Lilly requests revocation of emergency use authorization for bamlanivimab alone to complete transition to bamlanivimab and etesevimab together for treatment of COVID-19 in the U.S.

April 16, 2021

- Final step in Lilly's planned transition to provide only bamlanivimab and etesevimab together in the U.S.

- Bamlanivimab and etesevimab together now fully available across the U.S.

- Lilly, in collaboration with Amgen, expects to manufacture sufficient supply for complete global transition by June 2021

INDIANAPOLIS, April 16, 2021 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) has requested the U.S. Food and Drug Administration (FDA) revoke the Emergency Use Authorization (EUA) for bamlanivimab (LY-CoV555) 700 mg alone. Lilly made this request due to the evolving variant landscape in the U.S. and the full availability of bamlanivimab and etesevimab together. This request is not due to any new safety concern.

This final step in Lilly's transition to only supply bamlanivimab and etesevimab for administration together in the U.S. for the treatment of COVID-19 – as planned with the FDA – follows the modification of contracts with the U.S. government to ensure adequate supply of etesevimab to be used together with bamlanivimab.

All sites in the U.S. now have access to obtain doses of etesevimab for administration with bamlanivimab—which together neutralize more of the emerging COVID-19 variants in the U.S. than bamlanivimab alone, including the rapidly growing B.1.427/B.1.429 California strain that currently accounts for 50 percent of the virus in California and over 10 percent across a number of additional states. In the U.S., bamlanivimab alone should no longer be administered. However, sites of care should not dispose of bamlanivimab supply; instead, they should order etesevimab to pair with it.

"Lilly moved quickly to make bamlanivimab alone available as a potentially lifesaving medicine at a time when Americans were hardest hit by COVID-19," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific officer and president of Lilly Research Laboratories. "With the growing prevalence of variants in the U.S. that bamlanivimab alone may not fully neutralize, and with sufficient supply of etesevimab, we believe now is the right time to complete our planned transition and focus on the administration of these two neutralizing antibodies together."

Lilly's bamlanivimab was the first neutralizing monoclonal antibody to receive emergency use authorization from the FDA as a treatment for mild to moderate COVID-19 — providing a valuable treatment at a time when cases were at their highest in the U.S. More than 400,000 patients have been treated with bamlanivimab – more than any other neutralizing antibody – potentially preventing more than 20,000 hospitalizations and at least 10,000 deaths during the worst of the pandemic in the U.S.

Lilly developed bamlanivimab and etesevimab for administration together to meet the potential challenge of treatment-resistant variants likely to resist treatment with either monoclonal antibody used alone. Due to the rapidly evolving and geographically diverse nature of the SARS-CoV-2 virus, continued scientific innovation remains critical to develop additional treatments. Lilly remains committed to developing complementary neutralizing antibodies to address potential SARS-CoV-2 variants that may arise in the future.

Bamlanivimab and/or bamlanivimab administered with etesevimab are authorized under special pathways in 20 countries outside the U.S. spanning four continents. Both bamlanivimab alone and bamlanivimab and etesevimab together retain the neutralization effects against the vast majority of variants, including the UK (B.1.1.7.) variant, present in these other countries and remain an important treatment option. The degree of neutralization of the virus does not necessarily equate to improved clinical outcomes.

Lilly is not requesting the withdrawal of emergency authorization for bamlanivimab alone in any other jurisdiction at this time. However, its use together with etesevimab, where authorized and available, is preferred over bamlanivimab alone. Lilly, in collaboration with Amgen, expects to manufacture sufficient supply of bamlanivimab and etesevimab together to meet global supply needs. Going forward, Lilly will submit only bamlanivimab administered with etesevimab together for authorization globally with a full transition expected by June 2021.

For more information about the use of bamlanivimab and etesevimab together for the treatment of mild to moderate COVID-19 in high-risk patients under the FDA's emergency use authorization, contact Lilly's 24-hour support line at 1-855-LillyC19 (1-855-545-5921). Patients and physicians can visit covid.infusioncenter.org or the HHS Therapeutics Distribution locator to find a potential treatment location.

For media resources, including product images and fact sheets, please click here.

Important Information about bamlanivimab and etesevimab together

Bamlanivimab and etesevimab together have not been approved by the FDA for any use. It is not known if bamlanivimab and etesevimab together are safe and effective for the treatment of COVID-19.

Bamlanivimab and etesevimab together are authorized under Emergency Use Authorization only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under Section 564(b)(1) of the Act, 21 U.S.C § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Healthcare providers should review the Fact Sheet for information on the authorized use of bamlanivimab and etesevimab together and mandatory requirements of the EUA. Please see the FDA Letter of Authorization, Fact Sheet for Healthcare Providers, and Fact Sheet for Patients, Parents and Caregivers (English) (Spanish) for bamlanivimab and etesevimab together.

Authorized Use and Important Safety Information

Bamlanivimab and etesevimab together are authorized for use under EUA for treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to

severe COVID-19 and/or hospitalization.

Limitations of Authorized Use

- Bamlanivimab and etesevimab together are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Treatment with bamlanivimab and etesevimab together has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Important Safety Information
There are limited clinical data available for bamlanivimab and etesevimab together. Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab and etesevimab together.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions
Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of bamlanivimab with and without etesevimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of bamlanivimab and etesevimab together. These reactions may be severe or life threatening. Signs and symptoms of infusion-related reactions may include:

- fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (e.g. atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, and diaphoresis.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Clinical Worsening After Bamlanivimab Administration
Clinical worsening of COVID-19 after administration of bamlanivimab has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, sinus tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to bamlanivimab use or were due to progression of COVID-19.

