I BVGH history and Mission

In 2010, the World Health Organization (WHO) classified a group of seventeen (17) bacterial, viral, and parasitic diseases as “neglected” because they lacked safe, effective, and affordable drugs, vaccines, and diagnostics to prevent, diagnose, and treat them. Globally, over one billion people are directly affected by these diseases. While these seventeen diseases often are not fatal, they can result in permanent disfigurement, disrupted childhood development, and increased work and school absenteeism. These neglected tropical diseases (NTDs) are endemic to over 140 countries worldwide, with the majority of infections occurring in low- and middle-income countries (LMICs) located in Africa, Asia, and Latin America. The economic effects of NTDs compound the financial challenges faced by these developing economies and stifle their growth. For example, the WHO has estimated that dengue virus infections alone directly and indirectly cost over US$2 billion annually. Thus NTDs pose a crippling burden to some of the world’s poorest nations.

The biopharmaceutical industry has historically paid little attention to NTDs and other diseases that predominantly affect the poor (poverty-related diseases [PRDs]). This inattention is primarily due to the lack of market opportunity and inability to secure a return on the large investment in research and development (R&D) that is needed to bring a medical product to the market. However, in 2004, driven by the growing need for the development of solutions to address the unmet medical needs of the developing world – including NTDs – the Biotechnology Innovation Organization (BIO), the world’s largest biopharmaceutical, diagnostic, and life sciences trade organization, established BIO Ventures for Global Health (BVGH). BVGH was created to develop and implement programs that engage BIO’s stakeholders and leverage their assets to impact global health. This included publishing business cases for the development of specific

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products targeting PRDs,\textsuperscript{5} and establishing partnerships to accelerate product development.\textsuperscript{5} One such program was BVGH’s Global Health Primer – a compilation of information about twenty-five PRDs and the products in use or in development for their management. Through these and other programs, BVGH initiated dialogue between BIO’s stakeholders and the global health community and encouraged industry’s involvement in R&D of products for the many unmet medical needs of the developing world.\textsuperscript{7}

One major barrier hindering the development of products to prevent, diagnose, and treat NTDs is that the diseases’ experts have had limited access to the biopharmaceutical industry’s small molecules, technologies, and know-how. Conversely, the biopharmaceutical industry’s lack of attention to and expertise in these diseases impedes their development of much needed products.\textsuperscript{8} These challenges can be addressed by developing platforms through which disease experts can access industry’s knowledge and assets and by creating strategic public–private partnerships (PPPs) that leverage the respective strengths of each sector.

The drivers of industry’s attention to NTDs and PRDs are varied. Globalization over past decades has raised awareness of PRDs and the health care needs of the millions living in poverty. Through corporate social responsibility (CSR) programs, companies are contributing their resources to address these diseases. In addition, companies recognize that Africa, Latin America, and South Asia will become crucial markets and are investing significant capital in R&D of products for diseases affecting these regions. BVGH’s programs encourage companies to recognize the benefits of addressing PRDs and the possibilities of building new partnerships within these regions to address health care needs.

This chapter will explore two open innovation platforms co-led by BVGH – the Pool for Open Innovation against Neglected Tropical Diseases (POINT) and WIPO Re:Search – that encourage and support biopharmaceutical companies’ contributions to NTD R&D through PPPs. The necessity of a partner responsible for proactively establishing collaborative projects between participating organizations and managing established alliances to ensure challenges are addressed and projects are successful is discussed. This chapter concludes with a description of how the WIPO Re:Search Consortium governs the sharing of intellectual property between organizations and the Consortium’s alignment with the United Nations Sustainable Development Goals (SDGs).

\textsuperscript{5} BVGH & PATH, The Case for Investment in Enterotoxigenic \textit{Escherichia coli} Vaccines (2011).
\textsuperscript{7} According to Carl Feldbaum, President Emeritus of the Biotechnology Innovation Organization and a member of the BVGH Board of Directors since its launch, “BVGH was established to help bridge a great divide between BIO’s stakeholders – public and private companies, academic and research institutions – and approximately 6 billion people living in the developing world, especially those suffering from neglected tropical diseases.” When interviewed in 2014, Mr. Feldbaum expressed his disappointment that industry’s initial progress had been slow; however, he was encouraged by the shift in the pharmaceutical industry’s perception of developing world markets.
\textsuperscript{8} Dent, Graef, and Shivanand, supra note 6 at 1–5.
II Pool for Open Innovation against Neglected Tropical Diseases (POINT)

Established in February 2009 by GlaxoSmithKline (GSK) as part of the company’s larger plan to aid the developing world, POINT was created to allow universities and government research institutes to access GSK’s small molecules, patents, and know-how on favorable terms to bolster and accelerate their neglected disease drug development. Sir Andrew Witty, GSK’s Chief Executive Officer, proposed the voluntary “patent pool” and called on other biopharmaceutical firms to open up access to their intellectual property (IP) assets relevant to NTDs. This proposal followed Witty’s announcement that GSK would cap its prices for patented medicines in poor countries at 25 percent of what it charged in developed countries and reinvest 20 percent of the profit it made from selling medicines in poor nations into health care infrastructure projects in those countries.9

At its inception, the pool contained approximately eight hundred (800) patents. Within less than a year, Alnylam Pharmaceuticals, the Massachusetts Institute of Technology, and South Africa’s Technology Innovation Agency announced their participation in POINT.10 These organizations’ contributions expanded the pool of IP assets to include over twenty-three hundred (2,300) patents.11

