REZOLVE-AD Phase 2b Study of Rezpegaldesleukin Meets Primary and Key Secondary Endpoints in Patients with Moderate-to-Severe Atopic Dermatitis

June 24, 2025

Achieved statistical significance on primary endpoint at week 16 for mean percent change in EASI score from baseline for all rezpegaldesleukin arms versus placebo

Achieved statistical significance for key secondary endpoints at week 16 of disease reduction, including EASI-75, EASI-90, Itch NRS, vIGA-AD and BSA

Rapid onset of EASI reduction and magnitude of itch improvement show potential differentiation of this novel regulatory T-cell mechanism as a first and best-in-class immune-modulator

Robust dose-dependent reduction of inflammatory biomarkers in atopic dermatitis including TARC/CCL17, periostin, MDC/CCL22, and IL-19

Safety profile consistent with previously reported results

Data expected in Q1 2026 from continued treatment of patients with atopic dermatitis in long-term maintenance part of REZOLVE-AD study

Top-line Phase 2b data for rezpegaldesleukin in alopecia areata expected in Q4 2025

Conference call and webcast with management and atopic dermatitis experts today at 8:15 am ET / 5:15 am PT

SAN FRANCISCO, June 24, 2025 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR), a clinical-stage biotechnology company focused on development of novel immunology therapies, today announced statistically significant data from the 16-week induction period of the ongoing Phase 2b REZOLVE-AD study of investigational rezpegaldesleukin, an IL-pathway agonist and regulatory T-cell (Treg) proliferator.

The global Phase 2b study is being conducted in 393 patients with moderate-to-severe atopic dermatitis. Patients were randomized (3:3:3:2) to receive subcutaneous treatment with three doses of rezpegaldesleukin: a high dose of 24 µg/kg every two weeks (q2w), a middle dose of 18 µg/kg every two weeks (q2w), and a low dose of 24 µg/kg every four weeks (q4w), or placebo q2w. The primary endpoint and secondary endpoints were assessed at week 16. Following a 16-week induction period, rezpegaldesleukin-treated patients who achieved EASI percent score reductions of ≥50 were re-randomized (1:1) to continue at the same dose level on a q4w or q12w regimen through week 52 in a blinded maintenance period. Placebo patients with EASI percent score reductions of ≥50 percent continue to receive placebo q4w.

Rezpegaldesleukin Achieved Primary and Key Secondary Efficacy Endpoints at Week 16

The trial met its primary endpoint of the mean improvement in Eczema Area and Severity Score (EASI) from baseline at week 16 for all three dose arms of rezpegaldesleukin versus placebo ($p<0.001$).

All three dose arms also achieved statistical significance at week 16 for the key secondary endpoints of EASI-75 (percent of patients who achieve ≥75% reduction in EASI from baseline), EASI-50 (percent of patients who achieve ≥50% reduction in EASI from baseline) and BSA (mean percent improvement in Body Surface Area score from baseline).

The q2w arms of rezpegaldesleukin (high and middle doses) achieved statistical significance at week 16 for the key secondary endpoints of vIGA-AD 0/1 (percent of patients achieving a score of 0 or 1 on the validated Investigator's Global Assessment for Atopic Dermatitis with ≥ 2-point reduction from baseline) and Itch NRS (percent of patients with baseline ≥ 4 who experienced a ≥ 4-point reduction in the Itch Numerical Rating Score from baseline).

In addition, at week 16, the high dose of 24 µg/kg q2w achieved statistical significance on EASI-90 (percent of patients who achieve ≥ 90% reduction in EASI from baseline).

When evaluating EASI-75 and EASI-90 by disease severity using baseline vIGA-AD score, similar responses were observed in severe patients (baseline vIGA-AD of 4) as in moderate patients (baseline vIGA-AD of 3).

