NEKTAR®

NEW PATHWAYS TO SMARTER MEDICINE™

# 42nd Annual J.P. Morgan Healthcare Conference

January 2024

# Forward-looking Statements

*This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, unaudited year-end cash and investments and sufficiency of working capital and future availability of clinical trial data. Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 8, 2023. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.*

# Nektar Therapeutics: Targeting Immunology and Inflammation with Immune Modulating Therapies

## Deep Understanding of Immunology

Novel approaches to address the imbalance and dysfunction of T regulatory cells (Tregs) to restore the body's self-tolerance mechanisms and achieve immune homeostasis

## Novel Targets and Differentiated Candidates

Lead candidate (Ph2), REZPEG, is a first-in-class IL-2 pathway agonist selective Treg therapy

Preclinical TNFR2 agonist antibody (NKTR-0165) is designed to potentiate suppressive effects of Tregs

## Compelling Proof-of-Concept Data

Promising Phase 1b data for REZPEG in atopic dermatitis suggest potential as a differentiated remittive and disease modifying therapy

## Large Indications with High Unmet Need

REZPEG is being studied in two large, randomized Phase 2b studies in atopic dermatitis and alopecia areata with data expected in first half of 2025

## Well Capitalized Through Upcoming Catalysts

Ended the year with $329M in cash and cash equivalents

Cash runway into the middle of 2026

# Immunology Focused Pipeline & Oncology Assets

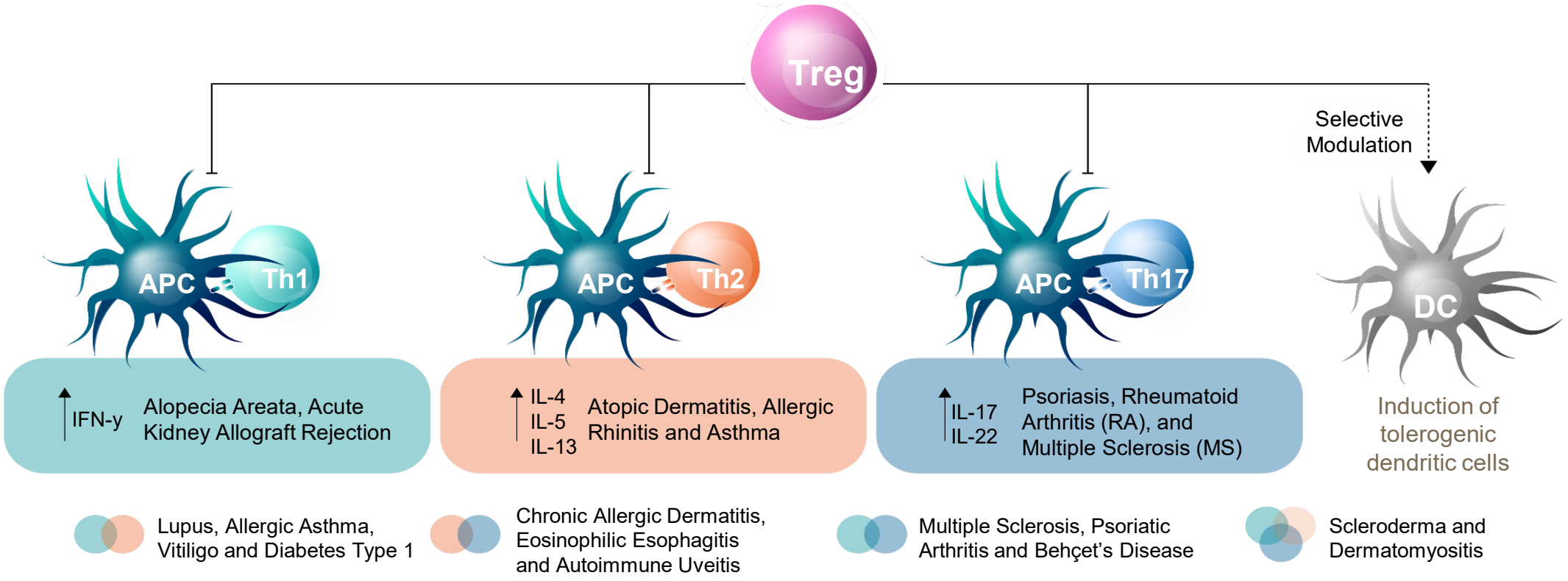
| Program | Indication | Stage | Preclinical | Phase 1 | Phase 2 | Phase 3 | Partner |
|---|---|---|---|---|---|---|---|
| REZPEG | Atopic Dermatitis | Initiating Phase 2b Trial in Q4 2023 | | | | | |
| REZPEG | Alopecia Areata | Initiating Phase 2b Study in Q1 2024 | | | | | |
| NKTR-0165 | Multiple Sclerosis & Other Autoimmune Indications | Preclinical | Preclinical | | | | BiolojicDesign |
| PEG-CSF1 | Fibrotic Diseases & Other Indications | Preclinical | Preclinical | | | | |

**REZPEG:** IL-2 T Regulatory Cell Stimulator
**NKTR-0165:** Bivalent Agonistic Antibody Targeting TNFR2

| Program | Indication | Stage | Preclinical | Phase 1 | Phase 2 | Phase 3 | Partner |
|---|---|---|---|---|---|---|---|
| NKTR-255 | Oncology | Multiple partnered and investigator-sponsored trials ongoing in various indications | | | Exploring Partnership Options | | MERCK KGaA Darmstadt, Germany; AbelZeta |
| NKTR-288 | Oncology | Preclinical | Preclinical | | | | |

**NKTR-255:** IL-15 Receptor Agonist
**NKTR-288:** PEG-conjugate of Interferon Gamma

# The Central Role of T Regulatory Cells in Immune Homeostasis



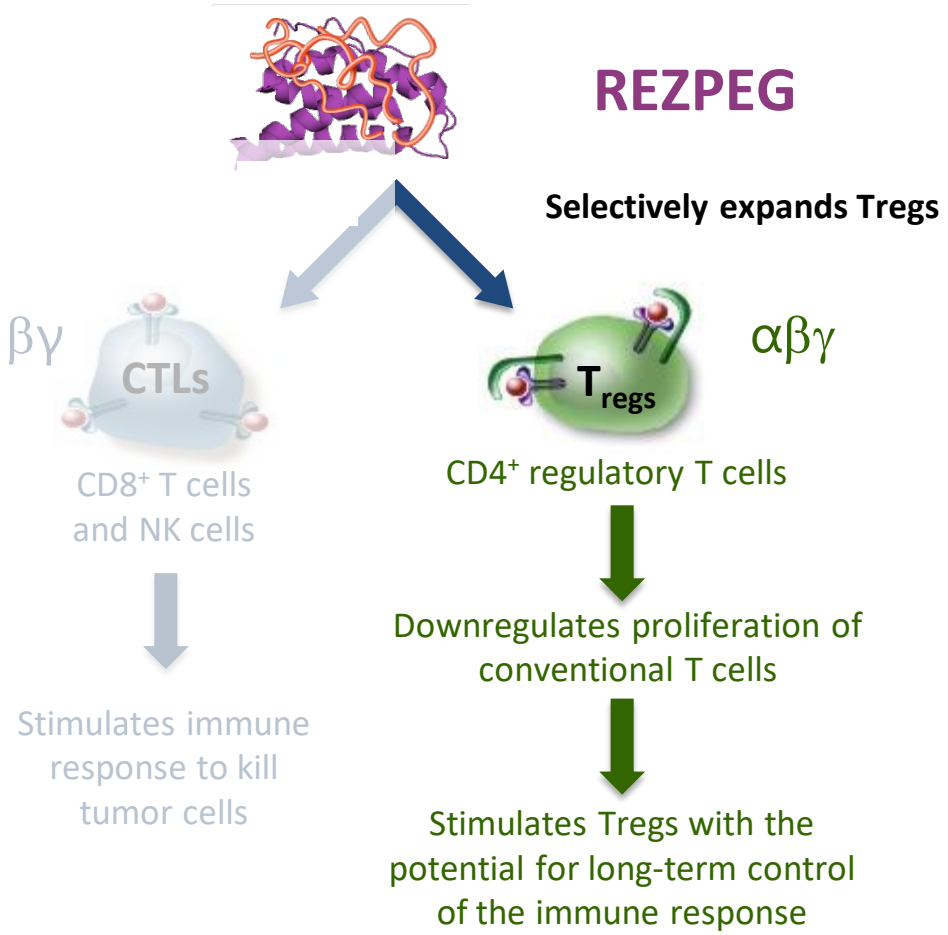

**Tregs are crucial for immune homoeostasis and the prevention of autoimmune conditions.**[1]

- ***IL-2 pathway agonism***
- ***TNFR2 agonism***



**Sources:** [1] Lykhopiy V, et al. *Genes Immun.* (2023) Epub ahead of print

# REZPEG: IL-2 Pathway Agonist that Selectively Induces Tregs and their Suppressive Activity




**Compared with native IL-2, REZPEG has:**[1]

- An altered binding profile, eliciting a lower binding affinity for IL-2Rβ and a different binding bias for IL-2Rα and IL-2Rβ
- Selectivity for the stimulation of regulatory T cells (Tregs) over conventional T cells (Tcons)
- An increased half-life