During the development of POINT, GSK engaged BVGH to manage the program and promote the program’s independence from GSK.12 Following POINT’s launch, BVGH helped to facilitate POINT’s first collaboration between GSK, iThemba, and Emory University. While this partnership demonstrated the impact an IP-sharing platform could have, and the value of company contributions, it was recognized that additional company assets would be beneficial. BVGH also recognized that a stagnant pool of IP assets does not attract researchers’ interests. Instead, potential IP users must be proactively engaged and presented with novel partnership ideas based on the assets in the pool and aligned with the areas of interest and research needs of the IP users. A model involving thoughtful partnership development and alliance management would need to be employed to meet the program’s objectives.

III WIPO Re:Search

POINT’s demonstration of an IP-sharing, open innovation platform dedicated to accelerating product development for diseases of poverty began to garner the interest of a wider group of biopharmaceutical companies. As the world’s leading institution in overseeing and shaping global IP policies, the World Intellectual Property Organization (WIPO) was an obvious partner in a new initiative. WIPO has a mandate to lead the development of a balanced IP system that enables innovation and creativity for the benefit of all.13 When approached by interested companies in 2010, WIPO expressed an interest in exploring a new and broader model to exhibit this open access concept and to demonstrate that IP is not a barrier to research and development. WIPO, BVGH, and

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11 Dent, Graef, & Shivanand, supra note 6 at 1–5.
eight biopharmaceutical companies\textsuperscript{14} (Alnylam, AstraZeneca, Eisai, GSK, MSD [known as Merck & Co., Inc. in the US and Canada], Novartis, Pfizer, and Sanofi) created a new platform that leveraged WIPO’s infrastructure, built upon the ideas and momentum created by POINT, and expanded the scope of the pool to include diagnostics and vaccines. These efforts led to the establishment of the WIPO Re:Search Consortium, a platform through which the biopharmaceutical industry’s IP assets and resources are connected to qualified academic and nonprofit neglected disease researchers through collaborative research agreements. The goal of the Consortium is to accelerate the development of new drugs, vaccines, and diagnostics for NTDs, malaria, and tuberculosis.\textsuperscript{15}

The activities and administration of WIPO Re:Search are coordinated jointly by WIPO and BVGH. Each organization has distinct and complementary responsibilities within their respective roles as the Partnership Hub Administrator (BVGH) and the Secretariat (WIPO). Leveraging its IP expertise and authority, WIPO hosts IP training workshops for Consortium Members. WIPO is also responsible for organizing the WIPO Re:Search annual (or biennial) meeting, coordinating teleconferences between all Members, and managing the WIPO Re:Search Database,\textsuperscript{16} an online database of IP assets made available by Provider Members.\textsuperscript{17} Through its role as the Partnership Hub Administrator, BVGH is responsible for establishing research collaborations between

\textsuperscript{14} As of 2016, ten companies are participating in WIPO Re:Search: Alnylam; Eisai; GSK; Janssen, the Pharmaceutical Companies of Johnson & Johnson; MSD; Merck KGaA, Darmstadt, Germany; Novartis; Pfizer; Sanofi; and Takeda.

\textsuperscript{15} Jennifer Dent et al., WIPO Re:Search: A Consortium Catalyzing Research and Product Development for Neglected Tropical Diseases, 2 PHARMACEUTICAL PAT. ANALYST 591 (2013).

\textsuperscript{16} Anatole Krattiger, Thomas Bombelles, and Ania Jedrusik, Driving Innovation for Global Health Through Multi-stakeholder Partnerships, Chapter 3, supra (in this volume).

\textsuperscript{17} Institutions join the Consortium as “User,” “Provider,” and/or “Supporter” Members. Provider Members – most notably the Founding Pharmaceutical Members – are those organizations that have expressed a willingness to share their IP assets, such as know-how, expertise, materials, and services, with other Members. User Members subsequently utilize these contributed assets to accelerate their neglected disease R&D activities. Supporter Members join the Consortium to demonstrate their approval of the WIPO Re:Search mission and its innovative and open access to IP.
WIPO Re:Search Members and providing alliance management and support to all ongoing research projects. BVGH also leads the recruitment of new WIPO Re:Search Members. Both BVGH and WIPO are responsible for communicating the activities and achievements of WIPO Re:Search to Members and the greater global health and IP communities.

IV Targeted Recruiting

A Consortium membership composed of research organizations from different sectors and geographies ensures not only a diversity of collaborations, but also a variety of ideas and capacities directed toward the development of products for neglected infectious diseases. At its inception in 2011, thirty-two organizations were Members of WIPO Re:Search.18 During the subsequent three years, BVGH focused a significant portion of its efforts toward expanding the WIPO Re:Search membership. This included a specific emphasis on recruiting User Members from Africa – where NTDs predominate. By the end of 2014, ninety-one organizations from twenty-six countries – including eighteen from Africa – were Members of WIPO Re:Search.

