Summary of the Efficacy and Safety of Galcanezumab in Phase 3, Randomized, Double-Blind, Placebo-Controlled Studies

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Phase 3 Trial Methods

- Patients were randomized 1:1:2 to subcutaneous injections of galcanezumab (GBM) 120 mg/month with a loading dose of GBM 240 mg, GBM 240 mg/month, or placebo.

- Primary endpoint: overall mean change from baseline in the number of monthly migraine headache days (MHD) during the double blind treatment period.

- Key secondary endpoints:
  - Response rates (≥50%, ≥75%, and 100% reduction in monthly MHD)
  - Reduction in monthly MHD requiring acute migraine treatments
  - Change on the Role Function-Restrictive (RF-R) domain score of the Migraine-Specific Quality of Life Questionnaire (MSQ)
  - Change on Patient Global Impression-Severity of Illness (PGI-S)
A Phase 3 Placebo-Controlled Study of Galcanezumab in Patients with Chronic Migraine: Results from the 3-Month Double-Blind Treatment Phase of the REGAIN Study
Primary Objective

• To determine if GMB, a humanized monoclonal antibody that selectively binds to the calcitonin gene-related peptide (CGRP), is superior to placebo in the prevention of chronic migraine at doses of 120 mg or 240 mg/month.
### REGAIN Study Design

**Eligibility**

- The eligibility period is determined between a minimum of 30 days and a maximum of 40 days.

**Randomization**

- Patients randomized to the 120 mg dose received a loading dose of 240 mg at the first injection only (Visit 3).

**First injection of open-label extension**

- At Visit 7, all patients who entered the open-label extension received galcanezumab at a dose of 240 mg.

**Dosing**

- At Visit 8, all patients received galcanezumab at a dose of 120 mg.

- Starting at Visit 9, dosing was flexible (galcanezumab 120 mg or 240 mg) at the discretion of the investigator.

**Abbreviations:**

- OLE = open-label extension
- SP = Study period

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**Timeline**

<table>
<thead>
<tr>
<th>Month</th>
<th>Visit</th>
<th>Dosing</th>
<th>Randomization</th>
<th>First injection of open-label extension</th>
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<tr>
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<td>14</td>
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<td>15</td>
<td>18</td>
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</table>

*Eligibility period determined between a minimum of 30 days and a maximum of 40 days.

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### REGAIN Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=558</th>
<th>GMB 120 mg N=278</th>
<th>GMB 240 mg N=277</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>41.63 (12.08)</td>
<td>39.66 (11.88)*</td>
<td>41.05 (12.40)</td>
</tr>
<tr>
<td>Gender (female), %</td>
<td>86.56</td>
<td>85.25</td>
<td>81.59</td>
</tr>
<tr>
<td>Race (white), %</td>
<td>77.42</td>
<td>80.22</td>
<td>81.16</td>
</tr>
<tr>
<td>Duration of migraine illness, years, mean (SD)</td>
<td>21.94 (12.85)</td>
<td>20.37 (12.74)</td>
<td>20.06 (12.72)*</td>
</tr>
<tr>
<td>Number of comorbidities, mean (SD)</td>
<td>4.39 (3.70)</td>
<td>4.08 (3.33)</td>
<td>4.21 (3.19)</td>
</tr>
<tr>
<td><strong>MHD per month, mean (SD)</strong></td>
<td><strong>19.55 (4.59)</strong></td>
<td><strong>19.36 (4.27)</strong></td>
<td><strong>19.17 (4.60)</strong></td>
</tr>
<tr>
<td>Headache days per month, mean (SD)</td>
<td>21.54 (4.10)</td>
<td>21.24 (3.97)</td>
<td>21.44 (4.10)</td>
</tr>
<tr>
<td><strong>MHD with acute medication use per month, mean (SD)</strong></td>
<td><strong>15.51 (6.57)</strong></td>
<td><strong>15.12 (6.25)</strong></td>
<td><strong>14.49 (6.25)</strong>*</td>
</tr>
<tr>
<td>Prior preventive treatment, %</td>
<td>77.96</td>
<td>75.90</td>
<td>79.42</td>
</tr>
<tr>
<td>Failed ≥2 preventives, %</td>
<td>29.21</td>
<td>24.46</td>
<td>35.02††</td>
</tr>
<tr>
<td>Medication overuse, %</td>
<td>63.38</td>
<td>64.26</td>
<td>64.13</td>
</tr>
<tr>
<td>Concurrent migraine preventive medication use, %</td>
<td>14.70</td>
<td>13.31</td>
<td>15.52</td>
</tr>
<tr>
<td><strong>MSQ RF-R, mean (SD)</strong></td>
<td><strong>38.37 (17.18)</strong></td>
<td><strong>39.29 (17.30)</strong></td>
<td><strong>38.93 (17.31)</strong></td>
</tr>
<tr>
<td><strong>PGI-Severity of Illness, mean (SD)</strong></td>
<td><strong>4.91 (1.22)</strong></td>
<td><strong>4.79 (1.24)</strong></td>
<td><strong>4.87 (1.31)</strong></td>
</tr>
<tr>
<td><strong>MIDAS total score, mean (SD)</strong></td>
<td><strong>68.66 (57.36)</strong></td>
<td><strong>62.46 (49.48)</strong></td>
<td><strong>69.17 (64.08)</strong></td>
</tr>
</tbody>
</table>

