Society for Investigative Dermatology, 2026 Annual Meeting

# Preclinical characterization of IMG-007, a high-affinity, non-depleting anti-OX40 monoclonal antibody for the treatment of inflammatory and autoimmune disease

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# Disclosures

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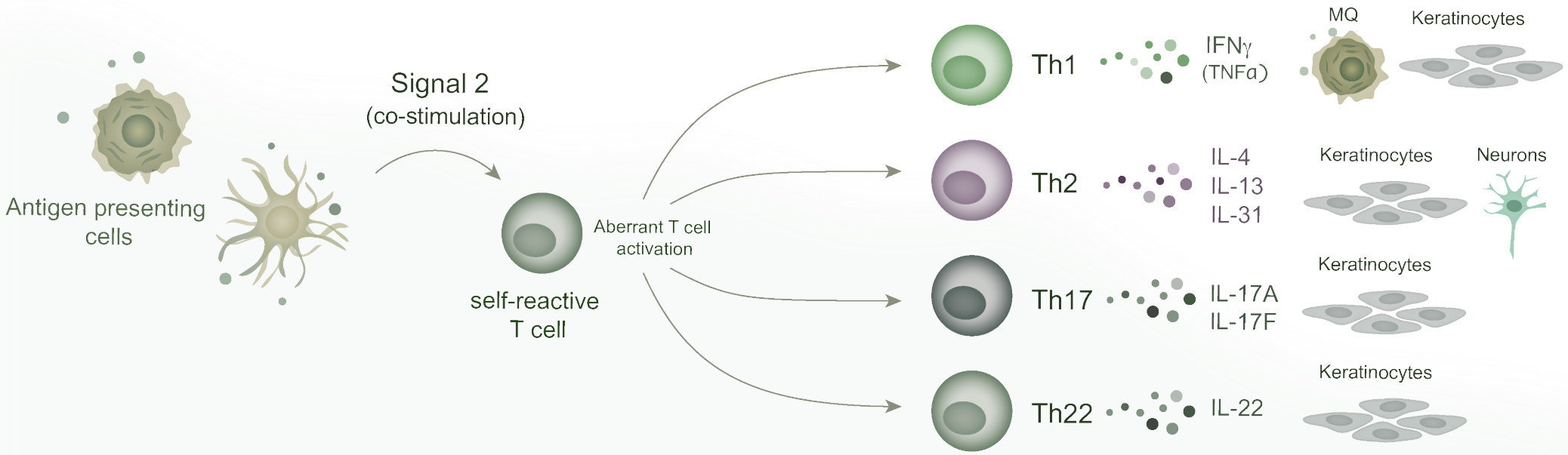
Jonatan Tuncel, Kurinji Pandiyan, Ben Porter-Brown, and Kristin Yarema are employees of ImageneBio and may hold equity interests.

Chongtian Guo is an employee of Miragene, may hold equity interests, and is a former employee of the private company Inmagene, which conducted several of the studies presented.

No other relevant financial relationships to disclose.

# Atopic dermatitis is a heterogeneous disease with high unmet need, underpinned by diverse immune endotypes

- ✓ AD is a chronic heterogeneous inflammatory disease with several immune endotypes
- ✓ ~40-50% of patients show incomplete or no response to Type 2 biologics (e.g., dupilumab)[1]


No approved Th1-selective biologics in AD

Several approved type 2 biologics in AD

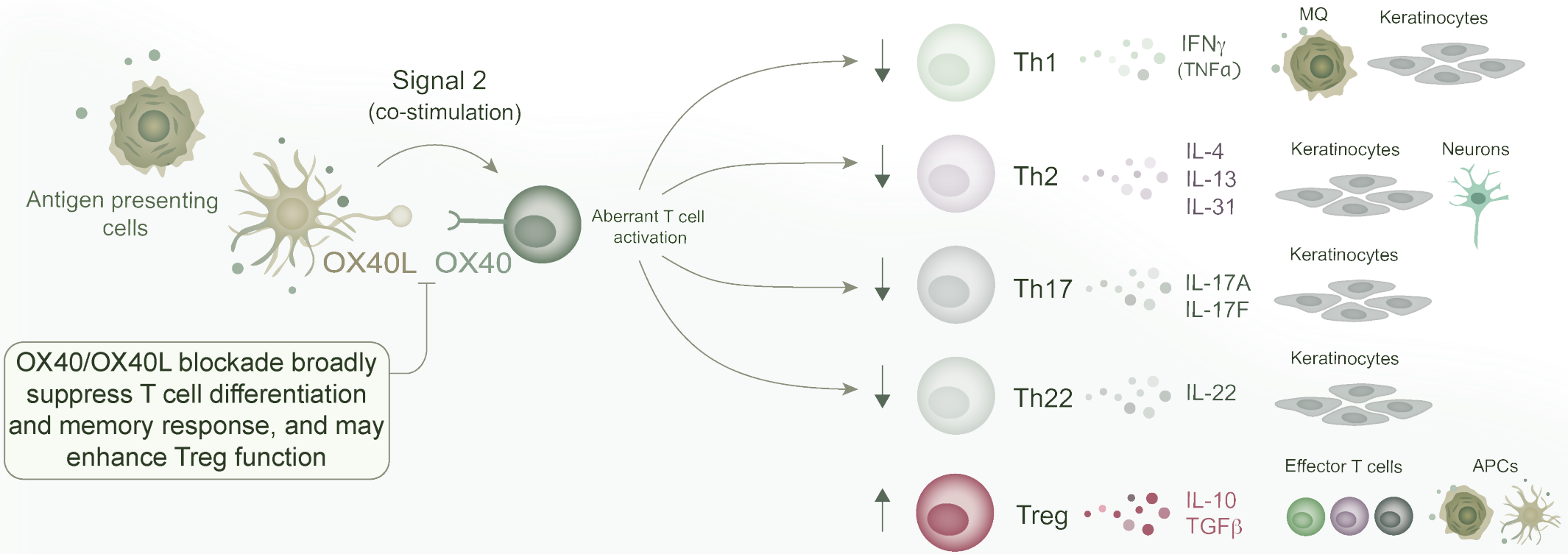
No approved Th17-selective biologics in AD

