# 5 Advancing Innovation and Access to Medicines

## The Achievements and Unrealized Potential of the Product Development Partnership Model

*Marcela Fogaça Vieira, Ryan Kimmitt, Danielle Navarro, Anna Bezruki and Suerie Moon*

### Introduction: Partnerships and the Global Pharmaceutical Research and Development System

When the Sustainable Development Goals (SDGs) were agreed in 2015, Goal 3 called upon the world to "ensure healthy lives and promote well-being for all." Achieving this ambitious objective depends, in part, on the development of and access to health technologies such as drugs, diagnostics, vaccines and medical devices (hereinafter referred to either as "health technologies" or "medicines"). Specific targets for SDG 3 include providing access to medicines (Target 3.8) and supporting research and development (R&D) for "diseases that primarily affect developing countries" (Target 3.b) (United Nations n. d.). The COVID-19 pandemic is a remainder to the world of what has long been recognized in the health community – that access to medicines is essential for health (WHA 60.29, World Health Assembly 2007).

Health technologies are not ordinary consumer goods but rather essential goods, just like food and water. However, current systems for the R&D and delivery of medicines do not meet the needs of most of the world's population. Nearly 2 billion people lack access to essential medicines (WHO 2017) and about 90 million people globally are pushed below the poverty line each year due to health care expenditure (WHO 2020b). The World Health Organization (WHO) estimates that more than 1.7 billion people every year require treatment for at least one neglected tropical disease (WHO 2020a).

The pharmaceutical R&D system that has emerged over the past century – and been globalized in part through the World Trade Organization and its Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) – is based on intellectual property rights, which provide a time-limited monopoly to the rights-holder. Firms are expected to invest in R&D and later recoup those investments through product sales. Potential market size and profitability drives R&D priorities and investment, and firms can charge the highest price the market (or state regulator) will bear during the monopoly period. This system promotes R&D

DOI: 10.4324/9781003148371-8

investment in lucrative areas where product development risk is manageable, but neglects diseases where the risk is too high and/or the market is too small. High prices are built into the system by design. This traditional approach to R&D does not deliver affordable, relevant innovation for low- and middle-income countries (LMICs). The challenges for high-income countries are also increasingly clear; high prices of new medicines are straining the sustainability of health systems and restricting access, even in the wealthiest countries (Morgan et al. 2020). Furthermore, there is insufficient R&D investment for novel antibiotics, outbreak-prone diseases ("pathogens of pandemic potential"), and many rare and/or pediatric diseases that affect all countries.

The question has arisen as to whether different approaches to organizing, financing or incentivizing R&D – sometimes referred to as "alternative" or "new" business models of R&D – can address some of the shortcomings of this traditional approach (Suleman et al. 2020). One area where there has been significant experimentation in alternative business models is that of neglected diseases (also known as neglected tropical diseases or poverty-related neglected diseases), which predominantly affect people in LMICs. It has long been recognized that commercial R&D models did not and would not generate innovative health technologies for these diseases because the market incentive is inadequate to do so (Trouiller et al. 2001). Thus, approximately two dozen public-private product development partnerships (PDPs) were founded around the turn of the millennium to spur R&D into medicines for neglected diseases, such as malaria or sleeping sickness. While PDPs constitute an important category within the larger universe of health partnerships, their impact has been less extensively studied than those of global financing initiatives, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and Gavi, the Vaccine Alliance. However, with at least two decades of experience with PDPs, there is now a sizeable body of evidence to assess their effectiveness.

While there is significant variation in how they operate, a PDP is usually a non-profit organization with a separate and distinct legal identity that enables collaboration to advance the R&D of drugs, vaccines, diagnostics and other health technologies directed at unmet health needs. PDPs are generally funded by public and philanthropic contributions, which allows R&D to focus on health rather than market outcomes. PDPs usually bring together academic, government, industry and philanthropic actors to jointly develop new health technologies. Usually, they do not conduct R&D activities in-house but rather operate as "system integrators" that coordinate several partners who perform these activities (Munoz et al. 2015). A common objective among PDPs is to produce new health technologies that meet the following characteristics: "effective, high quality, acceptable to the target group, and available at an affordable price" (Munoz et al. 2015) with affordability and accessibility concerns built early into the R&D process.

The remainder of this chapter assesses PDPs' effectiveness, according to the five pathways of the typology discussed in Chapter 1 in this volume. There is a growing body of literature about PDPs, focusing on specific organizations, target diseases, projects and products, as well as how they operate, their funding and

governance structure, among many other aspects (Munoz et al. 2015; Moran et al. 2010; Moran et al. 2005; Policy Cures Research n. d.). We draw on this literature to summarize PDPs' effectiveness in terms of goal attainment (Pathway 1) and their impact on affected populations (Pathway 4); in terms of refilling empty development pipelines and bringing new products successfully through the long, costly and risky process of medicine development to reach patients. We then consider whether PDPs have demonstrated effectiveness in terms of creating value for partners (Pathway 2) and improving collaboration between them (Pathway 3), for example, by mobilizing resources or offering partners incentives to collaborate. We then turn to the Pathway 5 question of whether PDPs have influenced institutions outside the partnerships, for which we draw on a recent study (Moon, Vieira and Kimmitt 2020) comparing the costs and efficiency of PDPs against the traditional model of commercial product development. Specifically, we assess the extent to which PDPs are seen as self-contained exceptions to the rule that should be applied only in certain cases, or as a more disruptive business model that can address growing concerns that the traditional business model is unable to fully meet societal needs.

This chapter uses a mixed-methods approach to analyze the effectiveness of PDPs. Literature reviews had previously been conducted by the authors on a number of the topics mentioned here, e.g., PDPs (Navarro and Moon 2019), costs (Vieira and Moon 2020), timeframes and success rates of traditional pharmaceutical R&D (Kimmitt et al. 2020). We also collected and analyzed quantitative data (on costs, timeframes and attrition rates gathered through surveys) and qualitative data (gathered through interviews) on non-commercial R&D initiatives for a separate study prior to the writing of this chapter (Moon, Vieira and Kimmitt 2020). We draw on these literature reviews and original data sources to analyze the effectiveness of PDPs under the framework discussed in Chapter 1 of this volume. We offer more detailed descriptions of the methodology relevant to sections 3 and 4 at the start of those sections below.

## Goal Attainment and Impact on Affected Populations

After two decades, PDPs as a group have demonstrated that it is possible to develop medicines through alternative business models, as evidenced by significant increases in funding for neglected diseases R&D, a renewed pipeline and a number of new medicines now reaching patients.

Global funding for neglected diseases R&D has grown substantially in recent decades. It was up 38 percent in 2018, at USD 4.07 billion (Policy Cures Research n. d.), compared with just USD 2.95 billion in 2007 (Policy Cures Research 2020b), when tracking began. Yet, it still remains a small fraction of the total global investment in pharmaceutical R&D, which was estimated at USD 181 billion in 2018 (Statista 2020). A breakdown of total global funding for neglected disease R&D between 2007 and 2018 shows that, of an estimated USD 44.9 billion, the largest proportion came from public (67 percent) and philanthropic (19 percent) sources, with industry accounting for 14 percent. For comparison, in

2007, the proportions were public (70 percent), philanthropic (22 percent) and industry (8 percent) (Policy Cures Research 2020b). Sources of PDP funding have thus consistently been driven largely by public and philanthropic organizations.[1]

PDPs receive a relatively small proportion of the total R&D funding for neglected diseases, accounting for 13.5 percent of the total (USD 553 million) in 2018 (Policy Cures Research 2020b). Total funding directed to PDPs themselves has remained relatively stable or even decreased proportionally to other recipient types. The growing global investment in overall R&D for neglected diseases indicates growing interest in developing medicines for these diseases and greater involvement from other actors in the field, such as academics.[2] In turn, the number of health technologies under development for neglected diseases has grown significantly in the past two decades. A 2005 analysis found that 75 percent of 63 projects for the development of health technologies for neglected diseases were led by PDPs (Moran et al. 2005). A 2015 analysis found a significant increase – with 485 product candidates in the pipeline, 58 percent of them had come from PDPs and other public-private partnerships (Policy Cures 2015). While there was a decline in the proportion of total products under development by PDPs, there was an increase in the absolute number of projects from PDPs as well as a greater involvement of other actors. As of August 2019, there were 585 products in the pipeline (Policy Cures Research 2019). This increase in the development of health technologies for neglected diseases has been called a "remarkable quiet revolution" "that could dramatically improve the way we prevent, treat and diagnose neglected diseases" (Policy Cures 2015), potentially saving millions of lives and promoting the well-being of many more.

