# Lilly provides comprehensive update on progress of SARS-CoV-2 neutralizing antibody programs

October 7, 2020

**- Lilly submitted request for emergency use authorization (EUA) for monotherapy to U.S. Food and Drug Administration (FDA)**

**- New data show combination therapy met primary and secondary endpoints, reducing viral load, symptoms and hospitalizations; EUA request to follow**

**- Plan to initiate a large open-label pragmatic study in COVID-19 outpatients in October**

**- Media and investor call to be held at noon EDT today**

INDIANAPOLIS, Oct. 7, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced additional details on its SARS-CoV-2 neutralizing antibody programs – including interim data on combination therapy in recently diagnosed patients with mild-to-moderate COVID-19 – and plans to make these therapies broadly available to patients.

"Our teams have worked tirelessly the last seven months to discover and develop these potential antibody treatments," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific officer and president of Lilly Research Laboratories. "We believe the data generated to date provide sufficient evidence that both monotherapy and combination therapy may be effective to treat COVID-19 in patients with a high risk for serious outcomes. Lilly is diligently working with regulators around the world to make these treatments available."

Investors, media and the general public are invited to a conference call today at noon EDT, where Lilly will provide more data and discussion on these programs. The webcast information is available here. A replay will also be available on the website following the conference call.

*Combination therapy clinical trial data*

Data from a new interim analysis of the BLAZE-1 clinical trial showed that combination therapy with two of Lilly's SARS-CoV-2 neutralizing antibodies reduced viral load, symptoms and COVID-related hospitalization and ER visits. The randomized, double-blind, placebo-controlled Phase 2 study evaluated LY-CoV555 and LY-CoV016, which bind complementary regions of the SARS-CoV-2 spike protein, for the treatment of symptomatic COVID-19 in the outpatient setting. The combination cohort enrolled recently diagnosed patients with mild-to-moderate COVID-19, who were assigned to 2800 mg of each antibody (n=112) or placebo (n=156).

The combination therapy significantly reduced viral load at day 11 ($p=0.011$), meeting the primary endpoint of the study. Most patients, including those receiving placebo, demonstrated near complete viral clearance by day 11. Further, combination treatment reduced viral levels at day 3 ($p=0.016$) and day 7 ($p<0.001$)—earlier time points during the course of infection when higher viral loads are typically seen. Combination therapy also significantly reduced the time-weighted average change from baseline from day 1 to 11. An exploratory analysis showed that the proportion of patients with persistent high viral load at day 7 for combination therapy was lower (3.0 percent) versus placebo (20.8 percent), corresponding to a nominal p value of $p<0.0001$ without multiplicity adjustment. No emergent putative resistance variants have been observed thus far in patients treated with combination therapy.

Combination therapy also met prespecified clinical endpoints, including the time-weighted average change from baseline in total symptom score from day 1 to 11 ($p=0.009$). The improvement in symptoms was observed as early as three days after dosing and was similar in magnitude and timing to improvements previously seen with LY-CoV555 monotherapy. The rate of COVID-related hospitalization and ER visits was lower for patients treated with combination therapy (0.9 percent) versus placebo (5.8 percent), a relative risk reduction of 84.5 percent ($p=0.049$). This was also similar to observations for LY-CoV555 monotherapy.

Combination therapy has been generally well tolerated with no drug-related serious adverse events. In LY-CoV555 monotherapy studies there have

been isolated drug-related infusion reactions or hypersensitivity that were generally mild (two reported as serious infusion reactions, all patients recovered). Treatment emergent adverse events were comparable to placebo for both LY-CoV555 monotherapy and combination therapy.

Lilly is working to publish the monotherapy and combination therapy data in peer-reviewed journals as soon as possible.

*Manufacturing and supply update*

To be able to quickly provide treatment to patients around the world, Lilly invested in large-scale manufacturing of both antibodies at risk – even before data demonstrated their potential to become a meaningful therapeutic option for COVID-19.

For monotherapy, Lilly is focused on the 700 mg dose of LY-CoV555 since similar clinical effects were seen across all dose levels tested in BLAZE-1. Lilly anticipates it could supply as many as one million doses of 700 mg LY-CoV555 monotherapy in Q4 2020, with 100,000 available in October. With respect to the supply of combination therapy, Lilly anticipates it will have 50,000 doses available in Q4 2020. The supply of combination therapy will increase substantially beginning in Q1 2021, as additional manufacturing resources come online throughout the year, including Lilly's recently announced manufacturing collaboration with Amgen (NASDAQ: AMGN). Lilly is also pursuing additional partnerships to provide antibodies to resource-limited countries.

