Pfizer Logo

EMA Issues Advice for Potential Early Use of Pfizer's Novel COVID-19 Oral Antiviral Candidate

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- *EMA's CHMP advice states that PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) can be used for treatment of adults with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe disease*
- *This advice could support authorities of EU Member States regarding the supply and use of PAXLOVID prior to the grant of EU conditional marketing authorization; rolling review is being conducted by the EMA in parallel*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued advice on the use of PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets), stating that PAXLOVID can be used to treat adults with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe disease. The CHMP also recommend that PAXLOVID should be administered as soon as possible after diagnosis of COVID-19 and within five days of the start of symptoms. The EMA issued this advice under Article 5(3) of Regulation 726/2004 to support authorities of European Union (EU) Member States who may decide to allow the supply and use of PAXLOVID, for example in emergency use settings, prior to EU conditional marketing authorization. PAXLOVID is currently not authorized for use in the EU.

"The CHMP's advice signifies the strength of our data for PAXLOVID in the treatment of high-risk adults diagnosed with COVID-19," said Albert Bourla, Chairman and Chief Executive Officer, Pfizer. "COVID-19 continues to take lives at an unprecedented pace globally and exacts a devastating toll on health care systems. If authorized, PAXLOVID has the potential to help save lives and reduce hospitalizations. We look forward to working with the EMA and other regulatory agencies worldwide to bring this potential treatment to patients as quickly as possible."

The CHMP based their advice on positive results from the Phase 2/3 EPIC-HR (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **H**igh-**R**isk Patients) interim analysis, which enrolled non-hospitalized adults with confirmed COVID-19 who are at increased risk of progressing to severe illness. The data demonstrated an 89% reduction in risk of COVID-19-related hospitalization or death from any cause in patients treated with PAXLOVID compared to placebo within three days of symptom onset, with no deaths in the treatment group. Similar results were seen with those treated within five days of symptom onset. Treatment-emergent adverse events were comparable between PAXLOVID (19%) and placebo (21%), most of which were mild in intensity. Pfizer recently announced that results from the final analysis of the primary endpoint from all patients enrolled in EPIC-HR were consistent with the interim analysis, confirming robust efficacy and a similar safety profile.

Pfizer has also initiated rolling submission with the EMA for potential EU conditional marketing authorization of PAXLOVID. If authorized, PAXLOVID could be prescribed as an at-home treatment to high-risk patients at

the first sign of infection, potentially helping patients avoid severe illness which can lead to hospitalization and death. PAXLOVID is also being studied in adults at standard risk of progressing to severe illness, as well as in adults who have been exposed to the virus through household contacts.

About PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets)

PAXLOVID is an investigational SARS-CoV-2 protease inhibitor antiviral therapy. It was developed to be administered orally so that, if authorized or approved, it can be prescribed at the first sign of infection or at first awareness of an exposure – potentially helping patients avoid severe illness (which can lead to hospitalization and death) or disease development following contact – subject to the successful completion of the remainder of the EPIC clinical development program. Nirmatrelvir [PF-07321332], which originated in Pfizer's laboratories, is designed to block the activity of the SARS-CoV-2-3CL protease, an enzyme that the coronavirus needs to replicate. Co-administration with a low dose of ritonavir helps slow the metabolism, or breakdown, of nirmatrelvir in order for it to remain active in the body for longer periods of time at higher concentrations to help combat the virus.

Nirmatrelvir is designed to inhibit viral replication at a stage known as proteolysis, which occurs before viral RNA replication. In preclinical studies, nirmatrelvir did not demonstrate evidence of mutagenic DNA interactions.

Current variants of concern can be resistant to treatments that are focused on the spike protein expressed on the surface of the SARS-CoV-2 virus, due to the mutations in this region. PAXLOVID, however, works intracellularly on the protease of the SARS-CoV-2 virus by inhibiting viral replication. Nirmatrelvir has shown consistent in vitro antiviral activity against the previously identified variants of concerns (i.e., alpha, beta, delta, gamma, lambda, and mu). In addition, nirmatrelvir potently inhibited the 3CL protease associated with Omicron in an in vitro biochemical assay. This indicates nirmatrelvir's potential to maintain robust antiviral activity against Omicron. Additional in vitro antiviral studies with this variant are underway.

If authorized or approved, PAXLOVID will be administered at a dose of 300 mg (two 150 mg tablets) of nirmatrelvir with one 100 mg tablet of ritonavir, given twice-daily for five days. One box contains five blister packs of PAXLOVID, as co-packaged nirmatrelvir tablets with ritonavir tablets, providing all required doses for a full five-day treatment course.

