# A Phase 2b, Randomized, Double-Blinded, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Rezpegaldesleukin in Adults with Severe to Very-Severe Alopecia Areata (Rezolve AA)

David Rosmarin[1], Neil Sadick[2,3], Timothy G. Rodgers[4], Edward Lain[5], Lawrence Osman[6], Stephen Schleicher[7], Adam Reich[8], Jacek C Szepietowski[9], Agnieszka Owczarczyk-Saczonek[10], Wojciech Baran[9], Bartlomiej Kwiek[11], Michal Torz[12], Jacek Zdybski[13], Sohail Chaudhry[14], Zachary Lee[14], Heng Xu[14], Yi Liu[14], Brian Lewis[14], Katie Mellskog[14], Lucinda M. Elko-Simms[14], Christie Fanton[14], Mary Tagliaferri[14], Jonathan Zalevsky[14], Charles W. Lynde[15,16]

[1]Indiana University School of Medicine, Indianapolis, IN, United States; [2]Department Of Dermatology, Weill Cornell Medicine, New York, NY, United States; [3] Sadick Research Group, New York, NY, United States; [4]North Texas Center for Clinical Research, Frisco, TX, United States; [5]Austin Institute for Clinical Reserach, Austin, TX, United States; [6]Osman Dermatology, Northridge, CA, United States; [7]DermDox Centers for Dermatology, Sugarloaf, PA, United States; [8]Department of Dermatology, Institute of Medical Sciences, Medical College of Rzeszow University, Rzeszow, Poland; [9]Department of Dermatology, Venereology, and Allergology, Wroclaw Medical University, Wroclaw, Poland; [10]Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology, University of Warmia and Mazury, Olsztyn, Poland; [11]Klinika Ambroziak Dermatologia, Lazarski University, Warsaw, Poland; [12]Dermaceum Centrum Badań Klinicznych, Wroclaw, Poland; [13]Dermedic Jacek Zdybski, Ostrowiec Świętokrzyski, Poland; [14]Nektar Therapeutics, San Francisco, CA, United States; [15]Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada; [16]Lynde Institute for Dermatology, Markham, ON, Canada

## BACKGROUND

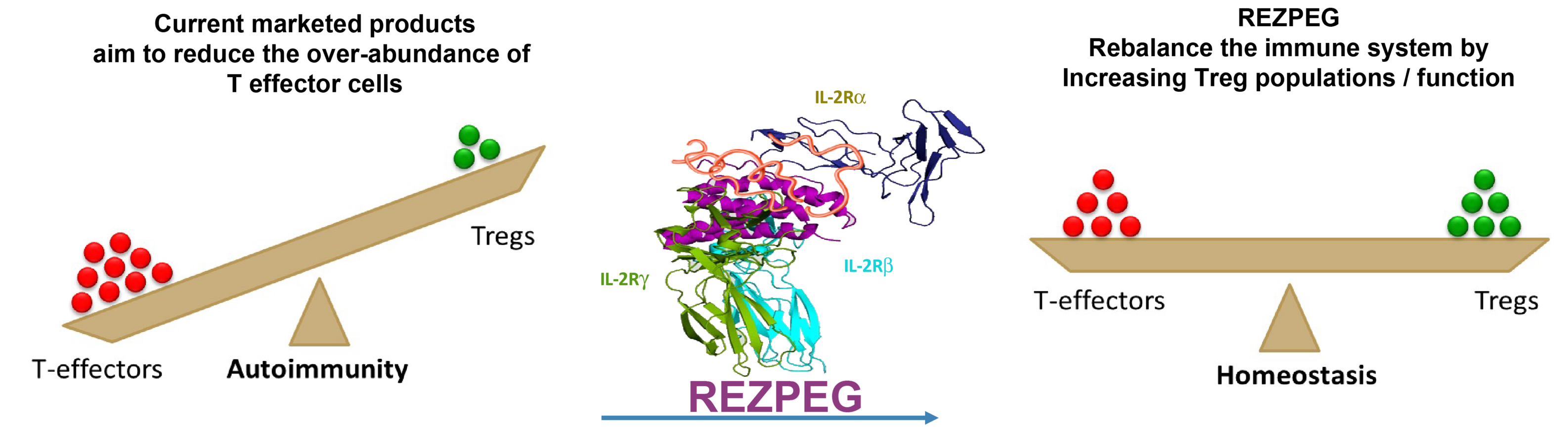
- Prevalence of alopecia areata (AA) is 0.1-0.2% with calculated lifetime risk of 2%[1]
- 6.7 million people in the US and 160 million worldwide have AA[1]
- AA can start at any age and 80% of patients are younger than age 40[2]
- Patchy alopecia areata, alopecia totalis, and alopecia universalis are the predominant types of alopecia areata[3]
- 10–20% of the patients will develop alopecia totalis[2]
- AA causes substantial emotional and psychosocial distress[1]
- Alopecia areata often occurs with other autoimmune conditions such as thyroid disease, atopic dermatitis, inflammatory bowel disease, rheumatoid arthritis, psoriasis, systemic lupus erythematosus and vitiligo[1]
- Biopsies from patients with AA show perifollicular lymphocytic infiltrate (CD4+ and CD8+ T cells) around the anagen phase hair follicle[4] and a significant reduction in regulatory T-cells (Treg)[5]