**REZPEG has shown:**

- Activity in animal models of systemic lupus erythematosus (SLE)[2] and cutaneous hypersensitivity[3]
- Selective stimulation of Tregs in healthy volunteers and patients with lupus[4]
- Clinical efficacy in Atopic Dermatitis, Psoriasis, and SLE

NEKTAR **Source:** 1. Fanton C, et al. Poster presented at the European Congress of Rheumatology (EULAR), 2020: THU0054.; 2. Dixit et al J Trans Autoimmun 2021; 3. Langowski J, et al. Poster presented at the American College of Rheumatology Annual Meeting, 2017: 2715.; 4. Fanton et al J Trans Autoimmun 2022

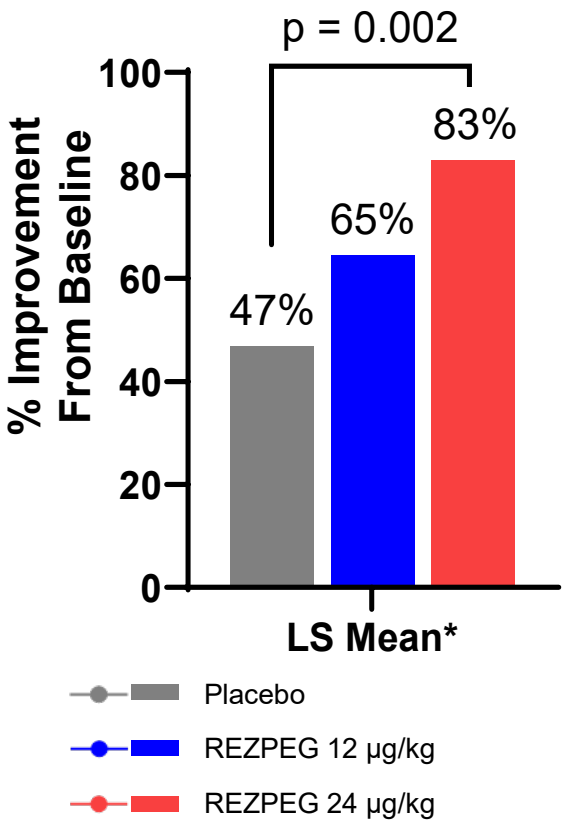
# 9 Clinical Trials Conducted for the REZPEG Program Provide a Roadmap for Development Success

- 382 patients with autoimmune conditions and 210 healthy volunteers have received REZPEG
- Consistent and highly-predictable Treg pharmacology observed across 9 clinical studies
- Clear evidence of clinical benefit in skin-related autoimmune conditions observed across 3 randomized placebo-controlled studies (atopic dermatitis, psoriasis & cutaneous lupus)
- Well tolerated biologic agent with minimal side effects

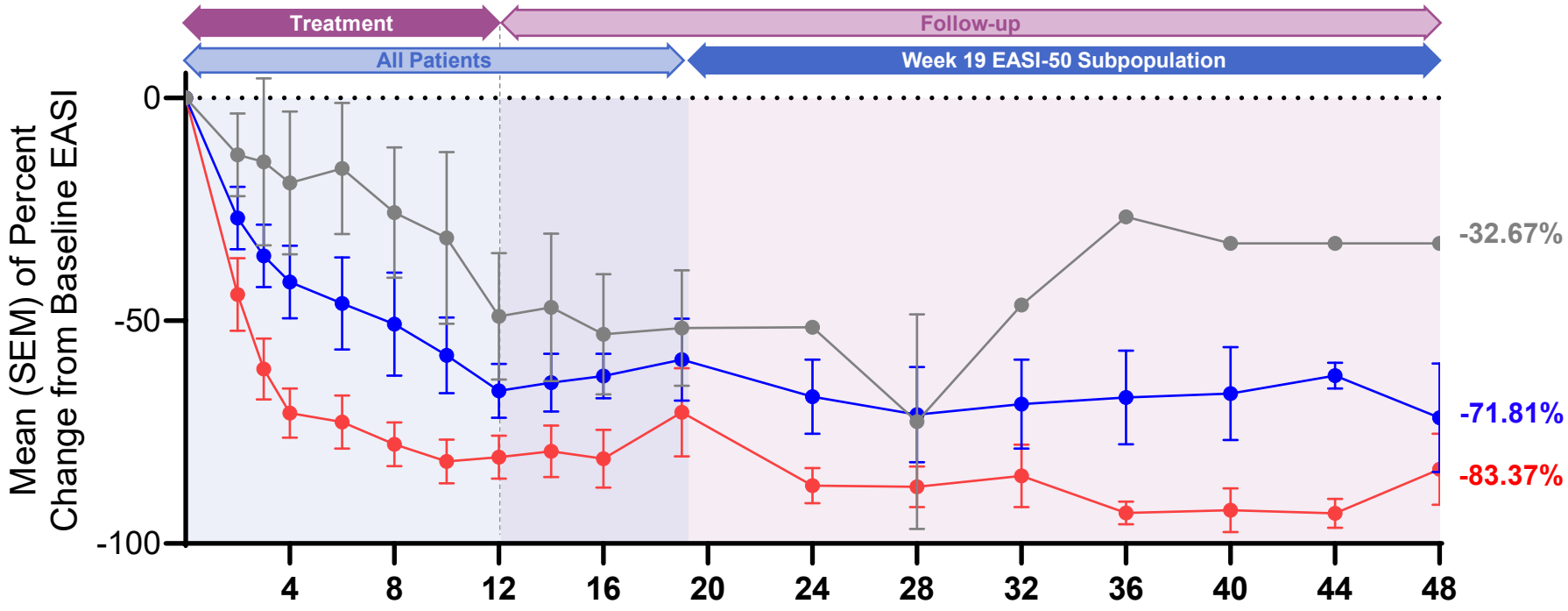
# Percent Change From Baseline EASI Score

***Statistically Significant and Sustained Improvement At Highest Dose***

## EASI Improvement at Week 12




## Percent Reduction from Baseline EASI




| Weeks | 0 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 14 | 16 | 19 | 24 | 28 | 32 | 36 | 40 | 44 | 48 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PBO, n | 10 | 8 | 6 | 8 | 6 | 8 | 5 | 7 | 5 | 5 | 6 | 1 | 2 | 1 | 1 | 1 | 1 | 1 |
| REZPEG 12 µg/kg, n | 16 | 16 | 15 | 15 | 14 | 14 | 12 | 12 | 12 | 12 | 12 | 7 | 5 | 5 | 5 | 4 | 3 | 4 |
| REZPEG 24 µg/kg, n | 17 | 16 | 16 | 15 | 15 | 14 | 13 | 12 | 13 | 13 | 13 | 8 | 9 | 9 | 7 | 7 | 7 | 7 |

