Belantamab Mafodotin (Belamaf) Accelerated Approval for Patients with Relapsed or Refractory Multiple Myeloma

July 14, 2020
GlaxoSmithKline
Oncologic Drug Advisory Committee
Belantamab Mafodotin (Belamaf)

Introduction

Axel Hoos, MD, PhD
Senior Vice President Oncology
GlaxoSmithKline
Belamaf Offers a Novel and Specific Mechanism of Action Targeting Myeloma

- First-in-class afucosylated anti-BCMA IgG1 antibody-drug conjugate (ADC)
- Multi-modal mechanism
  - Delivery of cytotoxic, MMAF
  - Immunogenic cell death (ICD)
  - Enhancing antibody-dependent cellular cytotoxicity (ADCC)
  - Inducing antibody-dependent cellular phagocytosis (ADCP)
Belamaf Provides Positive Benefit-Risk, Supporting Accelerated Approval

### Unmet Need
- Indicated population refractory to most effective classes
  - Anti-CD38 antibody, PI and IMiD
  - One approved option: Selinexor / dex
- Median OS 6-9 months\(^1\)
- Median DOR 4.4 months\(^2\)
- Need for novel MoA

### Efficacy
- Consistent and clinically meaningful responses
- Responses deep and durable\(^*\)
  - 31% ORR
  - DOR ≥ 9 months\(^\dagger\)
  - Estimated median OS 11.9 months

### Safety
- Manageable safety profile
- Mostly ocular AEs
  - Boxed warning in label
  - REMS with Elements to Assure Safe Use (ETASU)
- Disease related symptoms and QoL stable over time

\(1\) Gandhi, 2019; \(2\) Chari, 2019

\(*\) 9-month update, \(\dagger\) Worst-case sensitivity analysis
Comprehensive Characterization of Ocular Events

- DREAMM-2 collected various types of data
  - Patient symptoms
  - Objective eye examinations
  - Quality of life measures
  - Ongoing, long-term follow-up
  - Treatments available to correct ocular AEs
- Ocular event collection and grading
  - Keratopathy and Visual Acuity (KVA) scale and CTCAE
Ocular AEs Well Understood by Ophthalmologists and Can Be Monitored and Managed

- Ocular AEs often asymptomatic without meaningful change in visual acuity
  - No complete loss of vision
  - 3 patients discontinued due to ocular AE

Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU)

1. Education and mandatory ocular monitoring
2. Timely management and intervention
3. Restricted access and controlled administration
Proposed Indication for Accelerated Approval

- Belantamab Mafodotin is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor (PI), an immunomodulatory agent (IMiD)

- Recommended dose is 2.5 mg/kg once every 3 weeks
Breakthrough Therapy Designation (BTD) Granted Based on DREAMM-1 Data

DREAMM-1
Supportive (Phase I)
Enrolled heavily pretreated RRMM population
ORR 38%

DREAMM-2
Pivotal Study (Phase II)
Enrolled population consistent with BTD

- Patients with MM who were failed by ≥ 3 prior lines of therapy
  1. Anti-CD38 antibody
  2. Proteasome inhibitor (PI)
  3. Immunomodulatory agent (IMiD)
DREAMM-3: Randomized Controlled Study to Confirm Clinical Benefit of Belamaf in RRMM

- Includes heavily pretreated RRMM patients
- Enrollment ongoing

DREAMM-3

Confirmatory

Phase III
Randomized Controlled
Belamaf vs pom / dex

N = 320 Planned
Unmet Need in Patients with RRMM

Kenneth Anderson, MD
Professor of Medicine at Harvard Medical School
Director of the Lebow Institute for Myeloma Therapeutics
and Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
*Not compensated for time

Clinical Efficacy

Ira Gupta, MD
VP Medicine Development Leader Oncology
GlaxoSmithKline PLC

Overall Clinical Safety

Hesham A. Abdullah, MD, MSc, RAC
Senior VP, Head of Clinical Development, Oncology
GlaxoSmithKline PLC

Characterization of Corneal Safety and Monitoring

Kathryn Colby, MD, PhD
Louis Block Professor and Chair
Department of Ophthalmology & Visual Science, University of Chicago
*Compensated for time

REMS with ETASU

Hesham A. Abdullah, MD, MSc, RAC

Clinical Perspective

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Chief Medical Officer
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*Not compensated for time
Additional Experts

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Professor and Chair
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University of Maryland School of Medicine
*Compensated for time

