Investing for Global Health Impact in Product Development Partnerships

A Tideline Working Paper

Supported by the Bill & Melinda Gates Foundation

June 2017

About the Bill & Melinda Gates Foundation

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life. Based in Seattle, Washington, the foundation is led by CEO Dr. Susan Desmond-Hellmann and Co-chair William H. Gates Sr., under the direction of Bill and Melinda Gates and Warren Buffett.

About Tideline

Tideline is a consulting firm that provides tailored advice to clients developing impact investment strategies, products, and solutions. Tideline's mission is to help clients excel in realizing financial and societal value. The Tideline project team includes: Aaron Arnoldy, Amy Bell *(lead author)*, Alex Bergonia, Nadza Durakovic *(lead author)*, Christina Leijonhufvud, Bryan Locascio, and Ben Thornley.

Acknowledgements

We are grateful to the Bill & Melinda Gates Foundation for their support of the Product Development Partnerships Innovative Financing Initiative (PDP IFI). The project would not have been possible without the ideas, initiative, and deep collaboration of our PDP partners. Each made significant commitments of time and insight to the work. In particular, we are grateful for the leadership, support, and candor of: Catharina Boehme, Ranald Sutherland, and the staff of FIND; Mark Feinberg, Labeeb Abboud, and the staff of IAVI; and Amie Batson, Olivia Polius, and the staff of PATH. In addition, Tideline has benefitted from the input and guidance of a number of experts, for which we are appreciative, including: the members of the PDP IFI Working Group and Expert Investor Group (please see appendix for members) and Glenn Rockman of the Global Health Investment Fund. We also want to thank Dr. Mary Moran of Policy Cures Consulting, who has been an invaluable contributor and advisor to the project since its inception. Finally, thank you to the participants in the capstone PDP IFI workshop and to the Rockefeller Foundation for hosting the event.

About the Product Development Partnerships Innovative Financing Initiative

This paper presents findings from the PDP IFI, a project led by Tideline and supported by the Bill & Melinda Gates Foundation. The initiative seeks to bring clarity and practical guidance to the prospect of impact investment as a funding source for PDPs to complement ongoing financial support from public and philanthropic donors. The research is intended for an audience of global health actors and stakeholders, as well as current and potential investors in the global health market. The PDP IFI was launched in August 2016 and the project continued through May 2017.

CONTENTS

1. **Executive summary** 4

2. **Introduction** 9
   a. Background 9
   b. The market for global health R&D and PDPs 10

3. **The prospect of return-seeking capital for PDPs** 12

4. **Case studies of PDP investment opportunities** 14
   a. Overview of selected case studies 14
   b. Framework for assessing investment prototypes 15
   c. FIND case studies 17
      i. R&D Investment 17
      ii. Manufacturing buy-down 20
   d. IAVI case studies 26
      i. Technology spin-off 26
      ii. Services spin-off 32
   e. PATH case studies 37
      i. Private sector partnerships 37
      ii. PRV-linked investment 41

5. **Implications from the PDP case studies** 46
   a. Summary of the case study assessments 46
   b. Implications of the assessment findings 47
   c. Insights and recommendations from the assessments 49

6. **Recommendations** 56

7. **Conclusion: The potential for transformation** 58

Appendix 59

1. EXECUTIVE SUMMARY

The **Product Development Partnership Innovative Finance Initiative (PDP IFI)** was launched in 2016 with the objective of bringing clarity and practical guidance as to the prospect of impact investing as an additional, complementary funding source for product development partnerships (PDPs), alongside ongoing support from government and philanthropic donors. Attracting sustained funding for R&D beyond current sources is a critical priority, for both PDPs and the global health community at large.

In partnership with three PDPs, five hypothetical deals and one actual transaction have been examined to articulate the opportunities for attracting return-seeking investment and challenges to doing so. Identifying revenue-generating activities and designing an investment structure and strategy around them is a key challenge for PDPs, particularly given limited precedent for investment in global health R&D. In addition, PDPs will have to dedicate financial and operational resources to support these activities, accessing transactional expertise as needed, without disruption to the broader work and mission.

For PDPs, it will be essential to consider a range of strategies for enhancing their investability, including quantifying the potential financial value and articulating the risks to achieving it, accessing internal or external resources to manage and structure the ensuing deals, confirming broader stakeholder buy-in for the approach, aligning on key economic terms of any deal, and outlining a clear and resource-efficient implementation strategy.

The Role of PDPs

PDPs emerged as a non-profit model for addressing the gap between the health needs of emerging markets with the funding available to address them. Developing countries face 90 percent of the global disease burden, but only 10 percent of current medical R&D focuses on the neglected diseases that primarily affect low-income countries. Each PDP seeks to incentivize partnership between the pharmaceutical industry, academic research institutions, and the public sector to undertake the development of drugs, vaccines, and diagnostics for neglected diseases.

PDPs are entirely reliant on restricted donor and grant funding to support their work. These funds have been declining over time due to downward pressures affecting public sector and donor budgets, so there is growing interest in attracting impact investment as a source of flexible, diversified capital. Investors face numerous challenges to participating in global health R&D, including the need for specialized expertise, uncertainty around the timing and quantum of returns, and limited investment precedents. Although PDPs are increasingly identifying revenue-generating activities that could draw interest from investors, transforming them into investable opportunities will require significant effort.

To better explore this market opportunity, the PDP IFI project assessed a number of investment prototypes together with a select group of partner PDPs in order to test the suitability of these

"case studies" with impact investors.[1] Through an intensive process of research and interviews, **FIND**, **IAVI,** and **PATH** were selected for the assessment. Each PDP is described along with their case studies in the graphic below.

FIND focuses on high-quality, affordable diagnostics for neglected diseases.

- **R&D Investment:** Given dual-market applications of diagnostics in its portfolio, FIND would like to consider whether it could receive outside investment with returns linked to successful product launches.
- **Manufacturer Buy-down:** FIND is exploring whether a manufacturer buy-down of the price of one or more tests in the Hepatitis C diagnostics portfolio could result in a scale-up of access to tool(s) and also attract impact investors to support the upfront costs.

IAVI advances science and technology in pursuit of an HIV/AIDS vaccine.

- **Technology Spin-off:** A spin-off of IAVI's broadly neutralizing antibodies technology for HIV could help accelerate promising approaches to HIV prevention, treatment, and cure, and may present an attractive investment opportunity.
- **Services Spin-off:** Through its Human Immunology Lab (HIL), IAVI performs clinical trial testing services that have attracted outside interest, giving rise to the potential for establishing HIL as a for-profit, self-sustaining entity.

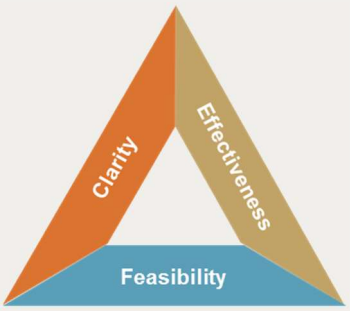
PATH accelerates the development and introduction of a portfolio of high-impact global technologies.

- **Private Sector Partnerships:** PATH's portfolio of diagnostics, devices and tools contains a number of private sector collaborations that could present opportunities for partnerships that generate financial value as well as global health impact for PATH.
- **PRV-linked Investment:** PATH negotiated an investment that will support development of a drug eligible for a Priority Review Voucher (PRV) and would allow all parties to share in the upside of any sale of the PRV.

To assess each of the selected case studies, a custom framework was developed to evaluate the potential for investment capital to support the PDP activities described within each case study. The framework considers those factors that help an investor determine whether a deal will produce results that meet its investment objectives—including the potential to produce a desired impact or benefit, in line with the dual impact and financial objective of impact investors.

[1] A full methodology and project overview can be found in the Appendix.

The framework categorizes the prototypical investor assessment into three elements to evaluate each case study's strengths and weaknesses as they relate to the potential for designing an investable opportunity:



Clarity: Is there certainty about the market opportunity, and what is the nature of the underlying economics?

Effectiveness: Does the concept deliver on global health impact objectives?

Feasibility: What is the experience of the PDP in commercial environments, are the time and cost to implement likely to be reasonable, and do the PDP's core stakeholders support the approach?

Each case study is considered against these three elements to assess the degree to which the opportunities could be developed into compelling impact investment structures that could be actionable and cost-efficient in the near-term. A summary of the assessment as applied across all of the case studies appears in the table below. At this stage, the assessment should not be interpreted as a recommendation or determination for or against any of the investment prototypes. In general, the set of case studies makes a compelling case to pursue impact investment as a new source of funding, though in nearly all instances, additional work needs to be completed to further confirm (a) the feasibility of the proposed strategy, and (b) that the benefits of pursuit outweigh the costs. The case study assessments helped to identify specific and actionable insights that would help support any future cost-benefit analyses.

PDP	CASE STUDY	CLARITY	EFFECTIVENESS	FEASIBILITY
FIND	R&D Investment	M	H	M
	Manufacturer Buy-down	M	H	L
IAVI	Technology Spin-off	M	H	L
	Services Spin-off	M	M	L
PATH	PRV-linked Investment	H	H	M
	Private Sector Partnerships	L	M	M

The insights and implications generated from the case study assessments helped to formulate a set of strategic recommendations for PDPs and their funders. The goal is to determine more definitively whether a PDP can attract impact investment capital and. In most cases, the recommendations may require extensive collaboration to be implemented, with the goal of creating more diverse, sustainable, and additive sources of funding for PDPs and the market more broadly. These recommendations include:

1. Clarify the opportunity: Sharpen the investment thesis and rationale for return-seeking capital, developing data, research, and/or precedents that demonstrate the efficacy of the proposed deal. Where possible, begin to engage with impact investors whose mandates align with the objectives of the PDP.

2. Engage management, operations, and funders: Determine the necessary resources to support and manage the activities underlying the investment opportunity, without disrupting the other activities of the organization. Engage funders to support development of the investment opportunity, including the hiring of external consultants, legal and tax counsel, and other subject-matter experts, as needed.

3. Ensure alignment on investment terms: Develop a view on the acceptable boundaries for key financial terms, as well as a definition of the PDP's role, rights, and ownership before entering conversations or negotiations with investors, leveraging legal and financial transaction experience (either internally or externally).

4. Leverage partnerships to maximize potential: Engage key internal and external stakeholders to identify any concerns they may have, as well as potential risks or conflicts of interest (donors, in particular, will have a view on if and how return-seeking capital can be

introduced in a way that is complementary and additive, rather than distracting or detrimental to a PDP's mission). Build organizational consensus and buy-in early in the investment design process to make negotiations more efficient. Identify a partner with transactional experience who is willing to provide feedback early on to help ensure that a prospective deal already integrates investor considerations and facilitates those conversations.

The appeal of attracting return-seeking capital as a means to both diversify funding streams and to access more flexible pools of capital is strong, although designing investable opportunities will require a significant strategic and operational shift for PDPs. As evidenced by the one completed transaction among the group of case studies explored here, PATH's ability to raise $25 million through a PRV-linked transaction indicates that PDPs can be successful in monetizing commercial opportunities or assets in their portfolio if they are willing to commit internal resources to develop an investor-ready deal. It took PATH considerable staff time, financial resources, and a willingness to manage risks and uncertainties to achieve this, but in their estimation, it was well worth it for a potentially significant source of unrestricted, diversified funding in the future. If PDPs can access the resources and leadership buy-in to make such a strategic shift and successfully execute upon it, the potential for PDPs—and the broader global health R&D market—could be transformational.

2. INTRODUCTION

Background

Developing countries face 90 percent of the global disease burden, but only 10 percent of current medical R&D focuses on the diseases that primarily affect low-income countries. The WHO estimates more than one billion people suffer from one or more these neglected diseases, yet the vast majority lack the means to access effective treatment and care.[2] In addition, infectious diseases account for one in eight deaths globally, with HIV/AIDS, malaria, tuberculosis, and diarrheal diseases imposing the heaviest burden. Beyond the suffering and deaths these diseases cause, the economic costs inflicted can be debilitating to the developing countries and their often underequipped healthcare systems. Their increased toll on productivity has had a serious effect on economic growth in some poor countries.[3]

Over the last two decades, product development partnerships (PDPs) have emerged to support the development of and access to drugs, vaccines, diagnostics, and vector control mechanisms that combat neglected diseases. PDPs were developed as nonprofit organizations with the goal of incentivizing partnership between the pharmaceutical industry, academic research institutions, and the public sector to undertake the development of products for neglected diseases. Currently, there are more than fifteen PDPs focused on research and development in different disease and product areas, but all share the common goal of combatting disease and improving health and life expectancy in the developing world.

PDPs have historically been funded through grants from government and philanthropic donors. In 2015, PDPs received a total of $450m for research and development, representing approximately 15 percent of all funding for neglected disease R&D.[4] This support has been on the decline—funding to PDPs fell by 13 percent between 2014 and 2015—largely due to grant funding cycles from major donors as well as general trends affecting government and philanthropic budgets.[5] In addition to this downward pressure, donor funding is often linked to programmatic objectives or specific initiatives, resulting in PDPs having less flexibility to respond to changes in the market.

> There is a need for creative solutions to facilitate increased and predictable funding streams to PDPs to ensure continued, successful product development work.

[2] National Institute of Health. "*Neglected Diseases FAQs.*" (2016)
[3] Fonkwo. "*Pricing Infectious Diseases: The economic and health implications of infectious diseases. EMBO Report*." (2016)
[4] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)
[5] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)

There is a need for creative solutions to facilitate increased and predictable funding streams to PDPs to ensure continued, successful product development work. Return-seeking investment capital that targets both financial and social impact objectives, or so-called "impact investment," has generated interest as a potential source of new capital for PDPs. The impact investing market is growing rapidly—an estimated 18 percent per year from 2013-15 to reach $77 billion in assets under management.[6] While compelling, there is limited precedent for the role of return-seeking capital, both in the global health R&D market and within PDPs. Tideline estimates that return-seeking investment currently represents between 1-3 percent of total funding in the global health R&D market. Investors currently active in the market operate at the margins due to numerous challenges like including the need for specialized expertise, uncertainty of market demand, scarce exit opportunities, and limited investment precedents. However, macro-level trends—including the emerging middle class, growing movement for market-based approaches, and improvements in technologies—are generally supportive of the longer-term opportunity to drive more investment capital into the global health R&D market.

The market for global health R&D and PDPs

Despite their burden, neglected diseases remain severely underfunded—out of the total $260 billion spent globally on health R&D, only 1-2 percent (or $3 billion) is channeled towards neglected diseases.[7] The paucity of funding has resulted in neglected disease product pipelines that tend to be underdeveloped, with few candidates moving beyond the early discovery and research stages. Only four out of the 336 new chemical entities registered between 2000 and 2011 were developed or approved for neglected diseases, and there are notably few neglected disease products close to commercialization.[8] [9]

The lack of resource allocation towards neglected diseases is primarily the result of the entrenched market failures that characterize global health R&D. The costs and scientific risks associated with the R&D process are high. Pharmaceutical companies may spend up to one billion dollars or more to develop and market a single successful drug. High attrition rates in the discovery and early R&D phases amplify those costs further. On the demand side, there is significant commercial uncertainty. Marginalized populations in many high-burden countries simply cannot afford the products coming to market or lack access to consistent distribution channels. Some 30,000 children in developing countries die each day from treatable diseases and around a third of the world's population lack consistent access to essential medicines.[10] Moreover, lack of data limits the market transparency and predictability that developers need to thoroughly assess potential product commerciality. Thus, developers have few incentives to invest in the R&D process for neglected diseases without the anticipated market demand that could justify the costs.

---

[6] Global Impact Investing Network. "*Impact Investing Trends: Evidence of a Growing Industry*." (2016)

[7] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)

[8] Chatelain and Ioset. "*Drug discovery and development for neglected diseases: the DNDi model. Drug Design Development and Therapy*." (2016)

[9] WHO. "*Health Product Research & Development Fund: Proposal for Financing and Operation*." (2016)

[10] MSH. "*Global Health Impact: Ensuring access to affordable, quality medicines*." (2015)

This has left much of the financial responsibility for R&D to donor governments and the philanthropic community.

> More recently, innovative financing tools have gained momentum as mechanisms to blend capital from the public and private sectors and leverage additional financing by underwriting R&D risks.

The Lancet Commission advocated for a doubling of funding for global health R&D to $6 billion a year by 2020 to meet the growing global health need. Given limits on the scope and size of public and philanthropic funding, innovative financing approaches could help to tap into new sources of funding. Pioneering investors like the Bill & Melinda Gates Foundation and the Global Health Investment Fund (GHIF), a $108 million fund investing in the development of global health products, provide important precedents by putting return-seeking capital to work in global health R&D through investments in developers that have promising products with neglected disease applicability. Nevertheless, return-seeking capital in global health R&D remains limited, and the few active investors tend to target more later-stage, lower-risk products closer to commercial viability. Early-stage products that offer the potential for highly impactful global health outcomes largely remain too risky for most investors.

More recently, innovative financing tools have gained momentum as mechanisms to blend capital from the public and private sectors and leverage additional financing by underwriting R&D and market risks. Established funding mechanisms, such as grants and PDPs, were designed to push new drug discovery through the development pipeline by subsidizing research inputs, thereby reducing the costs to developers. There has also been increasing interest in exploring pull mechanisms, such as the advanced market commitment and volume guarantees, which incentivize later stage R&D by securing or subsidizing demand and enhance the market opportunity for companies.[11]

[11] Kettler. "*Fostering incentives for research, development, and delivery of interventions for neglected tropical diseases: lessons from malaria.*" (2016)

3. THE PROSPECT OF RETURN-SEEKING INVESTMENT FOR PDPS

Most PDPs are focused on developing products for which there is insufficient market potential to justify the high risks and costs. However, PDPs also come across products or technologies that could have market potential. Some products have "dual-market" opportunities, which allow them to be adapted for the needs of both developing countries as well as higher-income countries, offering the possibility of attractive revenues and profits through tiered pricing structures. Other products present high volume, low margin opportunities for certain manufacturers. And, in select cases, investable opportunities are available through an incentivizing "pull mechanism," such as a manufacturer buy-down or the sale of a priority review voucher (PRV).