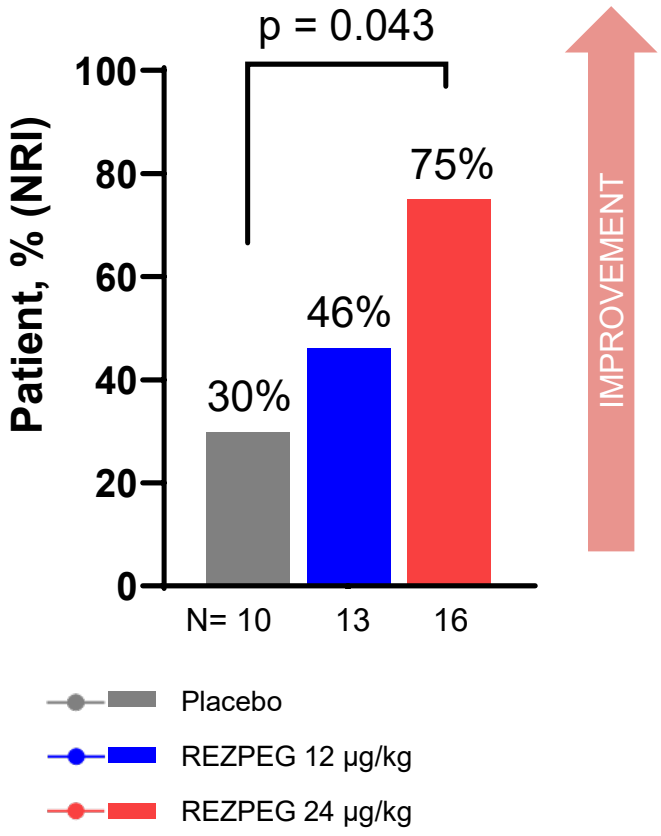
n = number of participants who were evaluated at each defined timepoint

NEKTAR SEM: Standard error of the mean; continuous endpoint using observed data; *EASI Improvement results are least squares (LS) mean percent change from baseline obtained from Mixed Model for Repeated Measures (MMRM) as specified in the statistical analysis plan (SAP) defined in the protocol (generated by independent statistical audit firm)

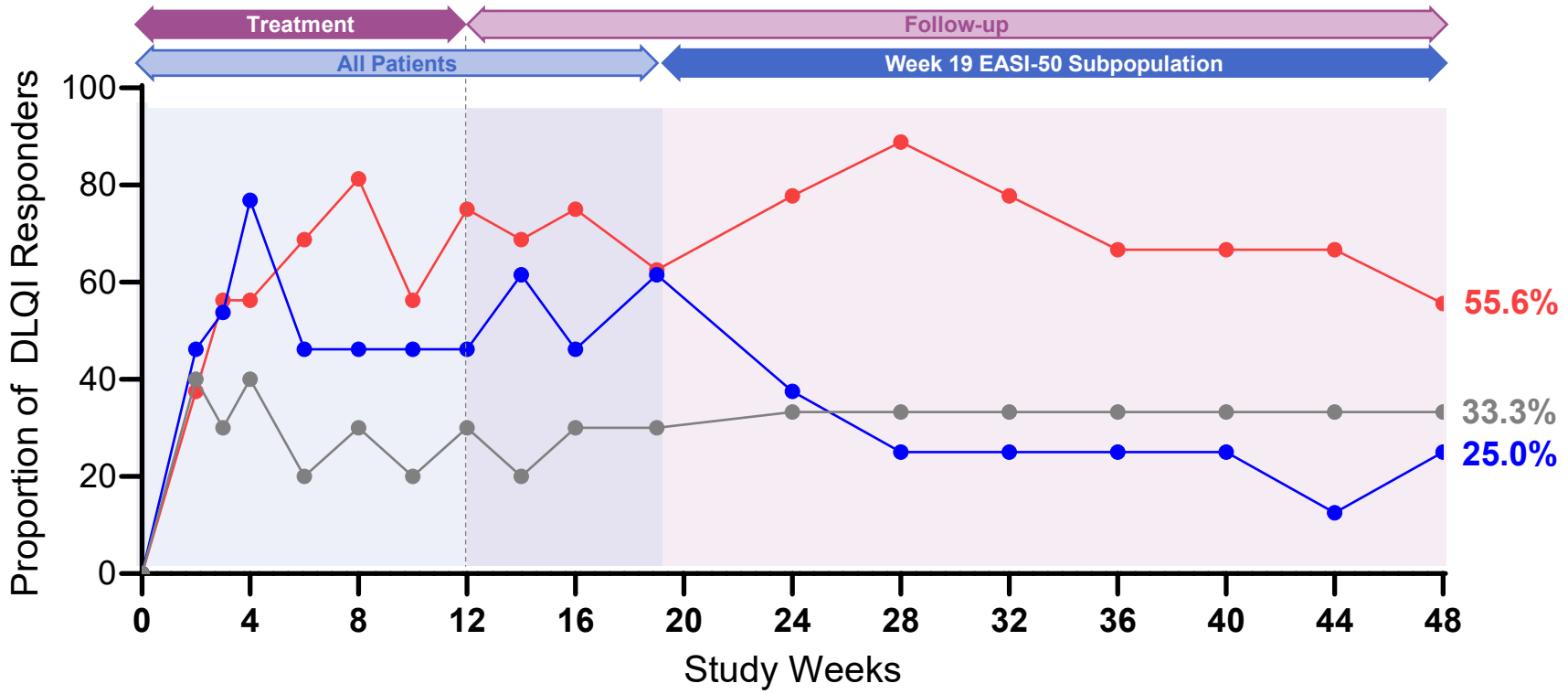
# DLQI (Dermatology Life Quality Index)

***Statistically Significant And Durable Improvement From Baseline***

## DLQI Responders at Week 12




## Proportion of DLQI Responders




| Weeks | 0 | 2 | 3 | 4 | 6 | 8 | 10 | 12 | 14 | 16 | 19 | 24 | 28 | 32 | 36 | 40 | 44 | 48 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PBO, n | N=10 | 4 | 3 | 4 | 2 | 3 | 2 | 3 | 2 | 3 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| REZPEG 12 µg/kg, n | N=13 | 6 | 7 | 10 | 6 | 6 | 6 | 6 | 8 | 6 | 8 | 3 | 2 | 2 | 2 | 2 | 1 | 2 |
| REZPEG 24 µg/kg, n | N=16 | 6 | 9 | 9 | 11 | 13 | 9 | 12 | 11 | 12 | 10 | 7 | 8 | 7 | 6 | 6 | 6 | 5 |

n = number of participants who achieved a DLQI response at each defined timepoint

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Patients were followed until Week 19 (10, 13, and 16 pts in the PBO, 12 µg/kg and 24 µg/kg groups), and those with ≥EASI-50 response at Week 19 (3, 8, and 9 pts in the PBO, 12 µg/kg and 24 µg/kg groups) were followed until Week 48 or until EASI-25 response criteria were no longer met; patients who were not EASI-50 responders at week 19 were excluded from the denominator for visits after week 19; NRI: non-responder imputation

***"We've never really been sure if the T reg hypothesis is true or not or if it was an epi phenomenon. These may be some of the most compelling data to-date for the field, proving at a high level, that if you causally increase T reg cells that you will take down inflammation and improve a disease state. To me, this is a proof of concept for so many things and an important finding for all of immunology."***

*- Dr. Jonathan Silverberg, Professor of Dermatology at The George Washington University School of Medicine and Health Sciences and Director of Clinical Research and Contact Dermatitis*

NEKTAR **Source:** Silverberg J, et al. Presentation at the European Academy of Dermatology & Venereology (EADV), 2023

# Atopic Dermatitis: Multi-Billion Dollar Market Opportunity Ahead

## *Still High Unmet Need, Especially For New Therapies With Remittive Effect*

**Atopic dermatitis (AD)** is a chronic autoimmune conditions that causes inflammation, redness and irritation of the skin. Moderate-to-severe AD is associated with unbearable itching that can result in significant disease burden and impacts to quality of life.