*p<.05 (vs. placebo); ††p<.01 (vs. GMB 120 mg)
REGAIN Patient Disposition: Double-Blind Period

Screened Patients
N=1903

Patients Enrolled and Randomized
N=1117

Did Not Meet Study Entry or Baseline Criteria
N=786

Placebo
N=558

Discontinued
N=49 (8.78%)
- Withdrawal by subject 18 (3.23%)
- Adverse Event 6 (1.08%)
- Lost to Follow Up 10 (1.79%)
- Protocol Deviation 6 (1.08%)
- Physician Decision 2 (0.36%)
- Pregnancy 2 (0.36%)
- Lack of Efficacy 5 (0.90%)

Completed
N=508 (91.04%)

Galcanezumab 120 mg
N=278

Discontinued
N=15 (5.40)
- Withdrawal by subject 4 (1.44%)
- Adverse Event 3 (1.08%)
- Lost to Follow Up 4 (1.44%)
- Protocol Deviation 1 (0.36%)
- Physician Decision 1 (0.36%)
- Pregnancy 2 (0.72%)
- Lack of Efficacy 0 (0.00%)

Completed
N=263 (94.60%)

Galcanezumab 240 mg
N=277

Discontinued
N=11 (3.97%)*
- Withdrawal by subject 7 (2.53%)
- Adverse Event 2 (0.72%)
- Lost to Follow Up 1 (0.36%)
- Protocol Deviation 0 (0.00%)
- Physician Decision 1 (0.36%)
- Pregnancy 0 (0.00%)
- Lack of Efficacy 0 (0.00%)

Completed
N=266 (96.03)**

Abbreviations: GMB=galcanezumab; N=number; PBO=placebo.
Note: 1 patient in placebo group not included due to data cutoff (16 March), but discontinued (withdrawal by subject)
*p<.05 (vs. placebo); **p<.01 (vs. placebo)

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REGAIN Overall Mean Change in the Number of Monthly Migraine Headache Days (MHD) Months 1-3

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LS Mean Change Difference (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=538)</td>
<td>-2.74</td>
</tr>
<tr>
<td>GMB 120 mg (N=273)</td>
<td>-4.83</td>
</tr>
<tr>
<td>GMB 240 mg (N=274)</td>
<td>-4.62</td>
</tr>
</tbody>
</table>

***p<.001
(statistically significant after multiplicity adjustment)
REGAIN Mean Change in Monthly MHD

Note: not statistically significant between GMB doses at any month

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REGAIN Mean Proportion of Patients Who Were Responders Over Months 1-3

50% Reduction in Monthly MHD

- Placebo (N=538): 15.4%
- GMB 120 mg (N=273): 27.6% (***p<.001 statistically significant vs placebo after multiplicity adjustment)
- GMB 240 mg (N=274): 27.5% (***p<.001 statistically significant vs placebo after multiplicity adjustment)

75% Reduction in Monthly MHD

- Placebo (N=538): 4.5%
- GMB 120 mg (N=273): 7.0% (*p<.05 not statistically significant after multiplicity adjustment)
- GMB 240 mg (N=274): 8.8% (***p<.001 statistically significant vs placebo after multiplicity adjustment)

<2% of patients had 100% reduction in monthly MHD with no significant differences between groups

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REGAIN Overall Mean Change in the Number of Monthly MHD with Acute Medication Use

Abbreviations: GMB=galcanezumab; LS=least square; MHD=migraine headache days; N=number; SE=standard error.

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REGAIN Mean Change from Baseline in MSQ Role Function-Restrictive at Month 3

**Abbreviations:** GMB=galcanezumab; LS=least square; MSQ=Migraine Specific Quality of Life questionnaire; N=number; SE=standard error.
REGAIN Mean Change from Baseline in Patient Global Impression-Severity of Illness at Month 3

- Placebo (N=494) -0.62
- GMB 120 mg (N=252) -0.76
- GMB 240 mg (N=253) -0.91

**p<.01
(statistically significant after multiplicity adjustment)
### REGAIN Overview of Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>Placebo N=558 n (%)</th>
<th>GMB 120 mg N=273 n (%)</th>
<th>GMB 240 mg N=282 n (%)</th>
<th>GMB Total N=555 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAEs</td>
<td>279 (50.00)</td>
<td>159 (58.24)*</td>
<td>160 (56.74)</td>
<td>319 (57.48)*</td>
</tr>
<tr>
<td>SAEs</td>
<td>4 (0.72)</td>
<td>1 (0.37)</td>
<td>4 (1.42)</td>
<td>5 (0.90)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>DCAEs</td>
<td>6 (1.08)</td>
<td>1 (0.37)</td>
<td>4 (1.42)</td>
<td>5 (0.90)</td>
</tr>
</tbody>
</table>