To have the greatest and most effective impact, WIPO Re:Search membership as a whole should have all the necessary assets, skills, and capabilities to move a product from discovery to the market. Furthermore, the membership should include organizations performing research and product development for all WIPO Re:Search diseases. As WIPO Re:Search entered its fourth year, BVGH honed its recruiting efforts toward those organizations that could bring key assets, skills, and capabilities to fill gaps in the WIPO Re:Search membership’s competencies. In late 2016 BVGH began the process of systematically mapping the assets and research activities of WIPO Re:Search User and Provider Members. Identification and organization of Members’ assets and capabilities will allow BVGH to manage the growing number of Members and resources while informing its approach to Member recruitment. By the end of 2016, a total of 109 organizations from 31 countries were WIPO Re:Search Members. These organizations include leading academic research centers with internationally renowned NTD experts, such as the University of California, San Diego (UCSD) and University of Georgia. They also include product development partnerships (PDPs), such as Medicines for Malaria Venture (MMV), Drugs for Neglected Diseases initiative (DNDi), and Foundation for Innovative New Diagnostics (FIND), as well as nonprofit organizations with experience conducting clinical trials in NTD-endemic regions, such as the Noguchi Memorial Institute for Medical Research. As BVGH continues to systematically map Members, it plans to recruit strategically relevant organizations to join and contribute to WIPO Re:Search.

18 Alnylam Pharmaceuticals; Assoc. of University Technology Managers (AUTM); AstraZeneca, Biotechnology Innovation Organization (BIO); California Institute of Technology (Caltech); Center for World Health & Medicine (CWHM); Drugs for Neglected Diseases initiative (DNDi); Eisai Co., Ltd.; Emory University; Fundação Oswaldo Cruz (Fiocruz); GlaxoSmithKline (GSK); Indian Council for Medical Research (ICMR); International Federation of Intellectual Property Attorneys (FICPI); iThemba; Kenya Medical Research Institute (KEMRI); Mahidol University; Massachusetts Institute of Technology (MIT); Medical Research Council—South Africa; Medicines for Malaria Venture (MMV); MSD; National Center for Genetic Engineering and Biotechnology (BIOTEC); Novartis; PATH; Pfizer; Sabin Vaccine Institute; Sanofi; Swiss Tropical and Public Health Institute (Swiss TPH); National Institutes of Health (NIH); US Patent and Trademark Office; University of California, Berkeley; University of California, San Francisco (UCSF); University of Dundee.
Proactive development and management of collaborations is key to the successful implementation of asset exchange programs. As the WIPO Re:Search Partnership Hub Administrator, BVGH is responsible for leveraging its close connection with WIPO Re:Search Members—including the participating biopharmaceutical companies—to establish and manage research partnerships. BVGH accomplishes this by proactively examining Member scientists’ research interests and needs and recommending collaborations with other Members that fulfill those needs. BVGH also fields asset requests from Members, identifies other Member organizations able to meet these requests, and then forges mutually beneficial collaborations with clearly defined roles, responsibilities, and objectives.

By the end of the Consortium’s first year, BVGH had established thirteen partnerships between Members. The partnership development momentum continued with twenty-eight and thirty-six collaborations established in 2013 and 2014, respectively. At the conclusion of its fifth year of operation, 108 collaborations, involving 56 members, had been established. Of these 108 partnerships, 25 were still ongoing at the end of 2016. These collaborations span thirteen different diseases and involve the sharing of several classes of IP assets: compounds, data and reagents, expertise and advice, samples, and technologies and assays.

How BVGH establishes collaborations depends on the Member it is seeking to engage. A primary objective of WIPO Re:Search is to leverage biopharmaceutical companies’

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19 Dent, supra note 14, at 591.
20 Id. at 593.
21 Fourteen diseases, including “other.”
assets to accelerate product development for neglected infectious diseases. Ten companies currently belong to WIPO Re:Search: Alnylam; Eisai; GSK; Janssen, the Pharmaceutical Companies of Johnson & Johnson; MSD; Merck KGaA, Darmstadt, Germany; Novartis; Pfizer; Sanofi; and Takeda. BVGH applies a customized approach to establishing partnerships for each of these companies. This customized approach includes the coordination of recurring discussions with each company, during which BVGH provides updates on the company’s partnerships. BVGH also inquires about the company’s current WIPO Re:Search partnership strategy: which assets it wishes to share, Members it is interested in engaging, and diseases it desires to focus on, as well as partnering bandwidth. Each company is encouraged to participate in WIPO Re:Search partnerships in a way that fits that company’s goals, resources, and capacity. For example, a company may choose to limit its participation to sharing its assets, whereas a different company may be more actively engaged in a partnership, not only sharing assets, but also scheduling regular updates with its partners, and contributing to the analysis of the data. BVGH works with each company to determine the style of participation that suits that company’s strategies and expectations.

BVGH applies a similar, customized approach to establishing collaborations with not-for-profit WIPO Re:Search Members. When a new Member joins WIPO Re:Search, BVGH reviews that Member’s researchers’ online profiles and publications, connects with those researchers to learn more about their interests, research plans, and needs, and suggests collaborations with other Members – both academic and for-profit – that could meet those needs.

VI Managing Alliances

WIPO Re:Search collaborations – as with other research endeavors – are planned and initiated with the best of intentions. A multitude of factors, including competing interests, funding changes, and lack of communication, can result in a collaboration not reaching its intended outcome. As the number and complexity of WIPO Re:Search collaborations expanded, BVGH augmented its partnering activities by creating a set of documents and implementing procedures to circumvent challenges before they can prevent a partnership from reaching a successful conclusion.

