# EVIDENCE FOR ACTIVITY OF GBR 830 (ANTI-OX40) IN EXTRINSIC AND INTRINSIC ATOPIC DERMATITIS (AD) IN A PHASE 2A STUDY

EMMA GUTTMAN-YASSKY, MD, PHD,[1] JANET S LEE, PHD,[2] ANA PAVEL, PHD,[1]
YACINE SALHI, PHD,[3] GERHARD WOLFF, MD, PHD[3]
[1]ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, NEW YORK, NY, USA; [2]SUBITO SCIENCE LLC, WEST ORANGE, NJ, USA;
[3]GLENMARK PHARMACEUTICALS INC., PARAMUS, NJ, USA

## ABSTRACT

**Rationale:** GBR 830, a humanized, monoclonal antibody against the co-stimulatory receptor OX40 on activated T-cells, was evaluated in subjects with Extrinsic and Intrinsic AD.

**Methods:** Moderate-to-severe AD subjects (affected body surface area ≥10%, Eczema Area and Severity Index [EASI] ≥12, history of inadequate response to topical treatments) received intravenous GBR 830 10 mg/kg on Day 1/baseline and Day 29. Clinical scores (EASI, SCORAD [Scoring Atopic Dermatitis] and IGA [Investigator Global Assessment]) were analyzed post hoc according to AD subtype (Intrinsic vs. Extrinsic, per investigator's judgment) and IgE level (>500 vs <500 U/mL). Biopsies were collected for biomarker measurement.

**Results:** For subjects treated with at least one dose of GBR 830 (n=46), baseline clinical scores did not show marked differences according to AD subtype or IgE level. Nonetheless, decreases in SCORAD were observed during the study regardless of AD subtype or IgE level. Responses were observed shortly after the first dose of GBR 830 and maintained through the second dose and beyond. Eotaxins were analyzed for subjects with skin biopsies (n=29). Baseline CCL18 levels were numerically greater in subjects with Extrinsic vs Intrinsic AD, but levels for CCL17 and CCL26 were not different. Post-treatment eotaxin levels did not change.

**Conclusions:** GBR 830 treatment showed clinical benefit in subjects, regardless of AD subtype or IgE level. Reductions in SCORAD clinical scores were observed throughout the treatment period.

PRESENTED AT:
THE AMERICAN ACADEMY OF ALLERGY, ASTHMA & IMMUNOLOGY ANNUAL MEETING
FEBRUARY 22-25, 2019 I SAN FRANCISCO, CA

# KEY FINDINGS

## METHODS

- Randomized, double-blind, placebo-controlled, repeated-dose study conducted in 17 North American centers
- Three phases: screening (up to 30 days), treatment (Day 1 [baseline] and Day 29), follow-up (through Day 85)
- Treatment: randomization 3:1 to intravenous GBR 830 or placebo; 2 repeated doses (each 10 mg/kg, administered intravenously) on Days 1 and 29
- Post hoc analysis: In the GBR 830 group, clinical scores (EASI, SCORAD, and IGA) and eotaxin levels were analyzed according to atopic dermatitis (AD) subtype (intrinsic vs extrinsic, per investigator's judgment) and/or IgE level (>500 U/mL vs <500 U/mL)
  - Extrinsic AD is characterized primarily by high serum IgE, as well as personal/family history of allergies (eg, specific IgEs to food or aeroallergens)[1]
  - Intrinsic AD shares a similar clinical phenotype but exhibits normal serum IgE, absence of other atopic diseases, and lack of allergen-specific IgEs[1]