**~30 million**[1]
Adults with AD in U.S.

**~220 million**[2]
Adults with AD globally

**~50%**[3]
Adults with AD have moderate-to-severe disease

**~8%**[4]
Patients with moderate/severe AD are treated with a biologic

Dupixent®: current market leader in atopic dermatitis exceeding $6.2B in annual sales, **but 50% of patients fail on therapy**[5, 6]

***High unmet need for a new therapy employing a new mechanism of action to:***

1. Induce a deep and potentially therapy-free remission
2. Offer dosing schedules without rebound effect
3. Favorable safety and tolerability profile for ease of use


Source: [1]Eczema stats. National Eczema Association. (2022, September 27). https://nationaleczema.org/research/eczema-facts/; [2]Eczema council. (n.d.). https://www.eczemacouncil.org/assets/docs/global-report-on-atopic-dermatitis-2022.pdf; 3Clarivate™ DRG Mature Markets Data 2023.; [4]DRG Epidemiology; [5]*N Engl J Med* 2016; 375:2335-2348 DOI: 10.1056/NEJMoa1610020; [6]Evaluate Ltd (accessed: 1/5/2023)

# Why We Need Additional Therapies for Atopic Dermatitis

## Current systemic treatment options fall short on safety and long-term disease control

- Majority of patients do not achieve adequate disease control by the end of the induction period[1]
- Currently available systemic therapies may be limited by their safety and efficacy profile:

### IL-13 Biologics

- Side effects include conjunctivitis, facial erythema*, arthralgia*[2]
- No dose flexibility
- Lack of efficacy with 50% of patients failing Dupixent® therapy[1]
- Lack of long-term disease control with patients rebounding once off treatment

### JAK Inhibitors

- Multiple black box warnings[3] (e.g. Serious infections, cardiovascular death, myocardial infarction, stroke, lymphoma, blood clots)
- Lab monitoring
- While treatment leads to rapid improvement in disease, once off therapy, patients rebound quickly

- Even patients with a favorable response experience loss of disease control following cessation of therapy[4-5]
- The limited armamentarium of approved drugs with an adequate benefit–risk ratio represent major challenges in the field[6]
- New strategies aimed at inducing deep and potentially therapy-free remission are needed[7]

* Reported with dupilumab; **Sources:** [1]Silverberg JI, et al. *Dermatol Ther (Heidelb)* (2022) 5:1181-1196; [2]Torres T, et al. *J Dermatolog Treat* (2022) 33(5): 2554-2559; [3]Mikhaylov D, et al. *Ann Allergy, Asthma, Immuno* (2023) 130(5) 577-592; [4]Gooderham et al. *JAMA Derm* (2019) 155(12): 137101379; [5]Blauvelt et al. *Am J Clin Dermatol.* (2022) 23(3): 365-383; [6]Bieber T. *Nature Reviews Drug Discovery* (2022) 21: 21–40; [7]Bieber T. *Nature Reviews Drug Discovery* (2023) 22: 662–680.

# Efficacy Comparison of Biologics in Patients with Atopic Dermatitis – Phase 2 Clinical Trials Vs. Nektar Phase 1b

| Endpoint | DUPIXENT (dupilumab) 300 mg Q2W[1] Regeneron | ADBRY (Tralokinumab) 300mg Q2W[2] Leo Pharma | Lebrikizumab 250mg Q2W[3] Lilly | Nemolizumab 30mg Q4W[4] Galderma | Rocatinlimab 300mg Q2W[5] Amgen | Amlitelimab 250mg Q4W LD[6] Sanofi | Rezpegaldesleukin (Phase 1b) 24 µg/kg Q2W Nektar |
|---|---|---|---|---|---|---|---|
| **Mechanism of Action** | IL-4 & IL-13 antagonist | IL-13 antagonist | IL-13 antagonist | IL-31 antagonist | OX40 antagonist | OX40 antagonist | IL-2Rα agonist |
| **Drug: EASI LS Mean % reduction from baseline** | 68% | 58% | 72% | 69% | 61% | 62% | 83% |
| **Placebo: EASI LS Mean % reduction from baseline** | 18% | 41% | 41% | 52% | 15% | 29% | 47% |
| **EASI-75** | ~53%# | 43%& | 51%-61%+ | 46% | 54% | 43% | 58% (OBS)<br>41% (NRI) |
| **EASI-90** | ~30%# | Not available | 44% | 30% | 37% | Not available | 33% (OBS)<br>24% (NRI) |
| **IGA/vIGA-AD ≥ 2 pt (0, 1) Responders** | 30% | 27% | 45% | 37% | 31% | 23% | 42% (OBS)<br>29% (NRI) |
| **Itch NRS ≥ 4 pt Responders** | 36-41%** | 20-25%** | 70% | ~50%^^ | 56% | 27% | 64%* (OBS)<br>47%* (NRI) |

*Analysis on patients with baseline score>=4; **Based on Phase 3 studies. # estimated from Figure 3 in manuscript 1. & excluded data after rescue medication and uses last observation carry forward (LOCF). +patients without baseline were excluded and missing data were imputed using Markov Chain Monte Carlo (MI-MCMC). ^^estimated from Figure 4 in manuscript 4

Acronyms: EASI = Eczema Area and Severity Index; LS = least squares; IGA = investigator global assessment; vIGA = validated investigator global assessment; pt = point; NRS = numerical rating scale; Q2W = every two weeks; Q4W = every four weeks; OBS = as observed; NRI = non-responder imputation. UNK=unknown. References: [1]Thaçi et al. *Lancet* (2016) 387(10013): 40-52; [2]Wollenberg et al. *J Allergy Clin Immunol* (2019) 143(1): 135-141; [3]Guttman-Yassky et al. *JAMA Dermatol.* (2020) 156(4): 411-420; [4]Silverberg et al. *J Allergy Clin Immunol.* (2020) 145(1): 173-182; [5]Guttman-Yassky et al. *Lancet* (2023) 401(10372): 204-214; [6] Weidinger et al. *Br J Derm* (2023), epub ahead (July 18, 2023)

# Phase 1b Data Suggest Potential for REZPEG as Differentiated Remittive Therapy

**Consistent clinical effects**

observed across all physician-assessed and patient-reported outcomes

**Rapid onset of effect**

with significant benefits in outcomes observed after just two doses of REZPEG

**Dose dependent responses**

suggest potential flexibility of dosing schedules

**Differentiated efficacy**

that is highly competitive with currently available systemic treatments

**Durability of response**

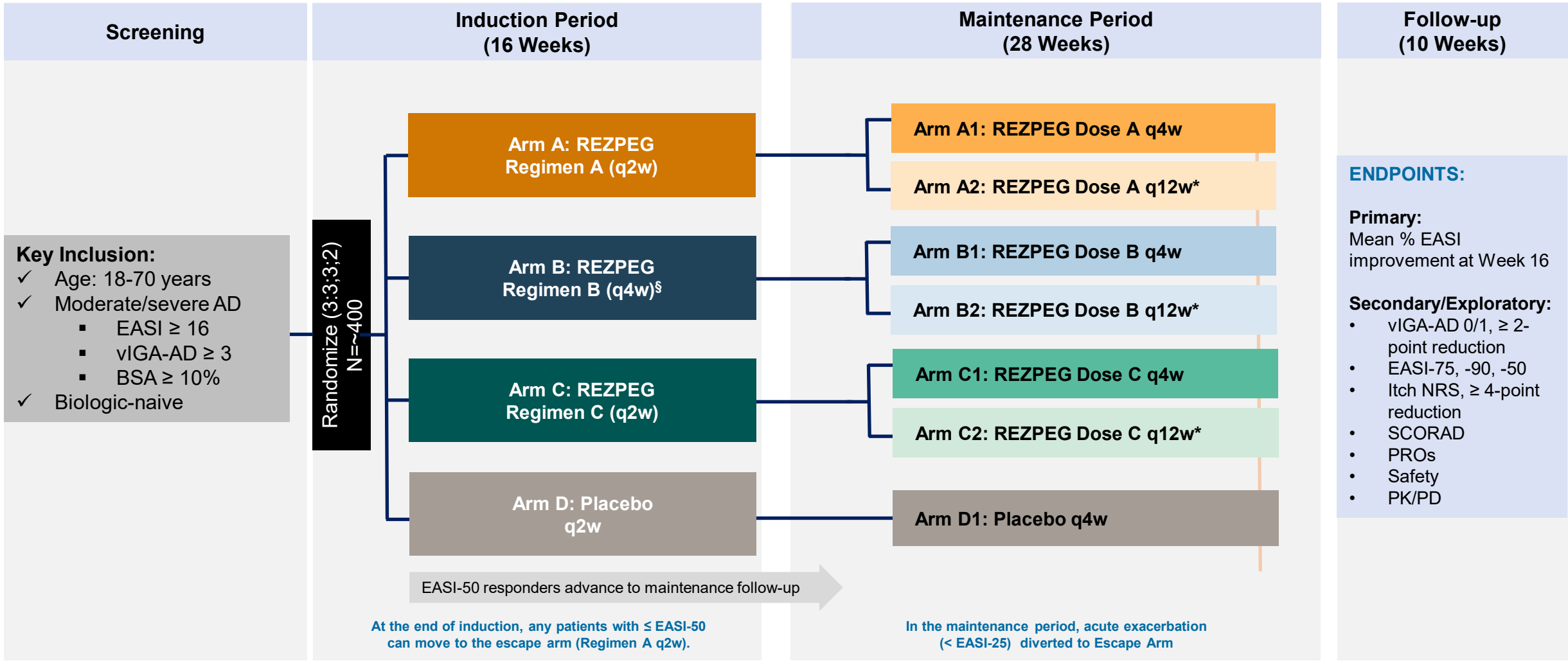
across all outcomes 36 weeks after end of REZPEG dosing suggests potential as a remittive therapy