As the R&D process is long, often extending over more than a decade, it has only recently been possible to assess how effective PDPs have been in actually bringing products to market. PDPs have demonstrated it is possible to develop medicines through alternative business models as evidenced by the growing list of products that have successfully been developed (see Table 5.1).

PDPs have not only developed products but the features of these products are an important aspect of their effectiveness. PDPs seek to develop products that are affordable, offer significant therapeutic advance and are suitable for use in resource-poor health systems (e.g., no need for refrigeration). In contrast, the traditional commercial R&D model that has evolved in industrialized countries allows products to be marketed at profit-maximizing prices, rewards the development of "me-too drugs" (which offer little or no therapeutic advance, but are less risky to develop and can claim market share) (Prescrire 2020) and are not designed for use in LMICs.

PDPs focus on areas of unmet health needs, so the products they develop usually offer at least some therapeutic advance over the status quo, although the baseline for neglected diseases is often quite low since there has been little investment in them previously. The Drugs for Neglected Diseases initiative (DND*i*), for example, received regulatory approval in 2018 for fexinidazole, which transformed treatment for the lethal disease known as sleeping sickness (Human African trypanosomiasis) (DND*i* 2018). Previously, the only available treatment was melarsoprol,

*Table 5.1* Products developed by PDPs

| *PDP* | *Product Name* | *Product Type* | *Therapeutic Area* | *Year of Approval* | *Sources* |
|---|---|---|---|---|---|
| DND*i* | Fexinidazole | Therapeutic | African trypanosomiasis (sleeping sickness) | 2018 (EMA) | 1 |
| DND*i* | Nifurtimox + eflornithine combination therapy (NECT) | Therapeutic | African trypanosomiasis (sleeping sickness) | 2009* (N/A) | 2 |
| DND*i* | Sodium stibogluconate + paramomycin | Therapeutic | Visceral leishmaniasis | 2010** (N/A) | 3 |
| DND*i* | Benznidazole | Therapeutic | Chagas disease | 2017 (US FDA) | 4 |
| DND*i* | Liposomal amphotericin B (intravenous, single dose); Liposomal amphotericin B (single dose) + miltefosine; Liposomal amphotericin B (single dose) + paromomycin | Therapeutic | Visceral leishmaniasis | 2010 (N/A) | 5 |
| DND*i* | Paromomycin + miltefosine | Therapeutic | Visceral leishmaniasis | 2010* (N/A) | 6 |
| DND*i* | Ritonavir + rifampicin (1:1 ratio) | Therapeutic | HIV and tuberculosis coinfection | 2016* (N/A) | 7 |
| DND*i* | Lopinavir/ritonavir (2-in-1 pelleets) | Therapeutic | HIV | 2015 (US FDA) | 8 |
| DND*i* and MMV | Artesunate-mefloquine (ASMQ) | Therapeutic | Malaria | 2012 (WHO PQ) | 9 |
| DND*i* and MMV | Artesunate/amodiaquine (ASAQ Winthrop®) | Therapeutic | Malaria | 2008 (WHO PQ) | 10 |
| FIND | Line probe assay for first-line TB drugs, 1st generation (GenoType MTBDRplus) | Diagnostic | Tuberculosis | 2008* (N/A) | 11 |
| FIND | Line probe assay for first-line TB drugs, 2nd generation (GenoType MTBDRplus V2) | Diagnostics | Tuberculosis | 2016* (N/A) | 12 |
| FIND | Line probe assay for first-line TB drugs 2nd generation (NTM+MDRTB detection kit 2) | Diagnostics | Tuberculosis | 2016* (N/A) | 13 |
| FIND | Line probe assay for second-line TB drugs (GenoType MTBDR*sl* version 1.0) | Diagnostics | Tuberculosis | 2016* (N/A) | 14 |
| FIND | Xpert HIV-1 Qual | Diagnostics | HIV | 2015 (WHO PQ) | 15 |
| FIND | Xpert HIV-VL | Diagnostics | HIV | 2017 (WHO PQ) | 15 |
| FIND | Xpert HCV-VL | Diagnostics | Hepatitis C | 2017 (WHO PQ) | 15 |
| FIND | Xpert Ebola | Diagnostics | Ebola | 2015 (US FDA) | 16 |
| FIND | Xpert MTB/RIF | Diagnostics | Tuberculosis | 2010* (N/A) | 15 |

| | | | | | |
|---|---|---|---|---|---|
| FIND | Xpert MTB/RIF Ultra | Diagnostics | Tuberculosis | 2017* (N/A) | 15 |
| FIND | TB LAM RDT (Determine™ TB LAM) | Diagnostics | Tuberculsosis | 2015* (N/A) | 15 |
| FIND | HAT RDT 1st generation (SD BIOLINE HAT) | Diagnostics | African trypanosomiasis (sleeping sickness) | 2013* (N/A) | 15 |
| FIND | HAT RDT 2nd generation (SD BIOLINE HAT 2.0) | Diagnostics | African trypanosomiasis (sleeping sickness) | N/A (N/A) | 15 |
| FIND | Malaria highly sensitive RDT | Diagnostics | Malaria | 2016 (N/A) | 15 |
| FIND | CRP/malaria combination test | Diagnostics | Fever/Malaria | N/A (N/A) | 15 |
| FIND | TB LAMP | Diagnostics | Tuberculosis | 2016* (N/A) | 15 |
| FIND | Malaria LAMP | Diagnostics | Malaria | 2014* (N/A) | 15 |
| FIND | Malaria *P. vivax* LAMP | Diagnostics | Malaria | N/A (N/A) | 15 |
| FIND | HAT LAMP | Diagnostics | African trypanosomiasis (sleeping sickness) | N/A (N/A) | 15 |
| FIND | Visceral leishmaniasis LAMP | Diagnostics | Visceral leishmaniasis | N/A (N/A) | 15 |
| FIND | MGIT liquid culture (TB and MDR-TB) | Diagnostics | Tuberculosis | 2007* (N/A) | 15 |
| FIND | MTB rapid speciation | Diagnostics | Tuberculosis | 2007* (N/A) | 15 |
| FIND | iLED fluorescent microscope | Laboratory equipment | Tuberculosis; malaria; leishmaniasis | 2009* (N/A) | 15 |
| FIND | TrueNat/TrueLab (TB and RIF) | Diagnostics | Tuberculosis | 2018* (N/A) | 15 |
| IPM | Dapivirine (vaginal ring) | Preventive Medicine | HIV | 2020 (EMA) | 17 |
| IVCC | Clothinandin (SumiShield™ 50 WG) | Vector control/ insecticide | Malaria | N/A (N/A) | 18 |
| IVCC | Clothinandin/deltamethrin (Fludora® Fusion) | Vector control/ insecticide | Malaria | N/A (N/A) | 19 |
| IVI | Bivalent killed whole-cell cholera vaccine (Shanchol™) | Vaccine | Cholera | 2011 (WHO PQ) | 20 |
| IVI | Bivalent killed whole-cell cholera vaccine (Euvichol®) | Vaccine | Cholera | 2016 (WHO PQ) | 21 |
| IVI | Bivalent killed whole-cell cholera vaccine (Euvichol-Plus®) | Vaccine | Cholera | 2017 (WHO PQ) | 22 |
| Lifebox | Pulse oximeter | Medical device | | N/A (N/A) | 23 |