*p<.05 (vs. placebo)

**Serious AEs.** Number (n) of patients with event:
- Placebo: alcoholic pancreatitis (1), epistaxis (1), gastritis (1), myocardial infarction (1)
- GMB 120 mg: colon cancer (1)
- GMB 240 mg: hypokalaemia (1), nephrolithiasis (1), acute pancreatitis (1), pulmonary embolism (1), renal colic (1)

**Discontinuation due to AEs.** Number (n) of patients with event:
- Placebo: abdominal pain (1), alopecia (1), headache (1), migraine (2), myocardial infarction (1)
- GMB 120 mg: weight increased (1)
- GMB 240 mg: depression (1), hepatic enzyme increased (1), injection site pain (1), acute pancreatitis (1)
# REGAIN Treatment-Emergent Adverse Events Occurring with ≥2% Frequency with Galcanezumab Total

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo N= 558 n (%)</th>
<th>GMB 120 mg N=273 n (%)</th>
<th>GMB 240 mg N=282 n (%)</th>
<th>GMB Total N=555 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥1 TEAE</td>
<td>279 (50.00)</td>
<td>159 (58.24)*</td>
<td>160 (56.74)</td>
<td>319 (57.48)*</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>24 (4.30)</td>
<td>17 (6.23)</td>
<td>20 (7.09)</td>
<td>37 (6.67)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>26 (4.66)</td>
<td>17 (6.23)</td>
<td>9 (3.19)</td>
<td>26 (4.68)</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>10 (1.79)</td>
<td>8 (2.93)</td>
<td>15 (5.32)**</td>
<td>23 (4.14)*</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>13 (2.33)</td>
<td>9 (3.30)</td>
<td>9 (3.19)</td>
<td>18 (3.24)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>5 (0.90)</td>
<td>4 (1.47)</td>
<td>13 (4.61)***†</td>
<td>17 (3.06)**</td>
</tr>
<tr>
<td>Nausea</td>
<td>23 (4.12)</td>
<td>9 (3.30)</td>
<td>8 (2.84)</td>
<td>17 (3.06)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>20 (3.58)</td>
<td>6 (2.20)</td>
<td>8 (2.84)</td>
<td>14 (2.52)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>10 (1.79)</td>
<td>6 (2.20)</td>
<td>6 (2.13)</td>
<td>12 (2.16)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>5 (0.90)</td>
<td>4 (1.47)</td>
<td>8 (2.84)*</td>
<td>12 (2.16)</td>
</tr>
</tbody>
</table>

Abbreviations: GMB = galcanezumab; N = number of subjects in safety population; n = number of subjects within each specific category; TEAE = treatment-emergent adverse event.

* p<.05 (vs. placebo)
** p<.01 (vs. placebo)
*** p<.001 (vs. placebo)
† p<.05 (vs. GMB 120 mg)
No clinically meaningful differences between galcanezumab and placebo were observed in laboratory analytes or any cardiovascular parameters such as blood pressure, quantitative ECGs or qualitative ECGs.

Injection site pain was similar in incidence with placebo and in both galcanezumab dose groups.

Injection site reaction, injection site erythema, and sinusitis were higher in incidence and statistically significant for GMB 240 mg compared to placebo.
Both galcanezumab doses were superior to placebo in overall reduction of monthly MHD, with significantly higher percentages of patients with ≥50% reduction in monthly MHD.

The 240 mg dose was also superior to placebo on key secondary endpoints: proportion of patients with ≥ 75% reduction in MHD, reduction in MHD with acute medication use, improvement in MSQ Role Function-Restrictive, and reduction in PGI-S.

Rates of discontinuation due to AEs were low, with no clinically meaningful differences from placebo on any safety parameters except for higher rates of injection-site reaction and erythema for the 240 mg dose.

The REGAIN study demonstrated that galcanezumab, at either 120 mg or 240 mg monthly, provided clinical benefit and improved function in patients with chronic migraine.
Two Phase 3 Studies (EVOLVE-1 and EVOLVE-2) of Galcanezumab in Episodic Migraine: Results of 6-Month Treatment Phase
To determine if galcanezumab (GMB), a humanized monoclonal antibody that selectively binds to the calcitonin gene-related peptide (CGRP), in doses of 120 mg or 240 mg/month, is superior to placebo in the prevention of episodic migraine.
EVOLVE-1 and EVOLVE-2 Study Design

Patients randomized to the 120 mg dose will receive a loading dose of 240 mg at the first injection only (Visit 3).