No approved Th22-selective biologics in AD

(1) 48-56% of patients failed to reach EASI-75 in SOLO 1 and 2, and 62-64% did not reach the primary outcome based on IGA (Simpson et al., NEJM (2016), Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis). Other references used: Müller et al., Allergy (2024), Treatment of atopic dermatitis: Recently approved drugs and advanced clinical development programs; Type 2 biologics are defined as monoclonal antibodies targeting cytokines or cytokine receptors primarily produced/expressed by Th2 cells. Abbreviations: (MQ) macrophages, (Th) T helper cell subset.

# OX40 inhibition has the potential to modulate multiple inflammatory pathways of relevance in AD

- ✓ OX40 is a key co-stimulatory pathway regulating T cell activation and effector function in AD[1]
- ✓ Upstream OX40 blockade broadly modulates T cell activation and effector differentiation across inflammatory pathways
- ✓ May reduce pathogenic memory T cell persistence and preserve or enhance Treg function[2]

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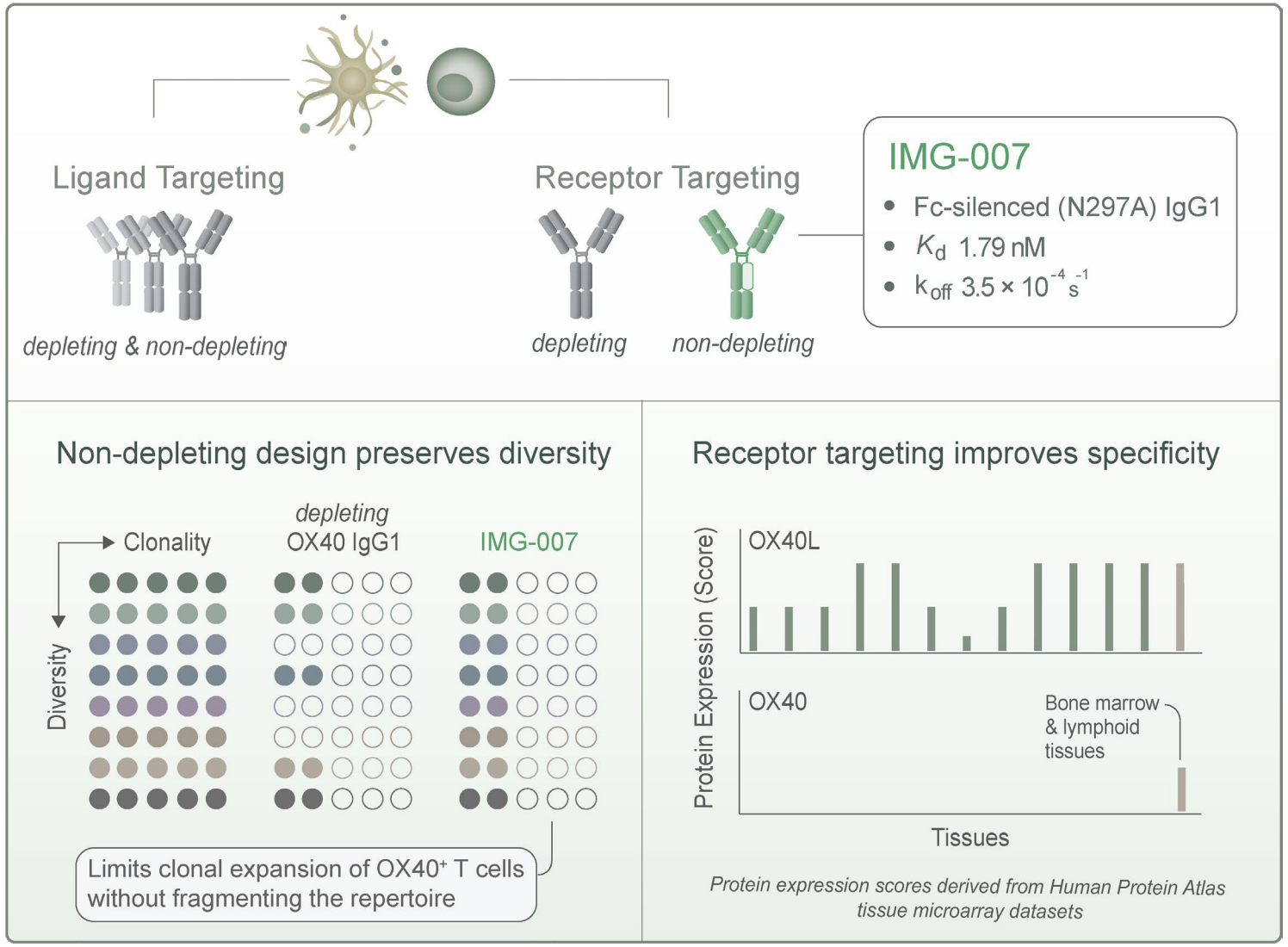
No approved Th17-selective biologics in AD