Peter Voorhees, MD
Professor of Medicine
Member, Plasma Cell Disorders Division
Director of Medical Operations and Outreach Services
Department of Hematologic Oncology and Blood Disorders
Levine Cancer Institute, Atrium Health
*Not compensated for time
Unmet Need in Myeloma Refractory to IMiD, PI and Anti-CD38 Therapy

Kenneth Anderson, MD
Professor of Medicine at Harvard Medical School
Director Lebow Institute for Myeloma Therapeutics and Jerome Lipper MM Center
Dana-Farber Cancer Institute
Multiple Myeloma is Second Most Common Hematologic Malignancy

- > 32,000 new cases in US in 2020\(^1\)
- > 12,800 deaths in US in 2020\(^1\)
- Median overall survival 5-10 years in newly diagnosed patients\(^2\)

1. NCI SEER, 2020; 2. Kumar, 2017
## Treatment Options for Patients with Multiple Myeloma

<table>
<thead>
<tr>
<th>Proteasome Inhibitor (PI)</th>
<th>Immunomodulatory Agent (IMiD)</th>
<th>Anti-CD38 Monoclonal Antibody</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfilzomib</td>
<td>Pomalidomide</td>
<td>Daratumumab</td>
<td>Panobinostat</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Lenalidomide</td>
<td>Isatuximab</td>
<td>Elotuzumab</td>
</tr>
<tr>
<td>Ixazomib</td>
<td>Thalidomide</td>
<td></td>
<td>Selinexor / dex</td>
</tr>
</tbody>
</table>

- Selinexor / dexamethasone only approved therapy for triple-class-refractory myeloma (accelerated approval)
MAMMOTH: Patients Refractory to IMiD, PI and Anti-CD38 Have Short Survival < 1 Year

<table>
<thead>
<tr>
<th>Refractory Status</th>
<th>Median OS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not triple-refractory</td>
<td>11.2 (5.4, 17.1)</td>
</tr>
<tr>
<td>Triple- and quad-refractory</td>
<td>9.2 (7.1, 11.2)</td>
</tr>
<tr>
<td>Penta-refractory</td>
<td>5.6 (3.5, 7.8)</td>
</tr>
</tbody>
</table>

1. Gandhi, 2019
Selinexor / Dex Demonstrates Difficulty in Treating Triple-Class-Refractory MM

**STORM Part 2**

<table>
<thead>
<tr>
<th>ORR (%)</th>
<th>26.2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median DOR (95% CI)</td>
<td>4.4 (3.7, 10.8)</td>
</tr>
</tbody>
</table>

**Median OS (95% CI)**

- 8.6 (6.2, 11.3)

1. Chari, 2019; 2. FDA.gov
## Selinexor / Dex Combination Limited by Tolerability Issues

<table>
<thead>
<tr>
<th>Event</th>
<th>STORM Part 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAEs</td>
<td>60%</td>
</tr>
<tr>
<td>AE leading to dose interruption</td>
<td>73%</td>
</tr>
<tr>
<td>AE resulting in dose reduction</td>
<td>49%</td>
</tr>
<tr>
<td>AE leading to treatment discontinuation</td>
<td>27%</td>
</tr>
<tr>
<td>AE resulting in death</td>
<td>10%</td>
</tr>
</tbody>
</table>
Diminished Quality of Life for Patients with RRMM

- QoL deteriorates with each relapse and subsequent line of therapy\(^1\)
- Physical functioning may be compromised
  - Reduced ability to carry out work, chores and leisure activities\(^1\)
- QoL impacted by disease burden and treatment-related AEs\(^2\)
  - Some treatments limited by tolerability and high discontinuation
- Stabilization of quality of life important

Patients Need Effective and Tolerable Therapies to Improve Clinical Response

- One option once disease becomes refractory to PI, IMiD and anti-CD38
- Survival is short, 6-9 months\(^1\)
- Urgent need for additional therapies with novel MoA
- Clinically meaningful responses
  - Durable response
  - Associated clinical benefit

\(^1\) Gandhi, 2019
Belantamab Mafodotin (Belamaf) Clinical Efficacy Results

Ira Gupta, MD
VP Medicine Development Leader Oncology
GlaxoSmithKline PLC
Belamaf Clinical Program Supporting Accelerated Approval

- Consistent evidence of efficacy in heavily pre-treated patients
- Failed ≥ 4 prior anti-myeloma therapies

