Accelerating R&D for Neglected Diseases through Global Collaborations

WIPO Re:Search Partnership Stories 2013–2015

A publication of collaborations facilitated by BVGH
"Many illnesses that primarily affect populations living in poverty do not have effective treatments or prevention methods, and we need new approaches to improve this situation," said NIH Director Francis S. Collins, M.D., Ph.D. "WIPO Re:Search is a new model to foster collaboration between researchers working across government, academia and pharmaceutical and biotech companies. The role of BVGH in WIPO Re:Search as an active facilitator of partnerships has clearly been an important element in the success of this effort."

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Dear Friends of WIPO Re:Search,

The World Intellectual Property Organization (WIPO) has a mandate to assist its 188 Member States to use intellectual property to meet society’s evolving needs. We do so by, inter alia, creating public-private sector partnerships and capacity-building programs to help developing countries gain access to valuable knowledge and facilitate technology transfer.

WIPO Re:Search is a particularly successful example of our work in the field of global health. The collaboration stories captured in this book are a sampling of our early progress and represent just the beginning of what we all expect to accomplish in the coming years.

In 2015, WIPO Re:Search recorded a milestone of 100 Members in total, including two new private sector companies, Takeda Pharmaceuticals of Japan and Johnson & Johnson of the United States of America. The growth in membership and the commitment of the private sector are clear signals of the success WIPO Re:Search has seen to date.

I hope you will enjoy the collaboration stories and WIPO Re:Search statistics included in this book.

Sincerely,

Francis Gurry, Ph.D.
Director General, World Intellectual Property Organization

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Dear Colleagues,

Since its launch in October 2011, WIPO Re:Search has exceeded our greatest expectations. We have made tremendous progress connecting researchers, facilitating collaborations, and advancing research and development in neglected tropical diseases, malaria, and tuberculosis. Members currently hail from 27 countries, with collaborations crossing oceans and spanning the globe. As of October 2015, BVGH has facilitated 95 agreements between WIPO Re:Search members. Of the 95 agreements, 47 are ongoing and eight have met important development milestones.

This second biennial storybook highlights how far we have come, the impact we have had, the wide range of projects we are facilitating, and where we are headed. Twenty-five collaborations are featured in the storybook along with an overview of the Consortium’s accomplishments. These stories illuminate the variety and breadth of WIPO Re:Search collaborations established to date.

I would like to express my sincere thanks to all WIPO Re:Search Members for their contributions to collaborations and their dedication to develop products to prevent, diagnose, and treat diseases of poverty.

All of us at BVGH look forward to working with you in 2016.

Sincerely,

Jennifer Dent
President, BVGH
WIPO Re:Search was founded by the World Intellectual Property Organization (WIPO) in partnership with BIO Ventures for Global Health (BVGH) and several leading pharmaceutical companies. The aim of the Consortium is to accelerate the development of new drugs, vaccines, and diagnostics for neglected tropical diseases (NTDs), malaria, and tuberculosis by connecting private industry assets and resources to qualified academic and non-profit researchers with product discovery or development ideas. Consortium membership includes academic and non-profit research institutions, governmental and non-governmental organizations, and biopharmaceutical companies.

The WIPO Re:Search consortium is supported through the financial contributions of the pharmaceutical company Members – Alnylam Pharmaceuticals; Eisai Co., Ltd.; GlaxoSmithKline; Johnson & Johnson; Merck KGaA, Darmstadt, Germany; Merck & Co., Inc.; Novartis AG; Pfizer Inc.; Sanofi S.A.; and Takeda Pharmaceutical Company Ltd. These companies and other Provider Members contribute a wide variety of intellectual property (IP) assets including compounds and compound libraries, expertise and advice, reagents, and technologies.

BIO Ventures for Global Health (BVGH)
BVGH was established in 2004 by the Biotechnology Industry Organization (BIO) to engage biopharmaceutical companies in global health initiatives. Today, BVGH continues to work closely with BIO and many other organizations to develop programs and create partnerships to improve health worldwide. As the Partnership Hub Administrator of WIPO Re:Search, BVGH plays a pivotal role in proactively identifying, establishing, and supporting collaborations.

World Intellectual Property Organization (WIPO)
WIPO is the United Nations agency dedicated to the use of IP to promote innovation for social, economic, and cultural development. WIPO manages a balanced and effective international IP system, in cooperation with its 186 member states and other relevant international organizations. As the Secretariat of WIPO Re:Search, WIPO plays a key role in overseeing the Consortium’s success. WIPO manages the online, publicly available WIPO Re:Search Database, which contains nearly 200 entries detailing Member contributions that range from compounds to diagnostic tools and more.

WIPO Re:Search Partnership Development Flow

- Identify opportunities
  - Search database for relevant assets
  - Communicate with Providers
  - Direct collaboration requests
  - Engage partners based on assets

- Establish partnerships
  - Establish mutual interest
  - Facilitate discussions
  - Align expectations and timelines

- Support partnerships
  - Track collaboration progress
  - Maintain communications
  - Resolve challenges

BIO Ventures for Global Health (BVGH)

- Manage assets
- Develop databases
- Recruit new User and Provider Members
- Member engagement
- Communications and publications
- Research collaborations
- Member workshops
- Search database for relevant assets
- Communicate with Providers
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WIPO Re:Search - catalyzing product research & development for NTDs, malaria, and tuberculosis
Collaboration Map

Distribution of Collaborations by Disease

Pipeline of Ongoing Collaborations

- Buruli ulcer
- Chagas disease
- Dengue fever
- Human African trypanosomiasis
- Leishmaniasis
- Lymphatic filariasis
- Malaria
- Neurocysticercosis
- Onchocerciasis
- Rabies
- Schistosomiasis
- Soil-transmitted helminthiases
- Tuberculosis

*Pipeline captures agreements put in place by October 15th, 2015*
Collaborations by Sector*
- Industry + Non-profit: 46
- Non-profit + Non-profit: 45

Collaborations by Current Stage of Development
- Basic research/Discovery: 35
- Screening for Repurposing: 27
- Hits ID: 13
- Hit to Lead: 8
- Preclinical Development: 12

Collaborations by Resources Shared
- Compounds: 37
- Data/Reagents: 15
- Expertise/Advice: 18
- Samples: 13
- Technology/Assay: 12

Collaboration Trends
- % Collaborations per Year:
  - 2012: 60%
  - 2013: 50%
  - 2014: 40%
  - 2015: 30%

*In addition, there are four Industry + Industry collaborations.

