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Pfizer Announces Additional Phase 2/3 Study Results Confirming Robust Efficacy of Novel COVID-19 Oral Antiviral Treatment Candidate in Reducing Risk of Hospitalization or Death

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- *Final data available from all high-risk patients enrolled in EPIC-HR study (n= 2,246) confirmed prior results of interim analysis showing PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) reduced risk of hospitalization or death by 89% (within three days of symptom onset) and 88% (within five days of symptom onset) compared to placebo; no deaths compared to placebo in non-hospitalized, high-risk adults with COVID-19*
- *The above data have been shared with the U.S. Food and Drug Administration (FDA) as part of an ongoing rolling submission for Emergency Use Authorization (EUA)*
- *Separately, interim analyses of an ongoing second study in standard-risk adults (EPIC-SR) showed a 70% reduction in hospitalization and no deaths in the treated population, compared to placebo, in the secondary endpoint; the novel primary endpoint of self-reported, sustained alleviation of all symptoms for four consecutive days, as compared to placebo, was not met. The study continues*
- *An approximate 10-fold decrease in viral load at Day 5, relative to placebo, was observed in both EPIC-HR and EPIC-SR, indicating robust activity against SARS-CoV-2 and representing the strongest viral load reduction reported to date for a COVID-19 oral antiviral agent*
- *Recent in vitro data confirm that nirmatrelvir is a potent inhibitor of the Omicron 3CL protease, which, combined with existing in vitro antiviral and protease inhibition data from other Variants of Concern (VoC) including Delta, indicates that PAXLOVID will retain robust antiviral activity against current VoCs as well as other coronaviruses*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced final results from an analysis of all 2,246 adults enrolled in its Phase 2/3 EPIC-HR (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **H**igh-**R**isk Patients) trial of its novel COVID-19 oral antiviral candidate PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets). These results were consistent with the interim analysis announced in November 2021, showing PAXLOVID significantly reduced the risk of hospitalization or death for any cause by 89% compared to placebo in non-hospitalized, high-risk adult patients with COVID-19 treated within three days of symptom onset. In a secondary endpoint, PAXLOVID reduced the risk of hospitalization or death for any cause by 88% compared to placebo in patients treated within five days of symptom onset, an increase from the 85% observed in the interim analysis. The EPIC-HR data have been shared with the U.S. Food and Drug Administration (FDA) as part of an ongoing rolling submission for Emergency Use Authorization (EUA).

“This news provides further corroboration that our oral antiviral candidate, if authorized or approved, could have a meaningful impact on the lives of many, as the data further support the efficacy of PAXLOVID in reducing hospitalization and death and show a substantial decrease in viral load. This underscores the treatment candidate’s potential to save the lives of patients around the world,” said Albert Bourla, Chairman and Chief Executive Officer, Pfizer. “Emerging variants of concern, like Omicron, have exacerbated the need for accessible treatment options for those who contract the virus, and we are confident that, if authorized or approved, this potential treatment could be a critical tool to help quell the pandemic.”

EPIC-HR Final Results

In the final analysis of the primary endpoint from all patients enrolled in EPIC-HR, an 89% reduction in COVID-19-related hospitalization or death from any cause compared to placebo in patients treated within three days of symptom onset was observed, consistent with the interim analysis. In addition, a consistent safety profile was observed.

0.7% of patients who received PAXLOVID were hospitalized through Day 28 following randomization (5/697 hospitalized with no deaths), compared to 6.5% of patients who received placebo and were hospitalized or died (44/682 hospitalized with 9 subsequent deaths). The statistical significance of these results was high ($p<0.0001$). In a secondary endpoint, PAXLOVID reduced the risk of hospitalization or death for any cause by 88% compared to placebo in patients treated within five days of symptom onset; 0.8% of patients who received PAXLOVID were hospitalized or died through Day 28 following randomization (8/1039 hospitalized with no deaths), compared to 6.3% of patients who received placebo (66/1046 hospitalized with 12 subsequent deaths), with high statistical significance ($p<0.0001$). Relative risk reduction was 94% in patients 65 years of age or older, one of the populations at highest risk for hospitalization or death; 1.1% of patients who received PAXLOVID were hospitalized through Day 28 (1/94 hospitalized with no deaths), compared to 16.3% of patients who received placebo (16/98 hospitalized with 6 deaths), with high statistical significance ($p<0.0001$). In the overall study population through Day 28, no deaths were reported in patients who received PAXLOVID as compared to 12 (1.2%) deaths in patients who received placebo.

In the EPIC-HR trial, in a secondary endpoint, SARS-CoV-2 viral load at baseline and Day 5 have been evaluated for 499 patients. After accounting for baseline viral load, geographic region, and serology status, PAXLOVID reduced viral load by approximately 10-fold, or 0.93 $\log_{10}$ copies/mL, relative to placebo, indicating robust activity against SARS-CoV-2 and representing the strongest viral load reduction reported to date for an oral COVID-19 agent.

