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Investigational Agents

All Company product candidates described or mentioned herein are investigational and have not yet been approved for marketing by any regulatory authority.
| Introduction | Welcome & Margetuximab Overview | Scott Koenig, M.D., Ph.D.  
President & Chief Executive Officer |
|--------------|---------------------------------|----------------------------------------------------------------------------------|
| Breast Cancer | SOPHIA Phase 3 Study: Primary PFS Analysis | Hope S. Rugo, M.D.  
University of California San Francisco  
Helen Diller Family Comprehensive Cancer Center |
| Gastric Cancer | HER2-positive Advanced Gastric Cancer: Current Treatments & Unmet Need | Daniel Catenacci, M.D.  
The University of Chicago Medical Center |
| Margetuximab Program | Planned Development | Jon Wigginton, M.D.  
Senior Vice President, Clinical Development & Chief Medical Officer |
| Summary | Key Takeaways & Future Program Milestones | Scott Koenig, M.D., Ph.D.  
President & Chief Executive Officer |
| Q&A | | |
Committed to Developing Life-Changing Medicines

*Engineering antibodies that leverage immune system to fight cancer*

- MacroGenics today – engineering broad array of antibody formats
  - Nine immuno-oncology product candidates in clinical development
  - Advancing to becoming fully-integrated biopharma company

All Company product candidates described or mentioned herein are investigational and have not yet been approved for marketing by any regulatory authority.

* MacroGenics retains rights to develop its pipeline assets in combination w/MGA012 (INCMGA0012) and to manufacture a portion of global clinical and commercial supply needs of MGA012.
Fc Optimization Platform Designed to Enhance Innate and Adaptive Immunity

- Selected known target for platform validation (HER2: margetuximab)
  - Reported positive Phase 3 SOPHIA study
  - Expanding to other HER2-positive cancers
- Applying technology to novel target (B7-H3: enoblituzumab)
- Combining Fc-optimized antibodies with checkpoint inhibitors to boost anti-tumor immunity
  - MGA012 (anti-PD-1)
  - MGD013 (PD-1 x LAG-3)
Capturing Full Potential of Margetuximab

Planned development strategy

1. Potential Approval
   - 3rd/4th Line mBC (w/chemo)

2. Follow-on Indications
   - 1st Line Gastric Cancer (w/checkpoints)
     - IND active, CFDA engaged
     - Ph. 2/3 initiation in 2H2019

3. Future Opportunities
   - Neoadjuvant breast cancer
   - Other HER2+ populations

Commercial Value

June 4, 2019 – ASCO 2019 Conference Call: Margetuximab
SOPHIA Phase 3 Study: Primary PFS Analysis

Hope S. Rugo, M.D.
Clinical Professor of Medicine, UC San Francisco’s Helen Diller Comprehensive Cancer Center
SOPHIA Primary PFS Analysis:
A Phase 3 Study of Margetuximab + Chemotherapy
vs Trastuzumab + Chemotherapy
in Patients With HER2+ Metastatic Breast Cancer
After Prior Anti-HER2 Therapies

Hope S. Rugo, MD,1 Seock-Ah Im, MD, PhD,2 Gail S. Wright, MD, FACP, FCCP,3 Santiago Escrivá-de-Romaní, MD,4 Michelino De Laurentiis, MD, PhD,5 Javier Cortes, MD, PhD,6 Shakeela W. Bahadur, MD,7 Barbara B. Haley, MD,8 Raul H. Oyola, MD,9 David A. Riseberg, MD,10 Antonino Musolino, MD, PhD, MSc,11 Fatima Cardoso, MD,12 Giuseppe Curigliano, MD, PhD,13 Peter A. Kaufman, MD,14 Mark D. Pegram, MD,15 Sutton Edlich,16 Shengyan Hong, PhD,16 Edwin Rock, MD, PhD,16 William J. Gradishar, MD,17 on behalf of the SOPHIA Study Group

1University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; 2Seoul National University Hospital Cancer Research Institute, Seoul, Korea; 3Florida Cancer Specialists & Research Institute, New Port Richey, FL, USA; 4Vall d’Hebron Institute of Oncology, Barcelona, Spain; 5National Cancer Institute Fondazione Pascale, Naples, Italy; 6IOB Institute of Oncology, Madrid & Barcelona; Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain; 7Bannerer MD Anderson Cancer Center, Gilbert, AZ, USA; 8University of Texas Southwestern Medical Center, Dallas, TX, USA; 9Northwest Georgia Oncology Centers, Marietta Cancer Center, Marietta, GA, USA; 10Mercy Medical Center, Baltimore, MD, USA; 11University Hospital of Parma, Parma, Italy; 12Champalimaud Clinical Center/Champalimaud Foundation, Lisbon, Portugal; 13University of Milano, European Institute of Oncology, Milan, Italy; 14University of Vermont Cancer Center, Division of Hematology/Oncology, Burlington, VT, USA; 15Stanford Women’s Cancer Center, Palo Alto, CA, USA; 16MacroGenics, Inc., Rockville, MD, USA; 17Northwestern University, Chicago, IL, USA
Persistent Unmet Need in HER2+ MBC After Anti-HER2 Therapy

• Current standard of care for HER2-positive MBC
  – First-line: trastuzumab and pertuzumab with chemotherapy\textsuperscript{1-3}
  – Second-line: T-DM1\textsuperscript{4,5}

• After the above therapies, there is no recognized standard of care
  – Subsequent therapies are poorly defined, including sequential chemotherapy with trastuzumab and/or lapatinib\textsuperscript{6,7}
  – Continued anti-HER2 therapy after progression is generally preferred, in combination with chemotherapy\textsuperscript{8-11}

HER2=human epidermal growth factor receptor 2; MBC=metastatic breast cancer; T-DM1=ado-trastuzumab emtansine.

Margetuximab: Fc-engineered to Activate Immune Responses

**Trastuzumab**

**Fab:**
- Binds HER2 with high specificity
- Disrupts signaling that drives cell proliferation and survival

**Fc:**
- Wild-type immunoglobulin G1 (IgG1) immune effector domains
- Binds and activates immune cells

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**Margetuximab**

**Fab:**
- Same specificity and affinity
- Similarly disrupts signaling

**Fc engineering:**
- ↑ Affinity for activating FcγRIIIA (CD16A)
- ↓ Affinity for inhibitory FcγRIIB (CD32B)

**Margetuximab Binding to FcγR Variants:**

<table>
<thead>
<tr>
<th>Receptor Type</th>
<th>Receptor</th>
<th>Allelic Variant</th>
<th>Relative Fc Binding</th>
<th>Affinity Fold-Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activating</td>
<td>CD16A</td>
<td>158F</td>
<td>Lower</td>
<td>6.6x ↑</td>
</tr>
<tr>
<td></td>
<td></td>
<td>158V</td>
<td>Higher</td>
<td>4.7x ↑</td>
</tr>
<tr>
<td></td>
<td>CD32A</td>
<td>131R</td>
<td>Lower</td>
<td>6.1x ↓</td>
</tr>
<tr>
<td></td>
<td></td>
<td>131H</td>
<td>Higher</td>
<td>↔</td>
</tr>
<tr>
<td>Inhibitory</td>
<td>CD32B</td>
<td>232I/T</td>
<td>Equivalent</td>
<td>8.4x ↓</td>
</tr>
</tbody>
</table>