## RESULTS

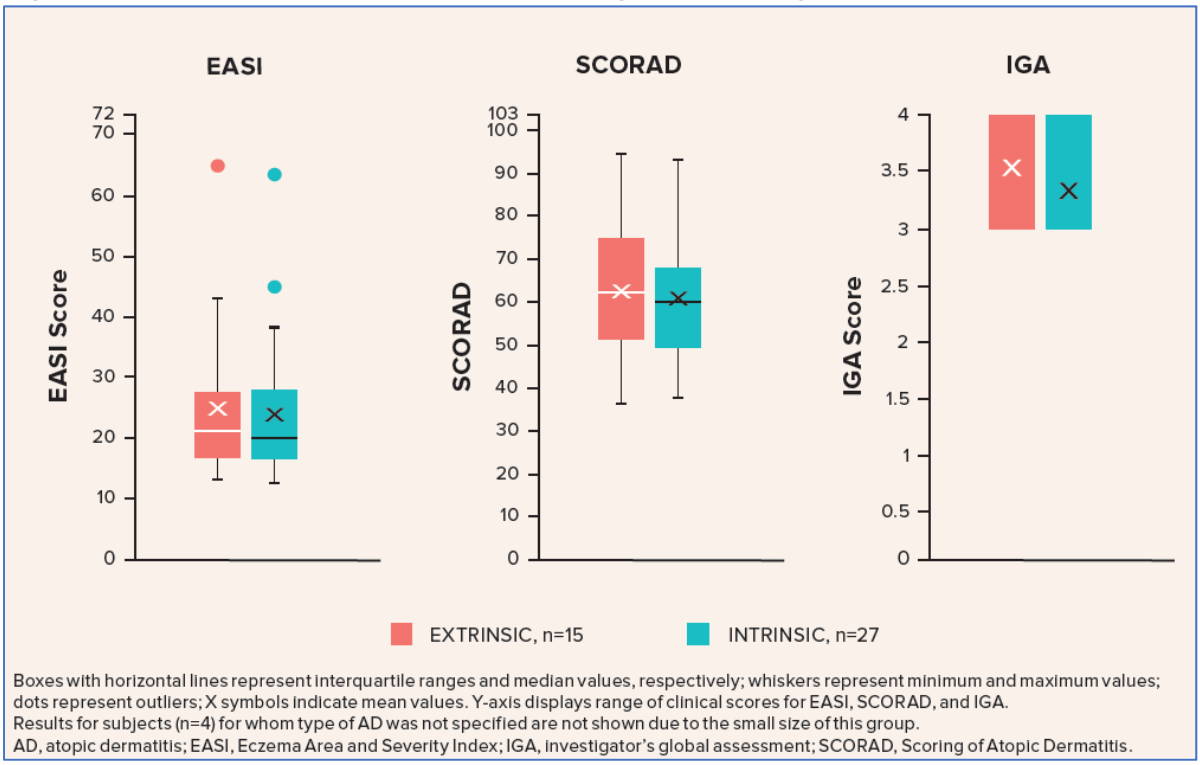
### Study Population

- Sixty-two randomized subjects (GBR 830, n=46; placebo, n=16) received ≥1 partial or full dose of study drug and were included in the analyses
  - Overall, mean age was 37.3 years, 48% were female, 68% were white, and mean affected body surface area was 1.85 $m^2$

### Post Hoc Analyses: Baseline Assessments

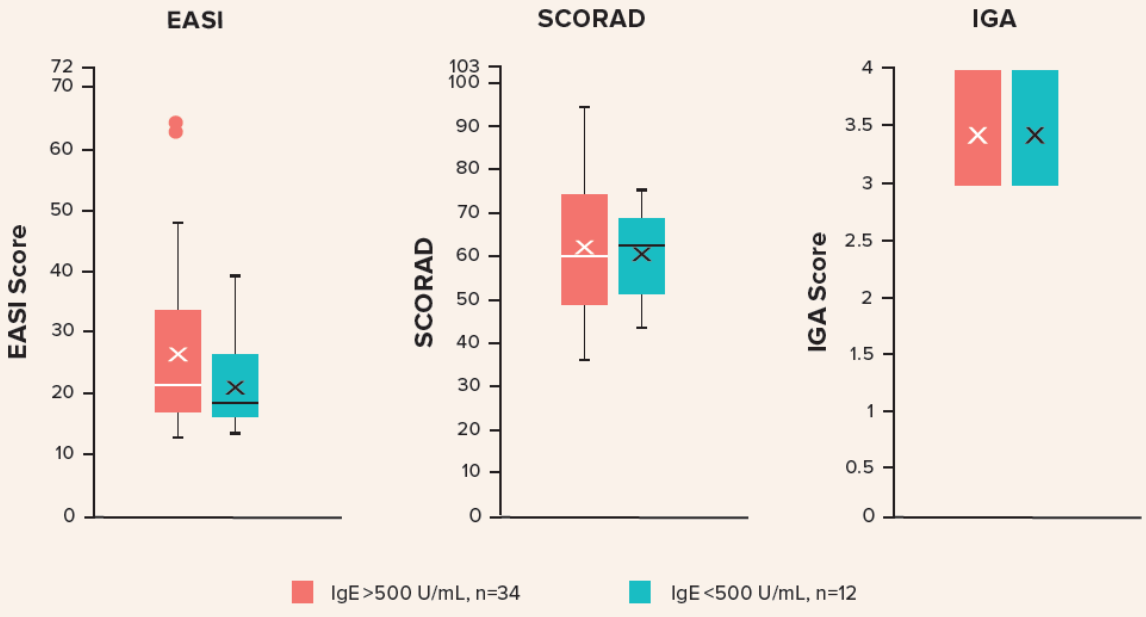
- Baseline clinical scores did not show marked differences according to AD subtype (**Figure 1**) or IgE level (**Figure 2**)

