WIPO | Re:Search
Sharing Innovation
in the Fight Against
Neglected Tropical Diseases

WIPO Re:Search
Partnership Stories 2016-2019
Driving R&D for Neglected Infectious Diseases Through Global Cross-Sector Collaborations

A publication of collaborations facilitated by BVGH

bvgh
BIO Ventures for Global Health

WIPO Re:Search

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Table of Contents

*MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA

Abbreviations and Acronyms

BIO	Biotechnology Innovation Organization
BVGH	BIO Ventures for Global Health
d³	Diagnostics, drug discovery, and development
EDCTP	European and Developing Countries Clinical Trials Partnership
FAST	Facilitated Access to Screening Technologies
GHIT	Global Health Innovative Technology
GIBH	Guangzhou Institutes of Biomedicine and Health
GSK	GlaxoSmithKline
GWU	The George Washington University
IDRI	Infectious Disease Research Institute
IEEE	Institute of Electrical and Electronics Engineers
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IP	Institut Pasteur
ISNTD	International Society for Neglected Tropical Diseases
J&J	Johnson & Johnson
JPMA	Japan Pharmaceutical Manufacturers Association
KNUST	Kwame Nkrumah University of Science and Technology
LES	Licensing Executives Society
LNBio	Laboratório Nacional de Biociências
MDR/RR-TB	Multidrug-resistant or rifampicin-resistant tuberculosis
MIT	Massachusetts Institute of Technology
MMV	Medicines for Malaria Venture
NGO	Non-governmental organization
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
PMV	Plasmepsin V
POINT	Pool for Open Innovation against Neglected Tropical Diseases
R&D	Research and development
SCRI	Seattle Children's Research Institute
SDGs	Sustainable Development Goals
***Sm*HMGR**	*Schistosoma* HMG-CoA reductase
SSGCID	Seattle Structural Genomics Center for Infectious Disease
TCAMS	Tres Cantos Antimalarial Set
UBC	University of British Columbia
UC	University of California
UN	United Nations
USF	University of South Florida
WEHI	Walter and Eliza Hall Institute of Medical Research
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization
WUSTL	Washington University in St. Louis

Introduction to
WIPO Re:Search

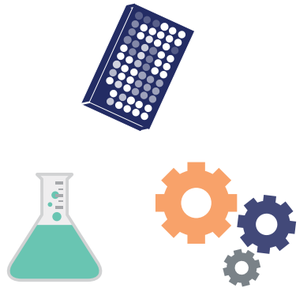
WIPO Re:Search is a global public-private consortium that accelerates drug, vaccine, and diagnostic research and development (R&D) to address unmet medical needs for neglected infectious diseases and drive progress toward the United Nations Sustainable Development Goals.

Established in 2011, WIPO Re:Search catalyzes royalty-free sharing of intellectual property—including compounds, data, clinical samples, technology, and expertise—among Consortium Members in targeted, mutually beneficial R&D collaborations.

WIPO Re:Search Unites:

Scientific know-how and creative thinking of academic, non-profit, and government investigators

Firsthand disease knowledge of researchers in endemic countries



Material assets and product development experience of global pharmaceutical companies

WIPO Re:Search promotes broad access to resulting products by requiring Members to agree to the Consortium's Guiding Principles, including:

- Royalty-free licenses for product use and sale in nearly 50 least-developed countries
- Good-faith consideration of product access for all developing countries

Neglected Infectious Diseases Covered by WIPO Re:Search

(See page 28 for more information on each disease)

Parasitic Diseases

Chagas disease
Cysticercosis
Dracunculiasis
Echinococcosis
Foodborne trematodiases*
Human African trypanosomiasis
Leishmaniasis
Lymphatic filariasis
Malaria
Onchocerciasis
Schistosomiasis
Soil-transmitted helminthiases