**DREAMM-1**
Supportive
Phase I
Open-Label, Dose Finding (0.03 – 4.6 mg/kg)
N = 79*

**DREAMM-2**
Pivotal
Phase II
Ongoing, Open-Label, Randomized, Two-Arm
N = 221

*73 with MM and 6 with lymphoma
Key inclusion criteria

- Confirmed diagnosis of multiple myeloma (IMWG*)
- ECOG 0-2
- ≥ 3 prior lines of anti-myeloma therapy
  - PI + IMiD-refractory
  - Failed anti-CD38
- Stratification based on number of prior therapies (> 4 and ≤ 4) and cytogenetic features [t(4;14), t(14;16), and 17p13del]

Belamaf 2.5 mg/kg Q3W
N = 97
Ocular sub-study (n = 17)

Belamaf 3.4 mg/kg Q3W
N = 99
Ocular sub-study (n = 13)

*Confirmation of MM based on International Myeloma Working Group criteria
DREAMM-2: Efficacy Endpoints

- **Primary endpoint**
  - Overall response rate (ORR) as assessed by an Independent Review Committee (IRC)

- **Secondary endpoints**
  - Duration of response (DoR)
  - Progression-free survival (PFS)
  - Overall survival (OS)

Secondary endpoints not multiplicity adjusted
**DREAMM-2: Patient Disposition**

- **Enrolled**
  - $N = 196^*$

- **Belamaf 2.5 mg/kg**
  - $N = 97$ (ITT)

- **Received Treatment**
  - $N = 95$

  - **Treatment Discontinued**
    - 73 patients
    - 59 due to progressive disease
    - 7 due to adverse event
    - 4 due to physician decision
    - 1 due to lack of efficacy
    - 1 due to lost to follow-up
    - 1 due to patient withdrawal

- **Ongoing**
  - $N = 60$

- 22 (23%) on treatment
- 38 (39%) in follow-up

*Note: $N=99$ patients in Belamaf 3.4 mg/kg group*
**DREAMM-2: Baseline Demographics Represent Patients with RRMM**

<table>
<thead>
<tr>
<th>Belamaf 2.5 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 97</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age; median years (range)</th>
<th>65 (39 - 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 75 years</td>
<td>13%</td>
</tr>
<tr>
<td>Male</td>
<td>53%</td>
</tr>
<tr>
<td>White</td>
<td>78%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>16%</td>
</tr>
<tr>
<td>United States</td>
<td>61%</td>
</tr>
</tbody>
</table>
**DREAMM-2: Heavily Pretreated Patients; Refractory to PI, IMiD and Failed Anti-CD38**

<table>
<thead>
<tr>
<th>Prior lines of therapy; median (range)</th>
<th>7 (3 - 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 4 prior lines</td>
<td>84%</td>
</tr>
<tr>
<td>Refractory to anti-CD38 antibody</td>
<td>100%</td>
</tr>
<tr>
<td>Refractory to proteasome inhibitor</td>
<td>100%</td>
</tr>
<tr>
<td>Refractory to immunomodulatory agent</td>
<td>100%</td>
</tr>
<tr>
<td>ECOG score ≥ 1</td>
<td>67%</td>
</tr>
<tr>
<td>ISS Stage II or III multiple myeloma</td>
<td>77%</td>
</tr>
<tr>
<td>High risk cytogenetics*</td>
<td>27%</td>
</tr>
</tbody>
</table>

*Includes t(4;14), t(14;16), and 17p13del
DREAMM-2: Primary Endpoint Demonstrates Clinically Meaningful Overall Response Rate

**Percent of Patients**

- PR: partial response
- VGPR: very good partial response
- CR: complete response
- sCR: stringent complete response

**ORR**

- 31% (20.8, 42.6)
- n=2
- n=1
- n=15
- n=12

Belamaf 2.5 mg/kg (N = 97)
**DREAMM-2: Duration of Response**

Not Reached at 6 Months

**Time (Months)**

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

**Mean DOR; months**

Not Reached

**Probability of Continuing Response**

78%

**Belamaf 2.5 mg/kg**
DREAMM-2: 72% Overall Survival Rate at 6 Months

Estimated Median OS; months (95% CI) 9.9 (8.9, NE)
6-month survival rate 72%

Number at Risk
Belamaf 2.5 mg/kg 97 91 81 76 69 63 50 40 19 8 1 0
Continued Clinically Meaningful Benefit Demonstrated with 9-Month Follow-Up

|                        | Belamaf 2.5 mg/kg |  
|------------------------|------------------|---
|                        | N = 97           | ---
| **Primary Analysis**   |                  |     |
| (6 months)             |                  |     |
| Median follow-up; months | 6.3             | 9.0 |
| ORR; patients (97.5% CI) | 31% (21, 43)       | 31% (21, 43) |
| Median DOR             | *Not reached*    | ≥ 9 months* |
| Median OS; months (95% CI) | 9.9 (8.9, no estimate) | 11.9 (9.4, 13.1) |

