

Report of the Medicines Patent Pool Expert Advisory Group on the Proposed Collaboration with Roche

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 on the proposed collaboration between MPP and F. Hoffman-La Roche (Roche).

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

Having reviewed the draft agreement, and upon receiving a briefing from the MPP on the proposed collaboration between the MPP and Roche,¹ 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 Roche.

Background, Overview of the Proposed Collaboration

The EAG was informed that MPP has been in negotiations with Roche since 2011 and that Roche currently has the following drugs of potential relevance to MPP's mandate to facilitate access to HIV treatment: saquinavir (SQV), enfuvirtide (ENF), and valganciclovir. During previous consultations, the MPP informed the EAG that the focus of the negotiations had shifted to valganciclovir, as neither SQV nor ENF are of medical priority in developing countries at this time in light of WHO guidelines.²

The MPP also informed that valganciclovir, while not an antiretroviral drug, is an important treatment for a common HIV-related opportunistic infection, cytomegalovirus (CMV). CMV is a virus that attacks immuno-compromised individuals, for example organ transplant patients who have been placed on immuno-suppressants and people living with HIV (PLHIV) with low levels of CD4. The retina is particularly susceptible to CMV infection in immuno-compromised individuals, and CMV-retinitis (CMV-r), if left untreated, can cause irreversible blindness. With the widespread availability of early antiretroviral therapy (ART) in high-income countries, HIV-related CMV-r has been largely eliminated there, but the problem persists in many developing

¹ The briefing took place in a conference call held on 3 June 2013 in which the following members of the EAG participated: Labeeb Abboud, Jonathan Berger, Alexandra Calmy, Shing Chang, Achal Prabhala, Maximiliano Santa Cruz and Wim Vandevelde. Due to scheduling conflicts, Gracia Violeta Ross, Carlos Correa, Lita Nelsen, and Eun-Joo Min could not attend the call and were briefed separately. Nelson Otwoma was unable to participate in the briefings.

² In the MPP's *ARV Priority List for the Medicines Patent Pool*, SQV was categorised as a level 3 priority, meaning that it is currently of low clinical priority, and ENF was not considered to be a priority for the MPP.

countries. The MPP informed the EAG that based on available data, CMV-r infections may affect as many as 14 percent of people living with HIV in Asia, 12 percent in Latin America, and 2.2 percent in Africa, according to a systematic review commissioned by the MPP in connection with the proposed collaboration (the review has been submitted for publication and is currently under peer review).

The alternative treatment to valganciclovir for treating CMV-r is ganciclovir. Unlike valganciclovir,³ ganciclovir cannot be administered orally, and the usual course of treatment for CMV-r with ganciclovir is a series of injections directly into the affected eye(s). Due in part to the current high costs of valganciclovir⁴ and the difficulty of administering intra-ocular injections of ganciclovir, the MPP informed the EAG that many HIV treatment programmes do not currently screen for CMV-r. Due to this lack of screening and treatment, there is currently very low demand for valganciclovir in treating HIV-related CMV-r. And due to this lack of demand, there is currently no low-cost generic available that meets stringent regulatory authority quality standards, and there appears to be little incentive for generic companies to enter the market with to serve the HIV-related CMV-r market in developing countries.

In an effort to break this "vicious cycle" of high prices leading to lack of demand, the MPP and Roche's proposed agreement envisions a two-phased approach: (1) to make Roche's valganciclovir available to a large number of developing countries at a steeply discounted price, then after greater market demand has been created for valganciclovir, (2) engage in licensing and technology transfer activities to ensure that affordable, quality-assured generics enter the market to address the need for HIV-related CMV-r treatment in developing countries. The salient features of the proposed agreement are as follows:

- **Price:** CHF 250/pack, with a minimum order of 40 packs (CHF 10,000).
- **Indication:** HIV-related CMV infection ('the Indication')
- **Eligible organisations:** non-profit HIV treatment organisations, including national HIV treatment programmes, those funded by the GFATM, PEPFAR, UNITAID, and organisations such as MSF, as well as other similar organisations proposed by the MPP and accepted by Roche (such acceptance not to be unreasonably withheld by Roche)
- **Territory:** 138 countries, as listed in Exhibit C of the proposed agreement, with possibility to expand territory if MPP can demonstrate unmet treatment needs in the Indication in low- and middle-income countries outside the Territory
- **Technology transfer and licensing:** after 2 years, Roche and the MPP will enter into negotiations for licensing and technology transfer to facilitate affordable, quality-assured generic versions of valganciclovir to enter the market both inside and outside the Territory

³ Valganciclovir is a pro-drug of ganciclovir that allows the body to absorb ganciclovir when taken orally.

⁴ Roche currently markets valganciclovir primarily to cater to the more lucrative organ-transplant market.

- **Term:** 5 years, renewable upon mutual consent; Roche may terminate sooner on a country-by-country basis *only if* there is a quality-assured generic version available at similar or lower cost
- **Offer for saquinavir:** Roche agrees to enter into negotiations for SQV in the event that the MPP identifies significant medical need for SQV

In addition to the initial discounted price, the MPP informed the EAG that it is engaged and will engage in a number of other activities in an effort to scale-up the screening, diagnosis and treatment of HIV-related CMV-r in developing countries, in order to test the hypothesis of whether increasing screening will contribute towards establishing a greater need for treatment. Such activities include commissioning a systematic review of the literature to demonstrate a significant unmet need for CMV-r treatment, advocating with the World Health Organization department to issue technical guidance for treatment of CMV-r and to include valganciclovir in the expression of interest for WHO prequalification, and engaging with organisations such as Médecins Sans Frontières and national treatment programmes to promote uptake of valganciclovir. The aim of these efforts would be to stimulate sufficient demand for valganciclovir so that the entry of generic competition is facilitated in developing countries.