Bacterial Diseases

Buruli ulcer
Leprosy
Trachoma
Tuberculosis
Yaws

Viral Diseases

Dengue
Rabies

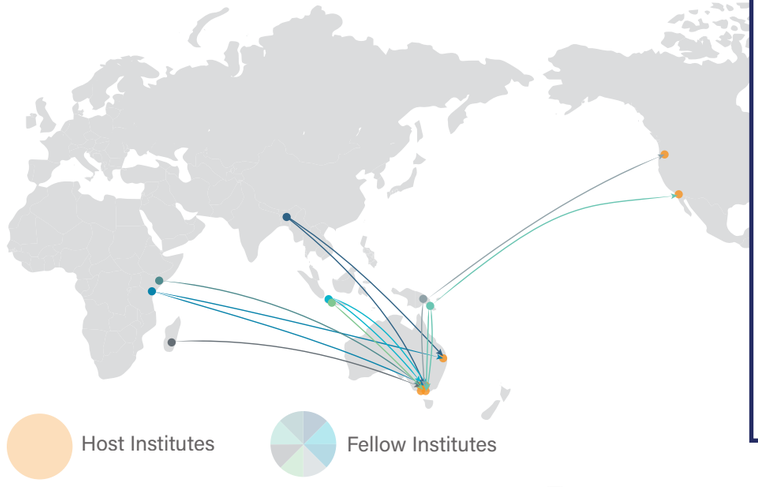
Other Conditions

Podoconiosis
Snakebite

* Clonorchiasis, fascioliasis, opistorchiasis, and paragonimiasis

WIPO Re:Search Fellowship Program

The **WIPO Re:Search Fellowship Program**, supported by the Government of Australia through WIPO Funds-in-Trust, organizes training sabbaticals in advanced laboratories to bolster the capacity of low- and middle-income countries to engage in neglected infectious disease R&D. BVGH matches fellows and hosts with complementary research interests and capabilities, with the aim of seeding long-term, mutually beneficial collaborative relationships.



Leadership

BIO Ventures for Global Health (BVGH) is a non-profit organization that connects the for-profit and non-profit sectors to solve global health challenges. BVGH leads Member engagement, partnering, and alliance management for R&D collaborations and fellowships.

World Intellectual Property Organization (WIPO) is a specialized agency of the United Nations and the global forum for intellectual property services, policy, information, and cooperation. As the WIPO Re:Search Secretariat, WIPO manages the WIPO Re:Search Resource Platform, an interactive tool that enables users to visualize and retrieve information about Consortium Members, collaborations, and assets.

WIPO Re:Search at a Glance

Membership

Eisai Co., Ltd. ▪ GlaxoSmithKline ▪ Johnson & Johnson ▪ Merck KGaA, Darmstadt, Germany ▪ MSD* ▪ Novartis ▪ Pfizer ▪ Takeda Pharmaceutical Company Limited

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R&D Collaborations

155 since 2011

>50 ongoing

Product Development Pathway

10 Advancing critical solutions for neglected infectious diseases along the product development pathway

Fellowships

20 Fellowships coordinated

100+ Months of training

11 Low- and middle-income countries benefitting from fellowships

Key outcomes and impacts

- **Grant funding (over US $750,000 for one fellow)**
- **Career promotions**
- **International publications and presentations**
- **Research collaborations**

WIPO Re:Search Value Drivers

Catalyzing Global Public-Private Partnerships for Neglected Infectious Diseases (pages 12-24)

BVGH proactively coordinates cross-sector WIPO Re:Search collaborations in alignment with Member interests and provides end-to-end alliance management support to help ensure successful outcomes.

Optimizing Collaborative R&D for Diseases of the World's Poor (pages 27-41)

WIPO Re:Search's innovative resource-matching model enables translation of novel ideas into new solutions in a risk-reducing, cost-effective manner.

Harnessing Open Innovation to Improve Global Health (pages 43-51)

WIPO Re:Search combines the power of BVGH's strategic partnering approach and industry open innovation to advance neglected infectious disease R&D worldwide.

Expanding Global Recognition of Members' Accomplishments (pages 54-61)

BVGH and WIPO share WIPO Re:Search successes with leaders and decision-makers worldwide to increase Member visibility and open doors to new opportunities.

WIPO Re:Search is a game changer for neglected infectious disease drug development. Thanks to the Consortium and the partnerships that BVGH has facilitated over the last few years, my team at the University of Buea has been able to achieve what some of our predecessors could not accomplish in a decade.

— Prof. Fidelis Cho-Ngwa, University of Buea

Value Driver 1:
Catalyzing Global Public-Private Partnerships
for Neglected Infectious Diseases

BVGH Utilizes a Unique Partnering Approach

BVGH's partnership development and alliance management approach prioritizes projects — termed targeted collaborations — that address the greatest needs and gaps for diseases of poverty. With over 150 WIPO Re:Search collaborations established to date, BVGH's partnering process catalyzes the sharing of intellectual property across sectors and geographies to drive product research and development (R&D) for malaria, tuberculosis, and neglected tropical diseases.

BVGH identifies WIPO Re:Search Members with complementary interests, capabilities, and needs; introduces the parties to determine if there is mutual interest in collaborating; coordinates communications between partners to align on collaboration milestones, roles, and responsibilities; and, once legal agreements are in place between the participating entities, provides alliance management support to help ensure successful outcomes.