(*Continued*)

*Table 5.1* Continued

| *PDP* | *Product Name* | *Product Type* | *Therapeutic Area* | *Year of Approval* | *Sources* |
|---|---|---|---|---|---|
| Meningitis Vaccines Project | Meningitis A vaccine (MenAfriVac) | Vaccine | Meningitis A | 2010 (WHO PQ) | 24 |
| MMV | Artemether-lumefantrine (Coartem® Dispersible) | Therapeutic | Malaria | 2008 (Swissmedic) | 25 |
| MMV | Artesunate (injectable) (Artesun®/Larinate®) | Therapeutic | Malaria | 2010 (WHO PQ) | 26 |
| MMV | Dihydroartemisininpiperaquine (DHA/PQP) (Eurartesim®) | Therapeutic | Malaria | 2011 (EMA) | 27 |
| MMV | Pyronaridine-artesunate (Pyramax®) | Therapeutic | Malaria | 2012 (EMA) | 28 |
| MMV | Sulfadoxine-pyrimethamine + amodiaquine (SPAQ-CO™/Supyra®) | Therapeutic | Malaria | 2014 (WHO PQ) | 29 |
| MMV | Pyronaridine-artesunate (Pyramax® Granules) | Therapeutic | Malaria | 2015 (EMA) | 30 |
| MMV | Artesunate (suppositories) | Therapeutic | Malaria | 2018 (WHO PQ) | 31 |
| MMV | Artesunate (suppositories) | Therapeutic | Malaria | 2018 (WHO PQ) | 32 |
| MMV | Tafenoquine (Krintafel®) | Therapeutic | Malaria | 2018 (US FDA) | 33 |
| MMV | Artesunate (injectable) (Larinate®) | Therapeutic | Malaria | 2018 (WHO PQ) | 34 |
| PATH | Malaria Ag P.f HRP2 ELISA | Diagnostics | Malaria | 2017** (N/A) | 35 |
| PATH | STANDARD™ G6PD | Diagnostics | Malaria | 2019** (N/A) | 36 |
| PATH | DMPA-SC (Depot-medroxyprogesterone acetate self-injectable) (Sayana® Press) | Contraception | Contraception | 2015 (UK MHRA) | 37 |
| TB Alliance | Isoniazid/rifampicin | Therapeutic | Tuberculosis | N/A (N/A) | 38 |
| TB Alliance | Rifampicin + isoniazid + pyrazinamide | Therapeutic | Tuberculosis | N/A (N/A) | 39 |
| TB Alliance | Pretomanid + bedaquiline + linezolid | Therapeutic | Tuberculosis | 2019 (US FDA) | 40 |

Source: Authors' elaboration, based on publicly available data (sources in Annex)
* Year that the therapy was recommended by the WHO.
** Year that the therapy was rolled out.
Note: This table is meant for illustrative purposes, as a snapshot of products brought to market by PDPs. It is compiled based on information available on PDPs' websites (see Annex for full details). Some information was not available from these websites, especially regarding the year of regulatory approval. This information has not been externally verified and may not include all available products.

a dangerous arsenic derivative that killed one in twenty patients treated. DND*i* had previously developed an improvement on melarsoprol by demonstrating that a combination of two preexisting drugs (nifurtimox and eflornithine) was safe and effective against the disease. However, this combination treatment required a painful diagnostic procedure (lumbar puncture), a hospital stay and a team of skilled health workers, which was a heavy burden on both individual patients and the health system. Fexinidazole could be given as a once-daily oral pill for ten days and without the need for a lumbar puncture. The product demonstrated the feasibility of developing medicines that offer both therapeutic advance and are well-suited for use in countries where costly health system resources, such as hospitals and physicians, are in scarce supply. Fexinidazole was also significant because it was a new chemical entity – that is, a molecule that had not previously received regulatory approval for any other disease. Many previous PDP projects had repurposed existing drugs for specific use against neglected diseases. To do so could certainly deliver significant therapeutic benefits but was not considered as technologically challenging or risky as developing a new chemical entity, exposing PDPs to the critique that they could carry out incremental innovation but not make big leaps forward. The approval of three new chemical entities developed by PDPs, the Medicines for Malaria Venture's tafenoquine, TB Alliance's pretomanid, as well as DND*i*'s fexinidazole, provides another indicator of effectiveness.

In addition to therapeutic advance and suitability for different contexts, affordability is a key metric for the success of a PDP's product. PDPs often consider affordability of the end product as a key criterion early in the R&D process, when they are considering multiple candidate technologies or manufacturing options. For example, the Meningitis Vaccine Project – a partnership initiative between the WHO and the non-governmental organization PATH with funding from the Bill and Melinda Gates Foundation – successfully developed the MenAfriVac vaccine by tapping the specific competencies of multiple public and private partners (Gordon, Røttingen and Hoffman 2014). The strategy for MenAfriVac was mainly influenced by the demand from African governments for a ceiling price of less than USD 0.50 per dose (Bishai et al. 2011; Gordon, Røttingen and Hoffman 2014; Kulkarni et al. 2015; Tiffay et al. 2015). Kulkarni et al. (2015) noted that the project succeeded due to "transparency and an intense and close collaboration" of the parties, which allowed for proper know-how and technology transfer, i.e., crucial nonexclusive patent licenses for the necessary technology. Ultimately, MenAfriVac was sold at the target price and was widely adopted by governments in the meningitis belt that stretches across West and Central Africa, causing cases of meningitis to fall steeply in the years following uptake of the vaccine (Gordon, Røttingen and Hoffman et al. 2014; Trotter et al. 2017). A similar approach was taken when DND*i* developed combination treatments for malaria (artesunate-mefloquine and artesunate-amodiaquine), for which target prices were set at levels affordable in malaria-endemic countries (Luiza et al. 2017; Wells Diap and Kiechel 2013).

A comprehensive assessment of all products developed by PDPs is beyond the scope of this chapter. Not all PDP products, however, will necessarily offer all

three key features identified here – therapeutic advance, ease of use in resource-poor settings, and affordability – since technological and other factors mean it is not always feasible to do so. We note, however, that these objectives, which are often articulated in target product profiles (Terry, Plasència and Reeder 2019), are usually core to a PDP's mission and constitute an important way in which their effectiveness should be assessed. It is also an important distinction between the objectives of PDPs vis-à-vis traditional commercial approaches to R&D.

The list of successfully developed products in Table 5.1 is testament to the effectiveness of PDPs in attaining their primary goal. The characteristics of those products – offering therapeutic advance at low-cost and adapted for use in resource-poor settings – suggests PDP-developed products are likely to have beneficial impacts on the health of their target populations. Studies tracking the health impact of new products are not always available, but the experience with the meningitis vaccine cited above offers a powerful illustration of what is possible.