CD16A Genotype May Predict Anti-HER2 Antibody Benefit

- Two retrospective studies of HER2+ MBC\(^1\) and early breast cancer\(^2\) suggest patients with lower affinity CD16A-158F allele have lower PFS and ORR with trastuzumab than those homozygous for higher affinity CD16A-158VV
  - Two other retrospective studies showed no association between Fc\(\gamma\)R genotypes and outcome with adjuvant trastuzumab in early breast cancer\(^3,4\)

- **Hypothesis**: Greater margetuximab benefit in lower binding CD16A-158F carriers
  - Increased affinity of margetuximab for CD16A-158F over trastuzumab (wild-type IgG1)

- **SOPHIA** is first prospective* analysis of Fc\(\gamma\)R genotype impact on anti-HER2 antibody efficacy

*SOPHIA* is first prospective* analysis of Fc\(\gamma\)R genotype impact on anti-HER2 antibody efficacy

*Non-alpha allocating, exploratory analysis.

ORR=objective response rate; PFS=progression-free survival.

Margetuximab Enhances Innate Immunity \textit{In Vitro}

Greater relative cytotoxicity of margetuximab with NK cells from CD16A-158F allele carriers

Preclinical Assay of Antibody-Dependent Cellular Cytotoxicity (ADCC)\(^1\)

**Effector Cells:** Human NK cells from donors with CD16A genotypes 158VV, 158FV, and 158FF

**Target Cells:** JIMT-1 HER2+ breast cancer cell line resistant to trastuzumab antiproliferative activity

**Cellular Assay:** 3:1 Effector:Target ratio; 24-hour incubation time; endpoint: % lactate dehydrogenase release

mAb=monoclonal antibody; NK=natural killer.

Margetuximab Enhances HER2-specific Adaptive Immunity\textsuperscript{1,2}

- Phase 1 margetuximab monotherapy study in 66 pretreated patients with HER2+ carcinomas\textsuperscript{3,4}:
  - Four (17\%) confirmed responses in 24 evaluable patients with HER2+ MBC\textsuperscript{3}
  - Three patients continue on margetuximab at least 4 to 6 years, as of 15-May-2019\textsuperscript{4}

- Enhanced HER2-specific T- and B-cell responses after margetuximab monotherapy\textsuperscript{5}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Antigen-specific T cells (per million PBMC, IFN$\gamma$ ELISpot)}
\end{figure}

Study CP-MGAH22-04 (SOPHIA) Design\textsuperscript{1,2}

**HER2+ advanced breast cancer**
- \(\geq 2\) prior anti-HER2 therapies, including pertuzumab
- 1-3 prior treatment lines in metastatic setting
- Prior brain metastasis ok if treated and stable

**Investigator’s choice of chemotherapy**
- capecitabine, eribulin, gemcitabine, or vinorelbine

### Sequential Primary Endpoints
- PFS (by CBA; \(n=257\); \(HR=0.67\); \(\alpha=0.05\); power=90%)
- OS (\(n=385\); \(HR=0.75\); \(\alpha=0.05\); power=80%)

### Secondary Endpoints
- PFS (Investigator assessed)
- Objective response rate (by CBA)
- Clinical benefit rate (CBR), duration of response (DoR)
- Safety profile, antidrug antibody
- Effect of CD16A, CD32A, and CD32B on margetuximab efficacy

### Tertiary/Exploratory Endpoints
- Margetuximab (15 mg/kg Q3W) + chemotherapy in 3-week cycles
- Trastuzumab (8 mg/kg loading → 6 mg/kg Q3W) + chemotherapy in 3-week cycles

**1:1 Randomization (\(N=536\))**

**Arm 1**
- Margetuximab (15 mg/kg Q3W) + chemotherapy in 3-week cycles

**Arm 2**
- Trastuzumab (8 mg/kg loading → 6 mg/kg Q3W) + chemotherapy in 3-week cycles

**Stratification:**
- Chemotherapy choice
- Prior therapies (\(\leq 2\) vs >2)
- Metastatic sites (\(\leq 2\) vs >2)

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HR=hazard ratio; CBA=central blinded analysis.
### ITT Population: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th><strong>Margetuximab + Chemotherapy (n=266)</strong></th>
<th><strong>Trastuzumab + Chemotherapy (n=270)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age</td>
<td>55</td>
<td>56</td>
</tr>
<tr>
<td>Female sex</td>
<td>266 (100%)</td>
<td>267 (98.9%)</td>
</tr>
<tr>
<td>Europe</td>
<td>152 (57%)</td>
<td>138 (51%)</td>
</tr>
<tr>
<td>North America</td>
<td>85 (32%)</td>
<td>102 (38%)</td>
</tr>
<tr>
<td>Other region</td>
<td>29 (11%)</td>
<td>30 (11%)</td>
</tr>
<tr>
<td><strong>Disease Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECOG PS 0</td>
<td>149 (56%)</td>
<td>161 (60%)</td>
</tr>
<tr>
<td>ECOG PS 1</td>
<td>117 (44%)</td>
<td>109 (40%)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>260 (98%)</td>
<td>264 (98%)</td>
</tr>
<tr>
<td>Locally advanced, unresectable</td>
<td>6 (2%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>Measurable disease by CBA</td>
<td>262 (99%)</td>
<td>262 (97%)</td>
</tr>
<tr>
<td>≤2 metastatic sites</td>
<td>138 (52%)</td>
<td>144 (53%)</td>
</tr>
<tr>
<td>&gt;2 metastatic sites</td>
<td>128 (48%)</td>
<td>126 (47%)</td>
</tr>
<tr>
<td>Hormone receptor positive</td>
<td>164 (62%)</td>
<td>170 (63%)</td>
</tr>
<tr>
<td>Hormone receptor negative</td>
<td>102 (38%)</td>
<td>98 (36%)</td>
</tr>
<tr>
<td><strong>Backbone chemotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capecitabine</td>
<td>71 (27%)</td>
<td>72 (27%)</td>
</tr>
<tr>
<td>Eribulin</td>
<td>66 (25%)</td>
<td>70 (26%)</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>33 (12%)</td>
<td>33 (12%)</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>96 (36%)</td>
<td>95 (35%)</td>
</tr>
</tbody>
</table>

ITT population (all randomized patients): N=536.
ECOG=Eastern Cooperative Oncology Group; hormone receptor positive=ER+ and/or PgR+; hormone receptor negative=ER- and PgR-; ITT=intention to treat; PS=performance status.