Abbreviations: SP = Study Period
## EVOLVE-1 Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=433</th>
<th>GMB 120 mg N=213</th>
<th>GMB 240 mg N=212</th>
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</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>41.33 (11.40)</td>
<td>40.93 (11.87)</td>
<td>39.07 (11.52)*</td>
</tr>
<tr>
<td>Gender (female), %</td>
<td>83.60</td>
<td>84.98</td>
<td>82.55</td>
</tr>
<tr>
<td>Race (white), %</td>
<td>82.22</td>
<td>79.34</td>
<td>77.83</td>
</tr>
<tr>
<td>Disease Characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of migraine illness, years, mean (SD)</td>
<td>19.89 (12.30)</td>
<td>21.12 (12.97)</td>
<td>19.30 (11.88)</td>
</tr>
<tr>
<td>Number of comorbidities, mean (SD)</td>
<td>4.81 (3.57)</td>
<td>4.67 (3.79)</td>
<td>4.44 (3.63)</td>
</tr>
<tr>
<td><strong>MHD per month, mean (SD)</strong></td>
<td>9.08 (2.97)</td>
<td>9.21 (3.05)</td>
<td>9.14 (2.91)</td>
</tr>
<tr>
<td>Migraine attacks per month, mean (SD)</td>
<td>5.79 (1.72)</td>
<td>5.61 (1.70)</td>
<td>5.74 (1.81)</td>
</tr>
<tr>
<td>Number of headache days, mean (SD)</td>
<td>10.57 (3.35)</td>
<td>10.59 (3.62)</td>
<td>10.94 (3.88)</td>
</tr>
<tr>
<td>MHD category ≥8, %</td>
<td>65.82</td>
<td>65.73</td>
<td>65.57</td>
</tr>
<tr>
<td><strong>MHD with abortive medication use per month, mean (SD)</strong></td>
<td>7.38 (3.48)</td>
<td>7.42 (3.68)</td>
<td>7.34 (3.30)</td>
</tr>
<tr>
<td>Prior preventive treatment, %</td>
<td>59.35</td>
<td>62.44</td>
<td>58.96</td>
</tr>
<tr>
<td><strong>MSQ RF-R, mean (SD)</strong></td>
<td>52.92 (15.41)</td>
<td>51.39 (16.20)</td>
<td>48.76 (16.82)**</td>
</tr>
<tr>
<td><strong>PGI-Severity of Illness, mean (SD)</strong></td>
<td>4.21 (1.12)</td>
<td>4.35 (1.08)</td>
<td>4.51 (1.12)**</td>
</tr>
<tr>
<td>MIDAS total score, mean (SD)</td>
<td>31.84 (27.31)</td>
<td>32.93 (28.18)</td>
<td>36.09 (27.76)</td>
</tr>
</tbody>
</table>

*p<.05 (vs. placebo); **p<.01 (vs. placebo)
## EVOLVE-2 Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=461</th>
<th>GMB 120 mg N=231</th>
<th>GMB 240 mg N=223</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, mean (SD)</strong></td>
<td>42.33 (11.30)</td>
<td>40.91 (11.15)</td>
<td>41.91 (10.77)</td>
</tr>
<tr>
<td><strong>Gender (female), %</strong></td>
<td>85.25</td>
<td>85.28</td>
<td>85.65</td>
</tr>
<tr>
<td><strong>Race (white), %</strong></td>
<td>70.50</td>
<td>71.86</td>
<td>68.16</td>
</tr>
<tr>
<td><strong>Disease Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of migraine illness, years, mean (SD)</strong></td>
<td>21.15 (12.75)</td>
<td>19.93 (11.73)</td>
<td>20.01 (12.12)</td>
</tr>
<tr>
<td><strong>Number of comorbidities, mean (SD)</strong></td>
<td>3.66 (3.08)</td>
<td>3.64 (3.41)</td>
<td>3.26 (2.75)</td>
</tr>
<tr>
<td><strong>MHD per month, mean (SD)</strong></td>
<td>9.19 (2.99)</td>
<td>9.07 (2.87)</td>
<td>9.06 (2.92)</td>
</tr>
<tr>
<td><strong>Migraine attacks per month, mean (SD)</strong></td>
<td>5.67 (1.82)</td>
<td>5.54 (1.76)</td>
<td>5.66 (1.80)</td>
</tr>
<tr>
<td><strong>Number of headache days, mean (SD)</strong></td>
<td>10.68 (3.53)</td>
<td>10.56 (3.42)</td>
<td>10.74 (3.70)</td>
</tr>
<tr>
<td><strong>MHD category ≥8, %</strong></td>
<td>66.59</td>
<td>66.67</td>
<td>67.71</td>
</tr>
<tr>
<td><strong>MHD with acute medication use per month, mean (SD)</strong></td>
<td>7.62 (3.40)</td>
<td>7.47 (3.34)</td>
<td>7.47 (3.25)</td>
</tr>
<tr>
<td><strong>Prior preventive treatment, %</strong></td>
<td>64.64</td>
<td>67.97</td>
<td>64.57</td>
</tr>
<tr>
<td><strong>MIDAS total score, mean (SD)</strong></td>
<td>34.25 (31.03)</td>
<td>30.87 (27.90)</td>
<td>32.75 (28.84)</td>
</tr>
<tr>
<td><strong>MSQ RF-R, mean (SD)</strong></td>
<td>51.35 (15.73)</td>
<td>52.47 (14.76)</td>
<td>51.71 (16.31)</td>
</tr>
<tr>
<td><strong>PGI-Severity of Illness, mean (SD)</strong></td>
<td>4.29 (1.22)</td>
<td>4.14 (1.19)</td>
<td>4.18 (1.17)</td>
</tr>
<tr>
<td><strong>Geography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>North America, %</strong></td>
<td>48.59</td>
<td>48.48</td>
<td>49.33</td>
</tr>
<tr>
<td><strong>Europe, %</strong></td>
<td>26.46</td>
<td>25.97</td>
<td>26.46</td>
</tr>
<tr>
<td><strong>Other, %</strong></td>
<td>24.95</td>
<td>25.54</td>
<td>24.22</td>
</tr>
</tbody>
</table>