Given current trends, traditional government and philanthropic capital will not be sufficient for accelerating necessary product innovation in global health R&D. Novel financing mechanisms that can effectively leverage available pools of capital and better align investor incentives to attract return-seeking investment will become increasingly essential to meet global health needs. To date, PDPs have served mainly as mechanisms for donors to provide "push" funding—monies that aim to incentivize innovation by subsidizing research inputs, helping defray costs and reduce scientific risk associated with early-stage R&D. While push mechanisms have been useful for stimulating R&D for neglected diseases, many market participants are turning to robust pull mechanisms as a necessary complement to help provide sufficient incentives to bring products to market.[12] [13] Unlike push mechanisms, pull mechanisms reward research outputs and help to mitigate market demand uncertainty. Pull mechanisms often focus on the development of specific products or product profiles. Since PDPs play an essential management role throughout the product development lifecycle, they can benefit from any assistance pull mechanisms provide in bringing products to market. These rewards can also play a vital role in enticing return-seeking capital to participate in a larger set of opportunities within global health R&D.

To date, private sector investment capital still plays a marginal, although growing, role in the global health R&D market. The annual G-FINDER survey has estimated private sector funding at $534 million, representing 16 percent of total funding, up by 28 percent since 2013.[14] Most of this comes from pharmaceutical and biotech companies that are increasingly investing in R&D for neglected diseases in the form of internal, strategic investments and, in some cases, through their Corporate Social Responsibility efforts. Their motivations tend to be qualitative and reputational in nature, with a focus on brand enhancement and employee engagement. Some companies also see an emerging opportunity in the developing world, making investments in neglected disease R&D an important component of a strategic expansion of their global footprint.

The pharmaceutical and biotech industry benefits from an expert understanding of potential synergies, benefits, and risks of investments into global health R&D. Third-party investors face

[12] Mueller-Langer. "*Neglected infectious diseases: Are push and pull incentive mechanisms suitable for promoting drug development research*?" (2013)

[13] Medecins Sans Frontieres. "*3P: Push. Pull. Pool. Better TB Treatment. Faster. Proposal to accelerate innovation and access to new treatment regimens for TB*." (2016)

[14] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)

more significant hurdles due to a lack of market infrastructure to help them evaluate and make investments. Of the $3.4 billion invested in R&D for neglected diseases in 2014, Tideline estimates only about 1 percent, or $40 million per year, is provided in the form of return-seeking investment capital from third parties.[15] There are a growing number of examples of successful transactions, including the $20 million Bill & Melinda Gates Foundation equity investment in the biotech KYMAB, which was founded as a spin-off from the Wellcome Trust Sanger Institute. Its proprietary technology platform has applicability for neglected diseases and represents a promising dual-market opportunity, and the investment ensured that KYMAB developed and retained a focus on malaria research.

As described in greater detail later in this document, some PDPs have begun to explore possible strategies for generating revenues to further their mission. This includes development of dual-market products, spin-offs of services and technologies with commercial appeal, and private sector partnerships. It has also raised the possibility of attracting third-party capital, given a small but growing set of precedents and potential impact investor interest.

Of the $3.4 billion invested in R&D for neglected diseases in 2014, Tideline estimates only about 1%, or $40 million per year, is provided in the form of return-seeking investment capital from third parties.

Nevertheless, finding new sources of capital is a significant challenge. Investing in R&D is a risky endeavor in many fields, given the long period between investment and payoff, the uncertainty about the exact characteristics of and need for the final product, and the scientific risks of the development process. These challenges are particularly acute in R&D for neglected diseases. Development of drugs and vaccines, in particular, takes many years and requires significant investments, especially for later-stage human trials. The market for these products is, moreover, very difficult to predict. Given limited data, it is challenging to determine the potential end market size. There are the risks, too, that a product fails in trials, does not make it through the regulatory process, or ends up being made obsolete by other advances in technology.

The lack of market infrastructure for investment in global health R&D more broadly provides an added challenge. The deals that have been done to date have often required significant investment of time and resources dedicated toward reconciling interests between diverse actors, developing legal agreements, and ascertaining tax consequences. This process will become more efficient as more deals take place, but there are currently still few precedents. The project at hand will help explore a number of potential opportunities that could establish helpful precedents for return-seeking investment in PDPs.

[15] Policy Cures. "*The Unrecognized Revolution in Global Health: 2015 Pipeline Report.*" (2015)

4. CASE STUDIES OF PDP INVESTMENT OPPORTUNITIES

Overview of selected case studies

In partnership with Tideline, the leadership at each PDP selected to support this research identified two internal opportunities that could serve as case studies for the project.[16] Tideline conducted deep research on the business opportunities identified to analyze their suitability for generating revenue for the PDP and potentially structuring the opportunity in a way that would be attractive to investors. While the presence of revenue streams offers the potential to attract impact investment capital, some of the opportunities identified are more actionable and realistic than others. To test the attractiveness of each business opportunity to potential investors, Tideline created investment prototypes structured as case studies, which were then shared with a select group of investors for feedback.

FIND focuses on high-quality, affordable diagnostics for neglected diseases.

- **R&D Investment:** Given dual-market applications of diagnostics in its portfolio, FIND would like to consider whether it could receive outside investment with returns linked to successful product launches.
- **Manufacturer Buy-down:** FIND is exploring whether a manufacturer buy-down of the price of one or more tests in the Hepatitis C diagnostics portfolio could result in a scale-up of access to tool(s) and also attract impact investors to support the upfront costs.

IAVI advances science and technology in pursuit of an HIV/AIDS vaccine.

- **Technology Spin-off:** A spin-off of IAVI's broadly neutralizing antibodies technology for HIV could help accelerate promising approaches to HIV prevention, treatment, and cure and may present an attractive investment opportunity.
- **Services Spin-off:** Through its Human Immunology Lab (HIL), IAVI performs clinical trial testing services that have attracted outside interest, giving rise to the potential for establishing HIL as a for-profit, self-sustaining entity.

PATH accelerates the development and introduction of a portfolio of high-impact global technologies.

- **Private Sector Partnerships:** PATH's portfolio of diagnostics, devices, and tools contains a number of private sector collaborations that could present opportunities for partnerships that generate financial value as well as global health impact for PATH.
- **PRV-linked Investment:** PATH negotiated an investment that will support development of a drug eligible for a Priority Review Voucher (PRV) and could allow all parties to share in the upside of any sale of the PRV.

[16] A full methodology and project overview can be found in the Appendix.

Framework for assessing investment prototypes

A custom framework has been developed to assess each of the selected case studies from the perspective of an impact investor. Generally, when investors evaluate potential opportunities, they consider a number of factors designed to help determine whether the deal could produce results that meet their investment objectives. In traditional investment markets, this assessment is primarily focused on quantifying the potential return and risks to achieving it by evaluating the market opportunity that will support the return-generating activities and the team's ability to execute on that opportunity. In the impact investment market, the approach is very similar, though investors are additionally assessing the potential to achieve a desired impact or benefit alongside the financial returns.

These conventions, which are well established, were adapted for the purpose of creating an assessment framework to evaluate the potential for investment capital to support the PDP activities described within each of the case studies. The framework categorizes the prototypical investor assessment into three elements—**Clarity**, **Effectiveness,** and **Feasibility**—to rigorously evaluate each case study and identify its strengths and weaknesses as they relate to the potential for designing an investable opportunity.

The dimensions of the assessment are further described below:

	DESCRIPTION	KEY DETERMINANTS OF INVESTABILITY
CLARITY	Evaluating the clarity and potential of the proposed **investment thesis**, by examining the rationale for return-seeking capital, as well as the profile of the proposed structure.	▪ **Certainty of market opportunity:** Can a structure be designed to attract impact investment to support the goals of the PDP? Is there precedent or other evidence to validate the approach and mitigate risk for an investor? ▪ **Nature of underlying economics:** Is there a means to generate significant, reliable revenues that could deliver a return?
EFFECTIVENESS	Considering the **expected impact** of the proposed investment, including global health outcomes, and any risks to achieving them.	▪ **Delivers on impact objectives:** Will the proposed structure directly support the global health objectives of the PDP? Does the introduction of return-seeking capital pose any risk to mission?
FEASIBILITY	Assessing the key **conditions** that would be conducive to success, including experience of the investee, implementation cost and time, and stakeholder alignment.	▪ **Experience of PDP in commercial environments:** Does the PDP have the appropriate organization and experience to successfully manage the opportunity? ▪ **Reasonable implementation time and cost:** What plans, processes, and legal steps need to be undertaken to reach investability? Do the prospective benefits of attracting investment outweigh the time and cost to do so? ▪ **Openness of core stakeholders:** Will external and internal stakeholders be supportive of the approach?

Each case study is ranked against these three elements, indicating the degree to which each opportunity could be developed into a compelling impact investment that would be actionable and cost-efficient in the near term. For example, a “high” ranking for a sub-element indicates that there is a more obvious pathway to an investable opportunity. A “low” ranking indicates that additional research or analysis is needed to develop the concept further to determine if an investable opportunity is achievable.

FIND CASE STUDIES

FIND was launched in 2003 at the World Health Assembly in Geneva, originally referred to as the Foundation for Innovative New Diagnostics. It is headquartered in Geneva, with additional country offices in South Africa, Uganda, India, and Vietnam. The organization focuses on high-quality and affordable diagnostics for neglected diseases, including tuberculosis, malaria, sleeping sickness, Hepatitis C, HIV, leishmaniasis, Buruli ulcer, and Chagas disease. Over the past twelve years, FIND has supported the development of 21 new diagnostics tools in previously neglected areas and worked with over 150 partners to ensure appropriate regulatory approval, introduction, and use. FIND has also facilitated the development of additional tools through the provision of samples and access to clinical sites.

R&D Investment

OPPORTUNITY SNAPSHOT: FIND R&D INVESTMENT

Overview

Given dual-market applications of certain diagnostics in its portfolio—particularly within the areas of anti-microbial resistance and tuberculosis—FIND would like to consider whether it could receive outside investment in development of these diagnostics with returns linked to successful product launches.

Assessment

Clarity	Medium
Effectiveness	High
Feasibility	Medium

Key insights

- Specialist expertise in global health R&D is likely to be needed—and ideally in diagnostics in the designated disease areas—to appropriately assess PDP investment opportunities
- Dual-market potential will be limited where there is not alignment between developed market and developing market priorities

Overview of potential investment

The FIND portfolio has a number of diagnostics with dual-market applications, in particular in the areas of anti-microbial resistance (AMR) and tuberculosis (TB). In one third of cases where antibiotics are given, patients do not need them, leading to the spread of AMR. Diagnostics that can more accurately identify the pathogen, particularly in disease areas like sepsis—which affects 30 million people annually, including 6 million infants and children—would help to address this global epidemic. In tuberculosis, a complex disease that affects more than 10 million people a year, more effective diagnostics could lead to more rapid treatment paths.

The case study explores whether return-seeking investment capital could be attracted to support the development of these tools, with investors sharing in the upside of any successful product launches (likely through royalties on sales). Although difficult to quantify on a general basis, an

upfront investment of $7-10m in an identified AMR-related or tuberculosis diagnostic has the potential to support development and launch a successful intervention. This assumes that the diagnostic test could be administered by an existing diagnostic platform, or that it is co-developed with a suitable platform (which may require additional capital).

R&D investment opportunity in context

Bacterial strains that are resistant to available antibiotics are emerging in hospital and community settings around the world, causing 700,000 deaths each year. Studies estimate that by 2050, 10 million lives a year and a cumulative $100 trillion of economic output will be at risk.[17] The rise in drug resistance is driven largely by the misuse of existing antibiotics, requiring a fundamental change in the way that antibiotics are prescribed and used. Effective diagnostics that can distinguish between bacterial and viral infections and accurately identify the cause of infection would be an essential tool in antibiotic management. Unfortunately, traditional diagnostic methods, such as blood cultures and drug susceptibility tests, lack the necessary accuracy and speed to effectively combat the rise in drug resistance.

FIND is currently pursuing mitigants to AMR risk as a theme across its diagnostics portfolio and has multiple clinical tools in development that may provide solutions. Both sepsis and tuberculosis serve as important cornerstones in the fight to combat AMR, since effectively tackling either could mitigate AMR risk. In the case of sepsis, which is the primary cause of death from infection globally, highly inaccurate and slow blood culture tests continue to command the global market.[18] Outdated diagnostics exacerbate the burden through misdiagnosis that can result in inaccurate treatment and drug resistance. Tuberculosis, an infectious disease with a fatality rate of 1.5 million people per year, suffers from a similar dearth of effective and accessible diagnostics. Of the 9 million cases of tuberculosis in 2013, only 58 percent of pulmonary tuberculosis patients were bacteriologically confirmed via a WHO-recommended test—the rest were likely managed on the basis of clinical suspicion or non-specific tests.[19] Such lack of effective diagnostics can result in incorrect treatment and an increased risk of multidrug-resistant tuberculosis developing.

A shift to faster, more accurate multiplex diagnostic platforms and point-of-care (POC) tests is a top priority.[20] FIND currently has a robust pipeline of febrile and tuberculosis disease diagnostics at varying stages of development. Nevertheless, differences in affordability and in the infrastructure of national healthcare systems suggest that a range of diagnostics may be appropriate. To date, the diagnostics market is concentrated in developed countries, with the United States, European Union, and Japan commanding 80 percent of global sales.[21] Developed countries have the means and the established health system infrastructure to administer more complex and sophisticated molecular tests. While molecular tests tend to be more accurate, their

[17] Review on Antimicrobial Resistance. "*Tackling drug-resistant infections globally*." (2016)
[18] Cohen et al., "*Sepsis roadmap for future research*." (2015)
[19] WHO. "*Global tuberculosis report*." (2014)
[20] Kik et al., "*Potential market for novel TB diagnostics: worth the investment?*" (2015)
[21] European Observatory and WHO. "*Ensuring innovative diagnostics for bacterial infections*." (2016)

cost (at more than $300 per test) and complexity can be prohibitive for developing countries. Simple, rapid POC tests may be more relevant solutions for resource-poor settings.[22]

Investability assessment

Investing in diagnostics with dual-market potential resonates with investors, as the structure to do so would mirror similar approaches in the market. For example, the GHIF has financed a number of companies whose products have applications to commercial markets in the developed world and are also needed in the developing world (e.g., a diagnostic for gestational diabetes and preeclampsia). Additional education and diligence is required to advance discussions of a transaction further, as most impact investors are not specialists in global health R&D, nor in the disease areas referenced.

Clarity

FIND has a diverse AMR and tuberculosis diagnostics portfolio, and most of its products have active private sector or academic partners. However, developed world priorities for diagnostics development are frequently different from the developing world, which could diminish the scale of the potential dual-market and/or constrain the R&D that would most benefit the developing world. Additional diligence on the FIND portfolio is necessary to understand the quantifiable dual-market opportunity and the product(s) that should be prioritized for exploring an investment.

In addition, a transaction like this is unprecedented for FIND, and the question of whether private sector partners would be open to sharing the upside from successful product launches merits further exploration. Structuring and negotiation expertise would be needed, either internally or as an external resource, to successfully and efficiently put a deal together.

Investors see this opportunity as worthy of further consideration if the above concerns could be appropriately addressed and reasonable terms negotiated. Most investors interviewed also highlighted that they knew little about the diagnostics pipeline within either AMR or tuberculosis, so deep education and diligence on the market opportunity—and FIND's position within it—would be an essential component of a first phase of consideration.

Effectiveness

There is a worldwide need for faster, more sensitive, and easier-to-use diagnostics that can combat AMR and provide more effective treatment pathways for tuberculosis patients. As a result, investments in FIND's robust AMR and tuberculosis diagnostics pipeline could produce more effective diagnostics that could have a dramatic impact on global health outcomes. By accessing return-seeking capital to support these development activities, FIND can reallocate donor-funded pools of capital to other critical areas.

[22] European Observatory and WHO. "*Ensuring innovative diagnostics for bacterial infections*." (2016)

Feasibility

FIND may want to explore establishing a separate legal entity to receive and manage investment capital, as there are limits to the types of capital that can be deployed into a nonprofit entity. This would require legal counsel and support, as well as some dedication of resources to be managed effectively, though it does offer the benefit of a clear separation between profit-making activities and the traditional donor-supported activities of the organization. Alternatively, FIND could negotiate a contractual agreement with an investor to share in the royalties that it receives from the commercialization of any of these products.

Along with considering time, cost, and resource implications of the above legal structures, FIND needs to verify whether its public sector partners (e.g., WHO) would be comfortable with either approach. There is concern that public sector partners may perceive conflicts of interest or risks to mission if investment capital were provided to a PDP. In general, issues of conflict of interest can be managed through buy-in from donors, clear expectation-setting, investment terms that protect the mission and ensure access, and walling off the activity receiving capital from other parts of the organization.

Manufacturing buy-down

OPPORTUNITY SNAPSHOT: FIND MANUFACTURING BUY-DOWN

Overview

FIND is exploring whether a manufacturer buy-down of the price of one or more tests in the Hepatitis C diagnostics portfolio could result in a scale-up of access to tool(s) and also attract impact investors to support the upfront costs.

