New data show treatment with Lilly's neutralizing antibodies bamlanivimab (LY-CoV555) and etesevimab (LY-CoV016) together reduced risk of COVID-19 hospitalizations and death by 70 percent

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- BLAZE-1 trial met primary endpoint and key secondary endpoints with high statistical significance
- Results from more than 1,000 high-risk patients were consistent with previous data
- Findings from BLAZE-4 trial provide data on lower doses of bamlanivimab and etesevimab together
- Media and investor call "SARS-CoV-2 Neutralizing Antibody Program Update" to be held at noon EST today; details below

INDIANAPOLIS, Jan. 26, 2021 /PRNewswire/ -- Bamlanivimab (LY-CoV555) 2800 mg and etesevimab (LY-CoV016) 2800 mg together significantly reduced COVID-19-related hospitalizations and deaths (collectively, "events") in high-risk patients recently diagnosed with COVID-19, meeting the primary endpoint of the Phase 3 BLAZE-1 trial, Eli Lilly and Company (NYSE: LLY) announced. Across 1,035 patients, there were 11 events (2.1 percent) in patients taking therapy and 36 events (7.0 percent) in patients taking placebo, representing a 70 percent risk reduction (p= 0.0004). There were 10 deaths total, all of which occurred in patients taking placebo, and no deaths in patients taking bamlanivimab and etesevimab together.

Bamlanivimab and etesevimab together also demonstrated statistically significant improvements on all key secondary endpoints, providing strong evidence that the therapy reduced viral load and accelerated symptom resolution.

"These exciting results, which replicate positive Phase 2 data in a much larger set of patients, add valuable clinical evidence about the role neutralizing antibodies can play in fighting this pandemic. While the preliminary nature of Phase 2 results from COVID-19 neutralizing monoclonal antibodies may have limited acceptance of treatment, these Phase 3 data further strengthen the available evidence," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific officer and president of Lilly Research Laboratories. "The death toll from COVID-19 continues to rise around the world and hospitalizations, particularly in the U.S., have reached record highs. These data further support our belief that bamlanivimab and etesevimab together have the potential to be an important treatment that significantly reduces hospitalizations and death in high-risk COVID-19 patients.

"Notably, the 70 percent decrease in risk of hospitalizations or death seen in this Phase 3 trial of bamlanivimab and etesevimab together is consistent with the reduction in risk of hospitalization or ER visits seen with bamlanivimab alone in the Phase 2 trial. Bamlanivimab alone is authorized for emergency use as a treatment for high-risk patients with mild to moderate COVID-19 in the U.S. and widely available for use," Skovronsky added.

In the trial, the safety profile of bamlanivimab and etesevimab together was consistent with observations from other Phase 1, Phase 2 and Phase 3 trials evaluating these antibodies. Serious adverse events were reported at a similar frequency in the bamlanivimab and etesevimab together and placebo groups. Across multiple clinical trials, Lilly has collected safety and efficacy data in more than 4,000 participants treated with Lilly's neutralizing antibodies, either bamlanivimab alone or bamlanivimab and etesevimab together.

BLAZE-4
Additionally, initial results from the ongoing BLAZE-4 trial provide viral load and pharmacodynamic/pharmacokinetic data which demonstrated lower doses, including bamlanivimab 700 mg and etesevimab 1400 mg together, are similar to bamlanivimab 2800 mg and etesevimab 2800 mg together. Lilly plans to explore even lower doses of bamlanivimab and etesevimab together, as lower doses can maximize available supply to treat more patients, allow potential for subcutaneous dosing, and potentially reduce the burden on the healthcare system and patients through reduced infusion times.

Availability and supply
Bamlanivimab is authorized for emergency use by the U.S. Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in high-risk patients, and it has also been granted authorizations in several additional countries. For more information about the use of bamlanivimab in the U.S., 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 Therapeutic Distribution locator to find a potential treatment location, or visit combatcovid.hhs.gov to find out more about antibody therapy.

In November, Lilly submitted a request to the FDA for emergency use authorization (EUA) for bamlanivimab and etesevimab together as another treatment for mild to moderate COVID-19 in high-risk patients. It remains under review by the FDA.

Lilly has received feedback from front-line nurses and doctors administering these infusions regarding the complexity and time requirements for preparation and administration. As a result, Lilly is working with the FDA to potentially reduce infusion times to be as short as 16 minutes – a significant reduction from the currently authorized time of 60 minutes. This potential change is aimed at simplifying administration and reducing the burden on the healthcare system.

Lilly has a robust, global supply chain in place to produce its neutralizing antibodies, with numerous manufacturing sites worldwide, and the supply is expected to increase substantially in 2021. Lilly continues to accelerate the manufacturing of etesevimab in collaboration with Amgen, providing up to 1 million doses of etesevimab for administration with bamlanivimab by mid-2021 – including more than 250,000 doses in the first quarter – for use around the world.

