GROWING OUR LEADERSHIP IN INFLAMMATION

OCTOBER 4, 2021

AMGEN®

SAFE HARBOR STATEMENT

This presentation contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd., Kyowa Kirin Co., Ltd., or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), or the Five Prime Therapeutics, Inc. acquisition, as well as estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes, effects of pandemics or other widespread health problems such as the ongoing COVID-19 pandemic on our business, outcomes, progress, or effects relating to studies of Otezla as a potential treatment for COVID-19, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this presentation and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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AGENDA

Introduction	**David Reese, M.D.—Executive Vice President, Research and Development**
Data Review	**Rob Lenz, M.D., Ph.D.—Senior Vice President, Global Development**
Commercial Landscape	**Murdo Gordon—Executive Vice President, Global Commercial Operations**
Q&A	**All**

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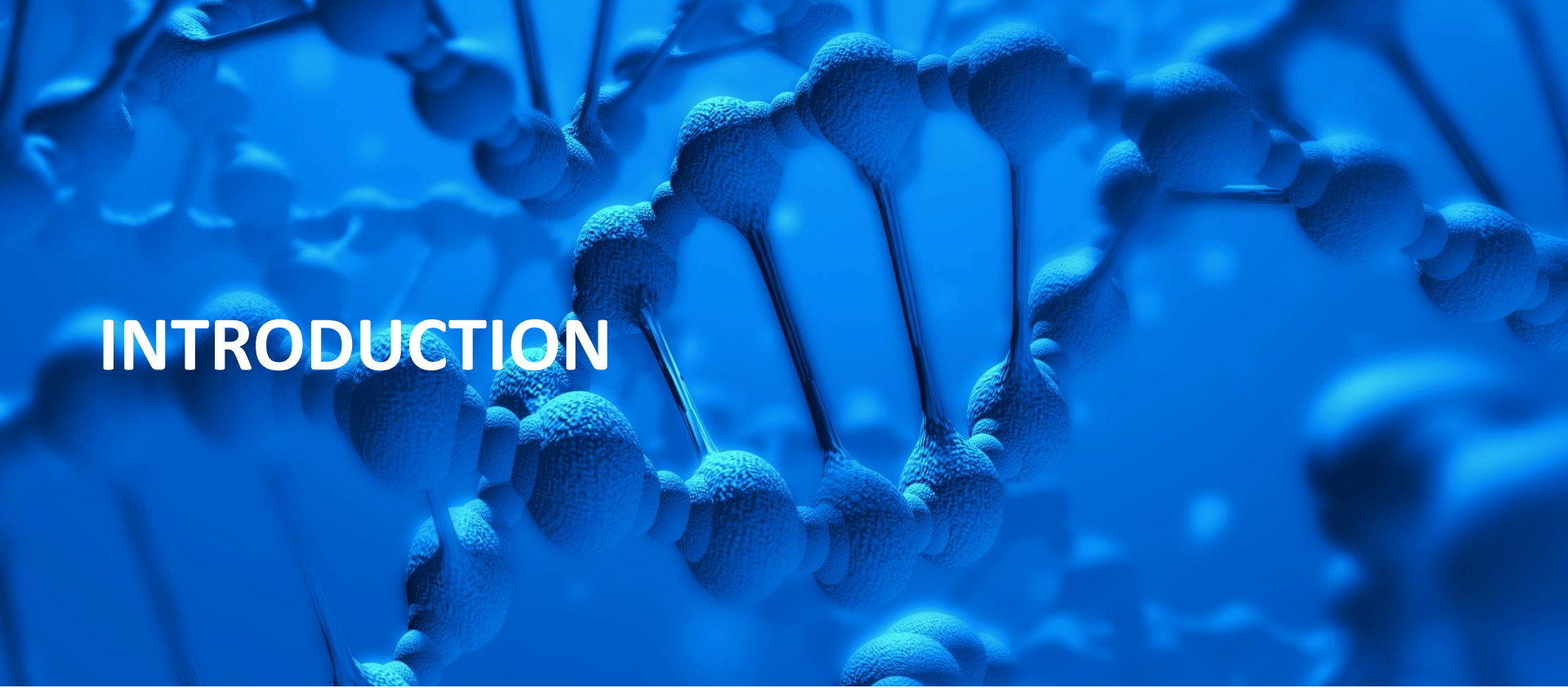

INTRODUCTION

DAVID REESE, M.D.

EXECUTIVE VICE PRESIDENT, RESEARCH AND DEVELOPMENT

AMGEN®

WE EXPECT INFLAMMATION TO BE A MEANINGFUL GROWTH DRIVER

- **Building on decades of established research, development, and commercial expertise**
- **Pursuing under-served markets with significant growth potential**
- **Launching first-in-class molecules, new indications and quality biosimilars in each of the next several years**
- **Leveraging human genetics — approximately half of our inflammation portfolio has human genetic validation**
- **Achieving significant near-term milestones for our late-stage programs**

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STEADY FLOW OF INFLAMMATION LAUNCHES AND LATE STAGE CLINICAL DATA THROUGH 2025

December 2021
Otezla®
U.S. approval
Mild-to-moderate
Psoriasis

Q1 2022
Tezepelumab
U.S. approval
Asthma

January 31, 2023
AMJEVITA™
U.S. launch*

H1 2024
Tezepelumab
Phase 3 completion*
Chronic Rhinosinusitis with Nasal Polyps

March 1, 2025
ABP 959
U.S. launch

H1 2022
AMG 451 / KHK4083
Phase 3 initiation
Atopic Dermatitis

H1 2023
Tezepelumab
Phase 2 completion*
Chronic Spontaneous Urticaria
Chronic Obstructive Pulmonary Disease

H1 2024
Efavaleukin alfa
Phase2 completion*
Systemic Lupus Erythematosus
Ulcerative Colitis

H2 2022
AMG 714 / PRV-015
Phase 2b completion
Celiac Disease

H2 2023
Rozibafusp alfa
Phase 2 completion*
Systemic Lupus Erythematosus

2022
ABP 654, ABP 938, ABP 959
Phase 3 completion*

Anticipated approval/launch denoted in green
AMJEVITA™ (adalimumab-atto) is a biosimilar candidate to HUMIRA®
ABP 654 is a biosimilar candidate to STELARA®
ABP 938 is a biosimilar candidate to EYLEA®
ABP 959 is a biosimilar candidate to SOLIRIS®

*Estimated Study Completion Date per clinicaltrials.gov; HUMIRA® is a registered trademark of AbbVie Biotechnology Ltd; STELARA® is a registered trademark of Janssen Pharmaceutica NV; EYLEA® is a registered trademark of Regeneron Pharmaceuticals, Inc.; SOLIRIS® is a registered trademark of Alexion Pharmaceuticals, Inc.; Tezepelumab is developed in collaboration with AstraZeneca; AMG 714 is developed in collaboration with Provention Bio.

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STEADY FLOW OF INFLAMMATION LAUNCHES AND LATE STAGE CLINICAL DATA THROUGH 2025

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Otezla®
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WE ARE PURSUING DIFFERENTIATED APPROACHES TO THE TREATMENT LANDSCAPE

Rebalancing the immune system

Block	Deplete	Tolerize	Repair
Inhibit well-validated targets using innovative modalities	Remove cells or molecules that cause disease	Enhance population of antigen-specific regulatory T cells	Regenerate cells that are damaged due to disease

We are leveraging our industry leading human genetics platform to advance innovative new therapies

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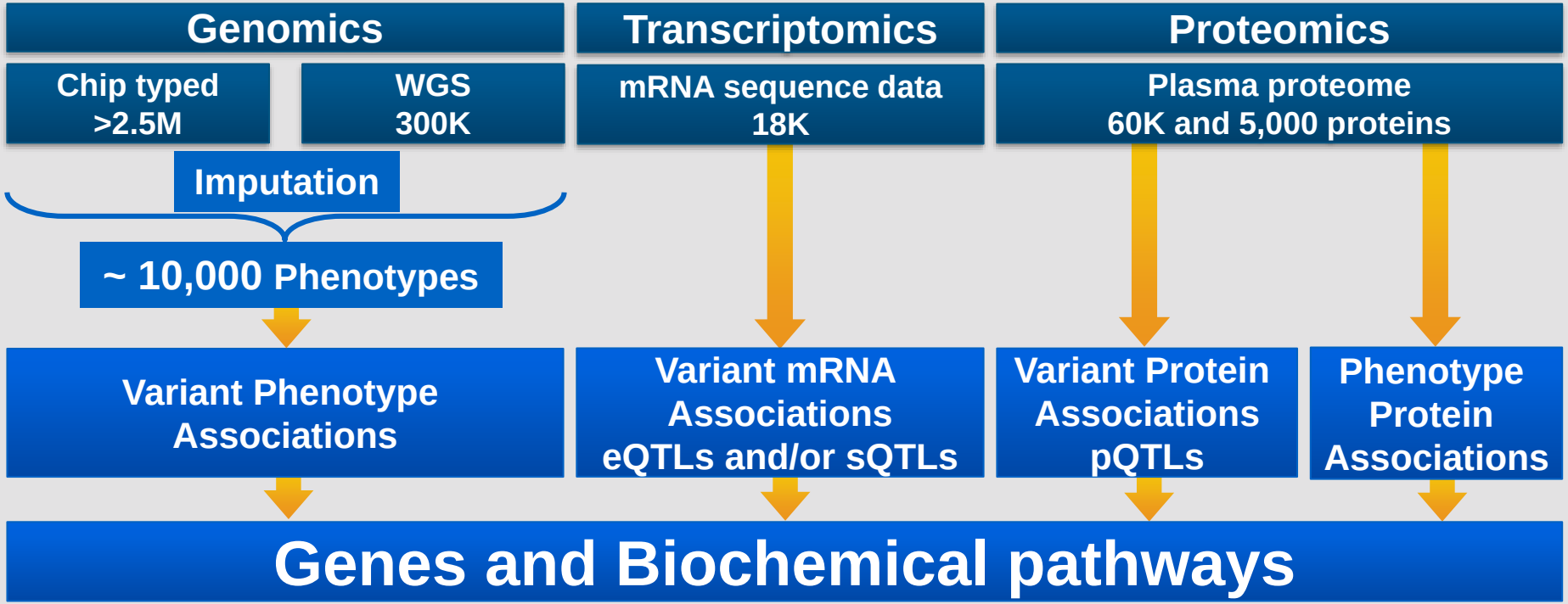
WE ARE LEVERAGING OUR INDUSTRY-LEADING HUMAN GENETICS PLATFORM TO ADVANCE INNOVATIVE NEW THERAPIES



WGS = whole genome sequencing; eQTL = expression quantitative trait loci; sQTL = splicing quantitative trait loci; pQTL = protein quantitative trait loci

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BROAD PORTFOLIO OF INFLAMMATION PRODUCTS*

Respiratory and Allergy

- Tezepelumab
  - Asthma
  - Chronic obstructive pulmonary disease
  - Chronic rhinosinusitis with nasal polyps
- AMG 714 / PRV015
  - Celiac disease

Gastrointestinal

- AMGEVITA™†
- AVSOLA™ Biosimilar to Remicade®*
- Efavaleukin alfa (AMG 592)
  - Ulcerative colitis
- ABP 654

Dermatology

- Enbrel®
- Otezla®
  - Psoriasis
  - Psoriatic arthritis
  - Palmoplantar pustulosis
- AMGEVITA™†
- AVSOLA™
- Tezepelumab
  - Chronic spontaneous urticaria
- AMG 451 / KHK4083
  - Atopic dermatitis
- ABP 654

Rheumatology

- Enbrel®
- Otezla®
  - Psoriatic arthritis
- AMGEVITA™†
- AVSOLA™
- Efavaleukin alfa
  - Systemic lupus erythematosus (SLE)
  - Graft vs. host disease
- Rozibafusp alfa (AMG 570)
  - Systemic lupus erythematosus
- ABP 654

*Phase 1 through marketed; †Approved in U.S. as AMJEVITA™; AVSOLA™ (infliximab-axxq) is a biosimilar to REMICADE®, a registered trademark of Janssen Biotech, Inc.

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INFLAMMATION PORTFOLIO REVIEW

ROB LENZ, M.D., PH.D.
SENIOR VICE PRESIDENT, GLOBAL DEVELOPMENT

MURDO GORDON
EXECUTIVE VICE PRESIDENT, GLOBAL COMMERCIAL OPERATIONS

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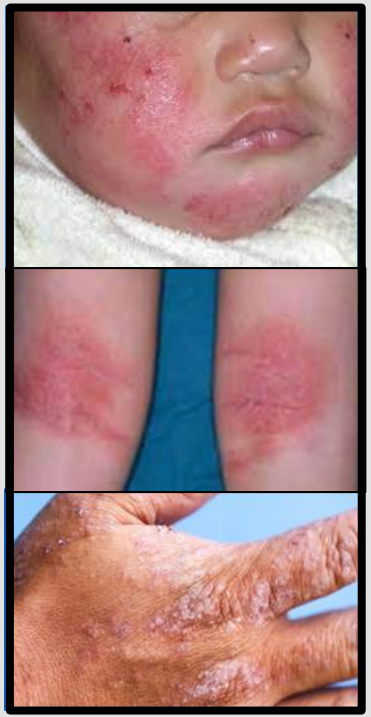
AMG 451 / KHK4083

A FIRST-IN-CLASS ANTI-OX40 MONOCLONAL ANTIBODY WITH POTENTIAL ACROSS INFLAMMATORY DISEASES

ATOPIC DERMATITIS IS A PREVALENT DISEASE WITH SIGNIFICANT UNMET NEED

- **Atopic dermatitis (AD) affects > 30 million people in major global markets, with particular unmet need in patients with moderate to severe disease**
  - **~ 15%-30% of children and up to 3% of adults**
  - **~ 1/3 have moderate to severe AD**
  - **~ 1/3 develop allergic rhinitis and ~ 1/3 develop asthma**
  - **Environmental triggers for flare-ups are highly unpredictable**
- **Symptoms include dry, scaly skin, pruritus (itching)**
- **New, effective therapies are needed in the current treatment paradigm**
  - **Topical corticosteroids and topical calcineurin inhibitors**
  - **Systemic immunosuppressant and biologics**



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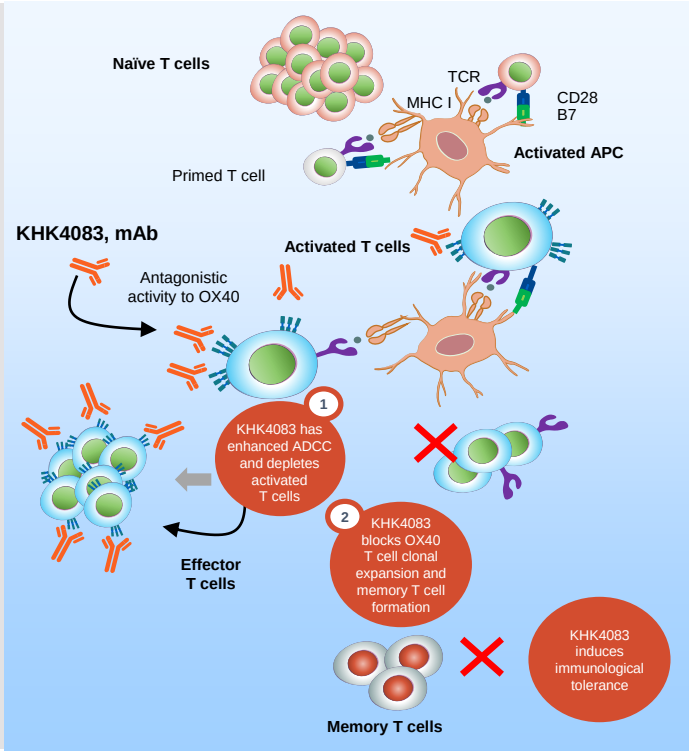
AMG 451 / KHK4083: PHASE 3-READY FOR ATOPIC DERMATITIS

- Activation of Th2 and other T cell subsets is central in atopic dermatitis
- The OX40–OX40L axis plays a critical role in long-lasting T cell responses
  - OX-40 ligand binding drives expression of pro-survival molecules and elevated cytokine production
- AMG 451 / KHK4083 is a fully human, afucosylated antibody with a dual mechanism of action
  - Blocks OX40 signaling
  - Depletes OX40 T cells
- T cell depletion reflected in clinical response
- Phase 3 initiation expected in H1 2022
- Amgen and Kyowa Kirin have a long history of successful collaboration on groundbreaking therapies



CD28 = cluster of differentiation 28; IgG = immunoglobulin G; MHC = major histocompatibility complex; mAb = monoclonal antibody; TCR = T cell receptor; Th2 = T-helper 2.

