Pioneering the Development of Engineered IgM Antibodies for the Treatment of Cancer

November 2019
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 its future financial condition, results of operations, business strategy and plans, and objectives of management for future operations. 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 potential results of our preclinical studies, clinical trials and our discovery programs; our ability to utilize our lgM antibody platform to generate and advance additional product candidates; our ability to advance product candidates into, and successfully complete, clinical trials; 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; 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 lgM 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 filing: 2020 (anticipated) |
| IL-15 x PD-L1 | Solid and Hem. Malignancies | IND filing: 2021 (anticipated) |

Proprietary IgM antibody technology: 22 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

$251.3M Cash and Investments Balance, September 30, 2019
# IGM’s Wholly-Owned Oncology Pipeline

## Lead Programs

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<th>Mode</th>
<th>Target</th>
<th>Indications</th>
<th>Phase of Development</th>
<th>Worldwide Commercial Rights</th>
<th>Anticipated Milestones</th>
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<tbody>
<tr>
<td><strong>T cell Engager</strong></td>
<td>IGM-2323 (CD20 x CD3)</td>
<td>NHL, CLL</td>
<td>Discovery</td>
<td></td>
<td>Initial Phase 1 data for R/R B cell NHL: 2020</td>
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<td><strong>Receptor Cross-linking Agonist</strong></td>
<td>IGM-8444 (DR5)</td>
<td>Solid and Hematologic Malignancies</td>
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<td><strong>Targeted Cytokines</strong></td>
<td>IL-15 x PD-L1</td>
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## Research and Discovery Programs

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<tr>
<td><strong>T cell Engagers</strong></td>
<td>CD123 x CD3</td>
<td>Acute Myeloid Leukemia</td>
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<td></td>
<td>CD38 x CD3</td>
<td>Multiple Myeloma</td>
<td></td>
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<td></td>
<td>Multiple Targets x CD3</td>
<td>Multiple Solid Tumors</td>
<td></td>
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<tr>
<td><strong>Receptor Cross-linking Agonists</strong></td>
<td>OX40</td>
<td>Solid and Hematologic Malignancies</td>
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<td></td>
<td>GITR</td>
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<tr>
<td><strong>Targeted Cytokines</strong></td>
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Why IgM?
Structural comparison of IgG and IgM antibodies

**LEGEND**
- Target binding domains
- Constant domains
- Joining chain (J chain)
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)
Dual Mechanisms of Action: TDCC plus CDC

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

![Graph showing the comparison of B cell depletion with different mechanisms of action.](image)
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

![Graph showing relative killing activity](image)

- IGM-2323
- Rituximab

~1,000x difference in killing activity at high antibody concentrations.
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

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Percent Killing

Antibody concentration (pM)

- IGM-2323
- Bispecific IgG
IgM: Potentially Safer T Cell Directed Bispecific Antibodies

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

IL-6

IL-2

IFN-γ

TNFα
IGM CD20 x CD3 Bispecific Antibody
Non-human primate cytokine release data

Peak plasma inflammatory cytokine levels in non-human primates following treatment with modified IGM-2323

- **IL-6**
  - Y-axis: IL-6 (pg/mL)
  - X-axis: Antibody dose (mg/kg)

- **IL-2**
  - Y-axis: IL-2 (pg/mL)
  - X-axis: Antibody dose (mg/kg)

- **IFNγ**
  - Y-axis: IFNγ (pg/mL)
  - X-axis: Antibody dose (mg/kg)

- **TNFα**
  - Y-axis: TNFα (pg/mL)
  - X-axis: Antibody dose (mg/kg)
Immune Synapses

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

MABEL (Minimally Active Biologic Effect Level)

**Expansion Cohorts**

R/R DLBCL

R/R FL

Potential Additional Expansion Cohorts

R/R CLL

**Single patient cohorts**

IGM 2323 1000 mg

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323

IGM 2323
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
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

Gastric PDX Model

![Graph showing tumor volume (mm³) over days with Vehicle and IGM-8444 treatments.](image)

IGM-8444 (5 mg/kg): ↑↑↑↑↑↑

*Image of graph showing tumor volume over days with Vehicle and IGM-8444 treatments.*
IL-15 delivered by high avidity PD-L1 IgM antibody

IL-15 activity when delivered *in vitro* by PD-L1 IgM antibody
Leadership Team

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Thank You