## Partnerships: Creating Value and Facilitating Collaboration, Not Competition

Turning now to Pathways 2 and 3 of this volume's framework, how effective have PDPs been in creating value for partners and facilitating collaboration between them? A full response to this question would require in-depth evaluation of each of these organizations, which is beyond the scope of this chapter. But we can develop some insights by referring to the literature and identifying concretely what PDPs have done to try to achieve these goals. PDPs often mobilize financial and knowledge-based resources from partners and combine them into a structured framework that provides incentives for partners to collaborate, and, ultimately, advance R&D. How do they do so? Bishai et al. (2011) characterized PDPs' organizational structure as having a "lattice form," that is, they stitch together resources available across a broad range of partners, connecting funding to intellectual property to research and production capacities in order to collectively co-produce new medicines. Gordon, Røttingen and Hoffman et al. (2014) also noted that this type of structure lowered the project's risk "as it enables switching among partners for specific deliverables and contributions," when demanded by circumstances and according to their expertise. Taylor and Smith (2020) analyzed the role of three PDPs in developing and delivering new health technologies for sleeping sickness: DND*i* (as described above), the Foundation for Innovative New Diagnostics (FIND) and the Global Alliance for Livestock Veterinary Medicines (GALVmed). They found that "all three organizations have been responsible for delivering new innovations for diagnosis and treatment through brokering and incentivizing innovation and private sector involvement" and conclude that "it is doubtful that these innovations would have been delivered without them" (Taylor and Smith 2020, p.1).

We identified additional ways in which PDPs create value and facilitate collaboration between partners through a study we conducted on non-commercial R&D initiatives (Moon, Vieira and Kimmitt 2020). The study we present here

mainly focused on gathering and analyzing evidence on the costs and efficiency (i.e., timeframes and attrition rates) of non-commercial R&D and analyzing how they compared to averages from commercial R&D. In addition to quantitative data (presented in the next section), we also collected qualitative data from a number of PDPs and/or experts on such initiatives. We contacted 48 non-commercial R&D initiatives to request their participation in the study and collected quantitative data from 8 organizations on 83 candidate products and qualitative data through interviews with 20 individuals from 12 organizations, many of which were PDPs. Out of those, 18 individuals provided their perspectives based on projects conducted within their own organizations and two were experts with knowledge of a range of PDPs. The quantitative data referred to a range of different types of health technologies (vaccines, diagnostics, drugs), but given the limitations of our dataset and the impossibility of comparison across organizations for diagnostics and vaccines, the results include only quantitative data related to drugs (more specifically, to 16 new chemical entities or NCEs). The qualitative data refer to all types of health technologies. Data was collected between June and September 2019. The participating organization (PO) and individual names were anonymized for confidentiality and quotes were edited for brevity and clarity.

In our interviews with actors engaged in PDPs, we identified six roles that PDPs play to enable collaboration among different partners and how these roles create different types of value that partners expect from joining a PDP.

First, interviewees emphasized the relevance of a non-profit organization playing the role of a broker across a portfolio of candidate technologies spanning multiple organizations. This role was especially relevant in making decisions concerning which product candidates to move forward, especially in the context of limited availability of funds.

> [We conduct] head-to-head comparisons among many candidates from different organizations. It is important to note that our mandate is to develop a technology, to promote a cure being found. It is not tied to a single candidate. Industry prioritizes single drug development. (PO 05)

> We see everybody's data. So, if you come to me with a new compound, we can tell you is this new or not. And that requires a model in which somebody like us can establish a reputation for being an honest broker. (PO 08)

> We have a portfolio management group that looks across vaccine candidates and does some down selecting based on the data shared and established criteria. … There is limited funding, so researchers and developers understand that it's better to act jointly, go to the funders and present this as a collaborative research effort across the field. (PO 11)

Second, the potential for knowledge and data sharing was raised by interviewees as one of the main characteristics and strengths of engaging in PDPs. It was highlighted that data sharing was easier and more frequent in non-commercial

R&D initiatives, with PDPs playing a role in facilitating and fostering knowledge exchange.

> Over the years that [practice] has built up, and people are really sharing data with each other. We facilitate knowledge exchange among research institutions in our collaborative network. … We have had a pretty good history of people sharing pre-publication data and results at our Annual Meeting where most of our consortium's researchers gather. … they see the advantage of the discovery, preclinical and clinical people talking and interacting with each other. (PO 11)

Third, another factor mentioned was the expert knowledge that PDPs have of the diseases as well as their social contexts and markets in LMICs, which can improve the quality of the product developed and its utilization in low-resource settings since the technologies can be better tailored to the context in which they are to be used.

> We try to identify in which areas we can help…[I'm] talking about access to biobanks, clinical trials, engagement with WHO and communities, understanding the markets and willingness to pay in comparison to other products. And these are areas where we provide a lot of value. (PO 04)

> We have experience in engaging communities in clinical trials. Community involvement adds a significant budget. Pharmaceutical companies recognize it is not in their expertise and they do not want to take responsibility for it. Rigorous community engagement efforts lead to additional costs, which pharmaceutical companies usually do not have to carry, but it also leads to better outcomes. (PO 05)

> We also bring our expertise, and we have a technical team as well as disease experts who can say what will work and not work in a particular setting. We try to bring reality to the product development to say what kind of things they should be focusing on to make development more sustainable. So we are, in a way, offsetting some of the early marketing or research, so that a company might not have to invest to understand the marketplace. We bring that to them. (PO 04)

A fourth important reason to engage in partnerships was access to centralized resources, such as compound libraries and biobanks, which can reduce costs and increase the speed of product development.

> We asked manufactures about what is the added value of working with us [PDP], and for example, having a biobank with access to different types of samples is super valuable for these companies, because for some diseases it is so hard to get access to them and without it, it wouldn't be possible [to conduct R&D]. I guess it is a case where, if you have collaboration, it facilitates and eases the R&D process, and reduces costs and time, definitely. (PO 04)

Fifth, resource mobilization for partner organizations was also highlighted as a significant incentive to engage in partnerships and work with PDPs. PDPs often apply for funding that can be distributed among partners, especially in the early stages of R&D, which was mentioned as a significant factor that de-risks later stage investment for other actors, including the private sector, and increases interest in developing products for neglected diseases.

> We don't have our own commercial interests; intellectual property remains with researchers and vaccine developers, enabling our organization to be a neutral and honest broker among R&D partners, global stakeholders and funders. Most of our scientific partners collaborate in developing and implementing a large R&D grant which we mobilize, which provides a common incentive to produce results. (PO 11)

> We essentially act as a bridge between funders or donors, the ones that fund us to build upon these technologies. So, in a way, we are providing funding to offset some of the early costs for these companies that are working with us. In other words, what we're doing is trying to bring down the early R&D costs, for instance, for a company which might not otherwise have invested so early a couple of million dollars or even larger sums, by bringing some donor dollars into that area. So, in a way, we effectively reduce the cost to the company. In return, what we ask for is that they reduce the cost when they go sell this in our target market, which is low- and middle-income countries. (PO 04)

> Some of the areas that we work on, most private companies have not thought of putting investments in, because it's not usually lucrative or commercially viable. We are not talking about making lots of money, but we are incentivizing players to come into certain areas where the critical needs are there but nobody is paying attention. That is one way in which we catalyze development. (PO 04)

Lastly, some private actors may benefit from the knowledge that is generated through collaborating with a PDP, which may generate spillover into more profitable areas:

> Let's say that for some studies a company gives us a drug free of charge so that we can set up the studies. After we conduct studies with a drug that already has a marketing authorization, the company may have an interest because we are doing studies as a pilot or proof of concept in special populations that may interest the company, [they can possibly obtain] a marketing authorization extension for it. The company is always interested in collaborating to find out what is happening with this treatment." (PO 01)

The findings outlined here underscore that PDPs can facilitate collaboration by offering resources that partners value, thereby bringing them into the fold.

Different types of resources offered by PDPs were highlighted in the interviews, including funding and de-risking later investments, knowledge of the diseases, social contexts and markets in developing countries, facilitating decisions on which products should move forward in the development pipeline and fostering knowledge and data sharing among partners. All of these resources – funding, information and knowledge – are ways PDPs reduce the costs and risks that product developers face, thereby lowering the barriers to goal attainment.