[1]Nakagawa H et al. J Dermatol Sci. 2020; 99(2):82–89; [2]Papp KA et al. J Eur Acad Dermatol Venereol. 2017, 31(8):1324–1332.

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Efficacy and Safety Results of KHK4083/AMG 451 (Anti-OX40 mAb) in Subjects With Moderate to Severe Atopic Dermatitis: A Phase 2, Multicentre, Randomized, Double-blind, Parallel-Group, Placebo-Controlled Study

Emma Guttman-Yassky,[1] Eric Simpson,[2] Kristian Reich,[3] Kenji Kabashima,[4] Ken Igawa,[5] Hidetoshi Takahashi,[6] Keizo Matsuo,[7] Yoshihiko Katahira,[8] Kazutomo Toyofuku,[9] Masatoshi Abe,[10] Margrit Simon,[11] Oliver Weirich,[12] Tetsuya Suzuki,[13] Shunichiro Orihara,[13] Takeshi Matsui,[13] Ehsanollah Esfandiari,[14] Masutaka Furue[15]

[1]Icahn School of Medicine at Mount Sinai, New York, USA; [2]Oregon Health & Science University, Portland, USA; [3]Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [4]Kyoto University, Kyoto, Japan; [5]Dokkyo Medical University Hospital, Tochigi, Japan; [6]Takagi Dermatological Clinic, Hokkaido, Japan; [7]Matsuo Clinic, Fukuoka, Japan; [8]Katahira Dermatology Clinic, Kagoshima, Japan; [9]Yamate Dermatological Clinic, Tokyo, Japan; [10]Sapporo Skin Clinic, Hokkaido, Japan; [11]Interdisciplinary Study Association GmbH, Berlin, Germany; [12]Rosenpark Research GmbH, Darmstadt, Germany; [13]Kyowa Kirin Co., Ltd., Tokyo, Japan; [14]Kyowa Kirin International Plc, London, UK; [15]Kyushu University, Fukuoka, Japan

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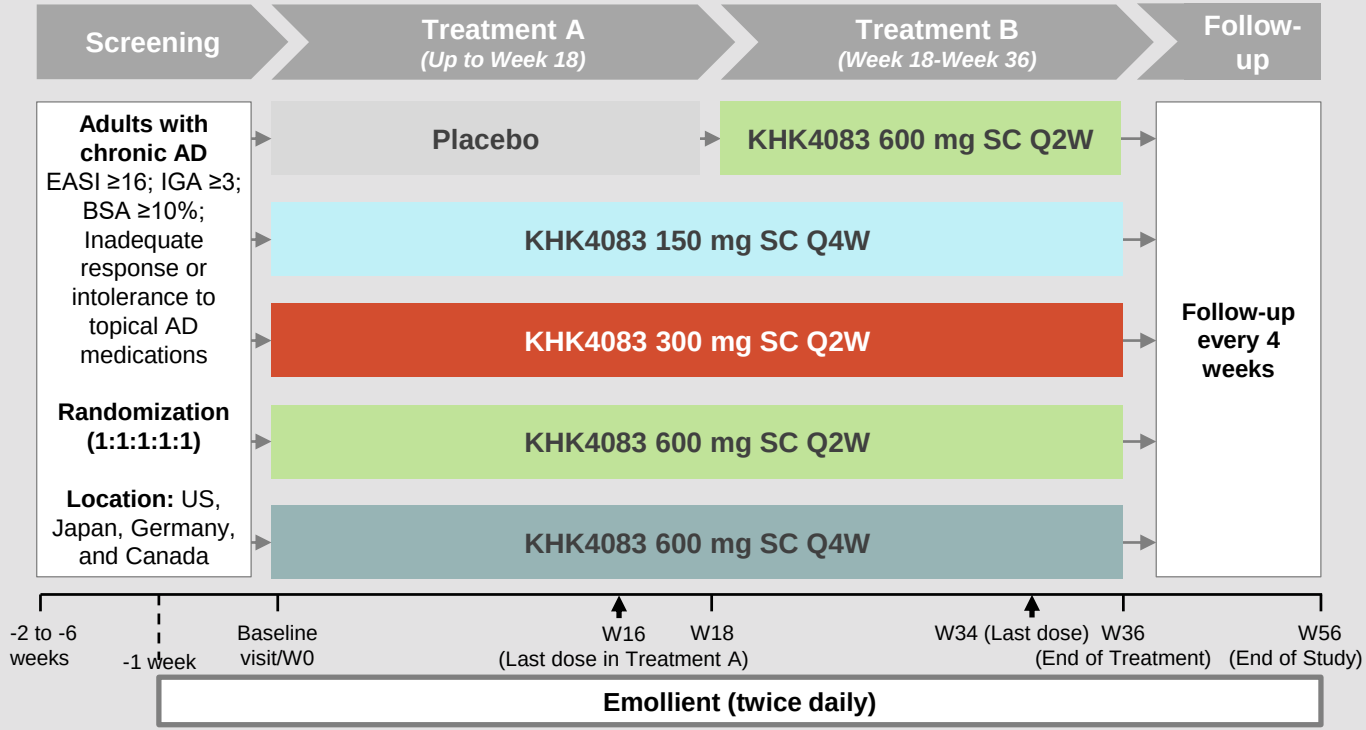
PHASE 2 STUDY DESIGN (NCT03703102)



Primary efficacy endpoint

- Percentage change in EASI score from baseline to Week 16

Secondary efficacy endpoints

- Reduction of ≥50%, ≥75%, and ≥90% in EASI score (EASI 50/75/90) from baseline
- Achievement of an IGA score of 0/1 and a reduction of ≥2 points from baseline (IGA0/1)
- Achievement of a reduction of ≥4 points in Pruritus-NRS score from baseline

Safety evaluations

- Adverse events

BSA =body surface area; EASI = Eczema Area and Severity Index; IGA = Investigator's Global Assessment; IP = Investigational product; NRS = Numerical Rating Scale; Q2W = every 2 weeks; Q4W = every 4 weeks; SC = subcutaneous; W = Week; Patients receiving rescue treatment before W36 assessment discontinued the IP and underwent end-of-study assessment.

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BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS (SAFETY ANALYSIS SET)

All baseline parameters were generally well-balanced among the treatment groups

Characteristics*		KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	Placebo/ KHK4083 600 mg Q2W N=57	Total N=273
Age, years		37.4 ± 13.6	38.9 ± 14.6	37.5 ± 14.1	37.3 ± 16.3	38.7 ± 14.4	38.0 ± 14.5
Sex, male, n (%)		37 (68.5)	31 (58.5)	31 (56.4)	30 (55.6)	31 (54.4)	160 (58.6)
Race, n (%)	Asian: Japanese	30 (55.6)	28 (52.8)	32 (58.2)	30 (55.6)	30 (52.6)	150 (54.9)
	Asian: Other	6 (11.1)	4 (7.5)	5 (9.1)	3 (5.6)	7 (12.3)	25 (9.2)
	Black or African American	3 (5.6)	1 (1.9)	2 (3.6)	1 (1.9)	6 (10.5)	13 (4.8)
	White	14 (25.9)	20 (37.7)	16 (29.1)	20 (37.0)	14 (24.6)	84 (30.8)
	Other	1 (1.9)	0	0	0	0	1 (0.4)
Body mass index at screening, kg/m^2		24.99 ± 4.81	24.69 ± 5.69	26.69 ± 7.24	25.19 ± 6.49	24.26 ± 5.23	25.16 ± 5.97
Duration from diagnosis of AD to randomization, years		6.47 ± 6.59	8.40 ± 8.32	8.59 ± 9.58	6.42 ± 5.69	6.41 ± 5.98	7.26 ± 7.32
Severity of AD - IGA, n (%)	3	30 (55.6)	28 (52.8)	30 (54.5)	29 (53.7)	31 (54.4)	148 (54.2)
	4	24 (44.4)	25 (47.2)	25 (45.5)	25 (46.3)	26 (45.6)	125 (45.8)
Pruritus-NRS score		7.8 ± 1.6	7.5 ± 2.3	7.5 ± 1.6	7.6 ± 1.9	7.2 ± 2.3	7.5 ± 2.0
EASI score		32.8 ± 13.1	32.5 ± 12.7	32.2 ± 13.4	31.1 ± 11.8	29.2 ± 13.3	31.5 ± 12.8
SCORAD score		68.75 ± 12.57	69.44 ± 13.64	68.52 ± 14.36	68.79 ± 14.36	66.35 ± 14.05	68.34 ± 13.76
Percent BSA		59.5 ± 23.7	59.1 ± 25.2	56.8 ± 21.8	55.3 ± 23.4	54.3 ± 23.5	56.9 ± 23.5
Previous use of biological products for treatment of AD, n (%)		7 (13.0)	5 (9.4)	8 (14.5)	8 (14.8)	9 (15.8)	37 (13.6)

*Data presented as mean ± SD, unless specified otherwise. Data presented from safety analysis set, which included patients who received at least 1 dose of KHK4083; 273 of the 274 randomized patients were included in the safety analysis set. SCORAD, Severity scoring of atopic dermatitis.

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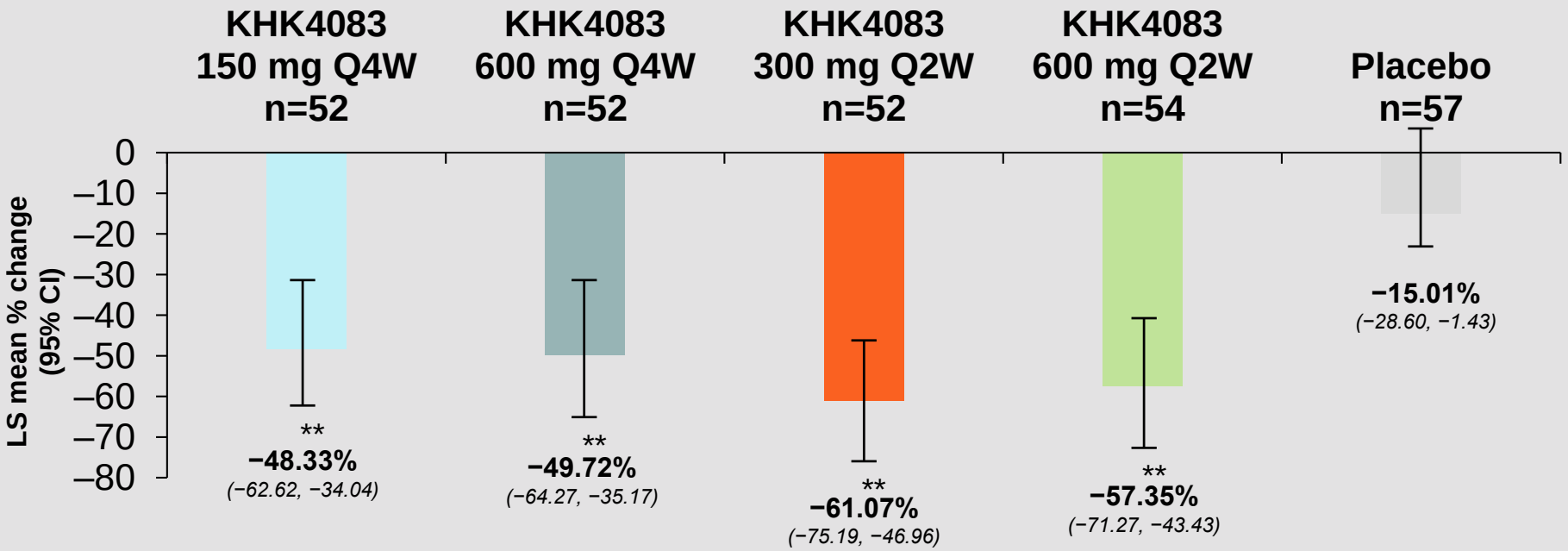
PRIMARY ENDPOINT: % CHANGE IN EASI SCORES (WEEK 16) FROM BASELINE (LAST OBSERVATION CARRIED FORWARD, FULL ANALYSIS SET)

All KHK4083-treated groups achieved the primary endpoint



**p<0.001 for difference versus placebo; LS = least square.

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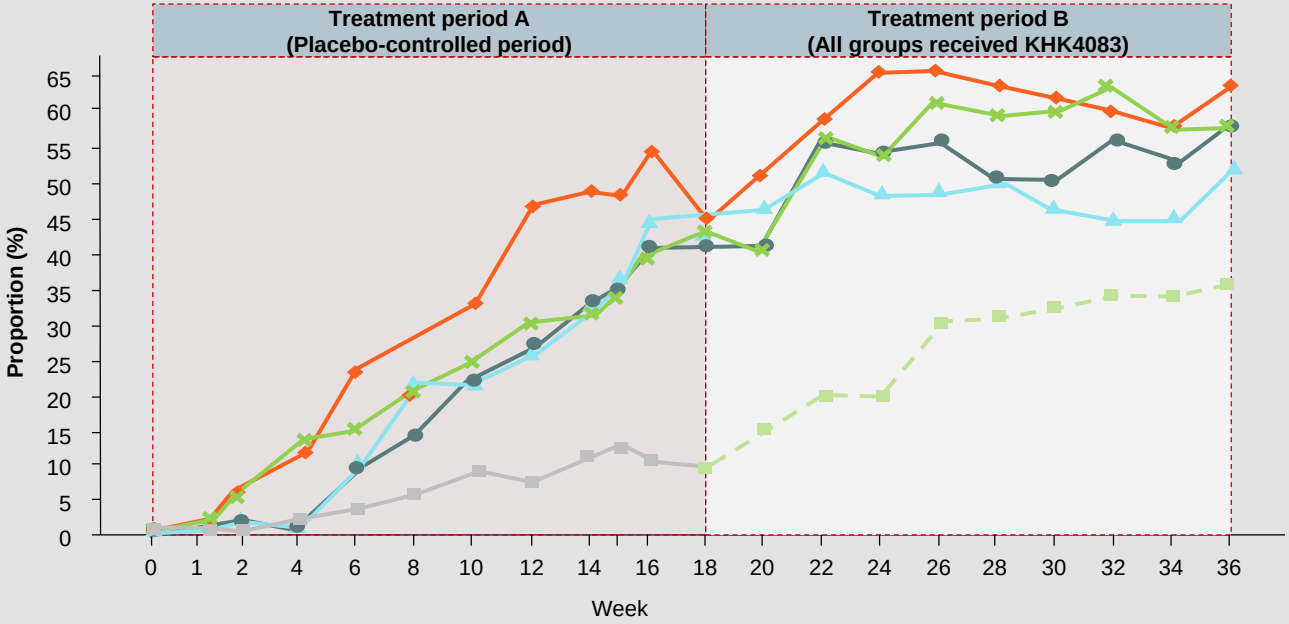
PROPORTION OF PATIENTS WHO ACHIEVED EASI-75 (NON-RESPONDER IMPUTATION, FULL ANALYSIS SET)