### Why We Need Additional Therapies for Severe Alopecia Areata

- Majority of patients do not achieve adequate disease control with the standard of care therapies (baricitinib and ritlecitinib)[6]
- Currently available systemic therapies may be limited by their safety profile
  - JAK inhibitors (like baricitinib, ritlecitinib) carry multiple black boxed warnings[7]
- AA frequently recurs after a patient stops taking oral JAK inhibitors[8]
- The limited armamentarium of approved drugs with an adequate benefit–risk ratio represent major challenges in the field[9]
- New strategies aimed at inducing deep and potentially therapy-free remission are needed[9]

**Figure 1: Rezpegaldesleukin (REZPEG): Novel Treatment Approach for Auto-immune Disorders**

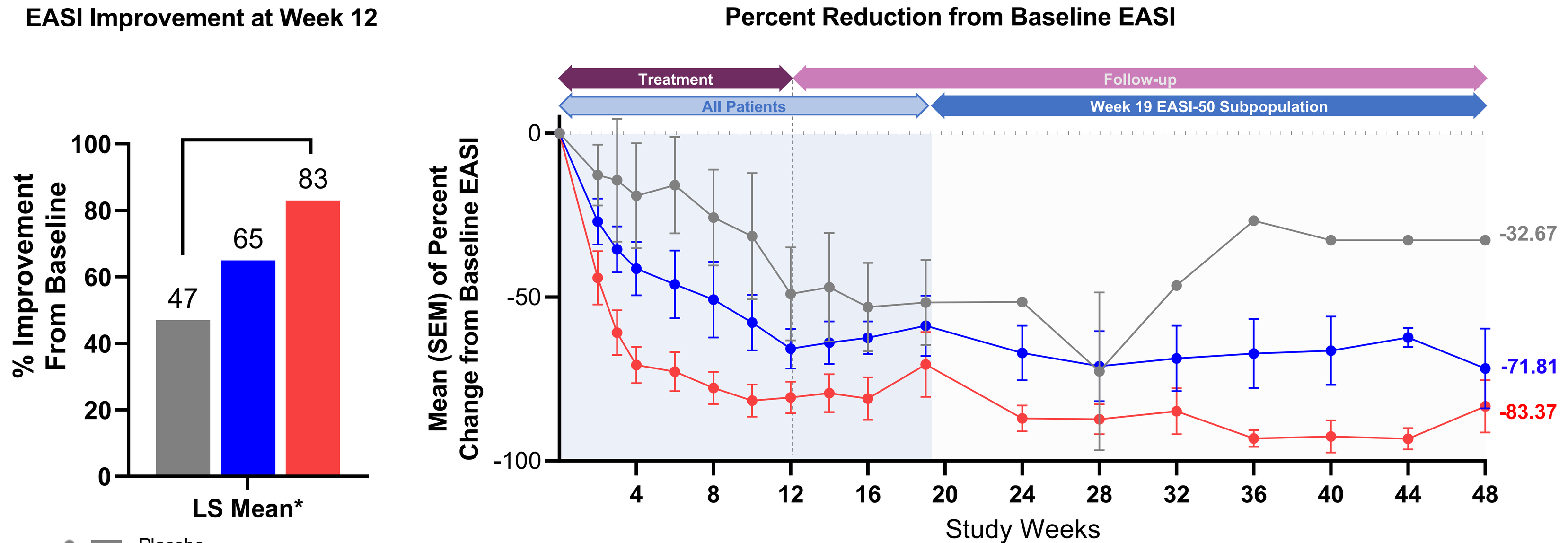
**Novel mechanistic approach:** Resolution/restoration of immune system