Before initiating discussions between potential collaborators, BVGH circulates its collaboration guidelines (Appendix A), which outline how BVGH will work with the potential collaborators to establish and track their WIPO Re:Search collaboration. This includes a description of the documents that must be completed prior to beginning and upon completion of a collaboration. The guidelines also describe the metrics that BVGH will track – such as project milestones reached, manuscripts published, and funding awards obtained. To further circumvent potential challenges and set expectations, BVGH has developed a collaboration outline document (Appendix B) that must be completed and approved by all participants of a WIPO Re:Search collaboration. This document requires a description of the research project and objectives, IP assets to be shared, expected timelines, and the source of funding for the project.

After establishing each collaboration, BVGH provides partnership support and alliance management – tracking each collaboration’s progress, maintaining communications between all participants, and resolving any challenges and roadblocks that arise. BVGH also engages the collaborators to schedule timeline-appropriate check-in dates.
and recurring meetings to encourage continuous communication and early resolution of challenges. As needed, BVGH identifies and engages additional WIPO Re:Search Member scientists to add further resources and expertise in order to move the research project to the next stage of product development. For example, BVGH brought an additional partner with expertise in solving the structures of pathogens’ proteins to a WIPO Re:Search schistosomiasis drug discovery project. This additional partner agreed to attempt to solve the structure of the Schistosoma mansoni protein targeted by the drug discovery project. With the structure in hand, the researchers will be able to perform rational drug design and synthesize compounds that preferentially interact with the S. mansoni protein over to the homologous human protein.

BVGH evolves and augments its partnering and alliance management procedures to meet the needs and goals of the Consortium and its Members. Upon reaching the completion of a WIPO Re:Search collaboration, BVGH requests that each collaborator complete a “collaboration close-out form,” which requests feedback and impressions of the collaboration.

VII Evolving Outputs

Aligning with the Consortium’s primary objective of engaging biopharmaceutical companies in neglected infectious disease research and product development, the majority of collaborations established by BVGH in the first two years after the Consortium’s inception involved a for-profit Member contributing its assets – most often compound sets and libraries – to a nonprofit or academic Member researcher. As WIPO Re:Search membership grew and BVGH strengthened its relationships with User Members, the collaborations established by BVGH shifted to those solely involving nonprofit/academic Members. These nonprofit + nonprofit partnerships are often multifaceted, with both partners equally contributing assets and expertise to a research project. By the end of 2016, fifty-three of the collaborations included an industry and a nonprofit/academic partner. Forty-nine collaborations involved only nonprofit/academic partners.22 Four collaborations between two for-profit entities were also established.

The diversity of projects stemming from WIPO Re:Search expanded as well. The overwhelming majority of collaborations established during the Consortium’s first year focused on drug development. However, diagnostics discovery and basic research have become more prominent over time. Correlating with the changing landscape of Members participating in a collaboration, the majority of diagnostics and basic research projects have involved two nonprofit entities.

VIII Measuring Impact

The first WIPO Re:Search collaboration was established in early 2012. While a metric such as the number of diseases eradicated or number of lives saved will be the ultimate measure of the success of the Consortium, these metrics cannot yet reflect the early performance of the Consortium and its research projects. Current analyses estimate that

it can take upwards of ten years to move a drug from discovery to the market. The majority of WIPO Re:Search collaborations were initiated at an early discovery stage and would thus require at least an additional six years to reach the market.

Until such a time when a product would be expected, BVGH has established alternative metrics to evaluate its performance as well as the impact of the collaborations it has established. Similar to the pharmaceutical industry, where the quality of a given company’s pipeline may be measured by the number of viable candidates under development, BVGH measures its performance by the number of meaningful partnerships it has established between Members, the number of Members it has engaged in those collaborations, the diversity of research questions the collaborations were established to answer, and the variety of diseases and products those collaborations address.

To date, BVGH has engaged 65 percent of the WIPO Re:Search User and/or Provider Members in a research collaboration. Thirteen of the twenty-one WIPO Re:Search diseases have been the focus of a collaboration. Research projects focused on basic research as well as drug, vaccine, and diagnostic discovery and development have been established. These collaborations span the various stages of product development – from discovery to screening, hits identification to optimization, preclinical to clinical research.

While the depth of the WIPO Re:Search Partnership Pipeline demonstrates BVGH’s prolific partnering abilities, other metrics are more reflective of the collaborations’ potential

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**Figure 4.3.** At the Consortium’s inception, the majority of collaborations BVGH established focused on drug development. As time advanced, diagnostics development and basic research became more prominent (a). While the majority of collaborations established during the Consortium’s first two years and to date involve a for-profit and nonprofit organization, in recent years, nonprofit + nonprofit partnerships have increased, outpacing for-profit + nonprofit collaborations in 2014 and 2015 (b).

Source: BIO Ventures for Global Health.

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24 The full partnership pipeline can be viewed at: https://bvgh.org/bio-ventures-global-health/wipo-research/wipo-research-collaborations/
impacts. The goal of the Consortium is to accelerate product development for neglected infectious diseases. A collaboration’s movement into the next stage of development is a good indication of its quality and potential for impact. Of the 107 agreements established to date, 15 have met important development milestones, including 4 that are still active within the Consortium.\textsuperscript{25} The number of peer-reviewed publications accepted and funding awards obtained also indicate the strength and potential for impact of a collaboration. Participants of a WIPO Re:Search collaboration are encouraged to publish the results of their collaborations, and to date, six articles have been published. Moreover, participants of two WIPO Re:Search collaborations have jointly applied for and received funding. These two funding awards totaled over US$380,000 (£250,000 GBP).