*Treatment arms overall balanced*
### ITT Population: Prior Cancer Therapy

<table>
<thead>
<tr>
<th>Setting of prior therapy</th>
<th>Margetuximab + Chemotherapy (n=266)</th>
<th>Trastuzumab + Chemotherapy (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant and/or neoadjuvant</td>
<td>158 (59%)</td>
<td>145 (54%)</td>
</tr>
<tr>
<td>Metastatic only</td>
<td>108 (41%)</td>
<td>125 (46%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior metastatic lines of therapy</th>
<th>Margetuximab (n=266)</th>
<th>Trastuzumab (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>175 (66%)</td>
<td>180 (67%)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>91 (34%)</td>
<td>90 (33%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior anti-HER2 therapy</th>
<th>Margetuximab (n=266)</th>
<th>Trastuzumab (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>266 (100%)</td>
<td>270 (100%)</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>266 (100%)</td>
<td>269 (100%)</td>
</tr>
<tr>
<td>T-DM1</td>
<td>242 (91%)</td>
<td>247 (92%)</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>41 (15%)</td>
<td>39 (14%)</td>
</tr>
<tr>
<td>Other HER2</td>
<td>6 (2%)</td>
<td>6 (2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior chemotherapy</th>
<th>Margetuximab (n=266)</th>
<th>Trastuzumab (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taxane</td>
<td>252 (95%)</td>
<td>249 (92%)</td>
</tr>
<tr>
<td>Anthracycline</td>
<td>118 (44%)</td>
<td>110 (41%)</td>
</tr>
<tr>
<td>Platinum</td>
<td>34 (13%)</td>
<td>40 (15%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior endocrine therapy</th>
<th>Margetuximab (n=266)</th>
<th>Trastuzumab (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>126 (47%)</td>
<td>133 (49%)</td>
<td></td>
</tr>
</tbody>
</table>

**Treatment arms overall balanced**
PFS Analysis in ITT Population

**24% Risk Reduction of Disease Progression**
Central Blinded Analysis (Primary Endpoint)

- **Margetuximab + Chemotherapy**
  - (n=266)
  - # of events: 130
  - Median PFS: 5.8 months (95% CI: 5.06–6.67)
- **Trastuzumab + Chemotherapy**
  - (n=270)
  - # of events: 135
  - Median PFS: 4.9 months (95% CI: 4.17–5.59)

HR by stratified Cox model, **0.70**
(95% CI, 0.59–0.98)
Stratified log-rank **P=0.033**

**30% Risk Reduction of Disease Progression**
Investigator Assessed (Secondary Endpoint)

- **Margetuximab + Chemotherapy**
  - (n=266)
  - # of events: 160
  - Median PFS: 5.6 months (95% CI: 5.06–6.67)
- **Trastuzumab + Chemotherapy**
  - (n=270)
  - # of events: 177
  - Median PFS: 4.2 months (95% CI: 3.98–5.39)

HR by stratified Cox model, **0.76**
(95% CI, 0.59–0.98)
Stratified log-rank **P=0.033**

- PFS analysis was triggered by last randomization on October 10, 2018, after 265 PFS events occurred

ITT population: N=536. CI=confidence interval.
# PFS Subgroup Analyses

<table>
<thead>
<tr>
<th></th>
<th>Median PFS (95% CI), Months</th>
<th>HR by Unstratified Cox Model</th>
<th>95% CI</th>
<th>Unstratified Log-Rank P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, n=536</td>
<td>5.8 (5.52–6.97)</td>
<td>0.78</td>
<td>(0.61–0.99)</td>
<td>0.044</td>
</tr>
<tr>
<td>Capecitabine, n=143</td>
<td>8.3 (5.55–11.50)</td>
<td>0.77</td>
<td>(0.47–1.26)</td>
<td>0.302</td>
</tr>
<tr>
<td>Eribulin, n=136</td>
<td>6.0 (3.81–8.05)</td>
<td>0.66</td>
<td>(0.42–1.05)</td>
<td>0.080</td>
</tr>
<tr>
<td>Gemcitabine, n=66</td>
<td>5.4 (4.07–11.01)</td>
<td>0.58</td>
<td>(0.29–1.18)</td>
<td>0.128</td>
</tr>
<tr>
<td>Vinorelbine, n=191</td>
<td>5.6 (4.24–6.97)</td>
<td>0.90</td>
<td>(0.60–1.35)</td>
<td>0.606</td>
</tr>
<tr>
<td>&gt;2 metastatic sites, n=254</td>
<td>6.3 (5.42, 8.08)</td>
<td>0.63</td>
<td>(0.44–0.89)</td>
<td>0.009</td>
</tr>
<tr>
<td>≤2 metastatic sites, n=282</td>
<td>5.7 (4.47, 6.97)</td>
<td>0.94</td>
<td>(0.67–1.31)</td>
<td>0.702</td>
</tr>
<tr>
<td>Hormone Receptor-, n=200</td>
<td>5.8 (4.80, 7.23)</td>
<td>0.58</td>
<td>(0.39–0.86)</td>
<td>0.007</td>
</tr>
<tr>
<td>Hormone Receptor+, n=334</td>
<td>5.7 (5.52, 8.18)</td>
<td>0.88</td>
<td>(0.64–1.19)</td>
<td>0.393</td>
</tr>
<tr>
<td>HER2 IHC 3+, n=291</td>
<td>6.9 (5.55, 8.31)</td>
<td>0.64</td>
<td>(0.46–0.90)</td>
<td>0.011</td>
</tr>
<tr>
<td>HER2 ISH amplified, n=245</td>
<td>5.5 (4.01, 6.60)</td>
<td>1.01</td>
<td>(0.71–1.42)</td>
<td>0.972</td>
</tr>
<tr>
<td>Age &gt;60 years, n=170</td>
<td>6.9 (5.52, 10.51)</td>
<td>0.58</td>
<td>(0.36–0.92)</td>
<td>0.020</td>
</tr>
<tr>
<td>Age ≤60 years, n=366</td>
<td>5.6 (4.24, 6.97)</td>
<td>0.87</td>
<td>(0.66–1.16)</td>
<td>0.337</td>
</tr>
<tr>
<td>Prior (neo)adjuvant Tx: yes, n=303</td>
<td>6.3 (5.55–8.05)</td>
<td>0.67</td>
<td>(0.48–0.93)</td>
<td>0.014</td>
</tr>
<tr>
<td>Prior (neo)adjuvant Tx: no, n=233</td>
<td>5.6 (3.71–6.97)</td>
<td>0.99</td>
<td>(0.68–1.42)</td>
<td>0.935</td>
</tr>
</tbody>
</table>

Hormone receptor positive=ER+ and/or PgR+; hormone receptor negative=ER- and PgR-; IHC=immunohistochemistry; ISH=in situ hybridization; Tx=treatment.
Planned* Exploratory PFS Analyses by FcγR Genotypes (CBA)