Collaboration: Any sharing of IP assets, data, and expertise to advance research and development of NTDs, malaria, and tuberculosis.

Industry: A pharmaceutical or biotechnology company.

Non-profit: Academic institutions, research institutions, and product development partnerships.

Portfolio of Select Diseases

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<tr>
<th>Disease</th>
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<td>Dengue</td>
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*In addition, there are four Industry + Industry collaborations.
The following stories represent some of the many collaborations that have been catalyzed through WIPO Re:Search. This publication features collaborations that have been established since 2013.

**Collaboration Stories**

**Glossary of Icons used in the Stories**

**Disease Causing Organism**
- Bacteria
- Virus
- Protozoa
- Worms

**Product**
- Drugs
- Vaccines
- Diagnostics

**Stage of Development**
- Basic research/Discovery
- Screening for Repurposing
- Hits ID
- Hit to Lead
- Preclinical Development

**Resource Shared**
- Compounds
- Expertise/Advice
- Reagents
- Technology

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**Cerebral malaria (CM)** is the most severe neurological complication of the infection by the parasite *Plasmodium falciparum*, resulting in seizures, coma, and death. With over 500,000 cases annually, children in sub-Saharan Africa are the most affected. Mortality is high, and around 25% of survivors develop neurological complications and cognitive impairment.

The pathology of CM is not fully understood but is thought to involve interactions between *P. falciparum*-infected erythrocytes (IE) and host endothelial cells. In a recent study in Malawi, brain swelling was found to be strongly linked with fatal outcomes in CM. The cause of this swelling is probably multi-factorial, involving inflammation, cell death, and IE accumulation. Recent work from Dr. Alister Craig, Dr. Chris Moxon, and colleagues at the Liverpool School of Tropical Medicine (LSTM) and University of Liverpool identified a role for protease-activated receptor (PAR) 1 in this pathway. Their research has shown that during *P. falciparum* cerebral infection, PAR1 may be activated by an alternate pathway. This altered activation causes the PAR1 pathway to initiate a pro-inflammatory response, causing coagulation and inflammation.

Dr. Craig's group has developed a live endothelium model co-cultured with IE to study these interactions *in vivo*. Given the critical role of PAR1 in the altered signaling process, Dr. Craig wanted to test a range of PAR1 inhibitors using this model. His hypothesis is that this PAR1-mediated coagulation/inflammation pathway plays a significant role in endothelial barrier loss in CM, and that adjunct treatments targeting PAR1 could reduce mortality and, potentially, post-CM neurological complications. BVGH connected Dr. Craig to vascular biology experts at Eisai Co., Ltd. (Eisai) who have PAR1 inhibitors to contribute to his research. Dr. Craig has obtained encouraging results after his first round of screening. BVGH is currently working with Dr. Craig and the scientists at Eisai to explore different approaches to move this project forward.

"WIPO Re:Search provides a proactive approach to identifying potential research groups that could benefit from input from industrial partners. This is particularly important for diseases that principally affect areas of the world with limited resources by providing a platform for researchers often working within academia to gain added value from the investment in people and research delivered by industry." - Dr. Alister Craig, LSTM

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**Eisai Co., Ltd.**

**Liverpool School of Tropical Medicine**
K

Polo-like kinases (Plks) are important regulators of cell cycle progression and mitosis. In mammals there are five Plks (Plk 1-5). SmPlk1 and SmSak—homologous to Plk1 and Plk4 respectively—are expressed in the parasitic worm Schistosoma mansoni. Dr. Conor Caffrey of the Center for Discovery and Innovation at the University of California, San Diego. He and his team are particularly focused on basic and applied biology of tropical parasitic diseases including schistosomiasis, hookworm disease, and African trypanosomiasis.

Given the usefulness and versatility of these inhibitors, GSK is currently collaborating with over 100 researchers to explore the full use of the compounds. A few notable diseases being studied through WIPO Re:Search include tuberculosis, malaria, and schistosomiasis. Described below is one such collaboration.

To accelerate drug discovery, Dr. Gerd Pluschke from the University of British Columbia (UBC) in Canada have discovered that certain avermectins, a family of compounds with anthelmintic activities used to treat river blindness in people and roundworms in pets, were active as antibiotics against \textit{Mycobacterium tuberculosis}, the bacterium closely related to the causative agents of tuberculosis (\textit{Mycobacterium leprae}). Although Buruli ulcer can be effectively treated, current therapeutic options are limited, lengthy, and unpleasant. To further support the growing list of collaborations based on kinase inhibitor sharing, GSK licensed PKIS1 and PKIS2 to UBC.

Boston University Global Health (BVGH) connected Dr. Pluschke with Drs. Charles Thompson and Santiago Ramon-Garcia to discuss the possibility of assessing these avermectins against \textit{M. leprae}. Dr. Pluschke and his Associate Researcher, Dr. Nicole Scherr, assessed the set of avermectins provided by UBC against the bacterium. The data from these assays, together with an appraisal of published pharmacokinetic properties of the avermectins, demonstrated that selamectin was most promising for clinical application (recently published in PLOS Neglected Tropical Diseases 9: e0003996 doi: 10.1371/journal.pntd.0003996, 2015).

The results of this collaboration have paved the way for the development of a new, alternative treatment option for Buruli ulcer. Given these exciting results, new partners who will bring in the expertise and the infrastructure needed to move this project forward are being sought.