## Impact Outside of PDPs: Comparing Non-commercial and Commercial R&D

An important but often under-emphasized aspect of effectiveness concerns the impact of a PDP on institutions and collaboration outside the partnership itself (Pathway 5 in this volume's framework). In the context of pharmaceutical R&D, the external impact of PDPs could be considered as the extent to which their business model could be applied beyond the niche area of neglected diseases. Understanding the extent to which this is feasible requires further analysis of whether the PDP model could be applied more broadly.

In the previous section, we analyzed the role that PDPs play in facilitating scientific collaboration, rather than competition. Scientific knowledge is a cumulative endeavor. It is widely understood that science progresses more quickly and is of higher quality when individual researchers and organizations share information and data, so that each may benefit from the knowledge of others. This is the key principle behind the well-established scientific practices of peer review and publication, and more recent moves toward open innovation approaches. Yet commercial R&D is primarily competitive, with strong incentives for secrecy and exclusivity. The ability of PDPs to broker collaboration is an important aspect that could be emulated beyond neglected diseases, a point to which we will return in the conclusion.

A second key question is the extent to which PDPs are comparable in costs and efficiency to commercial R&D models. If so, this would imply that non-commercial R&D could potentially be extended to other disease areas. We address this issue based on the study described above (Moon, Vieira and Kimmitt 2020) in which we gathered and analyzed evidence on the costs and efficiency (i.e., timeframes and attrition rates) of non-commercial R&D initiatives and compared them to averages from commercial R&D. We summarize the key findings here:

### *Costs, Timeframes and Success or Failure Rates*

Our study found that non-commercial R&D differs in many significant ways from commercial R&D. However, it is possible that the sum of these differences would cancel each other out so that total costs and efficiency would be largely in line with commercial averages. Given the small size and heterogeneity of our dataset, our study provides hypotheses for further testing against a larger dataset, rather than conclusions. Nevertheless, to the best of our knowledge, it is the first study since 2005 that examines costs and efficiency, across more than one

non-commercial R&D organization, and compares it to commercial benchmarks (a ground-breaking study was conducted by Moran et al. (2005), but with a very small dataset given that these organizations were only a few years old at the time). Pharmaceutical R&D (product development) is characterized as being a long, costly and risky process. It typically consists of several stages and multiple phases, beginning with basic research and early discovery, followed by preclinical studies and Phase I (small-scale), II (medium-scale), and III (large-scale) clinical trials, before submitting to regulatory (marketing) approval. The process can vary according to different technology types, leading to a wide range of estimates available for costs, timeframes and success rates.

Regarding costs, the collected quantitative data on non-commercial R&D were largely in line with commercial benchmarks (Portfolio to Impact (or P2I) model estimates), with some variation by phase of development. For the technology type "simple new chemical entities," total costs for non-commercial R&D were 13 percent higher than the P2I estimates (USD 52 million for non-commercial vs. USD 46 million for commercial). The largest differences were in the preclinical stage and Phase I, where the costs in our sample of PDPs were more than double the commercial estimates. Conversely, Phase II and III trials were less expensive for simple new chemical entities in our data but by a small margin. For "complex new chemical entities," total costs were similar – 8 percent lower than commercial averages, (USD 54 million for non-commercial vs. USD 59 million in P2I). In contrast to simple new chemical entities, non-commercial preclinical and Phase I costs for complex new chemical entities were lower than for commercial. Notably, Phase II costs were much higher in our dataset (USD 12.7 million vs. USD 6.4 million for commercial). This could be in part due to the higher proportion of Phase II/III trials in our dataset than in the commercial data. Phase III costs were substantially lower than the commercial estimates, which may be explained by the fact that many pivotal trials were in Phase II. The opportunity to forgo Phase III testing would drive up Phase II costs while lowering Phase III costs. The proportion of pivotal Phase II tests may differ between commercial averages and our dataset. The sample size is too small for statistical significance testing or to generalize to other organizations working on non-commercial R&D more broadly; rather, the findings suggest a hypothesis that overall costs to develop simple and complex new chemical entities are similar between non-commercial R&D initiatives and commercial benchmarks.

The qualitative data identified many more reasons why non-commercial costs would be lower than commercial R&D, but did not shed light on the magnitude of these effects. The overall emerging hypothesis is that direct costs of non-commercial R&D are expected to be equivalent or somewhat lower than commercial. Indirect costs for commercial R&D are expected to be higher due to greater overheads and capital costs.

In total, we identified twelve factors that drove costs up or down in the different phases of product development: Three factors pushed costs upward, and five factors pushed costs downward for non-commercial R&D in comparison with commercial (Table 5.2). Four factors were categorized as indeterminate, as

they would affect both non-commercial and commercial R&D in the same way. Table 5.2 presents a summary of the factors influencing costs (Moon, Vieira and Kimmitt 2020).

Regarding timeframes of product development, the emerging hypothesis is that non-commercial R&D timeframes are expected to be equivalent or somewhat longer than commercial. The quantitative data for simple new chemical entities shows that timeframes between non-commercial and commercial R&D averages were roughly similar. Non-commercial R&D had shorter preclinical times (1.65 years vs. 2.49 years for commercial) and longer Phase I times (2.61 vs. 1.80 years for commercial). Non-commercial R&D also had much shorter Phase II times (1.75 vs. 3.38 years for commercial), while Phase III times were slightly higher (3.67 vs. 3.18 years for commercial). Overall, our dataset suggested modestly faster timeframes for non-commercial simple new chemical entity development (taking 9.67 years vs. 10.85 years in the commercial averages). For complex new chemical entities, the non-commercial preclinical stage was much shorter (1.00 vs. 2.87 years commercial), Phase I testing slightly shorter (1.67 vs. 1.93 years commercial), Phase II longer (4.25 vs. 3.51 years commercial), and Phase III longer (4.0 vs. 2.8 years commercial). Overall, non-commercial development time was nearly identical for complex new chemical entities, at 10.92 compared to 11.11 years for commercial.

We identified twelve factors influencing timeframes for non-commercial R&D (summarized in Table 5.3). As with costs, the identified factors were categorized by their potential to push timeframes up or down for non-commercial R&D in comparison to commercial R&D. Seven factors were likely to lengthen timeframes for non-commercial R&D, no factors were likely to shorten timeframes and five factors were categorized as indeterminate. Yet, while the qualitative data identified many more reasons why non-commercial timeframes would be longer than commercial, it did not shed light on the magnitude of the effects.

*Table 5.2* Factors influencing costs for non-commercial (vs. commercial) R&D

| *Costs Pushed Upward* | *Indeterminate* | *Costs Pushed Downward* |
|---|---|---|
| Infrastructure building and training at LMIC's trial sites | Number of arms of the trial | Type of technology (i.e., simpler) |
| Involvement of affected community in product development | Duration of treatment or disease progression | Trial location in LMICs (vs. high-income countries) |
| Limited scientific understanding of the disease | Prevalence or incidence of the disease | Organizational costs (i.e., non-profits) |
| - | Predictive model and attrition profile | Advances beyond existing standards of care easier to show with smaller trial size |
| - | - | Lower input prices for non-profit organizations |

Source: Moon, Vieira and Kimmitt (2020).

*Table 5.3* Factors influencing timeframes for non-commercial (vs. commercial) R&D

| *Timeframes longer* | *Indeterminate* | *Timeframes shorter* |
|---|---|---|
| Lower availability of funding | Need to develop regimens of multiple products (rather than single products) | - |
| Slower decision-making processes | Combined Phase 2/3 trials | - |
| Longer time to negotiate access to candidate compounds | Duration of treatment and/or disease progression | - |
| Longer regulatory/ethical review | Seasonality of disease incidence | - |
| Multiple simultaneous related trials, longer time to reach conclusions | Prevalence or incidence of the disease | - |
| Smaller organization scale or less mature organization | - | - |
| Time for capacity building in LMICs | - | - |

Source: Moon, Vieira and Kimmitt (2020).