IX WIPO Re:Search Case Studies

A GlaxoSmithKline and the University of California, San Diego

Kinases are involved in many key cellular processes and are chemically tractable drug targets. However, less than 5 percent of the human kinome has been explored with selective small molecule inhibitors.\textsuperscript{26} To enable research on this historically understudied portion of the kinome, GlaxoSmithKline (GSK) compiled two sets of kinase inhibitors, Published Kinase Inhibitor Set 1 (PKIS1) and Set 2 (PKIS2), and openly shared these sets with academic researchers to be used as tools to advance biological evaluation and pharmacological understanding of the unmapped human kinome.\textsuperscript{27}

Polo-like kinases are important regulators of cell cycle progression and mitosis. In mammals there are five of these (Plk 1–5). SmPlk1 and SmSak – orthologous to human Plk1 and Plk4, respectively – are expressed in the parasitic worm, Schistosoma mansoni. Researchers at UCSD have evidence from whole-organism screens that specific inhibition of SmPlk1 by commercially available inhibitors of human Plk1 kills the helminth. To further the investigation of SmPlk1 as a potential target for disease intervention, BVGH connected UCSD and GSK. GSK agreed to provide the UCSD researchers with PKIS1 and PKIS2. The sets, which contain 367 and 539 compounds, respectively, include potent and selective inhibitors of human Plk1. Based on their studies of PKIS1 and PKIS2, the UCSD scientists have identified a number of potent anti-Schistosoma compounds as well as further demonstrated SmPlk1 as a potential schistosomiasis drug target.\textsuperscript{28}

\textsuperscript{25} Six collaborations involved AstraZeneca, which left the Consortium in 2014. At the time of AZ’s departure, these six collaborations had progressed to the next stage of development. BVGH no longer tracks the outcomes of these collaborations, and as such, it is unknown whether these projects are still active. One collaboration involved 60 Degrees Pharmaceuticals (60P), which left the Consortium in 2015.

\textsuperscript{26} NIH Phase-II-UNCID as Bio-Inert Interface for Anti-Thrombogenicity Applications, SBIR STTR, www.sbir.gov/sbirsearch/detail/677614.

\textsuperscript{27} Thavy Long et al., Structure-Bioactivity Relationship for Benzimidazole Thiophene Inhibitors of Polo-Like Kinase 1 (PLK1), a Potential Drug Target in Schistosoma mansoni, PLOS NEGLECTED TROPICAL DISEASES (Jan. 11, 2016), www.ncbi.nlm.nih.gov/pmc/articles/PMC4709140/.

\textsuperscript{28} Id.
With half of the world’s population living in areas at risk for transmission, malaria is one of the most severe public health concerns worldwide.\(^{29}\) The disease has two stages in the human host – an obligatory asymptomatic liver-stage followed by a symptomatic blood stage. Treating malaria symptoms requires clearing blood-stage parasites, and appropriately, most antimalarial drug discovery efforts have largely focused on developing therapeutics against blood-stage parasites. However, inhibiting the liver stage, when the lower parasite burden might delay resistance development, presents a more attractive approach for prophylaxis. Yet presently there are no approved liver-stage therapies with the exception of primaquine, which is contraindicated during pregnancy and in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency, a widespread phenotype across malaria-endemic regions.\(^{30}\)

Accordingly, a researcher at the National Institute of Immunology (NII) in Delhi, India is working to identify a drug target for liver-stage malaria. He has found four host-based transcription factors that he believes affect the severity of liver-stage malaria infection. In order to analyze their role, he is interested in knocking down these genes in the \textit{in vitro} and \textit{in vivo} models that he has developed. One approach to knocking down genes is through RNA interference. Given their expertise in this field, BVGH connected the NII researcher with scientists at Alnylam Pharmaceuticals in Cambridge, Massachusetts. Alnylam designed and synthesized optimized small interfering RNAs (siRNAs) against the four host transcription factor genes identified by the NII researcher.

Another challenge in getting efficient gene knockdown is the delivery and targeting of the siRNAs within the tissue. To complete this puzzle, BVGH introduced a third collaborator from Northeastern University in Boston, Massachusetts. The Northeastern University researcher, who is an expert in target-specific delivery systems, encapsulated the siRNAs in nanoparticles that target them to hepatocytes (liver cells). The NII researcher confirmed that the siRNAs knocked down expression of the target genes and subsequently assessed the effect this knock-down had on malaria parasite growth \textit{in vitro}. Knock-down of three of the four transcription factors resulted in significant inhibition of the malaria parasite’s growth in hepatocytes. The researcher will subsequently test the effect the siRNAs have on liver-stage malaria \textit{in vivo}.

Ultimately these analyses will help the team identify host proteins that could then be targeted for novel drug development for liver stage-malaria thus addressing a significant therapeutic void.

Soil-transmitted helminths infect approximately 1.5 billion people worldwide, resulting in diarrhea, abdominal pain, general malaise, and weakness. The helminths responsible for these infections – roundworms (\textit{Ascaris}), whipworms (\textit{Trichuris}), and hookworms


(Necator and Ancylostoma) – are transmitted through contact with or consumption of soil contaminated with parasite egg-ridden feces. Improving sanitation in endemic regions can dramatically reduce the incidence of these infections.

