Lilly's EBGLYSS™ (lebrikizumab-lbkz) demonstrated meaningful improvement in skin clearance and itch relief in the majority of patients with moderate-to-severe atopic dermatitis who discontinued dupilumab

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In first dedicated study of a selective IL-13 inhibitor in patients previously treated with dupilumab, the majority of patients had a history of inadequate response to dupilumab

EBGLYSS also provided meaningful improvements in difficult-to-treat face and hand dermatitis

The safety profile of EBGLYSS was consistent with previous Phase 3 studies and of the patients who reported eye-related events, facial dermatitis or inflammatory arthritis as the reason for prior dupilumab discontinuation, none reported similar events with EBGLYSS

INDIANAPOLIS, Oct. 25, 2024 /PRNewswire/ -- New results show Eli Lilly and Company's (NYSE: LLY) EBGLYSS improved skin (including hand and face) and itch among patients with moderate-to-severe atopic dermatitis (eczema) who were previously treated with dupilumab. These results from the Phase 3b ADapt study will be presented at the Fall Clinical Dermatology (FCD) Conference from Oct. 24-27 in Las Vegas.[1]

EBGLYSS is an interleukin-13 (IL-13) inhibitor that selectively blocks IL-13 signaling with high binding affinity.[2,3,4] The cytokine IL-13 is key in atopic dermatitis, driving the type-2 inflammatory cycle in the skin, leading to skin barrier dysfunction, itch, skin thickening and infection.[5,6]

"Treatment isn't one-size-fits-all, and many patients with moderate-to-severe atopic dermatitis remain in need of an effective medicine to help manage the impact of the disease, especially in difficult-to-treat areas like face and hands," said Linda Stein Gold, M.D., investigator of the ADapt study, director of dermatology research and head of the Division of Dermatology for Henry Ford Health System in Detroit, Michigan. "These data showed that EBGLYSS improved skin symptoms and reduced itch for the majority of patients who had stopped using dupilumab and complement previously presented EBGLYSS data in biologic-naive patients, further supporting that a broad range of patients could benefit from this new and effective treatment option."

The ADapt study evaluated the efficacy and safety of EBGLYSS in patients with moderate-to-severe atopic dermatitis who were previously treated with dupilumab. To qualify for ADapt, patients must have discontinued dupilumab treatment due to inadequate response, intolerance or an adverse event, or other reasons (including cost or loss of access to the medicine). View an EBGLYSS patient photo from the ADapt study here.[1]

The primary endpoint of the study was measured by at least 75 percent improvement in the Eczema Area and Severity Index (EASI-75) score at 16 weeks, which evaluates the extent and severity of the skin disease. Secondary endpoints at 16 and 24 weeks included Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction of at least two points from baseline and at least a four-point improvement in Pruritus NRS from baseline. Other secondary and exploratory endpoints were also included.[1] The reported endpoints were as observed.

With EBGLYSS, 57 percent of patients at Week 16, and 60 percent of patients at Week 24 who were previously treated with dupilumab, achieved EASI-75. These results are similar to what was observed in the Phase 3 monotherapy trials of EBGLYSS in patients without prior exposure to dupilumab (ADvocate 1 and ADvocate 2). In addition, 46 percent of patients who were inadequate responders to dupilumab achieved EASI-75 response with EBGLYSS at Week 16.[1]

Fifty-three percent and 62 percent of ADapt patients who discontinued dupilumab and began treatment with EBGLYSS also experienced itch relief (Pruritus NRS) with at least a four-point improvement from baseline at Week 16 and Week 24 respectively.[1]

Patients in this study saw improvements in difficult-to-treat areas when treated with EBGLYSS. More than half of patients (52 percent) treated with EBGLYSS saw clear or almost clear face dermatitis at Week 24 (F-IGA 0,1 with a reduction of at least two points from baseline). Among patients with moderate-to-severe hand dermatitis at baseline (defined as ≥12), patients' modified total lesion symptom score (mTLSS), which measures extent and severity of hand dermatitis, decreased by 75 percent at Week 24.[1]*

Less than six percent of patients treated with EBGLYSS experienced an adverse event that led to treatment discontinuation.[1]

The safety profile of EBGLYSS in ADapt was consistent with previous EBGLYSS Phase 3 studies in patients with moderate-to-severe atopic dermatitis, and no new safety signals were observed. The majority of adverse events were mild or moderate. Reported treatment-related side effects in the study were conjunctivitis and injection site reactions.