*Not reached at 9-month data cut, estimated median DOR based on worst case sensitivity analysis
Belamaf Provides Clinically Meaningful Response in Patients with RRMM

- Responses were deep and durable
  - Median DOR still not reached at 9 months*
  - Median OS estimated to be 11.9 months*
- Data from DREAMM-1 support findings from DREAMM-2

*Based on 9-month follow-up
Belantamab Mafodotin (Belamaf) Clinical Safety Results

Hesham A. Abdullah, MD, MSc, RAC
Senior Vice President
Head of Clinical Development Oncology
GlaxoSmithKline PLC
# DREAMM-2: Overall Safety Profile

<table>
<thead>
<tr>
<th>Event</th>
<th>Belamaf 2.5 mg/kg (N = 95)</th>
<th>Belamaf 3.4 mg/kg (N = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>98%</td>
<td>100%</td>
</tr>
<tr>
<td>AEs Grade 3 or 4</td>
<td>82%</td>
<td>82%</td>
</tr>
<tr>
<td>SAEs</td>
<td>40%</td>
<td>47%</td>
</tr>
<tr>
<td>AEs leading to death</td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>AEs leading to dose reduction</td>
<td>29%</td>
<td>41%</td>
</tr>
<tr>
<td>AEs leading to dose interruption</td>
<td>54%</td>
<td>62%</td>
</tr>
<tr>
<td>AEs leading to treatment discontinuation</td>
<td>8%</td>
<td>10%</td>
</tr>
</tbody>
</table>
# DREAMM-2: Belamaf Exposure

<table>
<thead>
<tr>
<th></th>
<th>Belamaf 2.5 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 95</td>
</tr>
<tr>
<td><strong>Number of cycles; median (range)</strong></td>
<td>3.0 (1 – 11)</td>
</tr>
<tr>
<td><strong>Dose intensity; median (mg/kg/3 weeks)</strong></td>
<td>2.5 (0.7 – 2.6)</td>
</tr>
<tr>
<td><strong>Time on treatment; median weeks (range)</strong></td>
<td>9.1 (2 – 40)</td>
</tr>
</tbody>
</table>
DREAMM-2: Most Common AEs by CTCAE Grade for Belamaf 2.5 mg/kg

Any grade in ≥ 10% of patients

Keratopathy
Thrombocytopenia*
Anemia
Nausea
Pyrexia
Vision blurred*
Infusion related reaction*
AST increased
Fatigue*
Dry eye*
Hypercalcemia
Lymphocyte count decreased
Neutropenia*
Constipation
Diarrhea
Decreased appetite
Upper respiratory tract infection*

Any Grade
Grade 1-2
Grade 3-4

* AEs based on pooled terms

Any grade in ≥ 10% of patients
# DREAMM-2: Dose Delays and Reductions Allowed Patients to Remain on Treatment (≥ 3%)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Dose Delay</th>
<th>Dose Reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any patient</td>
<td>54%</td>
<td>29%</td>
</tr>
<tr>
<td>Keratopathy</td>
<td>47%‡</td>
<td>20%</td>
</tr>
<tr>
<td>Vision blurred*</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Pneumonia*</td>
<td>3%</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia*</td>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>Dry eye*</td>
<td>3%</td>
<td>0</td>
</tr>
</tbody>
</table>

‡69% of patients re-started treatment

* AEs based on pooled terms
DREAMM-2: AEs Leading to Discontinuation in ≥ 2 Patients for Belamaf 2.5 mg/kg

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Belamaf 2.5 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE leading to treatment discontinuation</td>
<td>8%</td>
</tr>
<tr>
<td>Keratopathy</td>
<td>2%</td>
</tr>
</tbody>
</table>
Overall Safety Conclusions

- Belantamab mafodotin has a manageable safety profile
- Low frequency of AEs, other than corneal events
- Few patients discontinued
  - Attesting to tolerability and utility of dose modifications
- No new safety signals based on 9-month update
- Proposed label and REMS with ETASU for corneal events
Characterization of Corneal Safety and Monitoring

Kathryn Colby, MD, PhD
Louis Block Professor and Chair
Department of Ophthalmology & Visual Science
University of Chicago
President, Cornea Society
Ocular Events with Belamaf

- Ophthalmologists routinely identify and manage ocular events
  - Common and manageable findings
  - Keratopathy from medications not uncommon (eg amiodarone and Ara-C)
- Ophthalmologist – hematologist collaboration important
  - Ophthalmologist identify findings in timely fashion
  - Hematologists/oncologists treat myeloma with appropriate dosing
Anatomy of the Eye: AEs Experienced on Superficial Layer of Cornea
“The epithelium as the outer barrier is constantly self-renewing and has the highest regenerative capacity, as epithelial cells are replenished every 7–10 days.”