Assessment

Clarity	Medium
Effectiveness	High
Feasibility	Low

Key insights

- Evidence of the thesis—in this case, the success of the prior manufacturing buy-down—makes a more compelling case for investment
- Balancing simplicity in structure with the concerns and demands of donors will be essential to attracting return-seeking investment

Overview of potential investment

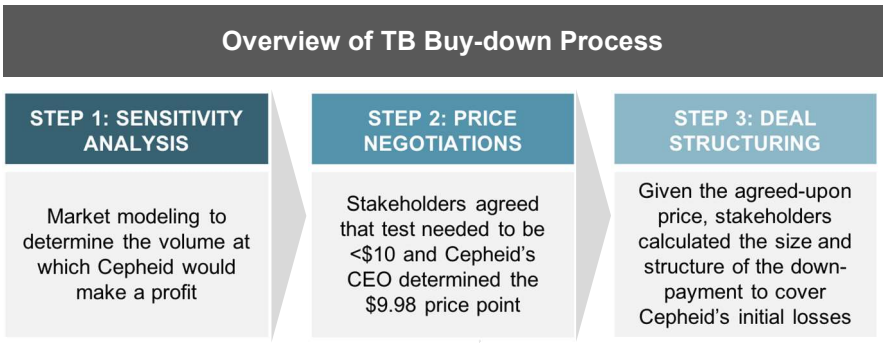
FIND is exploring the potential of a manufacturer buy-down—the use of donor funds to subsidize the price of a diagnostic to a level more affordable for the developing world—to catalyze development of products in its Hepatitis C (HCV) diagnostics portfolio. Alongside the buy-down, FIND is assessing whether the proposed transaction would provide a compelling incentive for an impact investor to finance the upfront costs.

A few years ago, several donors partnered together to provide a price buy-down on a tuberculosis (TB) diagnostic developed by Cepheid, a leading molecular diagnostics company, and supported by FIND. The donors funded $11 million to cover Cepheid's losses until volumes on the tuberculosis diagnostic reached a profitable level at the lower price. The transaction led to the rapid deployment of the diagnostic tool with significant global health benefit—approximately 24 million tests have been performed in 130 countries since 2010.[23] FIND believes its current HCV portfolio presents a similar opportunity and that the growing impact investment market offers the possibility to explore a financial innovation. Rather than the donors providing all the funding upfront, an impact investor would be approached to provide a loan to the manufacturer to support the manufacturing ramp-up period.

Manufacturing buy-down opportunity in context

Precedent analysis of tuberculosis buy-down

In 2010, the WHO endorsed Cepheid's Xpert MTB/RIF test, a molecular assay for tuberculosis that can detect the disease and resistance to rifampicin in under two hours. Cepheid's overall platform and testing system, known as GeneXpert, was also attractive because it can be used outside of conventional laboratories (i.e., in low-resource settings) and does not require specialized training. However, the $16.86 cost per cartridge proved to be a barrier to the introduction and widespread use of the test in developing countries. Through negotiations, Cepheid agreed to partner with FIND as well as UNITAID, USAID, PEPFAR, and Gates Foundation to buy down the cost of the diagnostic to $9.98. The price was determined through careful negotiation to be acceptable to the ministries of health in the recipient countries and sustainable for Cepheid. The agreement further ensured that the price would not increase for 10 years (until 2022).



[23] WHO. "*Status of Xpert rollout*." (2016)

At this pricing level, Cepheid would have incurred losses in the initial years, so the donors collectively pooled and disbursed $11 million in grants to Cepheid upfront to cover those losses until volumes reached a financially sustainable level at the negotiated price. The donors also agreed to commit an additional $1 million at a later stage if volumes did not reach a defined level in order to further mitigate risk for Cepheid. The volumes were easily met within the first year, so the final $1 million payment was not disbursed. Globally, about 24 million Xpert tests have been performed in 130 countries since 2010, galvanizing stakeholders and paving the way for universal drug susceptibility testing.[24]

Two important considerations have emerged in commentary from discussions with key stakeholders. First, the $9.98 price for the test is still considered expensive relative to need, and some participants theorize that uptake could have been even greater at a lower price point. However, it's not clear that Cepheid would have agreed to a lower price or that it would have been sustainable to do so. Secondly, the existence of an agreement with a single manufacturer has raised concerns that the buy-down essentially created a monopoly that would make it more difficult for other product developers to enter the market. There is not strong evidence to support this concern—at the time of the agreement there was no other comparable test in development, and there is some indication that the rollout instead helped to attract new product developers to tuberculosis, resulting in a more robust molecular diagnostic pipeline.

Opportunity in Hepatitis C

Hepatitis C (HCV) has been called the 'silent pandemic' as it remains largely undiagnosed due to the complexity and cost of existing diagnostic tools, with only 1 percent of infected patients aware of their status. Approximately 130-150 million people suffer from chronic HCV infection globally with an estimated 350,000 to 500,000 deaths annually. Gilead has recently developed an HCV cure, marketed as Sovalid, which makes the need to effectively identify and diagnose patients even more pressing and urgent. FIND is exploring molecular tests as well as core antigen tests for its HCV program. Molecular tests present the lowest technical risk and highest sensitivity, and there is a clear market opportunity in the United States and European Union; however, they are costly and difficult to use. Core antigen test are cheaper and portable, making them more suitable for low-income countries (LICs); however, they not as accurate.

A similar approach taken in the case of the Cepheid tuberculosis test could be taken in the case of HCV diagnostics and would likely have a significant global health impact, but the lack of a potential dual-market opportunity and saturation of platform developers need to be considered.

[24] Albert et al., "*Development, roll-out and impact of Xpert MTB/RIF for tuberculosis: what lessons have we learned and how can we do better?*" (2016).

	HCV CONTEXT	XPERT COMPARISON	CONSIDERATIONS
PRICE	• Costs of HCV testing currently can exceed $300 per test, and while new molecular tests under development may cost as low as $20, that is still considered too high for market need	• Cepheid introduced a faster, more reliable, and easier to use tool to the market, but its high costs limited uptake	• FIND estimates that molecular tests will have to reach $5 per test while core antigen tests have to fall below $3 per test to ensure sufficient uptake
PRODUCTS	• While the molecular test has market opportunities in both the US and Europe, an antigen POC immunoassay would be a better solution for LICs due to lower cost and ease of use	• The Xpert's dual-market potential created an investment incentive, as Cepheid could charge a higher market price in developed countries to further offset losses in LICs	• None of the HCV diagnostics candidates have a true dual-market opportunity, which would impact potential volumes and the size of any subsidy required
COMPETITION	• HCV's competitive landscape is crowded: FIND estimates there are more than 80 developers for molecular platforms and 40 for core antigen tests • The large number of HCV diagnostics developers and varying target product profiles suggests that a buy-down in the HCV market could consider a portfolio approach that supports complementary diagnostic solutions targeting different populations	• At the time of the Xpert buy-down, Cepheid was the only developer with a comparable tuberculosis diagnostic on the market • This allowed Cepheid to achieve sufficient scale quickly but ultimately led to criticism that the buy-down distorted the market by creating a monopoly	• While a portfolio approach could eliminate concerns around creating a market monopoly, it would add complexity to the eventual deal structure • Stakeholders will need to consider whether the requisite volumes can be achieved by subsidizing multiple developers (i.e., each will have to scale independently)

Economic considerations

An analysis that FIND performed to examine the economics of the tuberculosis buy-down was adapted to similarly assess the economics of a potential HCV buy-down. As a proxy for the upfront investment that would be required to be made by an investor, the peak cumulative losses for a single, hypothetical manufacturer are calculated with variations shown for different LIC test prices and for the proportion of tests that are sold to LIC markets.

Illustrative Analysis with a Single Manufacturer

Peak cumulative losses over 10-year period ($m)

LIC market price per test ($)	LIC volume as % of total tests sold				
	90.0%	**87.5%**	**85.0%**	**82.5%**	**80.0%**
$8.00	$103.2	$84.8	$63.0	$47.5	$34.3
$10.00	$21.4	$18.5	$15.5	$13.3	$11.0
$12.00	$6.0	$5.0	$3.8	$6.8	$5.6

At the base case price of $10.00 per test, cumulative losses range from $11-21 million, depending on the proportion of tests sold in LIC markets. Industry research indicates that LIC markets will represent a larger portion of total test demand for HCV than was assumed for tuberculosis (based on prevalence rates), which will mean a higher upfront investment and lower lifetime profits for the manufacturer.

A second analysis repeats the approach above but splits the test volume between two manufacturers, to demonstrate the economic impact of addressing concerns that an agreement with a single manufacturer creates a monopoly and/or constrains innovation.

Illustrative Analysis with Multiple Manufacturers

Peak cumulative losses over 10-year period ($m)

LIC market price per test ($)	LIC volume as % of total tests sold				
	90.0%	**87.5%**	**85.0%**	**82.5%**	**80.0%**
$8.00	$212.1	$191.9	$168.3	$141.3	$109.8
$10.00	$57.3	$42.9	$33.6	$45.9	$37.8
$12.00	$20.5	$16.9	$12.9	$8.4	$5.6

The analysis results in much larger upfront costs at the target $10.00 price of $38-57 million due to the additional time required for each manufacturer to reach a profitable level at the lower negotiated price.

Investability assessment

There seems to be a strong degree of interest in replicating the buy-down, though proposed adjustments to the structure increase the difficulty of execution and the ability to attract return-seeking capital.

Clarity

While pull mechanisms have rarely been used in the diagnostics market, the buy-down in its initial use was an effective way to increase developing world access to critical tests; however, it has received some criticism given its support of a single test and platform—and, by extension, a single manufacturer (Cepheid)—which raised concerns about potentially creating a monopoly and stifling or slowing innovation for second generation products. To mitigate this concern and garner sufficient donor support, an HCV buy-down should be structured with the capacity to include multiple tests (that use different manufacturer platforms). UNITAID, a lead donor in the first buy-down, has expressed interest in exploring this concept with that change incorporated. With that adjustment, a key challenge will be sizing the buy-down to accommodate scaling multiple manufacturers, which—as the economic analysis shows—is likely to require significantly more upfront capital than in the case of the tuberculosis buy-down where there was a single manufacturer. Nevertheless, supporting a portfolio of products and manufacturers may allow multiple solutions with distinctly useful applications to come to market.

Investors also noted that it may be difficult to justify extending a loan to the manufacturer without advanced purchase commitments or some other mechanism in place that would assure the investment could be repaid in a reasonable time frame (ideally 3-7 years).

Effectiveness

FIND's HCV diagnostics portfolio comprises a couple of near-term test candidates that could have a significant global health impact if priced appropriately. Since HCV remains largely undiagnosed due to the complexity and cost of existing diagnostics, more effective and accessible diagnostic tools could help to prevent a significant number of fatalities annually. To ensure the full potential benefits are achieved, stakeholders should consider whether the healthcare systems within target markets can appropriate administer tests and manage results.

Feasibility

There is no precedent of using a buy-down as a means to attract upfront investment capital, so the feasibility of the concept needs to be further explored with investors. The inclusion of multiple manufacturers is likely to complicate the discussions by increasing the number of stakeholders FIND would have to negotiate with, which would necessitate additional capital and legal expenses to draft a buy-down agreement that addresses the needs of all investors and donors.

IAVI CASE STUDIES

The International AIDS Vaccine Initiative (IAVI) was launched in 1996 and works with partners in 25 countries to research, design and develop AIDS vaccine candidates. It is headquartered in New York, with regional offices in the Netherlands, Kenya, South Africa, and India. The organization also conducts policy analysis and serves as an advocate for the AIDS vaccine field. It supports a comprehensive approach to addressing HIV and AIDS that balances expansion and strengthening of existing HIV prevention and treatment programs with grants targeted toward designing and developing new tools to prevent HIV.

Technology spin-off

OPPORTUNITY SNAPSHOT: IAVI TECHNOLOGY SPIN-OFF

Overview

A spin-off of IAVI's broadly neutralizing antibodies technology for HIV could help accelerate promising approaches to HIV prevention, treatment and cure, and may also present an attractive investment opportunity.

Assessment

Clarity	Medium
Effectiveness	High
Feasibility	Low

Key insights

- Further demonstration of the potential of the technology, as well as the ability to generate consistent revenues, will be necessary to appropriately assess the investment opportunity
- Development of a business plan that articulates roles and responsibilities in the new entity for IAVI and The Scripps Research Institute (TSRI), what resources will need to be dedicated and the revenue potential is an important next step to assessing whether to pursue this strategy

Overview of potential investment

Through its discovery and development work, IAVI and its collaborators have identified a number of broadly neutralizing antibodies that may form the basis for innovative approaches to HIV prevention, treatment, and cure. Additional efforts to improve performance, scale manufacturing, and explore optimal delivery of these antibodies are underway or being considered. If successful, these approaches would make the delivery of a globally accessible product achievable and affordable and, as a result, may be attractive to companies working in HIV, as well as impact investors, given the existing commercial market for HIV prevention and therapy.

Several of the IAVI-discovered broadly neutralizing antibodies are already the subject of commercial interest, and have either been licensed to industry or are currently under discussion for licensing. IAVI anticipates that, working in partnership with The Scripps Research Institute (TSRI), the organization has the ability to discover other potent broadly neutralizing antibodies with additional commercial applications. IAVI also believes that scaled-up, low-cost

manufacturing options and effective delivery options will further enable this initiative to contribute to improved HIV prevention, treatment, or cure approaches, which are well aligned with IAVI's core mission and ultimately could generate significant commercial revenues that could be used to support IAVI's vaccine development activities.

By spinning out the antibody discovery and development work into an affiliated entity, IAVI may be able to more effectively access the partnerships and funding required to accelerate this effort. If successful, the initiative may, first and foremost, help address the HIV epidemic, and also generate additional unrestricted funding for IAVI and its partners through licensing revenues (e.g., milestone payments and product royalties). These revenues may provide the means to attract return-seeking capital.

Technology spin-off opportunity in context

Market context

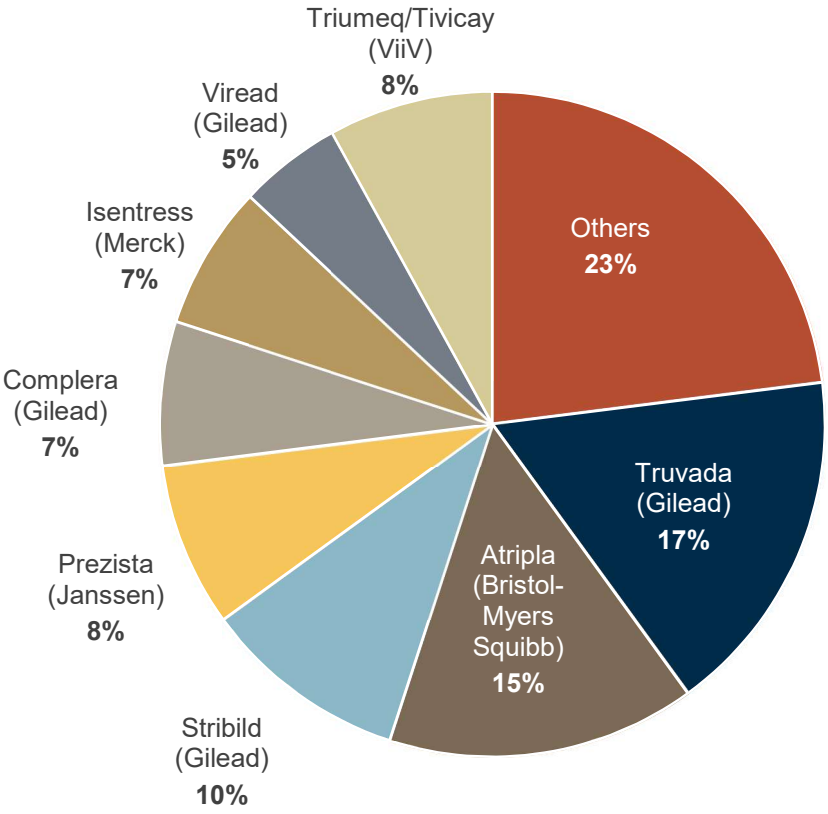
Despite a decrease by almost one-third in new HIV infections and AIDS-related deaths since the early 2000s, HIV remains a substantial global health challenge. As of 2015, 37 million people worldwide were living with HIV, with developing countries bearing a disproportionate amount of the burden and accounting for 98 percent of all AIDS-related deaths.[25] Access to appropriate antiretroviral therapy is vital to prevent HIV morbidity and mortality, yet only an estimated 37 percent of all infected individuals received treatment in 2015. The main cause for the treatment gap seems to be lack of effective diagnosis, as only about 54 percent of HIV-infected individuals are aware of their condition.