No approved Th22-selective biologics in AD

No approved Treg-selective biologics in AD

(1) Abdelhalim et al. Dermatol Ther (2024), A Narrative Review of the OX40-OX40L Pathway as a Potential Therapeutic Target in Atopic Dermatitis: Focus on Rocatinlimab and Amlitelimab; (2) Zhang et al., Cell Rep (2018) OX40 Costimulation Inhibits Foxp3 Expression and Treg Induction via BATF3-Dependent and Independent Mechanisms

# IMG-007: A non-depleting OX40 antagonist designed to suppress pathogenic immunity while preserving immune balance




## High affinity supports potent inhibition of OX40–OX40L engagement

- ✓ Limits effector T cell activation and polarization
- ✓ Reduces clonal expansion of pathogenic memory T cells
- ✓ May enhance Treg suppressive function

## Non-depleting design (N297A/Fc-silenced)

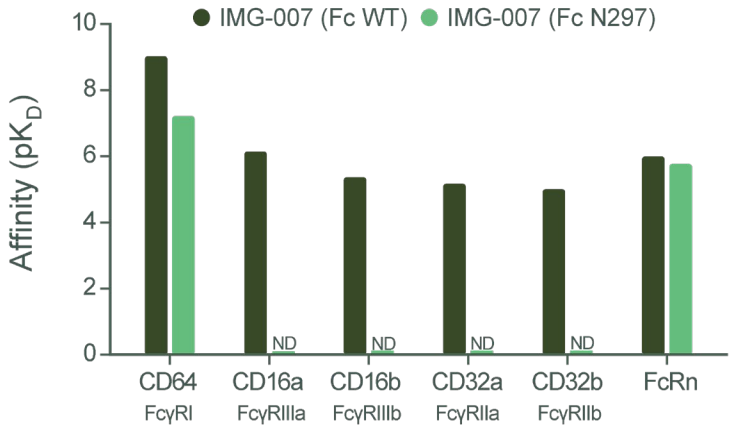
- ✓ Preserves T cell diversity and immune surveillance
- ✓ Preserves tissue Tregs

* Data show antibody-based tissue microarrays using 1 mm cores across normal and cancer tissues (normal: n = 144 individuals, 44 tissue types; cancer: n = 216 patients, 20 cancer types). As specimens were derived from surgical material, tissues may include pathological variation. Each bar represents the highest expression score found in a particular group of tissues. Protein expression scores are based on a best estimate of the "true" protein expression from a knowledge-based annotation

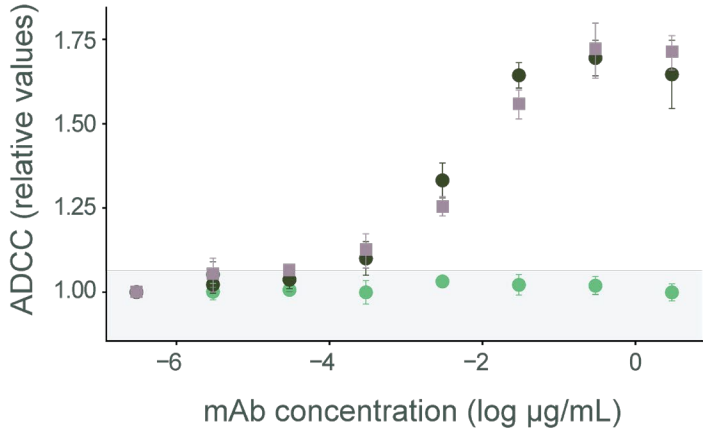
# Minimal Fcγ receptor binding prevents depletion of OX40+ cells through ADCC

- ✓ IMG-007 show minimal FcγR binding across FcγRI/II/III, with only residual CD64 interaction and fully preserved FcRn binding
- ✓ No NK cell–mediated cytotoxicity (ADCC) across concentrations tested
- ✓ Minimal release of NK-derived inflammatory cytokines, potentially lowering AE risk

IMG-007 shows minimal Fcγ receptor binding, with the exception of CD64, while maintaining FcRn affinity

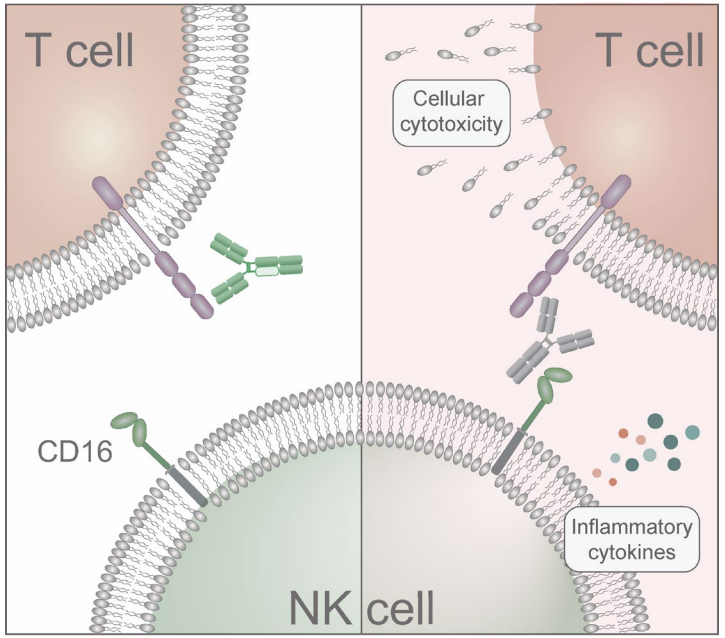



IMG-007 does not elicit NK cell–mediated cytotoxicity (ADCC)