Of the 14 patients who discontinued dupilumab due to an adverse event, two patients discontinued EBGLYSS due to an adverse event. Of the 10 patients who discontinued dupilumab due to eye-related events, facial dermatitis or inflammatory arthritis, none reported similar events with EBGLYSS.[1]

"This trial supports the growing body of data showing that health care providers can have confidence prescribing EBGLYSS as a first-line biologic treatment for moderate-to-severe atopic dermatitis, and reinforces that EBGLYSS provided a meaningful benefit among individuals who have already tried another biologic treatment such as dupilumab and may have more difficult-to-treat disease," said Mark Genovese, M.D., senior vice president of Lilly Immunology development.

Lilly will also present additional data at the Fall Clinical Dermatology conference, including new analyses from the ADjoin long-term extension study with data up to three years.

EBGLYSS was approved in the U.S. by the Food and Drug Administration (FDA) last month as a first-line biologic treatment for adults and children 12 years of age and older who weigh at least 88 pounds (40 kg) with moderate-to-severe atopic dermatitis that is not well controlled with topical prescription therapies.

EBGLYSS 250 mg/2 mL injection is dosed as a single monthly maintenance injection following the initial phase of treatment. The recommended initial starting dose of EBGLYSS is 500 mg (two 250 mg injections) at Week 0 and Week 2, followed by 250 mg every two weeks until Week 16 or later when adequate clinical response is achieved; after this, maintenance dosing is a single monthly injection (250 mg every four weeks).[1]

EBGLYSS was also approved in the European Union in 2023, as well as in Japan in January 2024, with additional markets expected later this year.

Lilly has exclusive rights for development and commercialization of EBGLYSS in the U.S. and the rest of the world outside Europe. Lilly's partner Almirall S.A. has licensed the rights to develop and commercialize EBGLYSS for the treatment of dermatology indications, including eczema, in Europe.

*mTLSS is a composite measure of intensity of seven hand dermatitis signs and symptoms (erythema, edema, desquamation, fissures, hyperkeratosis/lichenification, pruritus/pain, and vesiculation, with total scores ranging from 0 to 21), used to assess improvement in hand dermatitis.

About ADapt
ADapt (NCT05369403), is an open-label, Phase 3b, 24-week study that evaluated the efficacy and safety of EBGLYSS in adults and adolescents (12 to less than 18 years of age and weighing ≥40 kg) with moderate-to-severe atopic dermatitis who were previously treated with dupilumab. Four or more weeks after discontinuing dupilumab, patients were treated with EBGLYSS and received a starting dosing of 500 mg (two 250 mg injections) at Week 0 and Week 2, followed by 250 mg every two weeks until Week 16. IGA 0,1 or EASI-75 responders at Week 16 received 250 mg once monthly and non-responders continued on 250 mg every two weeks until Week 24. Patients were allowed to stay on low and mid-potency topical corticosteroids.[1]

From baseline to Week 16, data from the ADapt study was analyzed as observed and with non-responder imputation/multiple imputation (NRI/MI). After Week 16, Q2W and Q4W data from the ADapt study were pooled and analyzed as observed and with NRI/MI.[1]

INDICATION AND SAFETY SUMMARY
EBGLYSS ™ (EHB-glihs) is an injectable medicine used to treat adults and children 12 years of age and older who weigh at least 88 pounds (40 kg) with moderate-to-severe eczema (atopic dermatitis) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. EBGLYSS can be used with or without topical corticosteroids.

It is not known if EBGLYSS is safe and effective in children less than 12 years of age or in children 12 years to less than 18 years of age who weigh less than 88 pounds (40 kg).

Warnings - Do not use EBGLYSS if you are allergic to lebrikizumab-lbkz or to any of the ingredients in EBGLYSS. See the Patient Information leaflet that comes with EBGLYSS for a complete list of ingredients.

Before using

Before using EBGLYSS, tell your healthcare provider about all your medical conditions, including if you:

- Have a parasitic (helminth) infection.
- Are scheduled to receive any vaccinations. You should not receive a "live vaccine" if you are treated with EBGLYSS.
- Are pregnant or plan to become pregnant. It is not known if EBGLYSS will harm your unborn baby. If you become pregnant during treatment with EBGLYSS, you or your healthcare provider can call Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979) to report the pregnancy.
- Are breastfeeding or plan to breastfeed. It is not known if EBGLYSS passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Possible side effects

EBGLYSS can cause serious side effects, including:

- **Allergic reactions. EBGLYSS can cause allergic reactions that may sometimes be severe.** Stop using EBGLYSS and tell your healthcare provider or get emergency help right away if you get any of the following signs or symptoms:
  - breathing problems or wheezing
  - itching
  - swelling of the face, lips, mouth, tongue or throat
  - fainting, dizziness, feeling lightheaded
  - skin rash
  - hives
  - cramps in your stomach area (abdomen)
- **Eye problems.** Tell your healthcare provider if you have any new or worsening eye problems, including eye pain or changes in vision, such as blurred vision.