With over 2 million new HIV infections in 2015, efforts to improve effective HIV prevention and treatment options remain a global health priority. The antiretroviral (ARV) pipeline remains robust and includes several promising candidates. The existing global HIV drug market is fragmented across a number of manufacturers and generated $24 billion in sales in 2015. Sales are projected to reach $25 billion by 2019 with an average growth of 9 percent from 2010-2015. The United States was the dominant national market for HIV therapies, accounting for about 66 percent of total sales by value. In contrast, the market for ARVs in low- and middle-income countries, where the highest HIV burden remains, is estimated at $1.5 billion, which represents 6 percent of the monetary value of the global ARV market. International donors continue to play an important role financing HIV interventions in the developing world. Total donor funding was estimated at $19 billion in 2015, of which a significant portion was dedicated for treatment purchases. Yet donor-led procurement has resulted in consolidation on both the supply and demand side for ARVs in developing countries, with a relatively small number of manufacturers engaged in product development

[25] WHO. *"Global Health Observatory Data: HIV/AIDS."*

and sales for low- and middle income markets. Such a concentrated market effectively limits competition and creates price pressures.[26] [27] [28] [29]

GLOBAL HIV DRUG MARKET



$24 BILLION IN SALES IN 2015

Despite the large number of drugs approved for HIV, distinct unmet needs exist for an efficacious medication with a strong safety profile that 1) offers a simple treatment regimen, and 2) is accessible to developing countries. The R&D focus has shifted to new, extended-duration ARVs for both therapy and prevention. Moreover, the early-stage R&D pipeline includes a number of broadly neutralizing antibodies.[30] From what was a small handful of broadly neutralizing antibodies just seven years ago, researchers have now amassed hundreds of these powerful infection-fighting proteins to have them guide vaccine design, aid in HIV

[26] Nature Reviews. *"The HIV Therapy Market."* (2016)

[27] Clark and Gohil. *"In the crowded HIV market, there is room for innovation."* (2015)

[28] Transparency Market Research. *"HIV Market – Global industry analysis, size, share, growth, trends and forecast 2014-2020."* (2014)

[29] Note on pie chart: Gilead, Merck, and BMS have all participated in the development and/or distribution of Atripla; J&J and Gilead have both participated in the development and/or distribution of Complera

[30] TAG and i-base. "*HIV & TB Pipeline Report*." (2016); also referenced press releases, and data from IAVI

prevention more broadly, serve as a potential long-acting HIV treatment, and even to explore them as a component of an eventual cure strategy.

ANTIBODY	DISCOVERER / OWNER	STAGE (# OF TRIALS)
VRC01	National Institute of Allergy & Infectious Disease (NIAID)	Phase I/II (4)
3BNC117	Rockefeller University	Phase I/II (2)
10-1074	Rockefeller University	Phase I (1)
PGT-121	IAVI/TSRI/Theraclone	Phase I
PGDM 1400	IAVI/TSRI/Cornell University	Phase I (to start by 2018)

Industry has also been pursuing various approaches to HIV therapy and cure, using broadly neutralizing antibodies or newly developed antibody approaches. IAVI-generated antibodies, co-discovered and co-owned with TSRI and Theraclone Sciences, were commercially licensed by Theraclone to Gilead for HIV therapy. Additional antibodies are currently the subject of licensing discussions with industry.

Spin-off opportunity

Companies with proprietary platform technologies can generate revenue by: (a) licensing a part of their technology to larger pharmaceutical companies and (b) creating spin-off companies that develop specialized tech applications for specific disease areas. These spin-offs tend to use the parent company's technology as the foundation to create disease-specific platforms that have their own management, responsibility for funding, and business development. Some may even remain partially owned by the parent company.

Determining an appropriate structure and business plan, as well as identifying potential funding sources, will be critical to assessing the viability of this option for IAVI. TSRI has a depth of experience spinning out companies, with more than 70 spin-offs since 1980. To date, IAVI and TSRI have partnered to isolate antibodies from samples provided through IAVI's global research. The potential new entity would be structured so that TSRI and IAVI continue to contribute subject matter expertise and IAVI provides the samples, additional necessary resources, and partnership coordinating capacity to support the spin-off in executing on its strategy. In addition, it is notable that there is precedent among PDPs for this type of structure. The Infectious Disease Research Institute (IDRI) has spun out technologies opportunistically to access small business grants and development funding, as well as to out-license indications for these technologies that were outside of IDRI's primary scope to identify and develop new diagnostics, drugs, and vaccines for infectious diseases.

Economic and structural considerations

The potential economic value of an investment in a new entity could be compelling if the passive administration of antibodies proves to be effective in preventing or treating HIV in clinical trials. IAVI has begun to map the additional efforts that will be required in HIV antibody discovery, development, manufacturing, and delivery, to optimize the probability of success of antibody-based HIV interventions.

Further, the portfolio of existing and newly developed antibodies may provide attractive licensing opportunities, which could generate revenues to support the initiative; however, these revenues will be highly dependent upon the entity's ability to structure licensing agreements, as well as the technical feasibility of developing a successful product and the sales it generates. Interest from investors will be driven by an understanding of antibody technology and its promise within the HIV prevention, treatment, and cure market; and likely mission alignment around developing solutions for HIV.

IAVI is considering the establishment of a new affiliated entity, in partnership with TSRI, and potentially other collaborators. In its initial phases, the entity would largely be supported by IAVI with the staffing, coordination, and resources required to drive the initiative. The structure and shareholding arrangement is still to be determined, although careful consideration will need to be given to a structure that provides enough incentives for all stakeholders and remains flexible enough to engage additional partners deemed complementary to the initiative.

IAVI would retain rights to use the antibodies as a tool to develop vaccines (where the antibody will not be part of the final construct) while the new entity would have the rights to use the antibodies in products for prevention, treatment, and cure. Out-licensing of antibody rights to industry collaborators could generate additional revenue streams for the initiative. Likewise, future product royalties would be another potential revenue stream. Mission alignment for global health goals would be ensured by either reserving license rights for certain fields or geographies or through access commitments from industry collaborators.

Investability assessment

Early indicators are positive for establishing an antibody-focused spin-off, although there are a number of hurdles to developing it into a financially sustainable, mission-driven enterprise capable of attracting outside investment.

Clarity

The use of broadly neutralizing antibodies in HIV prevention, treatment, or potentially cure strategies is currently being actively explored by both academic researchers and industry. However, proof of concept has not yet been established in humans. If technical feasibility can be demonstrated and strategies for monetizing rights to the antibodies (or antibody-based products) can be developed, investors will be more willing to explore a potential investment opportunity, given the size of the HIV prevention, treatment, and cure market. Broadly

neutralizing antibodies have been licensed previously, so the contemplated proposal would build on that experience and encompass advances that are being made in the technology.

The entity's ability to generate revenues depend on whether it can effectively advance product development and out-license rights in exchange for milestone payments and royalties, making the revenues variable and unpredictable. This creates a risk profile that may be unsuitable for many investors other than venture capital or early-stage biotech investors, in addition to certain impact investors.

Effectiveness

IAVI's broadly neutralizing antibodies could have potential uses for HIV prevention, treatment and cure (in addition to possible use in an HIV vaccine), which could have significant positive global health impact for one of the world's major diseases. Broadly neutralizing antibodies could form an important basis for an efficacious HIV intervention with a strong safety profile that offers both a simple treatment regimen and is accessible to developing countries.

Feasibility

IAVI will need to generate a business plan that clearly articulates the need, opportunity, and feasibility of this initiative, as well as the team required and the various collaborations that will be needed, along with funding needs. This will require additional discussion at the senior management and board level, as well as external consultation with outside counsel and other experts. In addition, the organization would likely need to establish a separate legal entity and dedicate resources to coordinate and drive the initiative in a mutually beneficial partnership with TSRI that allows for additional collaboration partners. IAVI and TSRI will need to agree on a resource plan and an appropriate sharing of rights, roles, responsibilities, and benefits as part of the partnership. While these activities are feasible, the time and cost to implement them is likely to be extensive and should be measured against the potential benefit.

In addition to considering time, cost, and resource implications of any legal structure, consultation with IAVI's key funders and partners would also be an important part of the process. PDPs will need to manage existing funder relationships to ensure that any new activity or strategic shift is perceived and understood as a constructive and positive evolution of the activities already being funded by donors. Donors will certainly have a view on if and how return-seeking capital can be introduced in a way that is complementary and additive, rather than distracting or detrimental to a PDP's mission.

Services spin-off

OPPORTUNITY SNAPSHOT: IAVI SERVICES SPIN-OFF

Overview

Through its Human Immunology Lab (HIL), IAVI performs clinical trial services that have attracted outside interest, giving rise to the potential for establishing the HIL as self-sustaining entity.

Assessment

Clarity	Medium
Effectiveness	Medium
Feasibility	Low

Key insights

- Evolution of the HIL activities, structure, and business model creates potential risks in prioritizing IAVI's mission, which will require active mitigation
- Development of a business plan that includes the HIL's go-to-market strategy and clarity on IAVI's role and relationship to the new entity is essential to engaging investors in a constructive conversation

Overview of potential investment

IAVI established the Human Immunology Lab (HIL) at Imperial College London in 2001 as the central repository for samples collected in IAVI-sponsored HIV vaccine trials and epidemiology studies. Since then, the HIL has taken on contract work for vaccine development in HIV and other disease areas. With a 15-year track record for high-quality, rigorous clinical immunology and sample management, pharmaceuticals, and biotech firms have begun to approach the HIL for contract work, which presents a potential pathway for transforming the lab into a self-sustaining business.

Currently, the HIL is pursuing new service contracts with industry partners that could generate significant revenues over the next 24 months. These contracts are structured to include operating margins that would support growth and strengthen HIL service offerings (all other nonprofit-related contract work is priced pursuant to the funder's terms and conditions). If the team can successfully differentiate itself in the contract research organization (CRO) market, this represents a first step on a pathway towards financial self-sustainability for the HIL. Further, if a business and growth strategy can be defined that would provide sufficient cash flows, IAVI could consider how impact investment could support expansion of the HIL's work either directly or through an investment in IAVI.

Services spin-off opportunity in context

Pharmaceutical R&D is a complex and risky undertaking that can take 10-15 years and cost up to a billion dollars or more, with only a limited number of evaluated compounds ultimately receiving FDA approval. Certain market-level innovative financing mechanisms, such as volume guarantees, have tried to mitigate and offset that risk by underwriting market demand

uncertainty and guaranteeing a margin to developers. As a result, pharmaceutical companies have increasingly sought to introduce efficiencies into their operational models. By outsourcing some of their development activities to specialized contract research organizations (CROs), pharmaceutical, biotech, and medical device companies can effectively reduce their fixed costs. These CROs, which initially served as providers of discrete services and additional capacity, have grown to a $30 billion industry that has become an integral element to the global R&D process.[31]

IAVI initially established the HIL in 2001, as an internal infrastructure development project with the aim to build out IAVI's capacity for sample collection and processing for its HIV vaccine trials and epidemiology studies. Over time, the HIL has evolved to become a core component of IAVI's clinical development efforts and a well-reputed provider of clinical immunology services and contract work to IAVI's partners, constituting an important source of revenue for the PDP. Leveraging IAVI's expertise in vaccine development and evaluation, the HIL has been successful in attracting key partnerships with larger pharmaceutical companies (e.g., GSK, Johnson & Johnson, and Merck) and other PDPs, including PATH's Malaria Vaccine Initiative (MVI), as a reference laboratory for clinical immunology services.

It is those partnerships that help the HIL distinguish itself in an increasingly more crowded CRO market landscape. Other CRO immunology service providers, which differ in scale and global reach, often set themselves apart through greater specialization in product and disease focus. As IAVI considers a growth strategy for the HIL, it will need to identify its distinct competitive advantages and consider how to position itself vis-à-vis its peer group.

[31] Harris Williams & Co. "*Contract Research Organization Industry Overview*." (2014)

	SERVICE OVERVIEW	FUNDING	DIFFERENTIATION
HIL	• Reference clinical immunology lab • Assay development • Biobanking • Training and capacity building	• Government • Foundations • Commercial	• Key existing partnerships with larger pharmas, governments, and foundations
PROIMMUNE	• Preclinical and clinical immunology research management and support	• Commercial	• Specializes in immunology and pentamers development
HIV VACCINE TRIAL NETWORK	• HIV vaccine development across all phases of clinical trials	• NIAID • Bill & Melinda Gates Foundation	• Key partnerships with Duke University and specialty in HIV
ADVANCED BIOSCIENCE LABS	• Manufacturing and lab research for vaccine and therapy development	• Government • Commercial	• Global reach and decades of experience
EUROFINS	• Analytical testing services across a broad range of biopharma services	• Commercial	• Global footprint across a range of industries

Economic and structural considerations

To better understand the potential economic impact of a standalone services business, different scenarios for growth and profitability were modeled for the HIL business. The following assumptions underpin the analysis:

- Growth rates are shown in a range around a midpoint of 6 percent, the current growth rate of the clinical trial subsegment of the CRO industry.
- Operating margins are based on reaching different levels of profitability by year 10, ranging from a low of 5 percent (representing a conservative case where operations do not scale efficiently) to a high of 11 percent (consistent with operating margins at publicly traded peers).
- For illustrative purposes, it was assumed that IAVI would receive 25 percent of any operating margin as a dividend to arrive at a 10-year cumulative dividend figure, the results of which are shown across different growth rates and operating margin levels.

Illustrative 10-year Cumulative Dividends to IAVI ($000s)

Target operating margin \ Annual revenue growth	0.0%	3.0%	6.0%	9.0%	12.0%
5.0%	358	423	502	598	713
8.0%	495	592	710	854	1,027
11.0%	632	761	918	1,109	1,341

The various assumptions produce a range of $360,000 to $1.3 million for the 10-year cumulative dividend, as seen in the table above. As the results demonstrate, the level of growth and margin can produce meaningful differences in the cash flow generated by the HIL, which should inform its growth and financing strategies.

As for structural considerations, additional assessment is needed to determine whether the HIL would operate as a for-profit subsidiary of IAVI or as a separate standalone entity with IAVI retaining some ownership stake. IAVI must also evaluate the cost and benefit of various structural options, including the HIL remaining at Imperial College or relocating to a lower-cost jurisdiction. These decisions will impact the structure and terms of any potential investment into the HIL.

IAVI will need to determine with the HIL leadership what the mission of the standalone services business will be. If not explicitly linked to global health objectives, it will be difficult to attract impact investment capital and it may result in longer-term mission drift. The current intent of both IAVI and the HIL is to link the mandate and strategy of the spun-out entity to IAVI's mission and also to support the broader field of global health.

Investability assessment

Early indicators are positive for establishing the HIL as a standalone services business, though there are a number of hurdles to developing it into a financially sustainable, mission-driven enterprise.

Clarity

The services business has the potential to attract outside capital given general growth and interest in the CRO industry, which could facilitate the growth of the HIL enabling it to expand to provide contributions more broadly in the field of global health and also potentially generate additional unrestricted income to IAVI. There are a number of key economic terms that need to be further evaluated to assess the financial viability of a standalone services business and, further, its ability to attract outside investment:

- Appropriate pricing model and balance between margin-generating contracts and those delivered at cost,
- Top-line growth plan and supporting go-to-market plan,
- Resource and staffing model to support growth plan, and
- IAVI's ownership share in the entity.

IAVI and the HIL's leadership are beginning to evaluate the appropriate structure for a potential evolution of the HIL to a for-profit business: whether to keep it embedded in Imperial College or spin it out as a standalone entity, potentially relocating to a more affordable location. It should further be considered whether the Imperial College relationship could support the building or marketing of the business. These details will significantly impact the costs to run the business and the terms of any investment.

Effectiveness

As a standalone CRO, the HIL can provide significant value-add to larger developers and allow for more efficiency in clinical immunology and sample management, although the global health impact will depend on the HIL's mission—which is intended to remain linked to IAVI's—and the balance of work they undertake for nonprofit clients (e.g., IAVI, Bill & Melinda Gates Foundation) as opposed to for-profit clients (e.g., pharmaceuticals).

Feasibility

The HIL differentiates itself through its ability to deliver high-quality, customized services that meet global regulatory standards. The organization has successfully demonstrated its value-add through the provision of clinical trial immunology and sample management services and support with a range of external partners across disease areas, including HIV, malaria, tuberculosis, and Ebola. To ensure the success of a spin-off, a go-to-market strategy needs to be developed to determine the competitive strategies that will support growth.

Further, IAVI and the HIL need to agree on a standalone mission for the business that has the means to attract impact investment and ensures that the business can continue to support both IAVI's mission and a growing portfolio of third-party vaccine work. Similar to the technology spin-off, the activities required to spin out the HIL and maximize its potential for success are likely to be time- and resource-intensive and should be considered against the potential benefits.

PATH CASE STUDIES

PATH was launched in 1977 with modest seed funding from the Ford Foundation. Its early goals focused on improving access to contraceptive technologies, but its focus has since expanded to an array of health technologies. It is headquartered in Seattle, with 43 offices around the world that implement projects in more than 70 countries. The organization works across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that seek to scale innovations, with a particular focus on women and children.

Private sector partnerships

OPPORTUNITY SNAPSHOT: PATH PRIVATE SECTOR PARTNERSHIPS

Overview

PATH's portfolio of diagnostics, devices, and tools contains a number of private sector collaborations that could present an opportunity for partnerships that generate financial value as well as global health impact for PATH.

Assessment

Clarity	Low
Effectiveness	Medium
Feasibility	Medium

Key insights

- Pursuit of a revenue-generating opportunity presents a shift in strategy that may introduce mission drift or conflicts of interest; these costs and risks have to be measured against the potential benefit to assess whether PATH should continue exploring this concept
- Demonstrates need to build consensus with internal and external stakeholders as part of the development and evaluation of the investment opportunity

Overview of potential investment

PATH engages with private sector actors across its portfolio of development work. In particular, its portfolio of diagnostics, devices, and tools often attracts private sector collaboration in development and distribution because of the ability to apply or implement the underlying technologies in commercial, developed market settings. This signifies an opportunity for PATH to more strategically and intentionally explore the ability to generate revenue from these collaborations in exchange for access to the technologies, tools, and expertise within PATH. Further, the dual-market opportunities offer the potential for PATH to consider arrangements that would generate financial value as well as impact. The structure for each relationship will vary depending on the nature of the collaboration and the potential market for the product selected.

The case study examines a sample of existing products and partnerships to consider the conditions necessary to structure a revenue-generating arrangement for PATH. If the partnerships could be designed to generate reliable and significant revenue streams, they could provide the means to attract outside investment in PATH's work.