### Figure 1. Baseline Clinical Scores According to AD Subtype




Boxes with horizontal lines represent interquartile ranges and median values, respectively; whiskers represent minimum and maximum values; dots represent outliers; X symbols indicate mean values. Y-axis displays range of clinical scores for EASI, SCORAD, and IGA.
Results for subjects (n=4) for whom type of AD was not specified are not shown due to the small size of this group.
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, investigator's global assessment; SCORAD, Scoring of Atopic Dermatitis.

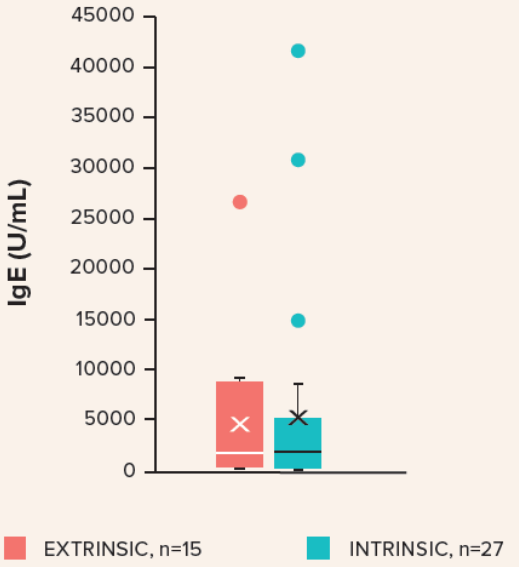
## Figure 2. Baseline Clinical Scores According to IgE Level




Boxes with horizontal lines represent interquartile ranges and median values, respectively; whiskers represent minimum and maximum values; dots represent outliers; X symbols indicate mean values. Y-axis displays range of clinical scores for EASI, SCORAD, and IGA.
EASI, Eczema Area and Severity Index; IGA, investigator's global assessment; IgE, immunoglobulin E; SCORAD, Scoring of Atopic Dermatitis.

- Serum IgE levels were also similar between subjects with extrinsic versus intrinsic AD (**Figure 3**)

