



Report of the Medicines Patent Pool Expert Advisory Group on the Proposed Licence Agreement between MPP and PF PRISM HOLDINGS B.V. (Pfizer) on PF-07321332

Introduction

The Expert Advisory Group (EAG) of the Medicines Patent Pool (MPP) submits the following report to the Governance Board of the Medicines Patent Pool (Board) on the proposed License Agreement (the Agreement) between MPP and Pfizer for PF-07321332 ('332) for treatment of mild and moderate COVID-19.

This report reflects the outcome of consultations with the EAG on 11 November 2021 (chaired by Peter Beyer and joined by EAG members Giten Khwairakpam, Ellen 't Hoen, Jan Gheuens, Manuel Gonçalves, Jordan Jarvis, and Jennifer Cohn. Additional input via correspondence was received from EAG members Alexandra Calmy, Valérie Paris, Fatima Suleman, Martha Gyansa-Lutterodt, and François Venter from the Scientific Advisory Panel (SAP)).

The Terms of Reference for the EAG pose two questions that the EAG must address in assessing the results of final negotiations: (i) do the results sufficiently meet the requirements set out in the Statutes, and (ii) do the negotiation results offer sufficient added value over the *status quo*?

Background, Overview of the Proposed Agreement

On November 05, 2021, Pfizer issued a press release on the interim Phase 2/3 trial results for Pfizer's '332 (PAXLOVID™), an investigational oral antiviral medicine for the treatment of mild and moderate Covid-19. Apart from this announcement, Pfizer has not published any clinical trial results yet. Pfizer claims that the early trial results showed that '332 in combination with ritonavir reduces risk of hospitalization or death by 89% when administered to patients within the first three days of the onset of symptoms.

MPP entered into negotiations with Pfizer for '332 in October 2021. Pfizer did not engage in bilateral negotiations with generic companies and does not plan to issue bilateral license agreements outside the MPP license.

Key aspects of the proposed Agreement are as follows:

Scope of Grant of Licence. The proposed Agreement would grant MPP a nonexclusive licence to the Pfizer patents/patent applications and documentary know-how with the ability to grant nonexclusive, royalty-bearing sublicences to eligible API and finished product manufacturers anywhere in the world for purposes of supplying API or finished product into the Territory for use in the prevention and/or treatment of Covid-19.

Field of Use. The Field of Use in the proposed Agreement is the treatment and/or prevention of Covid-19.

Licensed Products. The proposed Agreement specifies that Licensed Products would be the co-packaged ‘332 + ritonavir which would include the option to develop a fixed-dose combination. Other combinations would require Pfizer’s prior written approval subject to separate terms and conditions.

Patent Status. As evidenced by the patent exhibit, Pfizer pursues patents in many different jurisdictions.

Royalties. Royalties are set at 5% of net sales for governments and other public purchasers (including NGOs) in the Territory, and at 10% of net sales to commercial entities in the Territory, except that there are no royalties for sales in LICs. Royalties are only payable where there is a patent/patent application in the country of manufacture or sale, or for the duration of regulatory exclusivity in place. The Agreement is royalty-free until the World Health Organization (WHO) declares the end of the Public Health Emergency of International Concern regarding COVID-19 (PHEIC).

Territory. The Territory of the proposed Agreement consists of 95 countries. The list includes all low-income countries, lower-middle income countries, upper-middle income countries in Sub-Saharan Africa, and upper-middle income countries that have graduated into such status within the last five years.

Other key public health-oriented terms and conditions. The proposed Agreement contains other important public health-oriented terms and conditions, such as the requirement that Pfizer provides regulatory waivers. Anti-diversion restrictions are limited to those countries outside the Territory where there is a Non-Territory Patent.

Compatibility with TRIPS flexibilities. The proposed Agreement contains language that provides that nothing in the Agreement shall be interpreted as preventing activities that would not infringe upon Pfizer’s patents and/or know-how and/or use Pfizer’s Confidential Information, and expressly makes clear that this applies where a country outside the Territory has issued a compulsory licence.

