



Report of the Medicines Patent Pool Expert Advisory Group on the Proposed Licence Agreement with AbbVie, Inc.

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 Licence Agreement (the Agreement) between MPP and AbbVie, Inc. (AbbVie) for lopinavir (LPV) and ritonavir (RTV or r) individually or in combination, for paediatric use.

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

Background, Overview of the Proposed Agreement

MPP formally entered into negotiations with AbbVie in the fourth quarter of 2013 for paediatric formulations of LPV and RTV. LPV boosted with RTV (LPV/r) is recommended by WHO as a component of second-line treatment regimens for adults and children, and as a component of the preferred first-line treatment regimen for children under three years. Additionally, RTV is recommended by WHO as a booster for other protease inhibitors, atazanavir and darunavir.

Although LPV/r is a key component of paediatric treatment, the currently available formulations suffer from a number of shortcomings, particularly for children under 3 years of age that have difficulty in swallowing tablets. The currently available oral solution suffers from unpalatability, a high alcohol content, and the need for refrigeration – something not dependably available in resource limited settings. There is a need to develop suitably taste-masked, heat-stable and easily administered formulations of LPV/r, preferably in combination with lamivudine (3TC) and either abacavir (ABC) or zidovudine (AZT), in line with WHO recommendations.

The proposed Agreement between MPP and AbbVie seeks to facilitate the development of such adapted paediatric formulations, and to ensure wide availability in the event that they are developed. The proposed Agreement consists of a main Agreement between MPP and AbbVie that grants MPP the right to sublicense in the form of the Sublicense Agreement attached as a schedule to the Agreement. The Sublicense Agreement is a bilateral and royalty free agreement



to be signed between MPP and the potential Sublicensee, and allows for the manufacture and sale of both active pharmaceutical ingredients (API) and finished products worldwide for use within the Territory, defined as 102 countries, covering, according to MPP's estimates, 94.3% children living with HIV (CLHIV) in developing countries. Taking into account the countries outside the Territory where there are no AbbVie patents in force in which MPP licensees are permitted under the Agreement to sell, the effective coverage will be 130 countries, accounting for 98.9% CLHIV, according to the MPP's estimates.

During the EAG briefing, one EAG member sought clarification as to whether RTV as a paediatric stand-alone product could be manufactured under the licence. The MPP staff agreed that there was some ambiguity as to whether such a product would be covered under the Agreement, and agreed to take this issue to AbbVie to seek clarification. The EAG is pleased to learn that after further discussion with AbbVie, the parties have agreed to amend the definition of Licensed Products to make clear that stand-alone paediatric non-tablet formulations of RTV are permitted under the licence. The EAG views this as an important clarification, particularly as there may be a need to "super-boost" LPV with RTV in cases of TB co-infection.

Under the proposed Agreement, MPP has the right to enter into Sublicence Agreements with any entity, worldwide, to be identified by MPP with willingness and capacity to manufacture the Products following WHO pre-qualification standards or the standards of any Stringent Regulatory Authority, and in compliance with anti-bribery and anti-corruption practices. AbbVie will have a 30 days term to approve the suggested Sublicensee. Consent by AbbVie shall be understood as granted unless otherwise is notified to MPP in such 30 days term.

With respect to any new LPV/r formulation developed by an MPP licensee, AbbVie is granted the right of first refusal for either (i) a sole right to purchase such New Formulation for sale in the US, EU or (ii) a sole licence to any patents and know-how for the US and EU, in exchange for a 4% royalty payable from AbbVie to the MPP licensee. AbbVie will also have the option to either (i) purchase such New Formulation or (ii) a non-exclusive royalty-free license to any patents and know-how relating to the New Formulation for use outside the US, EU and outside the Territory. With respect to any new LPV/r formulations containing other active compounds (e.g., ABC/3TC; AZT/3TC), AbbVie is granted a right of first negotiation for the two options described above.

The proposed Licence Agreement contains a number important public health-oriented terms and conditions. In the preamble it is expressly mentioned that the Agreement aims to provide access to AbbVie Patents and not to create any non-patent-related barriers where AbbVie Patents do not exist. Towards this end, the Agreement specifies that nothing in the Agreement would prohibit MPP licensees from engaging in any activities that would not infringe an AbbVie Patent granted and in force, including where a country has issued a compulsory licence. In the EAG's view, this broad language would allow for sales of adult formulations both within and without the Territory where there are no AbbVie patents; sales of both adult and paediatric



formulations anywhere in the world where there are patent applications pending or during the pendency of an appeal; sales of both adult and paediatric formulations where the MPP licensee has developed a non-infringing version of an AbbVie product; and sales of both adult and paediatric formulations anywhere in the world where a compulsory licence has been issued.

Additionally, as in all previous MPP licences, AbbVie has agreed to waive any data exclusivity rights it may have within the Territory, and obligates MPP sublicensees from seeking such exclusivity to the extent that it may be available.