**REZPEG preferentially stimulates expansion of regulatory T cells with minimal effects on T-effectors[10]**

**Figure 2: Phase 1b Study of REZPEG in Atopic Dermatitis (AD)**

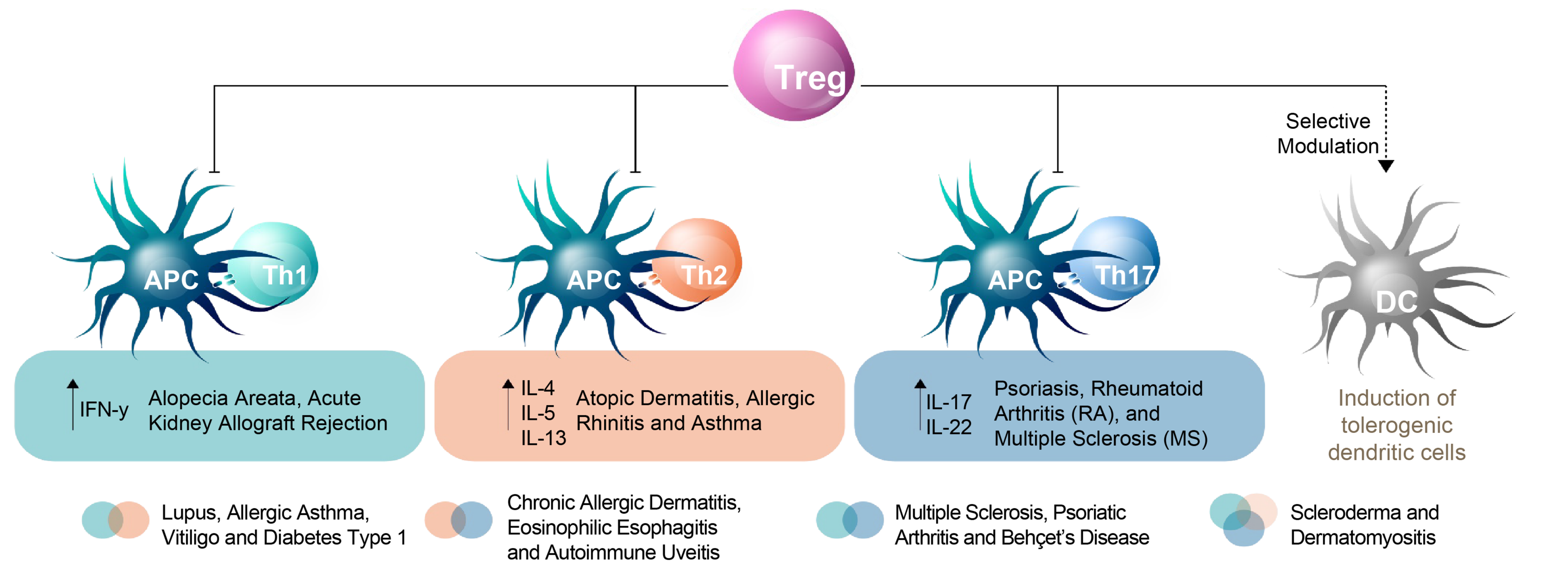
*Sustained Benefit Observed After 12-Weeks of Therapy[11]*




| 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 |

**Phase 2b Study Evaluating REZPEG Potential in Patients with Moderate-to-Severe AD is Ongoing (NCT06136741)**

**Figure 3. Central Role of T Regulatory Cells in Immune Homeostasis**




**Tregs are crucial for immune homoeostasis and the prevention of autoimmune conditions.[12]**

### Key eligibility criteria

- Adult patients (males aged 18-60 years; females aged 18-70 years)
- Stable extent of hair loss over the last 6-months
- Severe to very-severe AA:
  - SALT ≥50
  - No other causes of alopecia
- Systemic Biologic and JAK-inhibitor naïve

