Developing new medicines is a lengthy, high-risk and costly process involving numerous partners. However, for diseases, such as malaria, that mainly affect the world’s poorest populations, drug development projects are unlikely to have a positive, risk-adjusted, net present value (NPV) — the standard criterion for whether a project is financially worthwhile to pursue — if full development costs are included and the final product is priced at a level that allows access for those in need.

One strategy that has been successfully used to address this ‘market failure’ for malaria drugs (as well as those for neglected tropical diseases) is to share the development costs and risk associated with promising projects in a product development partnership (PDP) model that engages key partners such as academic institutions, the pharmaceutical industry, disease foundations and governments. For malaria, a not-for-profit organization, Medicines for Malaria Venture (MMV), contributes syndicated funding from donor governments and foundations, as well as expertise and portfolio management, to support partners to develop new antimalaria medicines.

The need for responsible management of intellectual property (IP) is a key factor in our partnership model. Although entirely open-source projects have some appeal, the lack of ownership means that no partner is clearly tasked with the responsibility of driving them forwards. Our strategy is to keep all the IP, both patents and know-how, clearly together in one place. We thus ensure clear ownership, and with clear ownership we ensure clear responsibility to provide equitable access for patients and affordable pricing.

A diversity of partners
MMV’s partnerships come in various flavours. We have partnerships with major companies that have end-to-end expertise in drug R&D, such as GlaxoSmithKline, Novartis and Sanofi, but for many of our projects, the partnerships require a more complicated structure. The majority of the skills needed to find new molecular targets are in the academic sector, and most of the skills needed to test molecules clinically are in the health-care sector. However, the expertise and knowledge on how to progress from a target to a clinical candidate is, with a handful of exceptions, in the pharmaceutical industry. About half of MMV’s development candidates come from academic collaboration networks. Once these networks have produced candidates with good activity in cells, these candidates need to be tested in humans, which can involve an array of partners.

Infectious diseases such as malaria have a further complication — the need for combinations of new active ingredients to protect against resistance. Advancing the best possible combinations often requires collaboration between at least two groups of scientists and their supporters, and clarity in understanding what is being brought to the table by whom is a critical success factor.

Our portfolio also includes collaborations with companies that have a strong role in generic medicines, such as Shin Poong Pharmaceuticals (Korea), Guilin Pharmaceutical (China) and Cipla (India). These companies are experts in surviving in market places in which gross margins are vanishingly small. For some partnerships, the active ingredient is no longer protected by patents. However, a degree of IP protection still applies: the companies have know-how that was developed in collaboration with us, including an understanding of registration, which enables us to establish provisions that ensure equitable access.

Managing IP to ensure access to medicines
Projects only move forwards if someone takes responsibility for them: this transfers the responsibility for solving market failure from the greater scientific community and makes it a personal responsibility. By linking the IP with this responsibility, we create a clear line of sight. The discovery, development and delivery of new medicines for neglected populations is a relay race: the project...
is passed on at different stages in the process. To ensure success, it is important to have a well-defined ‘bundle’ of knowledge that can be passed between partners. Much of the success of MMV’s discovery pipeline has come through open innovation: the ability to share ideas in a protected environment, or ‘walled garden’ model. Once a promising antimalarial candidate is selected, we need to have clarity, freedom to operate and protection of the asset, as it may have to be passed from one partner to the next. Patents offer a well-defined structure that clarifies ownership and rights to the molecule.

**IP ownership as a foundation for partnership**

It may seem counter-intuitive that a not-for-profit foundation would invest in clearly defined IP ownership to develop a medicine for a disease with market failure. However, later-stage clinical development, manufacturing and the distribution of medicines require pharmaceutical expertise, for which IP ownership must be clearly defined at the start of the partnership. In our model, potential partner companies review the initial animal data as part of a bidding process, in which freedom to operate and control the project is a key motivating factor. Each applicant can then submit a proposal outlining what they can bring to a project, and this forms the basis of a contractual negotiation. Within such a contract, MMV requires clear provisions for equitable access, and also sets pricing expectations. For MMV, these partner investments substantially reduce the amount of government and foundation money that needs to be invested. The partner companies need to see clarity of IP rights, and are reassured by clearly defined IP protection.

Two recent examples underline this process. DDD107498, a first-in-class plasmodial EF2 inhibitor, was discovered by a collaboration led by the Drug Discovery Unit at the University of Dundee, UK, who characterized it as a preclinical candidate. Through the subsequent competitive bidding process, Merck KGaA was selected; the first human studies are planned for 2017. AZ13721412 (MMV253) is a first-in-class ATPase inhibitor originally identified by the AstraZeneca research group in Bangalore, India. When AstraZeneca were unable to progress the project, then contractually it returned to MMV. After an open bidding process, a contract was negotiated with the Indian company Zydus Cadila, which is completing the preclinical programme, thus retaining the specific Indian heritage of this molecule.

Along with the desire to have clarity about what they are investing in today, our partners need clarity on how their investment will develop in the future. Although these malaria projects currently have a negative or neutral NPV, some of our partners want clear ownership should this change. Other applications for the molecule may be found: we continually monitor whether any of our molecules would have an application in a commercially attractive market or in animal health applications. Our pharmaceutical partners need to have clarity on the ownership of data in such cases. Another potential upside is provided by the introduction of transferable priority review vouchers (PRVs) in the United States, which are awarded by the FDA to companies that gain regulatory approval for a drug for defined neglected diseases and have been traded for up to US$350 million. It is difficult to predict what value they would have a decade ahead, or even if new incentives will be developed, but clear IP ownership underlines that any upside is shared proportionately with those who invested time, expertise and money in the antimalarial project, with little or no return.

**Responsibility of the IP holder**

Our work on collaborations in an area of market failure has enabled us to develop an IP strategy based on responsibility, rather than simply on rights. The owner of the rights to a molecule has a contractual responsibility to either develop or return an asset: MMV has the responsibility to find new partners in the latter case. When MMV transfers the IP rights to a commercial partner, the partner commits to ensuring that the final product is made available, according to quality specifications outlined under the product’s stringent regulatory approval, at an affordable price in malaria-endemic countries (around $1—2 for a course of treatment). Failure to deliver on these commitments would mean a revocation of the rights granted by MMV to the commercial partner. Under a conventional understanding of IP ownership, especially with a single entity as holder, the drug development race can stop for any reason — for example, a change of focus for the company, a merger or acquisition, or a change in the competitive landscape. Under the relay model of IP ownership, rights bring the responsibility to either finish the race or pass the baton. In order to ask our partners to take on such a large responsibility, we need to offer something substantial in return. For us, IP fills that need.

**Summary**

There has been some debate recently that the development of affordable medicines would be more effective if no IP was used. However, the process of discovering, developing and delivering drugs is long and complex, and often involves numerous partners, akin to a relay race. To date, no new medicine has been launched in this century without the involvement of the private sector. At MMV, clarity of IP ownership is a key driver for keeping the private sector involved in diseases of market failure. Without such involvement, it is difficult to see how new medicines could be progressed, and how the needs of many millions of patients addressed.


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**Competing interests statement**

The authors declare no competing interests.