Nektar Announces Promising New and Corrected Rezpegaldesleukin Efficacy Data Which Were Previously Reported in 2022 and Incorrectly Calculated by Former Collaborator Eli Lilly & Company

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EASI-Related and PASI-Related Clinical Efficacy Endpoints in Atopic Dermatitis and Psoriasis Studies Were Incorrectly Calculated by Lilly and Were Reported Erroneously at EADV 2022

SAN FRANCISCO, Aug. 7, 2023 /PRNewswire/ -- Nektar Therapeutics (Nasdaq: NKTR) today announced that efficacy data previously generated by Eli Lilly & Company for rezpegaldesleukin (REZPEG) that were presented at the September 2022 EADV Congress were incorrectly calculated by Lilly. The erroneous data is from two Phase 1b studies for REZPEG that were conducted by Lilly. The new and corrected data highlight the important potential of REZPEG to help patients battling atopic dermatitis (AtD), a chronic skin condition that afflicts nearly 10% of Americans.

Specifically, the new and corrected data from the atopic dermatitis study demonstrate that 12 weeks of REZPEG therapy at the highest dose resulted in a mean Eczema Area and Severity Index (EASI) score improvement of 83% with a p-value of 0.002 as compared to placebo and an EASI-75 response rate of 41% (see corrected data found in Tables 1 and 2 below). REZPEG also provided a more rapid and steep drop in EASI scores immediately after therapy initiation than the previously reported erroneous data indicated. This efficacy benefit was also maintained for 36 weeks without additional treatment after the 12-week induction period.

Nektar discovered the EASI-related and Psoriasis Area and Severity Index (PASI)-related clinical efficacy endpoints were incorrectly calculated by Lilly after all rights to REZPEG were returned to Nektar and the raw data files from the REZPEG clinical studies were transferred to Nektar. This transfer of the raw data files to Nektar was the first opportunity for Nektar to review the complete patient data files. Subsequently, an independent statistical firm was employed to analyze the raw data *de-novo,* and the firm provided the new and corrected data in the tables below.

The internal statistical and clinical teams in charge of the two studies at Lilly were made aware that Nektar discovered the data errors. Lilly confirmed the errors in written communications with Nektar.

"These corrected data importantly demonstrate that REZPEG, a novel and differentiated T regulatory cell mechanism, holds great promise for treating patients with atopic dermatitis," said Howard W. Robin, President & CEO of Nektar Therapeutics. "The data further reinforce the importance of Nektar's renewed strategic focus on advancing REZPEG into a robust Phase 2b study in biologic-naïve patients with moderate to severe atopic dermatitis by October of this year."

Hyperlink to Supporting Slide Set

SECTION A: Corrected efficacy endpoints for the Phase 1b study in atopic dermatitis

TABLE 1:

Study Arm	EADV 2022 INCORRECT INTERIM DATA REPORTED[1] *Mean % improvement in EASI score from baseline at 12-weeks*	p-value	CORRECTED INTERIM DATA (INDEPENDENT STATISTICAL AUDIT) *Mean % improvement in EASI score from baseline at 12-weeks*	p-value
Placebo	49		47	
12 µg/kg	53	NS	65	NS
24 µg/kg	66	NS	83	0.002

TABLE 2:

Study Arm	EADV 2022 INCORRECT INTERIM DATA REPORTED[1]	CORRECTED INTERIM DATA (INDEPENDENT STATISTICAL AUDIT)	CORRECTED INTERIM DATA (INDEPENDENT STATISTICAL AUDIT)

	Proportion of Patients Who Achieved an EASI-75 Score (NRI calculation)	*Proportion of Patients Who Achieved an EASI-75 Score (NRI calculation)*	*Proportion of Patients Who Achieved an EASI-75 Score (as observed)*
Placebo	20 %	20 %	29 %
12 µg/kg	25 %	25 %	33 %
24 µg/kg	29 %	41 %	58 %

Note: Corrected results utilize a 72-point EASI scale, and all patient data were included in the analyses. The continuous endpoint of % improvement in EASI score from baseline is calculated from observed data using a mixed model for repeated measures (MMRM) as specified in the statistical analysis plan (SAP) defined in the protocol. All statistical analyses on the efficacy endpoints are post-hoc exploratory per the SAP.

SECTION B: Corrected efficacy endpoints for the Phase 1b study in psoriasis:

TABLE 3:

Study Arm	**EADV 2022 INCORRECT FINAL DATA REPORTED[2] LS Mean % improvement in PASI score from baseline at 12-weeks (as observed)**	**p-value**	**CORRECTED FINAL DATA (INDEPENDENT STATISTICAL AUDIT) LS Mean % improvement in PASI score from baseline at 12-weeks (as observed)**	**p-value**
Placebo	19	NS	24	NS
24 µg/kg	40	NS	44	NS

TABLE 4:

Study Arm	**EADV 2022 INCORRECT FINAL DATA REPORTED[2]** *Proportion of Patients Who Achieved a PASI-50 Score (NRI)*	**CORRECTED FINAL DATA (INDEPENDENT STATISTICAL AUDIT)** *Proportion of Patients Who Achieved a PASI-50 Score (NRI)*	**CORRECTED INTERIM DATA (INDEPENDENT STATISTICAL AUDIT)** *Proportion of Patients Who Achieved a PASI-50 Score (as observed)*
Placebo	20 %	20 %	20 %
24 µg/kg	26 %	32 %	55 %

TABLE 5:

Study Arm	**EADV 2022 INCORRECT FINAL DATA REPORTED[2]** *Proportion of Patients Who Achieved a PASI-75 Score (NRI)*	**CORRECTED FINAL DATA (INDEPENDENT STATISTICAL AUDIT)** *Proportion of Patients Who Achieved a PASI-75 Score (NRI)*	**CORRECTED INTERIM DATA (INDEPENDENT STATISTICAL AUDIT)** *Proportion of Patients Who Achieved a PASI-75 Score (as observed)*
Placebo	0	0	0
24 µg/kg	11 %	21 %	36 %

Note: Corrected results utilize a 72-point PASI scale. The continuous endpoint of % improvement in PASI score from baseline is calculated from observed data using a mixed model for repeated measures (MMRM) as specified in the SAP defined in the protocol. All statistical analyses on the efficacy endpoints are post-hoc exploratory per the SAP.