Key Features of BVGH's Approach

Aimed at Improving Health and Saving Lives in Low- and Middle-Income Countries

BVGH focuses on deploying Members' assets within targeted collaborations that

- Address **unmet medical needs** in areas of interest
- Employ **innovative approaches or technologies**
- **Align with the priorities and interests** of major global health funders and other stakeholders
- Are positioned to **attract the financing and partners** needed to transition innovation into impactful products

Customized and Flexible

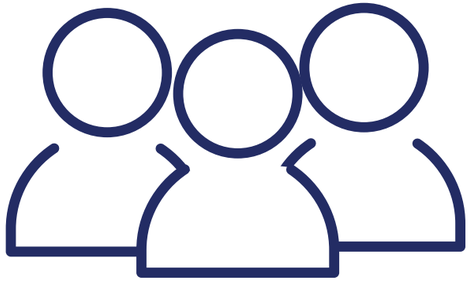
BVGH's services are driven by and evolve with Members' partnering interests, including but not limited to

- Diseases
- Expected products (drugs, diagnostics, vaccines)
- Assets to be shared (such as compounds, data, clinical samples, technology, expertise)
- Specific researchers, institutions, countries, or regions
- Number and scope of collaborations

Sharing of assets and participation in collaborations is always optional. Members are empowered to make such decisions on a case-by-case basis.

Proactive Profiling, Scouting, and Vetting

Experienced BVGH scientists and alliance managers regularly reach out to Members to discuss collaboration interests. Informed by those discussions, BVGH actively searches for researchers—both within and beyond the existing WIPO Re:Search network—who best fit the Members' needs. BVGH's objective is to find the most suitable partners for each Member and collaboration, regardless of institution or location. Before introducing potential partners to a Member, BVGH conducts a rigorous vetting process to confirm their readiness for WIPO Re:Search collaborations.



> ***I think of BVGH as our external scouting arm for collaborations involving neglected tropical disease indications — we work closely with them to identify high-caliber collaborators for endeavors where MSD* can bring a unique asset to the table to impact a particular disease.***
>
> **— Dr. David Olsen, Distinguished Scientist and Neglected Tropical Diseases Discovery Lead, MSD**

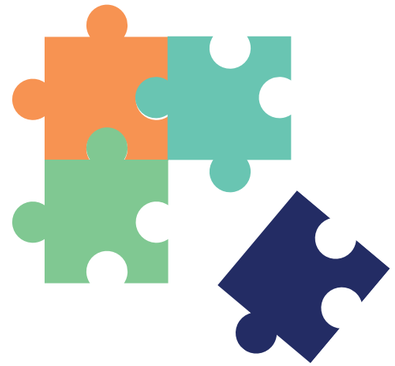
Robust Global R&D Network

In scouting potential collaborators for Members, BVGH taps into WIPO Re:Search's international network, spanning over 140 corporate, academic, non-profit, and government organizations in over 40 countries on six continents. Disease-endemic regions are well represented; Africa alone is home to over 30 Member institutions. In the event that a Member's needs cannot be met by the current network, BVGH recruits new Members to expand the breadth and impact of collaborations.

*MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA

Connecting Expertise and Assets

BVGH-facilitated WIPO Re:Search collaborations unite the scientific expertise and creative thinking of academic, non-profit, and government researchers; the in-depth disease knowledge of investigators in endemic countries; and the material assets and product development experience of global companies for optimal efficiency and impact.



End-to-End Planning, Support, and Communication

Realizing the full value of a collaboration requires not only a well-matched partnership, but also alliance management support from beginning to end. BVGH coordinates communications between partners to solidify collaboration details and responsibilities; organizes regular update calls to discuss progress and roadblocks; and recruits additional partners as needed.

BVGH also helps collaborators identify high-value award opportunities to fund continued development of promising product candidates. Examples include Wellcome Trust awards secured for an onchocerciasis drug development collaboration between **Merck KGaA, Darmstadt, Germany** and the **University of Buea** in Cameroon (read about this collaboration on page 39), and an antimalarial drug development partnership between **MSD** and the **Walter and Eliza Hall Institute of Medical Research** (see page 36 for more information about this collaboration).

WIPO Re:Search Leverages Company Assets to Drive Drug Discovery

Through WIPO Re:Search, Member companies contribute valuable assets—both tangible and intellectual—to neglected infectious disease drug discovery initiatives. BVGH connects company decision makers with investigators who have targeted collaboration needs. If a company decides to proceed with a collaboration and share a resource, BVGH oversees and guides the partnership so that the investigators can focus on what matters – advancing their work toward new drugs, diagnostics, and vaccines.