Researchers at the University of South Florida (USF) have developed a solar-chemical toilet that sanitizes waste products; however, to determine the efficacy of the treatment, they need to assess the viability of parasite eggs post-treatment. The process of isolating eggs from sewage or environmental samples to assess their viability requires the filtration of large quantities of samples as well as multiple sedimentation and flotation steps. Due to the nature of these samples, the filters are easily and routinely clogged by solid debris and the process can take two days. An alternative device that could swiftly and cost-effectively isolate and concentrate helminth eggs from sewage and bio-solids samples would greatly aid the USF researchers’ assessment of the solar-chemical toilet.

To assist the USF scientists with their work, BVGH connected them to a biomicrofluidics expert at McMaster University in Canada. After several discussions the McMaster University researcher and his group developed a compact, portable, and low-cost tangential flow filtration device that separates particles according to their size without the use of any sophisticated instrumentation. The device can retain particulates as minute as two microns as well as worm eggs as large as 400 microns, and it is particularly useful in concentrating Ascaris eggs from a variety of samples. The USF and McMaster scientists have collaborated extensively over the past year on developing and testing various designs of this device. The USF scientists are already comparing an improved, second generation filtration device’s ability to isolate eggs from environmental and fecal samples to that of the WHO-standard technique (Kato Katz). If successful, this device could become the routine method to use when testing clinical and environmental samples for the presence of parasite eggs, thus helping to detect the parasites at their source and stemming their transmission.

D  NINA Heater: Bringing Malaria Testing to the Field

One of the main barriers to eliminating malaria is accurate and timely diagnosis of the disease. There are methods available to screen for Plasmodium falciparum infection; however, many are not affordable, are unable to detect asymptomatic cases, or have long turnaround times. These challenges often result in asymptomatic people not being diagnosed and treated, resulting in continued malaria transmission. Newer methods, such as loop-mediated isothermal amplification (LAMP), have been created with these challenges in mind. However, these are still dependent upon consistent electricity – something that is commonly unavailable in many malaria-endemic regions.

In order to address this issue, a team of researchers and engineers at PATH developed a technology known as a noninstrumented nucleic acid amplification (NINA) heater. The NINA heater uses an exothermic chemical reaction to generate the heat necessary for DNA amplification such that no external electricity source is needed. A malaria LAMP assay combined with the NINA heater is a tool suitable for field use.
E. PATH and the University of Calgary

BVGH connected the scientists at PATH with an infectious disease doctor and researcher at the University of Calgary in Canada, who works on implementing effective malaria diagnostics that can be used in low-resource settings.

The University of Calgary scientist tested a pan-Plasmodium/Plasmodium falciparum-specific LAMP assay with the NINA heater, first in his laboratory at the University of Calgary and then in the field in Ethiopia. The results of his studies demonstrated that the NINA-LAMP combination was more sensitive than microscopic diagnosis and comparable to a nested PCR test.32

F. PATH and the Centre Pasteur du Cameroun

A researcher at the Centre Pasteur du Cameroun (CPC) developed two reverse transcription-LAMP-based assays (RT-LAMP) – one to detect gametocytes, the transmissible form of the Plasmodium parasite, and one to detect low-level parasitemia in malaria patients. Developing an assay to detect the gametocytes will help to determine the risk of transmission from humans back to mosquitoes. Detecting low-level parasitemia will help to minimize the number of false negative malaria diagnoses obtained using other available malaria diagnostics. Both of these are important factors as the world moves toward malaria elimination. BVGH connected the CPC researcher with the PATH scientists, who agreed to share their NINA heater. The CPC researcher assessed both of his RT-LAMP assays with the NINA heater. These tests have yielded encouraging results including a peer-reviewed publication describing the low-level parasitemia assay. The two groups also expect to publish the results of the gametocyte assay.

X. Managing IP

Transparent management of IP rights is an important aspect of any collaborative project, including those established through WIPO Re:Search. Drawing on POINT’s access and affordability principles, the Consortium and its activities are governed by the WIPO Re:Search Guiding Principles (Principles or Guiding Principles).33 These Principles are incorporated into all collaboration agreements and dictate ownership of new IP and access and affordability of products resulting from a WIPO Re:Search collaboration.34 The majority of partnerships established through WIPO Re:Search were initiated following the execution of a material transfer agreement (MTA). Other partnerships have been governed by a broader memorandum of understanding (MOU) or confidential disclosure agreement (CDA). Regardless of the type of agreement partners prefer to use, the Guiding Principles are expected to be incorporated.

34 Krattiger et al., supra note 16.
XI Partnerships as Implementers of Sustainable Development Goals

The Sustainable Development Goals (SDGs) build on the momentum of the Millennium Development Goals (MDGs) and are designed to shape development, align stakeholders, and indicate global progress toward ending poverty, protecting the planet, and ensuring prosperity for all.\(^{35}\) PPPs have historically been, and will continue to be, key instruments of delivery for development initiatives, such as the SDGs, due to their adaptability as well as shared risk and resources model.\(^{36}\) Going forward, it will be essential for PPPs to align their strategies and activities to the SDGs to collectively make the greatest possible impact on development.

