Report of the Medicines Patent Pool Expert Advisory Group
on the Proposed Licence Agreement with Pharco Pharmaceuticals

Introduction

The HCV sub-group of 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 Licence Agreement (the Agreement) between MPP and Pharco Pharmaceuticals, Inc. (Pharco) for ravidasvir (RAV).

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 the Memorandum of Understanding (MoU) between the MPP and UNITAID, and (ii) do the negotiation results offer sufficient added value over the *status quo*?

Having reviewed the draft Agreement, and having received a briefing from the MPP on the proposed collaboration between the MPP and Pharco, the EAG answers both questions in the affirmative and recommends that the Board request the Executive Director of the MPP to finalise and execute the necessary documents with Pharco.

Background, Overview of the Proposed Agreement

Ravidasvir was developed by the biotechnology company Presidio Pharmaceuticals Inc.

One of Presidio's licensing partners is Pharco Pharmaceuticals, the largest manufacturer of pharmaceuticals in Egypt. Pharco focuses on research, formulation, manufacturing and commercialization of pharmaceutical products in the MENA region.

Pharco performed a Phase III clinical trial in Egypt specifically for HCV genotype 4 using ravidasvir in combination with sofosbuvir with or without ribavirin, which showed approximately 100% cure rate in non-cirrhotic patients and 94% cure rate in cirrhotic patients.

Presidio Pharmaceuticals entered into a non-exclusive licence agreement with the Drug for Neglected Diseases *Initiative* (DNDi) on March 21, 2016. As part of its initiative on HCV, DNDi will perform Phase II/III clinical studies in Malaysia and Thailand on the combination sofosbuvir+ravidasvir. Pharco and DNDi publicly announced that once approved, the combination will be available at a price of USD 294 or less per treatment.

According with the DNDi's strategy paper on HCV, Presidio will consider entering into negotiations with the MPP for the granting of additional non-exclusive licences in order to accelerate and broaden the manufacture and distribution of ravidasvir.

Certain key countries were not included in the DNDi-Presidio licence because Presidio had already given exclusive rights to certain countries to Pharco. Thus, the MPP sought to further expand on the number of people potentially able to benefit from the DNDi initiative by entering into negotiations with Pharco on the countries to which it had exclusive rights.

The proposed Agreement on RAV consists of a Licence Agreement between MPP and Pharco, that grants MPP the right to negotiate and grant sublicences under terms and conditions consistent with the Licence Agreement.

The MPP acquires a non-exclusive licence over the patents and technology with the ability to grant non-exclusive royalty bearing sublicences to eligible sublicensees.

Sublicensees will be selected by MPP between entities with willingness and capacity to manufacture the Licensed Compound and/or Licensed Products in a manner consistent with MPP's Quality Policy. Sublicensees could be based anywhere in the world.

Royalties will be payable by Sublicensees to Pharco over net sales of the Products in the Territory, at 4% for sales to countries classified as Low Income Countries (LIC) by the World Bank, 8% for sales to countries classified as Middle Income Countries (MIC) and 12% for sales to countries classified as High Income Countries (HIC).

Pharco will provide MPP with a copy of all documents and information necessary for the development and manufacture of the Compound and Product. MPP will share this technology with Sublicensees.

The territory of the licence is 19 countries, including high HCV prevalence countries such as Russia, Ukraine, Egypt and Iran. Taken together with the licensed territory in the DNDi-Presidio Agreement, and the ability of MPP licensees to supply in countries where there is no patent, the EAG understands that up to 139 low and middle-income countries (LMICs) accounting for over 85% of HCV the burden in LMICs can potentially have access to RAV.

The proposed Licence Agreement contains a number of other important public health-oriented terms and conditions. Pharco agrees to waive any data exclusivity rights it may have within the Territory, provide documentation to assist in local registration, allows licensee to combine RAV with other drugs to make, e.g., fixed-dose combinations, and sets timelines on licensees to ensure prompt development and registration of the licensed product.

Assessment of the Proposed Collaboration in Light of MPP's Statutes and MoU

MPP's Statutes and MoU with UNITAID contain guiding principles against which the results of negotiations are assessed. The HCV sub-group of the EAG finds that the proposed collaboration meets the requirements in both the Statutes and MoU with UNITAID, as summarised in the tables below.

(i) 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 benefits, taking into account the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property of the WHO (GSPOA); Doha Declaration	• No restrictions on ability of licensees to challenge patents • Agreements to waive data exclusivity rights; prevention of further data exclusivity rights • Allows for any activity outside the Territory where such activities would not infringe a patent granted and in force, including where a country outside the territory has issued a compulsory licence
Entering into licence agreements with patent holding entities, and sublicence agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and no-discriminatory basis	• MPP retains the right to issue non-exclusive sublicences to any qualified entity in the world. Pharco to receive a copy of the Sublicence Agreement once signed