Manufacturing: The license agreement allows worldwide manufacturing for the territory (thus manufacturing could take place outside the territory for shipping to the territory).

Assessment of the Proposed Agreement in Light of MPP's Statutes

MPP's Statutes contain guiding principles against which the results of negotiations are assessed. The EAG finds that the proposed licence agreement meets the requirements in the Statutes, as summarised in the table below.

Relevant Considerations in the Statutes of the Medicines Patent Pool

Statutes	Terms in Proposed Licence
Negotiating terms and conditions of licence agreements with aim to maximize public health	Provisions ensuring that sales inside or outside the Territory are not a breach of the

benefits, taking into account the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property of the WHO (GSPOA); WTO Doha Declaration	Agreement if the sales do not infringe Pfizer intellectual property and/or misappropriate Pfizer know-how and/or use Pfizer Confidential Information. Explicit reference to compulsory licences as an example. No limitations to use TRIPS flexibilities.
Entering into licence agreements with patent holding entities, and sublicense agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and non-discriminatory basis	MPP to enter into non-exclusive licences with licensees chosen through MPP's Expression of Interest Portal. No parallel bilateral license agreements with generic companies.
As and when necessary, enforcing terms and conditions of licence agreements, with appropriate dispute resolution mechanisms	MPP takes on significant obligations to monitor and enforce terms of agreements; specifies stepwise approach including mediation at WIPO in case of dispute, and arbitration.
Requiring stringent quality criteria for licensed products	Requires all licensed products to be made in accordance with WHO PQ or Stringent Regulatory Authority standards, or through any provisional or emergency use authorizations available from WHO or an SRA.
Including anti-diversion and traceability mechanisms	Licensees required to implement a system of batch control as a means of tracing of product to monitor potential diversion.

Assessment of the Proposed Agreement in Light of the *Status Quo*

The EAG finds that the terms and conditions of the proposed Agreement represent a significant added value over the *status quo*. Subject to the final outcome and the assessment of the clinical trial data once published, the added value would consist of

- the potential medical significance of enabling affordable access to an effective oral antiviral treatment in 95 countries around the world, as well as
- the strategic and norm-setting significance of demonstrating MPP's contribution in meaningfully engaging in the fight against Covid-19.

From a medical standpoint, the EAG stresses the importance of a rigorous review of the clinical trial data as it is not possible to make an assessment of the product based on the press statements. In general, an effective all-oral antiviral treatment available to high-risk patients outside the hospital setting would form an important component of the Covid-19 response by reducing the risk of hospitalisation and death. As the EAG has stated previously, the need for access to affordable Covid-19 treatments is all the more evident in light of the ongoing disparities of access to vaccines against Covid-19.

In line with standard MPP practice, the EAG recognizes the value in moving forward with this proposed Agreement even before the drug has been granted emergency use approval to enable early access to



generic treatments if the clinical development is ultimately successful and the drug finally approved by regulatory authorities. The EAG notes the importance of generating and reviewing data regarding certain populations not included in the trials (*e.g.* pregnant or breastfeeding women, potentially people of African origin depending on the current study population). These are important clinical considerations to monitor closely.

As compared to MPP's recently announced licence with MSD for molnupiravir (MOL), there are many similarities but with some notable improvements in the terms and conditions. For example, where the Field of the MOL agreement was treatment only, the Field in the proposed agreement includes prevention as well, which could potentially prove significant if eventually '332 is found to prevent Covid-19 in addition to its therapeutic benefits. . To date, no data have been released on the efficacy of '332 for post-exposure prophylaxis and the results of an ongoing clinical trial will need to be assessed.

