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Pfizer Announces Submission of New Drug Application to the U.S. FDA for PAXLOVID™

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- *Submission seeks approval for the treatment of COVID-19 in both vaccinated and unvaccinated individuals at high risk for progression to severe illness from COVID-19; consistent with current emergency use authorization*
- *Final results from EPIC-HR study showed an 86% reduction in relative risk of hospitalizations or death from any cause; no deaths were observed in patients treated with PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) through Week 24, compared to 15 deaths observed with placebo*
- *50-60% of the U.S. population is estimated to have at least one risk factor for progressing to severe COVID-19 illness*
- *Available safety data generally consistent in more than 3,500 PAXLOVID-treated participants across EPIC clinical development program*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for approval of PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) for patients who are at high risk for progression to severe illness from COVID-19. PAXLOVID is currently authorized for emergency use for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg [88 lbs]) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. The submission provides the longer-term follow-up data necessary for acceptance and potential approval.

According to the U.S. Centers for Disease Control and Prevention (CDC), 50-60% of the U.S. population is estimated to have one or more risk factors for progressing to severe COVID-19 illness.[1] These risk factors include any of the following: being aged 65 and older, obesity, diabetes, hypertension, smoking, physical inactivity, chronic kidney or liver disease, and immunocompromised conditions such as cancer, among others.[2]

“As the COVID-19 pandemic continues to evolve and be highly unpredictable, we must remain vigilant in protecting those who are at greatest risk of getting very sick from COVID-19, as they remain vulnerable to potential hospitalization or even death,” said Albert Bourla, Chairman and Chief Executive Officer, Pfizer. “Data from our clinical development program, coupled with the more than 1.7 million patients around the world who have been prescribed our oral treatment to date, reinforce PAXLOVID as an important treatment option for mild-to-moderate COVID-19 in patients at greater risk of progression to severe symptoms, regardless of vaccination status. We look forward to working with the FDA toward full regulatory approval for PAXLOVID.”

The NDA submission is supported by non-clinical and clinical data for PAXLOVID. It includes results from the Phase 2/3 EPIC-HR study (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **H**igh-**R**isk Patients), which found that, compared to placebo, treatment with PAXLOVID reduced the risk of hospitalization or death from

any cause by 88% in non-hospitalized, high-risk adult patients treated within five days of symptom onset; results from the final Clinical Study Report showed an 86% reduction in relative risk. The submission is also comprised of the most recent analyses from the Phase 2/3 EPIC-SR study (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **S**tandard-**R**isk Patients), which included data from both vaccinated patients with, and unvaccinated patients without, risk factors for severe COVID-19. While the novel primary endpoint of self-reported, sustained alleviation of all symptoms for four consecutive days was not met, the data were supportive of the efficacy and safety data observed in EPIC-HR for use in patients at increased risk of progression to severe COVID-19 illness. The NDA submission also includes:

- An integrated analysis of data across the EPIC-HR and EPIC-SR studies, which showed an 84% reduction ($p<0.0001$) in hospitalizations or death, compared to placebo and regardless of vaccination status, in patients with at least one risk factor for progression to severe COVID-19 illness who were treated with PAXLOVID (12/1,400 [0.857%] PAXLOVID-treated patients versus 73/1,406 [5.192%] placebo recipients) within five days of symptom onset.
    - In EPIC-HR, there was an 86% relative risk reduction in hospitalizations or death through Day 28 in PAXLOVID-treated patients [9/1,039] with no deaths, compared to placebo [66/1,046] which included twelve deaths.
    - In EPIC-SR, there was a 57% relative risk reduction in hospitalizations or death through Day 28 in PAXLOVID-treated patients [3/361] with no deaths, compared to placebo [7/360] which included one death.
- Available safety data for PAXLOVID, which have been generally consistent in more than 3,500 PAXLOVID-treated participants across the EPIC clinical development program, including EPIC-HR, EPIC-SR, and EPIC-PEP[3] studies, as well as in reported post-authorization safety experience.
- Data from the EPIC-HR, EPIC-SR and EPIC-PEP studies which showed a consistent reduction in viral load with PAXLOVID, including across both the Delta and Omicron variants.
- Data which show that the frequency of return of detectable nasal viral RNA following PAXLOVID treatment was low and generally similar among PAXLOVID and placebo recipients.