*Table 5.4* Factors influencing attrition rates for non-commercial (vs. commercial) R&D

| *Attrition Rate Higher* | *Indeterminate* | *Attrition Rate Lower* |
|---|---|---|
| Limited availability or use of optimization tools | Type of technology or product | Lower preexisting standard of care means easier to demonstrate benefit of candidate product |
| Limited scientific understanding of disease | Testing for multiple indications | - |
| Wide prevalence or incidence of the disease means broad target population across which a drug must be shown to be effective | Combinations or regimens | - |
| - | Reluctance to stop the project | - |
| - | Differing non-commercial vs. commercial reasons for attrition | - |

Source: Moon, Vieira and Kimmitt (2020).

Regarding success/attrition rates of product development, the quantitative data were not sufficient for analysis. The qualitative data uncovered more reasons why attrition rates might be higher in non-commercial R&D, but also provided a number of reasons why there might be no difference. Again, the magnitude of the effects is not quantified. The overall very tentative hypothesis that emerges is that success/attrition rates for non-commercial R&D would be equivalent to commercial R&D.

The qualitative data identified nine factors influencing success/attrition rates for non-commercial R&D (summarized in Table 5.4). As with costs and timeframes, the

identified factors were categorized as likely to drive attrition rates higher or lower for non-commercial R&D in comparison to commercial R&D. Three factors were identified as pushing attrition rates higher for non-commercial R&D, one factor as pushing attrition rates lower and five factors were categorized as indeterminate.

If non-commercial R&D is characterized by equivalent or lower direct costs (excluding indirect costs and costs of capital), equivalent or longer timeframes and equivalent attrition rates to commercial R&D, then overall, non-commercial R&D (including PDPs) would be expected to perform as efficiently as commercial R&D. The final expected direct costs and quantity of products resulting from a pipeline of non-commercially developed candidate technologies, then, would largely be equivalent to those resulting from commercial R&D.

## Discussion and Conclusion

Ever since their emergence, PDPs have demonstrated effectiveness across Pathways 1–4 of the volume's analytical framework, highlighting their potential contribution to expanding access to medicines as a key dimension of SDG 3. This is evidenced by increased funding, renewed product pipelines, and finished products reaching patients on the ground. PDP-developed medicines often offer significant therapeutic advance, are designed to be easy to use in resource-poor settings, with affordability built-in from the early stages of the R&D process. PDPs have also demonstrated the capacity to offer value to partners and facilitate collaboration by playing a number of roles within partnerships. In contrast to commercial pharmaceutical firms for whom effectiveness is measured through financial returns for shareholders, the criteria against which PDP effectiveness must be assessed are more numerous and complex.

What has made these PDPs effective? Our data suggest that at least three of this volume's proposed four conditions for effectiveness (internal to a partnership) are directly relevant to PDPs: Fostering innovation, sophisticated contracting and credible commitment of resources. The *raison d'être* of PDPs is to foster technological innovation, but this has not been enough: They have also had to adopt innovative practices in order to do so. More concretely, PDPs have carved out a very specific role as "orchestra conductors" within the broader pharmaceutical R&D ecosystem, bringing together public and private actors to work in ways they were not used to. Bringing disparate actors together usually required sophisticated contracting, both to clarify actor roles and ensure that each would deliver what the partnership needed. Control over valuable resources, such as funding, scientific data and access to biobanks, were important levers that PDPs used to secure the contractual provisions with partners that were necessary for goal attainment. In turn, ensuring that the PDP could secure those resources required a credible commitment of funds, usually in the form of multi-year grants from public and philanthropic sources. In this way, the three conditions are intertwined. Assessing the relevance of the fourth proposed condition – adaptability – would require further research on individual PDPs that is beyond the scope of this study. More in-depth analysis of specific PDPs

may also yield valuable insights as to why some are more effective than others and why some enjoy greater longevity, productivity and organizational growth than others.

While PDPs have demonstrated significant effectiveness overall, when considering their influence on institutions outside their own niche (Pathway 5), PDPs' impact has been limited. In recent years, there has been only one new PDP created focused on developing new antibiotics (the Global Antibiotic Research and Development Partnership, GARDP), and one PDP (DND*i*) has expanded its portfolio to address hepatitis C and COVID-19, neither of which are considered neglected diseases; it is no coincidence that GARDP was a project originally incubated at DND*i*. Meanwhile, some even foresee a potential shift away from PDPs as the main model for addressing neglected diseases. The Bill and Melinda Gates Foundation (BMGF) has been the single largest funder of PDPs (Policy Cures Research 2020b). However, in 2018 it created the Bill and Melinda Gates Medical Research Institute as a "non-profit biotech" to focus on clinical product development for malaria, tuberculosis and other neglected diseases, despite the existence of (Gates-funded) PDPs already focused in these areas (Bill and Melinda Gates Medical Research Institute n. d.). The future of PDPs thus remains vulnerable to the ebb and flow of philanthropic and developmental aid financing. One reason PDPs have not made waves beyond their own niche area may be how they are framed or understood. Neglected disease R&D is often characterized as a market failure, with the corollary that the market works well for other diseases. Yet, the problems of limited therapeutic advance and high prices of new medicines suggest the market is not working perfectly for other diseases either. But as long as PDPs are seen as acts of charity, rather than as alternative business models, their broader applicability will remain under-recognized.

Our research suggests that various aspects of the PDP model could be applied more broadly to health R&D and possibly beyond. The hypothesis emerging from the empirical data is that non-commercial R&D can be comparable to commercial R&D in terms of costs and efficiency. At the same time, PDPs offer important advantages over commercial R&D in terms of incentivizing therapeutic advances, scientific collaboration, affordability and products well-suited for use across countries of all income levels. Alternative approaches to traditional R&D could use the model of PDPs to generate better outcomes for society. The PDP model may also be usefully applied to needs for technological innovation for sustainable development more broadly, such as for low-cost clean energy technologies, drought-resistant or low-pesticide agricultural technologies, sustainable packaging or clean water (Anadon et al. 2016). In each of these areas, reducing costs and risks and facilitating data and knowledge-sharing to advance innovation – and equitable access to it – could contribute substantially to sustainability.

Two major issues need to be addressed, however, if PDP-type models are to be more widely applied. The first is to identify incentives for scientific collaboration in a competitive commercial environment. A key feature of PDPs has been that they focus on diseases with no commercial potential. This enables them to attract contributions and collaborations among commercial entities, since there

is no potential loss of profit at stake. Contributions to PDPs from pharmaceutical firms are usually considered acts of corporate social responsibility, not core to the business strategy of the firm. For diseases where significant profits are at stake and big rewards go to the first firm to develop a breakthrough product, collaboration will be far more complex to design.

The second is credible commitment of resources, the absence of which has been the Achilles' heel of PDPs. PDPs rely on public and philanthropic money. Governments and philanthropists would need to allocate sustained funding for R&D, in many cases by pooling this funding internationally, yet most have not demonstrated the willingness to do so. Various proposals have been elaborated over the years, for example, for an R&D treaty that would create binding commitments on public R&D investment (WHO 2012) or the creation of an R&D fund at the Special Program for Research and Training in Tropical Diseases, hosted by WHO (WHO 2016). Yet none of these proposals has attracted major financial support. Significant public sums have been mobilized, however, for R&D for novel antibiotics (CARB-X n. d.) and epidemic threats (Coalition for Epidemic Preparedness Innovations n. d.). The COVID-19 pandemic catalyzed an unprecedented surge in public R&D investment, mobilizing more than USD 9.1 billion in the first ten months of the pandemic from at least 38 countries (Policy Cures Research 2020a), demonstrating that it is certainly feasible. Yet sustained internationally pooled funding of health technology R&D has not yet been realized. In the absence of long-term public or philanthropic funding, PDPs or other non-commercial initiatives have to find other ways to finance their R&D, for example through sales, limited-profit models or other means.