*Margetuximab benefit appears to be increased in low-affinity CD16A-158F allele carriers

<table>
<thead>
<tr>
<th></th>
<th>Median PFS (95% CI), Months</th>
<th>HR by Unstratified Cox Model</th>
<th>95% CI</th>
<th>Unstratified Log-Rank P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Margetuximab + Chemotherapy</td>
<td>Trastuzumab + Chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>5.8 (5.52–6.97)</td>
<td>4.9 (4.17–5.59)</td>
<td>0.78</td>
<td>(0.61–0.99)</td>
</tr>
<tr>
<td><strong>Activating function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD16A/F carrier (FV or FF), n=437</td>
<td>6.9 (5.55–8.15)</td>
<td>5.1 (4.14–5.59)</td>
<td>0.68</td>
<td>(0.52–0.90)</td>
</tr>
<tr>
<td>CD16A/FF, n=192</td>
<td>8.2 (5.52–10.51)</td>
<td>5.6 (4.50–8.31)</td>
<td>0.69</td>
<td>(0.46–1.05)</td>
</tr>
<tr>
<td>CD16A/FV, n=245</td>
<td>6.3 (5.52–7.23)</td>
<td>4.3 (4.01–5.59)</td>
<td>0.71</td>
<td>(0.50–1.01)</td>
</tr>
<tr>
<td>CD16A/VV, n=69</td>
<td>4.8 (2.46–5.65)</td>
<td>5.6 (2.86–11.04)</td>
<td>1.78</td>
<td>(0.87–3.62)</td>
</tr>
<tr>
<td><strong>Inhibitory function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD32A/RR, n=122</td>
<td>5.7 (4.80–10.55)</td>
<td>5.5 (2.76–8.21)</td>
<td>0.69</td>
<td>(0.41–1.17)</td>
</tr>
<tr>
<td>CD32A/RH, n=247</td>
<td>6.9 (5.55–8.15)</td>
<td>5.6 (4.17–4.67)</td>
<td>0.74</td>
<td>(0.52–1.06)</td>
</tr>
<tr>
<td>CD32A/HH, n=137</td>
<td>5.6 (3.29–8.28)</td>
<td>4.1 (2.79–5.59)</td>
<td>0.80</td>
<td>(0.49–1.30)</td>
</tr>
<tr>
<td>CD32B/II†, n=380</td>
<td>5.8 (5.55–7.66)</td>
<td>5.5 (4.17–5.65)</td>
<td>0.85</td>
<td>(0.64–1.13)</td>
</tr>
<tr>
<td>CD32B/IT†, n=117</td>
<td>6.0 (4.14–NA)</td>
<td>5.5 (2.79–7.16)</td>
<td>0.63</td>
<td>(0.36–1.10)</td>
</tr>
</tbody>
</table>

*Non-alpha allocating, exploratory analysis.
†CD32B/TT not included on forest plot because n=9 is too small (5 on margetuximab, 4 on trastuzumab) to make analysis meaningful.
Planned Exploratory PFS Analysis by CD16A Genotype, by CBA
506 patients genotyped (94%)

FF or FV, n=437 of 506 (86%)

<table>
<thead>
<tr>
<th></th>
<th>Margetuximab + Chemotherapy (n=221)</th>
<th>Trastuzumab + Chemotherapy (n=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of events</td>
<td>103</td>
<td>112</td>
</tr>
<tr>
<td>Median PFS (95% CI)</td>
<td>6.9 months (5.55–8.15)</td>
<td>5.1 months (4.14–5.59)</td>
</tr>
</tbody>
</table>
| HR by unstratified Cox model | 0.68 (95% CI, 0.52–0.90) | Unstratified log-rank *P=0.005*

VV, n=69 of 506 (14%)

<table>
<thead>
<tr>
<th></th>
<th>Margetuximab + Chemotherapy (n=37)</th>
<th>Trastuzumab + Chemotherapy (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of events</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>Median PFS (95% CI)</td>
<td>4.8 months (2.46–5.65)</td>
<td>5.6 months (2.86–11.04)</td>
</tr>
</tbody>
</table>
| HR by unstratified Cox model | 1.78 (95% CI, 0.87–3.62) | Unstratified log-rank *P=0.110*
Planned Exploratory PFS Analysis by CD16A Genotype, by CBA
506 patients genotyped (94%)

FF, n=192 of 506 (38%)

- Margetuximab + Chemotherapy (n=102)
  - # of events: 48
  - Median PFS (95% CI): 8.2 months (5.52–10.51)
- Trastuzumab + Chemotherapy (n=90)
  - # of events: 43
  - Median PFS (95% CI): 5.6 months (4.50–8.31)
  - HR by unstratified Cox model: 0.69 (95% CI, 0.46–1.05)
  - Unstratified log-rank P = 0.080

FV, n=245 of 506 (48%)

- Margetuximab + Chemotherapy (n=119)
  - # of events: 55
  - Median PFS (95% CI): 6.3 months (5.52–7.23)
- Trastuzumab + Chemotherapy (n=126)
  - # of events: 69
  - Median PFS (95% CI): 4.3 months (4.01–5.59)
  - HR by unstratified Cox model: 0.71 (95% CI, 0.50–1.01)
  - Unstratified log-rank P = 0.055
October 2018 Interim OS* for ITT vs CD16A-158F Carriers

158 (41%) of 385 events needed for final OS analysis

ITT population, n=536

<table>
<thead>
<tr>
<th></th>
<th>Margetuximab + Chemotherapy (n=266)</th>
<th>Trastuzumab + Chemotherapy (n=270)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of events</td>
<td>78</td>
<td>80</td>
</tr>
<tr>
<td>Median OS (95% CI)</td>
<td>18.9 months (16.16–25.07)</td>
<td>17.2 months (15.80–33.31)</td>
</tr>
<tr>
<td>HR by stratified Cox model</td>
<td>0.95 (95% CI, 0.69–1.31)</td>
<td></td>
</tr>
</tbody>
</table>

CD16A/FF or FV, n=437 of 506 (86%)

<table>
<thead>
<tr>
<th></th>
<th>Margetuximab + Chemotherapy (n=221)</th>
<th>Trastuzumab + Chemotherapy (n=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of events</td>
<td>59</td>
<td>65</td>
</tr>
<tr>
<td>Median OS (95% CI)</td>
<td>23.6 months (16.56–NA)</td>
<td>16.9 months (15.41–20.53)</td>
</tr>
<tr>
<td>HR by unstratified Cox model</td>
<td>0.82 (95% CI, 0.58–1.17)</td>
<td></td>
</tr>
</tbody>
</table>

*First interim overall OS analysis at time of PFS analysis (Oct 10, 2018) was immature with 41% of 385 deaths needed for final OS analysis; stopping boundary was not crossed.