**IMG-007** OX40 blockade without CD16 engage-ment and ADCC

**Non-Fc silenced IgG1** Depletion of OX40+ cells through ADCC



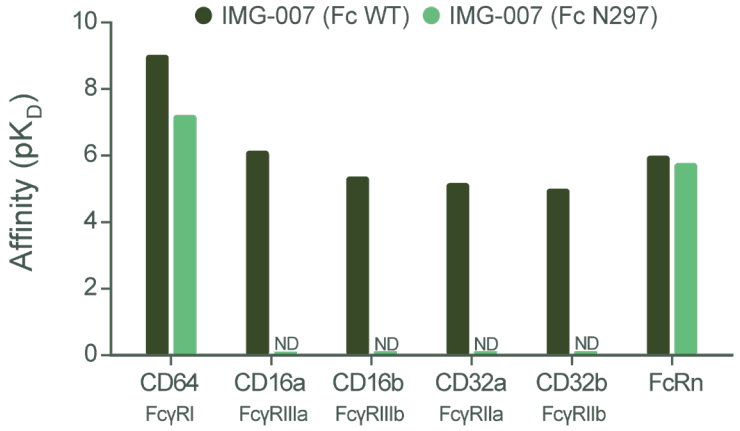

GBR 830 (Fc WT) IMG-007 (Fc WT) IMG-007 (Fc N297A) Background (isotype-matched N297A control)

The left panel shows surface plasmon resonance (SPR) used to assess binding of Fc modified (N297A) and non-modified IMG-007 to FcγR and FcRn. FcRn was measured by anti-His capture with multi-cycle kinetics (pH 6.0) while FcγR binding (assessed separately) was characterized under 1:1 kinetic conditions. The middle panel shows relative killing of OX40-overexpressing HEK293 target cells after 2 h co-culture with primary NK cells in the presence of anti-OX40 mAb, normalized to a no-antibody control.

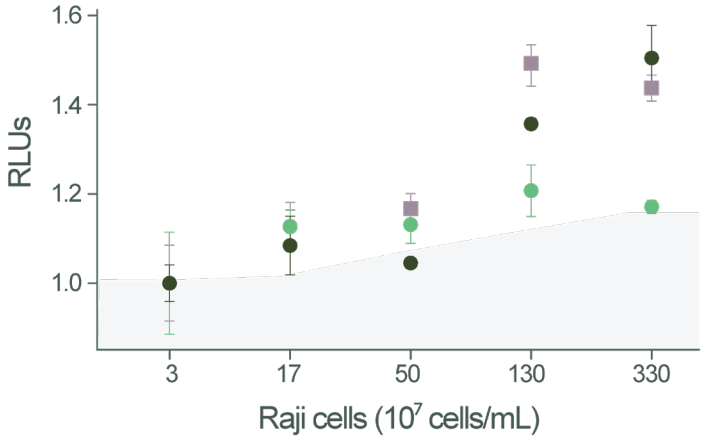
# Minimal Fcγ receptor binding limits agonistic signaling by preventing OX40 crosslinking

- ✓ IMG-007 show minimal FcγR binding across FcγRI/II/III, with only residual CD64 interaction and fully preserved FcRn binding
- ✓ No meaningful agonistic signaling detected across a broad set of test conditions

IMG-007 shows minimal Fcγ receptor binding, with the exception of CD64, while maintaining FcRn affinity

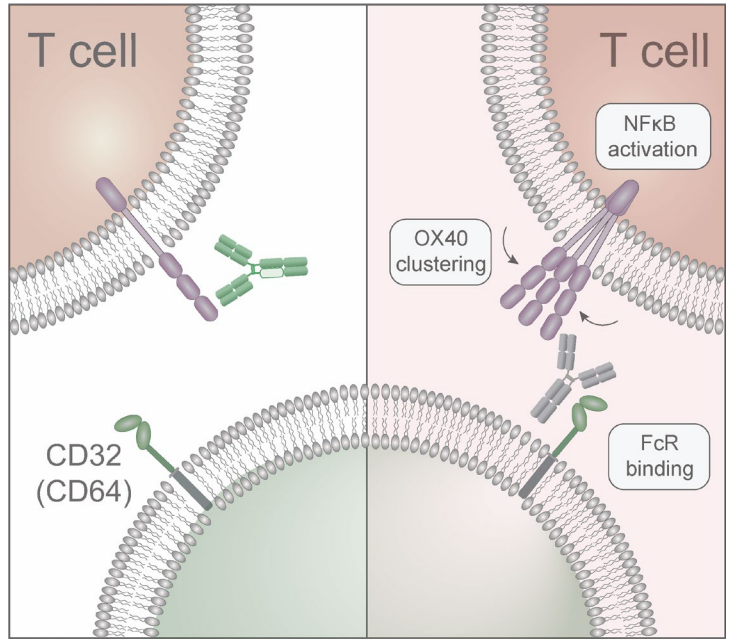



IMG-007 shows minimal agonistic activity in co-culture with FcR-expressing Raji cells