Proportions of EASI-75 responders at Week 16 were significantly higher in all KHK4083-treated cohorts versus placebo



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	44.2**	48.1	51.9
KHK4083 600 mg Q4W, %	40.4**	53.8	57.7
KHK4083 300 mg Q2W, %	53.8**	65.4	63.5
KHK4083 600 mg Q2W, %	38.9**	53.7	57.4
Placebo/KHK4083 600 mg Q2W, %	10.5	19.3	35.1

**p<0.001 vs placebo, assessed at Week 16

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

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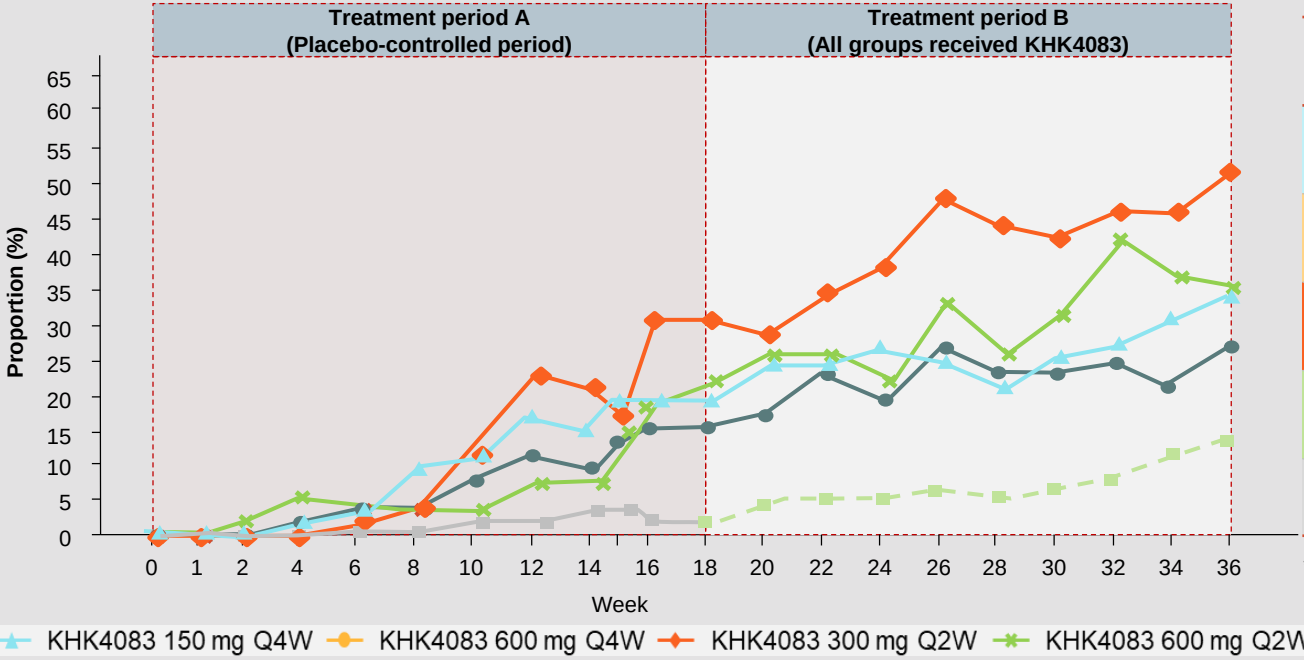
PROPORTIONS OF PATIENTS WHO ACHIEVED AN IGA SCORE OF 0/1 AND A REDUCTION OF ≥2 POINTS FROM BASELINE (NON-RESPONDER IMPUTATION, FULL ANALYSIS SET)

In all KHK4083 groups, the proportion of subjects who achieved IGA score 0/1 gradually increased up to Week 36



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	19.2*	26.9	34.6
KHK4083 600 mg Q4W, %	15.4*	19.2	26.9
KHK4083 300 mg Q2W, %	30.8**	38.5	51.9
KHK4083 600 mg Q2W, %	18.5*	22.2	35.2
Placebo/KHK4083 600 mg Q2W, %	1.8	5.3	14.0

*p<0.05, **p<0.001 vs placebo, assessed at Week 16

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

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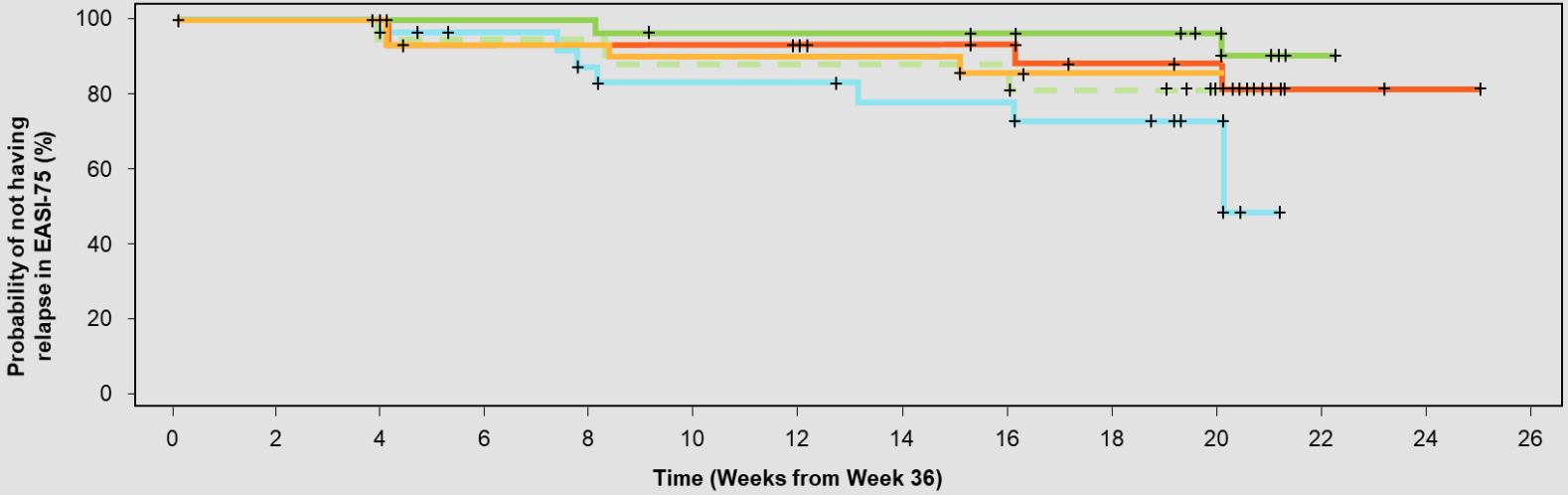
DURABILITY OF EASI-75 RESPONSE AFTER TREATMENT DISCONTINUATION IN SUBJECTS WHO ACHIEVED EASI-75 AT WEEK 36

EASI-75 response was durable even after discontinuation of KHK4083 at Week 36



KHK4083 150 mg Q4W	27	26	26	22	19	17	17	15	15	13	9	0	0	0
KHK4083 600 mg Q4W	30	29	29	27	27	26	26	26	24	22	16	0	0	0
KHK4083 300 mg Q2W	33	30	29	25	25	25	24	22	21	18	13	2	1	0
KHK4083 600 mg Q2W	31	27	27	25	25	21	21	21	20	19	17	1	0	0
Placebo/KHK4083 600 mg Q2W	20	18	18	16	16	13	13	13	13	11	7	0	0	0

+: censored; Note: Subjects in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. The numbers below the figure represent the number of remaining subjects at each visit. Note: Relapse is the loss of EASI-75 after achieving EASI-75 at Week 36. Note: Censored cases are prohibited concomitant medications and/or therapies including rescue treatment started before the event confirmed, study completion without the event confirmed, and early termination of the study without the event confirmed.

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TEAES – TREATMENT A PERIOD (SAFETY ANALYSIS SET)

In Treatment A period, 81% TEAEs occurred in KHK4083 groups versus 72% in the placebo group

Category	KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	KHK4083 Total N=216	Placebo N=57
Any TEAEs	37 (68.5)	45 (84.9)	47 (85.5)	46 (85.2)	175 (81.0)	41 (71.9)
Serious TEAEs	3 (5.6)	1 (1.9)	3 (5.5)	1 (1.9)	8 (3.7)	1 (1.8)
TEAEs leading to treatment discontinuation	5 (9.3)	3 (5.7)	7 (12.7)	4 (7.4)	19 (8.8)	12 (21.1)
All deaths	0	0	0	0	0	0
TEAEs with severity grade of ≥3	6 (11.1)	1 (1.9)	5 (9.1)	4 (7.4)	16 (7.4)	2 (3.5)

TEAE = treatment-emergent adverse event; Note: n=number of patients reporting at least 1 TEAE in that category except for all deaths. Data are presented as n (%).
Data presented from safety analysis set, which included patients who received at least 1 dose of investigational product; 273 of the 274 randomized patients were included in the safety analysis set.

AMGEN®

TEAES IN >5% OF SUBJECTS IN THE TOTAL KHK4083 GROUP BY PREFERRED TERM - TREATMENT A PERIOD (SAFETY ANALYSIS SET)

- The most frequent TEAEs in KHK4083 groups were pyrexia, nasopharyngitis, worsening of AD, and chills
- Events of pyrexia and chills were mild to moderate in intensity and were mostly observed only after the first administration of KHK4083 and were not associated with any consequent treatment discontinuation
- No hypersensitivity reactions were observed

Preferred Term	KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	KHK4083 Total N=216	Placebo N=57
Pyrexia	7 (13.0)	10 (18.9)	9 (16.4)	10 (18.5)	36 (16.7)	2 (3.5)
Nasopharyngitis	8 (14.8)	7 (13.2)	7 (12.7)	8 (14.8)	30 (13.9)	9 (15.8)
Dermatitis atopic	8 (14.8)	5 (9.4)	8 (14.5)	7 (13.0)	28 (13.0)	17 (29.8)
Chills	2 (3.7)	3 (5.7)	7 (12.7)	12 (22.2)	24 (11.1)	0
Headache	4 (7.4)	6 (11.3)	4 (7.3)	5 (9.3)	19 (8.8)	1 (1.8)
Aphthous ulcer	3 (5.6)	8 (15.1)	3 (5.5)	1 (1.9)	15 (6.9)	0
Nausea	3 (5.6)	2 (3.8)	1 (1.8)	7 (13.0)	13 (6.0)	1 (1.8)

PT = Preferred Term; Note: Adverse events were coded using MedDRA version 23.0. Data are presented as n (%).

AMGEN®

AMG 451/KHK4083: A FIRST-IN-CLASS ANTI OX40 ANTIBODY WITH POTENTIAL ACROSS INFLAMMATORY DISEASES

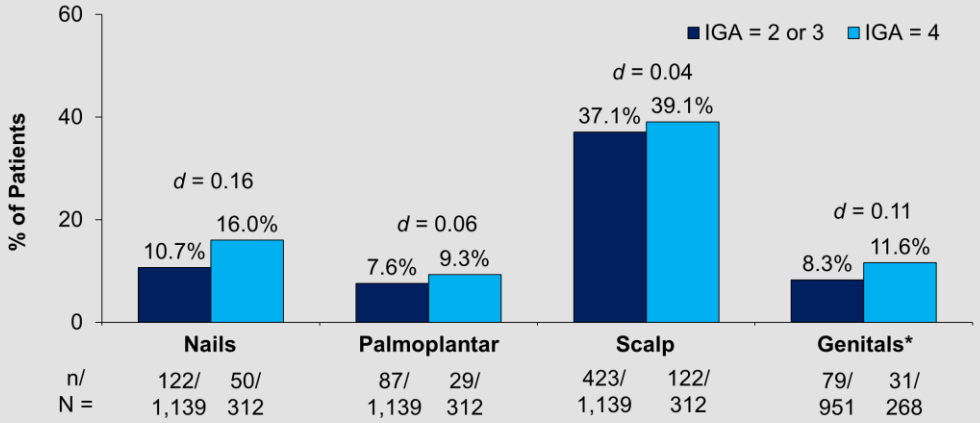
- **Novel mechanism of action blocks OX40 signaling and depletes OX40-expressing T cells**
- **Significant improvements in signs and symptoms of AD compared with placebo, across primary and secondary efficacy parameters at Week 16**
- **Progressive improvement in efficacy parameters beyond Week 16**
- **Sustained efficacy 20 weeks after treatment discontinuation**
- **May be a novel treatment option for patients with moderate-to-severe AD**
- **Given OX40 expression and proprietary human genetic data, we are exploring the potential in other inflammatory conditions**

OTEZLA®

POTENTIAL TO BE FIRST AND ONLY SYSTEMIC ORAL TREATMENT FOR ACTIVE PSORIATIC ARTHRITIS AND MILD TO SEVERE PSORIASIS

AMGEN®

BURDEN OF DISEASE IN MILD-TO-MODERATE PSORIASIS PATIENTS IS PERCEIVED TO BE THE SAME AS IN SEVERE PSORIASIS



*Genital morphology data were available for 951 patients with mild to moderate IGA and 268 patients with severe IGA.
d = standardized difference between groups; *d* > 0.1 considered a potentially meaningful difference.

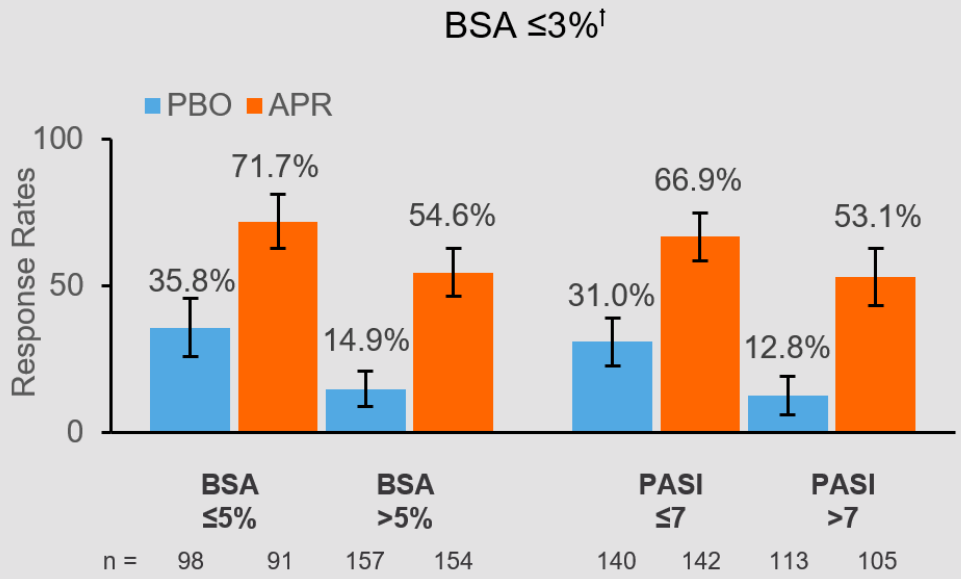
- **Systemic therapy-naïve patients with mild-to-moderate psoriasis were associated with**
  - **Bothersome symptoms, such as fatigue and psoriasis in special areas**
  - **Substantial quality-of-life burden**
  - **Overall burden of disease similarly high as severe psoriasis**

Data highlight the need for systemic oral therapies for mild to moderate psoriasis

Strober, et al. Abstract P1409 presented at EADV 30th Congress; 29 September–2 October 2021; IGA = investigator's global assessment.