"These data from REZOLVE-AD show a fast onset of both EASI response and itch relief within the first few doses of rezpegaldesleukin treatment, which are important metrics for physicians as they assess treatment options in atopic dermatitis," Prof. Jonathan Silverberg, MD, PhD, MPH Professor of Dermatology at George Washington University School of Medicine and Health Sciences. "This shows the advantage of a broad-based Treg mechanism over other immune-modulation approaches in development to treat the disease. Additionally, we don't see any increased risk of incidence of conjunctivitis, oral herpes, or oral

ulcers with this mechanism of action as we do with other mechanisms."

Week 16 Efficacy

	24 µg/kg q2w (high dose)	**18 µg/kg q2w (middle dose)**	**24 µg/kg q4w (low dose)**	**Placebo**
Primary Endpoint	N=104	N=106	N=110	N=73
Mean improvement in EASI score from baseline	61% *p<0.001*	58% *p<0.001*	53% *p<0.001*	31 %
Key Secondary Endpoints				
EASI-75	42% *p<0.001*	46% *p<0.001*	34% *p<0.05*	17 %
vIGA-AD 0/1	20% *p<0.05*	26% *p<0.01*	19% *ns*	8 %
EASI-90	25% *p<0.05*	18% *ns*	17% *ns*	9 %
*Itch NRS**	42% *p<0.01*	35% *p<0.05*	23% *ns*	16 %
Mean improvement in BSA score from baseline	54% *p<0.001*	48% *p<0.001*	43% *p<0.001*	17 %
EASI-50	66% *p<0.001*	66% *p<0.001*	55% *p<0.01*	34 %

**Patients with baseline Itch NRS ≥ 4 used as denominator for assessing Itch NRS response (N=63, 95, 92, and 102 for the placebo, 24 µg/kg q2w, 18 µg/kg q2w, and 24 µg/kg q4w arms); ns=not significant.*

"These REZOLVE-AD results present a new therapeutic hypothesis for treatment of dermatological diseases and the investigators are looking forward to rezpegaldesleukin advancing in development in atopic dermatitis," said Prof. David Rosmarin M.D., Chair, Department of Dermatology and Associate Professor of Dermatology, Indiana University School of Medicine. "With the establishment of this efficacy profile in the dermatological setting of atopic dermatitis, we are also eager to see the upcoming results from the ongoing REZOLVE-AA study in patients with severe to very-severe alopecia areata."

Across all three dose arms, translational blood biomarker data demonstrate robust on-target and dose-dependent pharmacological activity with an increase in total Tregs of up to 6-fold in the high dose arm. Sustained Treg cell proliferation was observed at week 16 as compared to baseline and was correlated with reduction of key T helper 2 (Th2) inflammatory markers: IL-19, TARC/CCL17, periostin, and MDC/CCL22.

"We believe that the REZOLVE-AD study results clearly demonstrate that Nektar has established a new biology and harnessed the promise of Tregs as an important potential therapeutic modality to treat inflammatory skin disorders and other autoimmune conditions," said Howard W. Robin, President and CEO of Nektar Therapeutics. "These compelling efficacy findings are further boosted by the translational data that show, for the first time, that rezpegaldesleukin also reduced key markers of Th2 inflammation in atopic dermatitis. With this validation in atopic dermatitis, we also look forward to reporting results in the fourth quarter of this year for rezpegaldesleukin in alopecia areata."

Nektar plans to submit these REZOLVE-AD 16-week induction results for presentation at a medical conference later in 2025.

Safety Profile Consistent with Previously Reported Results

The safety profile for the 16-week induction period for rezpegaldesleukin was consistent with previously reported results. The most common treatment-emergent adverse events (TEAEs) were local injection site reactions (ISRs), observed in 69.7% of all rezpegaldesleukin-treated patients, with the largest proportion of these being mild or moderate (99.6%). ISRs were self-resolving and <1% of patients discontinued because of an ISR. Across all rezpegaldesleukin doses administered in the study over the 16-week induction period, 55.9% had no reports of ISRs, 30.1% had mild reports, 13.8% had moderate reports, and only 0.2% were severe. Other TEAEs more commonly observed (≥5%) in the study treatment arms (n=320) versus placebo (n=73) include eosinophilia (7.8% vs. 2.7%), pyrexia (6.3% vs 2.7%), headache (6.3% vs. 4.1%) and arthralgia (5.0% vs 1.4%).