**IMG-007** Minimal Fcγ receptor binding limits agonistic potential

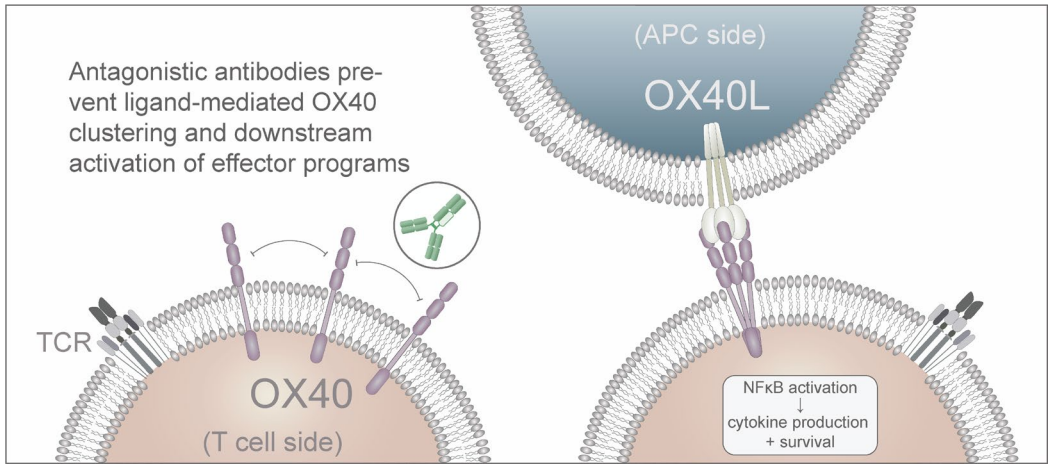
**Non-Fc silenced IgG1** Potentially greater risk for agonistic properties




GBR 830 (Fc WT) IMG-007 (Fc WT) IMG-007 (Fc N297A) Background (isotype-matched N297A control)

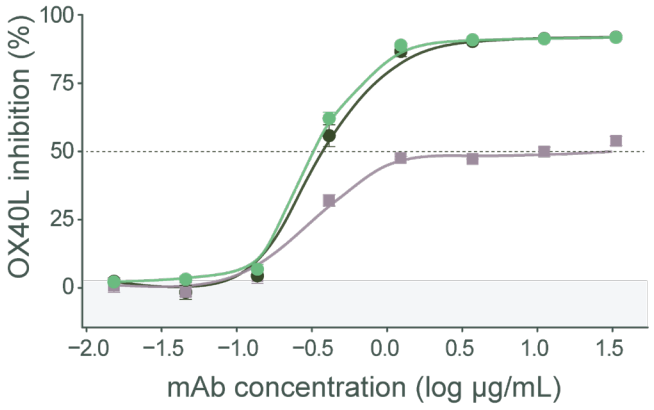
The left panel shows surface plasmon resonance (SPR) used to assess binding of Fc modified (N297A) and non-modified IMG-007 to FcγR and FcRn. FcRn was measured by anti-His capture with multi-cycle kinetics (pH 6.0) while FcγR binding (assessed separately) was characterized under 1:1 kinetic conditions. The middle panel shows NF-κB activation (RLU) in OX40-overexpressing HEK293T reporter cells after 6 h co-culture with FcγR-expressing Raji cells. Anti-OX40 mAb was added at a fixed concentration; activation reflects FcγR-mediated, antibody-dependent crosslinking of OX40 (agonistic activity).

# IMG-007 shows rocatinlimab-level OX40L inhibition without Fc-mediated effector function

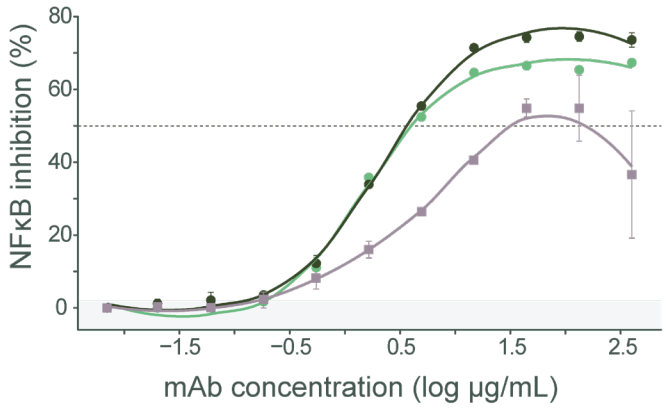



- ✓ IMG-007 is comparable to rocatinlimab in OX40L binding and downstream NFκB inhibition
- ✓ IMG-007 shows potent, dose-dependent suppression of IFNγ production in primary T cell assays

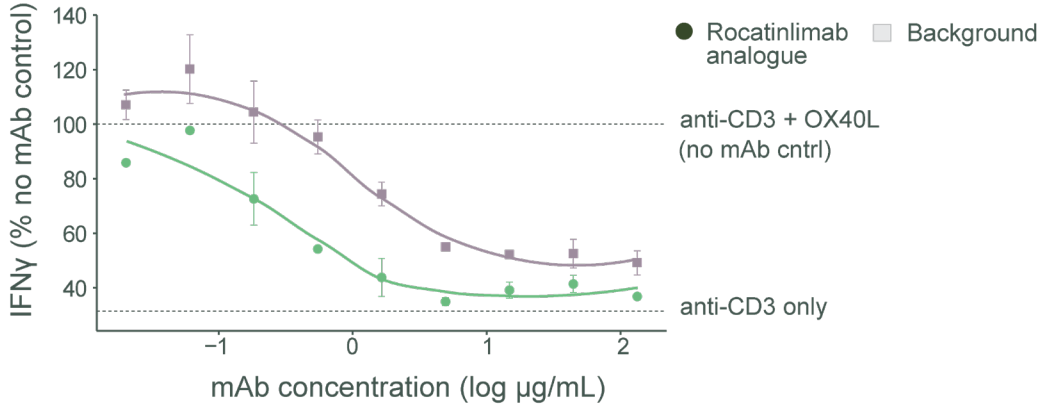
## Inhibition of OX40-OX40L interaction (ELISA)