The most common side effects of EBGLYSS include:

- eye and eyelid inflammation, including redness, swelling, and itching
- injection site reactions
- shingles (herpes zoster)

These are not all of the possible side effects of EBGLYSS. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

How to take

- **See the detailed "Instructions for Use" that comes with EBGLYSS for information about how to prepare and inject EBGLYSS and how to properly store and throw away (dispose of) used EBGLYSS prefilled pens and prefilled syringes.**
- Use EBGLYSS exactly as prescribed by your healthcare provider.
- EBGLYSS is given as an injection under the skin (subcutaneous injection).
- If your healthcare provider decides that you or a caregiver can give the injections of EBGLYSS, you or a caregiver should receive training on the right way to prepare and inject EBGLYSS. Do not try to inject EBGLYSS until you have been shown the right way by your healthcare provider. In children 12 years of age and older, EBGLYSS should be given by a caregiver.
- If you miss a dose of EBGLYSS, inject the missed dose as soon as possible, then inject your next dose at your regular scheduled time.

Learn more
EBGLYSS is a prescription medicine available as a 250 mg/2 mL injection prefilled pen or prefilled syringe. For more information, call **1-800-545-5979** or go to **ebglyss.lilly.com**

This summary provides basic information about EBGLYSS but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking to your doctor. Be sure to talk to your doctor or other healthcare provider about EBGLYSS and how to take it. Your doctor is the best person to help you decide if EBGLYSS is right for you.

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About EBGLYSS
EBGLYSS is a monoclonal antibody that selectively targets and neutralizes IL-13 with high binding affinity and a slow dissociation rate.[3,4,7] EBGLYSS binds to the IL-13 cytokine at an area that overlaps with the binding site of the IL-4Rα subunit of the IL-13Rα1/IL-4Rα heterodimer, preventing formation of this receptor complex and inhibiting IL-13 signaling. IL-13 is implicated as a primary cytokine tied to the pathophysiology of eczema, driving the type-2 inflammatory loop in the skin, and EBGLYSS selectively targets IL-13.[7]

The EBGLYSS Phase 3 program consists of five key global studies evaluating over 1,300 patients, including two monotherapy studies (ADvocate 1 and 2), a combination study with topical corticosteroids (ADhere), as well as long-term extension (ADjoin) and adolescent open label (ADore) studies. Further data results from ADjoin and ADmirable are expected to be shared in 2024 and early 2025.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about EBGLYSS (lebrikizumab-lbkz) as a treatment for patients with moderate-to severe atopic dermatitis and the timeline for future readouts, presentations, and other milestones relating to EBGLYSS and its clinical trials and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that future study results will be consistent with the results to date or that EBGLYSS will receive additional regulatory approvals, or that it will be commercially successful. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

1 Silverberg J, et al. Lebrikizumab improves atopic dermatitis and quality of life in patients with moderate-to-severe atopic dermatitis previously treated with dupilumab: Results from the ADapt Trial. 2024 Fall Clinical Dermatology Conference. October 25, 2024.
2 Simpson EL, et al. Efficacy and safety of lebrikizumab (an anti-IL-13 monoclonal antibody) in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical corticosteroids: A randomized, placebo-controlled phase II trial (TREBLE). J Am Acad Dermatol. 2018;78(5):863-871.e11. doi:10.1016/j.jaad.2018.01.017
3 Okragly A, et al. Binding, Neutralization and Internalization of the Interleukin-13 Antibody, Lebrikizumab. Dermatol Ther (Heidelb).

2023;13(7):1535-1547. doi:10.1007/s13555-023-00947-7
4 Ultsch M, et al. Structural basis of signaling blockade by anti-IL-13 antibody Lebrikizumab. J Mol Biol. 2013;425(8):1330-1339. doi:10.10116/j.jmb.2013.01.024
5 Bieber T. Interleukin-13: Targeting an underestimated cytokine in atopic dermatitis. Allergy. 2020;75(1):54–62. doi:10.1111/all.13954
6 Tsoi LC, et al. Atopic Dermatitis Is an IL-13-Dominant Disease with Greater Molecular Heterogeneity Compared to Psoriasis. J Invest Dermatol. 2019;139(7):1480-1489. doi:10.1016/j.jid.2018.12.018
7 EBGLYSS. Prescribing Information. Lilly USA, LLC.

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