“WIPO Re:Search was instrumental in bringing together the expertise needed to move this project forward. They definitely catalyzed this productive collaboration.” — Dr. Charles Thompson, UBC

“WIPO Re:Search has been very important in facilitating collaborations and furthering the various research agendas for NTDs. This is greatly appreciated.” — Dr. Conor Caffrey, UCSD

Note:
The team of GSK scientists that developed PKIS1 and PKIS2 recently moved to the University of North Carolina (UNC), Chapel Hill (https://pharmacy.unc.edu/research/sgc-unc/). In order to further support the growing list of collaborations based on kinase inhibitor sharing, GSK licensed PKIS1 and PKIS2 to UNC. Interested parties can reach out to the UNC team with questions about the kinase inhibitor sharing initiative by sending an e-mail to sgc-unc@unc.edu.
Merck & Co., Inc.
Walter and Eliza Hall Institute of Medical Research

Since the early 2000s, the estimated global mortality rates due to malaria have decreased by 47%. Emerging parasite resistance to current therapies threatens this progress and resistance to anti-malarial drugs has been documented in three of the five malaria species known to affect humans.

Researchers are actively looking for new anti-malarial drugs, that are less likely to result in resistance. One approach involves targeting plasmodopin V (PMV), a Plasmodium enzyme that is encoded by a highly conserved gene and therefore may offer a target with a high barrier to resistance. PMV regulates the export of Plasmodium proteins that remodel the host's infected red blood cells (RBC). This RBC remodeling is essential for the parasite's survival, enabling it to acquire nutrients and evade the host immune response.

Dr. Alan Cowman, a Howard Hughes Medical Institute investigator at the Walter and Eliza Hall Institute of Medical Research (WEHI) in Australia, and his colleagues, Dr. Justin Boddey and Dr. Brad Sleebs, are studying the function of proteins involved in parasite invasion and host cell remodeling. They have developed a high-throughput assay to screen for compounds that can inhibit PMV in both P. falciparum and P. vivax, the two parasites responsible for the vast majority of malaria cases. The Cowman/Boddey/Sleebs laboratories are interested in identifying aspartyl protease inhibitors that are specific to Plasmodium, an aspartic acid proteolytic enzyme. At the US-based pharmaceutical company, Merck & Co., Inc. (known as MSD outside the United States and Canada), Dr. Tanweer Khan recognized that the company had many drug-like aspartyl protease inhibitors in its chemical libraries that could potentially impact the replication of malaria. Merck approached BVGH with an interest in possibly repurposing these inhibitors, previously made for other therapeutic targets, as agents against malaria. BVGH connected the two organizations.

This work forms part of Merck’s long-standing commitment to discovering, developing, and delivering novel medicines in the global fight against infectious disease through both in-house research and engagement with external partners (http://www.merckresponsibility.com/access-to-health/infectious-diseases/).

By screening Merck’s set of small molecule aspartyl protease inhibitors using WEHI’s high-throughput assay, the team expects to identify chemically tractable hits that target PMV. The initial results of the screen seem promising, and Merck will continue to share medicinal chemistry expertise to help advance initial hits. Recognizing the need to find additional financial support for this progressing collaboration, BVGH suggested that Merck and WEHI jointly apply for a Wellcome Trust funding opportunity aimed at stimulating partnerships between non-profit and for-profit entities. The parties successfully obtained financial support for this progressing collaboration, and the team hopes to advance the development of a new, broad-spectrum anti-malarial drug into development.

"BVGH was the conduit that allowed for facile discussions that moved quickly to agreement negotiations and signature. Working with Alan’s team of expert scientists is exactly the kind of partnership we look for whereby we can employ an important company asset and our drug-hunting expertise in collaboration with world expert scientists to address a disease area of incredible medical need. Doing science like this is not work – it is fun and incredibly rewarding for all involved.”

- Dr. David Olsen, MSD

University of California, San Diego

Chagas disease and leishmaniasis, two parasitic diseases caused by pathogens belonging to the Trypanosomatidae family, collectively infect nearly 22 million people worldwide and result in approximately 60,000 deaths annually. Current treatments for both are often long, expensive, and limited by significant side effects. Despite the availability of treatment options, chronic Chagas disease and visceral leishmaniasis—the most advanced forms of the diseases—are not curable.

The sterol biosynthesis pathway is an attractive target to develop new treatments as sterols are critical in maintaining proper stability of eukaryotic cell membranes. Specifically, Trypanosoma cruzi (T. cruzi, the causative agent of Chagas disease) and Leishmania require membrane ergosterols for growth and viability. Interestingly, ergosterols are absent in mammalian cells, making the parasite enzymes responsible for catalyzing ergosterol synthesis ideal drug targets. CYP51 and squalene synthase—enzymes involved in the multistep catalysis of ergosterol—have been demonstrated to be promising drug targets in T. cruzi and Leishmania.

Targeting multiple enzymes within a single metabolic pathway is an accepted method of limiting the development of drug resistance. Having previously demonstrated that CYP51 inhibitors are effective against T. cruzi and Leishmania, Drs. Larissa Podust, Jim McKerrow, and Jair Siqueira-Neto from the University of California, San Diego (UCSD) were interested in identifying inhibitors of an additional enzyme in the parasites’ ergosterol synthesis pathways.

Eisai Co., Ltd. (Eisai), a founding member of the WIPO Re:Search consortium, contributed E5700, a novel squalene synthase inhibitor originally developed to treat atherosclerosis, to the WIPO Re:Search Database. Based on previous studies by Dr. Julio Urbina and colleagues establishing E5700’s important role in targeting the catalysis of ergosterol, Dr. McKerrow hypothesized it would be an ideal drug candidate to co-administer with a novel CYP51 inhibitor. BVGH conveyed Dr. McKerrow’s interest and request to Eisai, and they agreed to share E5700 with the UCSD researchers. Dr. Podust, McKerrow, and Siqueira-Neto will assess E5700 alone and in combination with a novel CYP51 inhibitor for efficacy against both T. cruzi and Leishmania. If synergistic effects are observed, these compounds could be further optimized into a potentially more efficient and effective treatment for Chagas disease and leishmaniasis.

"WIPO Re:Search continues to play a key role for us in brokering collaborations with biotech and pharma. Because we are working on neglected tropical diseases, having WIPO/BVGH on the lookout for new drug candidates or technology is an invaluable resource.”