This analysis has shown that there is potential for PDPs to catalyze more disruptive changes to the pharmaceutical R&D business model. However, to date this potential remains unrealized, and PDPs have treated only one symptom of an R&D system in need of more comprehensive intervention.

## Notes

1 From 2007-2018, PDPs received a total of USD 6.6 billion, of which 44 percent from public and 56 percent from philanthropic donors for neglected disease R&D. In 2007, total funding was USD 567 million (41 percent public and 58 percent philanthropic) and in 2018, USD 553 million (59 percent public and 40 percent philanthropic). A break-down by funder shows that the Gates Foundation (philanthropic) has been the main funder, accounting for 52 percent of total funding from 2007-2018 (a low of 38 percent in 2018, down from 52 percent in 2007), followed by government funds from high-income countries mostly the US (US NIH and USAID) and the UK (UKDFID), with 18 percent and 11 percent, respectively (2007: US - 22 percent, UK – 4 percent; 2018: US – 21 percent, UK 21 percent) (Policy Cures Research 2020b).

2 Academic institutions accounted for USD 521 million or 18 percent of total funding in 2007 and USD 1.64 billion or 40 percent of total in 2018. Industry was USD 263 million or 9 percent in 2007 and USD 903 million or 22 percent in 2018. Funding for national government agencies represented 13 percent in both 2007 and 2018, USD 374 million and USD 695 million, respectively (Policy Cures Research 2020b).

## References

Anadon, Laura Diaz, Gabriel Chan, Alicia G. Harley, KiraMatus, SuerieMoon , Sharmila L.Murthy and William C.Clark . 2016. Making Technological Innovation Work for Sustainable Development. *Proceedings of the National Academy of Sciences*, 113:35, 9682–9690.

Bill and Melinda Gates Medical Research Institute. n.d. Factsheet. Available at https://www.gatesmri.org/user/themes/quark/assets/GatesMRI_Factsheet.pdf.

Bishai, David M., Claire Champion, Michael E. Steele and Lindsay Thompson. 2011. Product Development Partnerships Hit Their Stride: Lessons from Developing a Meningitis Vaccine for Africa. *Health Affairs*, 30:6, 1058–1064.

CARB-X. n.d. Combating Antibiotic-resistant Bacteria. Available at https://carb-x.org/.

Coalition for Epidemic Preparedness Innovations. n.d. Priority Diseases. Available at https://cepi.net/research_dev/priority-diseases/.

DND*i*. 2018. European Medicines Agency Recommends Fexinidazole, the First All-Oral Treatment for Sleeping Sickness. Available at https://dndi.org/press-releases/2018/ema-recommends-fexinidazole-first-all-oral-treatment-sleeping-sickness/.

Gordon, Rachel, John-Arne Røttingen and Steven Hoffman. 2014. The Meningitis Vaccine Project. Global Health Education and Learning Incubator at Harvard University. Available at http://repository.gheli.harvard.edu/repository/10691.

Kimmitt, Ryan, Marcela Vieira, Suerie Moon and Anna Bezruki. 2020. *Research Synthesis: Time and Success Rate of Pharmaceutical R&D. Knowledge Portal on Innovation and Access to Medicines*. Geneva: Global Health Centre, Graduate Institute of International and Development Studies. Available at https://www.knowledgeportalia.org/r-d-time-success.

Kulkarni, Prasad S., Muriel Socquet, Suresh S. Jadhav, Subhash V. Kapre, F. Marc LaForce and Cyrus S. Poonawalla. 2015. Challenges and Opportunities While Developing a Group a Meningococcal Conjugate Vaccine Within a Product Development Partnership: A Manufacturer's Perspective from the Serum Institute of India. *Clinical Infectious Diseases*, 61:suppl_5, S483–S488.

Luiza, Vera Lucia, Gabriela Costa Chaves, Tayná Marques Torres Barboza, Luciana de Paula Barros Gonçalves and Eric G. Stobbaerts. 2017. Desafios de uma parceria para o desenvolvimento de produtos: o caso de um tratamento para malária. *Ciência and Saúde Coletiva*, 22:7, 2197–2211.

MoonSuerie, , Marcela Vieira and Ryan Kimmitt. 2020. Do Costs, Timeframes and Attrition Rates Differ Between Non-Commercial and Commercial Biomedical R&D? A Study of Neglected Diseases R&D and the P2I Model. Geneva, Graduate Institute of International and Development Studies, Global Health Centre. Available at https://repository.graduateinstitute.ch/record/298834.

Moran, Mary, Anne-Laure Ropars, Javier Guzman, Jose Diaz and Christopher Garrison. 2005. The New Landscape of Neglected Disease Drug Development. Wellcome Trust. Available at https://www.mmv.org/newsroom/publications/new-landscape-neglected-disease-drug-development.

Moran, Mary, Javier Guzman, Anne-Laure Ropars and Alexandra Illmer. 2010. The Role of Product Development Partnerships in Research and Development for Neglected Diseases. *International Health*, 2:2, 114–122.

Morgan, Steven G., Hannah S. Bathula and Suerie Moon. 2020. Pricing of Pharmaceuticals is Becoming a Major Challenge for Health Systems. *British Medical Journal*, 368, 14627.

Munoz, Viviana, Fabiana Visentin, D. Foray and Patrick Gaule. 2015. Can Medical Products be Developed on a Non-Profit Basis? Exploring Product Development Partnerships for Neglected Diseases. *Science and Public Policy*, 42:3, 315–338.

Navarro, Danielle and Suerie Moon. 2019. *Research Synthesis: Product Development Partnerships. Knowledge Portal on Innovation and Access to Medicines*. Geneva: Global Health Centre, Graduate Institute of International and Development Studies Available at https://www.knowledgeportalia.org/product-development-partnerships.

Policy Cures. 2015. The Unrecognized Revolution in Global Health. Available at http://policycures.org/downloads/ND%20Pipeline%20Report%202015%20web.pdf.

Policy Cures Research. 2019. R&D Pipeline Tracker. [database]. Policy Cures Research. Available at https://www.policycuresresearch.org/pipeline-database.

Policy Cures Research. 2020a. COVID-19 R&D Tracker Analysis. [database]. Policy Cures Research. Available at https://www.policycuresresearch.org/media_release/vaccines-clinical-trial-results-summary/.

Policy Cures Research. 2020b. Public Search. [database]. Policy Cures Research. Available at https://gfinderdata.policycuresresearch.org/pages/data-visualisations.

Policy Cures Research. n.d. G-FINDER. [database]. Policy Cures Research. Available at http://gfinder.policycuresresearch.org/.

Prescrire. 2020. Prescrire's Ratings of New Products and Indications over the Past 10 Years: 2010–2018. Available at https://english.prescrire.org/en/81/168/58567/0/NewsDetails.aspx.

Statista. 2020. Total Global Spending on Pharmaceutical Research and Development from 2012 to 2026. Available at https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/.

Suleman, Fatima, Marcus Low, Suerie Moon and Steven G. Morgan. 2020. New Business Models for Research and Development with Affordability Requirements are Needed to Achieve Fair Pricing of Medicines. *British Medical Journal*, 368:l4408.

Taylor, Emma M. and James Smith. 2020. Product Development Partnerships: Delivering Innovation for the Elimination of African Trypanosomiasis? *Tropical Medicine and Infectious Disease*, 5:1, 11.

Terry, Robert F., Antoni Plasència and John C. Reeder. 2019. Analysis of the Health Product Profile Directory: A New Tool to Inform Priority-Setting in Global Public Health. *Health Research Policy and Systems*, 17:1, 97.

Tiffay, Kathleen, Luis Jodar, Marie-Paule Kieny, Muriel Socquet and F. Marc LaForce. 2015. The Evolution of the Meningitis Vaccine Project. *Clinical Infectious Diseases*, 61:suppl_5, S396–S403.