**Favorable safety profile**

with no serious or severe adverse events, no conjunctivitis and no ADA

# REZPEG Phase 2b Study Initiating in Q4 2023

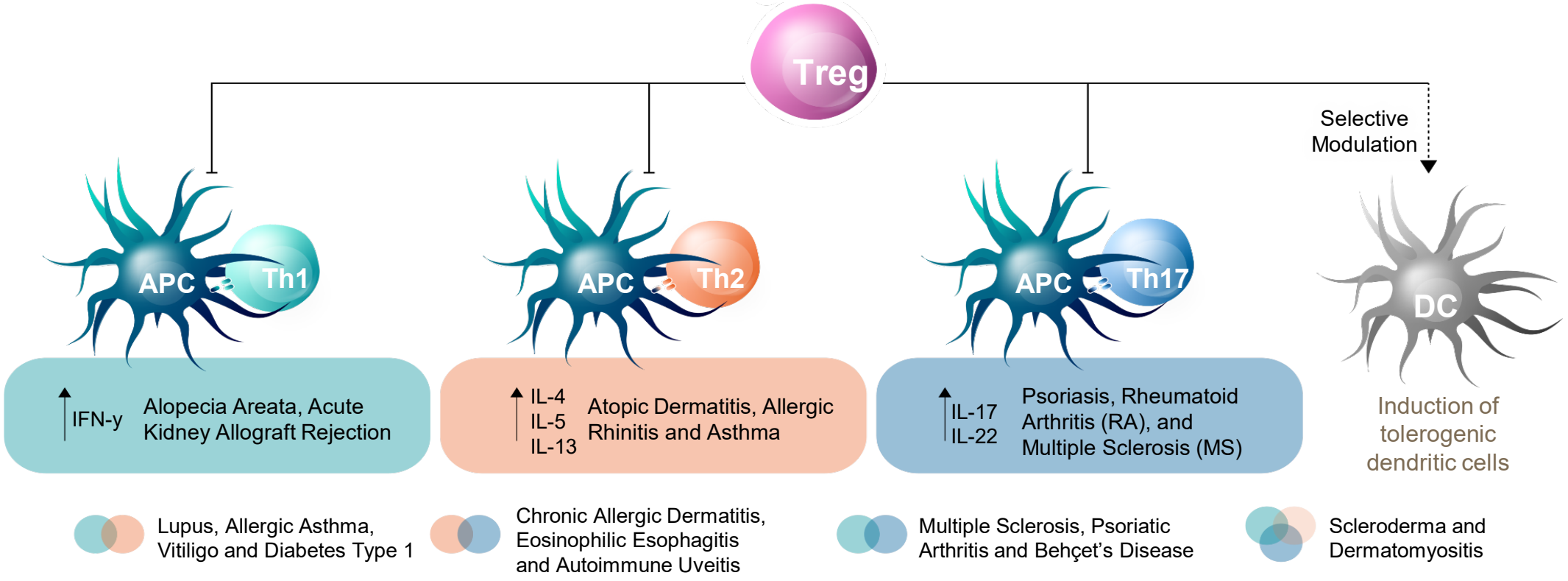
## *Moderate-to-Severe Atopic Dermatitis*




§ Patients assigned to Arm B during induction will be administered placebo on Weeks 4, 8, 12, and 16 to satisfy the q2w induction dosing schedule.
* Patients assigned to q12w arms during maintenance will be administered placebo on Weeks 22, 26, 34, and 38 to satisfy the q4w maintenance dosing schedule.

# Rezpegaldesleukin (REZPEG)

## *The Central Role of T Regulatory Cells in Immune Homeostasis*




**Tregs are crucial for immune homoeostasis and the prevention of autoimmune conditions.**[1]



**Sources:** [1] Lykhopiy V, et al. *Genes Immun.* (2023) Epub ahead of print

# REZPEG In Alopecia Areata

## *Phase 2b Clinical Study Expected To Initiate In Q1 2024*

**Alopecia areata (AA)** is a disease that happens when the immune system attacks hair follicles and causes hair loss[1]

- Nearly 6.7 million people in the US have had it or will have it in their lifetime. ~700,000 people currently have alopecia areata in US. [2]
- ~160 million people worldwide have alopecia areata or have had, or will have it[2]
- 80% of patients show signs of alopecia before 40[2]
- Many patients are refractory to available therapies, and long-term use is associated with troublesome side effects and safety risks[3]
- Only systemic treatments approved for alopecia are JAK inhibitors with multiple Blackbox warnings. High relapse rates upon discontinuation of these therapies[3]

***Represents additional opportunity to expand REZPEG***

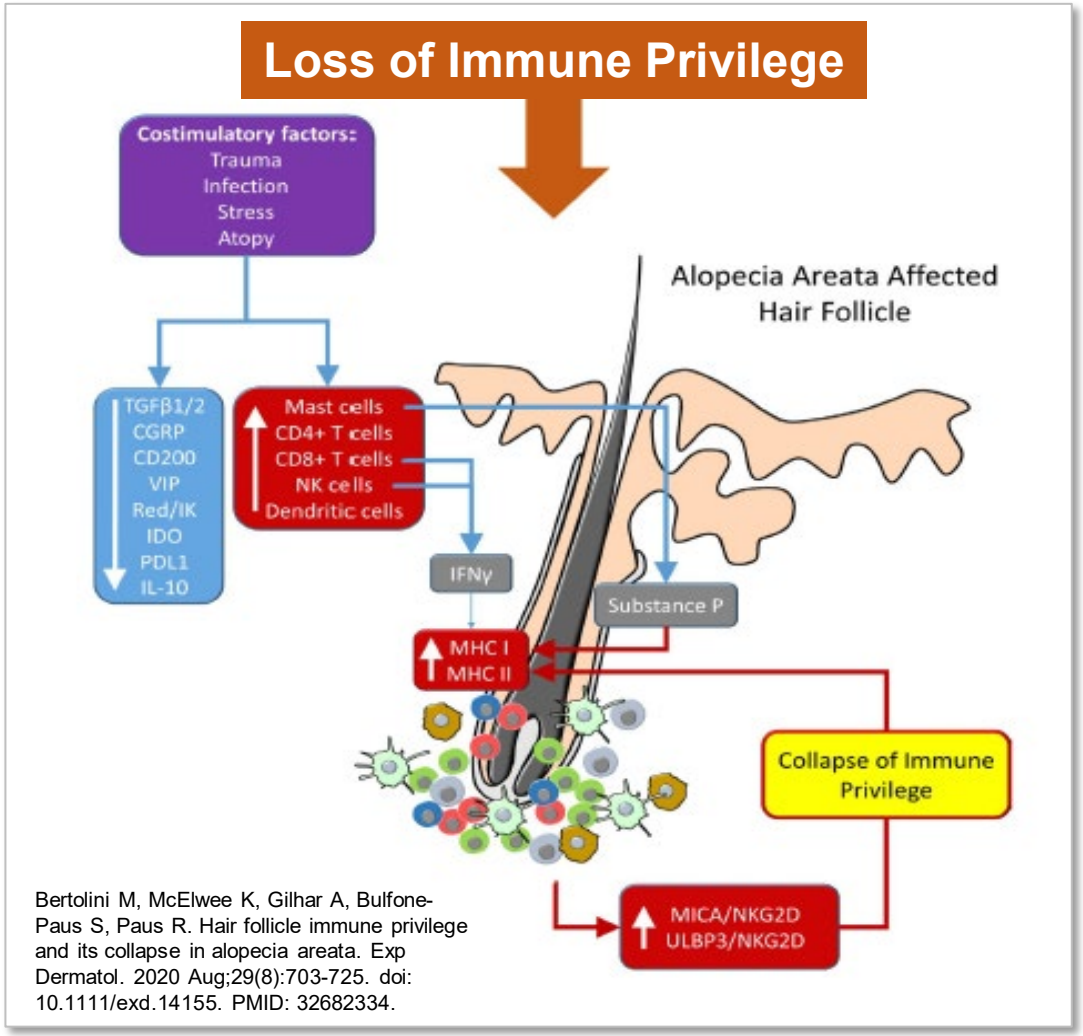
NEKTAR **Sources:** 1. NIH; 2. National Alopecia Areata Foundation; 3. DRG – Unmet Needs of Alopecia Areata