- Dr. Jim McKerrow, UCSD

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The connections made by BVGH and the opportunities that have been presented to my students and me through WIPO Re:Search have been invaluable,” stated Dr. Wellington Oyibo, Director, Research and Innovation, University of Lagos, Nigeria. “My laboratory and students have benefited through the many research partnerships and scientific exchanges facilitated. The impact of these experiences will be long-lasting for each of us and for the University.”

University of Lagos faculty to Novartis:
BVGH coordinated a research placement for Dr. Oyibo at Novartis’ headquarters in Basel, Switzerland. Dr. Oyibo gained experience in product development processes, as well as insights into clinical trial management. Funding for this program was secured by WIPO from the Australian government.

With the shift in focus from malaria control to malaria elimination, Dr. Oyibo is interested in developing diagnostics that can detect asymptomatic malaria. After receiving samples from Nigerian patients with severe or asymptomatic malaria and from healthy individuals, Dr. Bach will use a proteomic approach to identify differently expressed biomarkers in the three population types that could be incorporated into a suitable platform for malaria diagnosis.

University of Lagos PhD student to NIPD/China:
BVGH facilitated the placement of a graduate student from Dr. Oyibo’s laboratory, Uche Igbasi, in Dr. Jun-Hu Chen’s laboratory at NIPD (see inset below).

University of Lagos PhD student to Stanford:
BVGH facilitated the placement of a graduate student from Dr. Oyibo’s laboratory, Chika Okangoba, in Dr. Ben Pinsky’s laboratory (Stanford) to advance student education and training (see story on page 28).
Onchocerciasis: One Disease, Two Approaches

Onchocerciasis, commonly known as river blindness, is a debilitating neglected tropical disease that affects approximately 26 million people across the world, causing visual impairment in up to 1-2 million people, of which 276,000 people are rendered completely blind. This disease, which is predominant in sub-Saharan Africa, is caused by the parasitic worm *Onchocerca volvulus* and is spread via the bite of black flies of genus *Simulium damnosum*.

Despite being the second leading infectious cause of blindness globally, there is no available treatment that can cure or resolve the infection. Ivermectin is currently the only recommended drug. It kills the juvenile worms (microfilariae) but is ineffective against the microfilariae-producing adult worms. To completely clear the parasite, infected individuals must take ivermectin annually over the entire life span of the adult worm—up to 14 years. Mass drug administration (MDA) of ivermectin has eliminated or significantly reduced the burden of the disease in many endemic villages. Unfortunately, concomitant killing of the microfilariae of the African eye worm *Loa loa* by ivermectin can cause severe adverse events in humans, including encephalopathy and death. Therefore, ivermectin MDA was halted in many endemic regions. Onchocerciasis is currently the only recommended drug. It kills the microfilariae of the African eye worm *Onchocerca volvulus*, without also killing *Loa loa* microfilariae. Below is the description of two collaborations involving *Onchocerca* and *Loa loa*

**Collaboration with Merck KGaA, Darmstadt, Germany**

Heat shock protein 90 (Hsp90) is a molecular chaperone involved in the trafficking of proteins in the cell. It is one of the most highly expressed cellular proteins across all species and is essential in all eukaryotes. Previous work has shown that Hsp90 inhibitors are potent against *Bosca pahangi* microfilariae and adults. *B. pahangi* is a microfilarial nematode similar to *O. volvulus*. Thus, the Hsp90 of *Onchocerca* is expected to be a similarly efficacious drug target. Merck KGaA, Darmstadt, Germany has 2.5 million diverse small molecules in its portfolio, including Hsp90 inhibitors. Merck KGaA, Darmstadt, Germany will provide Dr. Cho-Ngwa with a subset of these highly potent molecules, mostly Hsp90 inhibitors, to screen against *Onchocerca*. Dr. Cho-Ngwa will follow the initial screening to counter-select against *Loa loa*. This will involve both in vitro and in vivo screens. The best leads will be advanced in subsequent steps by the concerted efforts of both Merck KGaA, Darmstadt, Germany, the University of Buea, and other partners, if required.

**BVGH’s FundFinder program was used to secure funding for this important initiative. BVGH identified the Wellcome Trust PathFinder award—a funding opportunity aimed at stimulating partnerships between pharmaceutical companies and academic research institutes. Dr. Cho-Ngwa jointly applied with Merck KGaA, Darmstadt, Germany and was successful in securing funding from the Wellcome Trust.**

**Dr. Fidelis Cho-Ngwa, of the Biotechnology Unit at the University of Buea in Cameroon, has developed an innovative screen for small molecules that have the potential to be developed into new drugs to treat river blindness, and he has identified crude extracts of several African plants that show promising activity. We are excited to be helping his research by identifying the chemical structures of the active natural products in his active crude extracts.** - Dr. Raymond Andersen, UBC

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**“This platform demonstrates how intellectual property can be activated to be a promoter of access rather than a barrier. WIPO Re:Search will provide the opportunity for Merck to share its vast compound library with experts in the global research community focused on developing novel compounds to combat infectious diseases.” - Dr. Arno Hartmann, Head of Patents Pharmaceuticals, Merck KGaA, Darmstadt, Germany**

**“I am delighted that BVGH introduced me to Professor Cho-Ngwa from the University of Buea. Professor Cho-Ngwa has developed an innovative screen for small molecules that have the potential to be developed into new drugs to treat river blindness, and he has identified crude extracts of several African plants that show promising activity. We are excited to be helping his research by identifying the chemical structures of the active natural products in his active crude extracts.” - Dr. Raymond Andersen, UBC**
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. 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 liver 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.

Accordingly, Dr. Agam P. Singh 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 in vitro and in vivo models that he has developed. One approach to knocking down genes is through RNA interference (RNAi). Given their expertise in this field, BVGH connected Dr. Singh with academic and industry partners working on areas where industry otherwise would not be working. Another important contribution of BVGH Re:Search is in facilitating connections between diverse researchers with complementary expertise towards a larger goal. “I am very positive about this collaboration and expect it to unlock some very important targets for malaria eradication.”