Corneal Epithelial Exam Findings With Belamaf

Slit lamp microscopic image of microcyst-like epithelial changes (MECs)\(^1\)

Confocal microscopy images of the corneal plane

Normal corneal epithelial cells

Deposits in epithelium

1. Image from Shaohui Liu, MD, PhD
Progression and Resolution of MECs in Epithelium

Microcyst-like deposits larger for representation, not to scale. Schematic example
DREAMM-2: Comprehensive Assessments of Ocular Events

Corneal Data Collection

- AEs as Reported by Patients
  - Collected and graded by investigator using CTCAE
  - Subjective symptoms of blurred vision, dry eye, etc.

- Corneal Exam Findings*
  - Graded by investigator based on pre-defined criteria KVA Scale
  - Corneal findings coded under preferred term of keratopathy graded per CTCAE

- Best Corrective Visual Acuity
  - Objective findings informed dose modifications

*Patients had to undergo routine ophthalmologic exams prior to every dose
Grading of Exam Findings: Rigorous Method Used to Determine Dose Modifications

- KVA scale
  - Protocol specified criteria
  - Grades events based on
    - Objective findings in cornea
    - Changes in visual acuity
    - Used to determine dose modifications

- CTCAE criteria
  - Standard for AE reporting
  - Grades events based on severity of subjective patient experience
### Objective Corneal Exam Findings by Maximum Grade

<table>
<thead>
<tr>
<th>Keratopathy</th>
<th>Evaluation of keratopathy</th>
<th>KVA N = 95 N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Mild, superficial</td>
<td>8 (12%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Moderate, superficial with patchy MECs</td>
<td>17 (25%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Severe, superficial with diffuse MECs</td>
<td>42 (62%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Corneal epithelial defect</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

- Any grade keratopathy: 68 (72%)

Data based on 9-month update; MECs = microcyst-like epithelial changes
Recovery of Keratopathy

<table>
<thead>
<tr>
<th>Patients with Keratopathy (Grade ≥ 2)</th>
<th>N = 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered from first occurrence (%)</td>
<td>75%</td>
</tr>
<tr>
<td>Recovered as of last follow up (%)</td>
<td>29 (48%)*</td>
</tr>
<tr>
<td>Median time to resolution, days (range)</td>
<td>78 (11, 232)</td>
</tr>
<tr>
<td>Still on treatment or in follow-up ‡</td>
<td>16 (27%)</td>
</tr>
<tr>
<td>Lost to follow-up/death**</td>
<td>15 (25%)</td>
</tr>
</tbody>
</table>

- 77% of patients Grade 3-4 recovered to Grade 2 or better as of last follow-up

Data based on 9-month update
*Resolution defined as Grade 1 or better. 17% were resolving as of last follow up
**Median time from last dose to last exam = 23 days
‡ Still on treatment (n=13); In follow-up (n=3)
Objective Finding of Keratopathy Frequently Reported, Few Patients Discontinued

Data based on 9-month update

3 / 95 (3%) patients discontinued due to corneal events
Keratopathy Does Not Always Lead to Patient Symptoms or Meaningful Changes in Vision

Data based on 9-month update

*Visual acuity change = 20/50 or worse in better seeing eye
**Symptomatic = AE by PT or ≥ 2 lines visual acuity change

83% of patients without meaningful visual acuity change*
Examination of Visual Acuity

20/20  20/50  20/200
Limited Number of Patients Experienced Clinically Meaningful Reductions in Visual Acuity

<table>
<thead>
<tr>
<th>Belamaf 2.5 mg/kg N = 95</th>
<th>Bilateral BCVA 20/50 or Worse</th>
<th>Bilateral BCVA 20/200 or Worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>16 (17%)</td>
<td>1 (&lt; 1%)</td>
</tr>
<tr>
<td>Time to onset; median days (range)</td>
<td>64.5 (20-190)</td>
<td>21.0 (21-21)</td>
</tr>
<tr>
<td>Time to resolution; median days (range)</td>
<td>22 (7-64)</td>
<td>22 (22-22)</td>
</tr>
<tr>
<td>Resolved as of last assessment</td>
<td>15 (94%)</td>
<td>1 (100%)</td>
</tr>
</tbody>
</table>