AMGEN®

EFFICACY OF OTEZLA® IN MILD-TO-MODERATE PSORIASIS PATIENTS REGARDLESS OF DISEASE EXTENT AT BASELINE



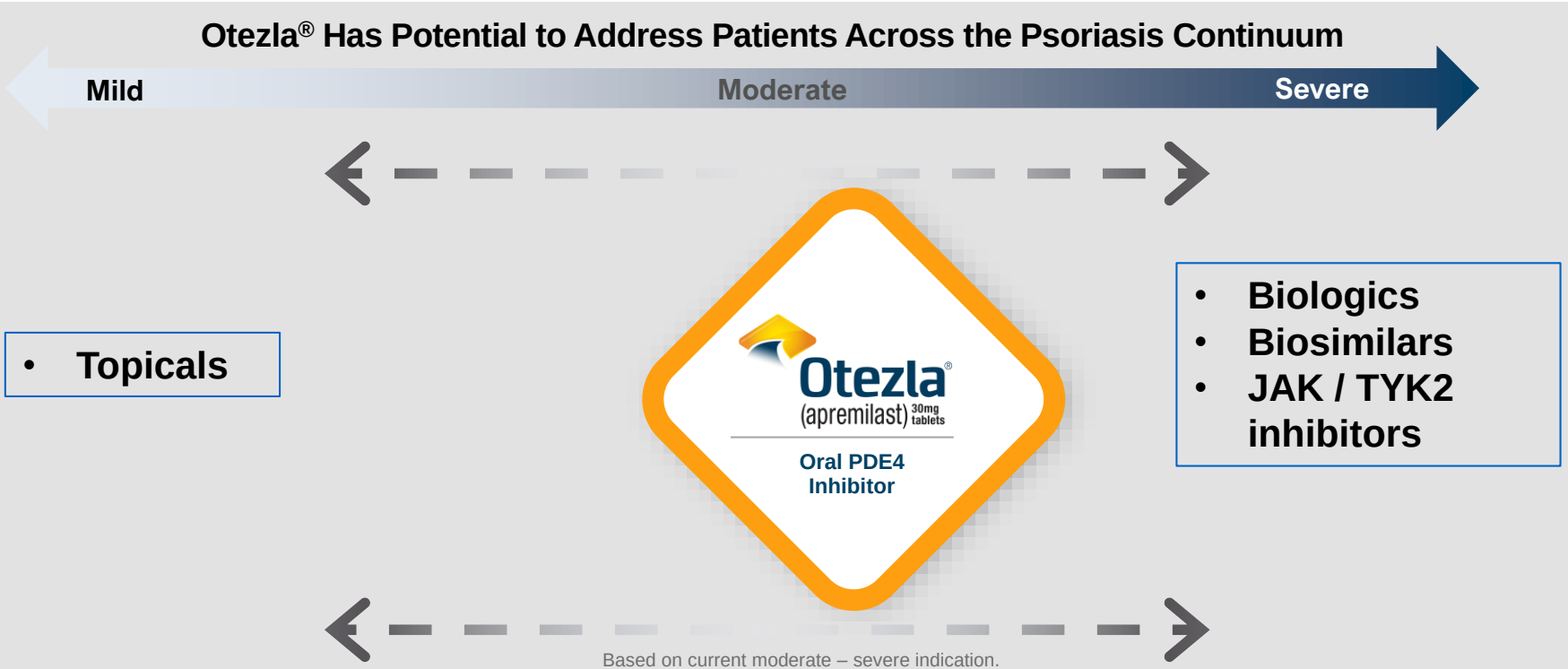
- **More than half of patients achieved target of BSA<3 at Week 16**
- **No new safety signals were identified**

ADVANCE study inclusion: Adults with mild-to-moderate plaque psoriasis (static Physician Global Assessment [sPGA] score of 2-3, with BSA of 2%-15% and PASI score of 2-15) who were biologic-naive and inadequately controlled with or intolerant to ≥1 topical therapy

Gold et al. Abstract P1334 presented at **EADV 30th Congress; 29 September–2 October 2021;** ITT population, multiple imputation was used for missing data. Error bars represent 95% CI.
*$p \leq 0.0001$ vs PBO by CMH test. †In patients with BSA >3% at baseline. PBO = placebo; APR = apremilast; BSA = body surface area; PASI = psoriasis area and severity index.

AMGEN®

MILD-TO-MODERATE PSORIASIS INDICATION COULD HELP OTEZLA® MOVE INTO EARLIER LINES OF TREATMENT



PDE4 = phosphodiesterase 4; JAK = janus kinase

Provided October 4, 2021, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

AMGEN®

OTEZLA® IS WELL-POSITIONED FOR CONTINUED GROWTH

- **Potential to be the first and only systemic oral treatment indicated for active psoriatic arthritis (PsA) as well as mild-to-severe psoriasis (PsO)**
- **Long-term safety profile, with no required lab monitoring or prescreening**
- **Over 90% of commercially insured lives have biologic step-free coverage for Otezla® in both PsA and PsO**
- **More than 700,000 patients have been treated across over 40 countries**
- **Approved in China—anticipated launch in 2022**

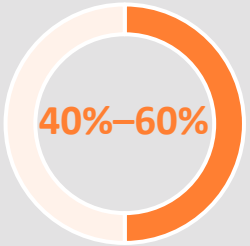
Approximately 1.5M additional patients to address in the mild-to-moderate psoriasis setting

TEZEPELUMAB

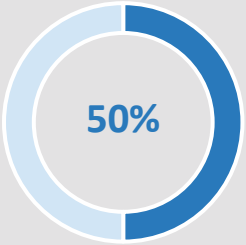
A FIRST-IN-CLASS INVESTIGATIONAL ANTI-TSLP MONOCLONAL ANTIBODY WITH DEMONSTRATED EFFICACY ACROSS A BROAD POPULATION OF PATIENTS WITH SEVERE UNCONTROLLED ASTHMA

AMGEN®

SIGNIFICANT UNMET MEDICAL NEEDS REMAINS IN TREATING SEVERE ASTHMA



of patients started on biologic therapy continue to experience ≥ 1 exacerbations per year[1]



have multiple drivers of inflammation[2,3]

have EOS < 300 in which current biologics have sub-optimal efficacy[4]

EOS = eosinophils; 1. Llanos et al. *J Asthma Allergy* 2020; 13:77-87. 2. Lambrecht BN, Hammad H. *Nat Immunol*. 2015;16(1):45-56. 3. Tran TN, Zeiger RS, Peters SP, et.al. *Ann Allergy Asthma Immunol*. 2016;116(1):37-42. 4. Symptom burden of severe uncontrolled asthma and its impact on patient qualify of life and productivity loss - a NOVELTY analysis of baseline data.

AMGEN®

SIGNIFICANT UNMET NEED IN PATIENTS WITH SEVERE UNCONTROLLED ASTHMA

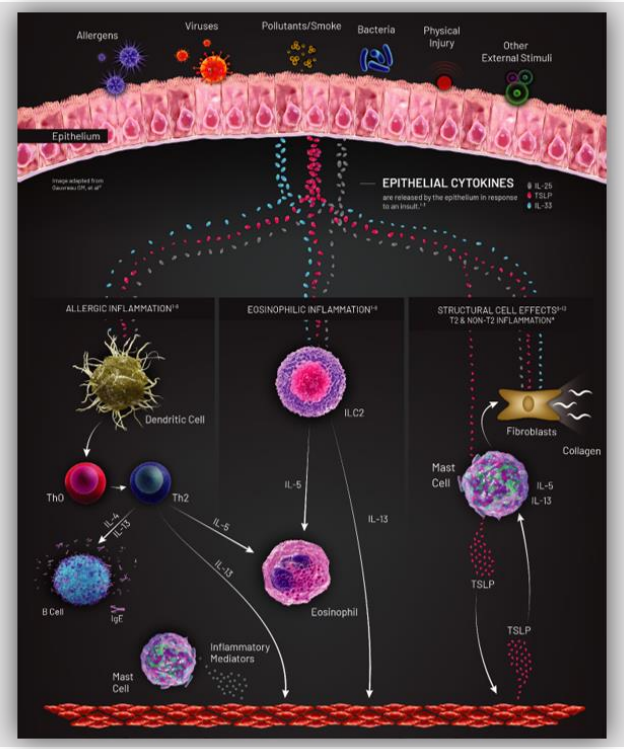
- **Patients with severe uncontrolled asthma experience significant symptoms that impact their quality-of-life**
  - **Frequent exacerbations requiring systemic/oral corticosteroids[1]**
  - **Serious exacerbations requiring 1.6M emergency room visits and 180K hospitalizations per year in the U.S.[2]**
- **Severe uncontrolled asthma accounts for 50% of asthma-related costs[3]**

1. American Lung Association. www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/learn-about-asthma/what-is-asthma. Accessed February 3, 2021; 2. Most Recent National Asthma Data, Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm; accessed September 24, 2021; 3. Nunes C, et al. *Asthma Res Pract*. 2017;3:2-11.

AMGEN®

TEZEPELUMAB: A DIFFERENTIATED, FIRST-IN-CLASS INVESTIGATIONAL THERAPY FOR SEVERE ASTHMA

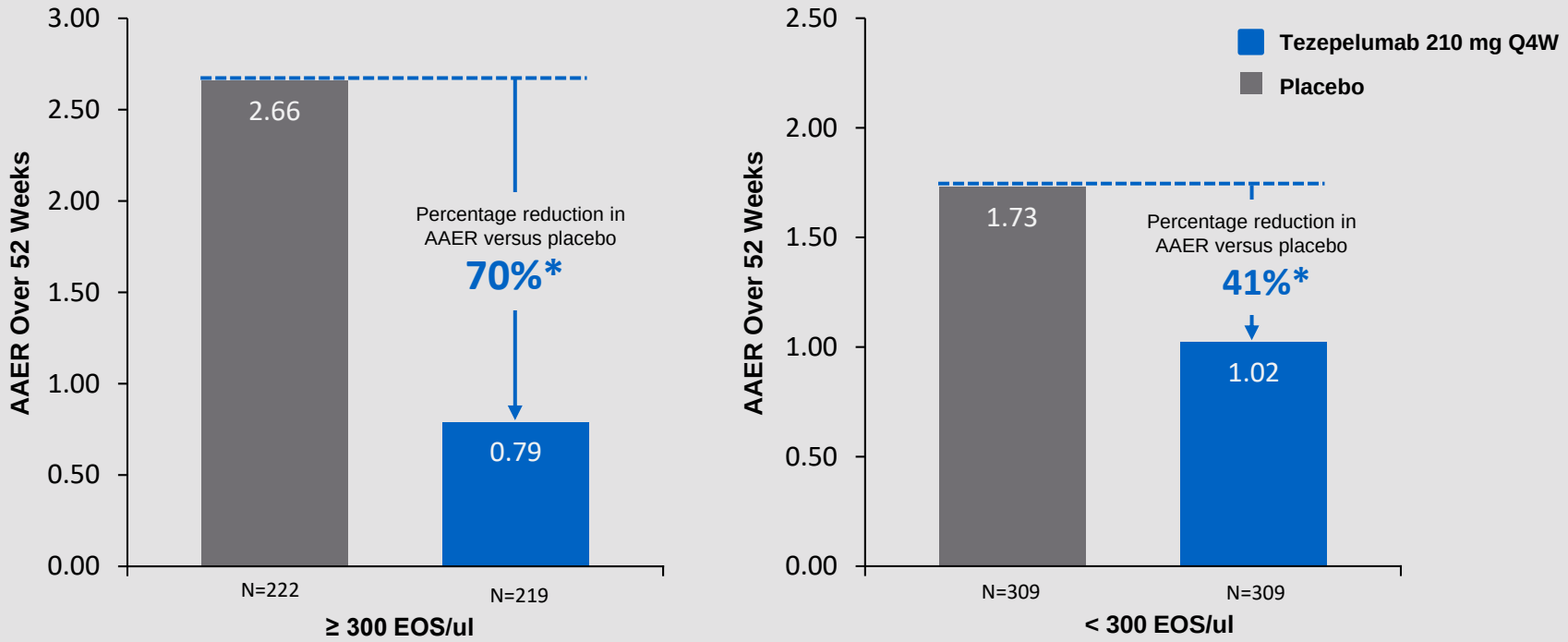
- **Tezepelumab is the first human monoclonal antibody that specifically blocks TSLP, a key epithelial cytokine at the top of the inflammatory cascade**
- **In response to insults, the airway epithelium releases alarmins, including TSLP, which can play a key role in driving allergic, eosinophilic, and non-T2 inflammation[1-4]**
- **Asthma is an epithelial-driven disease: the airway epithelium is a key source of an overreactive immune response[1-3]**
- **The airway epithelium is the first point of contact for viruses, allergens, pollutants, and other environmental insults[1-3]**
- **This immune response can lead to increased inflammation, causing continued asthma symptoms and exacerbations[1-6]**



TSLP = Thymic stromal lymphopoietin; 1. Gauvreau GM et al. *Expert Opin Ther Targets*. 2020;24:777–792. 2. Lambrecht BN, Hammad H. *Immunity*. 2019;50(4):975-991. 3. Lambrecht BN, Hammad H. *Nat Immunol*. 2015;16(1):45-56. 4. Brusselle G et al. *Nat Med*. 2013;19:977–979. 5. Brusselle G, Bracke K. *Ann Am Thorac Soc*. 2014;11(suppl 5):S322–S328. 6. Kaur D et al. *Chest.* 2012; 142(1):76-85. Tezepelumab is developed in collaboration with AstraZeneca.

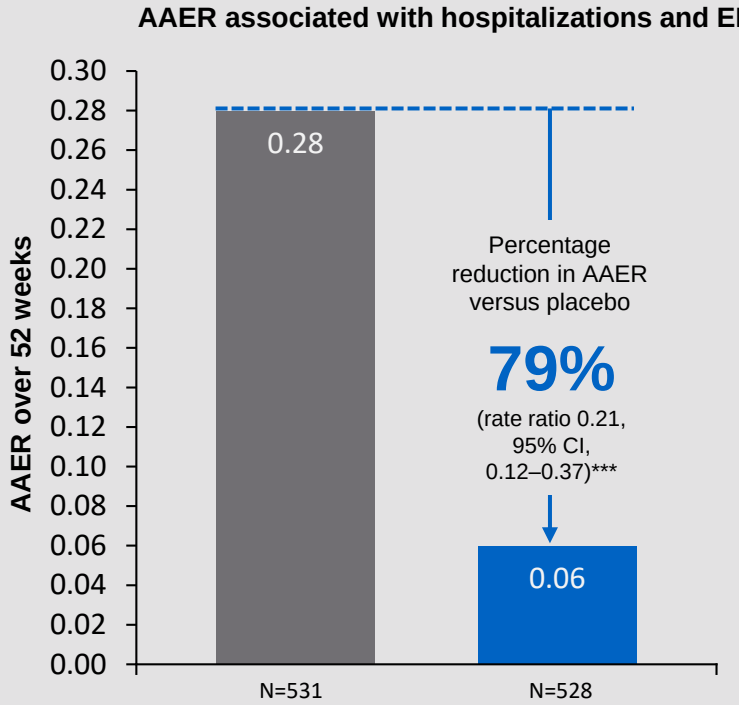
AMGEN

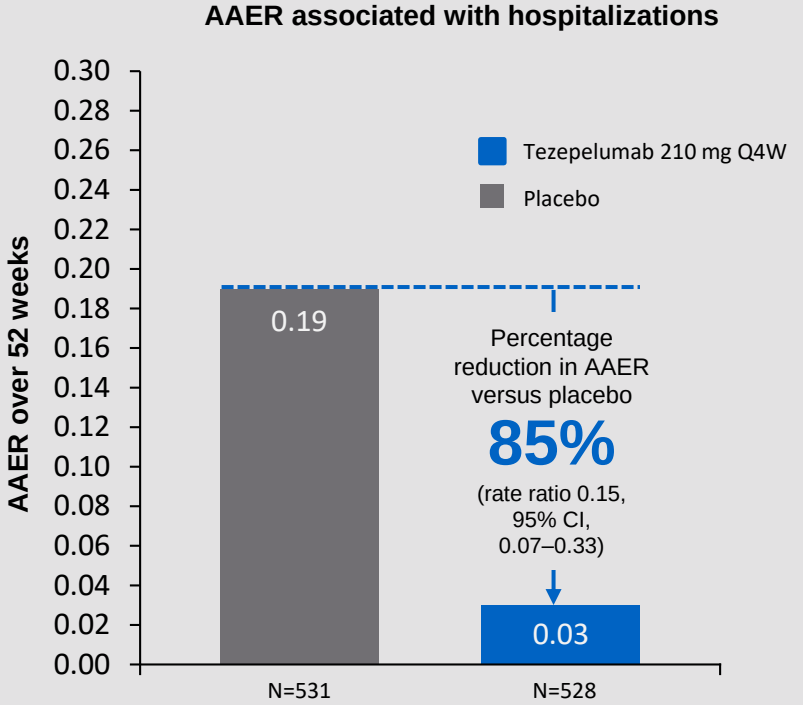
TEZEPELUMAB REDUCED EXACERBATIONS IRRESPECTIVE OF BASELINE EOSINOPHIL COUNTS AND ALLERGIC STATUS