Second interim OS analysis will occur after 270 deaths. Final OS analysis will occur after 385 deaths. NA=not achieved.
## Overall Response and Clinical Benefit Rates Complement PFS

<table>
<thead>
<tr>
<th>Objective Response Rate</th>
<th>Margetuximab + Chemotherapy (n=262)</th>
<th>Trastuzumab + Chemotherapy (n=262)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CR+PR), n (%) [95% CI]</td>
<td>58 (22.1%) [17.3–27.7]</td>
<td>42 (16.0%) [11.8–21.0]</td>
<td>0.060*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Benefit Rate</th>
<th>Margetuximab + Chemotherapy (n=262)</th>
<th>Trastuzumab + Chemotherapy (n=262)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CR+PR+SD&gt;6 months), n (%) [95% CI]</td>
<td>96 (36.6%) [30.8–42.8]</td>
<td>65 (24.8%) [19.7–30.5]</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best Overall Response, n (%)</th>
<th>Margetuximab + Chemotherapy (n=262)</th>
<th>Trastuzumab + Chemotherapy (n=262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>7 (2.7%)</td>
<td>4 (1.5%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>51 (19.5%)</td>
<td>38 (14.5%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>149 (56.9%)</td>
<td>147 (56.1%)</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>35 (13.4%)</td>
<td>46 (17.6%)</td>
</tr>
<tr>
<td>Not Evaluable/Not Available</td>
<td>20 (7.6%)</td>
<td>27 (10.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of Response (CR, PR), median months (95% CI)</th>
<th>Margetuximab + Chemotherapy (n=262)</th>
<th>Trastuzumab + Chemotherapy (n=262)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1 (4.11–9.13)</td>
<td>6.0 (4.01–6.93)</td>
<td>0.541†</td>
<td></td>
</tr>
</tbody>
</table>

Response evaluable population (randomized patients with baseline measurable disease): N=524.

*Stratified Mantel-Haenszel test P value (2-sided). †Unstratified log-rank P value (2-sided).
## Summary of Adverse Events (AEs)

### Similar overall safety profiles

<table>
<thead>
<tr>
<th></th>
<th>Margetuximab + Chemotherapy (n=264)</th>
<th>Trastuzumab + Chemotherapy (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any grade AE, n (%)</strong></td>
<td>258 (97.7)</td>
<td>255 (96.2)</td>
</tr>
<tr>
<td><strong>Grade ≥3 AE, n (%)</strong></td>
<td>138 (52.3)</td>
<td>128 (48.3)</td>
</tr>
<tr>
<td><strong>SAE, n (%)</strong></td>
<td>39 (14.8)</td>
<td>46 (17.4)</td>
</tr>
<tr>
<td><strong>AE leading to treatment discontinuation, n (%)</strong></td>
<td>8 (3.0)</td>
<td>7 (2.6)</td>
</tr>
<tr>
<td><em><em>AEs resulting in death,</em> n (%)</em>*</td>
<td>2 (0.8)†</td>
<td>2 (0.8)‡</td>
</tr>
</tbody>
</table>

Safety Population (randomized patients who received any study treatment): N=529.

*No AEs resulting in death were considered related to anti-HER2 study therapy.

†Pneumonia (n=1), pneumonia aspiration (n=1).

‡Pneumonia (n=1), acute kidney injury (n=1).

SAE=serious AE.
### AEs Regardless of Causality

<table>
<thead>
<tr>
<th>Most common AEs, n (%)</th>
<th>Margituximab + Chemotherapy (n=264)</th>
<th>Trastuzumab + Chemotherapy (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>103 (39.0)</td>
<td>92 (34.7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>81 (30.7)</td>
<td>84 (31.7)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>73 (27.7)</td>
<td>51 (19.2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>59 (22.3)</td>
<td>62 (23.4)</td>
</tr>
<tr>
<td>Anemia</td>
<td>48 (18.2)</td>
<td>55 (20.8)</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>32 (12.1)</td>
<td>35 (13.2)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>8 (3.0)</td>
<td>12 (4.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AEs of special interest, n (%)</th>
<th>Margituximab + Chemotherapy (n=264)</th>
<th>Trastuzumab + Chemotherapy (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion-related reaction (IRR)‡</td>
<td>34 (12.9)</td>
<td>10 (3.8)</td>
</tr>
<tr>
<td>Left ventricular dysfunction</td>
<td>6 (2.3)</td>
<td>7 (2.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discontinuation due to IRRs, n (%)</th>
<th>Margituximab + Chemotherapy (n=264)</th>
<th>Trastuzumab + Chemotherapy (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 (1.1)</td>
<td>0</td>
</tr>
</tbody>
</table>


*Incidence ≥20% in either treatment group.
†Incidence ≥5% in either treatment group.
‡All patients received prior trastuzumab. In pivotal trials of trastuzumab, IRRs occurred in 21% to 40% of patients (US package insert).
Conclusions

• Margetuximab is a novel Fc-engineered HER2 targeted antibody that stimulates mechanisms of both innate and adaptive immunity

• In patients with HER2+ MBC progressing after trastuzumab, pertuzumab, chemotherapy, and T-DM1:
  - Margetuximab plus chemotherapy improved PFS (CBA: HR=0.76, \( P=0.033 \); Inv: HR=0.70, \( P=0.001 \)), ORR, and CBR, compared with trastuzumab plus chemotherapy

• This is the first prospective analysis of CD16A genotype as predictor of efficacy from anti-HER2 therapy
  - Enhanced PFS benefit with margetuximab in exploratory subpopulation of low-affinity CD16A-158F carriers (HR=0.68, \( P=0.005 \))

• Acceptable safety, similar to trastuzumab\(^1\)
  - Increased IRRs (primarily low grade) on margetuximab (13% vs 4%), managed with premedications

• Next milestone: second interim OS analysis, expected late 2019

Acknowledgments

• We gratefully acknowledge the patients who participated and their families

• We also thank SOPHIA investigators and the clinical study teams

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**Poland** – I Bartosz, B Bauer-Kosinska, D Garnarek-Lange, B Itrych, T Jankowski, Z Nowecki, T Pieńkowski, T Sarosiek, P Wysocki

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**Puerto Rico** – M Acosta


**United Kingdom** – P Bezecny, S Chan, A Dhadda, J Graham, C Harper-Wynne, M Hogg, C Intrivici, J Mansi, C Poole


HER2-positive Advanced Gastric Cancer: Current Treatments & Unmet Needs

Daniel Catenacci, M.D.
Associate Professor of Medicine, The University of Chicago
Gastroesophageal Adenocarcinoma (GEA) Standard Therapy

- Cytotoxics: 5FU, platinum, irinotecan, taxane, TAS102
  1L (FOLFOX) $\rightarrow$ 2L (FOLFIRI) $\rightarrow$ 3L (FOLTAX) $\rightarrow$ 4L (TAS102)

- Few targeted therapies incorporated into routine care:

<table>
<thead>
<tr>
<th>Marker</th>
<th>Incidence</th>
<th>Treatment</th>
<th>Therapy Line</th>
<th>Approval</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2++</td>
<td>~15%</td>
<td>Chemo + Trastuzumab</td>
<td>1L</td>
<td>2010</td>
<td>HR 0.65</td>
</tr>
<tr>
<td>none</td>
<td>100%</td>
<td>Chemo + Ramucirumab</td>
<td>2L</td>
<td>2014/15</td>
<td>HR 0.8</td>
</tr>
<tr>
<td>MSI-High</td>
<td>~2-3%</td>
<td>Pembrolizumab</td>
<td>2L+</td>
<td>2017</td>
<td>HR? (great)</td>
</tr>
<tr>
<td>PD-L1+ ≥1%</td>
<td>~50-60%</td>
<td>Pembrolizumab</td>
<td>3L+</td>
<td>2017*</td>
<td>HR? (marginal)</td>
</tr>
</tbody>
</table>
GEA vs Breast Cancer
Anti-HER2 Therapy Phase III

**1L**
- Breast: Chemo +/- tras
  - Slamon et al, NEJM 2001
- Breast: Chemo +/- lap
  - Guan et al, JCO 2013
- Breast: Chemo-T +/- pert
  - Baselga et al, NEJM 2012
  - CLEOPATRA
- Breast: Tax-T vs T-DM1 vs T-DM1/pert
  - Ellis et al, ASCO 2015 Abstr 507
  - MARIANNE
- Breast: Cape +/- lap
  - Geyer et al, NEJM 2006
- Gastric: Cis/FP +/- tras
  - Bang et al, Lancet 2010
  - TOGA
- Gastric: Cis/FP +/- lap
  - Hecht et al, JCO 2015
  - LOGiC
- Gastric: Cis/FP-T +/- pert
  - Tabernero et al, Lancet Oncol 2019
  - JACOB
- Gastric: Paclitax +/- lap
  - Satoh et al, JCO 2014
- Gastric: T-DM1 vs Taxane
  - Kang et al, GI ASCO 2016
  - GATSBY

**2L**
- Breast: Cape +/- lap/Cape
  - Verma et al, NEJM 2012
  - EMILIA
- Gastric: T-DM1 vs lap/Cape
  - Verma et al, NEJM 2012
  - EMILIA

**TOGA**
- Cis/FP +/- tras
  - Bang et al, Lancet 2010
Intra-patient Heterogeneity Over Time: Mechanisms of Therapy Resistance

HER2 Expression Over Time – Mass Spec

Stage IV GEJ

41 months

Primary Tumor

LIVER

Seppallan et al. Therapeutically induced changes in Her2, Her3, and Egfr protein expression for treatment guidance. JNCCN 2016
Overall Survival, CPS ≥1

Shitara et al. Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): a randomised, open-label, controlled, phase 3 trial. Lancet 2018
Rationale for Margetuximab + Anti-PD-1 Combination

Coordinate engagement of innate and adaptive immunity to mediate tumor regression

Innate Immunity

Cancer Cells

Macrophages

NK Cells

Enhanced ADCC

Tumor Destruction

Sensitize T Cells

Margetuximab

Adaptive Immunity

Exhausted T Cells

Counter T-cell Exhaustion

T Cells

Enhanced Adaptive T-cell-mediated Antitumor Immunity

Anti-PD-1 Antibody

June 4, 2019 – ASCO 2019 Conference Call: Margetuximab
# Fully Enrolled Phase 2 Study in Advanced HER2+ Gastric Carcinoma

**Update provided at ASCO GI Symposium 2019**

## Dose Escalation
(n=3-6 per margetuximab dose)

- **Margetuximab 10 – 15 mg/kg q3w**
- **+ pembrolizumab 200 mg q3w**

## Dose Expansion #1
(margetuximab 15 mg/kg q3W + pembrolizumab 200 mg q3W)

- Gastric and Gastroesophageal (n=60)

## Dose Expansion #2
(margetuximab 15 mg/kg q3W + pembrolizumab 200 mg q3W)

- Gastric (HER2 3+) (n=25)

---

### Clinical Supply Agreement

**Dose Escalation**

- Potential for chemotherapy-free regimen
- **Margetuximab and pembrolizumab** administered day 1 of every 3 week cycle

### Inclusion/Exclusion Criteria

- Received ≥ 1 prior line of chemotherapy treatment
- No prior immunotherapy

### Endpoints

- Primary: safety, tolerability and efficacy (as evaluated by objective response rate (ORR)) of combo
- Secondary: PFS, OS, immunogenicity

---

**Data presented at ASCO GI 2019**
Summary of Patient Demographics

Ninety-two patients have been treated at recommended Phase 2 dose

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Gastric Cancer (n=61)</th>
<th>GEJ Cancer (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>61.4 ± 13.6</td>
<td>57.9 ± 11.1</td>
</tr>
<tr>
<td>Median (Range)</td>
<td>62.0 (19.0, 85.0)</td>
<td>60.0 (35.0, 79.0)</td>
</tr>
<tr>
<td><strong>Gender [n(%)]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48 (78.7)</td>
<td>27 (87.1)</td>
</tr>
<tr>
<td>Female</td>
<td>13 (21.3)</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td><strong>Race [n (%)]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>48 (78.7)</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>White</td>
<td>9 (14.8)</td>
<td>25 (80.6)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.6)</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>3 (4.9)</td>
<td>0</td>
</tr>
<tr>
<td><strong>ECOG Status [n (%)]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (32.8)</td>
<td>13 (41.9)</td>
</tr>
<tr>
<td>1</td>
<td>41 (67.2)</td>
<td>18 (58.1)</td>
</tr>
</tbody>
</table>

* Data cut-off January 8, 2019
Treatment with Combo of Margetuximab and Pembrolizumab is Well Tolerated

- 64% of patients experienced treatment related AE (TRAE) irrespective of grade
- 18% of patients with TRAE ≥ Grade 3
- Most common TRAE: pruritis (16.8%)
- 8 Treatment-related serious adverse events: autoimmune hepatitis [2], hyponatremia [1], diabetic ketoacidosis [1], and pneumonitis [1], hypotension [1], confusional state [1], dizziness [1]
- 17 Adverse events of special interest reported: infusion related reaction [11], autoimmune hepatitis [2], pneumonitis [1], endocrinopathy [1], others [1], LVEF dysfunction [1]

