Efficacy and safety of amlitelimab (an anti-OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 24-week results from a Phase 2b trial (STREAM-AD)

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Presenter: Wendell Valdecantos11

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OX40L-OX40 Signaling as a Therapeutic Target in AD

- **Unmet needs in AD**\(^1,2\):
  - Targeting heterogeneous immune activation
  - Innovative treatment options with long-term durable response on- and off-drug
  - Extended dosing regimens
  - Drugs with minimal side effects

- **OX40 ligand (OX40L)-OX40 axis is a secondary co-stimulatory pathway**\(^1,3,4\):
  - Ox40L-Ox40 regulates:
    - Th2 and Th1/Th17/Th22 cell proliferation and survival\(^1,3-5\)
    - Secretion of pro-inflammatory cytokines\(^1,3\)

- **Amlitelimab is a fully human, non-depleting, anti-OX40L mAb**\(^1,5\):
  - Binds OX40L on APCs to prevent interaction with OX40\(^+\) activated T cells\(^1,5\)
  - Targets antigen presentation to prevent inflammation escalation\(^1,5\)

A Phase 2a trial of amlitelimab IV high (500 mg/250 mg Q4W) and low (200 mg/100 mg Q4W) doses versus placebo in adults with moderate-to-severe AD met its primary endpoint of change in EASI from baseline to Week 16 while also showing acceptable safety\(^1\)

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**Diagram:**
- Activated T cell
- APC
- B7 (CD80/CD86)
- CD28
- OX40
- OX40L
- Amlitelimab
- CD40
- CD40L
- Th2
  - IL-4
  - IL-13
- Th17
  - IL-17
- Th22
  - IL-22
- Th1
  - IFN\(\gamma\)
- Mast cells
- Neutrophils
- Eosinophils
- T cells
- B cells secreting IgE

**Legend:**
- APC: antigen-presenting cell
- CD: cluster of differentiation
- EASI: Eczema Area and Severity Index
- IgE: immunoglobulin E
- IFN\(\gamma\): interferon \(\gamma\)
- IL: interleukin
- IV: intravenous
- mAb: monoclonal antibody
- Q4W: every 4 weeks
- Th: helper T cell

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AD, atopic dermatitis; APC, antigen-presenting cell; CD, cluster of differentiation; EASI, Eczema Area and Severity Index; IgE, immunoglobulin E; IFN\(\gamma\), interferon \(\gamma\); IV, intravenous; mAb, monoclonal antibody; OX40L, OX40 ligand; Q4W, every 4 weeks; Th, helper T cell.


STREAM-AD Phase 2b Trial Design (NCT05131477)

Part 1: 24-week results presented today

**Primary endpoint**

- Percentage change in EASI from baseline to Week 16
- Percentage of patients with:
  - EASI-75 at Week 16/24
  - IGA 0/1 at Week 16/24
  - Reduction of weekly average of PP-NRS ≥4 with a baseline PP-NRS of ≥4 from baseline to Week 16/24

**Secondary endpoints**

- Incidence of TEAEs
- Change in soluble protein blood biomarkers
- ADA titers and incidence

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**Part 1 - Focus of today’s presentation**

- **Week 0**
  - Randomized: 1:1:1:1:1 (n=390)
  - Treated*: (n=388)

- **Week 4 to 0**
  - Screened: N=589

- **Week 0**
  - 500 mg LD
  - 250 mg SC Q4W (n=77)

- **Week 16**
  - 250 mg SC Q4W (n=78)

- **Week 24**
  - 125 mg SC Q4W (n=77)

- **Week 52**

- **Week 68**

**Part 2**

- Week 24 Response: YES
  - Withdrawal (placebo)‡
  - Pre-Week 24 dose‡
  - Safety follow-up‡

- Week 24 Response: NO
  - Enter LTE or Safety follow-up

- Completed to Week 24: n=333
  - Discontinued study: n=33
  - Other: n=6

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*Two patients found to be not eligible after randomization. †Met EASI-75 and/or IGA 0/1 randomized to Withdrawal (placebo) or Pre-Week 24 dose groups; not EASI-75 and IGA 2/3/4 entered to LTE or Safety follow-up. ‡Patients demonstrating loss of clinical response during Part 2 are entered preferably into the LTE (or Safety follow-up). §Completed to Week 24 are patients who have reached Week 24 regardless of whether they completed treatment period. ¶Six patients did not show as completed or discontinued study prior to Week 24: 5 patients discontinued the study without an 'end of study visit' (effort to reach patients will continue until the closure of the study), and 1 was in the safety follow-up period.