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EVOLVE-1 Patient Disposition

Screened Patients
N=1671

Did Not Meet Study Entry or Baseline Criteria
N=809

Patients Enrolled and Randomized
N=862

Completed
N=351 (81.06%)

Did not receive PBO
N=1

Discontinued
N=82 (18.94%)

Withdrawal by subject 33 (7.62%)
Adverse Event 10 (2.31%)
Lost to Follow Up 18 (4.16%)
Protocol Deviation 2 (0.46%)
Physician Decision 7 (1.62%)
Pregnancy 2 (0.46%)
Lack of Efficacy 10 (2.31%)

Completed
N=177 (83.10%)

Did not receive GMB
N=2

Discontinued
N=37 (17.45%)

Withdrawal by subject 16 (7.55%)
Adverse Event 7 (3.30%)
Lost to Follow Up 5 (2.36%)
Protocol Deviation 2 (0.94%)
Physician Decision 2 (0.94%)
Pregnancy 3 (1.42%)
Lack of Efficacy 2 (0.94%)

Completed
N=175 (82.55%)

Did not receive GMB
N=1

Discontinued
N=36 (16.90%)

Withdrawal by subject 11 (5.16%)
Adverse Event 9 (4.23%)
Lost to Follow Up 9 (4.23%)
Protocol Deviation 2 (0.94%)
Physician Decision 3 (1.41%)
Pregnancy 1 (0.47%)
Lack of Efficacy 1 (0.47%)

Completed
N=177 (83.10%)

Placebo
N=433

Galcanezumab 120 mg
N=213

Discontinued
N=36 (16.90%)

Galcanezumab 240 mg
N=212

Discontinued
N=37 (17.45%)

Did not receive PBO
N=1

Did not receive GMB
N=2

Did not receive Placebo
N=1

Did not receive GMB
N=1

Abbreviations: GMB=galcanezumab; N=number; PBO=placebo.
EVOLVE-2 Patient Disposition

Screened Patients
N=1696

Patients Enrolled and Randomized
N=922

Did Not Meet Study Entry or Baseline Criteria
N=774

Did not receive PBO
N=2

Did not receive GMB
N=2

Did not receive GMB
N=3

Placebo
N=461

Discontinued
N=74 (16.05%)

Withdrawal by subject 39 (8.46%)
Adverse Event 8 (1.74%)
Lost to Follow Up 10 (2.17%)
Protocol Deviation 5 (1.08%)
Physician Decision 4 (0.87%)
Pregnancy 1 (0.22%)
Terminated by Sponsor 1 (0.22%)
Lack of Efficacy 6 (1.30%)

Completed
N=387 (83.95%)

Completed
N=203 (87.88)

Galcanezumab 120 mg
N=231

Discontinued
N=28 (12.12%)

Withdrawal by subject 11 (4.76%)
Adverse Event 5 (2.16%)
Lost to Follow Up 7 (3.03%)
Protocol Deviation 2 (0.87%)
Physician Decision 0 (0.00%)
Pregnancy 2 (0.87%)
Terminated by Sponsor 0 (0.00%)
Lack of Efficacy 1 (0.43%)

Galcanezumab 240 mg
N=223

Discontinued
N=27 (12.11%)

Withdrawal by subject 14 (6.28%)
Adverse Event 9 (4.04%)
Lost to Follow Up 0 (0.00%)*†
Protocol Deviation 1 (0.45%)
Physician Decision 2 (0.90%)
Pregnancy 0 (0.00%)
Terminated by Sponsor 0 (0.00%)
Lack of Efficacy 1 (0.45%)