PAXLOVID is currently approved or authorized for conditional or emergency use in more than 65 countries across the globe to treat COVID-19 patients who are at increased risk for progressing to severe illness. As of the end of May 2022, Pfizer had shipped more than 12 million treatment courses of PAXLOVID to nearly 40 countries around the world.

Please see Full Emergency Use Authorization (EUA) Prescribing Information available at www.fda.gov and www.PAXLOVID.com

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

PAXLOVID is a SARS-CoV-2 main protease (M^{pro}) inhibitor (also known as SARS-CoV-2 3CL protease inhibitor) therapy. It was developed to be administered orally so that it can be prescribed early after infection, potentially helping patients avoid severe illness (which can lead to hospitalization and death). Nirmatrelvir [PF-07321332], which originated in Pfizer laboratories, is designed to block the activity of the M^{pro}, 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 work by binding to the spike protein found on the surface of the SARS-CoV-2 virus. PAXLOVID, however, works intracellularly by binding to the highly conserved M^{pro} (3CL protease) of the SARS-CoV-2 virus to inhibit viral replication. Nirmatrelvir has shown consistent *in vitro* antiviral activity against the following variants: Alpha, Beta, Delta, Gamma, Lambda, Mu, and Omicron BA.1 and BA.2.

PAXLOVID is generally 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 carton 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 Access

Pfizer is committed to working toward equitable access to our oral COVID-19 treatment, PAXLOVID, for high-risk patients in need, aiming to deliver safe and effective oral treatment as soon as possible and at an affordable price. If authorized or approved, during the pandemic, Pfizer will offer its oral 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. To date, Pfizer has shipped more than 12 million treatment courses of PAXLOVID to nearly 40 countries around the world.

Pfizer has established a comprehensive strategy in close partnership with worldwide governments, international global health leaders, including WHO's Access to COVID-19 Tools Accelerator (ACT-A), and global manufacturers to optimize supply and access of PAXLOVID all around the world. This includes:

- ***Multilateral Supply Agreements*** : Signed agreement with **UNICEF** to supply up to 4 million treatment courses of PAXLOVID to low- and middle-income countries in 2022; Signed letter of intent with **Global Fund** for up to 6 million PAXLOVID treatment courses for supply to 130 Global-Fund eligible countries in 2022 and 2023, subject to the signing of a definitive agreement and regulatory approval or authorization.
- ***Expanding Access to Patent-Protected Medicines in Lower-Income Countries*** *:* Launched **An Accord for a Healthier World,** a first-of-its-kind initiative to enable sustained, equitable access to high-quality medicines and vaccines for 1.2 billion people living in lower-income countries. Pfizer has committed to provide its patent-protected medicines and vaccines available in the U.S. or European Union, including PAXLOVID, on a not-for-profit basis to 45 lower-income countries around the world and will collaborate with government and global health leaders to address barriers that limit access beyond supply, like diagnosis, education, infrastructure, storage and more.
- ***Accelerating Testing and Treatment*****:** Signed a letter of intent to join **COVID Global Accountability Platform (COVID GAP)**, a joint initiative of COVID Collaborative and Duke University, along with Open Society Foundations and the Clinton Health Access Initiative (CHAI). Subject to a definitive agreement, the company will provide treatment courses of PAXLOVID, as well as funding and expert resources, to support the consortium's efforts aimed at accelerating testing and improving access to treatment in under-resourced parts of the world.
- ***Treatment Donation:*** As part of its humanitarian response, Pfizer donated 200K treatment courses of PAXLOVID to **Ukraine**.
- ***Voluntary Licensing:*** Signed a voluntary license agreement with **Medicines Patent Pool (MPP)** to enable the development and distribution of generic versions of Pfizer's oral treatment to further expand long-term global supply and access. MPP has signed sublicense agreements with 38 manufacturers, who will supply the generic versions in 95 low- and lower-middle-income countries.