Treatment-emergent adverse events were comparable between PAXLOVID (23%) and placebo (24%), most of which were mild in intensity. Fewer serious adverse events (1.6% vs. 6.6%) and discontinuation of study drug due to adverse events (2.1% vs. 4.2%) were observed in patients dosed with PAXLOVID, compared to placebo, respectively.

All other secondary endpoints for this study, which are available on clinicaltrials.gov (NCT04960202), were not yet available for this review. Full study data are expected to be released later this month and submitted to a peer-reviewed publication.

EPIC-SR Interim Results

Interim analyses of the EPIC-SR (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **S**tandard-**R**isk Patients) Phase 2/3 study, which included unvaccinated adults who were at standard risk (i.e., low risk of hospitalization or death) as well as vaccinated adults who had one or more risk factors for progressing to severe illness, showed that the novel primary endpoint of self-reported, sustained alleviation of all symptoms for four consecutive days,

as compared to placebo, was not met.

The key secondary endpoint showed a 70% reduction in hospitalization and no deaths in the treated population for any cause compared to placebo. Additionally, there was approximately a 10-fold, or 1 $\log_{10}$ copies/mL, decrease in viral load compared to placebo, consistent with results from the Phase 2/3 EPIC-HR study.

The data were reviewed by an independent Data Monitoring Committee (DMC) and, based on the totality of the data available, the DMC recommended that the trial continue.

At the EPIC-SR interim analysis, which included 45% of the trial's planned enrollment, 0.6% of those who received PAXLOVID were hospitalized following randomization (2/333 hospitalized with no deaths), compared to 2.4% of patients who received placebo and were hospitalized or died (8/329 hospitalized with no deaths). A follow-on analysis at 80% of enrolled patients was consistent with these findings. In this analysis, 0.7% of those who received PAXLOVID were hospitalized following randomization (3/428 hospitalized with no deaths), compared to 2.4% of patients who received placebo and were hospitalized or died (10/426 hospitalized with no deaths); p=0.051.

Treatment-emergent adverse events were comparable between PAXLOVID (22%) and placebo (21%), most of which were mild in intensity. Rates of serious adverse events (1.4% vs. 1.9%) and discontinuation of study drug due to adverse events (2.1% vs. 1.2%) were also comparable between PAXLOVID and placebo.

All other secondary endpoints for this study, which are available on clinicaltrials.gov (NCT05011513), were not yet available for this review. The study is now fully enrolled, and further data will be released upon analysis of the full study data expected later this month.

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 avoid disease development following contact with a household member who contracts COVID-19 – subject to the clinical success of the rest of the EPIC development program. Nirmatrelvir [PF-07321332], which originated in Pfizer 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.

About the Phase 2/3 EPIC-HR Study Top-Line Results

The final analysis of the primary endpoint evaluated data from 2,246 adults who were enrolled by November 4, 2021. At the time of the decision to stop recruiting patients, enrollment was at 75% of the 3,000 planned patients from clinical trial sites across North and South America, Europe, Africa, and Asia, with 41% of patients located in the United States. Enrolled individuals had a laboratory-confirmed diagnosis of mild to moderate SARS-CoV-2 infection within a five-day period and were required to have at least one characteristic or underlying medical condition associated with an increased risk of developing severe illness from COVID-19. Each patient was randomized (1:1) to receive PAXLOVID or placebo orally every 12 hours for five days.

About the Phase 2/3 EPIC-SR Study Interim Analyses

The primary analysis of the interim data, consisting of the first 45% of patients enrolled in the study, included 673 adults, of whom 338 received PAXLOVID and 335 received placebo. At the time of the interim analyses, EPIC-SR had reached its planned enrollment of more than 1,140 adults from clinical trial sites across North and South America, Europe, Africa, and Asia, and the United States. Enrolled individuals had a laboratory-confirmed diagnosis of mild to moderate SARS-CoV-2 infection within a five-day period and were either unvaccinated adults who were at standard risk (i.e., low risk of hospitalization or death) or vaccinated adults who had one or more risk factors for progressing to severe illness from COVID-19. Each patient was randomized (1:1) to receive PAXLOVID or placebo orally every 12 hours for five days.

About the EPIC Development Program

The EPIC (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19) Phase 2/3 development program for nirmatrelvir; ritonavir 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 (**E**valuation of **P**rotease **I**nhibition for **C** OVID-19 in **H**igh-**R**isk Patients), a randomized, double-blind study of non-hospitalized adult patients 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. Food and Drug Administration (FDA), Pfizer ceased further enrollment into the study in early November 2021 due to the overwhelming efficacy demonstrated in results from an interim analysis. 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 patients with a confirmed diagnosis of SARS-CoV-2 infection who are at standard risk (i.e., low risk of hospitalization or death).

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. This trial is 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 14, 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 and Pfizer's investigational oral antiviral candidate PAXLOVID (including qualitative assessments of available data, including interim data, potential benefits, expectations for clinical trials, a submission to the FDA requesting Emergency Use Authorization (EUA), 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), 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 Phase 2/3 interim data and the other 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 EUA pending with the FDA), 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 https://www.sec.gov/ and www.pfizer.com.

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