Investors, media and the general public are invited to a conference call today at noon EST, where Lilly will provide more data and discuss Lilly's SARS-CoV-2 neutralizing antibody program. The webcast information is available here. A replay will also be available on the website following the conference call.

Important Information about bamlanivimab

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

Bamlanivimab is authorized under an Emergency Use Authorization (EUA) only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of bamlanivimab 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 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).

Authorized Use and Important Safety Information
Bamlanivimab 700 mg injection is 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 is 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.
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

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

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions
There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of bamlanivimab. 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. Signs and symptoms of infusion-related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

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

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

Adverse Events
Adverse events reported in at least 1% of BLAZE-1 clinical trial participants on bamlanivimab 700 mg and placebo were Nausea (3% vs 4%), Diarrhea (1% vs 5%), Dizziness (3% vs 2%), Headache (3% vs 2%), Pruritus (2% vs 1%) and Vomiting (1% vs 3%).

Use in Specific Populations

Pregnancy
There are insufficient data on the use of bamlanivimab during pregnancy. Bamlanivimab 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 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. 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.

Bamlanivimab is authorized in the U.S. for the treatment of mild to moderate COVID-19 in adults and pediatric patients 12 years and older with a positive COVID-19 test, who are at high risk for progressing to severe COVID-19 and/or hospitalization. Bamlanivimab should be administered as soon as possible after a positive COVID-19 test and within 10 days of symptom onset.

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 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. 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 BLAZE-1
BLAZE-1 (NCT04427501) is a randomized, double-blind, placebo-controlled Phase 2/3 study designed to assess the efficacy and safety of bamlanivimab alone or bamlanivimab and etesevimab together for the treatment of symptomatic COVID-19 in the outpatient setting. To be eligible, patients were required to have mild or moderate symptoms of COVID-19 as well as a positive SARS-CoV-2 test based on a sample collected no more than three days prior to drug infusion.

In the Phase 2 portion of BLAZE-1, cohorts of mild to moderate recently diagnosed COVID-19 patients, were randomized to one of three doses of bamlanivimab (700 mg, 2800 mg, and 7000 mg), bamlanivimab 2800 mg plus etesevimab 2800 mg, or placebo. 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*.

In the Phase 3 portion of BLAZE-1, the combination therapy arms enrolled mild to moderate, recently diagnosed COVID-19 patients who are at high risk for progressing to severe COVID-19 and/or hospitalization, studying bamlanivimab 2800 mg plus etesevimab 2800 mg versus placebo. The primary outcome measure for the Phase 3 portion of the BLAZE-1 trial was the percentage of participants who experience COVID-related hospitalizations or death from any cause by day 29. The key secondary endpoints were change from baseline to day 7 in SARS-CoV-2 viral load, persistently high SARS-CoV2 viral load on day 7, time to sustained symptom resolution, and COVID-related hospitalization, ER visit or death from any cause from baseline by day 29. Additional endpoints include change from baseline in viral load at other time points, symptom improvement, symptom resolution, as well as safety.

The study is ongoing with additional treatment arms. Across all treatment arms, the trial will enroll up to 3,300 participants.

About BLAZE-4
BLAZE-4 (NCT04634409) is a randomized, double-blind, placebo-controlled trial designed to assess the efficacy and safety of bamlanivimab alone, and bamlanivimab and etesevimab together, at various doses, versus placebo for the treatment of symptomatic COVID-19 in the outpatient setting. Across all treatment arms, the trial will enroll an estimated 1,000 participants in the United States and Puerto Rico.

The primary outcome measure is percentage of participants who have a viral load greater than 5.27 at day 7. Additional endpoints include change from baseline to day 7 in SARS-CoV-2 viral load, percentage of participants who experience COVID-related hospitalization, ER visit or death from baseline through day 29, as well as safety.

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 novel antibody treatments for COVID-19. Lilly is testing both single antibody therapy as well as combinations of antibodies as potential therapeutics 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) alone and bamlanivimab and etesevimab (LY-CoV016) together as potential treatments for patients with or at risk of infection from COVID-19, as well as collection of data regarding the effectiveness, and supply and delivery of these therapies. These statements reflect 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 alone or bamlanivimab and etesevimab together will prove to be a safe and effective treatment or preventative for COVID-19, that bamlanivimab alone or bamlanivimab and etesevimab together will receive regulatory approvals or additional authorizations, that patients will volunteer to participate in clinical trials or achieve positive outcomes or that we can provide an adequate supply of bamlanivimab alone or bamlanivimab and etesevimab together 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.

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