Risk Factors for Severe Illness Due to COVID-19

People with certain risk factors or medical conditions are more likely to become severely ill with COVID-19.[2] According to the U.S. Centers for Disease Control and Prevention, people more likely to get very sick with COVID-19 include those aged 65 and older and people with certain underlying conditions or risk factors such as cancer, chronic kidney, lung, or liver disease, cystic fibrosis, dementia or other neurological conditions, diabetes (type 1 or 2), disabilities, heart conditions, HIV infection, an immunocompromised condition or weakened immune system, mental health conditions, being overweight or obese, physical inactivity, pregnancy, sickle cell disease or thalassemia, smoking (current or former), recipients of a solid organ or blood stem cell transplant, stroke or cerebrovascular disease, substance use disorders, and tuberculosis.[2] Similarly, according to the World Health Organization, COVID-19 is often more severe in people aged 60 and older or with health conditions like lung or heart disease, diabetes, or conditions that affect their immune system.[?2]

About the 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 from 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 ($p<0.0001$). In the overall study population through Day 34, no deaths were reported in patients who received PAXLOVID as compared to 13 deaths in patients who received placebo.

Results from the final Clinical Study Report showed an 86% reduction in risk of COVID-19 related hospitalization or death from any cause through Day 28 in PAXLOVID-treated patients, relative to placebo. For the pre-specified endpoint of all-cause mortality at Week 24, no deaths were reported in patients who received PAXLOVID as compared to 15 deaths in patients who received placebo, representing a 100% relative risk reduction ($p<0.0001$).

In the EPIC-HR trial, in a secondary endpoint, SARS-CoV-2 viral load at baseline and Day 5 have been evaluated for 1,574 patients. After accounting for baseline viral load, geographic region, and serology status, PAXLOVID reduced viral load by approximately 10-fold relative to placebo when treatment was initiated within three days of symptom onset, indicating robust activity against SARS-CoV-2.

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) and EudraCT (2021-002895-38), were not yet available for this review.

U.S. FDA Emergency Use Authorization Statement

PAXLOVID has not been approved but has been authorized for emergency use by FDA under an EUA, for the 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 progression to severe COVID-19, including hospitalization or death.

The emergency use of PAXLOVID is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of the unapproved product PAXLOVID for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

LIMITATIONS OF AUTHORIZED USE

- PAXLOVID is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
- PAXLOVID is not authorized for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19
- PAXLOVID is not authorized for use for longer than 5 consecutive days

PAXLOVID may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which PAXLOVID belongs (i.e., anti-infectives).

PAXLOVID is not approved for any use, including for use for the treatment of COVID-19.

PAXLOVID is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of PAXLOVID under 564(b)(1) of the Food Drug and Cosmetic Act unless the authorization is terminated or revoked sooner.

IMPORTANT SAFETY INFORMATION

PAXLOVID is **contraindicated in patients with a history of clinically significant hypersensitivity reactions** (eg, toxic epidermal necrolysis [TEN] or Stevens-Johnson syndrome) to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.

Drugs listed in this section are a guide and not considered a comprehensive list of all drugs that may be contraindicated with PAXLOVID. The healthcare provider should consult other appropriate resources such as the prescribing information for the interacting drug for comprehensive information on dosing or monitoring with concomitant use of a strong CYP3A inhibitor such as ritonavir.

PAXLOVID is **contraindicated with drugs that are highly dependent on CYP3A** for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions:

- $Alpha_1$-adrenoreceptor antagonist: alfuzosin

- Analgesics: pethidine, propoxyphene
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- Antipsychotics: lurasidone, pimozide, clozapine
- Benign prostatic hyperplasia agents: silodosin
- Cardiovascular agents: eplerenone, ivabradine
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
- HMG-CoA reductase inhibitors: lovastatin, simvastatin
- Immunosuppressants: voclosporin
- Microsomal triglyceride transfer protein inhibitor: lomitapide
- Migraine medications: eletriptan, ubrogepant
- Mineralocorticoid receptor antagonists: finerenone
- Opioid antagonists: naloxegol
- PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension
- Sedative/hypnotics: triazolam, oral midazolam
- Serotonin receptor 1A agonist/serotonin receptor 2A antagonist: flibanserin
- Vasopressin receptor antagonists: tolvaptan