Trotter, Caroline L., Clément Lingani, Katya Fernandez, Laura V. Cooper, André Bita, Carol Tevi-Benissan, Olivier Ronveaux, Marie-Pierre Préziosi and James M Stuart. 2017. Impact of MenAfriVac in Nine Countries of the African Meningitis Belt, 2010–15: An Analysis of Surveillance Data. *The Lancet Infectious Diseases*, 17:8, 867–872.

Trouiller, Patrice, Els Torreele, Piero Olliaro, Nick White, Susan Foster, Dyann Wirth and Bernard Pecoul. 2001. Drugs for Neglected Diseases: A Failure of the Market and a Public Health Failure? *Tropical Medicine and International Health*, 6:11, 945–951.

United Nations. n.d. Sustainable Development Goals. Goal 3: Ensure Healthy Lives and Promote Well-Being for All at All Ages. Available at https://www.un.org/sustainabledevelopment/health/.

Vieira, Marcela and Suerie Moon. 2020. *Research Synthesis: Costs of Pharmaceutical R&D. Knowledge Portal on Innovation and Access to Medicines*. Geneva: Global Health Centre, Graduate Institute of International and Development Studies. Available at https://www.knowledgeportalia.org/cost-of-r-d.

Wells, Susan, Graciela Diap and Jean-René Kiechel. 2013. The Story of Artesunate–Mefloquine (ASMQ), Innovative Partnerships in Drug Development: Case Study. *Malaria Journal*, 12:1, 68.

WHO. 2012. Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination: Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination. Available at https://www.who.int/phi/cewg_report/en/.

WHO. 2016. Options for Sustainable Funding of a Voluntary Pooled Fund to Support Health Research and Development. Background document to EB140/21: "Follow-up of the Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination". Available at https://apps.who.int/iris/handle/10665/254831.

WHO. 2017. *Ten Years in Public Health, 2007–2017: Report by Dr. Margaret Chan, Director-General*. Geneva: World Health Organization.

WHO. 2020a. Neglected Tropical Diseases: Treating More than One Billion People for the Fifth Consecutive Year. Available at https://www.who.int/neglected_diseases/news/treating-more-than-one-billion-people-fifth-consecutive-year/en/.

WHO. 2020b. World Health Statistics 2020: Monitoring Health for the SDGs, Sustainable Development Goals. Available at https://apps.who.int/iris/bitstream/handle/10665/332070/9789240005105-eng.pdf?ua=1.

World Health Assembly. 2007. Resolution on Health Technologies (WHA60.29). Available at https://www.who.int/healthsystems/WHA60_29.pdf?ua=1.

## Annex

*Table 5.5* Products developed by PDPs - List of sources used for Table 5.1

1. DND*i*. https://dndi.org/research-development/portfolio/fexinidazole/
2. DND*i*. https://dndi.org/research-development/portfolio/nect/
3. DND*i*. https://dndi.org/research-development/portfolio/ssg-pm/
4. DND*i*. https://dndi.org/research-development/portfolio/paediatric-benznidazole/
5. DND*i*. https://dndi.org/research-development/portfolio/new-vl-treatments-asia/, https://www.who.int/leishmaniasis/research/978924129496_pp67_71.pdf
6. DND*i*. https://dndi.org/research-development/portfolio/new-vl-treatments-asia/, https://www.who.int/leishmaniasis/research/978924129496_pp67_71.pdf
7. DND*i*. https://dndi.org/research-development/portfolio/superbooster-therapy-paediatric-hiv/
8. DND*i*. https://dndi.org/research-development/portfolio/lpvr-pellets/
9. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/news/dndi-passes-ball-mmv, https://www.mmv.org/access/products-projects/asmq-artesunate-mefloquine
10. Medicines for Malaria Venture (MMV). https://www.mmv.org/access/products-projects/asaq-winthrop-artesunate-amodiaquine, https://www.mmv.org/newsroom/news/dndi-passes-ball-mmv
11. FIND. http://www.stoptb.org/wg/gli/assets/documents/LPA_test_web_ready.pdf, https://www.finddx.org/dx-developed/
12. FIND. https://www.finddx.org/dx-developed/, http://www.stoptb.org/wg/gli/assets/documents/LPA_test_web_ready.pdf
13. FIND. https://www.finddx.org/dx-developed/, http://www.stoptb.org/wg/gli/assets/documents/LPA_test_web_ready.pdf
14. FIND.https://www.finddx.org/dx-developed/, http://www.stoptb.org/wg/gli/assets/documents/LPA_test_web_ready.pdf
15. FIND. https://www.finddx.org/dx-developed/
16. FIND. https://www.fda.gov/media/91944/download; https://www.finddx.org/dx-developed/
17. IPM. https://www.ipmglobal.org/our-work/our-products/dapivirine-ring
18. IVCC. https://www.ivcc.com/market-access/sumishield-50wg/
19. IVCC. https://www.ivcc.com/market-access/fludora-fusion/
20. IVI. https://www.ivi.int/what-we-do/develop/
21. IVI. https://www.ivi.int/what-we-do/develop/
22. IVI. https://www.ivi.int/what-we-do/develop/
23. Lifebox. https://www.lifebox.org/purchase-oximeter/
24. Meningitis Vaccines Project. https://www.who.int/immunization/newsroom/menafrivac_20121114/en/#:~:text=Indian%20regulatory%20authorities%20granted%20marketing,quality%2C%20safety%2C%20and%20efficacy

25. Medicines for Malaria Venture (MMV). https://www.mmv.org/access/products-projects/coartem-dispersible-artemether-lumefantrine
26. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/news/mmv-supported-artesunate-injection-receives-who-prequalification
27. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/news/eurartesim-receives-stringent-regulatory-approval-ema
28. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/press-releases/pyramax-receives-positive-opinion-ema
29. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/news/guilin-s-spaq-added-who-s-list-prequalified-products
30. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/press-releases/pyramax-granules-becomes-first-paediatric-antimalarial-receive-ema-article, https://www.mmv.org/research-development/project-portfolio/pyramax-granules
31. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/press-releases/cipla-launches-quality-assured-rectal-artesunate-suppositories-severe, https://www.mmv.org/access/products-projects/artesunate-rectal-capsules, https://www.mmv.org/newsroom/press-releases/who-provides-first-ever-approval-rectal-artesunate-product-severe-malaria
32. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/press-releases/cipla-launches-quality-assured-rectal-artesunate-suppositories-severe, https://www.mmv.org/access/products-projects/artesunate-rectal-capsules, https://www.mmv.org/newsroom/press-releases/who-provides-first-ever-approval-rectal-artesunate-product-severe-malaria
33. Medicines for Malaria Venture (MMV). https://www.mmv.org/newsroom/press-releases/us-fda-approves-krintafel-tafenoquine-radical-cure-p-vivax-malaria
34. Medicines for Malaria Venture (MMV). https://www.mmv.org/access/products-projects/artesun-larinate-injectable-artesunate, https://www.mmv.org/node/12997/overlay
35. PATH. https://www.path.org/articles/finding-final-cases-malaria-using-more-sensitive-diagnostics/
36. PATH. https://www.path.org/articles/expert-review-panel-diagnostics-approval-expands-access-g6pd-deficiency-test-supports-p-vivax-malaria-treatment-and-elimination-initiatives/
37. PATH. https://www.path.org/articles/dmpa-sc/
38. TB Alliance. https://www.tballiance.org/portfolio/product/pediatric-fdc-continuation-phase
39. TB Alliance. https://www.tballiance.org/portfolio/product/pediatric-fdc-intensive-phase
40. TB Alliance. https://www.tballiance.org/portfolio/product/pretomanid-use-bpal.