- Dr. Agam P. Singh, NII

**“This collaboration between Alnylam, the National Institute of Immunology, and Northeastern University National Institute of Immunology could lead to more effective and safer therapies for malaria.”**

- Dr. Mansoor Amiji, NEU

**“Alnylam Pharmaceuticals/Northeastern University National Institute of Immunology”**

**“University of Washington Bothell Noguchi Memorial Institute for Medical Research”**

Metabolism of most drugs—such as those developed to treat HIV/AIDS, malaria, and tuberculosis—is mediated by members of the cytochrome P450 superfamily of monooxygenases (CYPs); most notably CYP3A4 and CYP2D6. Differences in drug response are influenced by these enzymes’ abilities to metabolize a drug, which in turn can be altered by single nucleotide polymorphisms (SNPs) in the CYP genes. Certain ethnic groups have unique SNPs that correlate with altered drug responses. As such, a comprehensive understanding of SNPs in the CYP genes within all populations is essential to ensure drugs are safe and efficacious for all.

Dr. Regina Appiah-Opong from the Noguchi Memorial Institute for Medical Research (NMIMR) in Ghana studies the potential of CYP-mediated drug-drug and herb-drug interactions of drugs and plant medicines used to treat malaria, tuberculosis, and HIV/AIDS (among others) in the Ghanaian population. In order to assess accurately the drug interaction potentials of these medicines, Dr. Appiah-Opong is focusing her research on CYP genes to identify the differences in SNPs between Caucasian and African ethnicities, particularly SNPs specific to Ghanaian people. To support her research efforts, BVGH connected Dr. Appiah-Opong with Dr. Susan Kraemer, a bioinformatics instructor at the University of Washington Bothell (UW Bothell).

The two researchers agreed to provide Dr. Kraemer’s undergraduate students with real-life bioinformatics experience; the students were instructed to analyze publicly available CYP gene sequences. These sequences include the recent data generated by the 1000 Genomes Project. Based on their analyses, the students identified genetic differences in CYP genes between African and Caucasian populations. Students in the first offering of the course found striking differences between particular alleles for CYP3A4 and CYP2D6 in the two populations. Due to the encouraging results and availability of human genome sequence data from a recently published African Genome variation project, Drs. Kraemer and Appiah-Opong were granted access to the Ghanaian DNA sequence information from the African Partnership for Chronic Disease Research (APCDR). Using these data, in addition to the data from the 1000 Genomes Project, Dr. Kraemer will lead another undergraduate class investigating the population-specific allelic differences. These analyses will improve our understanding of population variation of the CYP enzymes and will allow Dr. Appiah-Opong to clone Ghanaian-specific CYP vectors and conduct drug metabolism studies. Significant differences in drug metabolism between these enzymes and control CYPs would highlight the need for expanded clinical trials among different ethnicities. The results of this collaboration may lay the groundwork for changing approaches to drug approval in Ghana and in other regions of the world.

“**The collaboration between NMIMR and UW Bothell fostered by our partner, BVGH/WIPRe:Search, has been a great experience so far. The commitment and enthusiasm of each contributor, including students, toward this project’s biomedical research is remarkable. I am confident that the effort will culminate in more effective therapies not only for Ghanaians or Africans, but also various populations.”**

- Dr. Regina Appiah-Opong, NMIMR

**“I am very grateful to BVGH for establishing our collaboration. Undergraduate students received a ‘real world’ experience as well as an opportunity to learn from Regina. Working in partnership has made teaching undergraduate research more fun and meaningful – we also achieved great results. We plan to write a publication and grant proposal after the fall quarter!”**

- Dr. Sue Kraemer, UW Bothell
It is increasingly clear that a greater understanding of host-pathogen interactions—such as those between a human and malaria parasite—is essential to the development of new treatments and, most importantly, a vaccine for malaria. Entry into a host’s red blood cells (RBCs) is a key step in the complex life cycle of the malaria parasite that triggers downstream events leading to the development of the symptomatic phase of the infection. Malaria parasites have evolved to express several different molecules that induce entry following interaction with RBC surface receptors. Much is known about the interaction between RBCs and Plasmodium falciparum—the malaria parasite that causes the most severe form of malaria. However, the interaction between Plasmodium vivax (P. vivax), the parasite responsible for the most frequent and widely distributed form of recurring malaria, and host RBCs is less well understood.

Dr. Wai-Hong Tham, a malaria researcher at the Walter and Eliza Hall Institute of Medical Research (WEHI) in Melbourne, Australia, studies how malaria parasites enter RBCs and evade the host immune response. Dr. Tham is specifically interested in identifying high-affinity antibodies that block P. vivax proteins from binding to the surface of RBCs, thereby blocking entry. BVGH suggested a collaboration between Dr. Tham and Dr. Horacio Bach, who heads the antibody engineering facility at the University of British Columbia (UBC) in Vancouver, Canada. Using phage display, Dr. Bach is identifying human-derived, high-affinity recombinant antibodies against a specific P. vivax protein for Dr. Tham. Following Dr. Bach’s selection of high-affinity antibodies, Dr. Tham will determine which of these antibodies block P. vivax entry into RBCs. Dr. Tham will subsequently use the antibodies to map the protein epitopes that are required for RBC binding. Entry into RBCs results in the symptoms of malaria and is also essential for the parasite’s differentiation into its transmissible form. By understanding how P. vivax enters RBCs, Dr. Tham and other scientists will be better equipped to develop therapeutics or vaccines that mitigate symptoms and/or prevent P. vivax transmission.

“WIPO Re:Search is doing outstanding work by mediating collaborations of researchers in order to advance the understanding, diagnosis, and therapeutics of neglected diseases. In addition, BVGH follows up on collaborations, which allows us to track the development of our projects in a timely fashion. We strongly believe we can provide the basic tools required to accelerate the development of novel therapies and diagnostics in order to curb the expansion of neglected diseases.” - Dr. Horacio Bach, UBC

Infection with cercariae of the trematode genus Schistosoma (commonly known as blood flukes) leads to the devastating illness schistosomiasis. This neglected infectious disease afflicts more than 240 million people worldwide (mostly children), often in resource-deprived tropical and sub-tropical regions where exposure to contaminated water containing cercariae is unavoidable. The main anthelmintic used to treat schistosomiasis, praziquantel, is only effective in treating the adult worm. This limited efficacy, along with the potential of resistance development due to mass drug administration programs, highlights an urgent need for new therapies.