Limitations of Benefit and Potential Risk in Patients with Severe COVID-19
Treatment with bamlanivimab and etesevimab together has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. See Limitations of Authorized Use.

Adverse Events
Based on Phase 2 data from BLAZE-1, nausea was the most commonly reported adverse event, reported by 4% of subjects in both bamlanivimab and etesevimab together and placebo groups. Pruritus and pyrexia were more frequently reported from subjects treated with both bamlanivimab and etesevimab (2% and 1%) compared to placebo (1% and 0%, respectively).

Based on Phase 3 data from BLAZE-1, the most common adverse events were nausea, dizziness, and rash. These events each occurred in 1% of subjects treated with bamlanivimab and etesevimab together and in 1% of placebo subjects.

Use in Specific Populations
Pregnancy
There are insufficient data on the use of bamlanivimab and etesevimab together during pregnancy. Bamlanivimab and etesevimab together should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Breastfeeding
There are no available data on the presence of bamlanivimab or etesevimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

About bamlanivimab
Bamlanivimab is a recombinant, neutralizing human IgG1 monoclonal antibody (mAb) directed against the spike protein of SARS-CoV-2. It is designed to block viral attachment and entry into human cells, thus neutralizing the virus, potentially treating COVID-19. Bamlanivimab emerged from the collaboration between Lilly and AbCellera to create antibody therapies for the prevention and treatment of COVID-19. Lilly scientists rapidly developed the antibody in less than three months after it was discovered by AbCellera and the scientists at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center. It was identified from a blood sample taken from one of the first U.S. patients who recovered from COVID-19.

Lilly has successfully completed a Phase 1 study of bamlanivimab in hospitalized patients with COVID-19 (NCT04411628). A Phase 2/3 study in people recently diagnosed with COVID-19 in the ambulatory setting (BLAZE-1, NCT04427501) is ongoing. Results from the Phase 2 cohorts of BLAZE-1 were published in the *New England Journal of Medicine* and *The Journal of the American Medical Association*. A Phase 3 study of bamlanivimab alone or bamlanivimab and etesevimab together in residents and staff at long-term care facilities (BLAZE-2, NCT04497987) is also ongoing. In addition, bamlanivimab is being tested in the National Institutes of Health-led ACTIV-2 study in ambulatory COVID-19 patients.

About etesevimab
Etesevimab (LY-CoV016, also known as JS016) is a recombinant fully human monoclonal neutralizing antibody, which specifically binds to the SARS-CoV-2 surface spike protein receptor binding domain with high affinity and can block the binding of the virus to the ACE2 host cell surface receptor. Point mutations were introduced into the native human IgG1 antibody to mitigate effector function. Lilly licensed etesevimab from Junshi Biosciences after it was jointly developed by Junshi Biosciences and the Institute of Microbiology, Chinese Academy of Science (IMCAS). Junshi Biosciences leads development in Greater China, while Lilly leads development in the rest of the world.

Lilly has successfully completed a Phase 1 study (NCT04441931) of etesevimab in healthy U.S. volunteers to evaluate the safety, tolerability, pharmacokinetics and immunogenicity. A Phase 2/3 study in people recently diagnosed with COVID-19 in the ambulatory setting (BLAZE-1, NCT04427501) is ongoing. Results from the Phase 2 cohorts of BLAZE-1 were published in the *New England Journal of Medicine* and *The Journal of the American Medical Association*. Junshi Biosciences has completed a similar Phase 1 study in healthy volunteers in China and has initiated Phase 1b/2 trials in COVID-19 patients globally.

About Lilly's COVID-19 Efforts
Lilly is bringing the full force of its scientific and medical expertise to attack the coronavirus pandemic around the world. Existing Lilly medicines are being studied to understand their potential in treating complications of COVID-19, and the company is collaborating with partner companies to discover and develop novel antibody treatments for COVID-19. Click here for resources related to Lilly's COVID-19 efforts.

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/news. P-LLY

Lilly 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 bamlanivimab (LY-CoV555) and etesevimab (LY-CoV016) together as a potential treatment for patients with COVID-19, as well as bamlanivimab (LY-CoV555) alone and etesevimab (LY-CoV016) alone, the supply, distribution and contracts with the U.S. government relating to these therapies, and Lilly's development plans, and reflects Lilly's current beliefs and expectations. However, as with any such undertaking, there are substantial risks and uncertainties in the process of drug research, development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that bamlanivimab and etesevimab together or any other therapy will prove to be safe and effective treatments or successful preventative therapies for COVID-19, that bamlanivimab and etesevimab together or any other therapy will receive regulatory approvals or additional authorizations, that patients will volunteer to participate in clinical trials or achieve positive outcomes, that Lilly will obtain any additional purchase orders or supply contracts, or that Lilly can provide an adequate supply of bamlanivimab and etesevimab together or any other therapy in all circumstances. For a further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, please see Lilly's most recent Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Refer to:Dani Barnhizer; dbarnhizer@lilly.com; 317-607-6119 (Media)
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (Investors)

View original content to download multimedia:http://www.prnewswire.com/news-releases/lilly-requests-revocation-of-emergency-use-authorization-for-bamlanivimab-alone-to-complete-transition-to-bamlanivimab-and-etesevimab-together-for-treatment-of-covid-19-in-the-us-301270317.html

SOURCE Eli Lilly and Company