## Inhibition of NFkB activation (reporter assay)

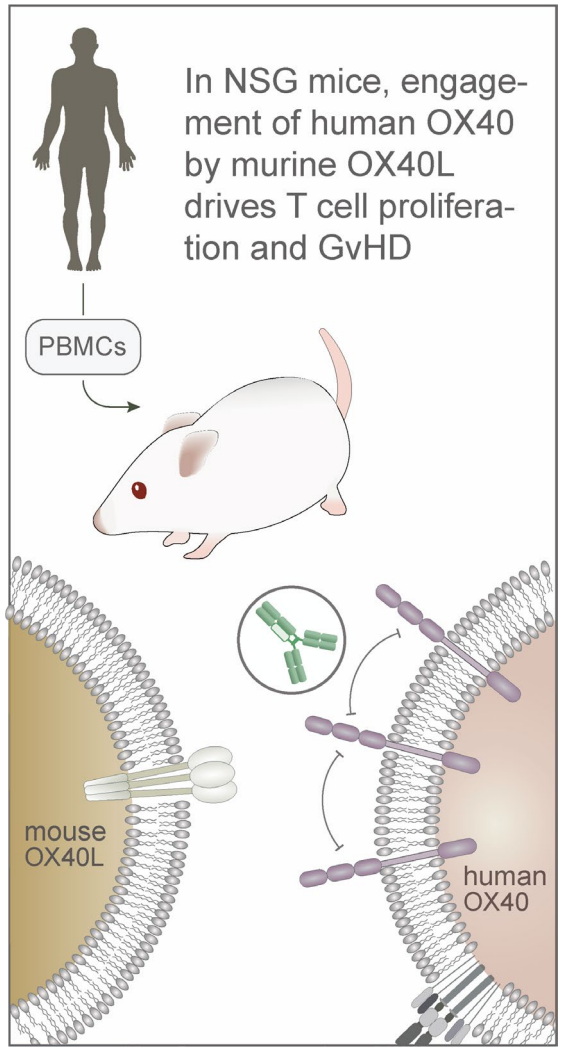



## Inhibition of T cell-mediated IFNγ production

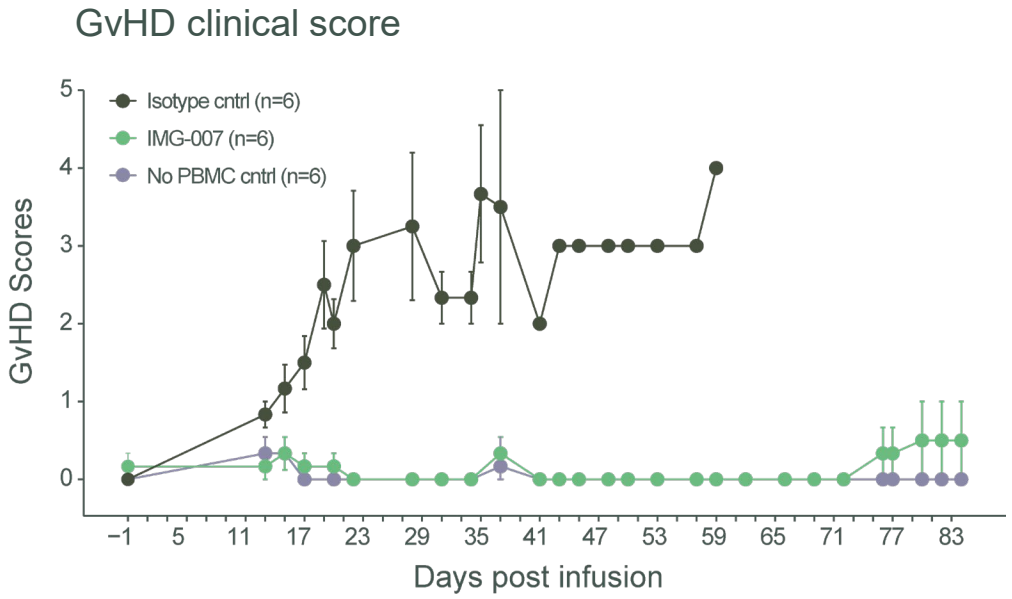


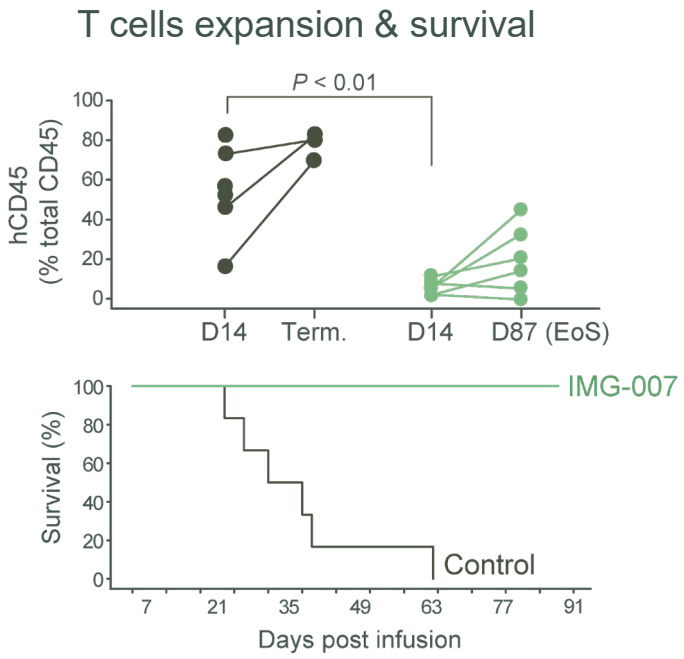

The left panel shows relative binding of soluble OX40L to plate-bound OX40 in the presence of varying concentrations of anti-OX40 mAb, normalized to a no-antibody control. Bound OX40L was detected using a biotinylated goat anti-OX40L antibody followed by streptavidin–HRP. The middle panel shows relative inhibition of NF-κB activation in OX40-expressing HEK293T-Luc cells stimulated with OX40L for 6 h in the presence of anti-OX40 mAbs. The right panel shows IFN-γ (ELISA) from primary T cells activated with plate-bound OKT3 (anti-CD3) and soluble OX40L in the presence of anti-OX40 mAb after 72 h. Tool compounds were generated based on publicly available sequence information; properties may not fully reflect the clinical molecule.