- No patients had complete vision loss

Data based on 9-month update; bilateral BCVA assessed vision changes in better seeing eye
Functional Impact of Reduced Vision Varies by Patient

- Temporary impact on activities of daily living
- National Eye Institute Visual Function Questionnaire (NEI-VFQ 25)
  - Assessment of patient reported outcomes related to visual function
NEI-VFQ-25: Worst Post-Baseline Change in Driving and Reading

Driving (N = 70)

- 53% No / Little Difficulty
- 10% Moderate Difficulty
- 1% Extreme Difficulty
- 16 (23%) Stopped Due to Eyesight

- 7/16 returned to driving

Reading (N = 83)

- 42% No / Little Difficulty
- 25% Moderate Difficulty
- 13% Extreme Difficulty
- 8 (10%) Stopped Due to Eyesight

- 7/8 returned to reading

Data based on 9-month update; *Patient remained with extreme difficulty driving throughout study; **9/10 patients improved
DREAMM-2: Global Health Status and QoL Stable Overtime

![Graph showing Global Health Status / QoL (EORTC QLQ-C30)](chart)

**Baseline Change**

- Improvement
- Worsening

**Patients at Risk**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Belamaf 2.5 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
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<tr>
<td>13</td>
<td>29</td>
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<tr>
<td>19</td>
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<td>37</td>
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<tr>
<td>43</td>
<td>13</td>
</tr>
<tr>
<td>49</td>
<td>4</td>
</tr>
</tbody>
</table>

Data based on 9-month update
Benefits Outweigh Risk from Ophthalmologic Perspective

- Keratopathy – identifiable exam finding
  - Manageable with dose modifications
  - Frequent but tolerable (3% discontinuation)
  - Exam findings improve with time
- Visual acuity changes can result from keratopathy
  - Less frequent and temporary
  - 94% of changes recovered
- Ophthalmologist and oncologist work together to treat patients
Proposed Labeling and Risk Evaluation and Mitigation Strategy (REMS)

Hesham A. Abdullah, MD, MSc, RAC
Senior Vice President
Head of Clinical Development Oncology
GlaxoSmithKline PLC
Boxed Warning in Proposed Belamaf Label

- Ophthalmic exams prior to each dose, and worsening of symptoms
- Use of dose interruptions and reductions
REMS with ETASU Goal to Support Consistent Monitoring and Management

1. Education and monitoring
   - Ocular exam before each dose by eye care professionals

2. Timely management and intervention
   - Prescriber utilizes ocular exam findings to guide treatment

3. Restricted access and controlled administration
# Multiple, Controlled, Recurring Activities to Identify and Manage Ocular AEs

<table>
<thead>
<tr>
<th>Integrated Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Education and Monitoring</td>
</tr>
<tr>
<td>2. Timely Management and Intervention</td>
</tr>
<tr>
<td>3. Restricted Access and Controlled Administration</td>
</tr>
</tbody>
</table>

### Activities

- **Ocular safety training**
- **Ocular exam prior to each dose**
- **Patient eye care resources and support**
- **Ocular report prior to each dose**
- **Dose modification guidance**
- **Focused intervention**
- **Automated alerts**
- **Controlled distribution**
- **Eligibility confirmation**
- **Authorized administration**
- **Audit of compliance**

### Shared feedback and collaboration

- **Prescriber**
- **Patient**
- **Eye care professional**
- **Infusion center**
- **Prescriber**
- **Patient**
- **Eye care professional**
- **Prescriber**
- **Patient**
- **Infusion center**
- **Specialty distributor**
Clinical Perspective

Sagar Lonial, MD, FACP
Chair and Professor
Department of Hematology and Medical Oncology
Anne and Bernard Gray Family Chair in Cancer
Chief Medical Officer
Winship Cancer Institute
Emory University School of Medicine
Patients with RRMM have High Unmet Medical Need and Poor Prognosis

- No consensus for treatments
- Only 1 approved agent for similar RRMM population
- Other available options are cytotoxics or reused
  - Significant issues with toxicity and morbidity
  - Lack effectiveness in refractory population
- Need to take advantage of new targets and new MoAs
Contextualizing Benefit-Risk

- Is the efficacy observed meaningful?
- Are safety events manageable?
- What is the impact of corneal events on the patient?
- How does the benefit-risk profile compare with other options in the same space?
- Does the benefit outweigh the risk?
DREAMM-2: Belamaf Demonstrated Deep and Durable Responses