The two double-blind, randomized, placebo-controlled studies of REZPEG evaluated safety, tolerability, and pharmacokinetics over a 12-week induction treatment period. Patients were followed for an additional 36 weeks after the end of the treatment period. The first study enrolled 44 patients with moderate-to-severe AtD who had progressed on topical corticosteroids and the second study enrolled 26 patients with plaque psoriasis who were candidates for systemic therapy or phototherapy.

For the AtD study, efficacy endpoints related to the Eczema Area and Severity Index (EASI), at an interim data cut-off date, were miscalculated for the validated 72-point EASI scoring system and excluded certain available patient data at the time of the interim. The EASI is a validated and widely used tool in atopic dermatitis studies that was clearly outlined in the REZPEG protocol. The EASI measures the severity of AtD for patients and scoring ranges from 0 (no disease) to 72 (maximal disease)[3]. The corrected and audited interim data analyses for the atopic dermatitis study utilizes the validated 72-point EASI scoring system and includes all patients in the 12-week induction period enrolled in the Phase 1b study.

For the psoriasis study, efficacy endpoints related to the Psoriasis Area and Severity Index (PASI), at the final data cut-off date, were miscalculated for the validated 72-point PASI scoring system. The PASI is a validated and widely used tool to measure the severity of psoriasis plaques for patients and scoring ranges from 0 (no disease) to 72 (maximal disease)[4]. The corrected and audited final data analyses for the psoriasis study utilizes the validated 72-point PASI scoring system from the Phase 1b study.

Nektar plans to hold an investor meeting with key opinion leaders in the coming weeks to discuss these corrected data as well as new and final data for the 36-week follow-up period for REZPEG. The final data strengthen the potential for REZPEG to provide a remittive effect. Nektar will also announce the new study design for the Phase 2b study of REZPEG in biologic-naïve patients with moderate to severe atopic dermatitis who have progressed on topical corticosteroids. This study is planned to start in October of this year.

Conference Call to Discuss Second Quarter 2023 Financial Results

Nektar management will host a conference call to discuss this press release and announce its financial results for the second quarter 2023 on Tuesday, August 8, 2023, beginning at 5:00 p.m. Eastern Time/2:00 p.m. Pacific Time.

This press release and live audio-only webcast of the conference call can be accessed through a link that is posted on the Home Page and Investors section of the Nektar website: http://ir.nektar.com/. The web broadcast of the conference call will be available for replay through September 8, 2023.

To access the conference call, please pre-register at Nektar Earnings Call Registration. All registrants will receive dial-in information and a PIN allowing them to access the live call.

About REZPEG
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. REZPEG 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 in order to stimulate proliferation of powerful inhibitory immune cells known as regulatory T cells. By activating these cells, REZPEG may act to bring the immune system back into balance.

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

About Nektar Therapeutics
Nektar Therapeutics is a biopharmaceutical company with a robust, wholly owned R&D pipeline of investigational medicines in immunology and oncology as well as a portfolio of approved partnered medicines. Nektar is headquartered in San Francisco, California, with additional manufacturing operations in Huntsville, Alabama. Further information about the company and its drug development programs and capabilities may be found online at http://www.nektar.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements which can be identified by words such as: "will," "may," "advance," "develop," "provide," "potential" and similar references to future periods. Examples of forward-looking statements include, among others, statements regarding the therapeutic potential of, and future development plans for rezpegaldesleukin, and our other drug candidates in research programs, the prospects and plans for our collaborations with other companies, the timing of the initiation of clinical studies and the data readouts for our drug candidates. 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, and our other drug candidates are based on preclinical and clinical findings and observations and are subject to change as research and development continue; (ii) rezpegaldesleukin and our other drug candidates are investigational agents and continued research and development for these

drug candidates is subject to substantial risks, including negative safety and efficacy findings in ongoing clinical studies (notwithstanding positive findings in earlier preclinical and clinical studies); (iii) rezpegaldesleukin and our other drug candidates are in various stages of 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 challenges caused by the COVID-19 pandemic, 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) we may not achieve the expected cost savings we expect from our 2022 corporate restructuring and reorganization plan or our 2023 cost restructuring plan and we may undertake additional restructuring and cost-saving activities in the future, (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 Annual Report on Form 10-Q filed with the Securities and Exchange Commission on May 10, 2023. 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.

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1. Schleicher et. al.: "*Efficacy and Safety of a Selective Regulatory T-Cell Inducing IL-2 Conjugate (LY3471851) in the Treatment of Atopic Dermatitis: A Phase 1 Randomised Study*"
2. Forman et. al: "*Efficacy and Safety of a Selective Regulatory T-Cell Inducing IL-2 Conjugate (LY3471851) in the Treatment of Psoriasis: A Phase 1 Randomised Study*"
3. *Hanifin, J. M.; Thurston, M.; Omoto, M.; Cherill, R.; Tofte, S. J.; Graeber, M. (2001). "The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group". Experimental Dermatology. 10 (1): 11–18. doi:10.1034/j.1600-0625.2001.100102.x. PMID 11168575. S2CID 25864663.*
4. https://doi.org/10.5070/D318w9j736

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