*p<0.001 compared with placebo group; AAER = Annualized Asthma Exacerbation Rate

TEZEPELUMAB SIGNIFICANTLY REDUCED EXACERBATIONS REQUIRING HOSPITALIZATIONS OR ER VISITS





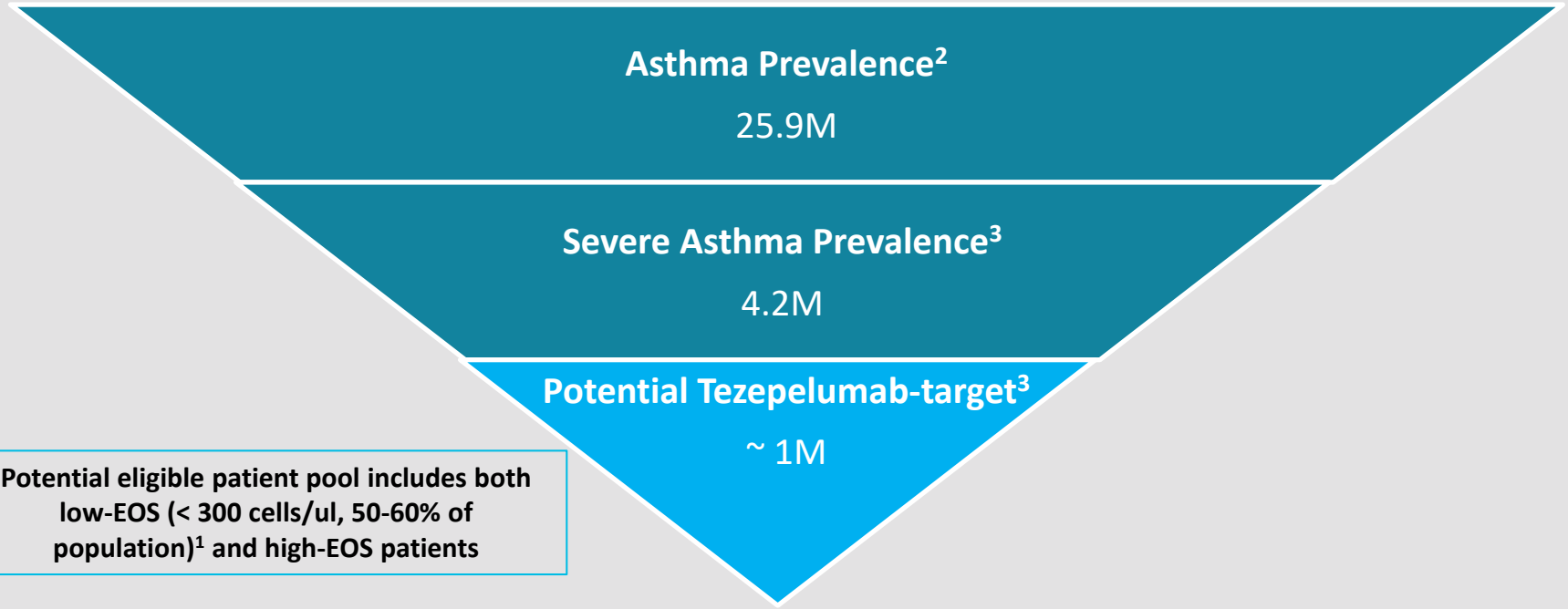
***p<0.001 compared with placebo group; AAER = Annualized Asthma Exacerbation Rate; ER = Emergency Room

AMGEN®

TEZEPELUMAB HAS THE POTENTIAL TO TRANSFORM CARE FOR PATIENTS WITH SEVERE ASTHMA

- **First and only biologic to demonstrate significant and clinically meaningful reductions in exacerbations irrespective of:**
  - **Eosinophil counts**
  - **Fractional exhaled nitric oxide levels**
  - **Allergic status**
- **No clinically meaningful differences in safety results vs. placebo**
- **Potential first-line biologic in broad population**
- **U.S. asthma submission under priority review, with PDUFA date in Q1 2022**

APPROXIMATELY 1 MILLION PATIENTS WITH SEVERE ASTHMA MAY BE ELIGIBLE FOR TEZEPELUMAB IN THE U.S.



Potential eligible patient pool includes both low-EOS (< 300 cells/ul, 50-60% of population)[1] and high-EOS patients

1. Symptom burden of severe uncontrolled asthma and its impact on patient qualify of life and productivity loss: a NOVELTY analysis of baseline data;
2. https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm accessed September 24, 2021; 3. IQVIA Longitudinal Access and Adjudication Data.

AMGEN®

TEZEPELUMAB LAUNCH WILL BENEFIT FROM AMGEN AND ASTRAZENECA'S SHARED CAPABILITIES

- **Commercialization of tezepelumab will reflect a "best of both" approach from Amgen and AstraZeneca**
  - **20 years of Amgen contracting and access in inflammation**
  - **50 years of AstraZeneca expertise in respiratory disease**
  - **Broad patient-support programs**
  - **Co-commercialization in U.S. and Canada, with coverage of both allergists and pulmonologists**
  - **Fully staffed respiratory sales force across Amgen & AstraZeneca**

The combined expertise of Amgen and AstraZeneca will be used to maximize the potential of tezepelumab to serve asthma patients

EXPLORING TEZEPELUMAB IN MULTIPLE INDICATIONS BEYOND SEVERE ASTHMA

- **Phase 3 study enrolling patients with chronic rhinosinusitis with nasal polyps**
- **Phase 2b study enrolling patients with chronic spontaneous urticaria**
- **Phase 2 study enrolling patients with COPD**

COPD = chronic obstructive pulmonary disease.

AMG 714 / PRV-015

FIRST-IN-CLASS INVESTIGATIONAL ANTI IL-15 MONOCLONAL ANTIBODY FOR THE TREATMENT OF CELIAC DISEASE

AMG 714 / PRV-015 – NOVEL APPROACH TO TREATING CELIAC DISEASE

- **Celiac disease is a serious autoimmune disease in genetically predisposed people where ingestion of gluten leads to small intestine damage**
  - **Affects ~ 0.7% of adults worldwide—up to 30% of patients have nonresponsive celiac disease (NRCD)[1,2]**
  - **There are no approved therapies for NRCD, and patients' quality-of-life can be significantly impaired**
- **IL-15 is upregulated in celiac disease and triggers an anti-apoptotic pathway, leading to accumulation of inflammatory lymphocytes**
- **AMG 714 is a human monoclonal antibody that binds to IL-15 and may restore intestinal lymphocyte apoptosis and reduce lymphocyte accumulation in the gut**
- **AMG 714 was well tolerated in 6 prior clinical trials with ~ 300 patients**
- **Proof of concept demonstrated in Phase 2a studies with no dose-limiting toxicities**
- **Phase 2b study is currently enrolling patients with NRCD**

1. Singh, et al. Clin *Gastroenterol Hepatol* 2018 ; 2. Rubio-Tapia, et al. *Am J Gastroenterol* 2013; IL-15 = interleukin 15; QoL = quality-of-life.

AMGEN®

EFAVALEUKIN ALFA

A NOVEL IL-2 MUTEIN DESIGNED TO SELECTIVELY INCREASE REGULATORY T CELLS

ROZIBAFUSP ALFA

A FIRST-IN-CLASS MULTISPECIFIC BIOLOGIC THAT TARGETS BAFF AND ICOSL SIMULTANEOUSLY

SYSTEMIC LUPUS ERYTHEMATOSUS IS AN AUTOIMMUNE DISEASE IN NEED OF NEW EFFECTIVE THERAPIES

- **Diagnosed prevalence estimate for SLE is ~ 250K in the U.S., ~ 500K in 7 major worldwide markets—expected to grow at 0.5% annually**
- **SLE is > 2X as prevalent in African Americans than other racial groups in the U.S.**
- **Females account for ~ 90% of the diagnosed prevalent cases; ~50% are of child-bearing age**
- **Fatigue and pain often result in missed work, job loss, and challenges with parenting and social relationships**
- **Only 2 therapies approved in the last 40 years**

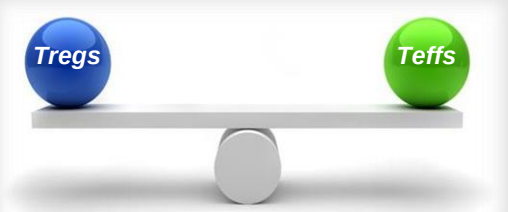
Sources: Barr et al. Patterns of disease activity in SLE, *Arth & Rheum.* 1999.;2. Harrison's Principles of Intern. Med. XII, p1922, 2009. Leerink Swann analysis, Adelphi 2015 SLE report.

EFAVALEUKIN ALFA

A NOVEL IL-2 MUTEIN DESIGNED TO SELECTIVELY INCREASE REGULATORY T CELLS

EFAVALEUKIN ALFA (AMG 592) IS AN IL-2 MUTEIN DESIGNED TO ADDRESS AUTOIMMUNE DISORDERS

- Regulatory T cells (Tregs) maintain balance in the immune system by negatively regulating other immune cells
- Treg impairment or deficiency has been reported in multiple human autoimmune conditions
- Phase 1a single ascending dose study in healthy volunteers demonstrated
  - Dose-dependent increases of Tregs and minimal to no increases in NK cells and T effector cells (Teffs)
  - Well tolerated
  - Phase 1b safety and PK data to be presented in Q4 ’21
- Studies underway in the following indications
  - Phase 2 for SLE in FDA’s Complex Innovative Trial Designs Pilot Program
  - Phase 2 for ulcerative colitis
  - Phase 1b for chronic graft vs. host disease



Normal Immune Homeostasis

NK = natural killer

Provided October 4, 2021, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

AMGEN®

ROZIBAFUSP ALFA

A FIRST-IN-CLASS MULTISPECIFIC BIOLOGIC THAT TARGETS BAFF AND ICOSL SIMULTANEOUSLY

AMGEN®

ROZIBAFUSP ALFA IS A FIRST-IN-CLASS, MULTISPECIFIC BIOLOGIC THAT TARGETS BAFF AND ICOSL SIMULTANEOUSLY

- T cell – B cell interactions are crucial in the production of autoreactive antibodies, a hallmark of autoimmune diseases such as SLE
- Interaction of inducible T cell co-stimulator (ICOS), with its sole ligand ICOSL, triggers key activities of T cells
- B-cell activating factor (BAFF) plays an important role in B-cell survival, maturation, and function
- Inhibition of both ICOSL and BAFF was more efficacious than single-target inhibition in preclinical models
- Rozibafusp alfa was successfully evaluated in Phase 1 clinical trials
  - Demonstrated acceptable safety, tolerability, and PK profile
  - Dose-dependent and reversible dual-target engagement (BAFF inhibition and high ICOSL receptor occupancy)
- Phase 2b study is enrolling patients with SLE

PK = pharmacokinetic.

AMGEN'S 20 YEARS OF LEADERSHIP IN INFLAMMATION

- TEZEPELUMAB
- AMG 451 / KHK4083
- AMG 714 / PRV-015
- AMG 570 (Rozibafusp alfa)
- AMG 592 (Efavaleukin alfa)
- Biosimilar candidates to
  - STELARA®
  - EYLEA®
  - SOLIRIS®

AMGEN®

SEVERAL INFLAMMATION BIOSIMILAR LAUNCHES TO GENERATE GROWTH

- **We commercialize biosimilars alongside our branded products, which creates a cost-effective selling model**
- **Successfully developed a $2 billion franchise**
- **EU leadership**
- **Broad portfolio that complements our branded products**
- **Sequential launch opportunities**
- **Large economic pool**

We see opportunity for meaningful portfolio growth from launches of additional biosimilars and expansion into new markets

BIOSIMILARS ARE ANNUALIZING AT $2 BILLION; FUTURE GROWTH TO BE DRIVEN BY SEQUENTIAL LAUNCHES

Originator Product	2020 WW Originator Sales	Therapeutic Area	Amgen Biosimilar	Amgen Biosimilar Status
AVASTIN®	~$5B	Hematology-Oncology	MVASI®	Launched in U.S. & EU
HERCEPTIN®	~$4B	Hematology-Oncology	KANJINTI®	Launched in U.S. & EU
Rituxan®	~$5B	Hematology-Oncology	RIABNI™	Launched in U.S.
Remicade®	~$4B	Inflammation	AVSOLA™	Launched in U.S.
HUMIRA®	~$20B	Inflammation	AMGEVITA™*	Launched in EU; 1/31/23 U.S. Launch
EYLEA®	~$8B	Inflammation	ABP 938	Phase 3
STELARA®	~$8B	Inflammation	ABP 654	Phase 3
SOLIRIS®	~$4B	Hematology-Oncology	ABP 959	Phase 3; 3/1/25 U.S. Launch
#9-11	~$27B	Undisclosed	Undisclosed	Process Development
Total	~$86B			

Our inflammation biosimilar candidates provide access to a market opportunity with ~ $40B of corresponding originator sales in 2020

*Approved in the U.S. as AMJEVITA™; MVASI® (bevacizumab-awwb) is a biosimilar to AVASTIN®, a registered trademark of Genentech, Inc.; KANJINTI® (trastuzumab-anns) is a biosimilar to HERCEPTIN®, a registered trademark of Genentech, Inc.; RIABNI™ (rituximab-arrx) is a biosimilar to Rituxan, a registered trademark of Biogen, Inc.

