TGA Approves Pfizer's Novel COVID-19 Oral Treatment in Australia

- *Therapeutic Goods Administration (TGA) approves PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) for supply to Australia.*
- *PAXLOVID is the first oral treatment of its kind; it includes nirmatrelvir, a 3CL (or main) protease inhibitor that was specifically designed to combat SARS-CoV-2.*
- *Pfizer Australia has entered an agreement with the Australian Government to supply 500,000 treatment courses over 2022.*

SYDNEY, AUSTRALIA, 20 January 2021 – Pfizer announced today that Australia's Therapeutic Goods Administration (TGA) has granted provisional approval for the supply and use in Australia of PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets. PAXLOVID has provisional approval for the treatment of coronavirus disease 2019 (COVID-19) in adults 18 years of age and older, who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.

PAXLOVID is the first oral antiviral of its kind; it includes nirmatrelvir, a 3CL protease (also known as Main protease or M^{pro}) inhibitor that was specifically developed in Pfizer's laboratories to combat SARS-CoV-2. Under this authorisation, PAXLOVID can be prescribed as an oral treatment to certain high-risk adults within the first 5 days of symptomatic infection, potentially helping patients avoid severe illness which can lead to hospitalisation or death.

"This milestone in Australia is an important moment in our continued fight against COVID-19, paving the way for use of PAXLOVID as cases continue to rise and we address the threat of a new variant of concern, Omicron," said Anne Harris, Pfizer Australia and New Zealand Managing Director. "This at-oral therapy, developed to reduce hospitalisations and save lives, has the potential to transform COVID-19 treatment and help lessen the devastating impact of the virus that has now taken over 5 million lives globally", Ms Harris said.

The TGA based its decision 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-hospitalised adults with confirmed COVID-19 who were at increased risk of progressing to severe illness. The data demonstrated an 89% reduction in risk of COVID-19-related hospitalisation or death from any cause in adults treated with PAXLOVID compared to placebo in those treated within three days of symptom onset, with no deaths in the treatment group. Similar results were seen in 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 efficacy with a similar safety profile. Additional Phase 2/3 clinical trials are ongoing in adults at standard risk of progressing to severe illness, and in those who have been exposed to the virus through household contacts.

In October 2021, Pfizer announced an agreement with the Australian Government to supply 500,000 treatment courses of PAXLOVID over 2022. With the oral treatment now approved for supply and use by the TGA, Pfizer will begin delivering the first treatment courses from Q1 2022.

About PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets)
PAXLOVID is a SARS-CoV-2 protease inhibitor antiviral therapy. It was developed to be administered orally so that it can be prescribed at the first sign of infection – potentially helping patients avoid severe illness (which can lead to hospitalisation and death) – subject to the clinical success of the rest of the EPIC development program. Nirmatrelvir [PF-07321332], which originated in Pfizer's laboratories, is designed to block the activity of the SARS-CoV-2-3CL (or main) 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.

Nirmatrelvir has shown consistent activity against the SARS-CoV-2 viral 3CL protease in all variants of concern to date and this efficacy has been confirmed in *in vitro* antiviral testing. Additional *in vitro* antiviral studies assessing expected similar activity against the Omicron variant are also currently underway.

PAXLOVID is authorised to 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 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 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. During the pandemic, Pfizer will offer its oral therapy, pending country approval, 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 to support the manufacturing and distribution of PAXLOVID, including exploring potential contract manufacturing options. It has entered into agreements with multiple 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 treatment to help expand access, pending country regulatory authorisation 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 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 randomised, double-blind study of non-hospitalised 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.

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 hospitalisation 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 (Evaluation of Protease Inhibition for COVID-19 in Post-Exposure Prophylaxis) 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 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 hospitalisation 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 hospitalised through Day 28 following randomisation

(5/697 hospitalised with no deaths), compared to 6.5% of patients who received placebo and were hospitalised or died (44/682 hospitalised with 9 subsequent deaths). The statistical significance of these results was high (p<0.0001). In a secondary endpoint, PAXLOVID reduced the risk of hospitalisation 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 hospitalised or died through Day 28 following randomisation (8/1039 hospitalised with no deaths), compared to 6.3% of patients who received placebo (66/1046 hospitalised 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 hospitalisation or death; 1.1% of patients who received PAXLOVID were hospitalised through Day 28 (1/94 hospitalised with no deaths), compared to 16.3% of patients who received placebo (16/98 hospitalised 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 log10 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 in the coming weeks.

About Pfizer Australia: Breakthroughs That Change Patients' Lives™
At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines. Our diversified global health care portfolio includes biologic and small molecule medicines and vaccines.

Consistent with our responsibility as one of the world's leading biopharmaceutical companies, we also collaborate with healthcare providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. For more information, please visit: www.pfizer.com.au

Disclosure Notice
The information contained in this release is as of 20 January 2022. 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, potential benefits, expectations for clinical trials, authorisation by the Therapeutic Goods Administration (TGA) for the supply and use in Australia of PAXLOVID in 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 authorisation, advanced purchase agreements and an agreement with MPP, efforts toward equitable access, the anticipated timing of data readouts, regulatory submissions, regulatory approvals or authorisations, 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 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; 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 commercialisation; 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 authorisation 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 authorisation 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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