University-Industry Partners Pursue Schistosomiasis Drug Discovery

The problem: An old treatment, and the risk of emerging resistance

Praziquantel is the only available treatment for schistosomiasis. Reliance on a single agent for mass drug administration increases the risk that resistance will develop.

Partner #1: Dr. Conor Caffrey, presenting a unique solution

Dr. Caffrey at the **University of California, San Diego** discovered that statins kill schistosome worms and prevent them from producing eggs by inhibiting an enzyme called *Schistosoma* HMG-CoA reductase (*Sm*HMGR).

What are statins?

Statins have been used worldwide for decades to reduce blood cholesterol, with well-documented safety and tolerability.

The decades of data on statins means that fewer studies will be needed to repurpose them for another medical condition, allowing scientists to bypass many of the time consuming, expensive, and risky stages of early drug discovery.

Roadblock : Finding a library of statins to test

Dr. Caffrey reached out to BVGH with interest in screening a statin library for schistosomiasis drug discovery.

Partner #2: MSD*, identified by BVGH, providing the statin library

MSD, a pioneer in statin drug discovery/development, invited BVGH to proactively present WIPO Re:Search collaboration ideas. After reviewing Dr. Caffrey's project outline, and under an appropriate agreement, MSD shared select statin compounds.

Roadblock: Pursuing structure-based drug design

Dr. Caffrey determined that certain MSD compounds (hits) had promising activity against schistosome worms.

His next step was to determine the crystal structure for *Sm*HMGR, to pursue structure-based drug design. However, he needed additional partners for the crystallization work.

Partners #3 and #4: Specialized experts, recruited by BVGH, solving a puzzle

BVGH searched its diverse network and connected Dr. Caffrey with crystallization experts at **Seattle Children's Research Institute (SCRI)** and **Seattle Structural Genomics Center for Infectious Disease (SSGCID).**

Roadblock: Producing *Sm*HMGR to determine its crystal structure

The SCRI/SSGCID experts had issues producing *Sm*HMGR protein.

They identified a specialized technology called codon-optimized gene constructs as a potential solution.

MSD contributes additional resources

MSD scientists provided codon-optimized gene constructs and technical input on protein expression/production.

Next steps

Once the crystal structure of *Sm*HMGR is obtained, the collaborators will optimize the hit compounds to improve *Sm*HMGR inhibitor activity.

BVGH will continue to identify additional partners and resources to bring the project ever closer to a new, and crucially needed, schistosomiasis drug.

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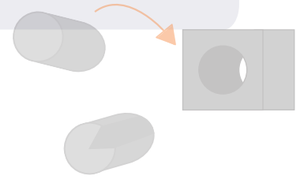
MSD
UC San Diego
SCRI
SSGCID

What is structure-based drug design?

Determining the three-dimensional crystal structure of a target protein such as *Sm*HMGR allows scientists to predict which compounds—based on characteristics including size and shape—will best bind the target and inhibit its activity.

Guided by those predictions, scientists can chemically modify the structures of hit compounds to improve their potency.



A Complicated Treatment Regimen in Need of Simplification

Current treatment regimens for tuberculosis are lengthy and complicated, often involving multiple drugs taken on varying schedules—some daily, some weekly—for up to two years. Given the complexities of treatment, it is not surprising that many patients discontinue therapy before being cured, threatening their health and their lives. Patient non-compliance has also contributed to the rise of multidrug-resistant and extensively drug-resistant tuberculosis. As resistance to current drugs grows, there is a critical need for medications with different mechanisms of action and shorter periods of administration.

Mycobacterium tuberculosis can survive and reproduce inside the macrophages of infected individuals, eventually killing the cells and suppressing the body's immune response to the disease. Dr. Yossef Av-Gay at the **University of British Columbia** previously identified a human protein that promotes the survival of *M. tuberculosis* within macrophages. Through a BVGH-facilitated WIPO Re:Search collaboration, Dr. Av-Gay is partnering with **Takeda Pharmaceutical Company Limited** to develop inhibitors of the protein to treat tuberculosis. Using Takeda's inhibitors—developed to treat other diseases—as a starting point, Dr. Av-Gay identified highly active hits in screening assays that inhibited *M. tuberculosis* growth with relatively low macrophage toxicity. Such low toxicity is critical—a drug must not only be effective against pathogens, but also safe for human use. University of British Columbia has filed a provisional patent application covering the use of the compound class as antitubercular drugs, and Dr. Av-Gay will advance several of the hits to animal studies in the near future. BVGH is now looking to connect Dr. Av-Gay with additional partners to continue moving the project toward human impact.