Completed
N=195 (87.44%)

Completed
N=195 (87.44%)

Note: 1 patient in 240 mg group not included due to data cutoff (16 March), but discontinued (lost to follow-up)
*p<.05 (vs. placebo); †p<.05 (vs. GMB 120 mg)

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EVOLVE-1 and EVOLVE-2
Overall Mean Change in Monthly MHD Months 1-6

EVOLVE-1

EVOLVE-2

Baseline total number of monthly MHD, mean (SD)
Placebo (N=425)
GMB 120 mg (N=210)
GMB 240 mg (N=208)

Placebo (N=450)
GMB 120 mg (N=226)
GMB 240 mg (N=220)

Abbreviations: GMB=galcanezumab; LS=least square; MHD=migraine headache days; SE=standard error.

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EVOLVE-1 and EVOLVE-2
Mean Change in Monthly MHD

Abbreviations: GMB=galcanezumab; LS=least square; MHD=migraine headache days; SE=standard error.

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EVOLVE-1 and EVOLVE-2
≥50% Response Rates
Percentages Over Months 1-6

**Abbreviations:** GMB=galcanezumab; N=number; SE=standard error.

**EVOLVE-1**
- Placebo (N=425)
- GMB 120 mg (N=210)
- GMB 240 mg (N=208)

**EVOLVE-2**
- Placebo (N=450)
- GMB 120 mg (N=226)
- GMB 240 mg (N=220)

**Mean % of Patients (SE)**
- **EVOLVE-1**
  - Placebo: 38.6% (SE), 62.3% (SE), 60.9% (SE)
  - GMB 120 mg: 62.3% (SE), 62.3% (SE), 62.3% (SE)
  - GMB 240 mg: 60.9% (SE), 60.9% (SE), 60.9% (SE)

**EVOLVE-2**
- Placebo: 36.0% (SE), 59.3% (SE), 58.5% (SE)
- GMB 120 mg: 59.3% (SE), 59.3% (SE), 59.3% (SE)
- GMB 240 mg: 58.5% (SE), 58.5% (SE), 58.5% (SE)

* ***p<.001 (statistically significant after multiplicity adjustment)
EVOLVE-1 and EVOLVE-2
≥75% Response Rates
Percentages Over Months 1-6

Abbreviations: GMB=galcanezumab; N=number; SE=standard error.
EVOLVE-1 and EVOLVE-2
100% Response Rates
Percentages Over Months 1-6

** Abbreviations: GMB=galcanezumab; N=number; SE=standard error. 

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EVOLVE-1 and EVOLVE-2 MHD with Acute Medication Use Months 1-6

**EVOLVE-1**

- Placebo (N=425)
- GMB 120 mg (N=210)
- GMB 240 mg (N=208)

- Improvement LS Mean Change from Baseline (SE)
  - Placebo: -2.15
  - GMB 120 mg: -3.96
  - GMB 240 mg: -3.76

***p<.001 (statistically significant after multiplicity adjustment)

**EVOLVE-2**

- Placebo (N=450)
- GMB 120 mg (N=226)
- GMB 240 mg (N=220)

- Improvement LS Mean Change from Baseline (SE)
  - Placebo: -1.85
  - GMB 120 mg: -3.67
  - GMB 240 mg: -3.63

***p<.001 (statistically significant after multiplicity adjustment)
EVOLVE-1 and EVOLVE-2
MSQ Role Function-Restrictive

**EVOLVE-1**

<table>
<thead>
<tr>
<th>Group</th>
<th>Average Months 4 - 6</th>
<th>LS Mean Change from Baseline (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=377)</td>
<td></td>
<td>24.69</td>
</tr>
<tr>
<td>GMB 120 mg (N=189)</td>
<td></td>
<td>32.43***</td>
</tr>
<tr>
<td>GMB 240 mg (N=184)</td>
<td></td>
<td>32.09***</td>
</tr>
</tbody>
</table>

**EVOLVE-2**

<table>
<thead>
<tr>
<th>Group</th>
<th>Average Months 4 - 6</th>
<th>LS Mean Change from Baseline (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (N=396)</td>
<td></td>
<td>19.65</td>
</tr>
<tr>
<td>GMB 120 mg (N=213)</td>
<td></td>
<td>28.47***</td>
</tr>
<tr>
<td>GMB 240 mg (N=210)</td>
<td></td>
<td>27.04***</td>
</tr>
</tbody>
</table>

Abbreviations: GMB=galcanezumab; LS=least square; MSQ=Migraine Specific Quality of Life questionnaire; N=number; SE=standard error.