# Anagen Hair Follicles Reside in a State of Immune Privilege

**Loss of Immune Privilege**

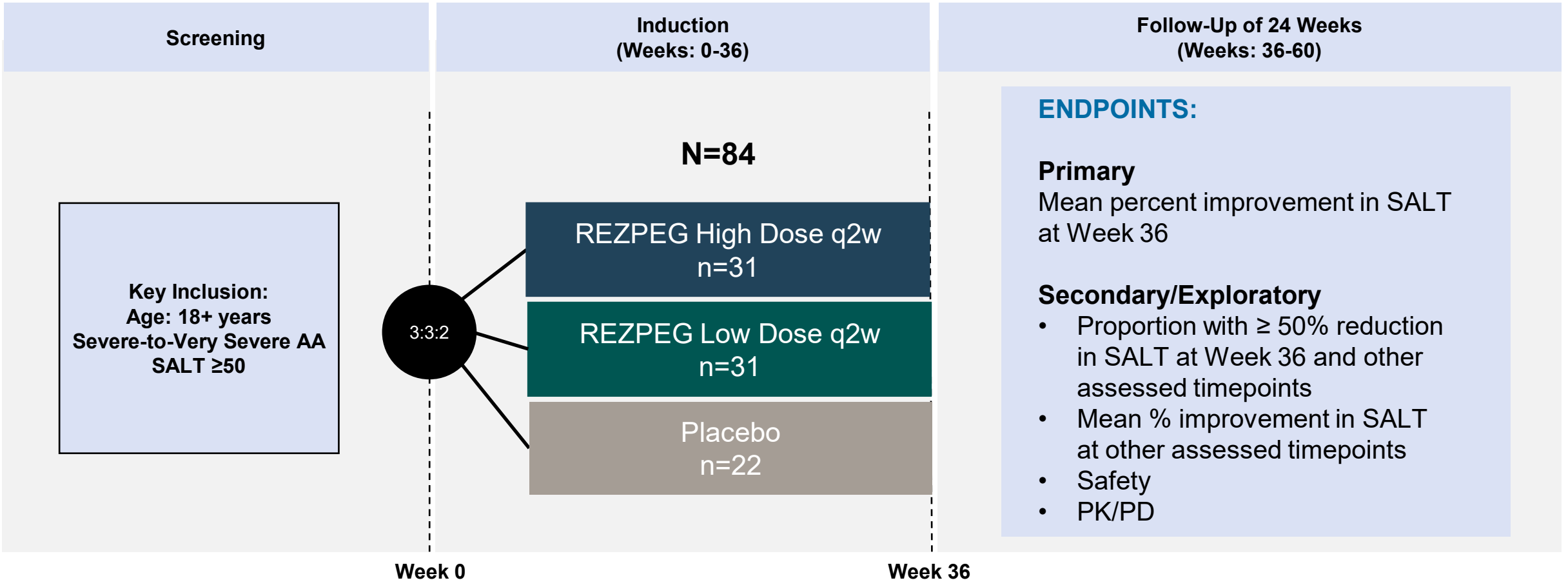
- Increase in expression of MHC Class I and MHC Class II, upregulation of danger ligands (such as NKG2D activating ligands MICA and ULBP molecules), increased levels of proinflammatory cytokines, and a robust immune cell infiltrate
- Immune cell infiltrates are predominantly $CD4^+$ and $CD8^+$ T cells. $CD8^+$ T cells in close association with the hair follicle were found to express NKG2D, an activating receptor commonly associated with the natural killer (NK) cell lineage and IFN gamma

- ***REZPEG preferentially stimulates expansion of Tregs without activation of effector T-cells***
- ***Rebalances immune system by increasing Treg population and function***




Bertolini M, McElwee K, Gilhar A, Bulfone-Paus S, Paus R. Hair follicle immune privilege and its collapse in alopecia areata. Exp Dermatol. 2020 Aug;29(8):703-725. doi: 10.1111/exd.14155. PMID: 32682334.

# Phase 2b Study for Patients with Alopecia Areata




**ENDPOINTS:**

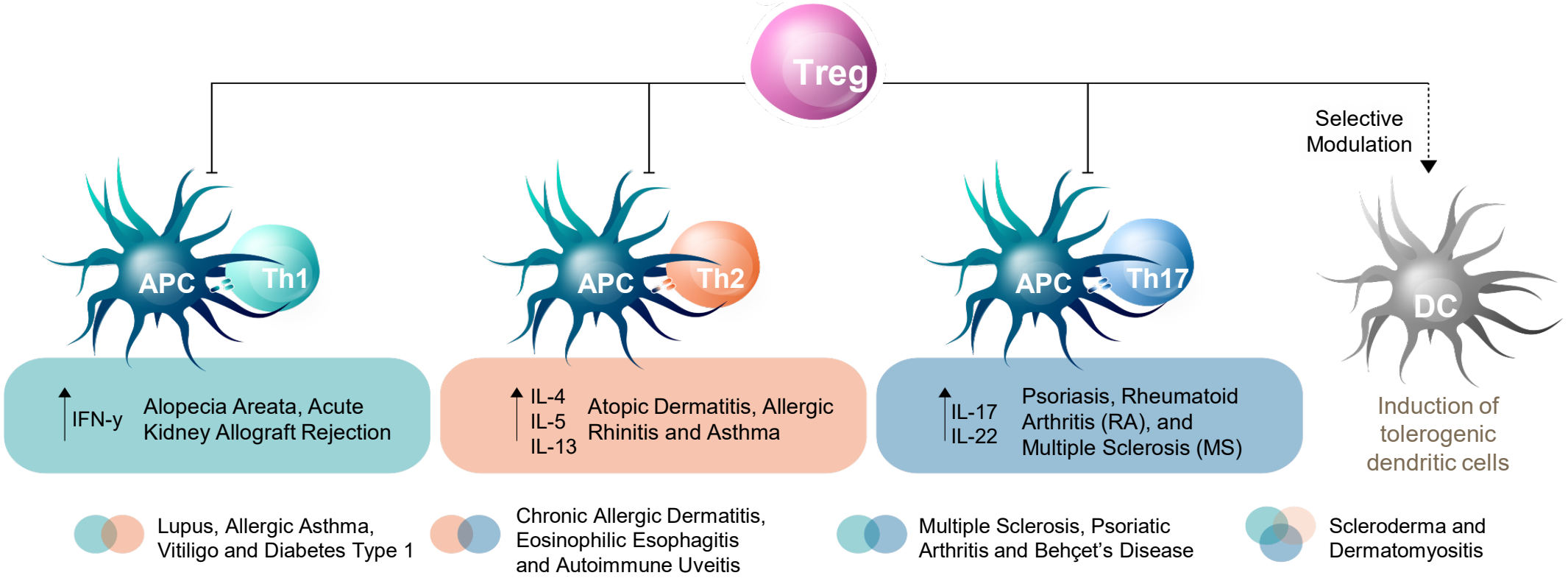
**Primary**
Mean percent improvement in SALT at Week 36