Private sector partnerships opportunity in context

	UNIJECT™ INJECTION SYSTEM	SILCS (CAYA) DIAPHRAGM	SE200 COMMUNITY CHLORINE MAKER	NIFTY INFANT FEEDING CUP
PRODUCT DESCRIPTION	Prefilled, auto-disposable injection system that can be administered in low-resource settings	Contraceptive alternative redesigned for fit, comfort, ease of use, and lower manufacturing cost	Portable, affordable device to generate chlorine solution that can treat 200L of water for safe drinking	Device for delivering milk to infants unable to breastfeed or other feeding difficulties
PRIVATE SECTOR PARTNER(S)	Becton Dickinson (BD)	Kessel medintim GmbH	Mountain Safety Research (MSR, subsidiary of Cascade Designs)	Laerdal Global Health (LGH, non-profit subsidiary of Laerdal Medical)
NATURE OF COLLABORATION	BD manufactures and sells Uniject	Product available in developing world at preferential pricing, exploring multi-purpose use (e.g., with ARVs)	Product available in developing world at preferential pricing (through donors and governments)	Product available in developing world at $1/cup through LGH
VALUE TO PATH	Manufacturing and marketing expertise of BD; distribution capabilities	Manufacturing and marketing expertise of Kessel; distribution capabilities	Technical, manufacturing, and marketing expertise of MSR; distribution capabilities	Manufacturing and distribution capabilities
VALUE TO PRIVATE SECTOR PARTNER	Access to PATH IP, PATH's knowledge of developing world and use cases for technology	Access to PATH IP, strategic fit of SILCS in existing offering, PATH's knowledge of developing world	Brand / reputation value, PATH's knowledge of developing world	Strategic fit of NIFTY cup in existing LGH offering, potential to market in developed world through parent
SOURCE OF REVENUE	Licensing fees for technology transfer and lump-sum payment in lieu of royalties on Uniject sales	Royalties on developed market sales of Caya	None	None; PATH co-developed design and decided with development partners to make it open source

The selected products above showcase the different approaches to collaboration PATH takes with the private sector. Revenues have only been possible when PATH has sole ownership of the IP and the private sector partner sees potential for financial and strategic value by accessing and using that IP.

More detail on the Uniject and SILCS partnerships arrangements reveals the conditions necessary to establish revenue-generating agreements. In the case of Uniject, the underlying injection technology was designed and developed by PATH and licensed to Becton Dickinson (BD). BD

paid licensing fees over five years to PATH to transfer the IP and agreed to pay a royalty on all sales of Uniject until the expiration of the patent. After the first few years of the license, PATH determined that it needed to address the perceived financial conflicts of interest around royalties on Uniject sales for use in developing countries. As a result, PATH monetized the Uniject royalty stream by taking a one-time, lump-sum payment in lieu of future royalties.

For the SILCS partnership, PATH was able to develop and realize an arrangement to market and distribute SILCS (under the brand name Caya) with Kessel because it was the "right product at the right time." Kessel is a smaller manufacturer with a focus on contraceptives, and the founder/CEO saw SILCS as an innovative design that would enhance and differentiate the company's product offering. SILCS also provided an opportunity for Kessel to respond to emerging European demand for non-hormonal contraceptive alternatives.

As PATH owns IP for the SILCS design, it was able to negotiate royalties on developed market sales of Caya (developing market royalties were intentionally excluded). To date, those sales have been limited, and the royalties PATH would receive do not exceed its cost to administer them. As a result, PATH has waived royalties until developed market sales reach a level where it would be profitable for PATH to receive them, and Kessel has committed to dedicating the waived royalty amounts to support marketing Caya in the developing world.

Based on a review of these two partnerships and contrasting them with the SE200 and Nifty Cup situations, it becomes clear there are three essential conditions to a successful revenue-generating private sector partnership for PATH:

- PATH has sole ownership of IP (either through creation or acquisition of product design or technical features);
- A private sector partner with a strategic, profitable opportunity to use the IP that compels them to provide licensing fees and, ideally, royalties; and
- To achieve PATH's global health objectives, the private sector partner should be willing to collaborate with PATH on the developing world opportunity (assuming they could do so at low-cost).

Investability assessment

Given PATH's successful track record of partnering with the private sector for commercialization of global health products, there is merit to considering a more intentional strategy for revenue generation, if internal concerns about conflicts of interest can be sufficiently addressed.

Clarity

Revenue-generating partnerships for PATH have been linked to design and technical features for which PATH owns the IP; however, due to a focus on leveraging existing products to quickly achieve global health impacts, its ability to generate IP in a reliable, ongoing fashion is limited. PATH's priority in pursuing projects is speed to market, which is more easily

executed through existing technologies and products, and as a result, creating and owning IP is not a strategic focus for PATH. To further its ability to generate revenues from private sector partnerships, PATH should consider how to incorporate the creation of IP as a strategic focus and consideration (while subordinating it to PATH's global health objectives).

Earning revenues from private sector actors who do not share the same global health priorities as PATH could potentially create reputational risks or conflicts of interest that need to be managed and contemplated as part of an agreement. Structuring in terms that allow PATH to engage with the private sector partner on product uses with applicability in the developing world is an approach to managing this risk. Generally, PATH needs to seek internal buy-in from senior management and its board to move forward, as such initiatives require adjustments to its strategy and add complexity to its relationships with private sector partners.

Effectiveness

Private sector partnerships offer the potential for PATH to consider arrangements that would generate financial value as well as impact, although the ultimate health outcomes will depend on the structure for each relationship, the nature of the collaboration, and the target market for the product selected.

Feasibility

If it can be shown that private sector partnerships present a reliable source of revenues as a strategic matter, investors will be more willing to explore a potential investment opportunity. The amounts of revenue that have been generated in prior partnerships, such as Uniject and SILCS, have been small and not sufficient nor reliable enough to support outside investment. Additional track record needs to be built to be able to engage with investors more concretely on this opportunity.

PATH management has demonstrated a commercial sensibility, and the organization has a deep track record of working with private sector partners to advance global health goals. Additional expertise is likely required, either internally or through outside resources, to develop a more strategic approach to identifying revenue-generating partnerships.

PRV-linked investment

OPPORTUNITY SNAPSHOT: PATH PRV-LINKED INVESTMENT

Overview

PATH negotiated and closed an investment that will support development of a drug eligible for a Priority Review Voucher (PRV) and would allow all parties to share in the financial upside of any sale of the PRV.

Assessment

Clarity	High
Effectiveness	High
Feasibility	Medium

Key insights

- Ability to link the investment returns to a potential PRV sale allowed both impact and commercial investors to participate and helped PATH justify the work needed to complete the transaction
- Highlights need for strong commitment from all parties—in terms of resources, time, and expense—to successfully execute a transaction

Overview of potential investment

PATH negotiated a $25 million investment from two investors—the GHIF and Clarus Ventures, a commercial biotech venture capital firm—that will support the development of tribendimidine, a potential treatment alternative to infections with soil-transmitted helminths (e.g., hookworm), which infect more than 1.6 billion people (including at least 800 million children). The treatment is eligible for a priority review voucher (PRV), so investor returns will be linked to cash generated from any sale of the PRV, once granted. Six PRV sale transactions have been completed thus far, with values ranging from $67 million on the low end to $350 million on the high end. The value of the PRV is linked to the buyer's economics (and the product it intends to use the PRV for) and the general market scarcity of PRVs available for sale to date.

This case study examines the $25 million investment, which will be completed in tranches: an initial tranche to support near-term development work followed by other milestone-linked tranches. Returns are funded through the sale of the PRV, with PATH and the consortium of developers keeping a portion of the proceeds and the remainder going to the two investors.

PRV-linked investment opportunity in context

The United States created the priority review voucher (PRV) program in 2007 to catalyze the development of drugs for neglected diseases. Under that program, a developer who registers an eligible drug is rewarded with both an expedited review for the eligible drug as well as a PRV for a drug of their choice. The FDA has awarded twelve PRVs since the inception of the program—eight vouchers for rare pediatric diseases and four for tropical diseases. Since PRVs can be sold, receipt of a voucher signals a potentially lucrative source of revenue that can offset part of the development costs and provide a return on investment to funders. To date, six recipients have sold their PRVs to other drug developers for amounts ranging from $67 million to $350 million.

COMPANY	PURCHASER	DATE	VALUE ($M)	USE OF PRV
BIOMARIN	Sanofi	July 2014	$67	Received FDA approval for cholesterol drug
KNIGHT THERAPEUTICS	Gilead	Nov 2014	$125	Received FDA approval for HIV treatment
ASKLEPION PHARMA	Sanofi	May 2015	$245	Redeemed for Type 2 diabetes drug process
UNITED THERAPEUTICS	AbbVie	Aug 2015	$350	Use undisclosed
UNKNOWN	Gilead	July 2016	Unknown	Disclosed in Gilead SEC filing; terms not included
SAREPTA	Gilead	Feb 2017	$125	Use undisclosed

A 2016 study concluded that the value of a PRV to its buyer is primarily driven by capturing market share and earlier-to-market sales, as well as barriers to entry for generic manufacturers.[32] A PRV can typically give a four-month market advantage to the recipient and is therefore considered a potential major windfall for a blockbuster drug. Scarcity seems to be another driver of value. With only 12 PRVs awarded to date, access is limited. If more than one PRV were available for sale at any one time, however, the value of each would fall to less than half of what it would be otherwise.[33] Since the number of potential PRV candidates is increasing, there is growing concern that future PRV awards may dilute market values. Nevertheless, the significant value PRVs have commanded thus far continues to draw attention to the program.

In 2015, GHIF announced the closing of a transaction that linked its returns to the sale of a PRV. The investment will support development of a treatment for river blindness in partnership with Medicines Development for Global Health. More details are in the case study below.

[32] Ridley and Regnier. "The commercial market for Priority Review Vouchers." (2016)
[33] Ridley and Regnier. "The commercial market for Priority Review Vouchers." (2016)

CASE STUDY: FIRST PRV-LINKED INVESTMENT

- Medicines Development for Global Health (MDGH), founded in 2005, is an Australia biopharma company working on development and delivery of medicines and vaccines that address unmet need
- In 2015, the GHIF committed $10 million to MDGH to complete registration of moxidectin (a drug for river blindness)
  - Development of moxidectin is eligible for a PRV
  - GHIF's investment was first-of-a-kind in linking the financial return to the awarding and subsequent sale of a PRV; there would be no means for a return otherwise
- If the drug is approved and wins a PRV, MDGH estimates that they could receive proceeds of ~$40 million and intends to use them to:
  - Provide a return on the GHIF investment
  - Support global access to moxidectin
  - Establish a drug development fund to support development of moxidectin for other neglected tropical diseases

Transaction overview

Based on precedent sale values of PRVs, a transaction linked to the sale of a PRV can provide compelling financial returns and thereby attract return-seeking capital to otherwise uninvestable projects, which is the goal of the PATH transaction. The $25 million investment in PATH will be deployed in tranches—an upfront investment with additional capital deployed based on reaching key development milestones. In the base case scenario, PATH believes a PRV could be received in 2020, with the sale taking place that same year; proceeds from the sale would be shared between the investors and PATH (who will share with a small consortium that is supporting the development work).

Illustrative Analysis of PRV-linked Transaction
Investor IRR assuming 60% of PRV sale value received

Year of PRV sale	Sale value of PRV (in $m)					
	$25	$50	$75	$100	$150	$200
Year 4	27.7%	10.3%	34.4%	52.8%	81.2%	103.4%
Year 5	17.4%	6.6%	22.2%	34.0%	52.0%	65.6%
Year 6	12.9%	4.9%	16.3%	24.8%	37.7%	47.4%
Memo: MOIC	*0.6x*	*1.2x*	*1.8x*	*2.4x*	*3.6x*	*4.8x*

Illustrative Analysis of PRV-linked Transaction
Investor IRR assuming 30% of PRV sale value received

Year of PRV sale	Sale value of PRV (in $m)					
	$25	$50	$75	$100	$150	$200
Year 4	67.5%	27.7%	-5.8%	10.3%	34.4%	52.8%
Year 5	38.7%	17.4%	-3.7%	6.6%	22.2%	34.0%
Year 6	28.7%	12.9%	-2.7%	4.9%	16.3%	24.8%
Memo: MOIC	*0.3x*	*0.6x*	*0.9x*	*1.2x*	*1.8x*	*2.4x*

While the specific terms are not disclosed, the analysis below looks at the sensitivity of investor returns based on a range of potential PRV sale values and the year in which the sale takes place (as compared to the year of the initial investment). This analysis treats the investment as being made by a single investor, and for an illustrative comparison, two scenarios are considered: one where the investor received 60 percent of the PRV sale value and another where it only receives 30 percent. If precedent PRV sale values hold, the financial return looks commercially attractive to an investor in most scenarios in the illustrative analysis.

Investability assessment

PATH's PRV-linked investment provides insights on investment structure, deal negotiation, and execution strategies relevant for any PDP transaction with return-seeking investors.

Clarity

PATH was able to attract impact investment capital from the GHIF and commercial investment capital from Clarus Ventures, a commercial biotech VC firm. The relatively low technical risk and the strength of PATH's track record of development experience were essential to convincing investors to participate, particularly Clarus. There is still risk related

to receiving the PRV and the ultimate sale of the PRV. There is no certainty there will be a buyer, and if additional PRVs came to market at the same time, it could diminish the potential return. Investors interviewed also agreed this structure should be attractive to venture capital and equity impact investors, assuming the PRV program does not end and that current sale precedents do indeed prove indicative of future sale values.

Effectiveness

Linking investment in its development work to the potential sale value of a PRV gives PATH the means to attract diverse and larger sources of capital to support its mission. Given the interest of Clarus—a traditional commercial investor—in the opportunity, PATH wanted to ensure there would be no risk to mission, so it insisted that GHIF be brought in as a partner and additional source of capital. Including GHIF in the process helped to ensure that global health goals were kept front and center of negotiations and appropriately incorporated into the transaction agreement.

Feasibility

PATH was able to monetize their familiarity with the global health landscape and their development capabilities without owning any IP, though evolving the proposal to the point that it attracted investment capital came at a high internal cost. Normally, the PDP funding model is focused on restricted project financing that does not allow staff to deploy their time towards non-project based activities. PATH benefited from a pool of flexible capital that allowed them to free up staff and engage them in this PRV-linked investment opportunity.

The negotiation process was long and expensive, due to the complexity of structuring a novel investment with actors driven by different motivations and preferences and coming from different cultural contexts. To counteract this, GHIF played an important role as “translator” during the deal process, helping bridge communication gaps between deal negotiators. Additionally, PATH was able to bring some internal transactional legal expertise to the table. While each of the participants has acquired skills and experiences that would make another negotiation process more efficient—and PATH will consider future PRV opportunities as a result—it is more difficult to transfer or share those benefits with different actors (particularly those in different legal or tax jurisdictions). Standardization of structure and terms should be pursued if additional deals are to be done by others in the field, and all involved parties should consider agreeing to cap the amount they want to spend on legal and transaction fees.

PATH’s senior management and board remained committed to the deal throughout and actively supported the deal negotiation and closing process. This internal buy-in is essential to cultural willingness to consider—and execute—unique transactions like these. The deal team cited the commercial expertise of the senior leadership and board, in addition to global health expertise, as being particularly helpful in navigating the negotiations. This commercial expertise will help ensure that PATH is able to manage reporting and communication with Clarus, whose needs in that regard differ from those of a traditional donor.

5. IMPLICATIONS FROM THE PDP CASE STUDIES

Summary of the case study assessments

While each of the investment prototypes is unique—representing a specific opportunity with its own set of potential benefits as well as challenges—collectively, the array of case studies reveals a number of common themes and insights related to the investability of PDPs more broadly. These points can be summarized within the investability framework presented at the outset this report:

- **Clarity:** Is there certainty about the market opportunity, and what is the nature of the underlying economics?
- **Effectiveness:** Does the concept deliver on global health impact objectives?
- **Feasibility:** What is the experience of the PDP in commercial environments, are the time and cost to implement likely to be reasonable, and do the PDP's core stakeholders support the approach?

For ease of reference, the assessment of the investment opportunity within each case study is summarized in the table below. At this stage, the assessment should not be interpreted as a recommendation or determination for or against any of the opportunities. In all cases—with the exception of the PRV-linked investment, which has already been completed—additional work needs to be done to confirm that (a) attracting impact investment may be feasible, and (b) the benefits of doing so outweigh the costs. The PDP assessments helped to identify specific and actionable insights that would help to support any future cost-benefit analyses.

PDP	CASE STUDY	CLARITY	EFFECTIVENESS	FEASIBILITY
FIND – Because diagnosis matters	R&D Investment	M	H	M
	Manufacturer Buy-down	M	H	L
IAVI – International AIDS Vaccine Initiative	Technology Spin-off	M	H	L
	Services Spin-off	M	M	L
PATH	PRV-linked Investment	H	H	M
	Private Sector Partnerships	L	M	M

As the table illustrates, some opportunities are at a more advanced stage of development than others. Some are also more likely to have promise as investment opportunities. By comparing across all six case studies, a number of core themes for further exploration and consideration can

be developed. The following section explores each of these themes in greater detail to help inform specific go-forward strategies for each opportunity, as well as to strengthen the investability of PDPs and their activities generally.

Implications of assessment findings

Promising opportunities

In the process of designing and developing products that support their mission, PDPs have created unique technologies, services, and strategies with broader potential applications. Where those applications have commercial value—e.g., a developed market opportunity or strategic value to private sector companies—there may be an opportunity to monetize that value. This provides a means to potentially generate diversified sources of revenue (which many PDPs have already begun to explore to mitigate reliance on a single funding strategy and as an evolution of the collaborations inherent to their strategies). In some cases, these revenue-generating activities may form the basis for an impact investment opportunity; however, as the case studies show, there are a number of factors that determine actionability beyond the ability to create financial value. This includes evidence of the ability to generate consistent returns, financial experience to manage deal structuring and negotiation, stakeholder buy-in to the approach, and a resource-efficient strategy to get there.