PAXLOVID is **contraindicated with drugs that are potent CYP3A inducers** where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. PAXLOVID cannot be started immediately after discontinuation of any of the following medications due to the delayed offset of the recently discontinued CYP3A inducer:

- Anticancer drugs: apalutamide
- Anticonvulsant: carbamazepine, primidone, phenytoin
- Cystic fibrosis transmembrane conductance regulator potentiators: lumacaftor/ivacaftor
- Herbal Products: St. John's Wort (*hypericum perforatum*)

There are limited clinical data available for PAXLOVID. **Serious and unexpected adverse events may occur** that have not been previously reported with PAXLOVID use.

Risk of Serious Adverse Reactions Due to Drug Interactions: Initiation of PAXLOVID, a CYP3A inhibitor, in patients receiving medications metabolized by CYP3A or initiation of medications metabolized by CYP3A in patients already receiving PAXLOVID, may increase plasma concentrations of medications metabolized by CYP3A. Initiation of medications that inhibit or induce CYP3A may increase or decrease concentrations of PAXLOVID, respectively. These interactions may lead to:

- Clinically significant adverse reactions, potentially leading to severe, life-threatening, or fatal events from greater exposures of concomitant medications
- Clinically significant adverse reactions from greater exposures of PAXLOVID
- Loss of therapeutic effect of PAXLOVID and possible development of viral resistance

Consult Table 1 of the Fact Sheet for Healthcare Providers for clinically significant drug interactions, including contraindicated drugs. Drugs listed in Table 1 are a guide and not considered a comprehensive list of all possible drugs that may interact with PAXLOVID. Consider the potential for drug interactions prior to and during PAXLOVID therapy; review concomitant medications during PAXLOVID therapy and monitor for the adverse reactions associated with the concomitant medications.

Hypersensitivity reactions have been reported with PAXLOVID including urticaria, angioedema, dyspnea, mild skin eruptions, and pruritus. Cases of anaphylaxis, TEN, and Stevens-Johnson syndrome have also been reported with components of PAXLOVID (refer to NORVIR labeling). If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue PAXLOVID and initiate appropriate medications and/or supportive care.

Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir. Therefore, caution should be exercised when administering PAXLOVID to patients with **pre-existing liver diseases, liver enzyme abnormalities, or hepatitis**.

Because nirmatrelvir is co-administered with ritonavir, there may be a **risk of HIV-1 developing resistance to HIV protease inhibitors** in individuals with uncontrolled or undiagnosed HIV-1 infection.

Adverse events in the PAXLOVID group (?1%) that occurred at a greater frequency (?5 subject difference) than in the placebo group were dysgeusia (6% and <1%, respectively), diarrhea (3% and 2%), hypertension (1% and <1%), and myalgia (1% and <1%). The proportions of subjects who discontinued treatment due to an adverse event were 2% in the PAXLOVID group and 4% in the placebo group.

The following adverse reactions have been identified during post-authorization use of PAXLOVID. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity reactions
Gastrointestinal Disorders: Abdominal pain, nausea
General Disorders and Administration Site Conditions: Malaise

Required Reporting for Serious Adverse Events and Medication Errors: The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events and medication errors potentially related to PAXLOVID within 7 calendar days from the healthcare provider's awareness of the event.

Submit adverse event and medication error reports to FDA MedWatch using one of the following methods:

- **Online:** https://www.fda.gov/medwatch/report.htm
- **Complete and submit a postage-paid** FDA Form 3500 **and returning by mail/fax**
- **Call** 1-800-FDA-1088 **to request a reporting form**

In addition, please provide a copy of all FDA MedWatch forms to: http://www.pfizersafetyreporting.com/ or by fax (1-866-635-8337) or phone (1-800-438-1985).

