Lilly, Vir Biotechnology and GSK Announce First Patient Dosed in Expanded BLAZE-4 Trial Evaluating Bamlanivimab (LY-CoV555) with VIR-7831 (GSK4182136) for COVID-19

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INDIANAPOLIS, SAN FRANCISCO and LONDON, Jan. 27, 2021 (GLOBE NEWSWIRE) -- Eli Lilly and Company (NYSE: LLY), Vir Biotechnology, Inc. (NASDAQ: VIR) and GlaxoSmithKline plc (LSE/NYSE: GSK) today announced a collaboration to evaluate a combination of two COVID-19 therapies in low-risk patients with mild to moderate COVID-19. Lilly has expanded its ongoing BLAZE-4 trial to evaluate the administration of bamlanivimab (LY-CoV555) 700mg with VIR-7831 (also known as GSK4182136) 500mg, two neutralizing antibodies that bind to different epitopes of the SARS-CoV-2 spike protein. This unique collaboration marks the first time that monoclonal antibodies from separate companies will be brought together to explore potential outcomes.

Bamlanivimab is a neutralizing antibody directed against the spike protein of SARS-CoV-2 designed to block viral attachment and entry into human cells, thus neutralizing the virus. Bamlanivimab emerged from the collaboration between Lilly and AbCellera to create antibody therapies for the prevention and treatment of COVID-19. Bamlanivimab is authorized for emergency use for the treatment of mild to moderate COVID-19 in patients who are at high risk for progressing to severe COVID-19 and/or hospitalization.

VIR-7831 is a dual-action monoclonal antibody that was selected for clinical development based on its potential to both block viral entry into healthy cells and clear infected cells, as well as its potential to provide a high barrier to resistance. In pre-clinical trials, the antibody has shown the ability to neutralize the SARS-CoV-2 live virus by binding to an epitope on SARS-CoV-2 shared with SARS-CoV-1, indicating that the epitope is highly conserved, which may make it more difficult for escape mutants to develop. Vir and GSK are advancing VIR-7831 as part of their collaboration to research and develop solutions for coronaviruses, including SARS-CoV-2.

“Bamlanivimab is a potent antibody – with data from multiple Phase 2 and 3 clinical trials, which have demonstrated robust evidence for both treating and preventing COVID-19,” said Daniel Skovronsky, M.D., Ph.D., Lilly’s chief scientific officer and president of Lilly Research Laboratories. “With a virus like SARS-CoV-2, it’s expected that variants could emerge that require new therapeutic options, which is why Lilly is studying bamlanivimab together with other neutralizing antibodies, including etesevimab. Adding VIR-7831 to our study is an important part of our commitment to develop therapies to treat current and future strains of COVID-19 until vaccines are widely available and utilized.”

“We believe that VIR-7831 has significant potential as a single agent, and we are optimistic about the pending interim data from two Phase 3 trials evaluating its potential for early treatment and in hospitalized patients,” said George Scangos, Ph.D., chief executive officer of Vir. “As the virus continues to evolve, we, along with Lilly and GSK, share the view that we should pursue all possibilities to help end the pandemic and maximize the number of lives that can be saved. This trial is a first step to assess whether the administration of VIR-7831, with its high barrier to resistance and potent effector function, alongside bamlanivimab, which has strong outcomes data in early treatment, can provide potential benefits beyond monotherapy.”

“Despite the significant progress on vaccines, there remains an urgent patient need for multiple therapeutic approaches to prevent the more severe consequences of COVID-19,” said Dr. Hal Barron, chief scientific officer and president R&D of GSK. “Partnering with Lilly to study VIR-7831 with bamlanivimab will provide the scientific community with further data on the important role these therapies could play in reducing the impact of this devastating pandemic.”

Bamlanivimab alone has been granted Emergency Use Authorization (EUA) by the U.S. Food and Drug Administration (FDA) based on interim data from the Phase 2 BLAZE-1 trial, which was published in the *New England Journal of Medicine*. These data show the therapy may help patients clear the virus and reduce COVID-19-related hospitalizations when given early in the disease course. The safety and efficacy of bamlanivimab is being evaluated with other neutralizing antibodies to provide a possible safeguard against potential viral resistance.

VIR-7831 is an investigational compound, not approved by the U.S. FDA or any other regulatory authority. VIR-7831 is also being evaluated in the global Phase 2/3 COMET-ICE (COVID-19 Monoclonal antibody Efficacy Trial - Intent to Care Early) trial for the early treatment of COVID-19 in adults at high risk of hospitalization.