AD, atopic dermatitis; ADA, anti-drug antibodies; EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LD, loading dose; LTE, long-term extension; NA, not applicable; PP-NRS, Peak Pruritus Numerical Rating Scale; Q4W, every 4 weeks; R, randomization; SC, subcutaneous; STREAM-AD, Study Testing Response Effect of KY1005 Against Moderate-to-Severe Atopic Dermatitis; TEAE, treatment-emergent adverse event.
### Key Inclusion Criteria

**Adult patients (18 to <75 years) with moderate-to-severe AD who have:**

- AD for $\geq 1$ year at baseline
- EASI score of $\geq 12$ at screening and $\geq 16$ at baseline
- IGA score of 3 (moderate) or 4 (severe) at baseline
- Body surface area involvement $\geq 10\%$ at baseline
- Peak Pruritus Numerical Rating Scale score $\geq 4$ at baseline
- Documented history, within 6 months prior to baseline, of either inadequate response to topical treatments or inadvisability of topical treatments
- Stable dose of topical emollient $\geq$ twice-daily for $\geq 7$ days prior to baseline

### Key Exclusion Criteria

- Previous treatment for AD before baseline within specified time periods
- Clinically significant disease or medical history that may interfere with trial procedures
- Known history of, or suspected, significant current immunosuppression
- Any malignancies or history of malignancies prior to baseline (except for non-melanoma skin cancer excised and cured $>3$ years prior to baseline; in situ cervical carcinoma excised and cured)
- Any active or chronic infection requiring systemic treatment within 2 weeks prior to baseline
- Treatment with a live (attenuated) immunization within 12 weeks prior to baseline
- Positive for HIV, hepatitis B or hepatitis C, current or past history of tuberculosis
- Weight $<40$ kg or $>150$ kg at baseline

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AD, atopic dermatitis; EASI, Eczema Area and Severity Index; HIV, human immunodeficiency virus; IGA, investigator global assessment; STREAM-AD, Study Testing Response Effect of Amlitelimab Against Moderate-to-severe Atopic Dermatitis.
## Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>Amlitelimab 250 mg Q4W LD</th>
<th>Amlitelimab 250 mg Q4W</th>
<th>Amlitelimab 125 mg Q4W</th>
<th>Amlitelimab 62.5 mg Q4W</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (FAS)</strong></td>
<td>N=77</td>
<td>N=78</td>
<td>N=77</td>
<td>N=79</td>
<td>N=79</td>
<td>N=390</td>
</tr>
<tr>
<td><strong>Age (years), mean (SD)</strong></td>
<td>36.3 (13.3)</td>
<td>40.8 (15.2)</td>
<td>37.9 (15.2)</td>
<td>37.6 (14.8)</td>
<td>36.4 (13.1)</td>
<td>37.8 (14.4)</td>
</tr>
<tr>
<td></td>
<td>18–64 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender (Male), n (%)</strong></td>
<td>75 (97.4)</td>
<td>72 (92.3)</td>
<td>72 (93.5)</td>
<td>74 (93.7)</td>
<td>77 (97.5)</td>
<td>370 (94.9)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td>47 (61.0)</td>
<td>43 (55.1)</td>
<td>38 (49.4)</td>
<td>42 (53.2)</td>
<td>49 (62.0)</td>
<td>219 (56.2)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td>61 (79.2)</td>
<td>63 (80.8)</td>
<td>63 (81.8)</td>
<td>60 (75.9)</td>
<td>60 (75.9)</td>
<td>307 (78.7)</td>
</tr>
<tr>
<td><strong>Region, n (%)</strong></td>
<td>56 (72.7)</td>
<td>57 (73.1)</td>
<td>56 (72.7)</td>
<td>57 (72.2)</td>
<td>57 (72.2)</td>
<td>283 (72.6)</td>
</tr>
<tr>
<td><strong>Duration of AD (years), mean (SD)</strong></td>
<td>22.0 (15.4)</td>
<td>21.5 (17.8)</td>
<td>22.4 (16.4)</td>
<td>23.3 (16.4)</td>
<td>22.2 (16.6)</td>
<td>22.3 (16.4)</td>
</tr>
<tr>
<td><strong>Weight (kg), mean (SD)</strong></td>
<td>79.8 (17.5)</td>
<td>73.3 (17.1)</td>
<td>76.8 (19.0)</td>
<td>72.8 (17.4)</td>
<td>79.0 (18.7)</td>
<td>76.3 (18.1)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²), mean (SD)</strong></td>
<td>27.3 (5.79)</td>
<td>25.0 (4.57)</td>
<td>26.8 (6.11)</td>
<td>25.2 (5.21)</td>
<td>27.1 (5.96)</td>
<td>26.3 (5.61)</td>
</tr>
</tbody>
</table>

Patient baseline demographics are generally balanced and reflective of the countries in which the trial is running, with all treatment arms containing a primarily young (<65 years old) population with more males than females.