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EVOLVE-1 and EVOLVE-2 Patient Global Impression-Severity of Illness

**EVOLVE-1**

Average Months 4 - 6

- Placebo (N=377)
- GMB 120 mg (N=189)
- GMB 240 mg (N=184)

**p<.01**

(statistically significant after multiplicity adjustment)

**LS Mean Change from Baseline (SE)**

-1.27
-1.59
-1.55

**EVOLVE-2**

Average Months 4 - 6

- Placebo (N=396)
- GMB 120 mg (N=213)
- GMB 240 mg (N=210)

*p<.05*

**p<.01**

(statistically significant after multiplicity adjustment)

**LS Mean Change from Baseline (SE)**

-0.94
-1.22
-1.17

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EVOLVE-1 Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>Placebo</th>
<th>GMB 120 mg</th>
<th>GMB 240 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=432 n (%)</td>
<td>N=206 n (%)</td>
<td>N=220 n (%)</td>
</tr>
<tr>
<td>Treatment-emergent AEs</td>
<td>261 (60.42)</td>
<td>135 (65.53)</td>
<td>149 (67.73)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>5 (1.16)</td>
<td>6 (2.91)</td>
<td>0 (0.00)†</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Discontinuation due to AEs</td>
<td>10 (2.31)</td>
<td>7 (3.40)</td>
<td>9 (4.09)</td>
</tr>
</tbody>
</table>

†p<.05 (vs. GMB 120 mg)

♦ Serious AEs. Number (n) of patients with event:
  • **Placebo**: cholelithiasis (2), deep vein thrombosis (1), pulmonary embolism (1), vertebral osteophyte (1)
  • **GMB 120 mg**: incarcerated incisional hernia (1), ligament rupture (1), pancreatitis acute (1), seroma (1), small intestinal obstruction (1), tendonitis (1), tubular breast carcinoma (1)

♦ Discontinuation due to AEs. Number (n) of patients with event:
  • **Placebo**: migraine (1), arthralgia (1), cholelithiasis (1), deep vein thrombosis (1), depression (1), dizziness (1), generalized anxiety disorder (1), sciatica (1), tinea capitis (1), vertebral osteophyte (1)
  • **GMB 120 mg**: migraine (1), injection site erythema (1), myalgia (1), peripheral swelling (1), rash generalized (1), tubular breast carcinoma (1), weight increased (1)
  • **GMB 240 mg**: migraine (4), dyspepsia (1), dyspnea (1), hypersensitivity (1), injection site swelling (1), nasopharyngitis (1)
# EVOLVE-1 Treatment-Emergent Adverse Events ≥2% Galcanezumab Total

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo N=432 n (%)</th>
<th>GMB 120 mg N=206 n (%)</th>
<th>GMB 240 mg N=220 n (%)</th>
<th>GMB Total N=426 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥ 1 TEAE</td>
<td>261 (60.42)</td>
<td>135 (65.53)</td>
<td>149 (67.73)</td>
<td>284 (66.67)</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>75 (17.36)</td>
<td>33 (16.02)</td>
<td>45 (20.45)</td>
<td>78 (18.31)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>31 (7.18)</td>
<td>9 (4.37)</td>
<td>15 (6.82)</td>
<td>24 (5.63)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>27 (6.25)</td>
<td>16 (7.77)</td>
<td>6 (2.73)†</td>
<td>22 (5.16)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>15 (3.47)</td>
<td>8 (3.88)</td>
<td>13 (5.91)</td>
<td>21 (4.93)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>11 (2.55)</td>
<td>10 (4.85)</td>
<td>9 (4.09)</td>
<td>19 (4.46)</td>
</tr>
<tr>
<td>Injection site pruritus</td>
<td>1 (0.23)</td>
<td>9 (4.37)***</td>
<td>10 (4.55)***</td>
<td>19 (4.46)***</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>4 (0.93)</td>
<td>7 (3.40)*</td>
<td>12 (5.45)***</td>
<td>19 (4.46)**</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>13 (3.01)</td>
<td>10 (4.85)</td>
<td>8 (3.64)</td>
<td>18 (4.23)</td>
</tr>
<tr>
<td>Nausea</td>
<td>15 (3.47)</td>
<td>5 (2.43)</td>
<td>8 (3.64)</td>
<td>13 (3.05)</td>
</tr>
<tr>
<td>Back pain</td>
<td>6 (1.39)</td>
<td>5 (2.43)</td>
<td>7 (3.18)</td>
<td>12 (2.82)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>11 (2.55)</td>
<td>6 (2.91)</td>
<td>5 (2.27)</td>
<td>11 (2.58)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>6 (1.39)</td>
<td>3 (1.46)</td>
<td>7 (3.18)</td>
<td>10 (2.35)</td>
</tr>
<tr>
<td>Cough</td>
<td>7 (1.62)</td>
<td>4 (1.94)</td>
<td>6 (2.73)</td>
<td>10 (2.35)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (2.78)</td>
<td>5 (2.43)</td>
<td>5 (2.27)</td>
<td>10 (2.35)</td>
</tr>
<tr>
<td>influenza</td>
<td>5 (1.16)</td>
<td>5 (2.43)</td>
<td>4 (1.82)</td>
<td>9 (2.11)</td>
</tr>
</tbody>
</table>

Abbreviations: GMB=galcanezumab; N=number of subjects in safety population; n=number of subjects within each specific category; TEAE=treatment-emergent adverse event.