## Figure 3. Baseline Serum IgE Levels According to AD Subtype

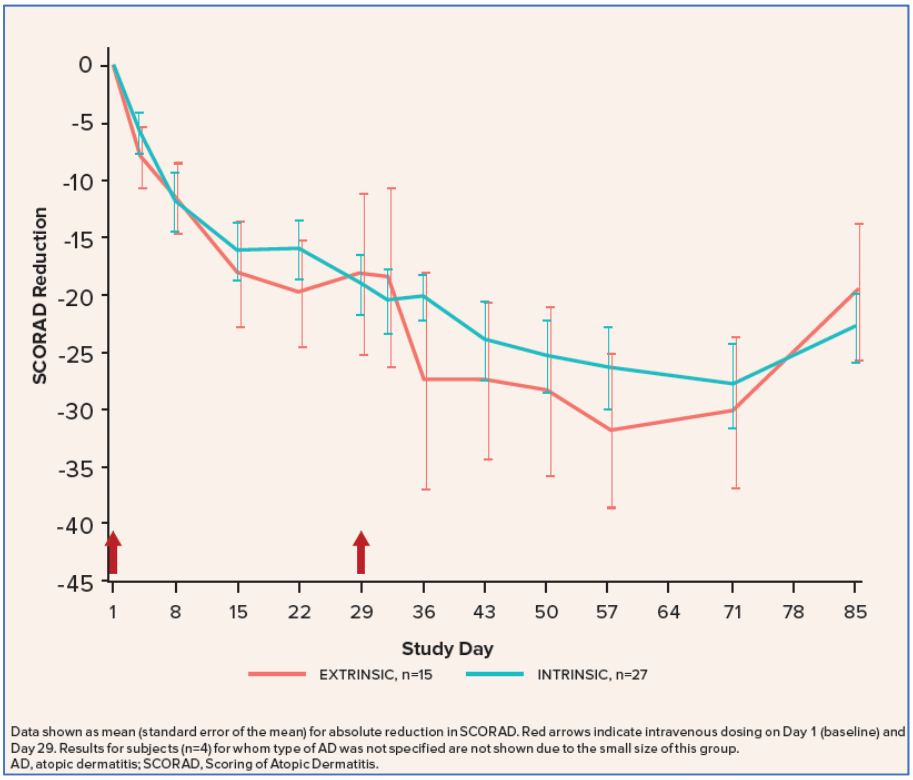



Boxes with horizontal lines represent interquartile ranges and median values, respectively; whiskers represent minimum and maximum values; dots represent outliers; X symbols indicate mean values.
Results for subjects (n=4) for whom type of AD was not specified are not shown due to the small size of this group.
AD, atopic dermatitis; IgE, immunoglobulin E.

## Post Hoc Analyses: Scoring of Atopic Dermatitis (SCORAD) Assessments

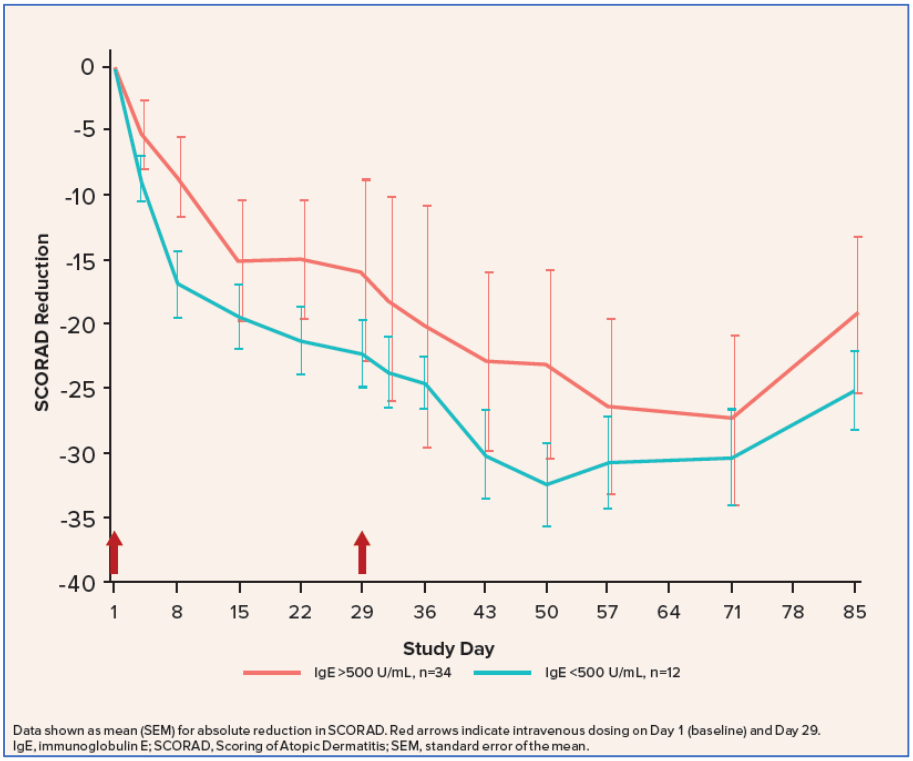
- Decreases in SCORAD were observed during the study regardless of AD subtype (**Figure 4**) or IgE level (**Figure 5**)

### Figure 4. SCORAD Change From Baseline Over Time According to AD Subtype




Data shown as mean (standard error of the mean) for absolute reduction in SCORAD. Red arrows indicate intravenous dosing on Day 1 (baseline) and Day 29. Results for subjects (n=4) for whom type of AD was not specified are not shown due to the small size of this group.
AD, atopic dermatitis; SCORAD, Scoring of Atopic Dermatitis.