AD, atopic dermatitis; BMI, body mass index; FAS, full analysis set (all randomized patients); LD, loading dose; SD, standard deviation; Q4W, every 4 weeks.
## Baseline Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Amlitelimab 250 mg Q4W LD</th>
<th>Amlitelimab 125 mg Q4W</th>
<th>Amlitelimab 62.5 mg Q4W</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (FAS)</td>
<td>N=77</td>
<td>N=78</td>
<td>N=77</td>
<td>N=79</td>
<td>N=390</td>
</tr>
<tr>
<td>EASI (0-72), mean (SD)</td>
<td>30.3 (11.7)</td>
<td>28.7 (10.5)</td>
<td>30.3 (12.4)</td>
<td>28.7 (10.1)</td>
<td>26.4 (7.9)</td>
</tr>
<tr>
<td>EASI ≤21 (moderate), n (%)</td>
<td>21 (27.3)</td>
<td>22 (28.2)</td>
<td>21 (27.3)</td>
<td>23 (29.1)</td>
<td>24 (30.4)</td>
</tr>
<tr>
<td>EASI &gt;21 (severe), n (%)</td>
<td>56 (72.7)</td>
<td>56 (71.8)</td>
<td>56 (72.7)</td>
<td>56 (70.9)</td>
<td>55 (69.6)</td>
</tr>
<tr>
<td>IGA 0-4, mean (SD)</td>
<td>3.3 (0.45)</td>
<td>3.3 (0.45)</td>
<td>3.3 (0.46)</td>
<td>3.3 (0.46)</td>
<td>3.3 (0.44)</td>
</tr>
<tr>
<td>IGA 3 (moderate)</td>
<td>53 (68.8)</td>
<td>56 (71.8)</td>
<td>55 (71.4)</td>
<td>57 (72.2)</td>
<td>59 (74.7)</td>
</tr>
<tr>
<td>IGA 4 (severe)</td>
<td>24 (31.2)</td>
<td>22 (28.2)</td>
<td>22 (28.6)</td>
<td>22 (27.8)</td>
<td>20 (25.3)</td>
</tr>
<tr>
<td>BSA involvement (%)</td>
<td>48.4 (19.2)</td>
<td>46.5 (19.7)</td>
<td>47.4 (20.3)</td>
<td>45.8 (20.0)</td>
<td>43.0 (15.7)</td>
</tr>
<tr>
<td>SCORAD (0-103), mean (SD)</td>
<td>67.08 (13.49)</td>
<td>67.78 (11.67)</td>
<td>68.83 (12.19)</td>
<td>66.22 (12.21)</td>
<td>66.00 (10.96)</td>
</tr>
<tr>
<td>N (FAS)*</td>
<td>N=76</td>
<td>N=77</td>
<td>N=77</td>
<td>N=78</td>
<td>N=386</td>
</tr>
<tr>
<td>PP-NRS (0-10), mean (SD)</td>
<td>7.31 (1.30)</td>
<td>7.35 (1.33)</td>
<td>7.31 (1.23)</td>
<td>7.24 (1.40)</td>
<td>7.38 (1.41)</td>
</tr>
</tbody>
</table>

Overall, patient populations are well-balanced, with no notable differences in disease severity, as determined by baseline EASI, IGA, PP-NRS, SCORAD, and BSA involvement.

*FAS population - number of randomized patients with observations at baseline.
BSA, body surface area; EASI, Eczema Area and Severity Index; FAS, full analysis set (all randomized patients); IGA, Investigator Global Assessment; LD, loading dose; PP-NRS, Peak Pruritus Numerical Rating Scale; Q4W, every 4 weeks; SD, standard deviation.
Study met primary and key secondary endpoints (percentage change in EASI), regardless of how rescue treatment was statistically handled and with the largest placebo-adjusted difference demonstrated using ‘treatment policy’ data across all doses.

250 mg Q4W with LD dose showed greatest placebo-adjusted difference at Week 16, which continued to improve through Week 24.

*Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16 and Week 24. All data are used for analysis regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are considered as non-responders at Week 16/Week 24.

CI, confidence interval; EASI, Eczema Area and Severity Index; LD, loading dose; LS, least squares; NRI, non-responder imputation; Q4W, every 4 weeks; WOCF, worst observation carried forward.

- Study met primary and key secondary endpoints (percentage change in EASI), regardless of how rescue treatment was statistically handled and with the largest placebo-adjusted difference demonstrated using ‘treatment policy’ data across all doses.

- 250 mg Q4W with LD dose showed greatest placebo-adjusted difference at Week 16, which continued to improve through Week 24.

Percentage Change in EASI From Baseline at Weeks 16 and 24

*Week 16 (NRI)*

*Week 24 (NRI)*

*Week 24 (All Data)*

LS mean % change

<table>
<thead>
<tr>
<th>Group</th>
<th>LS Mean % Change</th>
<th>LS Mean % Difference vs Placebo (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (with LD)</td>
<td>-61.5 (-43.9, -20.3)</td>
<td>-32.1 (-49.2, -15.6)</td>
</tr>
<tr>
<td>250 mg</td>
<td>-56.8 (-49.2, -26.1)</td>
<td>-37.6 (-47.1, -16.7)</td>
</tr>
<tr>
<td>125 mg</td>
<td>-64.8 (-49.8, -23.8)</td>
<td>-29.3 (-40.7, -17.9)</td>
</tr>
<tr>
<td>62.5 mg</td>
<td>-59.6 (-41.9, -18.5)</td>
<td>-30.2 (-43.9, -15.1)</td>
</tr>
<tr>
<td>Placebo</td>
<td>-68.4 (-44.3, -21.5)</td>
<td>-32.9 (-44.3, -21.5)</td>
</tr>
</tbody>
</table>

All p<0.0001
EASI-75 and IGA 0/1 From Baseline to Week 24 (NRI)*

**EASI-75**

<table>
<thead>
<tr>
<th>#Patients</th>
<th>BL</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (500 mg LD)</td>
<td>77</td>
<td>73</td>
<td>77</td>
<td>69</td>
<td>68</td>
<td>69</td>
<td>66</td>
<td>70</td>
</tr>
<tr>
<td>250 mg w/o LD</td>
<td>78</td>
<td>77</td>
<td>74</td>
<td>69</td>
<td>69</td>
<td>67</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>125 mg</td>
<td>77</td>
<td>75</td>
<td>76</td>
<td>74</td>
<td>70</td>
<td>71</td>
<td>70</td>
<td>69</td>
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<tr>
<td>62.5 mg</td>
<td>79</td>
<td>75</td>
<td>77</td>
<td>76</td>
<td>77</td>
<td>76</td>
<td>70</td>
<td>68</td>
</tr>
<tr>
<td>Placebo</td>
<td>79</td>
<td>78</td>
<td>75</td>
<td>72</td>
<td>67</td>
<td>67</td>
<td>60</td>
<td>58</td>
</tr>
</tbody>
</table>

Greatest increase from Week 16 to Week 24 with amlitelimab 250 mg Q4W with LD

**IGA 0/1**

<table>
<thead>
<tr>
<th>#Patients</th>
<th>BL</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (500 mg LD)</td>
<td>77</td>
<td>73</td>
<td>77</td>
<td>69</td>
<td>68</td>
<td>69</td>
<td>66</td>
<td>70</td>
</tr>
<tr>
<td>250 mg w/o LD</td>
<td>78</td>
<td>77</td>
<td>74</td>
<td>69</td>
<td>69</td>
<td>67</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>125 mg</td>
<td>77</td>
<td>75</td>
<td>76</td>
<td>74</td>
<td>70</td>
<td>71</td>
<td>70</td>
<td>69</td>
</tr>
<tr>
<td>62.5 mg</td>
<td>79</td>
<td>75</td>
<td>77</td>
<td>76</td>
<td>77</td>
<td>76</td>
<td>70</td>
<td>68</td>
</tr>
<tr>
<td>Placebo</td>
<td>79</td>
<td>78</td>
<td>75</td>
<td>72</td>
<td>67</td>
<td>67</td>
<td>60</td>
<td>58</td>
</tr>
</tbody>
</table>

No plateau observed with the 250 mg with LD arm for EASI-75 or IGA 0/1

*Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16/Week 24.