### Primary Endpoints

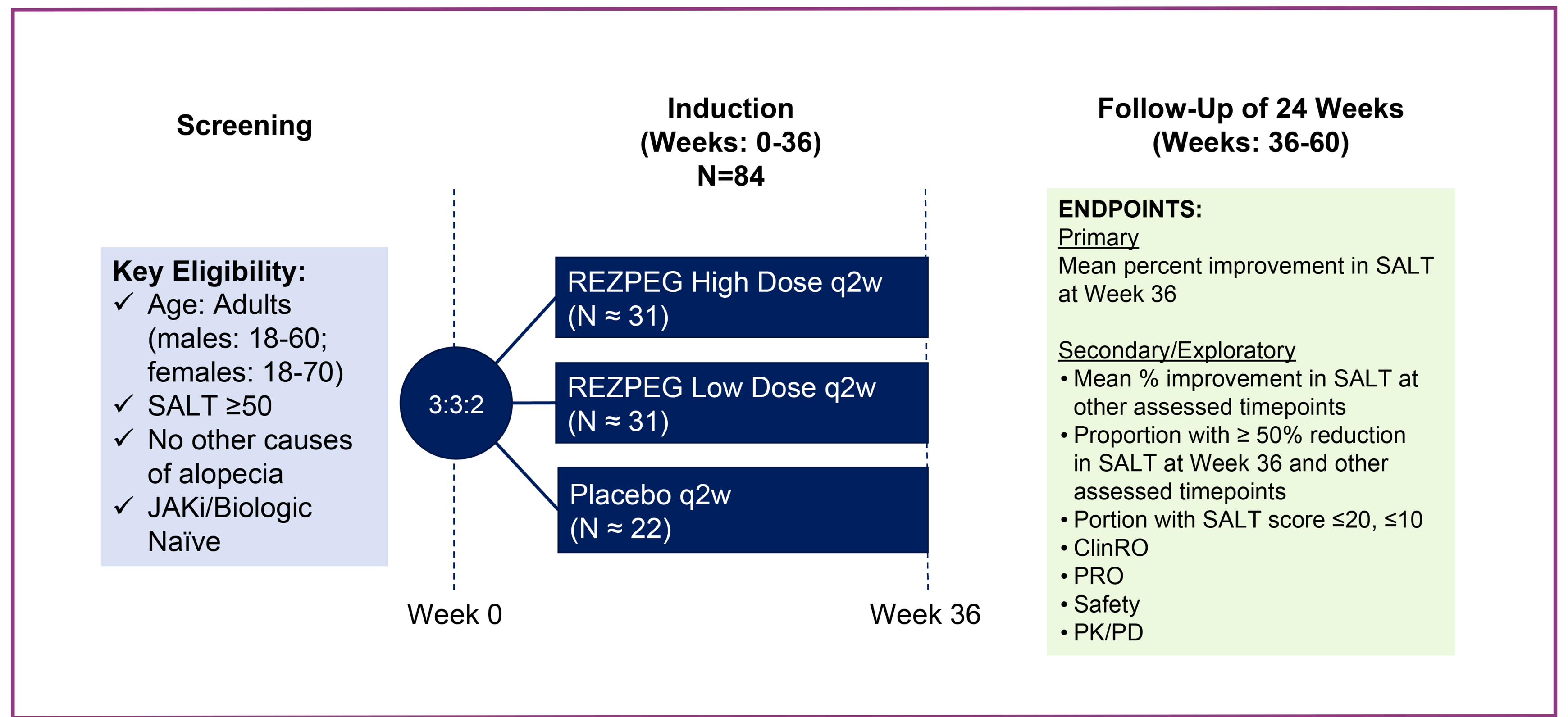
- The primary endpoint for this study is the least-square mean percent change from baseline in Severity of Alopecia Tool (SALT) score at Week 36.

### Secondary Endpoints

- Percent change from baseline in SALT score at other timepoints
- Proportion of patients achieving improvement in Severity of Alopecia Tool (SALT) ≥ 50%, ≥ 75%, ≥ 90%
- Proportion of patients achieving an absolute SALT score ≤ 10, ≤ 20, ≤ 30
- Safety and tolerability

## STUDY DESIGN

**Figure 4: Phase 2b Study for Patients with Severe Alopecia Areata**




### Phase 2b Study for Patients with Alopecia Areata

- This trial is a Phase 2b, randomized, double-blinded, placebo-controlled, international, multicenter study of REZPEG vs placebo for JAK-inhibitor and biologic-naïve patients with severe to very-severe AA.
- Patients will be randomly assigned in a 3:3:2 ratio to 2 different REZPEG dosing regimens vs. placebo, administered subcutaneously, during the 36-week treatment period.
- All patients will be followed for 24-weeks, following the treatment period.

## STUDY STATUS

### Location of Planned Study Sites

- International multicenter study
- Approximately 26 clinical sites across Canada, Poland and United States

- This study is initiating in North America and other parts of the world (**Figure 3**):
  - North America (Canada, United States)
  - Europe (Poland)
- Additional details are available at clinicaltrials.gov: NCT06340360
- Please contact the Sponsor (Nektar) with any questions

**ACKNOWLEDGMENTS**

This study is funded by Nektar Therapeutics, San Francisco, CA.
The study was or will be approved by the institutional review board of each participating site, and written informed consent from all patients is required for study participation.

**ABBREVIATIONS**

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

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Corresponding author David Rosmarin: drosmar@iu.edu

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