Responding to this need, researchers at Aberystwyth University in Wales, led by Prof. Karl Hoffmann, are developing new approaches for controlling parasitic helminths. Prof. Hoffmann’s group has partnered with Alnylam Pharmaceuticals (Alnylam) to explore the use of ribonucleic acid interference (RNAi) technology for gene silencing in S. mansoni (one of the three main trematode species that cause the disease in humans) to identify targets that are important for the survival of this medically important parasite.

Dr. Rachel Meyers, Senior VP, Alnylam, said, "Alnylam has a rich history of collaborating with academic and other research institutions to explore the use of RNA interference in identifying gene targets for the development of innovative medicines," Dr. Brian Bettencourt, a biometrics researcher at Alnylam, optimized a set of short interfering RNAs (siRNAs) for Prof. Hoffmann to assess in gene knockdown studies in S. mansoni. The optimized siRNAs designed by Alnylam were demonstrated to be more effective than previously tested siRNAs. Given these promising results, Alnylam supported the design of additional siRNAs against three S. mansoni genes. To optimize the knock-down, Alnylam is also providing lipophilic reagents and advice on the delivery of the siRNAs in S. mansoni. With this additional support from Alnylam, Prof. Hoffmann’s team plans to demonstrate proof-of-principle and establish an optimized protocol for gene silencing in schistosomes. Ultimately, the group envisages applying for funding to conduct a genome-wide screen in S. mansoni using siRNAs designed with Alnylam’s technology, with the aim of identifying gene targets for developing next-generation anthelmintics.

"Alnylam has a rich history of collaborating with academic and other research institutions to explore the use of RNA interference in identifying gene targets for the development of innovative medicines," said Rachel Meyers, Senior Vice President of Research at Alnylam. "We are happy to be working with the team at Aberystwyth University and providing materials that could enable the further development of a medicine for this neglected tropical disease."
Malariainduced by a microscopic parasite that spends part of its lifecycle inside human red blood cells (RBCs). The parasite metabolizes hemoglobin to obtain the necessary chemical ingredients to grow and reproduce but also produces toxic heme byproducts that dramatically reduce the deformability of host RBCs. In response, the malaria parasite sequosters toxic heme through its bocystatinization into met hemozoin. Since the inherent deformability of RBCs is essential to their function, this biophysical property of RBCs has a complex relationship with the pathology of the disease. On one hand, reduced deformability is thought to assist the removal of the parasite by inducing splenic clearance. On the other hand, reduced RBC deformability is known to cause microvascular occlusion and impairment of blood flow, symptoms associated with severe malaria.

To better understand the relationship between decreased RBC deformability and malaria pathogenesis, Dr. Hongshen Ma from the University of British Columbia (UBC) has developed a simple and high-throughput assay for measuring RBC deformability, known as "cell-phoresis." This method transports individual RBCs through a microstructured material in which the speed of transport depends on cell deformability. The final position of the cells can then be used as a simple, image-based readout for deformability, similar to DNA banding in gel electrophoresis. Using this approach, Dr. Ma’s team has made the surprising discovery that reduced infected RBC (iRBC) deformability is a universal feature of all clinical antimalarials. This finding suggests that reduced infected RBC (iRBC) deformability is perhaps a necessary characteristic of all antimalarials and could potentially be used as a physical biomarker in vivo. The final clearing of the parasites in vivo. Dr. Ma will assess the effect of these compounds on iRBC stiffness and correlate with the pathology of malaria.

In an attempt to accelerate antimalarial development, GlaxoSmithKline (GSK) developed the Tres Cantos Antimalarial Set (TCAMS) – a set of 13,500 compounds with activities against the blood stage form of P. falciparum. Through WIPO Re:Search, GSK has provided Dr. Ma with 15 compounds from the TCAMS that displayed ideal IC50s, had diverse effects on the parasite, and resulted in varying clearance times of RBCs in vivo. Dr. Ma will assess the effect of these compounds on RBC deformability and determine whether RBC stiffness correlates with efficient in vivo clearance. If the results are promising, GSK and Dr. Ma plan to assess the effect of these compounds on the parasite, and to screen for new drugs and adjunctive agents.

Oil-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 (Ascaris), whipworms (Trichuris), and hookworms (Necator and Ancylostoma)—are transmitted through contact with or consumption of soil contaminated with parasite egg-rich feces. Improving sanitation in endemic regions can dramatically reduce the incidence of these infections.

Dr. Ricardo Izurieta at the University of South Florida (USF) has developed a solar-chemical toilet that sanitizes waste products, however to determine the efficacy of the treatment, he needs 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. Due to the nature of these samples, the filters are easily and routinely clogged by solid debris. An alternative device that could swiftly and cost-effectively isolate and concentrate helminth eggs from sewage samples would greatly aid Dr. Izurieta’s assessment of the solar-chemical toilet.

To assist Dr. Izurieta with his work, BVGH connected him to Dr. P. Ravi Selvaganapathy, a biomicrofluidics expert at McMaster University in Canada. After several discussions with Dr. Izurieta, Dr. Selvaganapathy and his group have developed a tangential flow filtration device that uses minimal electricity to separate particles according to their size. The device can retain particulates as minute as two microns as well as worms as large as 400 microns, and it is particularly useful in concentrating Ascaris eggs from a variety of samples.

Dr. Selvaganapathy has finished developing the device and has confirmed its ability to filter and concentrate beads the size of Ascaris eggs. Dr. Izurieta will now compare the 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.
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 led by Dr. Robert Burton and Paul LaBarre developed a technology known as a non-instrumented 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.

PATH and the University of Calgary

BVGH connected the scientists at PATH with Dr. Dylan Pillai, 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.

Dr. Pillai 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 NINA-LAMP combination was more sensitive than microscopic diagnosis and comparable to a nested PCR test. The results obtained from these studies have been recently published, and the group plans to further examine the efficacy of this combination on samples from 800 asymptomatic malaria patients. The researchers plan to publish another paper with the results of these studies in the near future.