AMGEN®

SEQUENTIAL LAUNCHES OF BIOSIMILARS WILL STRENGTHEN OUR INFLAMMATION PRESENCE WITH PATIENTS

Phase 3 data will be followed by timely launches for our biosimilar candidates to STELARA®, EYLEA®, and SOLIRIS®

OUR BROAD INFLAMMATION PORTFOLIO BENEFITS FROM STRONG ACCESS CAPABILITIES

Respiratory and Allergy	Gastrointestinal	Dermatology	Rheumatology
			

- **Proven success in contracting over 20 years**
  - **Enbrel®: > 85% first-line coverage**
  - **Otezla®: > 90% first-line coverage**
- **Digital capabilities leveraged through the pandemic to address patients, healthcare providers, and payors**
- **Leading inflammation market-access account team**
  - **Amgen ranked #4 in 2021 Managed Care Account Management Performance survey**
- **Expanding capability through new Otezla® patient-access programs, upcoming tezepelumab launch, and biosimilars experience**

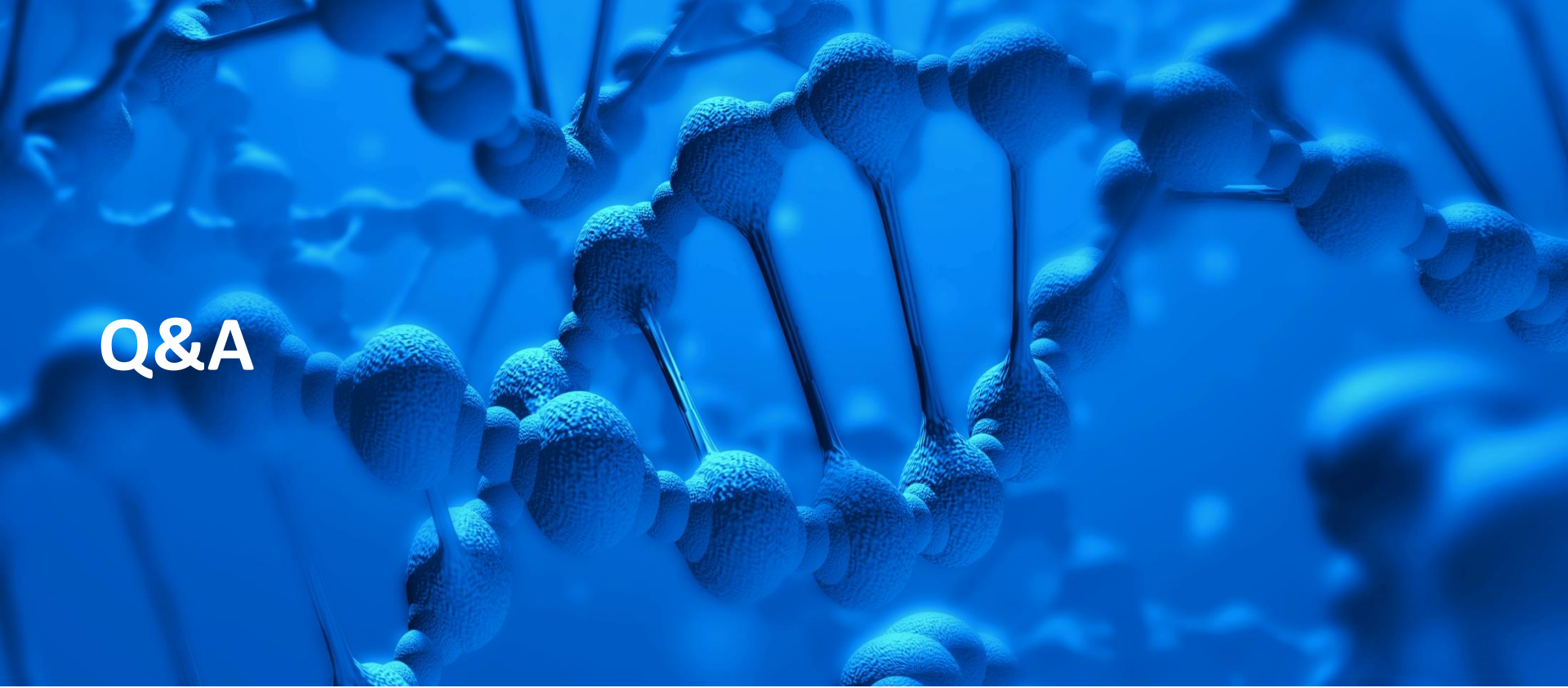
AMGEN®

WE EXPECT INFLAMMATION TO BE A MEANINGFUL GROWTH DRIVER

- Amgen is well-positioned to build on our ~20 years of leadership in inflammation
- We have near-term launch opportunities for multiple innovative molecules
  - Mild-to-moderate indication would allow Otezla® to treat patients across psoriasis continuum
  - Tezepelumab launch will leverage Amgen's and AstraZeneca's experience in inflammation
- We have a robust, innovative pipeline addressing areas of unmet need
  - Additional potential indications for tezepelumab and Otezla®
  - AMG 451 Phase 3 atopic dermatitis program anticipated to begin in H1 2022
  - Mid-stage pipeline of first-in-class programs in celiac disease (AMG 714/PRV-015), SLE (efavaleukin alfa, rozibafusp alfa), and UC (efavaleukin alfa)
- Biosimilars represent a meaningful growth opportunity
  - Phase 3 data for biosimilar candidates to STELARA®, EYLEA®, and SOLIRIS® expected in 2022

UC = ulcerative colitis.

AMGEN®


Q&A

AMG 451/KHK4083 PRESENTATION

AMGEN®

Efficacy and Safety Results of KHK4083/AMG 451 (Anti-OX40 mAb) in Subjects With Moderate to Severe Atopic Dermatitis: A Phase 2, Multicentre, Randomized, Double-blind, Parallel-Group, Placebo-Controlled Study

Emma Guttman-Yassky,[1] Eric Simpson,[2] Kristian Reich,[3] Kenji Kabashima,[4] Ken Igawa,[5] Hidetoshi Takahashi,[6] Keizo Matsuo,[7] Yoshihiko Katahira,[8] Kazutomo Toyofuku,[9] Masatoshi Abe,[10] Margrit Simon,[11] Oliver Weirich,[12] Tetsuya Suzuki,[13] Shunichiro Orihara,[13] Takeshi Matsui,[13] Ehsanollah Esfandiari,[14] Masutaka Furue[15]

[1]Icahn School of Medicine at Mount Sinai, New York, USA; [2]Oregon Health & Science University, Portland, USA; [3]Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [4]Kyoto University, Kyoto, Japan; [5]Dokkyo Medical University Hospital, Tochigi, Japan; [6]Takagi Dermatological Clinic, Hokkaido, Japan; [7]Matsuo Clinic, Fukuoka, Japan; [8]Katahira Dermatology Clinic, Kagoshima, Japan; [9]Yamate Dermatological Clinic, Tokyo, Japan; [10]Sapporo Skin Clinic, Hokkaido, Japan; [11]Interdisciplinary Study Association GmbH, Berlin, Germany; [12]Rosenpark Research GmbH, Darmstadt, Germany; [13]Kyowa Kirin Co., Ltd., Tokyo, Japan; [14]Kyowa Kirin International Plc, London, UK; [15]Kyushu University, Fukuoka, Japan

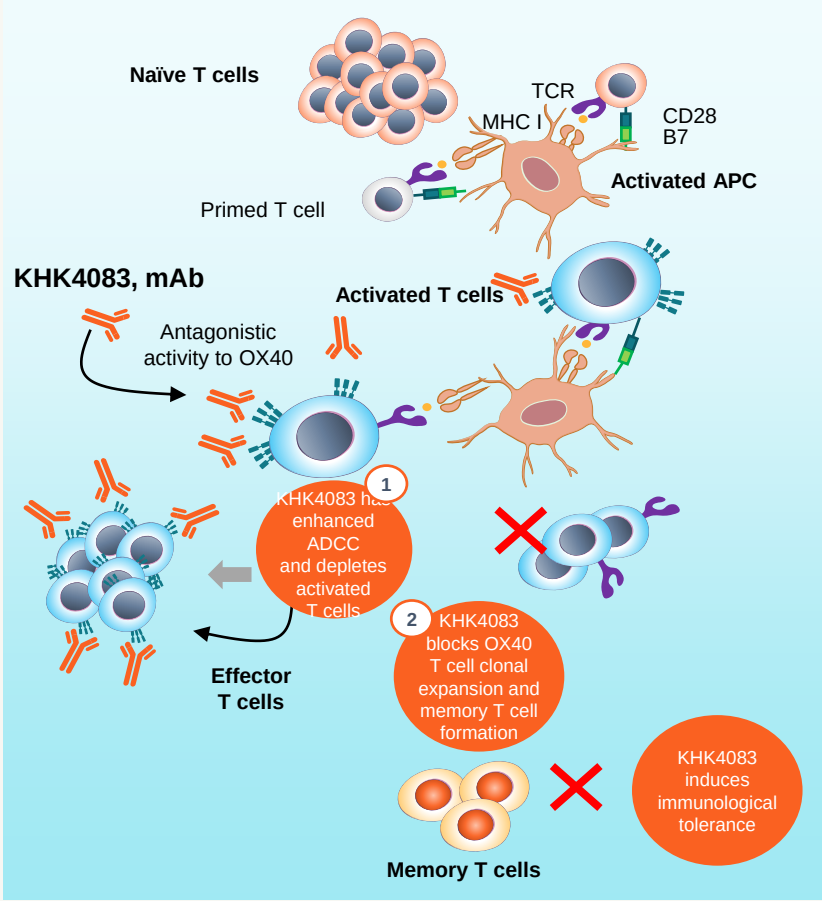
Speaker Disclosures

- Research support, consulting or lecture fees on atopic dermatitis received from Regeneron, Sanofi, Pfizer, Galderma, Celgene, Leo Pharma, Janssen, Medimmune, Dermira, Anacor, AnaptysBio, Glenmark, Novartis, Abbvie, GSK, Sun Pharma, Mitsubishi Tanabe, Vitae, Almirall, Asana Biosciences, Amgen, Immune, Gilead, Concert, Kyowa Kirin, DS Biopharma, Ralexar, Eli Lilly, UCB, Escalier, Boehringer, Botanix, Incyte, Sienna, Innovaderm, Cara Therapeutics, Dermavant, Union Therapeutics, Kiniksa, Arena, FLX Bio, Target

- No patents, ownership, or financial gain achieved from any atopic dermatitis drug

KHK4083/AMG 451 targets OX40 as a potential novel target for AD treatment

- Activation of Th2 and other T-cell subsets is central in atopic dermatitis (AD)
- The OX40–OX40L axis plays a critical role in long-lasting T-cell responses
  - OX40 is primarily expressed by activated T cells and binds OX40L on antigen-presenting cells (APCs), facilitating the effector function of T cells
- KHK4083/AMG 451 is a fully human, anti-OX40, non-fucosylated IgG1 monoclonal antibody with enhanced antibody-dependent cellular cytotoxicity (ADCC)[1]
  - It inhibits and depletes activated T cells, inhibiting T-cell clonal expansion and memory T-cell formation[2]

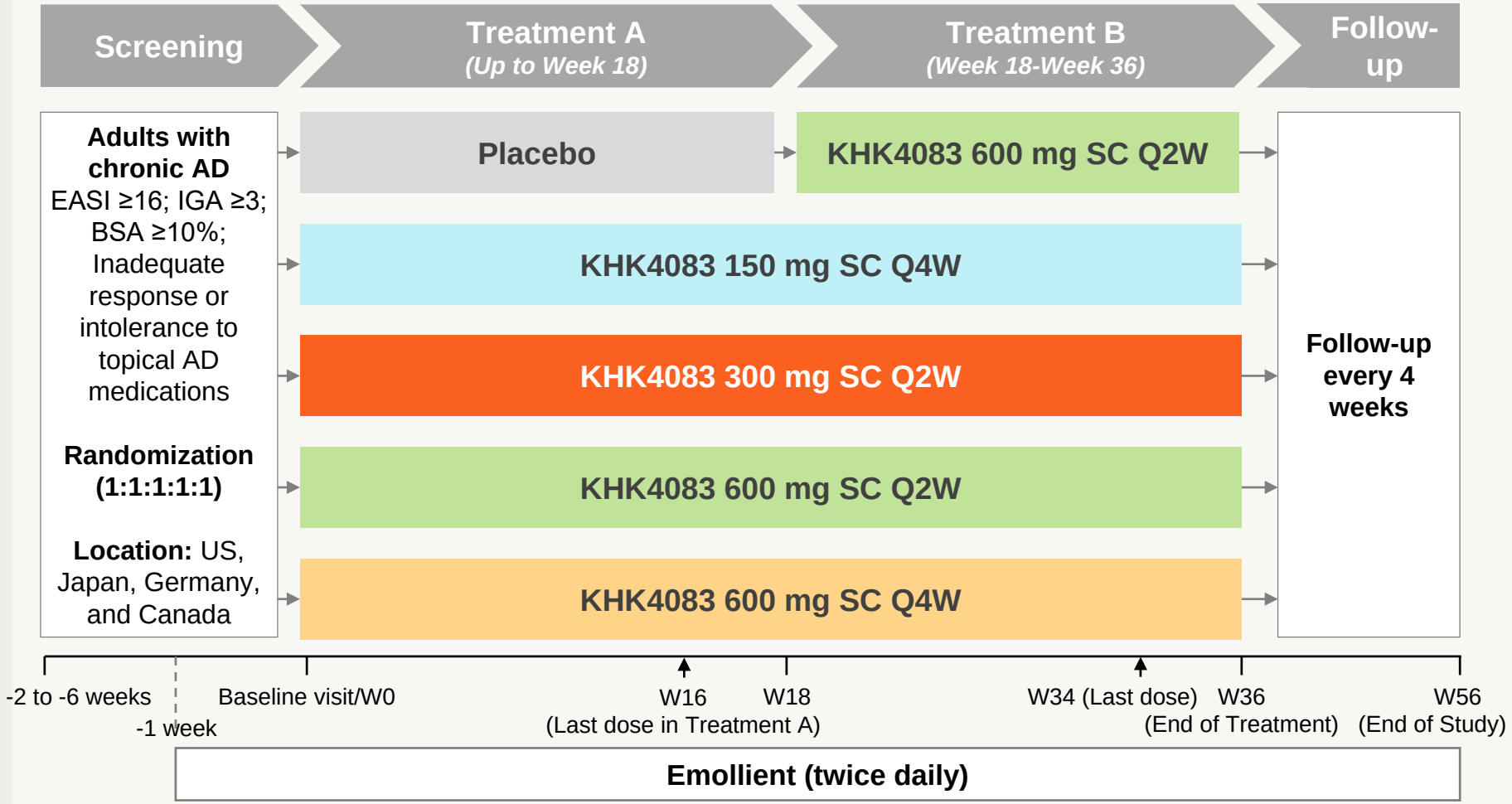


Mechanism of action of KHK4083[2]

CD28, cluster of differentiation 28; IgG, immunoglobulin G; MHC, major histocompatibility complex; mAb, monoclonal antibody; TCR, T-cell receptor; Th2, T-helper 2; TNF, tumor necrosis factor

[1]Nakagawa H et al. J Dermatol Sci. 2020; 99(2):82–89; [2]Papp KA et al. J Eur Acad Dermatol Venereol. 2017, 31(8):1324–1332.