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>All (N=95)*</th>
<th>≥Gr 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>61 (64.2)</td>
<td>17 (17.9)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>16 (16.8)</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14 (14.7)</td>
<td></td>
</tr>
<tr>
<td>Infusion related reaction</td>
<td>13 (13.7)</td>
<td>3 (3.2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (12.6)</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>7 (7.4)</td>
<td></td>
</tr>
<tr>
<td>Rash maculo-papular</td>
<td>5 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>5 (5.3)</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (4.2)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>4 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Lipase increased</td>
<td>4 (4.2)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>4 (4.2)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Chills</td>
<td>3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Amylase increased</td>
<td>3 (3.2)</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (2.1)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>2 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction decreased</td>
<td>2 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Blood alkaline phosphatase increased</td>
<td>2 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>2 (2.1)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2 (2.1)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>2 (2.1)</td>
<td>2 (2.1)</td>
</tr>
</tbody>
</table>

* Data cut-off January 8, 2019; Events occurring > 2% pts; includes all pts treated on study
Promising Activity in Gastric Cancer Population\(^{(a)}\)

### 33% ORR in HER2 3+ gastric cancer

<table>
<thead>
<tr>
<th>Gastric Cancer</th>
<th>N</th>
<th>ORR</th>
<th>DCR</th>
<th>mPFS</th>
<th>mOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 IHC 3+(^{(b)})</td>
<td>55</td>
<td>32.7% (18/55)</td>
<td>69.1% (38/55)</td>
<td>4.70 (2.66, 7.49)</td>
<td>NR (12.48, NR)</td>
</tr>
<tr>
<td>IHC3+/PD-L1+(^{(c)})</td>
<td>23</td>
<td>52.2% (12/23)</td>
<td>82.6% (19/23)</td>
<td>4.14 (2.60, 15.54)</td>
<td>NR (6.74, NR)</td>
</tr>
</tbody>
</table>

\(^{(a)}\) Data cut-off January 8, 2019. Includes patients who received at least one margetuximab and pembro dose in expansion phase, and had baseline measurable disease and at least one post-baseline disease assessment.

\(^{(b)}\) Immunohistochemistry (IHC) test gives score of 0 to 3+ that measures amount of HER2 receptor protein on surface of cells in cancer tissue sample. Score of 0 to 1+ is called “HER2 negative”, score of 2+ is called “borderline”, score of 3+ is called “HER2 positive.”

\(^{(c)}\) “PD-L1 Positive” reflects Combined Positive Score (per standard FDA approved assay) ≥1% (PD-L1 tested on archival tissue by IHC, clone 22C3 pharmDx).
Duration of Treatment in Overall Gastric Cancer Patients*

Presented at ASCO GI 2019

* Data cut-off January 8, 2019
Margetuximab + Anti-PD-1 Data in 2L Presents Opportunity to Advance to 1L

**HER2+ gastric cancer benchmarks**

<table>
<thead>
<tr>
<th></th>
<th>1st Line</th>
<th>2nd Line</th>
<th>3rd Line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent (Study)</strong></td>
<td>SOC</td>
<td>SOC</td>
<td>Failed</td>
</tr>
<tr>
<td>Trastuzumab + Chemo&lt;sup&gt;(a)&lt;/sup&gt; (TOGA)</td>
<td>Ramucirumab + Paclitaxel&lt;sup&gt;(b)&lt;/sup&gt; (RAINBOW)</td>
<td>Margetuximab+ Pembrolizumab&lt;sup&gt;(c)&lt;/sup&gt; (Ongoing Ph. 2)</td>
<td>Pembrolizumab&lt;sup&gt;(d)&lt;/sup&gt; (KEYNOTE-61)</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td>47%</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Median PFS</strong></td>
<td>6.7 mos.</td>
<td>4.4 mos.</td>
<td>4.7 mos.</td>
</tr>
<tr>
<td><strong>Median OS</strong></td>
<td>13.1 mos.</td>
<td>9.6 mos.</td>
<td>&lt;sup&gt;1&lt;/sup&gt; 16.8 mos. IHC 3+ GC; IHC3+/PD-L1+ (not reached)</td>
</tr>
<tr>
<td>≥ Grade 3 TRAEs</td>
<td>68%</td>
<td>Overall: N/A</td>
<td>&lt;sup&gt;2&lt;/sup&gt; 41% Neutropenia; 15% Hypertension; 12% Fatigue</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gastric/GEJ Patient Mix</strong></td>
<td>80/20%</td>
<td>80/20%</td>
<td>100%/0%&lt;sup&gt;3&lt;/sup&gt; (All IHC 3+ Gastric)</td>
</tr>
</tbody>
</table>

---

SOC = Standard of Care

<sup>(a)</sup> Data from Herceptin package insert; Bang, et al., Lancet, 2010;

<sup>(b)</sup> Data from Cyramza package insert; Wilkes, et al., Lancet Oncology, 2014;

<sup>(c)</sup> Data presented at ASCO GI 2019; Median OS for HER2 IHC 3+ gastric cancer as of April 2019.

<sup>(d)</sup> Data presented at ASCO 2018, Abstract 4062.

<sup>(e)</sup> Powell, et al., SABCS 2018, Poster P6-17-06, at 5.4 mg/kg dose in breast cancer patients (n=269), 5 cases of ILD reported, 2 x Gr1, 2 x Gr2, and 1 x Gr5; ILD is a well-characterized risk.
Margetuximab Program: Planned Development

Jon Wigginton, M.D.,
Chief Medical Officer, MacroGenics
Margetuximab: Hypothesized Mechanisms of Action

**Fab**
- Inhibit tumor cell signaling and proliferation

**Fc**
- Enhance *innate* immunity
  - NK cell activation and proliferation
  - NK cell expression of perforin and granzyme B
  - Enhance ADCC
- Enhance *adaptive* immunity
  - HER2-specific T-cell reactivity
  - Anti-HER2 antibody response

Tumor Regression
Capturing Full Potential of Margetuximab

Planned development strategy

1. Potential Approval
   - 3rd/4th Line mBC (w/chemo)

2. Follow-on Indications
   - 1st Line Gastric Cancer (w/checkpoints)
     - IND active, CFDA engaged
     - Ph. 2/3 MAHOGANY initiation in 2H2019

3. Future Opportunities
   - Neoadjuvant breast cancer
   - Other HER2+ populations

June 4, 2019 – ASCO 2019 Conference Call: Margetuximab
**MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer**

### Module A

<table>
<thead>
<tr>
<th>Margetuximab + Anti-PD-1 (Chemo-free Regimen)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HER2+ (IHC 3+) and PD-L1+ (≥1% CPS)</strong></td>
</tr>
<tr>
<td><em>Single Experimental Arm:</em> margetuximab + MGA012</td>
</tr>
<tr>
<td><em>(n=40)</em></td>
</tr>
<tr>
<td><strong>Go/No Go</strong></td>
</tr>
<tr>
<td><strong>ORR and Tolerability</strong></td>
</tr>
<tr>
<td><em>(add'l patients to support potential AA)</em></td>
</tr>
<tr>
<td><strong>Primary Endpoint:</strong> ORR</td>
</tr>
</tbody>
</table>