BL, baseline; EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LD, loading dose; NRI, non-responder imputation; Q4W, every 4 weeks; w/o, without.
### Key Secondary Endpoints Results Across All Doses at Weeks 16 and 24

*Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16/Week 24. All data are used for analysis, regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are considered as non-responders.*

<table>
<thead>
<tr>
<th>Percentage responders at Week 16</th>
<th>Amlitelimab 250 mg Q4W LD (N=77)</th>
<th>Amlitelimab 250 mg Q4W (N=78)</th>
<th>Amlitelimab 125 mg Q4W (N=77)</th>
<th>Amlitelimab 62.5 mg Q4W (N=79)</th>
<th>Placebo (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NRI*</td>
<td>All data†</td>
<td>NRI*</td>
<td>All data†</td>
<td>NRI*</td>
</tr>
<tr>
<td>IGA 0/1</td>
<td>22.1%</td>
<td>23.4%</td>
<td>14.1%</td>
<td>19.2%</td>
<td>19.5%</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0022</td>
<td>0.0078</td>
<td>0.0562</td>
<td>0.0315</td>
<td>0.0054</td>
</tr>
<tr>
<td>EASI-75</td>
<td>40.3%</td>
<td>42.9%</td>
<td>38.5%</td>
<td>46.2%</td>
<td>42.9%</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td>0.0008</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PP-NRS ≥4</td>
<td>24.7%</td>
<td>27.3%</td>
<td>19.2%</td>
<td>24.4%</td>
<td>20.8%</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0006</td>
<td>0.0002</td>
<td>0.0057</td>
<td>0.0006</td>
<td>0.0038</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Percentage responders at Week 24</th>
<th>Amlitelimab 250 mg Q4W LD (N=77)</th>
<th>Amlitelimab 250 mg Q4W (N=78)</th>
<th>Amlitelimab 125 mg Q4W (N=77)</th>
<th>Amlitelimab 62.5 mg Q4W (N=79)</th>
<th>Placebo (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NRI*</td>
<td>All data†</td>
<td>NRI*</td>
<td>All data†</td>
<td>NRI*</td>
</tr>
<tr>
<td>IGA 0/1</td>
<td>45.5%</td>
<td>49.4%</td>
<td>33.3%</td>
<td>42.3%</td>
<td>40.3%</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0008</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EASI-75</td>
<td>54.5%</td>
<td>61.0%</td>
<td>38.5%</td>
<td>50.0%</td>
<td>49.4%</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0040</td>
<td>0.0002</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PP-NRS ≥4</td>
<td>31.2%</td>
<td>32.5%</td>
<td>24.4%</td>
<td>32.1%</td>
<td>28.6%</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0002</td>
<td>0.0001</td>
<td>0.0038</td>
<td>0.0001</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LD, loading dose; NRI, non-responder imputation; PP-NRS, Peak Pruritus Numerical Rating Scale.
## Primary Analysis Safety Summary (1/2)

*Aggregated data presented only as Part 2 (maintenance/withdrawal phase) remains ongoing*

<table>
<thead>
<tr>
<th>TEAEs through Week 24</th>
<th>Amlitelimab pooled dose groups</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=310</td>
<td>N=78</td>
</tr>
<tr>
<td>Any TEAEs</td>
<td>209 (67.4%)</td>
<td>47 (60.3%)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any SAEs</td>
<td>8 (2.6%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Any AESIs</td>
<td>6 (1.9%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Any TEAE leading to treatment discontinuation</td>
<td>14 (4.5%)</td>
<td>5 (6.4%)</td>
</tr>
</tbody>
</table>

**Amlitelimab demonstrated an acceptable safety profile at the Week 24 primary analysis**

- No SAE term occurred in more than 1 patient
- Of patients who reported a TEAE: in the pooled amlitelimab groups 196 (93.8%) were mild or moderate, and in the placebo group 44 (93.6%) were mild or moderate

**Anti-drug antibodies**

ADA levels were generally low and not found to impact the PK of amlitelimab

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ADA, anti-drug antibody; AESI, adverse event of special interest; SAE, serious adverse event; PK, pharmacokinetics; TEAE, treatment-emergent adverse event.
Primary Analysis Safety Summary (2/2)

Aggregated data presented only as Part 2 (maintenance/withdrawal phase) remains ongoing