*Regulatory update*

Based on the combination therapy data, along with the previously disclosed findings for LY-CoV555 monotherapy, Lilly has engaged global regulators, including the FDA regarding potential EUA. Lilly has now submitted an initial request for EUA for LY-CoV555 monotherapy in higher-risk patients who have been recently diagnosed with mild-to-moderate COVID-19. We expect to submit a subsequent request for EUA for combination therapy in November, pending clinical trial enrollment, once additional safety data accumulate and sufficient supply is manufactured. Lilly anticipates having data to support a biologics license application (BLA) submission for combination therapy as early as Q2 2021. Conversations with global regulators are ongoing.

The BLAZE-1 clinical trial (NCT04427501) continues to enroll a confirmatory cohort of higher-risk patients who have been recently diagnosed with mild-to-moderate COVID-19, testing the ability of the antibody combination to reduce the number of patients with persistent high viral load and reduce COVID-related hospitalizations. In addition, Lilly is studying lower doses of combination therapy and alternative delivery options in planned or ongoing clinical trials. Other ongoing clinical trials include a Phase 3 study of LY-CoV555 monotherapy for the prevention of COVID-19 in residents and staff at long-term care facilities (BLAZE-2, NCT04497987). In addition, LY-CoV555 monotherapy is being tested in the National Institutes of Health-led ACTIV-2 and ACTIV-3 studies of ambulatory and hospitalized COVID-19 patients. Data from these other ongoing trials are not yet available. Thus far, over 850 trial participants have been dosed with LY-CoV555 (alone or in combination with LY-CoV016), contributing to the safety data supporting this potential treatment.

*Open-label pragmatic study in COVID-19 outpatients*

To generate additional efficacy and safety data, Lilly plans to initiate a pragmatic, open-label study in the coming weeks, enrolling patients treated with either monotherapy or combination therapy, with a focus on collecting data regarding hospitalizations, deaths and safety.

Moving forward, LY-CoV555 and LY-CoV016 will be referred to as bamlanivimab and etesevimab, respectively.

**About BLAZE-1**
BLAZE-1 (NCT04427501) is a randomized, double-blind, placebo-controlled Phase 2 study designed to assess the efficacy and safety of LY-CoV555 and LY-CoV016 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.

The monotherapy arms of the trial enrolled mild-to-moderate recently diagnosed COVID-19 patients, studying three doses of LY-CoV555 (700 mg, 2800 mg, and 7000 mg) versus placebo. The combination arm of the trial enrolled mild-to-moderate, recently diagnosed COVID-19 patients, studying LY-CoV555 2800 mg plus LY-CoV016 2800 mg versus placebo. Placebo patients were shared across all therapy arms in the completed cohorts.

The primary outcome measure for these completed arms of the BLAZE-1 trial was change from baseline to day 11 in SARS-CoV-2 viral load. Additional endpoints include the percentage of participants who experience COVID-related hospitalization, ER visit or death from baseline through day 29, as well as safety.

The study is ongoing with additional treatment arms. Across all treatment arms, the trial will enroll an estimated 800 participants.

**About bamlanivimab (LY-CoV555)**
LY-CoV555 is a potent, neutralizing 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 preventing and treating COVID-19. LY-CoV555 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 enrollment and primary safety assessments of LY-CoV555 in a Phase 1 study of hospitalized patients with COVID-19 (NCT04411628) and long-term follow-up is ongoing. A Phase 2 study in people recently diagnosed with COVID-19 in the ambulatory setting (BLAZE-1, NCT04427501) is ongoing. Lilly recently initiated a Phase 3 study for the prevention of COVID-19 in residents and staff at long-term care facilities (BLAZE-2, NCT04497987). In addition, LY-CoV555 is being tested in the National Institutes of Health-led ACTIV-2 and ACTIV-3 studies of ambulatory and hospitalized COVID-19 patients.

**About etesevimab (LY-CoV016)**
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 effectively 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. A SARS-CoV-2 challenge study was conducted in rhesus macaques and showed LY-CoV016 is effective for both prophylactic and therapeutic venues against SARS-CoV-2 infection. Lilly licensed LY-CoV016

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 LY-CoV016 in healthy U.S. volunteers to evaluate the safety, tolerability, pharmacokinetics and immunogenicity. LY-CoV016 has been well tolerated and no drug-related severe adverse events (SAEs) have been observed to date.

**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 now 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 media resources related to Lilly's COVID-19 efforts.

**About Eli Lilly and Company**
Lilly is a global healthcare 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 LY-CoV555 and LY-CoV016 as a potential treatment for patients with or at risk of infection from COVID-19 and reflects Lilly's current beliefs. However, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that LY-CoV555 and LY-CoV016 will prove to be a safe and effective treatment or preventative for COVID-19, that LY-CoV555 and LY-CoV016 will receive regulatory approvals or authorizations, or that we can provide an adequate supply of LY-CoV555 and LY-CoV016 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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