In the process of designing and developing products that support their mission, PDPs have created unique technologies, services, and strategies with broader potential applications.

Capacity and execution

The research revealed that management within the selected PDPs are clearly capable of thinking creatively about strategies for diversifying revenues; however, internal bandwidth is a real constraint in advancing these strategies. Further, establishing revenue-generating activities as a channel for attracting impact investment would be a challenge for many PDPs. In part, this is due to a lack of investment and transactional legal expertise to appropriately develop, assess, and implement investment structures on their own—a necessary complement to the deep scientific and operational experience the PDPs generally already possess. In addition, there is limited precedent for investments in global health R&D and almost none in PDPs. Lessons from the few existing transactions and partnerships have not been widely studied or shared, so they are difficult to reference and leverage.

Aside from the execution, legal, and tax considerations of these opportunities, most PDPs are also concerned about the implications for resources and operations, particularly given the aforementioned bandwidth constraints. While each case study presents an interesting opportunity for diversifying revenues and potentially attracting impact investment capital, the

underlying activity represents a small portion of the broader work each PDP is engaged in. Pursuing any of these opportunities further is likely to consume a disproportionate amount of time and resources, which needs to be managed.

Unintended consequences—particularly the creation of real or perceived conflicts of interest—are also a concern that PDPs need guidance in assessing.

Finally, unintended consequences—particularly the creation of real or perceived conflicts of interest—are also a concern that PDPs need guidance in assessing. This issue is often raised in the context of introducing a profit or revenue motive to mission-aligned organizations, and in the case of PDPs, this may create threats to culture, organizational mandates, or funder priorities. There is significant precedent in the impact investment industry of non-profit organizations successfully transitioning to self-sustaining, for-profit models through the support and integration of management, employees, funders, and other stakeholders during the process.

A couple of the case studies also incorporate private sector partners or investors who are mission-agnostic, which has been flagged as a difficult discussion with boards and funders. In particular, the perspective of donors and funders is a significant focus for PDPs, as these are their primary source of support. There is general wariness in the donor community about the private sector that needs to be addressed upfront through active dialogue and engagement. Although safeguards can be put into place within investment structures to protect or enhance impact, this needs to be front and center of any negotiation and there should be organizational and stakeholder consensus on the path forward.

Investor motivations and alignment

Although the featured investment prototypes demonstrate a variety of ways to increase unrestricted funding for the PDPs, not all of them naturally lend themselves to attracting return-seeking investment. Where there is precedent for a potential investment structure—such as the R&D investments in FIND, the IAVI services spin-off, or the PATH PRV-linked investment—the potential opportunity is more obvious. Where additional demonstration may be needed (e.g., IAVI's technology spin-off or PATH's private sector partnerships) or where an investment requires a degree of financial innovation or creativity (e.g., the manufacturing buy-down opportunity), the pathway to attracting return-seeking capital is murkier.

This idea was tested with a range of private investors with some knowledge of global health. In the conversations held, investors expressed more interest or curiosity in those possibilities that have a clearer opportunity for investment. In all cases though, any real consideration by a potential investor would have to come with further development and refinement of the ideas. It is difficult for an investor to assess an opportunity without an articulation of key terms (e.g., size, tenor, pricing) and risks.

Further, while there are some impact investors focused specifically on health, few have had much experience with investment opportunities in global health R&D; therefore, finding alignment with their investment strategies is challenging. Where there is potentially alignment, investors would prefer to see a lead or anchor investor with deep subject-matter expertise in global health R&D. Alternatively, investors may more readily consider an investment in these types of opportunities if they are part of a diversified investment strategy (i.e., through a large fund vehicle).

Insights and recommendations from assessments

To appropriately put the observations and implications above into context, further insight into the potential for impact investment to play a role in advancing the work of PDPs is provided below. The insights are organized against the investability assessment framework to provide more direct responses to the questions contained within each element of the framework. Examples from the case studies are drawn in to illustrate the different points made.

Clarity

Certainty of market opportunity: Can a structure be designed to attract impact investment to support the goals of the PDP? Is there precedent or other evidence to validate the approach and mitigate risk for an investor?

The first essential factor for investability is clarifying the market opportunity such that the means by which return-seeking capital could be deployed can be readily understood by potential investors. This includes not just the rationale for investment but, more specifically, the type and amount of capital needed and how it will be used. The **R&D investment opportunity for FIND** builds on the organization's diverse AMR and tuberculosis diagnostics portfolio, which has active private sector and academic partners. Investors see the potential in FIND's robust pipeline, but their interest is tempered by a lack of fundamental understanding of AMR and tuberculosis diagnostics. As there are very few specialist investors in global health R&D, PDPs looking to find return-seeking investors may have to further clarify the market opportunity through targeted education and information-sharing.

Beyond those elements, high-level terms like tenor and pricing need to be known to determine whether an investment is in scope for a potential investor's mandate. Impact investors often have specific objectives as well, so ensuring there is alignment between the mission of the PDP, the targeted impact of the investment, and potential investors is a critical initial step.

Certainty around the market opportunity can be affirmed most easily through precedent or comparable transactions. Evidence that an investment thesis has been successfully implemented in a deal with a similar risk profile provides a concrete demonstration of the efficacy of the strategy to potential investors and key stakeholders. For example, **IAVI's broadly neutralizing antibodies technology** is already the subject of commercial

interest, with certain antibodies and their rights having either been licensed to industry or currently under discussion for licensing. Spinning it off as a separate entity mirrors industry precedent for similarly bespoke technologies (e.g., TSRI, IAVI's partner in the work, has spun out more than 70 companies since 1980).

Nature of underlying economics: Is there a means to generate significant, reliable revenues that could deliver a return?

Related to the question of certainty of the market opportunity, the fundamental economics of the underlying asset or project will drive the attractiveness of an investment, both to the potential investor and the PDP, as a primary beneficiary of the deal. The core assumption is that the revenues generated will provide a source of return for an investor. Those revenues generated need to be significant enough to be shared between the PDP and the investor, such that each receives a meaningful source of funding. In the case of the PDP, this should equate to a sum that exceeds the ongoing costs of managing the revenue-generating activity and administering an investment. In the case of the investor, a meaningful source of return will be one that meets its target or benchmark return.

In addition to the amount of possible revenues, the reliability with which they can be earned and shared is another critical element to assessing the underlying economics of the opportunity. The regularity with which returns can be delivered will inform the type of investment (whether equity or debt or some other instrument) and the investor's analysis of the opportunity. This will be assessed through a fuller articulation and review of the risks to generating revenue as the balance of risk and return will be a critical consideration for any investor. Precedent transactions or other data that demonstrate the ability to overcome risks and generate revenue would facilitate assessment of a given opportunity.

In the case of **IAVI's broadly neutralizing antibodies spin-off**, the technology is still emerging as a viable therapeutic solution. As a result, there is a high degree of uncertainty around the timing of licensing cash flows and the ability to monetize the technology. Since revenue generation is linked to the potential for out-licensing rights in exchange for milestone payment royalties, the revenues are likely to be variable and unpredictable. While the size of the HIV market is attractive to investors, the onus will be on IAVI to develop an agreement that can minimize the revenue uncertainty and risk.

Although **PATH's PRV-linked investment proposal** builds on an emerging set of in-process or closed transactions that provide precedent, the PDP faces revenue uncertainty associated with the sale of the PRV. PATH cannot guarantee they will be able to find a buyer, and additional PRVs coming to market may diminish expected returns. It remains to be seen whether current sale precedents ranging from $67 - $350 million do indeed prove indicative of future sale values. Similarly, **PATH's private sector partnerships proposal** needs to show that partnerships can present a reliable source of revenue. Here, precedent indicates

that prior partnerships have generated limited amounts of revenue—as in the case of Uniject and SILCS. This revenue, moreover, is not reliable enough to support outside investment, and additional track record is needed to better clarify revenue opportunities.

Effectiveness

Delivers on impact objectives: Will the proposed structure directly support the global health objectives of the PDP? Does the introduction of return-seeking capital pose any risk to mission?

When evaluating any of the proposed projects, the effectiveness of the concept to deliver on global health outcomes is another important factor in assessing investability. Ultimately, any investment of capital, time, and capacity will need to show a measurable return on health outcomes that align with the mission of the PDP. Most of the investment opportunities proposed by the PDPs are based on products or services that could provide a significant impact, although the type and extent of the eventual health outcomes will depend on the structure of the project and the terms of the investment deal.

FIND's proposal to invest in its AMR or tuberculosis pipeline, for example, could produce more effective diagnostics with a dramatic impact on global health outcomes, while directly supporting FIND's core capacities and mission. Yet the impact of such an R&D investment will only be realized if it results in appropriately priced diagnostics and accessibility for target populations.

Similarly, **IAVI's services spin-off opportunity** will provide significant value-add to larger developers and allow for more efficiency in immunology and sample management. Yet the eventual global health impact will depend on the standalone mission of the spin-off as well as the balance of work between nonprofit clients and for-profit clients. Careful consideration will need to be given to strategic partnerships and structural elements to ensure that the impact is appropriately incorporated into the final agreement and design of the spin-off.

As some of the investment opportunities may offer attractive risk-return profiles, there is a possibility that return-seeking investment could divert the opportunity away from the PDP's overall global health mission. The **private sector partnerships opportunity**, for example, offers PATH the potential to generate financial value as well as impact by commercializing global health products. Yet private sector partners who do not share the same global health priorities as PATH could potentially create risks or conflicts of interest that need to be carefully managed and contemplated as part of any agreement.

While some of the investment opportunities present more obvious and direct global health outcomes than others, all of them will require careful and thoughtful consideration on how to more effectively integrate impact into the mission, business model, or deal structure.

Feasibility

Experience of PDP in commercial environments: Does the PDP have the appropriate organization and experience to successfully manage the opportunity?

Return-seeking investors have different motivations from traditional donors, and the success of an investment opportunity hinges on the PDP's ability to navigate often conflicting expectations. Some PDPs have already established partnerships with commercial partners that signal the viability of the opportunity to the market. **IAVI's HIL** supports a range of external partners across disease areas, including a number of global pharmaceutical companies. As IAVI considers spinning out the HIL, the established partnerships are a significant value-add and differentiating factor. In such a case, the outstanding questions focus on the structure of the spin-off, and whether embedding it within a current partner (Imperial College) or structuring it as a standalone entity will enable or hamper its ability to market the business and develop new partnerships.

Other PDPs have a significant track record in dealing with commercial partners and highly experienced deal teams that provide the necessary expertise to overcome the challenges of complex negotiations. **PATH, for example, negotiated and closed a $25 million investment** that will support the development of a neglected tropical disease drug eligible for a PRV. The negotiation process was long and expensive, due to the complexity of structuring a novel investment with actors comprising different motivations and preferences. In that case, the commercial expertise of PATH's deal team proved essential, particularly in managing investors with different expectations from traditional donors.

In other cases, the PDPs have no established precedent or expertise and would have to carefully consider how to structure the investment opportunity in a way that overcomes the lack of experience and internal capacity. In the case of FIND, **the R&D investment** is an unprecedented opportunity with a high potential upside. Yet FIND needs to explore whether the partners that would manufacture, sell, and distribute products would be open to sharing in that upside. Finding such aligned investors with an intimate knowledge of AMR or tuberculosis diagnostics may be a significant hurdle. FIND would also need to build up its internal negotiating expertise or consider hiring an experienced third party to help structure the investment.

As PDPs explore their various investment opportunities, they need to strategically consider whether their existing expertise, partnerships, and internal capacities are appropriate for successfully managing commercial investors.

Reasonable implementation time and cost: What plans, processes, and legal steps need to be undertaken to reach investability? Do the prospective benefits of attracting investment outweigh the time and cost to do so?

Nearly all of the case studies featured in this report would represent new strategies or changes in approach to the way each PDP fulfills its respective mission. Careful planning is essential to successfully establishing a new channel for accessing different sources of funding and should consider the potential benefits and costs, as well as any risks of execution. This would also include establishing a realistic timeframe for exploring and testing the idea, completing any necessary demonstration of the efficacy of the approach, and then reaching a scale at which the activity can attract investment capital. Business plans will need to be developed, and the PDP will need to identify a process for engaging the appropriate stakeholders to approve or participate in the initiative.

Many of the PDPs are considering multiple approaches, and further clarity on the costs and benefits of each is paramount. **FIND's manufacturer buy-down proposal**, for example, weighs supporting a single manufacturer against supporting a portfolio approach. Including multiple manufacturers may limit the risk of inadvertently creating a market monopoly or stifling innovation, but it is likely to complicate the discussions, given the need for additional capital to cover losses of multiple manufacturers over a longer scale-up period and to cover legal expenses for a buy-down agreement that addresses the needs of investors and donors.

In certain cases, a separate legal structure needs to be established as well to receive investment capital and/or to house the technology or services that are generating strategic and commercial value for the partners involved. Most of the ideas proposed initially in the investment prototypes, where this point is relevant, are fairly standard from a legal perspective. In considering the legal structure of both the **technology and services spin-offs**, for example, IAVI needs to explore establishing separate entities with dedicated resources to coordinate and drive the initiative in a way that is beneficial to IAVI and its partners. This requires an understanding of the process for setting up a new entity and any legal and tax implications for the PDP and potential investors.

Each PDP will need to assess whether it can manage these implementation-related activities on its own or whether outside expertise from subject-matter experts, consultants, or lawyers may be needed to guide the planning process. Either way, each PDP would have to commit time and resources to the upfront development of the activities supporting the potential investment, as well as to ongoing management.

The benefits of moving forward should be articulated early in the planning process and, ideally, quantified and compared against the costs for developing and launching the initiative and seeking investment. While there may be long-term benefits of bringing in return-seeking investment as a funding source, both for the PDP and for global health R&D more broadly, the time and expense need to be considered relative to those benefits.

Openness of core stakeholders: Will external and internal stakeholders be supportive of the approach?

A distinct and important element of assessing feasibility is determining whether key internal stakeholders (e.g., senior management, board of directors) and external stakeholders (e.g., funders, development partners) will support the initiative. Typically of concern for these groups is the potential for mission drift, conflicts of interest (real or perceived), and distractions from the organization's strategy or other core activities. Internally, there may also be cultural barriers to introducing a strategy that more directly engages the private sector or return-seeking investment.

In the case of **PATH's private sector partnerships opportunity**, there is clear consensus that PATH will need to engage in a process to develop a strategy that would appropriately balance mission with the desire to more strategically seek revenue-generating partnerships. This will require internal buy-in from senior management and could represent a cultural and operational shift within the affected parts of the team, since the opportunity would deepen and add complexity to PATH's relationships with private sector partners. PATH learned that lesson from its **PRV-linked investment** negotiations. Internal buy-in was essential to the cultural willingness to consider and execute such a unique transaction. PATH also strategically used the GHIF as a 'translator' to facilitate communication with the commercial investor and ensure that mission was kept front and center of negotiations.

Stakeholders also play a significant role in influencing the direction of an investment opportunity. As **FIND explores the manufacturing buy-down**, criticism that stakeholders perceived the prior tuberculosis diagnostic buy-down as a mechanism that inadvertently created a monopoly has led FIND to consider a portfolio approach, with multiple platforms and manufacturers. The Hepatitis C pipeline presents a more robust set of products to choose from, which makes a multiple product strategy more feasible.

Buy-in from key stakeholders is helpful prior to engaging with outside investors to ensure that support is in place. In the short term, this will be critical during any negotiation process; in the medium- to long-term, it will be critical for evolving and advancing the strategy.

PERSPECTIVES FROM IMPACT INVESTORS

- A group of impact investors was invited to the PDP IFI workshop held in March 2017 to participate in a panel and discuss their perspectives on the topic of investability.
- The investors on the panel represented years of deep experience in impact investing across a spectrum of deals and markets and, as a result, were able to comment on the factors at work in the growth of other analogous impact investing sectors, including:
  - **Communities of practice:** the importance of investor education and the role affinity groups can play in bringing investors with similar impact interests together to learn and share information
  - **"Teeing up" investment opportunities:** the need to recognize the idiosyncratic needs and constraints of different types of investors and the importance of designing (or working with intermediaries to design) projects or products that meet investors where they are
  - **Working toward replicability and scalability:** the value in thoughtfully building the groundwork for more replicable, scalable transactions so that, over time, deal structures and terms become familiar, learnings can be shared, a track record of performance can be developed, and deals can be completed with fewer transaction costs and less subsidy

6. RECOMMENDATIONS

The following section summarizes a number of recommendations for PDP management, boards, and funders to incorporate into any planning and development of revenue-generating activities that could then potentially form the basis for an investment opportunity. The assessment revealed several key insights related to the potential role for return-seeking, mission-aligned capital to advance global health R&D objectives in partnership with PDPs. In most cases the recommendations assume that the type of extensive collaboration—between donors, philanthropic funders, and industry—required to create PDPs in the first place is once again needed to help the field take another innovative step forward, with the goal of creating more diverse, sustainable sources of funding for PDPs and the market more broadly.

Clarify investment opportunity

For all of the case studies, PDPs will need to sharpen the investment thesis and the rationale for return-seeking capital. This entails articulating—with as much specificity as possible—the type of capital needed, how it will be put to use (and over what timeframe), and when and how the financial returns and impact objectives will be met.

Additionally, PDPs should seek out or develop data, research, and/or precedents that support the proposed investment thesis to provide clarity and confidence to potential investors. For example, the PDPs should seek further demonstration of the efficacy of a technology or service, as well as evidence of the ability to generate significant and reliable revenues when there is opportunity to do so. As part of that process, it is important for PDP team members to be cognizant of those indicators of success that will resonate with potential investors, as well as internal and external stakeholders. This demonstration should take place prior to developing more specifics around a potential investment structure to affirm that moving forward does indeed make sense.