The WIPO Re:Search Consortium’s core tenets align with the SDGs. WIPO Re:Search focuses its activities on malaria, tuberculosis, and NTDs. Along with HIV/AIDS, SDG Target 3.3 underscores the need to end the epidemics of tuberculosis, malaria, and NTDs, as well as combat hepatitis, water-borne illnesses, and other communicable diseases. Furthermore, SDG Target 3.b focuses on supporting R&D for health care products for communicable and noncommunicable diseases that particularly affect developing regions.\(^ {37}\) WIPO Re:Search is helping to meet this Target by establishing collaborations to stimulate and accelerate drug, vaccine, and diagnostic development for NTDs, malaria, and tuberculosis. The WIPO Re:Search Guiding Principles, which inform the Consortium’s approach to IP ownership and product accessibility, require any product resulting from a WIPO Re:Search collaboration to be sold royalty-free in LDCs and that affordability should be considered in all other developing regions.\(^ {38}\) These principles further align with SDG Target 3.b, which emphasizes the need to ensure access to affordable medicines and vaccines.

SDG Goal 9 concentrates on promoting sustainable industrialization, resilient infrastructure, and innovation across the world, with an emphasis on developing countries. Target 9.5 calls for the enhancement of scientific research in developing countries.\(^ {39}\) Many of the diseases that WIPO Re:Search focuses on disproportionately – if not entirely – affect people living in Africa. In an effort to tap into the research interests and knowledge of Africa, while also providing opportunities for African researchers to connect with leaders in the biopharmaceutical sciences, BVGH – with the support of the Consortium – made a concerted effort to recruit research centers from Africa. In 2012 and 2013, twelve of the new Members recruited were based in Africa. Of the 107 collaborations established by BVGH, 28 include an African partner. In certain instances, the collaborations also provided the researcher with the opportunity to gain new skills. Three collaborations have involved a capacity-building or training aspect. For example, BVGH established a collaboration between researchers at the University of Ibadan in Nigeria and the National Institute of Parasitic Diseases (NIPD), Chinese Center for Disease

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\(^ {35}\) Sustainable Development Goals, UN Dev. Program [www.undp.org/content/undp/en/home/sustainable-development-goals.html].


\(^ {38}\) WIPO, supra note 33.

Control and Prevention, in China to identify antigens from two *Schistosoma* species that could be incorporated into a diagnostic test. With funding from the Chinese government, a post-doctoral researcher from the University of Ibadan will travel to NIPD. While at NIPD, the scientist will work alongside his collaborators, receive training on NIPD’s antigen discovery platform, and use schistosomiasis patient samples from Nigeria to discover new diagnostic *Schistosoma* antigens.

With funding from IP Australia, BVGH was also able to arrange research training sabbaticals for six scientists from WIPO Re:Search member organizations in Africa. These scientists, who ranged from graduate students to laboratory heads, spent three months to one year at a leading research university or multinational pharmaceutical company. These training opportunities were customized to meet the specific training needs and research interests of each participating scientist.40 In 2015 IP Australia committed additional funding for research training sabbaticals. This second round of training opportunities will focus on building research capacity specifically in the Indo-Pacific region. Through these sabbaticals and research collaborations, WIPO Re:Search is actively promoting and augmenting scientific capacity in key developing regions.

SDG Goal 17 outlines the importance of PPPs as mechanisms for development that can unlock and mobilize private resources toward development issues. Goal 17 further emphasizes the need to create frameworks and incentives to support the establishment of PPPs to meet the other sixteen SDGs.41 WIPO Re:Search is a timely and germane example of how PPPs can be established and managed to support and impact global health. WIPO Re:Search collaborations leverage knowledge and skills and mobilize IP assets from the private, public, and civil sectors. The track record of WIPO Re:Search demonstrates that PPPs not only work, but that individuals and organizations across the globe and within all sectors are eager to combine resources and share risk to address the world’s greatest challenges.

Conclusion

Through globalization, the spread of people, ideas, and diseases is accelerating. Growing global interconnectedness is shedding light on diseases that have been neglected in the past and changing the ways society and the scientific community approach development. This is evident by the SDG Targets, which address tuberculosis, malaria, and NTDs, as well as through the global emphasis on PPPs as a means of implementation. Scientists and organizations are becoming less siloed in their infectious disease work. More collaborations, through PPPs and consortia, are directing R&D resources toward diseases historically neglected by the scientific community.

The biopharmaceutical industry is also recognizing the need for impactful global health efforts to relieve disease burden in developing countries and emerging markets. Through the creation of open innovation platforms, including POINT and WIPO Re:Search, as well as additional pragmatic approaches, the biopharmaceutical industry


is contributing to the advancement of NTD R&D. WIPO Re:Search and other PPPs provide the framework through which the biopharmaceutical industry can share its IP assets and resources with qualified infectious disease researchers. Leveraging IP to stimulate rather than hinder R&D is achievable by having clear guidelines, documented expectations, and an understanding of ownership. Refuting arguments that IP is inherently restrictive and hinders access to health products, open IP innovation platforms, like WIPO Re:Search, encourage and support the use of IP – within the legal IP framework – to benefit public health.