PAXLOVID is an inhibitor of CYP3A and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. Co-administration of PAXLOVID with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated. Co-administration with other CYP3A substrates may require a dose adjustment or additional monitoring.

Nirmatrelvir and ritonavir are CYP3A substrates; therefore, drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.

Pregnancy: There are no available human data on the use of nirmatrelvir during pregnancy to evaluate for a drug?associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published observational studies on ritonavir use in pregnant women have not identified an increase in the risk of major birth defects. Published studies with ritonavir are insufficient to identify a drug?associated risk of miscarriage. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy.

Lactation: There are no available data on the presence of nirmatrelvir in human or animal milk, the effects on the breastfed infant, or the effects on milk production. A transient decrease in body weight was observed in the nursing offspring of rats administered nirmatrelvir. Limited published data reports that ritonavir is present in human milk. There is no information on the effects of ritonavir on the breastfed infant or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PAXLOVID and any potential adverse effects on the breastfed infant from PAXLOVID or from the underlying maternal condition. Breastfeeding individuals with COVID?19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID?19.

Contraception: Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Advise patients using combined hormonal contraceptives to use an effective alternative contraceptive method or an additional barrier method of contraception.

Pediatrics: PAXLOVID is not authorized for use in pediatric patients younger than 12 years of age or weighing less than 40 kg. The safety and effectiveness of PAXLOVID have not been established in pediatric patients. The authorized adult dosing regimen is expected to result in comparable serum exposures of nirmatrelvir and ritonavir in patients 12 years of age and older and weighing at least 40 kg as observed in adults, and adults with similar body weight were included in the trial EPIC-HR.

Systemic exposure of nirmatrelvir increases in renally impaired patients with increase in the severity of renal impairment. No dosage adjustment is needed in patients with mild renal impairment. **In patients with moderate renal impairment (eGFR ?30 to <60 mL/min), reduce the dose of PAXLOVID** to 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days. Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID. Providers should counsel patients about renal dosing instructions. **PAXLOVID is not recommended in patients with severe renal impairment** (eGFR <30 mL/min based on CKD-EPI formula) until more data are available; the appropriate dosage for patients with severe renal impairment has not been determined.

No dosage adjustment of PAXLOVID is needed for patients with either mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. No pharmacokinetic or safety data are available regarding the use of nirmatrelvir or ritonavir in subjects with severe hepatic impairment (Child-Pugh Class C); therefore, **PAXLOVID is not recommended for use in patients with severe hepatic impairment**.

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 June 30, 2022. Pfizer assumes no obligation to update forward-looking statements contained in this statement 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 PAXLOVID (including qualitative assessments of available data, potential benefits, expectations for clinical trials, the anticipated timing of data readouts, regulatory submissions, regulatory approvals or authorizations, a new drug application submission in the U.S. for appropriate individuals at high risk of progression to severe illness and potential in high-risk COVID-19 patients, and efforts toward equitable access), 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; uncertainties regarding the commercial impact of the results of the EPIC-SR and EPIC-PEP trials; the ability of PAXLOVID to maintain efficacy against emerging virus variants; the risk that serious and unexpected adverse events may occur that have not been previously reported with PAXLOVID use; 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 applications or submissions for PAXLOVID that may be pending or filed (including the new drug application submission for PAXLOVID in the U.S. for appropriate individuals at high risk of progression to severe illness and 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 which may lead to reduced revenues or excess inventory; 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, 2021 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.

[1] Percentage of 12+ population derived from a) Analysis conducted flagging all diagnosed patients in claims data with diagnosed conditions that CDC considers to be "high-risk" except for "sedentary", smoking and obesity March – April 2022 b) RWE From July 2020-July 2021
[2] To learn more about who may be at high risk of progression to severe COVID-19, visit the Centers for Disease Control and Prevention or World Health Organization
[3] EPIC-PEP (**E**valuation of **P**rotease **I**nhibition for **C**OVID-19 in **P**ost-**E**xposure **P**rophylaxis)

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