**Secondary/Exploratory**
- Proportion with ≥ 50% reduction in SALT at Week 36 and other assessed timepoints
- Mean % improvement in SALT at other assessed timepoints
- Safety
- PK/PD

**SALT: The Severity of Alopecia Tool is widely used to assess the extent of scalp-hair loss in patients with alopecia areata. Guidelines define treatment success as a 50% improvement in scalp hair.**

# NKTR-0165: TNFR2 Agonist Antibody Program

## *The Central Role of T Regulatory Cells in Immune Homeostasis*



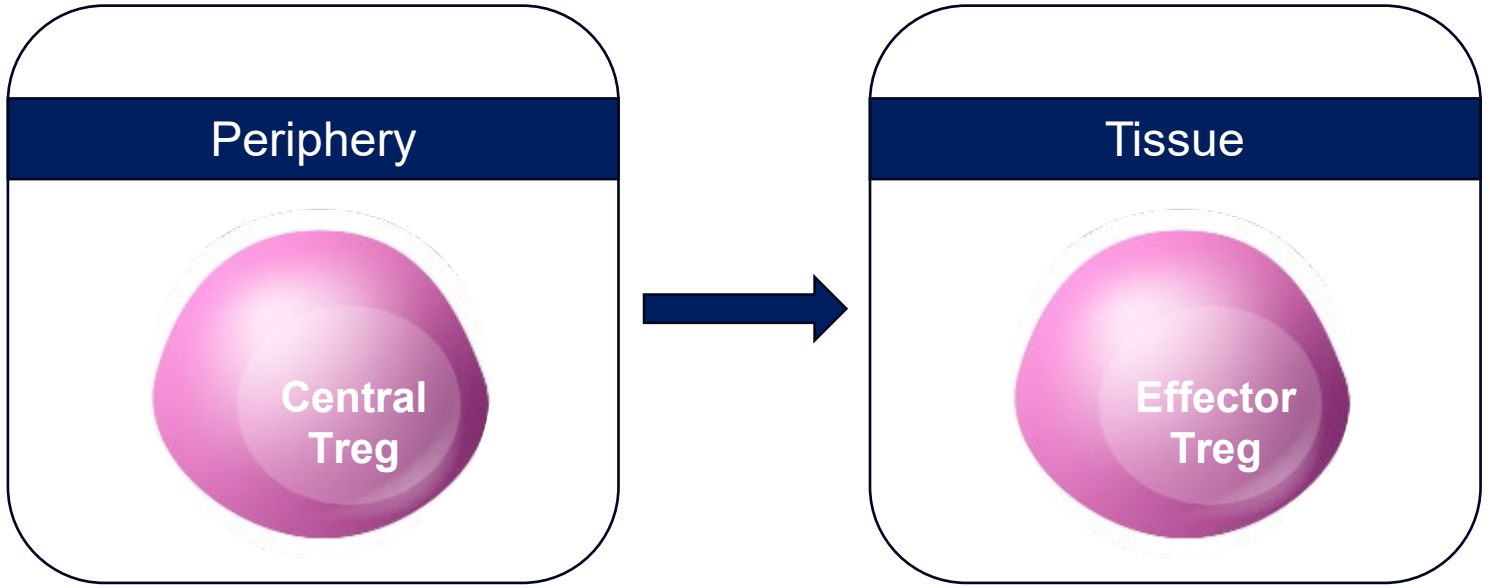

**Tregs are crucial for immune homoeostasis and the prevention of autoimmune conditions.**[1]



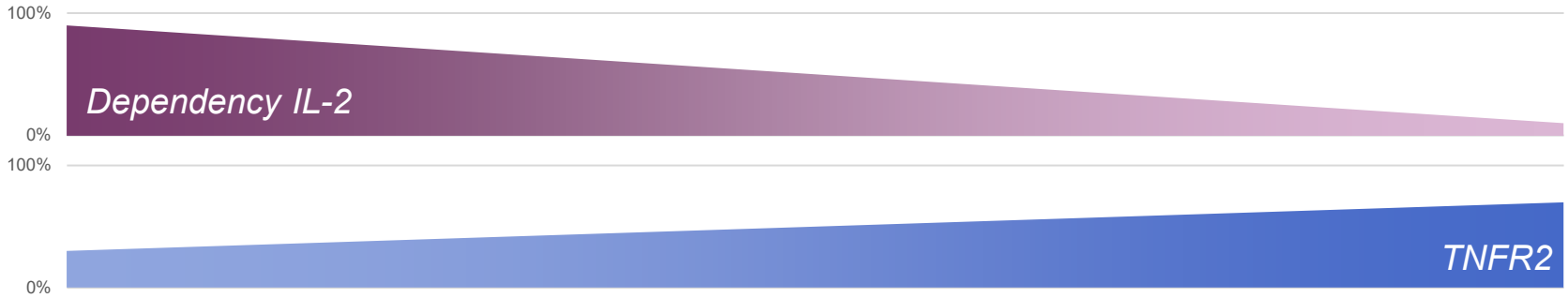
**Sources:** [1] Lykhopiy V, et al. *Genes Immun.* (2023) Epub ahead of print