Related to this point, PDPs should be seeking out relationships with impact investment groups whose impact mandates are aligned with the expected global health benefits of the proposed transaction. Boards and funders may be able to help facilitate those introductions and conversations.

Engage management and operations

Each PDP will need to consider, likely in consultation with its funders, the resource implications of the proposed transactions and prepare for them accordingly, should an opportunity merit further development. This includes dedicating the necessary resources to sustain the investment-supported activities in a way that helps to maximize successful execution without negatively impacting the rest of the organization. Funders should be willing to provide PDPs with the resources to improve internal team capacity or engage external experts where expertise may be lacking within the current team. For example, the structural complexities and related considerations increase when a separate legal entity will need to be formed to accept investment, so advice from experienced legal and tax counsel is essential.

Ensure alignment on investment terms

For those opportunities with potential for near-term investability, it is important that the PDPs develop a view on the acceptable boundaries for key financial terms before entering into conversation or negotiation with investors. This includes, at a high-level, the amount and type of investment required, the tenor of that investment, and the potential return (as well as an assessment of the risks to earning that return). Without these preliminary definitions, it is difficult to have meaningful or constructive conversation with potential investors. Here, in particular, is where legal and financial transaction experience will be critical, either within the current management and board or as outside experts.

Also, as many of the opportunities have been developed on the basis of monetizing a unique technology or service the PDP owns, each PDP should come to a view on what role, rights, and ownership it would ideally retain under the proposed transaction structure. This will be especially critical to ensuring adherence to global health mission for the duration of the investment, particularly when non-mission-aligned partners or capital are introduced. Consultants and lawyers with experience negotiating impact investments will be able to provide suggestions on approach based on market precedents.

Leverage partnerships to maximize potential

PDPs should begin a process of developing and leveraging existing and potential partnerships that will have a view on a strategy for pursuing return-seeking capital and can influence structuring and negotiations. Engaging with key internal and external stakeholders to identify any concerns they may have, potential risks, or conflicts of interest will be an essential step early on in the exploration and design phase for PDPs. Building organizational consensus and buy-in at the outset will also make negotiation with potential investors a more efficient process. In particular, PDPs will need to manage existing funder relationships to ensure that any new activity or strategic shift is perceived and understood as a constructive and positive evolution of the activities already being funded by donors. Donors will certainly have a view on whether and how return-seeking capital can be introduced in a way that is complementary and additive, rather than distracting or detrimental to a PDP's mission.

Given the novelty of deploying return-seeking capital to support global health R&D—and particularly with PDPs as partners—PDP management and funders should seek to identify a "friendly" investor or partner who is willing to provide feedback early on, as this could provide a lot of utility and efficiency to the investment structure development process. This will help to ensure that an initial term sheet or outline of a prospective deal already integrates investor considerations and facilitates those conversations.

7. CONCLUSION: THE POTENTIAL FOR TRANSFORMATION

While the appeal of attracting impact investment is strong—as a means to both diversify funding streams, as well as to access more flexible pools of capital—the strategic and operational shift that it requires for PDPs should not be underestimated. The pursuit of revenues requires staff capable of managing monetizable activities and a strategy that aligns those revenues with the desired impacts of the PDP. And relatedly, introduction of return-seeking investors, even with mission alignment, requires a different level of organizational accountability and discipline. This could be beneficial to the PDP but could also present operational distraction and, in a worst case, detract from the organization's mission. Additionally, the underlying activities referenced in each of the case studies represent only a narrow piece of the portfolio of work that each PDP manages, yet will likely consume a disproportionate share of the organization's resources to design an investment opportunity around them. Finally, the PDPs will likely require external financial and transactional expertise to evolve the concepts presented here into actionable opportunities. As they explore the feasibility of the opportunity, a PDP may discover that the benefits no longer outweigh the resourcing and implementation costs.

> The ideas and opportunities presented here demonstrate the ability of the PDPs to think entrepreneurially about their funding strategies and represent what are surely the initial steps down a pathway to more diversified, reliable sources of revenue.

It is also worth noting that the scale of impact investment capital potentially available to PDPs is largely unknown, as global health R&D has only recently become an area of focus and interest for a select group of impact investors. Still, the impact investing market represents over $77 billion in assets under management, and health is frequently cited as a sector of interest for impact investors, providing a window of opportunity to explore investments in PDP initiatives.[34]

The potential for PDPs could be transformational. Faced with constant budgetary pressures, PDPs that successfully leverage financial innovation can create a more sustainable strategy for growth. Consider, for example, the possibility that, due to the PRV, PATH fulfills the objectives of its deal with Clarus and GHIF and secures for itself a pool of unrestricted capital in the tens of millions of dollars. The ideas and opportunities presented here demonstrate the ability of the PDPs to think entrepreneurially about their funding strategies and represent the initial steps down a pathway to more diversified, reliable sources of revenue. With the ongoing growth and evolution in the impact investment field occurring in parallel, the promise to support the longer-term sustainability of PDPs for years to come may indeed become reality.

[34] Global Impact Investing Network. "*Impact Investing Trends: Evidence of a Growing Industry*." (2016)

APPENDIX

About Product Development Partnerships

Unique role of PDPs

Before the onset 20 years ago of what has been called the "Era of Partnerships", R&D for neglected diseases was quite scarce.[35] Only 20 drugs and projects focused on neglected diseases were developed between 1975 and 2000, all by industry participants (some of which were done in partnership with the WHO). Between 2000-2005, however, 55 drugs had been registered or were in development, 45 of those with the participation of PDPs.[36] As of 2015, there were 142 drugs (and 485 products in total) in the pipeline, with PDPs involved in 22 percent of those projects.[37]

In the 1990s, funders began to recognize the importance of and explore opportunities for greater partnership with product developers to further global health outcomes. These efforts led to some of the early investments in PATH, a non-governmental organization founded in the 1970s to house multiple public-private partnership efforts, as well as the founding of IAVI in 1996 as the first official "Product Development Public-Private Partnership," distinguished by its multi-candidate/portfolio management approach to coordinating vaccine development for a neglected disease (in IAVI's case, HIV/AIDS). As the culmination of a separate effort, MMV was launched in 1999 as the first PDP explicitly focused on drug development.[38] [39] Over a dozen more PDPs were launched between 1999 and 2003, including FIND, a PDP focused on developing diagnostics for neglected diseases. Many of those PDPs were launched with seed funding and support from the Rockefeller Foundation and the newly formed Bill & Melinda Gates Foundation.[40] Some support a single neglected disease or product type, while others support multiple diseases and product types, but all of the PDPs are focused on developing or adapting products for scale and use in developing countries.

The PDP model that emerged resembled the virtual drug development business in the private sector, except instead of being funded by private, return-seeking capital, PDPs would be funded by government and philanthropic dollars and have public health impact as their primary goal. PDPs channel the funding they receive into projects they manage that involve a number of different activities, including disease- and product-specific research, coordinating clinical trials, need and demand assessment (particularly in low-income countries), managing intellectual property, determining options for manufacturing, assisting with regulatory approvals, and

[35] Mahoney. "*Product Development Partnerships: Case studies of a new mechanism for health technology innovation*." (2015) —Mahoney divides the history of global health into four eras: the Era of the Public Sector (1850 to 1915), the Era of the Private Sector (1915 to 1970), the Era of Public Sector Reawakening (1970 to 2000), and the Era of Partnerships (2000 to present).

[36] Wellcome Trust and London School of Economics. "*New Approaches to Funding Drug R&D for Neglected Diseases*." (2005)

[37] Policy Cures. "*The Unrecognized Revolution in Global Health: 2015 Pipeline Report*." (2015)

[38] Widdus and White. "*Combating Diseases Associated with Poverty: Financing strategies for product development and the potential role of Public-Private Partnerships*." (1994)

[39] PATH was founded in 1977, but with an initial focus on contraceptives. Today, PATH's focus includes a wide array of health technologies and houses several PDPs, including the Vaccine Development Program (PATH-VAC), the Malaria Vaccine Initiative (MVI) and the Meningitis Vaccine Program (MVP). IDRI was founded in 1993 refers to itself as a "non-for-profit biotech". WHO/TDR was founded in the 1970s as well, and though its scope is broader than product development, it is included in G-FINDER as a "de facto" PDP.

[40] Malone. "*Strengthening Research Partnerships: The Bill & Melinda Gates Foundation's Perspective*." (2006)

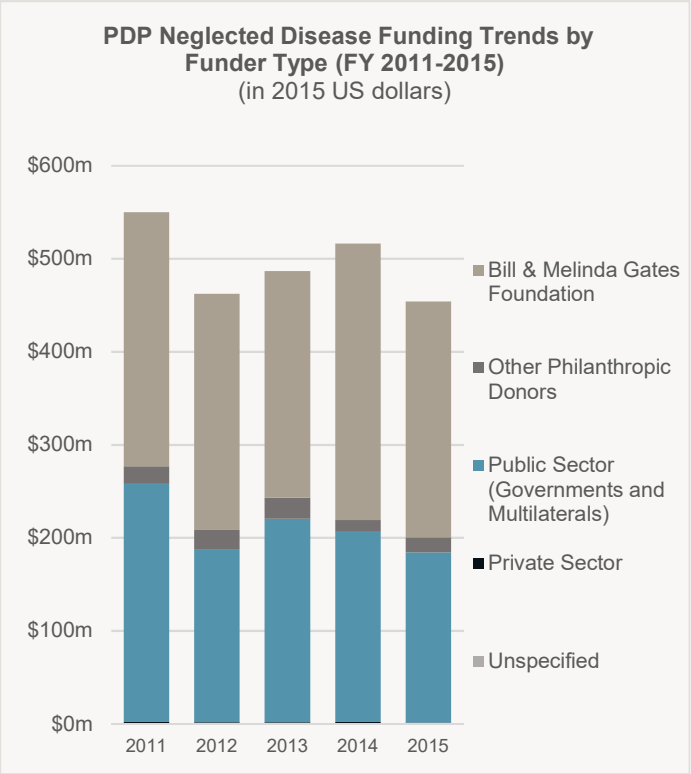
facilitating partnerships across sectors, including between pharmaceutical companies, academic research institutions, governments, and nonprofits.

For large pharmaceutical companies, the PDP model allows them to lend their strengths and expertise—often through their Corporate Social Responsibility (CSR) programs—without having to take on the full costs of product development for neglected diseases. For donors, the PDP model offers the opportunity to support a portfolio of projects that is selected by scientific and product development experts. Under the old model, donors supported a range of individual technologies at academic institutions without the benefit of the PDPs' ability to prioritize and manage product development.

Over the past two decades, PDPs have proven to be an important development in the field of global health, helping to improve availability and access for health products and technologies in developing countries. PDPs have helped advance the state of research for many diseases, and the products they have helped bring to market include better drugs, drug combinations, and insecticides for malaria; more efficient diagnostics for tuberculosis; new and improved vaccines for cholera, meningitis A, and Japanese encephalitis; and improved technologies for delivering vaccines in general. [41] [42]

PDP funding landscape

According to G-FINDER's 2016 report, PDPs received $450 million (20 percent) of the external grant funding provided for neglected disease R&D in 2015. This percentage is distorted by the large amount of grant funding provided by the US National Institutes of Health (NIH), however—when NIH funding is excluded, the PDPs managed about 39 percent of non-NIH grant funding provided in 2015.[43]

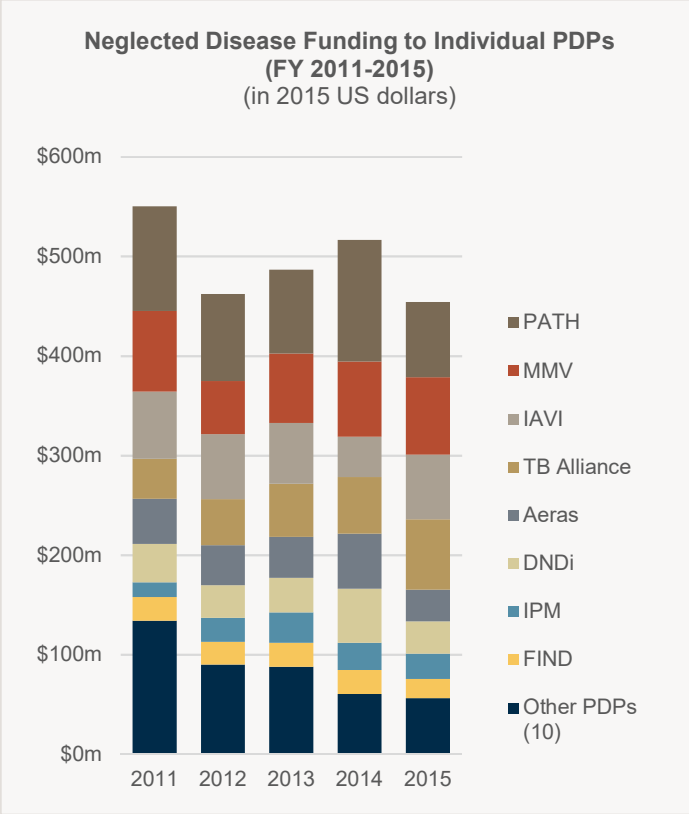


Much of the funding to PDPs is channeled to a few of the largest organizations. The funding received by MMV, PATH, and TB Alliance in 2015 represented half of all PDP funding that year.

The amount of neglected disease funding PDPs received in 2015 fell for the first time in three years, by 13 percent to $65 million, which the G-FINDER report explains as "reflecting

[41] Mahoney. "*Product Development Partnerships: Case studies of a new mechanism for health technology innovation*." (2011)
[42] Technopolois Group. "*Review of the Product Development Partnerships Fund 2011-2014: Final report to the Dutch Ministry of Foreign Affairs*." (2014)
[43] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)

the highly cyclical nature of grant funding to PDPs, especially from the [Bill & Melinda] Gates Foundation." A number of PDPs rely on the Bill & Melinda Gates Foundation for a considerable portion of their funding: In 2015, nearly half of all individual PDPs received a majority of their funding from the Bill & Melinda Gates Foundation.[44]



Funding from governments is highly concentrated in a few donors as well. Between 2011-2015, the United States, the United Kingdom, and the Netherlands provided, on average, over 75 percent of the public sector funding granted to the PDPs for disease research.

PDPs also experience the funding gap that persists in the field of global health R&D broadly. The degree of the funding gap is subject to debate and varies from disease to disease and on the goals and timeline for combatting, eliminating, or eradicating each. But many PDPs are concerned about sufficiency and sustainability of funding, especially as more products in their portfolios enter the significantly more expensive later stages of development involving large and time-consuming human trials to assess product safety and effectiveness.

PDPs do benefit from having a small set of dependable funders from an administrative and fundraising perspective, but having a few large funders makes organizations "more susceptible to the vagaries of external political, economic, and other forces."[45]

Furthermore, lack of sustainable funding complicates strategic planning for PDPs. Inability to forecast future revenues also puts the organizations in an unfavorable position in negotiations with partners, as the partner can see the uncertainty of the PDP's funding as a risk.[46] [47]

Exploring additional sources of revenue for PDPs could not only increase the number and variety of products for neglected diseases they are able to support, but could also benefit the PDP's effectiveness more broadly.

[44] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)
[45] Policy Cures Research. "*G-FINDER 2016, Neglected Disease Research and Development: A pivotal moment for global health*." (2016)
[46] Ganguly. "*Sustainability of PDPs' Model*." (2015)
[47] Expert consultations with staff at various PDPs.

Project Overview

The PDP Innovative Financing Initiative (IFI) was created to assess the potential for return-seeking investment as a funding source for PDPs. This potential was analyzed through a selection of case studies based on real-world opportunities with a sample of PDPs, the findings from which inform a set of broader strategic recommendations for PDPs to consider whether or not to pursue return-seeking capital.

Origins of the PDP IFI

Attracting sustained and additional funding for global health R&D beyond existing government and philanthropic capital is a critical priority, for both PDPs and the global health community at large. While there is limited precedent for return-seeking capital in global health R&D, the question of PDP investability has arisen previously. When the GHIF was established as one of the first return-seeking capital providers in the global health R&D market, several PDPs were considered as potential investees and partners. PDPs themselves have also been interested in exploring the idea of attracting investment capital, in order to help mitigate uncertain future funding flows and capitalize on revenue-generating activities. During the Bill & Melinda Gates Foundation's Product Development Forum in April 2016, PDP leaders expressed interest in finding ways to attract funding sources that could be supplemental to existing donor funding, including exploring ideas to increase PDPs' attractiveness to return-seeking investors. The particular question of PDP investability is one part of a broader, emerging interest in an expanded role for return-seeking capital in global health R&D writ large, an issue for which preliminary consideration has demonstrated significant potential and interest.[48] The PDP IFI is a response to the market need and interest, put forward as a public good to benefit the global health R&D market.

Project summary and objectives

The primary objective of the PDP IFI is to bring clarity and practical guidance on the prospect of impact investment as a complementary funding source for PDPs, in addition to ongoing support from government and philanthropic donors. To achieve this objective, the project has included the following key elements:

- Identification of a selection of PDPs best suited as collaborators for the project, in order to generate case studies for testing the potential for investment using real-world opportunities at these organizations;
- Definition of hypothetical investment opportunities based on these collaborations, which were tested with a selection of impact investors for their feedback; and
- Development of strategic recommendations for PDPs to determine whether to pursue impact investment capital and how best to attract it.