The EAG notes that the proposed collaboration with Roche is not a licence agreement as such, and so represents a somewhat unconventional approach as compared to the MPP's usual licensing activities. The MPP explained to the EAG that the discounted price should be seen as a measure to bridge the gap until the market conditions are such that promoting robust generic competition through licensing and technology transfer becomes appropriate. The MPP noted that the price offer in no way creates an obligation on the part of organisations to purchase *exclusively* from Roche, and that they are free to procure generic versions should they become available.

The EAG further notes that while a large number of countries are included, not all middle-income countries are eligible to receive the discounted price. The MPP informed the EAG that certain of Roche's country-level affiliates in the excluded countries were unable or unwilling to move forward with inclusion at this time. Nevertheless, the proposed agreement does however contemplate an expansion of the territory if the MPP can demonstrate "unmet treatment needs" in the excluded countries. The EAG expressed concern regarding the exclusion of certain countries, particularly in Eastern Europe, and the potential difficulty in identifying an "unmet treatment need" in those countries if no affordable treatment was made available. The EAG therefore strongly recommends that the MPP actively engage with excluded countries to determine whether there are any unmet treatment needs in these countries, and to continue working with Roche in defining reasonable criteria by which a demonstration of "unmet treatment needs" has been made.

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

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

Relevant Considerations in the Statutes of the Medicines Patent Pool

| Statutes | EAG Evaluation |
|--|--|
| <p>The Foundation may pursue all such lawful activities as may be appropriate to attain its purpose.</p> <p>The Foundation shall operate a Patent Pool through which intellectual property is made available, in order to reduce prices, improve access and facilitate the development and production of quality, safe and efficacious health products for use in low- and middle-income countries, considering the importance of technology transfer mechanisms, capacity building and local manufacturing in developing countries.</p> <p>In this context, the Foundation may, <i>inter alia</i>, pursue the following activities:</p> <ul style="list-style-type: none"> Responding to opportunities that may arise to maximize the uptake and health benefits of the Patent Pool. | <ul style="list-style-type: none"> Although the proposed collaboration with Roche is not a licence agreement, the MPP responded to an opportunity that arose to address a market failure in the availability of an important treatment for HIV-related CMV-r that should result in greater access to more affordable quality-assured medicines and help create the market conditions for robust generic competition There is agreement by MPP and Roche to seek licensing and technology transfer opportunities in order to promote generic entry There is agreement by Roche to enter into negotiations on SQV should a significant medical need for SQV arise in developing countries |

Relevant Considerations in the MoU between the Pool and UNITAID

| MoU | EAG Evaluation |
|--|---|
| <p>Engage potential licensors and sub-licensees of the Patent Pool and encourage them to collaborate with the Patent Pool and to develop and produce appropriate products taking into account <i>inter alia</i> the priority health products identified by UNITAID based on WHO recommendations.</p> | <ul style="list-style-type: none"> Future commitment to engage in licensing activities for valganciclovir and SQV (if necessary) |
| <p>Facilitate activities promoting transfer of technology, capacity building and local manufacturing of medicines in developing countries, consistent with the Purpose of the</p> | <ul style="list-style-type: none"> Future commitment to engage in technology transfer activities both within and outside the Territory |

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| Foundation, and in consultation with other international partners; | |
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Assessment of the Proposed Collaboration in Light of the *Status Quo*

The EAG finds that the proposed collaboration with Roche represents a significant improvement over the *status quo*. The proposed agreement will make available valganciclovir at a steeply discounted price, to a larger number of entities, and to a larger number of countries than is the case today: the lowest price at which Roche currently offers valganciclovir is CHF500/pack to just one entity, MSF. The EAG was informed by the MPP that retail prices for Roche's valganciclovir in some developing countries is up to ten times that of the price offered in the proposed agreement. Given the current high prices for valganciclovir and the absence of a readily available quality-assured generic alternative, the EAG is of the opinion that the discounted price may be an effective strategy to immediately improve access, while also laying the groundwork for potential generic entry, particularly with the prospect of the future commitment of licensing and technology transfer.

Finally, the EAG notes that the proposed agreement will be made public on MPP's website, contributing to the goal of injecting greater transparency in this field, a core mission of MPP.

Recommendation

The EAG concludes that the proposed collaboration with Roche is consistent with the MPP's mandate as defined in the Pool's Statutes and MoU with UNITAID, and represents a significant improvement over the *status quo*. Therefore, the EAG recommends that the Medicines Patent Pool Governance Board request the Executive Director to sign the proposed agreement between the MPP and Roche. The EAG also recommends that the MPP, following the Agreement, work actively with a variety of stakeholders including UNITAID, WHO and MSF towards facilitating the entry of quality-assured generics into the market, and to ensure that any unmet treatment needs are identified and addressed.

Signed,



Maximiliano Santa Cruz
Chair, Expert Advisory Group