# IMG-007 suppresses T cell expansion and T cell-driven pathology in a xenogeneic GvHD model




- ✓ Xenogeneic GvHD models provide a functional readout of T cell activation and expansion
- ✓ Relevant model systems for human OX40 biology, as murine OX40L engages OX40 on human donor T cells
- ✓ Weekly IMG-007 dosing limited expansion of engrafted T cells and prevented GvHD development

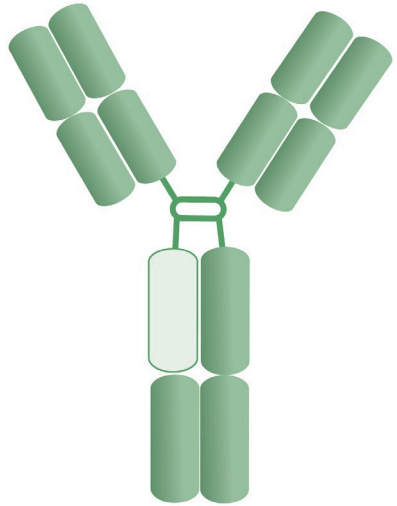


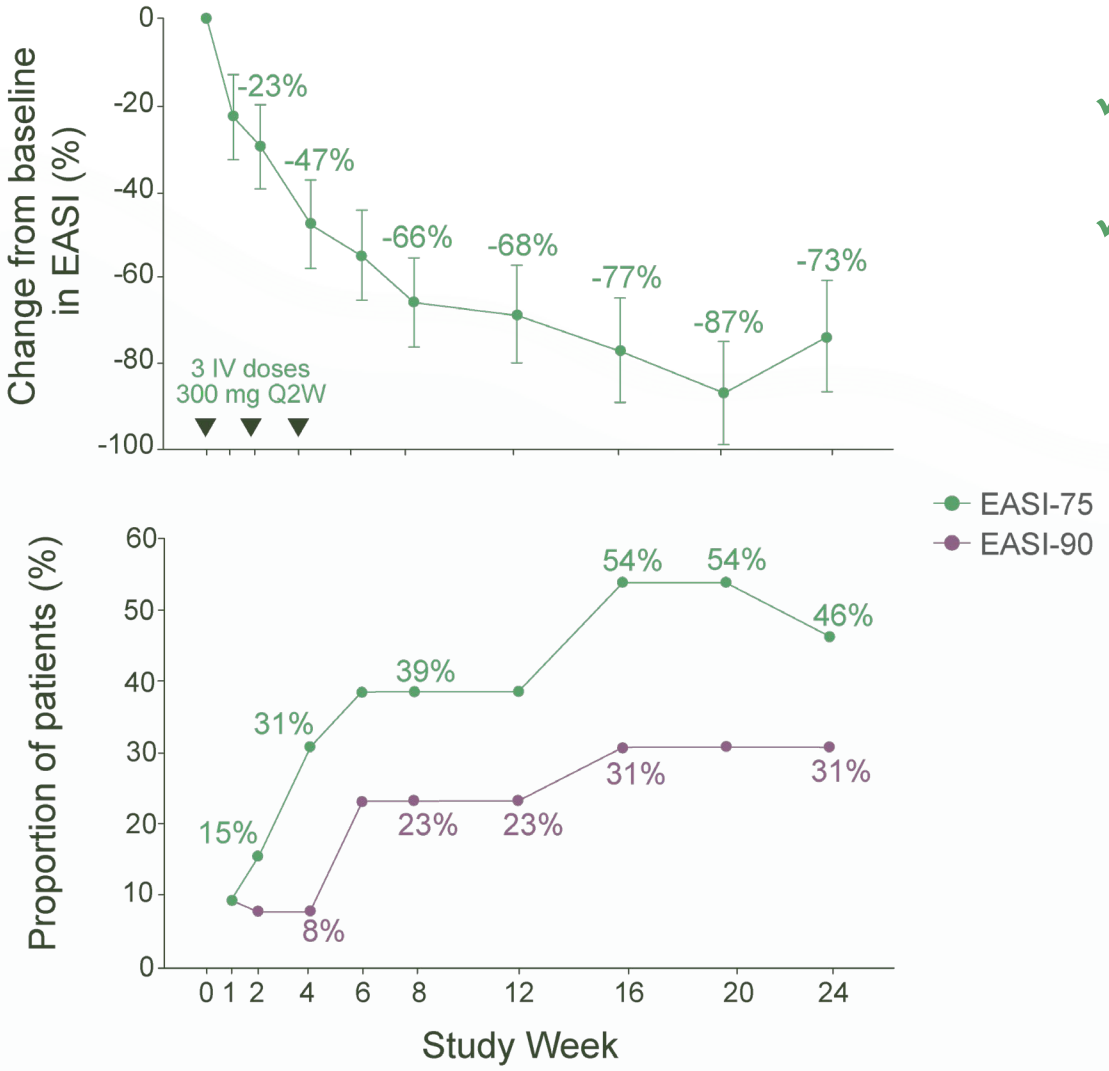

All mice were subjected to whole body irradiation 1 day prior to PBMC infusion. Antibodies were administered weekly at 1 mg/kg (i.v.) from PBMC infusion to end of study (EoS); peripheral exposure peaked ~1 h post-dose and remained detectable for ≥150 h. GvHD was assessed scoring system (fur texture, weight loss, posture, activity, skin integrity; 0–2 per parameter; Cooke KR et al., Blood, 1996). Day 14 group comparisons were performed using a two-sided Wilcoxon rank-sum test.