Phase 2 Study Design (NCT03703102)



Primary efficacy endpoint

- Percentage change in EASI score from baseline to Week 16

Secondary efficacy endpoints

- Reduction of ≥50%, ≥75%, and ≥90% in EASI score (EASI 50/75/90) from baseline
- Achievement of an IGA score of 0/1 and a reduction of ≥2 points from baseline (IGA0/1)
- Achievement of a reduction of ≥4 points in Pruritus-NRS score from baseline

Safety evaluations

- Adverse events

AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IP, Investigational product; NRS, Numerical Rating Scale; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; W, Week
Patients receiving rescue treatment before W36 assessment discontinued the IP and underwent end-of-study assessment

Baseline Demographics and Disease Characteristics (Safety Analysis Set)

All baseline parameters were generally well-balanced among the treatment groups

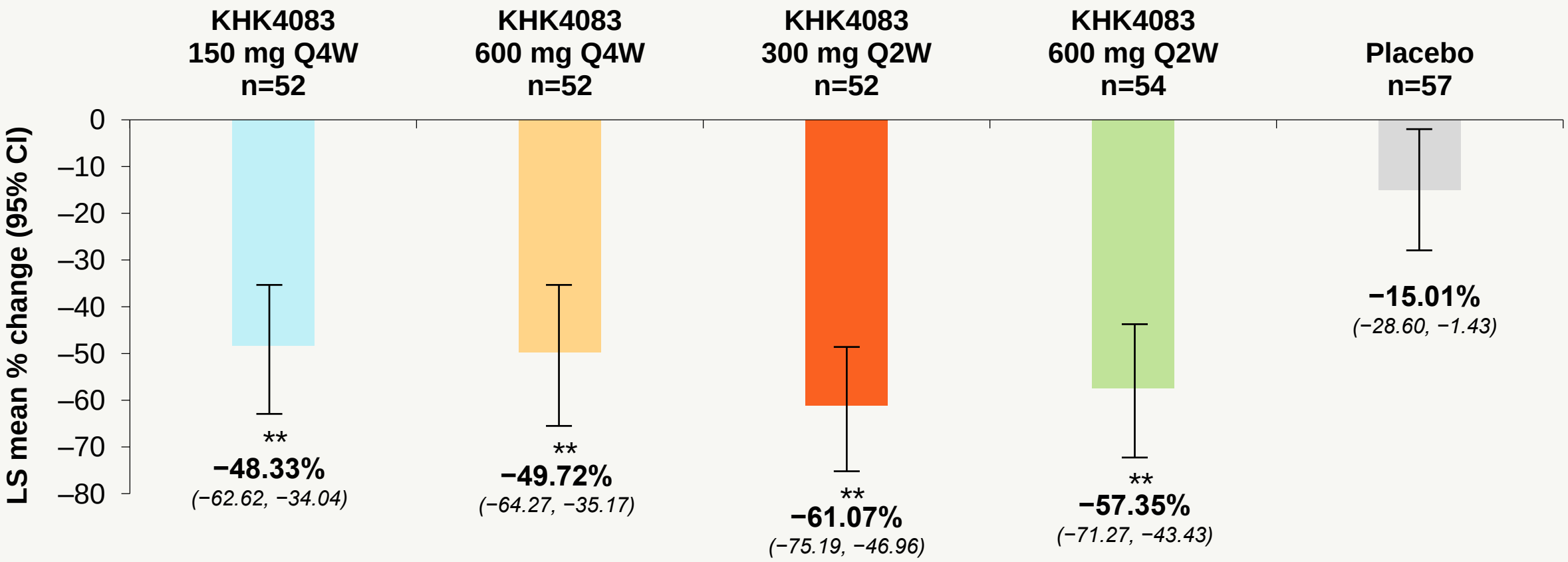
Characteristics*		KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	Placebo/ KHK4083 600 mg Q2W N=57	Total N=273
Age, years		37.4 ± 13.6	38.9 ± 14.6	37.5 ± 14.1	37.3 ± 16.3	38.7 ± 14.4	38.0 ± 14.5
Sex, male, n (%)		37 (68.5)	31 (58.5)	31 (56.4)	30 (55.6)	31 (54.4)	160 (58.6)
Race, n (%)	**Asian: Japanese**	30 (55.6)	28 (52.8)	32 (58.2)	30 (55.6)	30 (52.6)	150 (54.9)
	Asian: Other	6 (11.1)	4 (7.5)	5 (9.1)	3 (5.6)	7 (12.3)	25 (9.2)
	Black or African American	3 (5.6)	1 (1.9)	2 (3.6)	1 (1.9)	6 (10.5)	13 (4.8)
	White	14 (25.9)	20 (37.7)	16 (29.1)	20 (37.0)	14 (24.6)	84 (30.8)
	Other	1 (1.9)	0	0	0	0	1 (0.4)
Body mass index at screening, kg/m^2		24.99 ± 4.81	24.69 ± 5.69	26.69 ± 7.24	25.19 ± 6.49	24.26 ± 5.23	25.16 ± 5.97
Duration from diagnosis of AD to randomization, years		6.47 ± 6.59	8.40 ± 8.32	8.59 ± 9.58	6.42 ± 5.69	6.41 ± 5.98	7.26 ± 7.32
Severity of AD - IGA, n (%)	**3**	30 (55.6)	28 (52.8)	30 (54.5)	29 (53.7)	31 (54.4)	148 (54.2)
	4	24 (44.4)	25 (47.2)	25 (45.5)	25 (46.3)	26 (45.6)	125 (45.8)
Pruritus-NRS score		7.8 ± 1.6	7.5 ± 2.3	7.5 ± 1.6	7.6 ± 1.9	7.2 ± 2.3	7.5 ± 2.0
EASI score		32.8 ± 13.1	32.5 ± 12.7	32.2 ± 13.4	31.1 ± 11.8	29.2 ± 13.3	31.5 ± 12.8
SCORAD score		68.75 ± 12.57	69.44 ± 13.64	68.52 ± 14.36	68.79 ± 14.36	66.35 ± 14.05	68.34 ± 13.76
Percent BSA		59.5 ± 23.7	59.1 ± 25.2	56.8 ± 21.8	55.3 ± 23.4	54.3 ± 23.5	56.9 ± 23.5
Previous use of biological products for treatment of AD, n (%)		7 (13.0)	5 (9.4)	8 (14.5)	8 (14.8)	9 (15.8)	37 (13.6)

AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, Numerical Rating Scale; SCORAD, Severity scoring of atopic dermatitis; Q2W, every 2 weeks; Q4W, every 4 weeks

*Data presented as mean ± SD, unless specified otherwise. Data presented from safety analysis set, which included patients who received at least 1 dose of KHK4083; 273 of the 274 randomized patients were included in the safety analysis set.

Primary Endpoint: % Change in EASI Scores (Week 16) From Baseline (Last observation carried forward, Full Analysis Set)

All KHK4083-treated groups achieved the primary endpoint

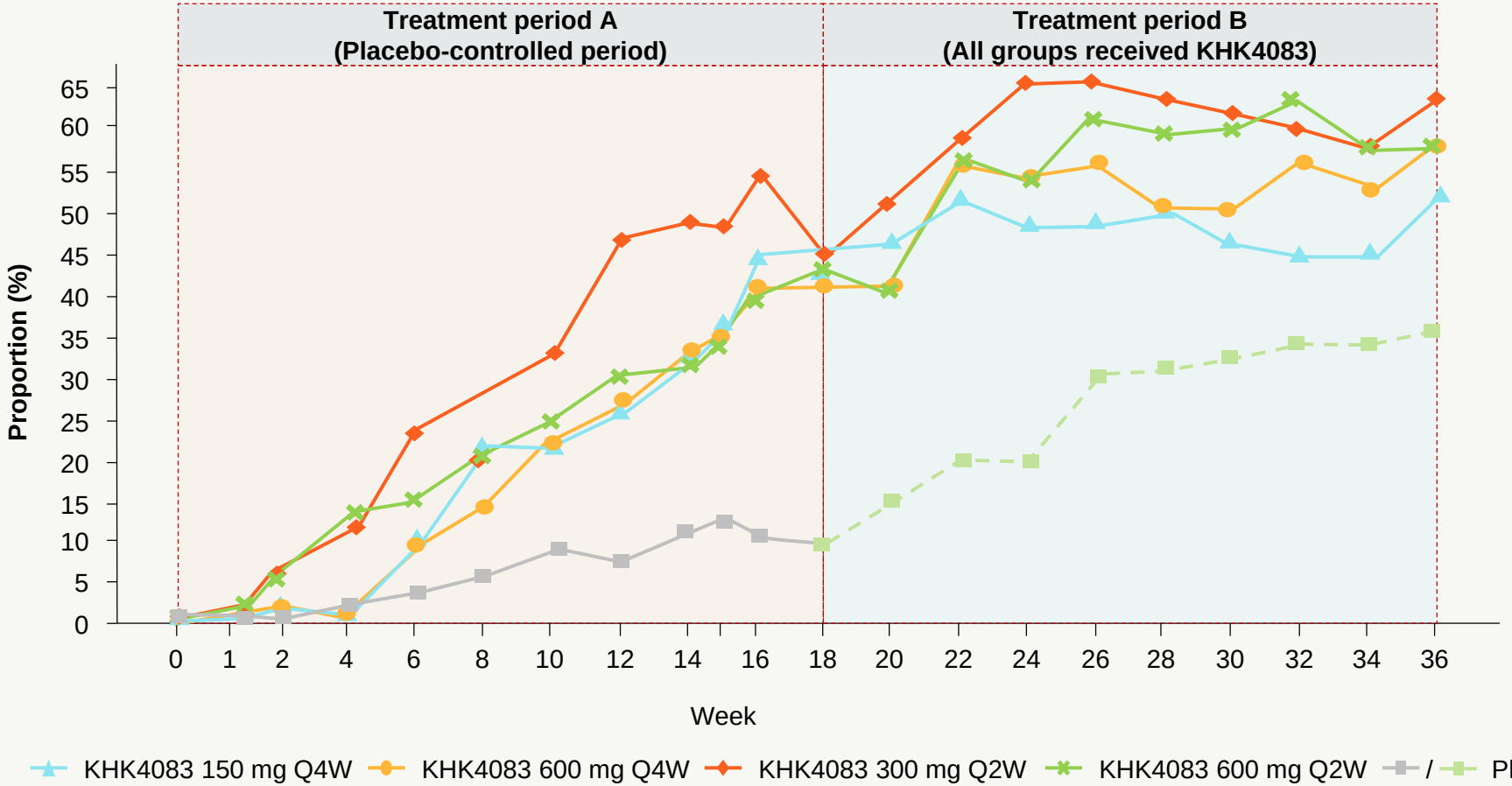


EASI, Eczema Area and Severity Index; LS, least square; Q2W, every 2 weeks; Q4W, every 4 weeks

**p<0.001 for difference versus placebo

Proportion of Patients Who Achieved EASI-75 (Non-responder Imputation, Full Analysis Set)

Proportions of EASI-75 responders at Week 16 were significantly higher in all KHK4083-treated cohorts versus placebo



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	44.2**	48.1	51.9
KHK4083 600 mg Q4W, %	40.4**	53.8	57.7
KHK4083 300 mg Q2W, %	53.8**	65.4	63.5
KHK4083 600 mg Q2W, %	38.9**	53.7	57.4
Placebo/KHK4083 600 mg Q2W, %	10.5	19.3	35.1

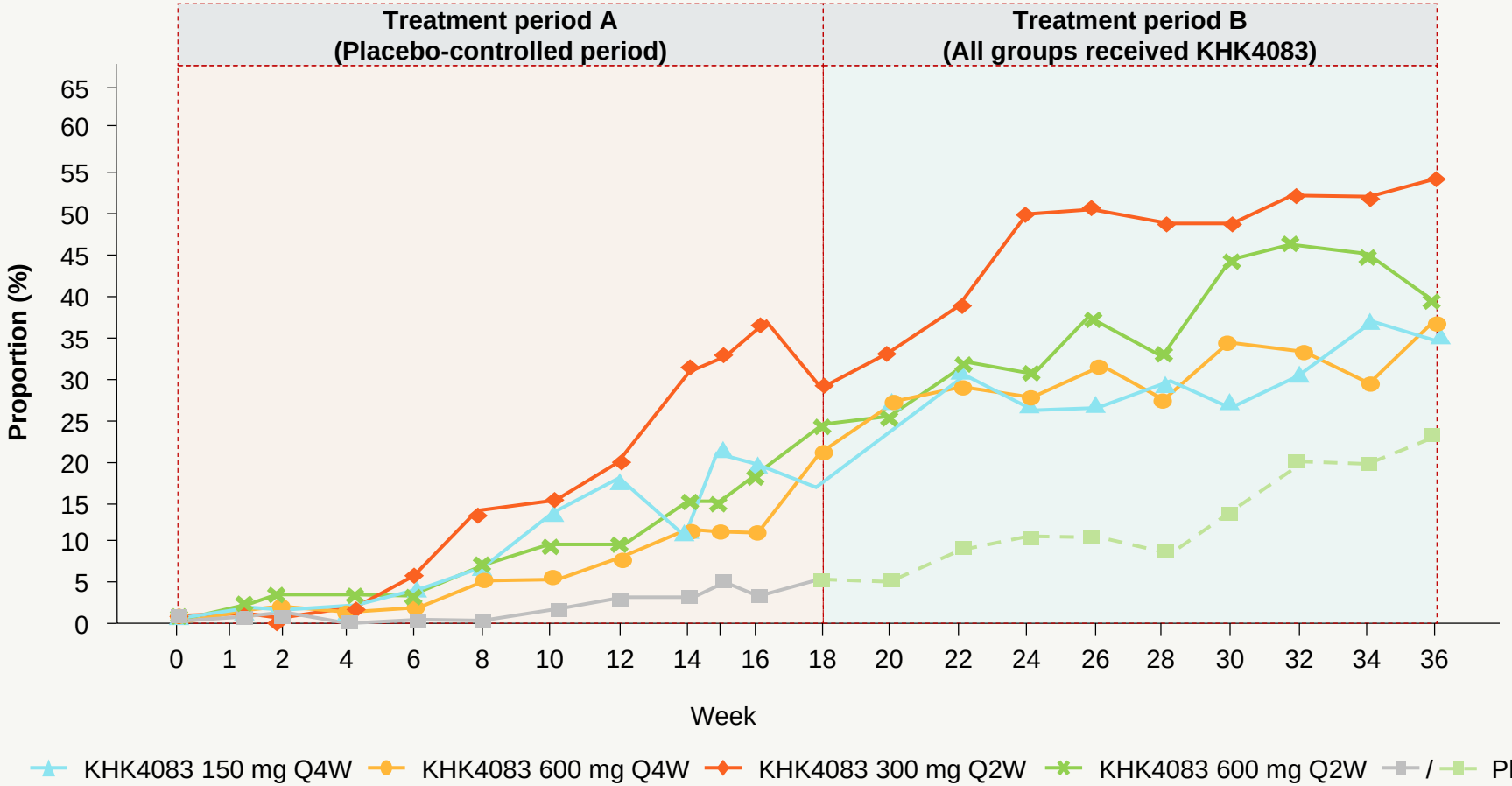
**p<0.001 vs placebo, assessed at Week 16

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; Q2W, every 2 weeks; Q4W, every 4 weeks

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

Proportion of Patients Who Achieved EASI-90 (Non-responder Imputation, Full Analysis Set)

Proportions of EASI-90 responders at Week 16 were significantly higher in most KHK4083-treated cohorts versus placebo



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	19.2*	26.9	34.6
KHK4083 600 mg Q4W, %	11.5	26.9	36.5
KHK4083 300 mg Q2W, %	36.5**	50.0	53.8
KHK4083 600 mg Q2W, %	18.5*	29.6	38.9
Placebo/KHK4083 600 mg Q2W, %	3.5	10.5	22.8