In the pooled rezpegaldesleukin arms, TEAEs, excluding ISRs, were reported in 60.3% of patients and in 57.5% of placebo-treated patients.

There was no increased risk of conjunctivitis, oral ulcers, or infections, including oral herpes, in the rezpegaldesleukin arms.

Safety over 16-Week Induction Period

	24 µg/kg q2w	18 µg/kg q2w	24 µg/kg q4w	Pooled drug arms	Placebo
	N=104	N=106	N=110	N=320	N=73
Patients with any TEAE, excluding ISRs	69 (66.3 %)	60 (56.6 %)	64 (58.2 %)	193 (60.3 %)	42 (57.5 %)
Patients with any Serious AE	1 (1.0 %)	4 (3.8 %)	0	5 (1.6 %)	0
Any Drug-Related Serious AE[1]	0	2 (1.9 %)	0	2 (0.6 %)	0
Patients with Severe AE	3 (2.9 %)	6 (5.7 %)	1 (0.9 %)	10 (3.1 %)	1 (1.4) %
Any Drug-Related Severe AE[2]	3 (2.9 %)	3 (2.8 %)	0	6 (1.9 %)	0
TEAEs leading to study drug discontinuation	8 (7.7 %)	5 (4.7 %)	5 (4.7 %)	18 (5.6 %)	0

1. *Serious TRAEs: Drug hypersensitivity – severe; Tonsillitis – moderate. Both events resolved.*
2. *Severe TRAEs (excluding Serious TRAEs): pyrexia (24 µg/kg q2w); two ISRs (24 µg/kg q2w); ISR, chest pain (18 µg/kg q2w). All five events resolved.*

Conference Call and Webcast to Discuss Results of Phase 2b REZOLVE-AD Trial

Nektar management will host a conference call and live webcast with Drs. Silverberg and Rosmarin today, June 24, 2025, to review the results at 8:15 a.m. Eastern Time / 5:15 a.m. Pacific Time.

The accompanying slides and the webcast of the conference call can be accessed through a link on Nektar's website on the investor relations page. To access the webcast directly, please click on the following link to register to join the Zoom webcast: *https://lifescievents.com/event/sro974rcsq260kbgiw59/*

The web broadcast of the conference call will be available for replay through July 25, 2025.

About REZOLVE-AD Phase 2b Study

The REZOLVE-AD trial was initiated in October 2023 and enrolled patients across approximately 110 sites globally with: 68% enrolled and treated in Europe, including Poland, Bulgaria, Germany, Czech Republic, Spain, Croatia and Hungary; 16% enrolled and treated in the United States; 11% enrolled and treated in Canada; and 5% enrolled and treated in Australia. Patient randomization was stratified based on baseline disease severity measured by vIGA-AD and geographic region. Key enrollment criteria in the study included a minimum EASI score of 16.0, a minimum Body Surface Area (BSA) of 10% and a minimum vIGA-AD of 3.

About Rezpegaldesleukin

Autoimmune and inflammatory diseases cause the immune system to mistakenly attack and damage healthy cells in a person's body. A failure of the body's self-tolerance mechanisms enables the formation of the pathogenic T lymphocytes that conduct this attack. Rezpegaldesleukin is a potential first-in-class resolution therapeutic that may address this underlying immune system imbalance in people with many autoimmune and inflammatory conditions. It targets the interleukin-2 receptor complex in the body to stimulate proliferation of powerful inhibitory immune cells known as regulatory T cells. By activating these cells, rezpegaldesleukin may act to bring the immune system back into balance.