*p<.05 (vs. placebo); **p<.01 (vs. placebo); ***p<.001 (vs. placebo); †p<.05 (vs. GMB 120 mg)

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## EVOLVE-2 Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>Placebo N=461</th>
<th>GMB 120 mg N=226</th>
<th>GMB 240 mg N=228</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-emergent AEs</td>
<td>287 (62.26)</td>
<td>147 (65.04)</td>
<td>163 (71.49)*</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>5 (1.08)</td>
<td>5 (2.21)</td>
<td>7 (3.07)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Discontinuation due to AEs</td>
<td>8 (1.74)</td>
<td>5 (2.21)</td>
<td>9 (3.95)</td>
</tr>
</tbody>
</table>

*P<.05 (vs. placebo)

- **Serious AEs.** Number (n) of patients with event:
  - **Placebo:** foot fracture (1), gallbladder polyp (1), hemorrhoids (1), migraine (1), rib fracture (1), road traffic accident (1), suicide attempt (1)
  - **GMB 120 mg:** adenocarcinoma of the cervix (1), bladder dysfunction (1), gastritis (1), pharyngitis bacterial (1), rectal polyp (1)
  - **GMB 240 mg:** acute myocardial infarction (1), cholelithiasis (1), disorientation (1), generalized tonic-clonic seizure (1), influenza (1), meniscus injury (1), pyrexia (1), transient ischemic attack (1)

- **Discontinuation due to AEs.** Number (n) of patients with event:
  - **Placebo:** dermatitis atopic (1), facial plain (1), fatigue (1), hypertension (1), pain in extremity (1), suicide attempt (1), syncope (1), vertigo (1)
  - **GMB 120 mg:** injection site reaction (1), adenocarcinoma of the cervix (1), bronchiectasis (1), gastritis (1), rash pruritic (1)
  - **GMB 240 mg:** injection site reaction (3), chest discomfort (1), hepatic enzyme increased (1), infection (1), influenza like illness (1), nasopharyngitis (1), skin ulcer (1)
## EVOLVE-2 Treatment-Emergent Adverse Events ≥2% Galcanezumab Total

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo N=461 n (%)</th>
<th>GMB 120 mg N=226 n (%)</th>
<th>GMB 240 mg N=228 n (%)</th>
<th>GMB Total N=454 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥1 TEAE</td>
<td>287 (62.26)</td>
<td>147 (65.04)</td>
<td>163 (71.49)*</td>
<td>310 (68.28)</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>39 (8.46)</td>
<td>21 (9.29)</td>
<td>20 (8.77)</td>
<td>41 (9.03)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>41 (8.89)</td>
<td>19 (8.41)</td>
<td>16 (7.02)</td>
<td>35 (7.71)</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>0 (0.00)</td>
<td>7 (3.10)***</td>
<td>18 (7.89)***†</td>
<td>25 (5.51)***</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>16 (3.47)</td>
<td>13 (5.75)</td>
<td>12 (5.26)</td>
<td>25 (5.51)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10 (2.17)</td>
<td>8 (3.54)</td>
<td>7 (3.07)</td>
<td>15 (3.30)</td>
</tr>
<tr>
<td>Influenza</td>
<td>14 (3.04)</td>
<td>3 (1.33)</td>
<td>10 (4.39)</td>
<td>13 (2.86)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>4 (0.87)</td>
<td>6 (2.65)</td>
<td>7 (3.07)*</td>
<td>13 (2.86)*</td>
</tr>
<tr>
<td>Injection site pruritus</td>
<td>0 (0.00)</td>
<td>6 (2.65)**</td>
<td>7 (3.07)***</td>
<td>13 (2.86)***</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (2.60)</td>
<td>6 (2.65)</td>
<td>5 (2.19)</td>
<td>11 (2.42)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>11 (2.39)</td>
<td>7 (3.10)</td>
<td>3 (1.32)</td>
<td>10 (2.20)</td>
</tr>
</tbody>
</table>

*p<.05 (vs. placebo); **p<.01 (vs. placebo); ***p<.001 (vs. placebo); †p<.05 (vs. GMB 120 mg)
EVOLVE-1 and EVOLVE-2 Conclusions

♦ Both doses of galcanezumab (in EVOLVE-1 and EVOLVE-2) met the primary and all key secondary objectives in patients with episodic migraine, after adjusting for multiplicity.

♦ Treatment effects were similar across galcanezumab doses for efficacy, tolerability, and safety.

♦ Both trials demonstrated that galcanezumab, at either 120 mg or 240 mg monthly, provided clinical benefit and improved function with discontinuations similar to placebo and few (<5%) discontinuations due to adverse events in patients with episodic migraine.