<table>
<thead>
<tr>
<th>Most frequent TEAEs by PT through Week 24 (≥5% in pooled amlitelimab groups)</th>
<th>Amlitelimab pooled dose groups</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) unique patients (N=388)</td>
<td>N=310</td>
<td>N=78</td>
</tr>
<tr>
<td>Worsening AD</td>
<td>53 (17.1%)</td>
<td>30 (38.5%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>34 (11.0%)</td>
<td>7 (9.0%)</td>
</tr>
<tr>
<td>COVID-19</td>
<td>24 (7.7%)</td>
<td>5 (6.4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>19 (6.1%)</td>
<td>2 (2.6%)</td>
</tr>
</tbody>
</table>

There were no reports of:
- Parasitic infections or serious opportunistic infections
- Malignancy
- Severe injection site reactions
- Chills or aphthous ulcers as TEAEs
- Pyrexia or influenza/influenza-like illness within 72 hours of injection

There were overall low incidences of:
- Conjunctivitis*, balanced across treatment arms and placebo (1.6% pooled amlitelimab vs 3.8% placebo)
- Herpes infections’ in pooled amlitelimab (2.3%) versus placebo (2.5%)

---
AD, atopic dermatitis; COVID-19, coronavirus disease 2019; PT, preferred term; TEAE, treatment-emergent adverse event.
Amlitelimab Reduced Eosinophils, TARC, and Th2/Th17/Th22 Cytokines Upregulated in AD

- Reduced AD biomarkers and eosinophil counts with amlitelimab versus placebo at Weeks 16 and 24
- Greatest observed reduction in the 250 mg with LD arm
- A consistent dose-dependent trend and substantial decrease in eosinophils by Week 4

**Fold-Change From Baseline to Week 24 (mean ± 95% CI)**

- **Eosinophils**
- **IL-13**
- **TARC**
- **IL-17A**
- **IL-22**

AD, atopic dermatitis; CI, confidence interval; IL, interleukin; LD, loading dose; TARC, thymus and activation-regulated chemokine; Th, helper T cell.
Amlitelimab 250 mg With LD Showed Greatest Efficacy, Reduction of Blood AD Biomarkers, and Was Well Tolerated

Continued improvement on lesions and pruritus up to Week 24

• Significantly greater proportion of patients achieving **clinically meaningful improvements** in AD lesions and pruritus with amlitelimab versus placebo
• Potential for **durable and meaningful efficacy** in moderate-to-severe AD

---

**IGA 0/1**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients With IGA 0/1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (with LD)</td>
<td>22.1 (627) (21,47)</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.1 (25,51)</td>
</tr>
</tbody>
</table>

Proportion difference vs placebo (95% CI)

- p=0.0022
- p<0.0001

**EASI-75**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients With EASI-75 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (with LD)</td>
<td>40.3 (16,42) (23,50)</td>
</tr>
<tr>
<td>Placebo</td>
<td>11.4 (25,53)</td>
</tr>
</tbody>
</table>

Proportion difference vs placebo (95% CI)

- p=0.0001

**PP-NRS ≥4 Points Reduction From Baseline**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients With PP-NRS ≥4 Points Reduction From Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mg (with LD)</td>
<td>24.7 (9,30)</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.1 (12,37)</td>
</tr>
</tbody>
</table>

Proportion difference vs placebo (95% CI)

- p=0.0006
- p=0.0002

• OX40L-OX40 blockade inhibited Th2/Th17/Th22 inflammatory biomarkers
• Early reduction in eosinophil counts

• Amlitelimab was well tolerated
  • No chills or aphthous ulcers as TEAEs
  • No pyrexia or influenza/influenza-like illness within 72 hours of injection
  • Low rates of conjunctivitis or herpetic infections
  • TEAEs balanced across amlitelimab and placebo

---

*Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16 and Week 24. *All data are used for analysis regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are considered as non-responders at Week 16/Week 24. AD, atopic dermatitis; CI, confidence interval; EASI, Eczema Area and Severity Index; IGA, investigator global assessment; LD, loading dose; OX40L, OX40 ligand; PP-NRS, Peak Pruritus Numerical Rating Scale; TEAE, treatment-emergent adverse event; Th, helper T cell.
Concluding Remarks

- Greatest numerical efficacy across primary and key secondary endpoints with amlitelimab 250 mg with LD
- Improvement across a broad range of doses provides an opportunity to alleviate treatment burden by reducing dosing frequency

- STREAM-AD Part 2 will give further insight into the maintenance of effect on- and off-drug beyond Week 24

- Larger scale Phase 3 studies are soon to be initiated to support the efficacy and safety profile observed in the Phase 2b study

LD, loading dose.
Thank You

The authors also thank the study patients, trial staff, and investigators for their participation.