In February 2025, the U.S. Food and Drug Administration (FDA) granted Fast Track designation for rezpegaldesleukin for the treatment of adult and pediatric patients 12 years of age and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Rezpegaldesleukin is being developed as a self-administered injection for a number of autoimmune and inflammatory diseases. It is wholly owned by Nektar Therapeutics.

About Atopic Dermatitis

Atopic dermatitis is the most common type of eczema, affecting approximately 30 million people in the United States.[1] AD is characterized by a defect in the skin barrier, which allows allergens and other irritants to enter the skin, leading to an immune reaction and inflammation.

About Nektar Therapeutics

Nektar Therapeutics is a clinical-stage biotechnology company focused on developing treatments that address the underlying immunological dysfunction in autoimmune and chronic inflammatory diseases. Nektar's lead product candidate, rezpegaldesleukin (REZPEG, or NKTR-358), is a novel, first-in-class regulatory T cell stimulator being evaluated in two Phase 2b clinical trials, one in atopic dermatitis and one in alopecia areata. Nektar's pipeline also includes a preclinical bivalent tumor necrosis factor receptor

type II (TNFR2) antibody and bispecific programs, NKTR-0165 and NKTR-0166, and a modified hematopoietic colony stimulating factor (CSF) protein, NKTR-422. Nektar, together with various partners, is also evaluating NKTR-255, an investigational IL-15 receptor agonist designed to boost the immune system's natural ability to fight cancer, in several ongoing clinical trials. Nektar is headquartered in San Francisco, California. For further information, visit www.nektar.com and follow us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "expect," "develop," "potential," "plan," and similar references to future periods. Examples of forward-looking statements include, among others, statements regarding the therapeutic potential and safety profile of, and future development plans for, rezpegaldesleukin, the results and timing for reporting the full 52-week data from REZOLVE-AD, the results and timing for reporting data from REZOLVE-AA, the potential for rezpegaldesleukin to be a first-in-class T regulatory cell therapy, the potential market opportunity in atopic dermatitis and alopecia areata, the advantage of a broad-based Treg mechanism over other immune-modulation approaches in development to treat atopic dermatitis, and the high unmet need for a new mechanism of action in atopic dermatitis and alopecia areata. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations, and assumptions regarding the future of our business, future plans and strategies, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results to differ materially from those indicated in the forward-looking statements include, among others: (i) our statements regarding the therapeutic potential of rezpegaldesleukin are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) rezpegaldesleukin is an investigational agent and continued research and development for this drug candidate is subject to substantial risks, including negative safety and efficacy findings in future clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) rezpegaldesleukin is in clinical development and the risk of failure is high and can unexpectedly occur at any stage prior to regulatory approval; (iv) the timing of the commencement or end of clinical trials and the availability of clinical data may be delayed or unsuccessful due to regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, changing standards of care, evolving regulatory requirements, clinical trial design, clinical outcomes, competitive factors, or delay or failure in ultimately obtaining regulatory approval in one or more important markets; (v) a Fast Track designation does not increase the likelihood that rezpegaldesleukin will receive marketing approval in the United States; (vi) patents may not issue from our patent applications for our drug candidates, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required; and (vii) certain other important risks and uncertainties set forth in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 9, 2025. Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

For Investors:

Corey Davis, Ph.D.
LifeSci Advisors
212-915-2577
cdavis@lifesciadvisors.com

For Media:

Madelin Hawtin
LifeSci Communications
603-714-2638
mhawtin@lifescicomms.com

[1] *Eczema stats. National Eczema Association (2022, September 27). https://nationaleczema.org/research/eczema-facts/*

View original content to download multimedia:https://www.prnewswire.com/news-releases/rezolve-ad-phase-2b-study-of-rezpegaldesleukin-meets-primary-and-key-secondary-endpoints-in-patients-with-moderate-to-severe-atopic-dermatitis-302489015.html

SOURCE Nektar Therapeutics