(ii) Relevant Considerations in the MoU between the MPP and UNITAID

MoU	Terms in Proposed Licence
Ensure that license agreements specify an alternative dispute resolution mechanism;	• Mediation by senior executives, before appealing to Mediation in accordance with WIPO Mediation Rules
Define the terms and conditions under which the sub-licensees must make insurance arrangements to cover liability risks linked to products produced under the sub-licence form the MPP;	• Product liability insurance obligation specified
Safeguard against diversion and ensuring traceability of products produced under sub-licence from the MPP by specifying sub-licence terms and conditions in accordance with the guidelines set out in Art. 2(b)(ii) of the Word Trade Organization's Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health;	• MPP to include usual terms and conditions in the sublicence agreements, such as differential trade mark, trade dress and packaging, and obligation to include in packaging that the product has been manufactured under a licence by the MPP
Broad geographical scope	• 19 countries + In the DNDi/Presidio Agreement, the possibility of MPP obtaining a licence is envisaged
Access to medicines through TRIPS and other mechanisms The MPP negotiates provisions that enable licensees to sell outside the licensed territory under certain circumstances, such as, for example: (a) In the event of a compulsory licence being issued, (b) In the event that sales do not infringe on any granted patents or patent challenges are successful (e.g. licence on dolutegravir), (c) By allowing generic manufacturers to terminate licences for which they no longer need a licence, thereby allowing them to sell in additional countries (e.g. licence on tenofovir disoproxil fumarate) MPP agreements also provide licensees the freedom to challenge the validity of the licensed patents	In the Whereas: "The intent of this Agreement is to provide access to patents and not to create any non-patent-related barriers where Patents do not exist" • No breach of the Agreement if sales made outside the Territory where there are no infringement of a patent granted and in force • No breach of the Agreement in case of sales to a country outside the Territory that has issued a compulsory licence • No restrictions on challenging patents • Termination of licence on country-by-country basis, until the expiration of the last to expire patent • Waiver of data exclusivity; prevention of further data exclusivity rights

Prompt availability of quality, low cost generic medicines (a) Ensure the speedy registration of licensed products through a waiver of the licensor's data exclusivity rights (where applicable) (b) Generic company products must meet internationally-recognised quality standards (c) MPP's generic partners must adhere to strict timelines for development and regulatory approval of products or face licence termination	• Waiver of data exclusivity; prevention of further data exclusivity rights • Quality provisions according to MPP's Quality Policy, which requires approval by WHO Prequalification, SRA or WHO Expert Review Panel • Timeline of 42 months to commence regulatory filings in the Territory, from availability of Phase-III data on the Licensed Products
Transparency of patent and licensing information (a) All MPP licences contain provisions to ensure that the MPP may publish the licences in full on the MPP website (b) Patent holders provide patent disclosure of relevant patents within (and sometimes outside) the licensed territory	• The Agreement will be published in MPP's web page, as well as the sublicence agreements signed by the MPP with generic manufacturers • Disclosure of Patents and Non-Territory Patents in the Exhibits of the Agreement
Promote robust generic competition (a) Licences are non-exclusive, pro-competitive and encourage the participation of a broad range of generic manufacturers — in most cases from anywhere in the world — in order to ensure sustained and effective competition (b) Potential generic manufacturers must demonstrate their ability to develop and manufacture quality-assured, affordable products promptly	• Sublicensees to be selected between entities with demonstrated willingness and capacity to manufacture Licensed Compound and/or Licensed Product in a manner consistent with MPP's Quality Policy. Sublicensees to be located anywhere in the world. • MPP's Quality Policy to date requires Sublicensees to seek regulatory approval by WHO Prequalification, SRA or WHO Expert Review Panel • Pharco will provide technology transfer necessary for the development and manufacture of the Compound and Product, to Sublicensees
Development of adapted medicines and FDCs Generic manufacturers can combine different medicines to develop appropriate FDCs	• Sublicensees to be free to combine the Compound with any other/others APIs.

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

The HCV sub-group of the EAG finds that the terms and conditions of the proposed Agreement represent a significant advance over the *status quo*, both in terms of geographic scope and in terms of promoting transparent, public health-oriented licensing terms and conditions.

Taken together with the DNDi-Presidio Agreement and the flexibilities included in the MPP agreement that allow for licensees to supply in countries where there is no patent, the effective geographical coverage of this collaboration is far broader than any HCV voluntary licence to date. In addition to the broad geographical scope, this proposed Agreement further strengthens the key public health-oriented terms and conditions of MPP-negotiated licences that are increasingly becoming the norm in voluntary licensing.

The HCV sub-group of the EAG also notes that the proposed Agreement will be made public on MPP's website, contributing to the goal of injecting greater transparency in the field of voluntary licensing, a core mission of the MPP. In this vein, the HCV sub-group of the EAG further encourages DNDi and Presidio to also make accessible to the public the text of their Licence Agreement, and expresses its expectation that this Agreement will contribute towards encouraging patent holders of other key pan-genotypic HCV drugs, such as Gilead and BMS, to expand number of people in LMICs who may benefit from their own voluntary licences.

Recommendation

The HCV sub-group of the EAG concludes that the proposed Agreement with Pharco is consistent with MPP's mandate as defined in its Statutes and MoU with UNITAID, and represents a significant improvement over the *status quo* in terms of the public health-oriented nature of the licensing terms and conditions.

The HCV sub-group of the EAG recommends that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed Agreement between Pharco and MPP.

Signed,

Maximiliano Santa Cruz
Chair, Expert Advisory Group

Note: Isabelle Andrieux-Meyer took part in this review, but disclosed that she has overlapping but not conflicting interests in her position at DND*i* working on its sofosbuvir-ravidasvir development project.