Based on 9-month update

<table>
<thead>
<tr>
<th>ORR % of Patients (95% CI)</th>
<th>n=12</th>
<th>n=3</th>
<th>n=2</th>
<th>n=13</th>
</tr>
</thead>
<tbody>
<tr>
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<td>CR</td>
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<tr>
<td>VGPR</td>
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<tr>
<td>PR</td>
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</tr>
</tbody>
</table>

Belamaf 2.5 mg/kg
N = 97

31% (20.8, 42.6)

Probability of Continuing Response

Median DOR at 9 months: Not Reached (NR)
Median DOR (worst-case analysis): 9.0 (4.2, 9.7)
## DREAMM-2: Overall Survival by Response in Patients Receiving Belamaf 2.5 mg/kg

### Survival Analysis by Response

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Number at Risk</th>
<th>ORR + MR</th>
<th>SD</th>
<th>PD / NE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>11</td>
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<tr>
<td>14</td>
<td>12</td>
<td>6</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

### Median OS (95% CI)

- **MR or better (n=35)**: NR (11.4, -)
- **SD (n=27)**: 7.7 (4.7, -)
- **PD / NE (n=35)**: 8.7 (1.9, 13.1)

Based on 9-month update.
## Contextualizing the Belamaf Data

<table>
<thead>
<tr>
<th></th>
<th>Belamaf</th>
<th>Selinexor/dex&lt;sup&gt;1,2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median prior lines of therapy</td>
<td>7 (3 - 21)</td>
<td>7 (3 - 18)</td>
</tr>
<tr>
<td>(range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR (%)</td>
<td>30.9%</td>
<td>26.2%</td>
</tr>
<tr>
<td>Median DOR</td>
<td>≥ 9 months&lt;sup&gt;*&lt;/sup&gt;</td>
<td>4.4 months</td>
</tr>
<tr>
<td>Median OS</td>
<td>11.9 months</td>
<td>8.6 months</td>
</tr>
<tr>
<td>SAEs</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>AE leading to dose interruption</td>
<td>54%</td>
<td>73%</td>
</tr>
<tr>
<td>AE resulting in dose reduction</td>
<td>29%</td>
<td>49%</td>
</tr>
<tr>
<td>AE leading to treatment discontinuation</td>
<td>8%</td>
<td>27%</td>
</tr>
<tr>
<td>AE resulting in death</td>
<td>3%</td>
<td>10%</td>
</tr>
</tbody>
</table>

1. Chari, 2019; 2. FDA.gov; *Not reached at 9-month data cut, estimated median; DOR based on worse case sensitivity analysis
Required Monitoring and Partnership to Manage Corneal Events

- Keratopathy occurred in 72% of patients
  - Many patients asymptomatic
  - 3 patients with corneal events discontinued
- Visual acuity changes time limited
  - Dose modifications allow continued therapy
  - 94% of patients’ vision returned to baseline or near baseline
- Partnership with ophthalmologist is required through REMS
Belamaf Data Supports a Positive Benefit-Risk

<table>
<thead>
<tr>
<th>Risk</th>
<th>Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients likely to experience a corneal event</td>
<td>Patients likely to experience a meaningful response</td>
</tr>
<tr>
<td>▪ Events managed with dose modifications</td>
<td>▪ BCMA most specific target for MM</td>
</tr>
<tr>
<td>▪ Objective keratopathy finding does not often correlate with meaningful changes in vision</td>
<td>▪ Unprecedented DOR in absence of dexamethasone</td>
</tr>
<tr>
<td>▪ Visual changes reversible</td>
<td>▪ Efficacy including OS improved with longer follow-up</td>
</tr>
<tr>
<td>▪ Present in 17% of patients</td>
<td>▪ Tolerable safety profile with 8% discontinuation</td>
</tr>
<tr>
<td>▪ 94% reversible</td>
<td></td>
</tr>
<tr>
<td>▪ Ophthalmic exam required (regardless of symptoms) will mitigate events</td>
<td></td>
</tr>
</tbody>
</table>
Patient Examples

- Two patients in mid to late 70s
  - Median 6-7 prior lines
  - Exhausted all available treatment options
- Both achieved meaningful clinical responses
  - One had keratopathy requiring dose modification
  - One had no changes in vision
- Both have received Belamaf for > 4 months
- Highlights importance of informed shared decision
Belantamab Mafodotin (Belamaf) Accelerated Approval for Patients with Relapsed or Refractory Multiple Myeloma

July 14, 2020
GlaxoSmithKline
Oncologic Drug Advisory Committee
Back-ups slides
Dose Modifications Did Not Appear to Significantly Impact Efficacy