PATH and the Centre Pasteur du Cameroun

Dr. Lawrence Ayong, a researcher at the Centre Pasteur du Cameroun (CPC), developed a reverse transcription-LAMP-based assay (RT-LAMP) to detect gametocytes—the transmissible form of the Plasmodium parasite. Developing an assay to detect the gametocytes will help to determine the risk of transmission from humans back to mosquitoes—an important factor as the world moves towards malaria elimination. BVGH connected Dr. Ayong with the PATH scientists, who agreed to share their NINA heater. Dr. Ayong’s tests of his RT-LAMP in the NINA heater yielded encouraging results, which he, along with the PATH team, plan to publish shortly.

“WIPO Re:Search facilitated connections with appropriate researchers and clinicians who have been essential in testing the emerging PATH NINA technology in low-resource settings and in receiving end-user feedback toward a more useful solution.” - Dr. Robert Burton, PATH

“Thanks to the WIPO Re:Search initiative, synergies are created between scientists from endemic countries and organizations with key technologies and products to allow for a variety of promising research projects that would have otherwise been largely inaccessible. Our collaboration with PATH is a clear example of how WIPO Re:Search is bridging the gap for NTDs and accelerating the development of more cost-effective and field-adaptable tools.” - Dr. Lawrence Ayong, CPC
Developing Diagnostics: Bringing Malaria Testing to the Field

Dengue fever and malaria, the two most prevalent mosquito-borne diseases worldwide, are not only difficult to treat, but also to diagnose. This is because their symptoms are non-specific and because the diseases are often co-endemic. In order to ensure more accurate diagnoses of febrile illnesses like dengue fever and malaria in developing regions, Drs. Jesse Waggoner and Benjamin Pinsky from Stanford University developed a highly sensitive real-time RT-PCR-based molecular diagnostic platform to simultaneously detect and distinguish nucleic acids from dengue virus and Plasmodium parasites. This platform can also be adapted to screen for other causes of undifferentiated systemic febrile illnesses, including leptospirosis, chikungunya, yellow fever, Rift Valley fever, and Zika fever. Drs. Waggoner and Pinsky are currently collaborating with two different partners to customize this platform to the diseases most common to Nigeria and Cameroon.

University of Lagos

Dr. Wellington Oyibo from the University of Lagos in Nigeria has collected samples from patients with febrile illnesses in Lagos state and was interested in determining the causes, besides malaria, of those illnesses. To address his interest, BVGH connected Dr. Oyibo with Drs. Waggoner and Pinsky. Following discussions, Drs. Waggoner and Pinsky secured a grant from the Stanford University Office of International Affairs, which allowed Dr. Oyibo’s graduate student, Chika Okangba, to visit Stanford for two months. During her stay, Chika learned how to collect and process patient samples, how to perform the Stanford multiplexed RT-PCR assay for dengue, malaria, and leptospirosis, and how to analyze the results. Chika, with the help of Dr. Alisha Mohamed-Hadley, a member of the Pinsky laboratory, used the multiplex assay to screen Dr. Oyibo’s sample collection. While few cases of dengue or leptospirosis were identified, Chika confirmed the diagnosis of malaria in a significant number of patients that tested negative by microscopy. Interestingly, the study showed that malaria detection using the Stanford molecular diagnostic on plasma and serum was more sensitive than, and equally specific to, microscopy in patients with P. falciparum malaria. A manuscript describing these findings has been accepted for publication in the Journal of Clinical Microbiology.

Given that the samples were from patients living in urban areas, Dr. Pinsky and Dr. Oyibo are planning to collect additional samples from urban populations where they believe the prevalence of dengue fever will likely be higher. Based on these results, the scientists plan to design a multiplexed RT-PCR assay specific to the non-malarial febrile illnesses of urban Nigeria.

Centre Pasteur du Cameroun

Drs. Waggoner and Pinsky are also working with Dr. Maurice Demanou, a virologist who is the Head of Arbovirus and Hemorrhagic Fever Virus Laboratory and Head of WHO National Reference Laboratory for yellow fever and measles at the Centre Pasteur du Cameroun (CPC). Dr. Demanou believes dengue fever is underestimated in Cameroon and is interested in determining the causes and prevalence of non-malarial fevers in the country. Accordingly, Dr. Demanou provided the Pinsky laboratory with blinded clinical samples from Cameroonian febrile patients collected and analyzed in CPC in the framework of ACIP Dengue A12-11 project funded by Institut Pasteur International Network). These samples were screened for dengue fever, chikungunya, malaria, and leptospirosis. Initial tests using this multiplexed RT-PCR assay identified a small number of dengue and chikungunya cases and a large proportion of malaria cases that were missed by conventional testing. Dr. Pinsky’s lab is currently screening the samples for an expanded set of arboviral diseases. Dr. Demanou has high expectations for this multiplex RT-PCR as the Cameroonian Government recently appointed his lab as the National Reference Laboratory for Chikungunya and Dengue. Therefore, Dr. Demanou hopes that he or a member of his team will obtain a grant from Stanford University to learn how to perform the Stanford multiplexed RT-PCR assay so as to implement it at CPC.

"This collaboration with Ben Pinsky at Stanford has provided a unique opportunity to train a graduate student while advancing our malaria research program. The experience Chika gained at Stanford will have a lasting impact on her scientific career. In addition, our partnership has achieved important milestones. We are currently planning to implement and evaluate the multiplex assay in febrile patients in Lagos." - Dr. Wellington Oyibo, University of Lagos

"Cameroon is considered to be endemic for several arboviruses and also has high malaria transmission. Unfortunately, the difficulty of clinical discrimination between these infectious agents and the lack of adequate local laboratories constitute a real threat to the prevention and diagnosis of these diseases. We therefore thank WIPO Re:Search for facilitating our collaboration with Stanford, which has allowed our reference lab to update our diagnostic platform and to develop further research projects on NTDs." - Dr. Maurice Demanou, CPC
Malaria is an acute tropical disease that first presents with fever, chills, headache, and vomiting. These symptoms, which can be mild and indistinguishable from those caused by other pathogens, can progress to more severe disease if a patient is not promptly diagnosed and treated with antimalarials. The World Health Organization currently recommends that microscopy or a rapid diagnostic test be used to diagnose malaria, however both methods have their shortcomings. Diagnosis via microscopy requires a trained technician, whereas a rapid diagnostic test may not detect a low-level infection. A malaria diagnostic able to quickly detect malaria parasites within a patient sample is essential to mitigate disease, reduce malaria deaths, and limit the parasites’ transmission.