Our Commitment to Equitable Access

Pfizer is committed to working toward equitable access to PAXLOVID for all people, aiming to deliver safe and effective antiviral therapeutics as soon as possible and at an affordable price. If authorized or approved, during the pandemic, Pfizer will offer our investigational oral antiviral therapy through a tiered pricing approach based on the income level of each country to promote equity of access across the globe. High and upper-middle income countries will pay more than lower income countries.

Pfizer will continue to invest up to approximately $1 billion to support the manufacturing and distribution of this investigational treatment candidate, including exploring potential contract manufacturing options. It has entered into agreements with several countries and has initiated bilateral outreach to approximately 100 countries around the world. Additionally, Pfizer has signed a voluntary license agreement with the Medicines Patent Pool (MPP) for its oral antiviral treatment to help expand access, pending regulatory authorization or approval, in 95 low- and middle-income countries that account for approximately 53% of the world's population.

About the EPIC Development Program

The EPIC (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19) Phase 2/3 development program for PAXLOVID consists of three clinical trials spanning a broad spectrum of patients, including adults who have been exposed to the virus through household contacts, as well as adults at both standard risk and high risk of progressing to severe illness.?

In July 2021, Pfizer initiated the first of these trials, known as EPIC-HR, a randomized, double-blind study of non-hospitalized adults with COVID-19, who are at high risk of progressing to severe illness. At the recommendation of an independent Data Monitoring Committee and in consultation with the U.S. FDA, Pfizer ceased further enrollment into the study in early November 2021 due to the overwhelming efficacy demonstrated in these results. Data have been submitted to the FDA as part of its submission for Emergency Use Authorization, and findings from the EPIC-HR interim analysis have been submitted to a peer-reviewed journal for publication.

In August 2021, Pfizer began the Phase 2/3 EPIC-SR (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **S**tandard-**R**isk Patients), to evaluate efficacy and safety in adults with a confirmed diagnosis of SARS-CoV-2 infection who are at standard risk (i.e., low risk of hospitalization or death). EPIC-SR includes a cohort of vaccinated adults who have an acute breakthrough symptomatic COVID-19 infection and who have risk factors for severe illness. Interim data from this study have been reported. In September, Pfizer initiated the Phase 2/3 EPIC-PEP (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **P**ost-**E**xposure **P**rophylaxis) to evaluate efficacy and safety in adults exposed to SARS-CoV-2 by a household member. These trials are ongoing.

For more information on the EPIC Phase 2/3 clinical trials for PAXLOVID, visit clinicaltrials.gov.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 170 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Disclosure Notice

The information contained in this release is as of December 16, 2021. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer's efforts to combat COVID-19, Pfizer's investigational oral antiviral candidate PAXLOVID (including qualitative assessments of available data, potential benefits, expectations for clinical trials, CHMP advice on the use of PAXLOVID for adults with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe disease, a rolling submission for potential EU conditional marketing authorization, advanced purchase agreements and an agreement with MPP, efforts toward equitable access, the anticipated timing of data readouts, regulatory submissions, regulatory approvals or authorizations, potential to maintain antiviral activity against

variants, planned investment and anticipated manufacturing, distribution and supply) and the positive CHMP opinions received by certain of Pfizer's pipeline of innovative medicines, involving substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as risks associated with preclinical and clinical data (including the data discussed in this release), including the possibility of unfavorable new preclinical, clinical or safety data and further analyses of existing preclinical, clinical or safety data, including the risk that final results from EPIC-SR could differ from the interim data; the ability to produce comparable clinical or other results including efficacy, safety and tolerability profile observed to date, in additional studies or in larger, more diverse populations following commercialization; the risk that preclinical and clinical trial data are subject to differing interpretations and assessments, including during the peer review/publication process, in the scientific community generally, and by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from these and any future preclinical and clinical studies; whether and when any drug applications or submissions to request emergency use or conditional marketing authorization for any potential indications for PAXLOVID may be filed in particular jurisdictions and if obtained, whether or when such emergency use authorization or licenses will expire or terminate; whether and when regulatory authorities in any jurisdictions may approve any such applications or submissions for PAXLOVID (including the submission for conditional marketing authorization in the EU, the submission for EUA pending with the FDA and rolling submissions in other jurisdictions), which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether it will be commercially successful; decisions by regulatory authorities impacting labeling or marketing, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of PAXLOVID, including development of products or therapies by other companies; risks related to the availability of raw materials for PAXLOVID; the risk that we may not be able to create or scale up manufacturing capacity on a timely basis or maintain access to logistics or supply channels commensurate with global demand, which would negatively impact our ability to supply the estimated numbers of courses of PAXLOVID within the projected time periods; whether and when additional purchase agreements will be reached; the risk that demand for any products may be reduced or no longer exist; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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Pfizer Contacts:
Media Relations
+1 (212) 733-1226
EUPress@Pfizer.com

Investor Relations
+1 (212) 733-4848
IR@pfizer.com

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