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 EAG finds that the proposed Agreement 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	Terms in Proposed Licence
<p>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</p>	<ul style="list-style-type: none"> • Preamble makes clear that Agreement is solely to provide access to IP where needed; not to create any contractual barriers to access. • No restrictions on ability of Sublicensees to challenge patents. • Agreements to waive data exclusivity rights; prevention of further data exclusivity rights. • Allows for sale outside the Territory where compulsory licence is issued. • Allows for sale outside the Territory where there are no patents in force.
<p>Entering into licence agreements with patent holding entities, and sublicense agreements with generic manufacturers and other appropriate sublicensees on a non-exclusive and no-discriminatory basis</p>	<ul style="list-style-type: none"> • MPP retains the right to issue non-exclusive sublicences to any qualified entity anywhere in the world. AbbVie to provide express consent in 30 days from notification. The lack of express notification will imply acceptance.

Relevant Considerations in the MoU between the Pool and UNITAID

MoU	Terms in Proposed Licence
Use all reasonable efforts to define standard terms and conditions of licence agreements	<ul style="list-style-type: none"> • Terms and conditions of Sublicence standardized across all sublicences via the form Sublicence Agreements • Increasingly, with each new licence the MPP negotiates, certain key terms are beginning to be standardized into all MPP licences, such as ability to supply outside the Territory where such activities would not infringe a patent; waiver of data exclusivity; stringent quality requirements, etc.
Define the terms and conditions of the licences and sublicences, respecting the differing patentability criteria across jurisdictions	<ul style="list-style-type: none"> • No breach of the Agreement if sales made outside the Territory where there are no infringement of AbbVie Patents granted and in force • No restrictions on challenging licensed patents
Ensure contracts with sublicensees specify that products must obtain approval from a stringent drug regulatory authority or WHO prequalification or temporary arrangements under WHO Expert Review Panel	<ul style="list-style-type: none"> • Quality provisions require approval by WHO Prequalification or from any SRA. Where such approvals are not yet available Licensee will obtain temporary approval through WHO Expert Review Panel
Ensure that licence agreements specify an alternative dispute resolution mechanism	<ul style="list-style-type: none"> • Binding arbitration specified in MPP-AbbVie licence; WIPO mediation in sublicense
Define the terms and conditions under which the sublicensees must make insurance arrangements to cover liability risks linked to products produced under sublicense from MPP	<ul style="list-style-type: none"> • Product liability insurance obligation specified
Safeguard against the diversion and ensuring the traceability of products...by specifying terms and conditions in accordance with WTO [30 Aug Decision] guidelines	<ul style="list-style-type: none"> • Obligation to bear mark and packaging distinctive from AbbVie • Product labeling will state that it has been manufactured under a licence from the MPP

<p>Facilitate activities promoting transfer of technology, capacity building and local manufacturing of medicines in developing countries, consistent with the Purpose of the Foundation, and in consultation with other international partners</p>	<ul style="list-style-type: none"> • Technical transfer package provided to all sublicensees • Sublicensees can be based anywhere in the world
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Assessment of the Proposed Collaboration in Light of the *Status Quo*

The EAG finds that the proposed Agreement with AbbVie represents a significant improvement over the *status quo*; both in terms of geographic scope and in terms of promoting transparent, public health-oriented licensing terms and conditions.

As mentioned, the licensed products have high public health importance, and better-adapted paediatric formulations of LPV/r and other combinations containing these products are needed in resource-limited settings. The development of appropriate LPV/r formulations for children under 3 years of age has been identified by the international community as a priority, and has been targeted by the recently launched Paediatric HIV Treatment Initiative as a target product.

The geographic scope of the proposed Agreement covers 102 countries, with a nominal coverage of 94.3% CLHIV, and an effective coverage of 130 countries representing 98.9% CLHIV. The EAG finds this to be a significant advance over the *status quo*, particularly in light of the fact that AbbVie has never before engaged in any type of access-oriented voluntary licensing for its HIV products.

In addition to the broad geographical scope, the EAG feels that this Agreement further strengthens the key public-health oriented terms and conditions of MPP-negotiated licences that are increasingly becoming the norm in the field of voluntary licensing in HIV products.

The EAG also notes that the proposed licence will be made public on MPP's website, contributing to the goal of injecting greater transparency in the field of HIV licensing, a core mission of MPP.

Recommendation

The EAG concludes that the proposed Agreement with AbbVie is consistent with MPP's mandate as defined in its Statutes and MoU with UNITAID, and represents a significant improvement over the *status quo*, both in terms of geographical scope and 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 MPP and AbbVie.

Signed,

A handwritten signature in black ink, appearing to read "Maximiliano Santa Cruz", written over a horizontal line.

Maximiliano Santa Cruz
Chair, Expert Advisory Group