As the head of the African Network for Drugs and Diagnostics Innovation (ANDI) Centre of Excellence for Malaria Diagnosis at the University of Lagos in Nigeria, Dr. Wellington Oyibo focuses on developing more sensitive, affordable, and user-friendly malaria diagnostics. Based on his interests, BVGH connected Dr. Oyibo with Dr. Paul Wiseman, a researcher at McGill University who is developing a diagnostic that detects a byproduct – hemozoin – produced by the malaria parasite. Upon entering a red blood cell, the malaria parasite must metabolize hemoglobin to obtain the necessary molecules required to reproduce. This metabolic process also produces a toxic heme byproduct, which the parasite sequesters into the inert heme crystals called hemozoin.

Dr. Wiseman is developing a diagnostic that detects hemozoin via laser excitation. In addition to being able to detect very low numbers of infected red blood cells, the diagnostic requires only a drop of blood and minimal user training, making it highly suitable for field studies and remote clinics.

Following a discussion with Dr. Wiseman, Dr. Oyibo agreed to share his collection of blood samples obtained from malaria patients and healthy donors from Lagos state. Dr. Wiseman will use these samples to validate the diagnostic, identify its limits of detection, and determine the diagnostic’s sensitivity. If the results are encouraging, Dr. Oyibo and Dr. Wiseman plan to apply for a joint grant to support the diagnostic’s further development into a portable device suitable for use throughout malaria-endemic regions.

“I am very excited to have been introduced to Dr. Oyibo and the collaboration is exciting for me due to his extensive knowledge and for providing us access to a large collection of well-characterized patient samples for us to test our method.” – Dr. Paul Wiseman

Impact on Product Development

The process of developing new products for diseases is complicated and lengthy. On average a product takes over ten years to move from the bench to market, at a cost of over one billion USD. This process is further complicated for neglected disease products where there is no financial incentive for the developer, scarce funding, and geographical and infrastructure constraints.

These stories highlight how WIPO Re:Search is addressing these challenges and accelerating product development.

Building Capacity

In addition to facilitating research and development collaborations, BVGH identifies training opportunities for scientists. BVGH presented an opportunity to attend a vaccinology training course, offered by the International Vaccine Institute (IVI) in Seoul, Korea, to Dr. Mathurm Toisokhem from the Centre Pasteur du Cameroun and Dr. Drissa Coulibaly at the University of Bamako, Mali. With support from BVGH, both researchers applied and were selected to participate in the program offered and funded by IVI.

Expediting R&D

60 Degrees Pharmaceuticals (60P), a company focused on developing therapeutics for dengue fever patients, was interested in repurposing modipafant to treat dengue fever. Modipafant was under development by Pfizer, but was discontinued. Pfizer disclosed the Investigator’s Brochure under confidentiality. The data helped 60P design its dengue fever clinical trial, saving both time and money. Recently, 60P received funding to conduct Phase II clinical trials using modipafant for dengue fever patients.

Access to Samples

Access to clinical samples can be a bottleneck for validation and development of diagnostics for NTDs, particularly when the R&D takes place in non-endemic countries. Through WIPO Re:Search, researchers have gained access to field sites and clinical samples for diagnostic testing (see NINA Heater story on page 26). These diagnostic collaborations have been facilitated in Cameroon, Nigeria, and Ethiopia and have provided the researchers with crucial data that will inform on their diagnostic’s design and development.

Identifying Expertise

Dr. Héla Kallel from the Institut Pasteur de Tunis (IPT) has developed an inactivated rabies vaccine. The vaccine should be highly thermostable to be suitable for use in tropical and sub-tropical regions. The US NIH has the resources to address vaccine thermostability. BVGH connected Dr. Kallel with the NIH, which will perform studies on stabilization and formulation of IPT’s rabies vaccine under the auspices of their preclinical services program.

Accelerating Product Development

Dr. Jim McKernon at UCSF is interested in testing ceftriaxone inhibitors for Chagas disease. Using BVGH FundFinder, BVGH identified a funding opportunity from the US NIH NCATS through a program called Discovering NTU+. Lasting Mectolox. Furthermore, Santé had contributed their ceftriaxone inhibitor to the NCATS program. BVGH connected Dr. McKernon with Dr. Christine Calvo at NCATS to apply for the NCATS NTU program to repurpose the Santé ceftriaxone inhibitor. Dr. McKernon’s application was successful and his group will receive both the compound and funding to further advance their research.
BVGH is incredibly proud of the progress WIPO Re:Search is making toward accelerating product development for neglected diseases. Since its inception in 2011, researchers around the world have come together across multiple sectors to combine efforts to repurpose industry assets, develop new technologies, evaluate products in the field, and much more. Going forward, BVGH will continue to bring Members together around innovative ideas while supporting alliances to achieve important product development milestones. We are committed to working in partnership with Members to make significant contributions toward advancing discoveries and ultimately helping patients suffering from these devastating neglected infectious diseases.

Dear Colleagues,

WIPO Re:Search clearly demonstrates the important contributions biopharmaceutical companies are making toward the development of new products for neglected tropical diseases.

The Biotechnology Industry Organization founded BVGH in 2004 with a mission to engage BIO members in impactful initiatives to improve global health. WIPO ReSearch is a prime example of how BVGH is achieving that purpose and how companies can participate in solving these challenges.

Intellectual property is a critical element in driving innovation and developing important new medicines that address unmet medical needs for patients around the world. I commend WIPO and BVGH on their partnership and combined effort to leverage intellectual property for the benefit of developing countries.

I am pleased to see a number of BIO members participating in WIPO ReSearch, and encourage more to join this consortium and contribute their resources to this fight.

Sincerely,

James Greenwood
President and CEO, Biotechnology Industry Organization
Developed in cooperation with our sponsors