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 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 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 with other neutralizing antibodies including VIR-7831 (GSK4182136) 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 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 for the prevention of COVID-19 in residents and staff at long-term care facilities (BLAZE-2, NCT04497987) is 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 VIR-7831 / GSK4182136
VIR-7831 (GSK4182136) is an investigational dual-action monoclonal antibody. Preclinical data suggest it has the potential to both block viral entry into healthy cells and clear infected cells. The antibody binds to an epitope on SARS-CoV-2 that is shared with SARS-CoV-1 (the virus which causes SARS), indicating that the epitope is highly conserved, which may make it more difficult for resistance to develop. VIR-7831 also has been designed to achieve high concentration in the lungs to ensure optimal penetration into airway tissues affected by SARS-CoV-2 and to have an extended half-life.

The COMET clinical development program for VIR-7831 includes a planned Phase 3 trial for the prevention of symptomatic infection. VIR-7831 is also being evaluated in a sub-trial of the National Institutes of Health's (NIH) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Program Phase 3 clinical trial. This trial is designed to evaluate the safety and efficacy of VIR-7831 for the treatment of hospitalized adults with COVID-19.

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. Visit Lilly's COVID-19 disease area page for resources related to Lilly's COVID-19 efforts.

GSK commitment to tackling COVID-19
GSK's response to COVID-19 has been one of the broadest in the industry with potential treatments and vaccine candidates in development.

GSK is collaborating with several organisations working on promising COVID-19 vaccines by providing access to our adjuvant technology. In a collaboration with Sanofi that brings together two of the world's largest vaccine companies, GSK is developing an adjuvanted recombinant protein-based COVID-19 vaccine candidate with a phase 2b study expected to start in February 2021. GSK also is collaborating with Medicago and Clover Biopharmaceuticals on adjuvanted, protein-based vaccine candidates, which are progressing into late-stage clinical trials. The use of an adjuvant is of particular importance in a pandemic situation since it may reduce the amount of vaccine protein required per dose, allowing more vaccine doses to be produced and therefore contributing to protecting more people.

GSK is also exploring potential therapeutic or treatment options for COVID-19 patients. We are collaborating with Vir Biotechnology to research and develop solutions for coronaviruses, including SARS-CoV-2, the virus that causes COVID-19. Currently, collaborating on the phase 3 clinical development of VIR-7831 (GSK4182136), a dual-action monoclonal antibody that has shown the ability in preclinical trials to both neutralize SARS-CoV-2 live virus in vitro and in vivo and kill already infected cells.

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.

About Vir Biotechnology
Vir Biotechnology is a clinical-stage immunology company focused on combining immunologic insights with cutting-edge technologies to treat and prevent serious infectious diseases. Vir has assembled four technology platforms that are designed to stimulate and enhance the immune system by exploiting critical observations of natural immune processes. Its current development pipeline consists of product candidates targeting hepatitis B virus, influenza A, SARS-CoV-2, human immunodeficiency virus and tuberculosis. For more information, please visit www.vir.bio.

About GSK
GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com/about-us.

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) as a potential treatment for patients with or at risk of infection from COVID-19, alone and in combination with other neutralizing antibodies, including VIR-7831 and etesevimab (LY-CoV016), Lilly's development plans and collaboration efforts, 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 and in drug collaborations. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that bamlanivimab alone or administered with VIR-7831or etesevimab will prove to be a safe and effective treatment or preventative for COVID-19, that bamlanivimab alone or administered with VIR-7831 or etesevimab will receive regulatory approvals or additional authorizations, that patients will volunteer to participate in a study of bamlanivimab alone or administered with VIR-7831 or etesevimab or achieve positive outcomes or that Lilly and its partners can provide an adequate supply of bamlanivimab alone or administered with VIR-7831 or etesevimab 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.

Vir Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "plan," "potential," "aim," "promising" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on Vir's expectations and

assumptions as of the date of this press release. Forward-looking statements contained in this press release include statements regarding the potential benefits of VIR-7831 as a single agent and in combination with bamlanivimab in the treatment of COVID-19, the potential benefits of participating in the BLAZE-4 trial, and the potential benefits of Vir, Lilly, and GSK's collaboration in addressing the current COVID-19 pandemic and future outbreaks of the disease. Many factors may cause differences between current expectations and actual results, including delays or failures in planned patient enrollment or retention, clinical site activation rates or clinical trial enrollment rates that are lower than expected, unexpected safety or efficacy data observed during preclinical or clinical studies, challenges in the treatment of hospitalized patients, difficulties in collaborating with other companies or government agencies, challenges in accessing manufacturing capacity, successful development and/or commercialization of alternative product candidates by our competitors, changes in expected or existing competition, delays in or disruptions to our business or clinical trials due to the COVID-19 pandemic, geopolitical changes or other external factors, and unexpected litigation or other disputes.

GSK's cautionary statement regarding forward-looking statements
GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D "Risk Factors" in the company's Annual Report on Form 20-F for 2019 and as set out in GSK's "Principal risks and uncertainties" section of the Q3 Results and any impacts of the COVID-19 pandemic.

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