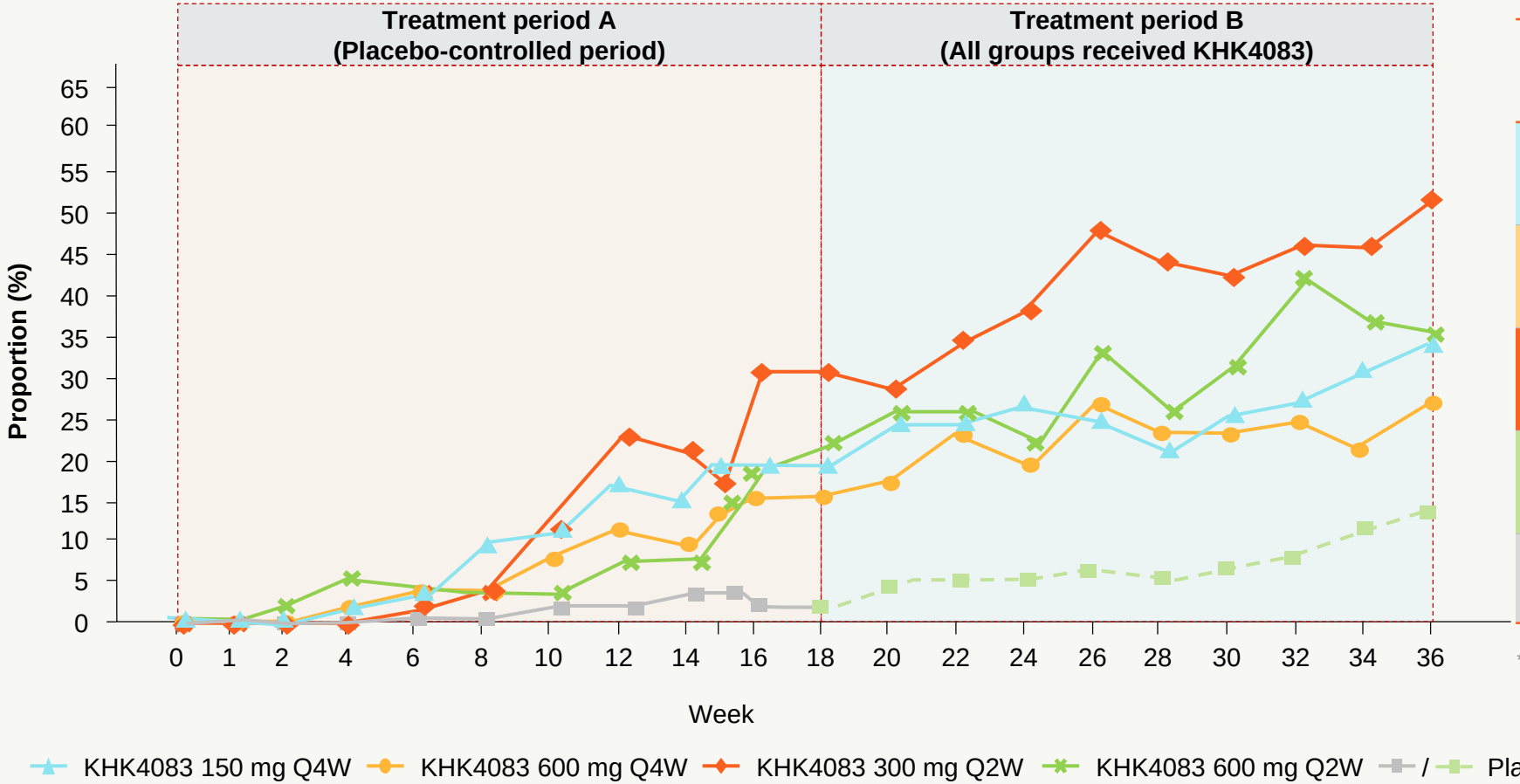
*p<0.05, **p<0.001 vs placebo, assessed at Week 16

EASI, Eczema Area and Severity Index; Q2W, every 2 weeks; Q4W, every 4 weeks

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

Proportions of Patients Who Achieved an IGA Score of 0/1 and a Reduction of ≥2 Points from Baseline (Non-responder Imputation, Full Analysis Set)

In all KHK4083 groups, the proportion of subjects who achieved IGA score 0/1 gradually increased up to Week 36



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	19.2*	26.9	34.6
KHK4083 600 mg Q4W, %	15.4*	19.2	26.9
KHK4083 300 mg Q2W, %	30.8**	38.5	51.9
KHK4083 600 mg Q2W, %	18.5*	22.2	35.2
Placebo/KHK4083 600 mg Q2W, %	1.8	5.3	14.0

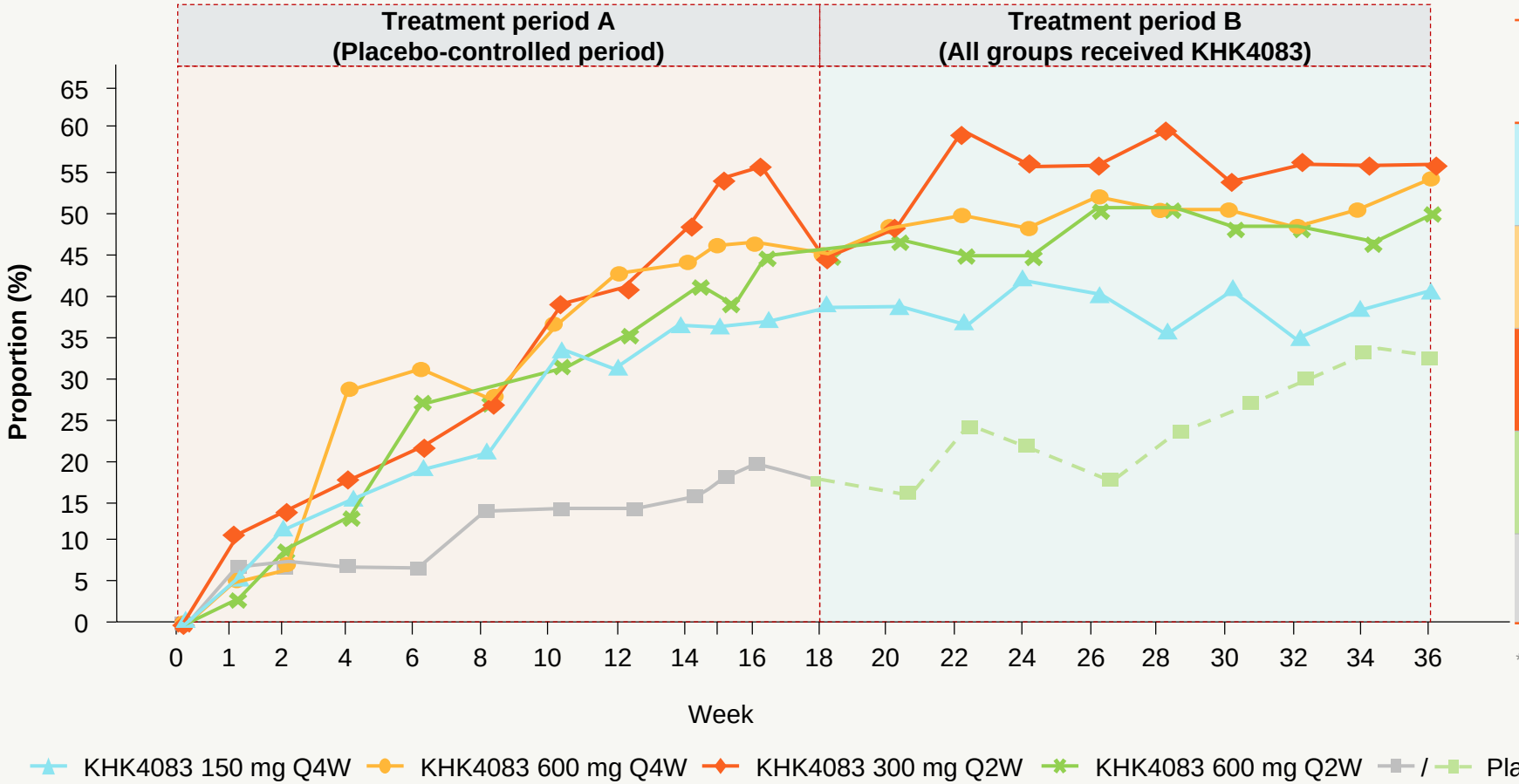
*p<0.05, **p<0.001 vs placebo, assessed at Week 16

IGA, Investigator's General Assessment; Q2W, every 2 weeks; Q4W, every 4 weeks

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

Proportions of Patients Who Achieved Reduction of ≥4 Points for Pruritus-NRS (Non-responder Imputation, Full Analysis Set)

Proportions of Pruritus-NRS responders at Week 16 were significantly higher in most KHK4083-treated groups versus placebo



	Week 16	Week 24	Week 36
KHK4083 150 mg Q4W, %	36.5	42.3	40.4
KHK4083 600 mg Q4W, %	46.2*	48.1	53.8
KHK4083 300 mg Q2W, %	55.8**	55.8	55.8
KHK4083 600 mg Q2W, %	44.4*	44.4	50.0
Placebo/KHK4083 600 mg Q2W, %	19.3	21.1	31.6

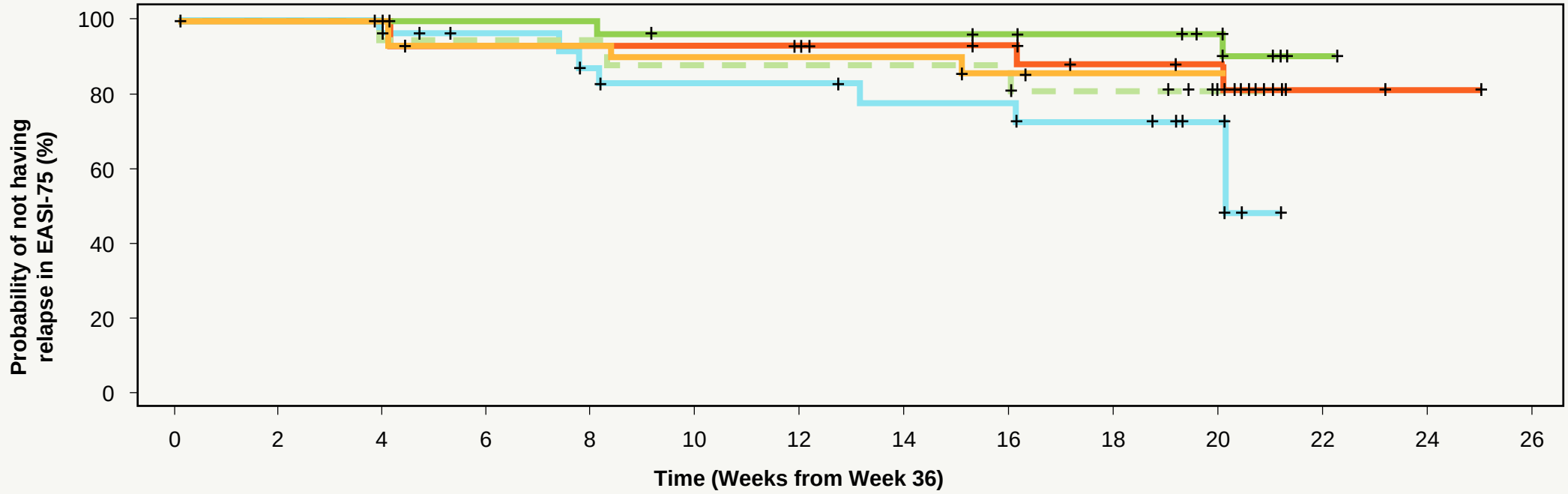
*p<0.05, **p<0.001 vs placebo, assessed at Week 16

NRS, Numerical Rating Scale; Q2W, every 2 weeks; Q4W, every 4 weeks

Note: Patients in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. These data are based on non-responder imputations and the patients who used rescue therapy (either topical or systemic) were treated as non-responders after the use of rescue therapy.

Durability of EASI-75 Response After Treatment Discontinuation in Subjects who achieved EASI-75 at Week 36

EASI-75 response was durable even after discontinuation of KHK4083 at Week 36



KHK4083 150 mg Q4W	27	26	26	22	19	17	17	15	15	13	9	0	0	0
KHK4083 600 mg Q4W	30	29	29	27	27	26	26	26	24	22	16	0	0	0
KHK4083 300 mg Q2W	33	30	29	25	25	25	24	22	21	18	13	2	1	0
KHK4083 600 mg Q2W	31	27	27	25	25	21	21	21	20	19	17	1	0	0
Placebo/KHK4083 600 mg Q2W	20	18	18	16	16	13	13	13	13	11	7	0	0	0

+: censored, EASI: Eczema Area and Severity Index, Q2W, every 2 weeks; Q4W, every 4 weeks

Note: Subjects in the placebo group were switched to KHK4083 600 mg Q2W after Treatment A period. The numbers below the figure represent the number of remaining subjects at each visit.

Note: Relapse is the loss of EASI-75 after achieving EASI-75 at Week 36.

Note: Censored cases are prohibited concomitant medications and/or therapies including rescue treatment started before the event confirmed, study completion without the event confirmed, and early termination of the study without the event confirmed.

TEAEs – Treatment A Period (Safety Analysis Set)

In Treatment A period, 81% TEAEs occurred in KHK4083 groups versus 72% in the placebo group

Category	KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	KHK4083 Total N=216	Placebo N=57
Any TEAEs	37 (68.5)	45 (84.9)	47 (85.5)	46 (85.2)	175 (81.0)	41 (71.9)
Serious TEAEs	3 (5.6)	1 (1.9)	3 (5.5)	1 (1.9)	8 (3.7)	1 (1.8)
TEAEs leading to treatment discontinuation	5 (9.3)	3 (5.7)	7 (12.7)	4 (7.4)	19 (8.8)	12 (21.1)
All deaths	0	0	0	0	0	0
TEAEs with severity grade of ≥3	6 (11.1)	1 (1.9)	5 (9.1)	4 (7.4)	16 (7.4)	2 (3.5)

TEAE, treatment-emergent adverse event; Q2W, every 2 weeks; Q4W, every 4 weeks
Note: n=number of patients reporting at least 1 TEAE in that category except for all deaths. Data are presented as **n (%).**
Data presented from safety analysis set, which included patients who received at least 1 dose of investigational product; 273 of the 274 randomized patients were included in the safety analysis set.

TEAEs in >5% of Subjects in the Total KHK4083 Group by Preferred Term - Treatment A Period (Safety Analysis Set)

- **The most frequent TEAEs in KHK4083 groups were pyrexia, nasopharyngitis, worsening of AD, and chills**
- **Events of pyrexia and chills were mild to moderate in intensity and were mostly observed only after the first administration of KHK4083 and were not associated with any consequent treatment discontinuation**
- **No hypersensitivity reactions were observed**

Preferred Term	KHK4083 150 mg Q4W N=54	KHK4083 600 mg Q4W N=53	KHK4083 300 mg Q2W N=55	KHK4083 600 mg Q2W N=54	KHK4083 Total N=216	Placebo N=57
Pyrexia	7 (13.0)	10 (18.9)	9 (16.4)	10 (18.5)	36 (16.7)	2 (3.5)
Nasopharyngitis	8 (14.8)	7 (13.2)	7 (12.7)	8 (14.8)	30 (13.9)	9 (15.8)
Dermatitis atopic	8 (14.8)	5 (9.4)	8 (14.5)	7 (13.0)	28 (13.0)	17 (29.8)
Chills	2 (3.7)	3 (5.7)	7 (12.7)	12 (22.2)	24 (11.1)	0
Headache	4 (7.4)	6 (11.3)	4 (7.3)	5 (9.3)	19 (8.8)	1 (1.8)
Aphthous ulcer	3 (5.6)	8 (15.1)	3 (5.5)	1 (1.9)	15 (6.9)	0
Nausea	3 (5.6)	2 (3.8)	1 (1.8)	7 (13.0)	13 (6.0)	1 (1.8)

PT, Preferred Term; TEAE, treatment-emergent adverse event; Q2W, every 2 weeks; Q4W, every 4 weeks
Note: Adverse events were coded using MedDRA version 23.0. Data are presented as **n (%)**.

Conclusions

- KHK4083/AMG 451 represents a novel mechanism of action and its use resulted in significant improvements in signs and symptoms of AD compared with placebo, across primary and secondary efficacy parameters at Week 16
- Importantly, KHK4083/AMG 451 demonstrated progressive improvement in efficacy parameters beyond Week 16
- KHK4083/AMG 451 demonstrated sustained efficacy for another 20 weeks after treatment discontinuation (until Week 56)
- KHK4083/AMG 451 was well-tolerated and did not show safety concerns
- KHK4083/AMG 451 may be a novel treatment option for patients with moderate-to-severe AD

Acknowledgments

The authors are grateful to all patients who participated in the trial, the investigators and the staff who helped in trial management, and Dr. Michael Croft at La Jolla Institute for Immunology who identified an important role of OX40 in maintaining T-cell proliferation and survival and in the formation of memory T cells and contributed to the development of the targeting rationale of KHK4083/AMG 451.

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