The proposed Agreement's provisions on royalties are likewise an improvement over the MOL agreement. While both agreements are royalty-free until WHO declares the end of the PHEIC, the proposed Agreement is additionally royalty-free for sales in LICs, and, critically, royalties elsewhere are only payable to the extent there is a Patent and/or existing regulatory exclusivity in the country of sale.

In terms of compatibility with TRIPS flexibilities, the non-infringement language is roughly the same as MOL, but with an express mention of compulsory licensing:

For the avoidance of doubt, nothing in this Agreement or the Sublicenses shall be construed to prevent Sublicensees from engaging in activities inside or outside the Territory where such activities would not (a) infringe the Patents and/or any other intellectual property rights of Pfizer; (b) use or misappropriate Licensed Know-How; and/or (c) use or require the use of any of Pfizer's Confidential Information. Pfizer expressly reserves all its rights under the Patents, except as expressly set forth in this Agreement and Sublicenses, and under any additional patents and/or patent applications Controlled (either as of the Effective Date or at any time during the term of this Agreement) by Pfizer or its Affiliates. For the avoidance of doubt, it shall not be deemed a breach by a Sublicensee to supply Compound, Product or Licensed Product outside the Territory into a country where the Government of such country has, to the extent permitted by Applicable Law, granted or required to be granted to Sublicensee a compulsory license under the Patents relating to such Compound, Product or Licensed Product allowing for the importation of such Compound, Product or Licensed Product into such country, provided that (a) such Sublicensee's supply of Compound, Product or Licensed Product into such country is solely within the scope and geographic range of such compulsory license and only for the duration that such compulsory license is in effect and (b) such Sublicensee does not use or misappropriate Licensed Know-How and/or misappropriate, use or require the use of any of Pfizer's Confidential Information.

As with the MOL Agreement, the absence of an express grant of right to commercialize outside the Territory is mitigated by the clear language in the first sentence that articulates that there is no breach for activities that do not infringe Pfizer Patents, use or misappropriate the Pfizer Know-How, or use or require Pfizer's Confidential Information. Regarding the Know-How and Confidential Information conditions, the Licensed Know-How excludes any know-how that may be specific to ritonavir, and there is no obligation for an MPP licensee to take the Pfizer data package that is available upon request. While the EAG interprets this non-infringement language as sufficient to cover situations where a country

outside the Territory has issued a compulsory licence, it views the express mention of such situations as covered under the provision as an improvement over the MOL licence simply for the added clarity.

The Territory in this proposed Agreement is roughly the same size in terms of population as the MOL agreement even where the number of countries in the Territory is slightly lower. However, the EAG notes that the proposed Agreement excludes several upper-middle income countries from the Territory of the licence, particularly in Latin America—one of the regions most impacted by the Covid-19 pandemic. The proposed Agreement excludes several UMICs that are hosting sites for the registrational clinical trial (Brazil, Colombia, Malaysia, and Thailand) as these countries do not fall into the criteria for country selection listed above. Pfizer’s announced plans regarding pricing and global access for ‘332 beyond the context of this proposed Agreement remain vague beyond a stated commitment to tiered pricing and investment in manufacturing and distribution. Thus, the EAG urges Pfizer to expand the territory and strongly recommends that MPP continue to work with Pfizer to further expand the Territory to ensure access and affordability in all low- and middle-income countries.

Lastly, the EAG is encouraged by the fact that Pfizer worked directly with MPP and did not opt to engage in any bilateral license agreements. The EAG encourages Pfizer to soon open discussions with MPP regarding Pfizer’s Covid-19 vaccine.

Recommendation

The EAG concludes that the proposed Agreement with Pfizer is consistent with MPP’s mandate as defined in its Statutes and represents a significant improvement over the *status quo* in terms of the public health-oriented nature of the licensing terms and conditions. Therefore, the EAG recommends that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed Agreement between Pfizer and MPP while urging Pfizer to work with the MPP on a further expansion of the territory.

Signed,



Peter Beyer
Chair, Expert Advisory Group
Date: 12 November 2021