# Summary of preclinical attributes of IMG-007

- IMG-007 is a novel OX40-targeting antibody combining potent pathway inhibition with an Fc-silenced backbone
- Aglycosylation (N297A) with limited Fcγ receptor binding confers silenced ADCC function and dominant antagonistic activity
- Preclinical studies demonstrated effective blockade of OX40L-mediated NFκB activation, cytokine production, and T cell proliferation
- The Fc-silenced design may support higher dosing and potentially a more favorable safety profile



# IMG-007 in AD: rapid clinical improvement with a favorable safety profile in Phase 1b/2a




- ✓ Four-week IMG-007 treatment with only three doses resulted in 87% mean reduction in EASI score from baseline at week 20
- ✓ Most patients achieved ≥75%, and nearly one-third achieved ≥90%, improvement in EASI by week 16.
- ✓ IMG-007 has shown a consistent safety profile across four studies to date, including AD, AA, and two healthy volunteer studies.

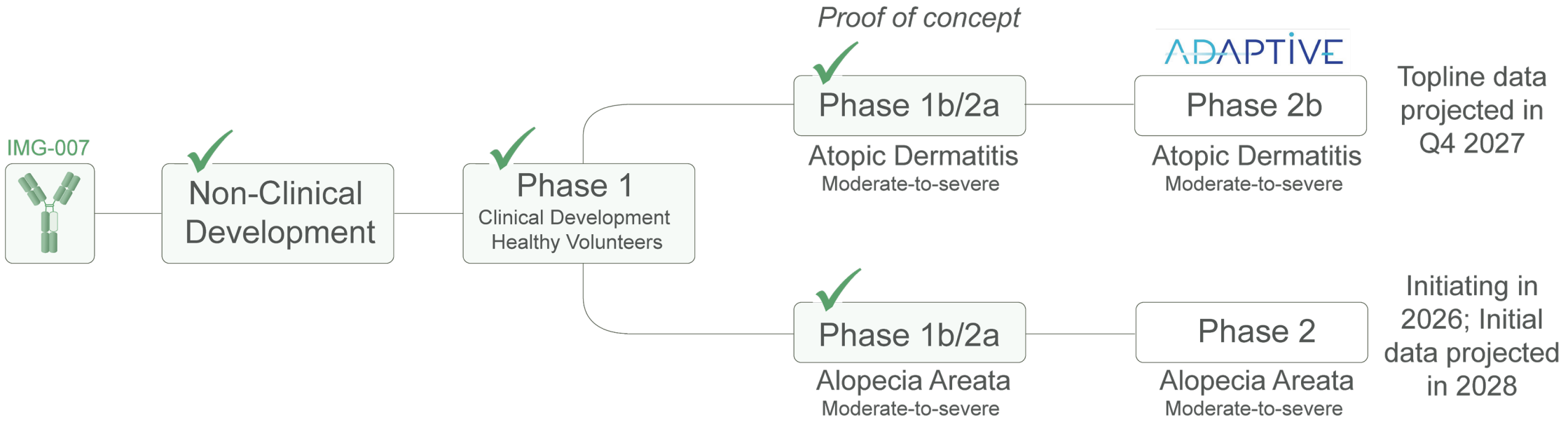
## Treatment-emergent adverse events in Phase 1b/2a

| | |
|---|---|
| Participants with at least one TEAE | 9 (69%) |
| Study treatment related TEAEs | 0 (0%) |
| Serious AE | 0 (0%) |
| TEAE by CTCAE grade | |
| Grade 1 (Mild) | 3 (23%) |
| Grade 2 (Moderate) | 5 (38%) |
| Grade 3 (Severe) | 1 (8%) |
| TEAE that are infusion-related reactions | 0 (0%) |
| TEAE of pyrexia (fever) or chills | 0 (0%) |
| TEAE leading to 4-week dosing period discontinuation | 0 (0%) |

Single arm study, n=13; Patients who received rescue therapies were counted as "non-responders"; Last observation carried forward (LOCF) imputation was used for missing data, except for missing data that arises following study discontinuation with reason 'lack of efficacy' (none in the study).
EASI: Eczema Area and Severity Index; EASI is a composite scoring system used in clinical trials to measure the extent (area) and severity of atopic eczema (dermatitis)

# IMG-007: the first non-depleting, antagonistic OX40 receptor–targeting antibody in advanced clinical development

*IMG-007 continues to be further characterized both biologically and clinically in an ongoing Phase 2 development program*



# Acknowledgment

The authors thank the patients, investigators, and study site personnel for their invaluable contributions to this research.

Please visit **Poster 1036**, "*Preclinical characterization of IMG-007, a high-affinity, non-depleting anti-OX40 monoclonal antibody for the treatment of inflammatory and autoimmune disease*," presented today from 4:30–6:00 PM during the poster session.