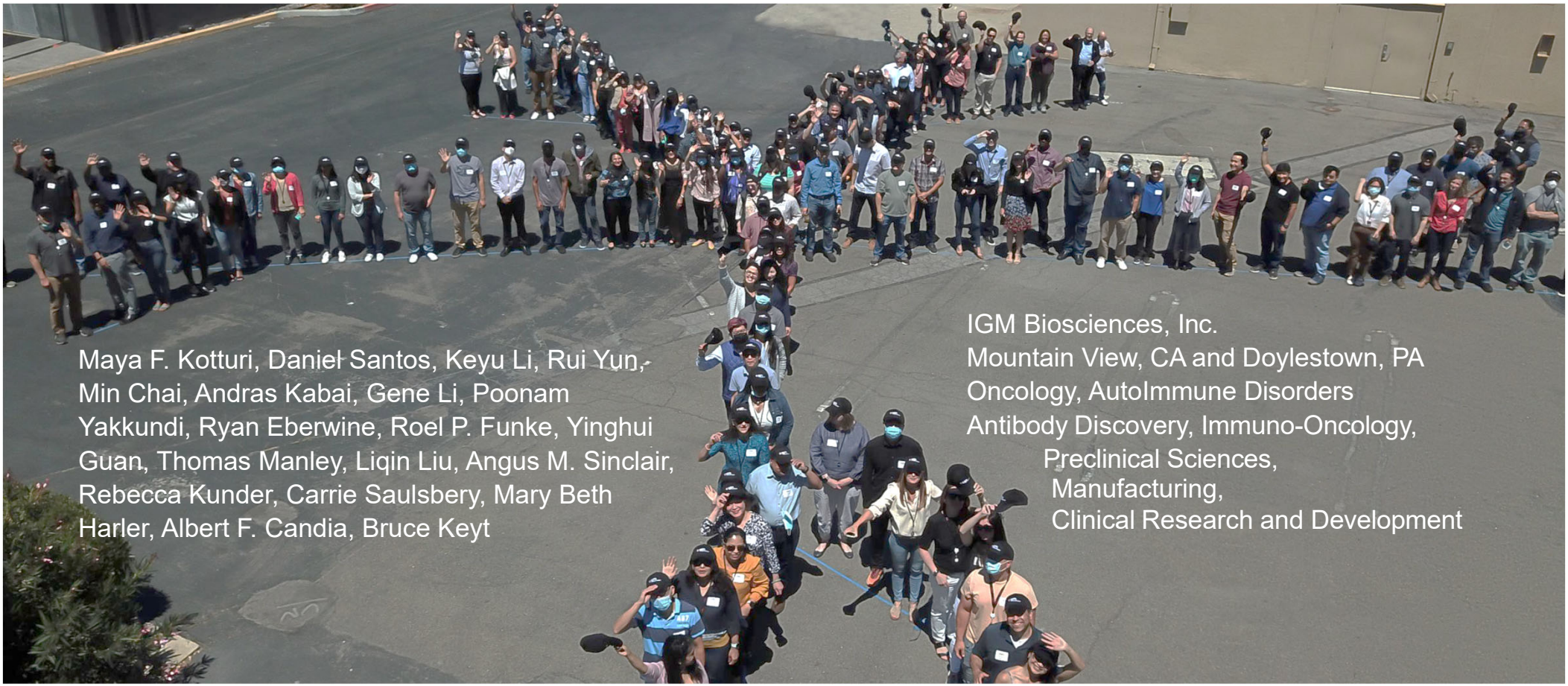
- Given the encouraging preclinical efficacy and safety profile, IGM-2644 has the potential to be a compelling CD38-targeted therapeutic agent

- IGM is planning clinical development of IGM-2644 for autoimmune disease with the goal of depleting CD38+ B cells to reduce pathogenic antibodies



Acknowledgments

AACR American Association for Cancer Research
ANNUAL MEETING
2024 • SAN DIEGO
APRIL 5-10 • AACR.ORG/AACR24 • #AACR24



Maya F. Kotturi, Daniel Santos, Keyu Li, Rui Yun, Min Chai, Andras Kabai, Gene Li, Poonam Yakkundi, Ryan Eberwine, Roel P. Funke, Yinghui Guan, Thomas Manley, Liqin Liu, Angus M. Sinclair, Rebecca Kunder, Carrie Saulsbery, Mary Beth Harler, Albert F. Candia, Bruce Keyt

IGM Biosciences, Inc.
Mountain View, CA and Doylestown, PA
Oncology, AutoImmune Disorders
Antibody Discovery, Immuno-Oncology,
Preclinical Sciences,
Manufacturing,
Clinical Research and Development