### Module B

<table>
<thead>
<tr>
<th>Margetuximab + Chemo + MacroGenics Checkpoint Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HER2+ (IHC 3+ or IHC 2+/FISH+) regardless of PD-L1 status</strong></td>
</tr>
<tr>
<td><em>(n=50 per arm)</em></td>
</tr>
<tr>
<td><strong>Standard of Care:</strong> trastuzumab + chemo</td>
</tr>
<tr>
<td><strong>Experimental Arm #1:</strong> margetuximab + chemo + MGA012</td>
</tr>
<tr>
<td><strong>Experimental Arm #2:</strong> margetuximab + chemo + MGD013</td>
</tr>
<tr>
<td><strong>Experimental Arm #3:</strong> margetuximab + chemo</td>
</tr>
<tr>
<td><strong>Futility Analysis</strong></td>
</tr>
<tr>
<td><strong>Assess Safety/efficacy of Experimental Arms #1 and #2</strong></td>
</tr>
<tr>
<td><em>(n=250 per arm)</em></td>
</tr>
<tr>
<td><strong>Standard of Care:</strong> Trastuzumab + chemo</td>
</tr>
<tr>
<td><strong>Experimental Arm:</strong> marge + chemo + CPI*</td>
</tr>
<tr>
<td><strong>Primary Endpoint:</strong> OS</td>
</tr>
<tr>
<td><strong>BLA</strong></td>
</tr>
</tbody>
</table>

* Pending chronic tox study (if regimen with MGD013 is selected).
### MGA012: Initial Activity Profile Similar to Approved Anti-PD-1 mAbs

**Global collaboration with Incyte; significant development effort across multiple studies**

| Function/ MoA | • Humanized, hinge-stabilized IgG4 mAb  
• Inhibits PD-1 |
|---------------|-------------------------------------------------|
| Status        | • Eleven monotherapy/combo studies ongoing  
• Initial monotherapy data projected in 2020*  
• Planned combination with margetuximab +/- chemo in Phase 2/3 MAHOGANY study in gastric cancer |
| Global Incyte Transaction | • $150M Upfront cash payment  
• Up to $750M in milestones ($15M received in 2018)  
• Tiered royalties of 15-24% on future MGA012 sales |
| MacroGenics’ Retained Rights | • Develop pipeline assets in combination with MGA012  
• Manufacture portion of global MGA012 supply |

* Ongoing studies in MSI-high endometrial cancer, Merkel cell carcinoma and anal cancer are potentially registration-directed.
MGD013: First Bispecific Checkpoint Molecule in Clinic

**Function/ MoA**
- Simultaneous and/or independent blockade of two checkpoint molecules
- Reactivation of exhausted T cells

**Targeted Indications**
- Patients with solid and liquid tumors:
  - Progressed on prior checkpoint inhibitor
  - Checkpoint-naïve

**Status**
- Ongoing Phase 1 dose expansion in nine tumor types
- Exploring correlative biomarkers (with Nanostring)
- Initiating Phase 2/3 MAHOGANY study with margetuximab and chemotherapy in gastric cancer

**MacroGenics’ Retained Rights**
- Global rights (excl. Greater China)
Rationale for MGD013: High LAG-3 Expression in Gastric Cancer

• LAG-3 positivity: 88% (30/34) observed across gastric cancer samples*

H&E and LAG-3 IHC profile for gastric cancer patient sample

* IHC performed using anti-LAG-3 mAb EPR43292(2); Positivity defined as detection of at least one LAG-3 positive Tumor Infiltrating Lymphocyte (TIL)

• cPR in 67 y.o. patient in MGD013 monotherapy Phase 1 study
  – Refractory to nivolumab
  – Complete resolution of target lesions
  – Treatment ongoing as of May 2019 for ~31 weeks
MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer

Seeks to establish chemotherapy-free regimen for treatment of HER2+/PD-L1+ patients in 1L setting

- Designed to establish meaningful clinical activity with favorable safety profile using single arm trial
- ≥Grade 3 AEs in 18% of patients treated with margetuximab/pembrolizumab
- Historical experience in patients treated with TOGA regimen: 68% ≥Grade 3 AEs
- Potential opportunity for accelerated approval in U.S. based on primary endpoint of ORR
- Planned initiation in 2H2019
MAHOGANY Phase 2/3 Study: Registration Path in 1L Gastric & GEJ Cancer

Integrates margetuximab and checkpoint inhibition in combination with standard chemotherapy

**Module B**

**Experimental Arm #3:** margetuximab + chemo + MGD013

**Experimental Arm #2:** margetuximab + chemo + MGA012

**Experimental Arm #1:** margetuximab + chemo

**Standard of Care:** trastuzumab + chemo

**Futility Analysis**

Assess Safety/efficacy of Experimental Arms #1 and #2

* Pending chronic tox study (if regimen with MGD013 is selected).

- Assess both **MGA012** (anti-PD-1) and **MGD013** (anti-PD-1 x LAG-3) based regimens
- Margetuximab+chemotherapy arm to help define contribution of components
- Primary endpoint: overall survival (OS); interim futility: ORR

**HER2+ (IHC 3+ or IHC 2+/FISH+) regardless of PD-L1 status**

**Primary Endpoint:** OS

**BLA**
Key Takeaways & Future Program Milestones

Scott Koenig, M.D., Ph.D.
President and Chief Executive Officer, MacroGenics
Margetuximab – Key Takeaways

• Margetuximab has shown ability to engage both innate and adaptive immunity

• SOPHIA Phase 3 demonstrates superiority to trastuzumab
  – Prolonged PFS in first sequential primary analysis
  – Consistent with putative mechanism of action, OS data is trending favorably at first interim analysis
  – Enhanced activity observed in CD16A F-carrier exploratory subpopulation
  – Comparable safety/tolerability profile with trastuzumab

• Seeking first approval in 3rd/4th line HER2-positive mBC

• Significant opportunity to expand commercial potential with additional indications
  – Phase 2/3 MAHOGANY trial in 1L gastric cancer
  – Neoadjuvant mBC study via investigator-sponsored trial (in discussion)
  – mBC bridging studies being planned in China (Zai Lab)
  – Checkpoint combinations align well with margetuximab’s mechanism of action
Margetuximab – Future Program Milestones

2H2019
- Initiate Phase 2/3 MAHOGANY first-line gastric study
- Conduct SOPHIA second interim OS analysis at 270 events
- Submit BLA in HER2-positive mBC

2020
- Potential U.S. approval in 3rd/4th line HER2-positive mBC
- Conduct SOPHIA final OS analysis at 385 events
- Submit application to EMA
Q&A Session

Scott Koenig, M.D., Ph.D.  President & Chief Executive Officer, MacroGenics
Jon Wigginton, M.D.  Chief Medical Officer, MacroGenics
Hope S. Rugo, M.D.  Clinical Professor of Medicine, UCSF Helen Diller Family Comprehensive Cancer Center
Daniel Catenacci, M.D.  Associate Professor of Medicine, The University of Chicago Medical Center
Thank You!

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