[48] Brookings Institute. "*Health Governance Capacity: Enhancing private sector investment in global health*." (2017)

Research methods

Extensive desk research was conducted on the global health R&D market to identify commercially viable segments of the market, unearth supply and demand dynamics for specific diseases and products, understand the motivations of key government and philanthropic funders, and assess the structure and experience of the PDPs. The desk research was complemented by expert consultations with PDP executives, key PDP stakeholders, and impact investors. Site visits to the three PDPs selected as partners were also conducted. To ensure diverse, representative input and feedback, two advisory groups were engaged throughout the project:

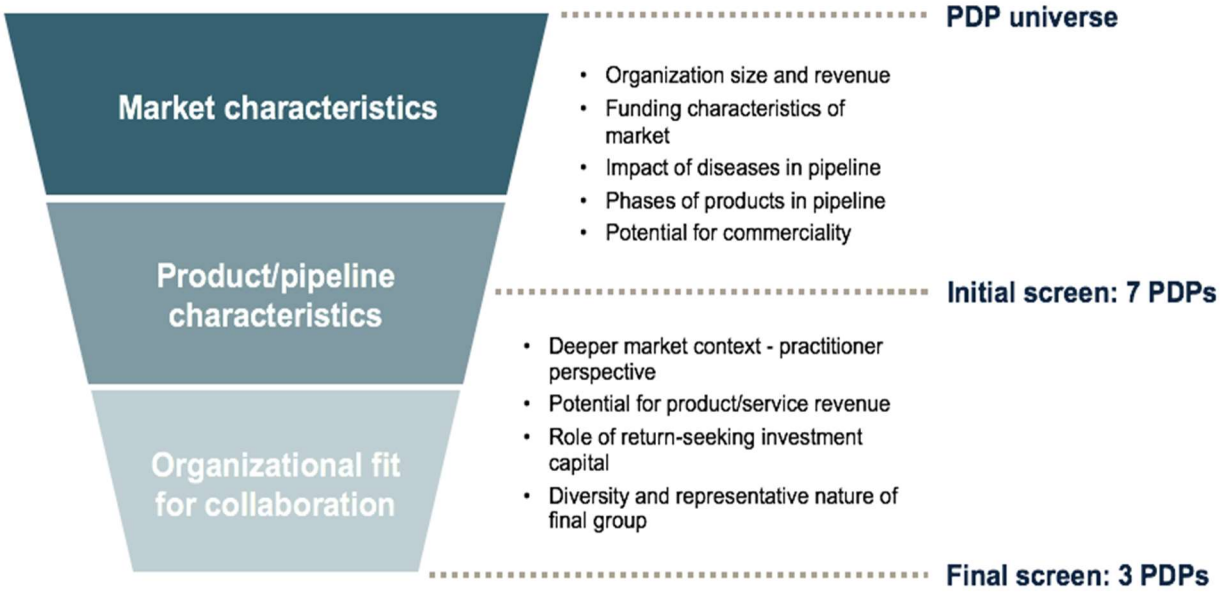
- **A Working Group** comprised of a variety of stakeholders and experts, convened regularly to guide the research, provide expert input, and test research findings; and
- **An Expert Investor Group** comprised of public and private sector impact investors with a degree of alignment with investment in global health R&D, which brought forward impact investors' interests and criteria and provided feedback on the hypothetical investment opportunities.

Purpose of the document

The purpose of the working paper is to share the findings from the PDP IFI with the field and serve as a basis for dialogue and shared understanding going forward. This working paper is the culmination of an exploratory phase of work, and includes recommended next steps and strategies for building on the findings. This work is intended to fill an important gap in knowledge and awareness on the opportunities, limitations, and practical considerations of utilizing impact investment as an additional funding source for PDPs.

Selection of PDPs

The selection process detailed below was established to identify the PDPs most suited for the purposes of the research and collaboration detailed in this paper:



Initial screen

The full range of PDPs was considered in a first round of desk research. This initial screen examined key characteristics of the organization, including:

- The story of each organization's founding and the evolution of its mission
- The funding history of the organization, including top donors and key stakeholders
- The organization's historical product development success, and the depth and breadth of the product pipeline
- The attractiveness of the end market for key products in development, including both commerciality and potential global health impact

Final screen

- In the final screen, the remaining seven PDPs were interviewed and researched more thoroughly. The final three were selected based on the interest of a PDP's leadership in participating in the project, the commercial nature of the products in development, and the identification of investable business activities that could generate additive revenue streams for the PDP and potentially attract third-party investors.
- At the culmination of the selection process, FIND, IAVI, and PATH were selected as collaborators in the assessment work based on their alignment with the project objectives and the diversity and representative nature of the final group.

PDP	OVERVIEW
FIND Because diagnosis matters	• **Year founded:** 2003 • **Headquarters:** Geneva, Switzerland • **Top funders:** Bill & Melinda Gates Foundation, BMBF, UK DFID, Australian DFAT, DGIS • **Funding received for R&D (FY 2015):** $19.4m* • **Focus:** FIND Is focused on developing diagnostic tests for tuberculosis, malaria, and kinetoplastids
iavi International AIDS Vaccine Initiative	• **Year founded:** 1996 • **Headquarters:** New York, NY • **Top funders:** USAID, DGIS, Bill & Melinda Gates Foundation, UK DFID, US NIH • **Funding received for R&D (FY 2015):** $65.1m* • **Focus:** IAVI is focused on the research and clinical assessment of candidate vaccines against strains of HIV/AIDS
PATH	• **Year founded:** 1977 • **Headquarters:** Seattle, Washington • **Top funders:** Bill & Melinda Gates Foundation, UK DFID • **Funding received for R&D (FY 2015):** $75.2m* • **Focus:** PATH has a wide focus area; products in development include vaccine, drugs, diagnostics, and devices for many disease areas including malaria, diarrheal disease, HIV/AIDS, Salmonella infections, and more

*Please note these figures reflect funding for product-related R&D for neglected diseases as reported by the G-FINDER survey for FY2015

Read-out from March 15 workshop

On March 15, 2017, the Bill & Melinda Gates Foundation and Tideline hosted a workshop to provide an opportunity for a select group of stakeholders and partners to review and comment on the PDP case studies and research findings. The goal was to distill and discuss a number of conclusions that seemed crucial to the success and viability of investments in PDPs based on the lessons and analysis from FIND, IAVI, and PATH, and reflect them in the strategic recommendations of the working paper.

In addition to the presentation of the various case studies, the workshop included an impact investor panel discussion (see 'March 15 workshop: Investor panel summary', also in the Appendix, for further detail) and a guest presentation by Dr. Mary Moran on 'The Dynamics of Collaboration'. Dr. Moran urged participants to revisit the data on global health trends and to account for the rapid development of a number of emerging economies, refining what today seems like a too-simplistic dichotomy in 'developed' and 'developing' world approaches to global health R&D. Policies need to be adapted to match a more fluid and flexible spectrum in global economic development, suggesting that high-volume/low-margin models (as opposed to more rigid dual-market opportunities) may be a more viable path forward. Moreover, established macro-level views and approaches ignore the inherent complexities within countries. After all, most people today live in middle income countries, with the biggest economic divisions manifesting within countries and across social classes.

Participants concluded the day by discussing key takeaways from the case studies and presentations, summarized below:

- **Resourcing and internal capacity:** PDPs may find it difficult to allocate enough internal bandwidth to replicate some of the presented opportunities. It was clear from PATH's PRV-linked investment case that internal financing expertise and a long and established track record in product development were essential to the success of the deal negotiation. PDPs, moreover, rely on inflexible donor funding that does not lend itself to pursuing non-project specific initiatives. PATH had the advantage of an unexpected pool of flexible capital they could reallocate towards resourcing the PRV-linked investment initiative.
- **Funding:** PDPs are intimately familiar with the donor space, yet few know how to navigate the investor market. There is a high upfront cost required to learn how to navigate the new landscape. PDPs would most likely benefit from more intentional collaboration and shared learnings with one another, necessitating a significant shift in thinking. Given the traditional donor funding model, PDPs have learned to operate in a scarcity mentality, competing for what they perceive is the same finite pot of money. To take full advantage of the opportunities, PDPs (and their public partners) would need to fully internalize that investment capital is not subject to the same scarcity issues as donor funding.
- **Need for intermediation:** Participants noted a clear need for a trusted proxy that could educate investors and help guide PDPs along an often complex negotiating process.

Participants also suggested that affinity groups could help play a valuable and critical role in creating a well-informed and aligned community of investors in global health. Most of the stakeholders present at the workshop recommended that the Bill & Melinda Gates Foundation play a more active intermediary role—supporting the development of investment prototypes and/or strategically convening affinity groups.

- **Investor motivations and alignment:** Finding aligned investors who understand the global health R&D space will be difficult. Beyond education in the space, it was clear that investors craved more clarity on the underlying economics and feasibility of each opportunity. PDPs will need to be very transparent on the tenor, risk, and return factors, and ideally present hard data that can demonstrate the viability of each investment case.

March 15 workshop: Investor panel summary

A group of impact investors was invited to the PDP Innovative Financing Initiative workshop held in March 2017 to participate in a panel discussion on the topic of investability. The investors brought a diversity of views informed by the varied corners of the impact investing market they operate in.

A summary of some of the key points raised during the panel follows:

- **Taking part in the growth of impact investing requires work:** While growing interest in "impact investing" is likely a megatrend, given the oft-cited interest and growing influence of women and millennials in investment decisions, much of the work of identifying and creating investment opportunities is undertaken at the sector level and takes dedicated effort. Building communities of shared practice and affinity groups to share knowledge and practices can help accelerate that work at the sector level.
- **Refining the investment thesis:** Profitability of a given product is not always a consideration for PDPs. Given an investor could alternatively invest directly in a small or medium-sized pharma or biotech, the case for including a PDP in a transaction--perhaps for their expertise, their impact orientation, their ownership of IP, or their ability to facilitate; should be well defined.
- **Categorizing investor types:** the various types of investors who might participate in global health R&D-related investments (i.e., development finance institutions, institutional foundations, high net worth individuals/family offices, health R&D venture capitalists) each have different needs and constraints. It may be difficult to find one investor who is willing to both finance the development risk for a product and be paid back with a stream of royalties over many years, but it may be possible to find two investors and match up their risk/return expectations and time horizons in a way that is suitable to each, allowing a transaction to take place that otherwise might not have.
- **Working toward repeatability and scalability:** There is value in thoughtfully building the groundwork for more repeatable transactions so that, over time, investors can become familiar with what to look for and how to implement certain kinds of deals, learnings can be shared, a track record can be developed, and transactions can gradually

take place with fewer transaction costs and less subsidy. This may mean moving from financing individual projects toward better identifying and supporting enterprises with the desired risk/return and impact characteristics.

- **Distinguishing between desirable and undesirable risks:** Some impact investors may be willing to take more risk than a traditional investor for the potential to create outsized global health impacts. One investor on the panel made a distinction between the risks related to business model, innovation, and execution they are willing to take and the risks related to management and operations they are not willing to take. Investors will look for a strong track record of management and operational expertise in just about any investment decision.
- **Coordinating with funder priorities:** Finding the overlap between programmatic priorities can be one challenge for funders and investors when they attempt to collaborate. Sometimes enterprises struggle as well when the capital they've been provided does not give them enough flexibility to adapt to a changing environment or grants in their market "crowd out" any potential for private capital. Thinking about grants as "propping up" enterprises rather than "sustaining" them could be a helpful shift.
- **Rightsizing transaction support:** Using philanthropic capital as a guarantee or for some other form of de-risking can help give an investor a margin of safety in a transaction with many real or perceived risks, but many investors are unwilling to do transactions that would not work on their own merits. A large amount of de-risking capital can sometimes be a negative signal and make investors question at a fundamental level why it is needed.

Members of the Project Working Group

NAME	ORGANIZATION	TITLE
Andrew Taylor	Grand Challenges Canada	VP of Investments
Cathy Clark	CASE at Duke University	Adjunct Professor & Director of CASE i3 Initiative on Impact Investing
Glenn Rockman	Global Health Investment Fund	Partner
Jens Bitsch-Norhave	Johnson & Johnson	Head of Business Development & Licensing, Johnson & Johnson Global Public Health
Mary Moran	Policy Cures	Founder and Chair of the Board
Renuka Gadde	BD	VP, Global Health
Ripley Ballou	GlaxoSmithKline	VP and Head of Global Vaccines US R&D Center
Sue Kinn	DFID	Research Manager at Department for International Development
Wendy Taylor	USAID (formerly)	Director, Center for Accelerating Innovation and Impact

Members of the Expert Investor Group

NAME	ORGANIZATION	TITLE
Beth Bafford	Calvert Foundation	Director, Investments
Chris McCahan	IFC	Chief Investment Officer
Christopher Egerton-Warburton	Lion's Head Global Partners	Partner
Ivo Knoepfel	onValues, Ltd.	Founder and Full Portfolio Advisor
Sachindra Rudra	Acumen	Chief Investment Officer

PDP IFI March 15, 2017 Workshop Participants

NAME	ORGANIZATION	TITLE
Labeeb Abboud	IAVI	General Counsel & SVP of Business Development and Strategy
Kate Antrobus	Lion's Head Global Partners	Executive Director
Aaron Arnoldy	Tideline	Director
Amie Batson	PATH	Chief Strategy Officer; Vice President, Strategy and Learning; and Acting Vice President, Technology Development and Introduction
Amy Bell	Tideline	Senior Director
Catharina Boehme	FIND	CEO
Thi Hanh Cao	DNDi	Senior Manager, Fundraising
Steve Cordial	IDRI	CFO
Nadza Durakovic	Tideline	Associate
Mark Feinberg	IAVI	President & CEO
Renuka Gadde	BD	VP, Global Health
Mỹ Lệ Thi Goel	Bill & Melinda Gates Foundation	Senior Program Officer
Nick Hamon	IVCC	CEO
Zach Katz	FIND	Chief Access Officer
Sue Kinn	DFID	Research Manager at Department for International Development
Christina Leijonhufvud	Tideline	Managing Partner
Bryan Locascio	Tideline	Associate
Andrea Lucard	MMV	Executive Vice-President for External Relations
Mary Moran	Policy Cures	Executive Director

PDP IFI March 15, 2017 Workshop Participants (continued)

NAME	ORGANIZATION	TITLE
Sally O'Keefe	Bill & Melinda Gates Foundation	Program Assistant
Olivia Polius	PATH	Chief Financial Officer and Vice President, Finance, Technology, and Infrastructure
Glenn Rockman	GHIF	Partner
Thomas Saugnac	DNDi	Operations Director
Mel Spigelman	TB Alliance	President & CEO
Wendy Taylor	-	Independent Consultant
Ben Thornley	Tideline	Managing Partner
Kim Wright-Violich	Tideline	Managing Partner

PDP IFI March 15, 2017 Investor Panel Participants

NAME	ORGANIZATION	TITLE
Brinda Ganguly	Rockefeller Foundation	Senior Associate Director
Bonny Moellenbrock	Investors' Circle	Executive Director
Glenn Rockman	GHIF	Partner
Brian Trelstad	Bridges Ventures	Partner
Adam Wolfensohn	Encourage Capital	Managing Partner

Acronyms

ACRONYM	DEFINITION
AMR	Anti-microbial resistance
ARV	Antiretroviral
BD	Becton Dickinson
BMGF	Bill & Melinda Gates Foundation
CRO	Contract research center
DFAT	Department of Foreign Affairs and Trade
DFID	Department for International Development
DGIS	Directorate-General for International Cooperation
FDA	Food and Drug Administration
GHIF	Global Health Investment Fund
HCV	Hepatitis C virus
HIL	Human Immunology Lab
HIV/AIDS	Human immunodeficiency virus/ Acquired immune deficiency syndrome
IAVI	International AIDS Vaccine Initiative
IDRI	Infectious Disease Research Institute
LGH	Laerdal Global Health
LIC	Low-income country
MDGH	Medicines Development for Global Health
MSR	Mountain Safety Research
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institute of Health

Acronyms (continued)

ACRONYM	DEFINITION
PDP	Product development partnership
PDP IFI	Product Development Partnership Innovative Financing Initiative
POC	Point of care
PRV	Priority review voucher
TB	Tuberculosis
TSRI	The Scripps Research Institute
USAID	United States Agency for International Development
WHO	World Health Organization

Disclaimer

The information in this report is based upon research, data, and forecasts conducted by Tideline and by research collaborators, contributors, and partners supplied to Tideline and reflects prevailing conditions and our views as of this date, all of which are accordingly subject to change. Opinions and estimates contained in the report constitute our judgment and should be regarded as indicative, preliminary and for illustrative purposes only. In preparing this report, Tideline has also relied upon and assumed, without independent verification, the accuracy and completeness of all information available from public sources or which was provided to us or which was otherwise reviewed by us. In addition, our analyses are not and do not purport to be appraisals of the value or business of any entity. Tideline makes no representations as to the actual value which may be received in connection with a transaction nor the legal, tax or accounting effects of consummating a transaction. Unless expressly contemplated hereby, the information in this presentation does not take into account the effects of a possible transaction or transactions.

IRS Circular 230 Disclosure: Tideline and its affiliates do not provide tax advice. Accordingly, any discussion of U.S. tax matters included herein (including any attachments) is not intended or written to be used, and cannot be used, in connection with the promotion, marketing or recommendation by anyone not affiliated with Tideline of any of the matters addressed herein or for the purpose of avoiding U.S. tax-related penalties.

Tideline is the marketing name for the activities of Tideline Advisors LLC, a consulting firm. Neither Tideline nor any of its affiliates is registered as an "investment adviser" under the U.S. Investment Advisers Act of 1940, nor is Tideline or any of its affiliates regulated by the U.S. Securities and Exchange Commission or any other state or federal entity.

This report should not be considered financial advice, nor does it constitute a commitment by any Tideline entity to underwrite, subscribe for or place any securities or to extend or arrange credit or to provide any other services.