- N=30 responders (Belamaf 2.5 mg/kg)
- **Dose delays:**
  - 90% of responders had dose delay and were able to re-start (n=27)
  - 5 progressed during delay (the delay was > 63 days in 2 pts)
- **Dose reductions**
  - 77% of responders had dose reduction (n=23)
    - n=4 progressed after dose reduction
    - No evidence that DoR impacted by lower dose intensity
- Given limited sample size further analyses not conducted
Efficacy Data from 9-Month and 13-Month Updates Provide Consistent Results with Primary Analyses

<table>
<thead>
<tr>
<th></th>
<th>Primary Analysis Belamaf 2.5 mg/kg N = 97</th>
<th>9-Month Update Belamaf 2.5 mg/kg N = 97</th>
<th>13-Month Update Belamaf 2.5 mg/kg N = 97</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR; patients (97.5% CI)</td>
<td>31% (21, 43)</td>
<td>31% (21, 43)</td>
<td>32% (21.7, 43.6)</td>
</tr>
<tr>
<td>Median DOR; months (95% CI)</td>
<td>Not reached</td>
<td>Not reached with 9-months of follow-up</td>
<td>11 (4.2, NR)</td>
</tr>
<tr>
<td>Median PFS; months (95% CI)</td>
<td>2.9 (2.1, 3.7)</td>
<td>2.8 (1.6, 3.6)</td>
<td>2.8 (1.6, 3.6)</td>
</tr>
<tr>
<td>Median OS; months (95% CI)</td>
<td>9.9 (8.9, NR)</td>
<td>11.9 (9.4, 13.1)</td>
<td>13.7 (9.9, NR)</td>
</tr>
</tbody>
</table>

Source: Tables 2.0010, 2.0060, 2.0080, 2.0150 (21-June-2019 data cut, primary analysis); Tables 2.0010, 2.0060, 2.0080, 2.0150 (20-Sep-2019 data cut; 90DU); ASCO 2020 poster [Tables 2.0010, 2.0060, 2.0080, 2.0150 (13-month update)].

13-Month data not reviewed by FDA under BLA 761158
Management of Keratopathy

- Universal use of preservative-free artificial tears
  - Four times daily
  - For comfort, lubrication, and to mitigate dry eye symptoms
- Symptomatic care such as warm or cool compresses, lid hygiene
- Eye care provider management as indicated (bandage contact lens, or topical antibiotics or steroids)

Prophylactic topical steroids showed no benefit in ocular sub-study
## Dose Modifications for Corneal Adverse Reactions in Proposed Labeling

<table>
<thead>
<tr>
<th>Corneal Adverse Reaction</th>
<th>Recommended Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 1</strong></td>
<td></td>
</tr>
<tr>
<td>Corneal examination finding(s): Mild Superficial keratopathy</td>
<td>Continue treatment at current dose</td>
</tr>
<tr>
<td>Change in BCVA:</td>
<td></td>
</tr>
<tr>
<td>Decline from baseline in 1 line of Snellen score</td>
<td></td>
</tr>
<tr>
<td><strong>Grade 2</strong></td>
<td></td>
</tr>
<tr>
<td>Corneal examination finding(s): Moderate Superficial keratopathy</td>
<td>Withhold until improvement in either exam findings or BCVA to Grade 1 or better and resume at current dose.</td>
</tr>
<tr>
<td>Change in BCVA:</td>
<td></td>
</tr>
<tr>
<td>Decline from baseline of 2 or 3 lines (and Snellen score not worse than 20/200)</td>
<td></td>
</tr>
<tr>
<td><strong>Grade 3</strong></td>
<td></td>
</tr>
<tr>
<td>Corneal examination finding(s): Severe Superficial keratopathy</td>
<td>Withhold until improvement in either exam or BCVA to Grade 1 or better and resume at a reduced dose of 1.9 mg/kg</td>
</tr>
<tr>
<td>Change in BCVA:</td>
<td></td>
</tr>
<tr>
<td>Decline from baseline by more than 3 lines (and Snellen score not worse than 20/200)</td>
<td></td>
</tr>
<tr>
<td><strong>Grade 4</strong></td>
<td></td>
</tr>
<tr>
<td>Corneal examination finding(s): Corneal epithelial defect</td>
<td>Permanently discontinue.</td>
</tr>
<tr>
<td>Change in BCVA:</td>
<td></td>
</tr>
<tr>
<td>Snellen score worse than 20/200</td>
<td></td>
</tr>
</tbody>
</table>