### Figure 5. SCORAD Change From Baseline Over Time According to IgE Level

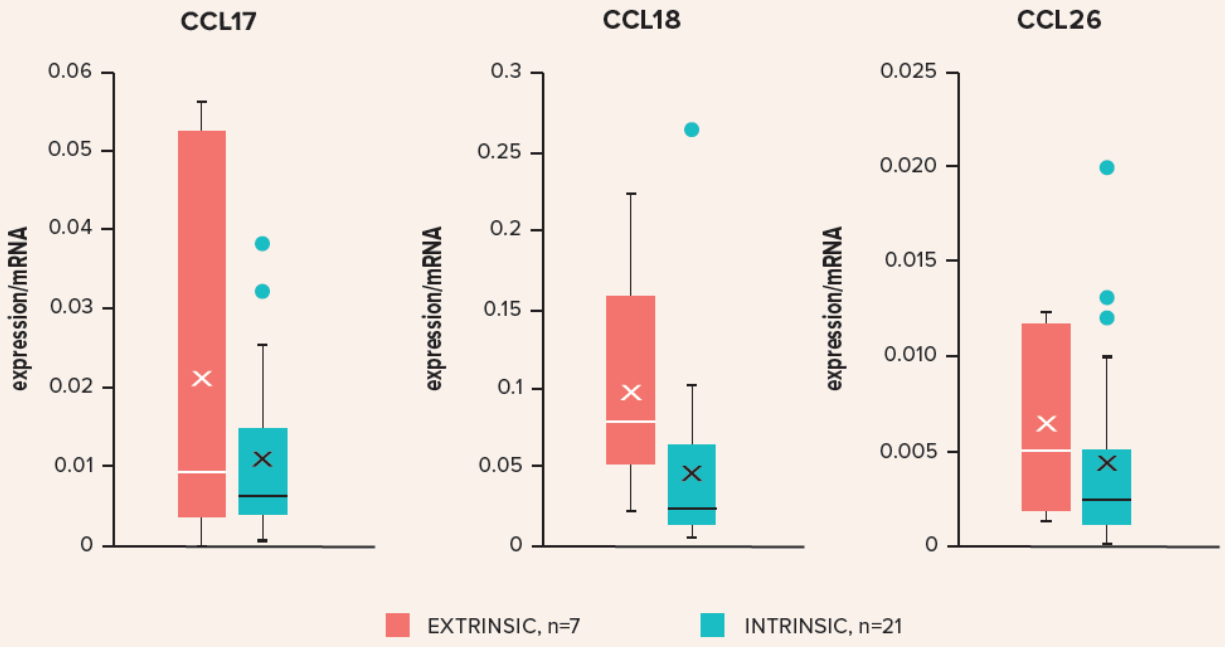



Data shown as mean (SEM) for absolute reduction in SCORAD. Red arrows indicate intravenous dosing on Day 1 (baseline) and Day 29.
IgE, immunoglobulin E; SCORAD, Scoring of Atopic Dermatitis; SEM, standard error of the mean.

### Post Hoc Analyses: Eotaxin Assessments

- Eotaxins (ie, CLL17, CCL18, and CCL26) were analyzed for GBR 830-treated subjects with skin punch biopsies (n=29)
- Median baseline CCL18 levels were numerically greater in subjects with extrinsic versus intrinsic AD, with smaller differences observed for CCL17 and CCL26 (**Figure 6**)
- By Day 29, change from baseline in post-treatment eotaxin levels was generally similar between the extrinsic and intrinsic groups (data not shown)

### Figure 6. Baseline Eotaxin Levels According to AD Subtype




Boxes with horizontal lines represent interquartile ranges and median values, respectively; whiskers represent minimum and maximum values; dots represent outliers; X symbols indicate mean values. Results for one subject for whom type of AD was not specified are not shown.
AD, atopic dermatitis.

## CONCLUSIONS

- In post hoc analyses, baseline clinical scores (EASI, SCORAD, IGA) did not show marked differences based on subject AD subtype (extrinsic vs intrinsic) or IgE level (>500 U/mL vs <500 U/mL)
- Reductions in SCORAD clinical scores were observed throughout the treatment period regardless of AD subtype or IgE level
- Although minor differences were observed in baseline eotaxin levels in subjects with extrinsic versus intrinsic AD, levels were generally similar post-treatment

## REFERENCE

1. Suárez-Fariñas M, Dhingra N, Gittler J, et al. *J Allergy Clin Immunol*. 2013;132(2):361-70.