In order for PPPs to be successful, it is crucial to develop a transparent framework for collaborations, thus ensuring a mutual understanding of expectations and ownership of resources. Equally important activities for effective PPPs include targeted recruitment to develop a well-rounded group of contributing members, proactive partnering engagement of members, alliance management, adaptability, and impact measurement. As the Partnership Hub of the WIPO Re:Search Consortium, BVGH is responsible for the aforementioned components of success. BVGH’s active alliance management and expectation-setting help align Members’ efforts to finding innovative solutions to advance product development for NTDs, malaria, and tuberculosis.

IP sharing and collaboration drive WIPO Re:Search activities. Given the growing interest in NTD, malaria, and tuberculosis research by PPPs and the global health community’s emphasis on these diseases, it is essential for WIPO Re:Search to be scalable and flexible. With the right foundation through the Guiding Principles, and an active partnership manager, WIPO Re:Search will continue to be a conduit between pharmaceutical companies’ assets and know-how and researchers’ innovative infectious disease solutions.
Appendix A: BVGH Collaboration Guidelines

BVGH strives to build successful WIPO Re:Search collaborations that achieve their scientific objectives. To ensure efficient and effective use of resources and assets, BVGH asks that all parties participating in a WIPO Re:Search collaboration follow the guidelines below.

Research Project and Goals

Prior to initiating a WIPO Re:Search collaboration, BVGH will ask User Members to complete the “WIPO Re:Search Collaboration Outline.” Each Outline should describe:

1. Clearly defined research objectives agreed upon by all collaborators
2. Key milestones (e.g., completion of first round of screening)
3. Go/no-go decision points, if applicable (e.g., funding requirements, meeting target IC50 values)
4. Project timelines based on availability of resources and other commitments

BVGH will use this information to facilitate communication between the partners and keep track of collaboration milestones and progress. Upon reaching a milestone, the BVGH team will work with collaborators to identify new partners and resources, if needed, to move the project forward.

Project Monitoring/Tracking and Close-out

After establishing a new collaboration, BVGH will schedule regular teleconferences with all project collaborators. The purpose of these discussions is to track project progress and resolve challenges.

All collaborators will be asked to complete the “WIPO Re:Search Collaboration Close-Out” document upon the conclusion of the project. This simple, half-page document provides collaborators with the opportunity to share their thoughts on the collaboration’s successes and challenges. This feedback will also help the BVGH team improve their support and alliance management services.

Metrics

In order to monitor WIPO Re:Search statistics, BVGH asks collaborators to track project metrics including the following:

1. Research milestones achieved
2. Publications and presentations arising from the collaboration
3. Grants applied for and any funding received
4. Number of students or postgraduates that received training as part of the collaboration

Publications and Presentations

To raise awareness of the Consortium and its achievements, BVGH requests that all Members acknowledge WIPO Re:Search when presenting or publishing the results of
their collaborations. BVGH suggests that the following or similar language be used in publications: “We thank BIO Ventures for Global Health (BVGH) for catalyzing this collaboration through WIPO Re:Search.”

BVGH encourages Members to contact Katy Graef at kgraef@bvgh.org about any WIPO Re:Search-related publications or presentations so that they can be mentioned in an issue of the monthly BVGH Partnership Hub Snapshot newsletter.
Appendix B: BVGH Collaboration Outline Document

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<tr>
<th>Requestor Information:</th>
<th>Date:</th>
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<tbody>
<tr>
<td>Name(s)</td>
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**Contact Information**  
(provide full contact information including address, phone number, email address)

**Primary Organization**  
Organization:  
Scientific Lead:

**Additional Organizations**  
Note all other organizations associated with the proposed work plan

**Other Agreements**  
Please describe any similar agreements or ongoing research projects.

**Request Overview**

**Research Objectives**

Briefly describe the collaboration: Background summary, research objectives, specific goals, and the question you hope to answer. If relevant, please describe what problem you are trying to solve. Include relevant citations as necessary.

Background:

Research objectives:

Specific goals for this collaboration:

**Description of Work**

Limit description to less than 100 words  
(Include experimental plan (assays), projected timeline, key project milestones, and go/no-go decision points, where applicable)

**Target Organisms**

List all organisms that will be tested, if applicable

**Asset(s) Requested/Shared**

**Asset requested/shared**

☐ Compounds (provide description below)  
☐ Expertise  
☐ Assay/Platform/Technology  
☐ Other (please specify, see below)

**For compound/chemical requests**

☐ Compound library: (provide description)  
☐ Compound class or series:  
☐ Probe compounds for mechanism of action studies:  
☐ Other:

**Format for delivery of compounds**

☐ Number of compounds:  
☐ Format: (in plates? Bold one: 96 / 384 / 1536 / 3456 well? Vials?)  
☐ Powder required? Y / N  Quantity (mg): ____  DMSO solution Y / N  ____ µL  
☐ Liquid stocks: Concentration: ____  Volume required: ____ mL  
☐ Blinded as to structure acceptable? (Y/N):  
☐ Other considerations (e.g.: special shipping/handling):

**Other assets requested**

Please provide a description of requested asset if it is not a compound/chemical

**Project support**

Do you have the necessary capacity and resources to complete the project as outlined above?  
If the research project involves multiple stages, do you anticipate the need for additional partners and/or resources? If so, please explain.  
How will this project be funded? Please provide the funding organization and grant type (e.g. NIH, Wellcome Trust)

**Project timeline**

- Estimated project initiation date:
- Estimated project completion date:
References