# Nektar's Programs Addressing Treg Biology

***REZPEG (IL-2 T Regulatory Cell Stimulator)***

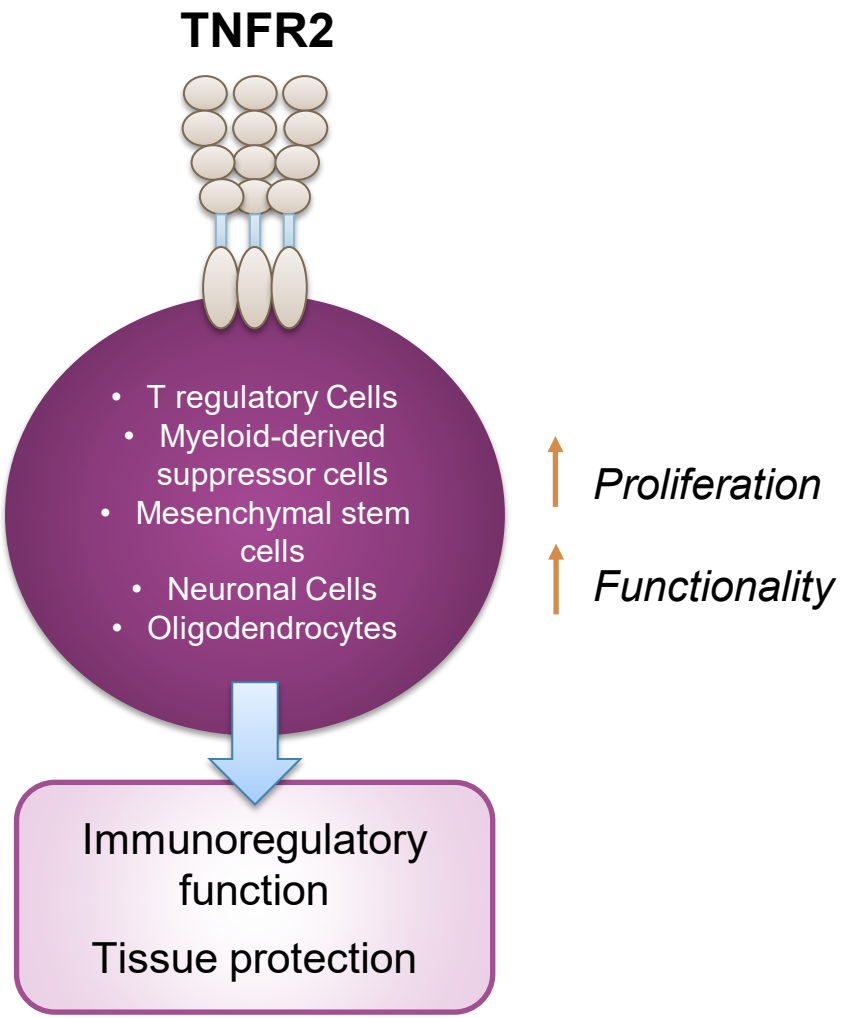



***NKTR-0165 (Bivalent Agonistic Antibody Targeting TNFR2)***



# NKTR-0165: TNFR2 Agonist Antibody Program

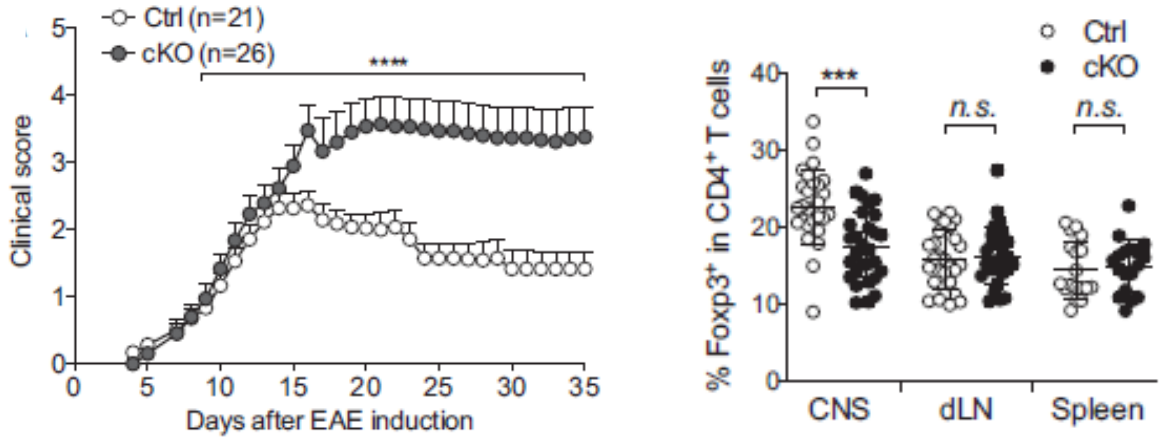
***Targeting TNF Receptor 2 (TNFR2) For The Treatment Of Autoimmune Conditions***




- TNFR2 signaling drives immunoregulatory function could provide direct protective effect for tissue cells
- Unique Nektar antibody candidates show selective T regulatory cell binding and signaling profiles enabling it to be developed for the treatment of autoimmune conditions
- Program targets multiple MOAs including suppression of inflammation, regrowth of myelin after demyelination (MS) and promotion of immune resolution.
  - Examples include Ulcerative Colitis, Multiple Sclerosis (i.e. myelin regrowth), Vitiligo and other autoimmune conditions
- Targeting IND enabling studies for NKTR-0165 in Q4 2024

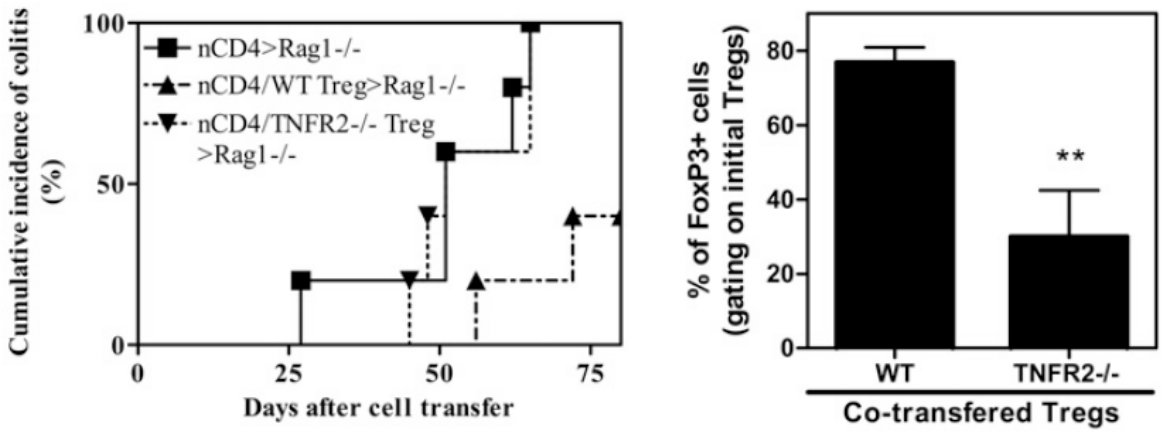
# Research Showing Importance of TNFR2 Expression on Regulatory T Cells in Mouse Disease Models

## EAE Model




*Proc Natl Acad Sci U S A. 2021 Mar 30;118(13)*

## Colitis Model




*J Immunol. 2013 Feb 1;190(3):1076-84*

**TNFR2 expression on regulatory T cells is critical to maintain the population and their immunosuppressive function in mouse disease models**

# Disease Prevalence of Ulcerative Colitis, Multiple Sclerosis & Vitiligo

**Ulcerative Colitis**

- Estimated ***5.8 million*** diagnosed cases of Ulcerative Colitis worldwide with 40% of these cases in major US and EU markets.
- Number of diagnoses forecast to increase by ***21%*** from 2021-2031.

**Multiple Sclerosis**

- Estimated ***2.9 million*** diagnosed cases of MS worldwide with 46% of these cases in major US and EU markets.
- Number of diagnosed cases worldwide forecast to increase by ***19%*** between 2022-2032.

**Vitiligo**

- Estimated ***24 million*** diagnosed cases of vitiligo worldwide with 10% of these cases in major US and EU markets.
- The number diagnosed cases forecast to increase by ***20%*** over 2023-2033.

NEKTAR **Source:** Clarivate™ DRG Mature Markets Data 2023

# NKTR-255: Ongoing Studies

## *IL-15 Receptor Agonist Designed To Boost Anti-Cancer Immunity*

| | |
|---|---|
| **In Combination with CD-19 CAR T-Cell Therapies for LBCL** | • Dose-escalation in two Phase 2 studies with approved CD19 CAR-T therapies YESCARTA® & BREYANZI®<br>• Phase 3 dose recommendation in mid-2025 |
| **In Combination with TIL Therapy for 2L NSCLC** | • Open-label study sponsored by Abel Zeta combining NKTR-255 with TIL therapy for patients with metastatic NSCLC who do not respond to chemotherapy and immune checkpoint inhibition in the first line setting |
| **In Combination with BAVENCIO (Anti PD-L1) for Bladder Cancer** | • Randomized, controlled clinical trial led by Merck KGaA combining NKTR-255 with BAVENCIO® as maintenance therapy for patients with locally advanced or metastatic bladder cancer |
| **In Combination with IMFINZI (Anti PD-L1) for Stage 3 Unresectable NSCLC (IST)** | • Clinical trial combining NKTR-255 with IMFINZI® to rescue the absolute lymphocyte count in patients with Stage 3, unresectable NSCLC whose disease has not progressed following concurrent chemo-radiation. |

**Continuing select development studies of NKTR-255**

in combination with cell therapies and checkpoint inhibitors while seeking strategic development partner

# Key Upcoming Milestones

| | |
|---|---|
| **Q1 2024** | Initiation of REZPEG Phase 2b study in alopecia areata |
| **H2 2024** | Interim results of NKTR-255 from the JAVELIN Bladder Medley Study |
| **Q4 2024** | IND enabling studies for NKTR-0165 (TNFR2 Agonist Antibody) |
| **2024** | Preclinical data for NKTR-0165 to be presented at medical conference |
| **2024** | Additional data for NKTR-255 from cell therapy studies |
| **H1 2025** | Topline data from REZPEG Phase 2b atopic dermatitis study |
| **H1 2025** | Topline data from REZPEG Phase 2b alopecia areata study |

**Ended the year with $329M in cash and cash equivalents**

**Cash runway into at least the middle of 2026**