Dr. Yossef Av-Gay, University of British Columbia

Sharing Drug Delivery Expertise

Malaria claimed over 435,000 lives worldwide in 2017. Committed to changing this narrative, Dr. Audrey Odom John at **Washington University in St. Louis*** and Dr. Cynthia Dowd at **The George Washington University** have developed an antimalarial drug candidate targeting a pathway essential for *Plasmodium falciparum* survival. The drug's target is found in parasites but not humans, reducing the risk of severe side effects.

Dr. Odom John and Dr. Dowd found that the drug candidate has a very short half-life in the bloodstream, meaning that it is quickly eliminated from the body and is unable to exert its antimalarial effects over a sustained period of time. Through WIPO Re:Search and BVGH, Dr. Odom John and Dr. Dowd requested a conversation with **Pfizer** regarding alternative ways to potentially formulate or deliver the drug to improve its half-life. A formulation expert at the company provided valuable information regarding two possible delivery approaches: an adhesive skin patch and an injectable gel. Dr. Odom John and Dr. Dowd will next perform a follow-up study leveraging this information, and then pursue the most appropriate delivery method based on the results.

*Dr. Odom John is now at Children's Hospital of Philadelphia

Dr. Audrey Odom John, Children's Hospital of Philadelphia

Dr. Cynthia Dowd, The George Washington University

WIPO Re:Search Investigators Pursue Natural Product Drug Discovery

For all of our tinkering in the laboratory, Mother Nature is the cleverest of us all. Thousands of years of evolution have led plants and fungi to produce molecules, or natural products, to help defend themselves from predators and adapt to their environment. Humans have also taken advantage of the therapeutic properties of natural products for millennia to prevent and treat a variety of ailments. A nexus is forming between traditional medicine and modern R&D, as it becomes increasingly clear the extent to which natural products are a source of novel, lifesaving treatments.

> ***As long as humans have walked the Earth, natural products have played a vital role in the treatment of diseases. The seemingly unending structural diversity found in plants represents a wealth of untapped therapeutic potential.***
>
> **— Dr. Edmund Ekuadzi, Kwame Nkrumah University of Science and Technology**

Famous Commercialized Natural Products

Aspirin, commercialized in the 1800s, is a derivative of a natural product called salicin, isolated from *Salix alba*, or white willow

Paclitaxel, a cancer drug, is derived from *Taxus brevifolia*, or the Pacific yew, a conifer native to the Pacific Northwest of North America

Artemisinin, used to combat multidrug-resistant malaria, is derived from the traditional Chinese plant *Artemisia annua*, or sweet wormwood

Former Novartis Fellow Seeking to Unleash the Medicinal Power of Ghanaian Plants

Leishmaniasis is an emergent public health problem with high rates of morbidity and mortality, and a more expansive geographical reach than ever before. Migration, climate change, deforestation, and urbanization are all contributing to the spread of leishmaniasis. Newer treatments are superior to older medicines but can still be highly toxic.

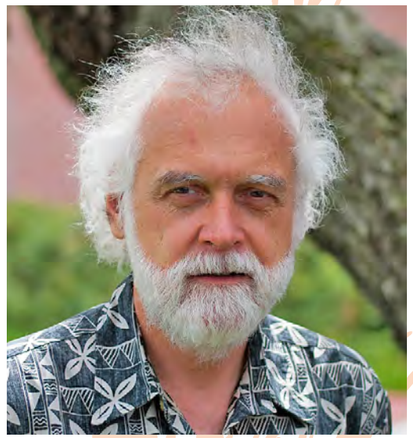
Dr. Edmund Ekuadzi outside the School of Life Sciences, University of Dundee, which hosts the Wellcome Centre for Anti-Infectives Research laboratories

Dr. Edmund Ekuadzi at the **Kwame Nkrumah University of Science and Technology Central Laboratory** in Ghana, a former **Novartis** Next Generation Scientist Program Fellow, is exploring the anti-leishmanial properties of Ghanaian plants used in traditional medicines. The Next Generation Scientist Program helps scientists and physicians from low- and middle-income countries further develop technical skills to be used in their research in their home countries. As part of WIPO Re:Search's collaborative work with Novartis, BVGH shares applicable opportunities, resources, and partnership connections with former Next Generation Scientist Fellows.

Upon learning that Dr. Ekuadzi was seeking advanced training in natural product isolation and fractionation, BVGH connected him with a fellowship opportunity at the Wellcome Centre for Anti-Infectives Research at the **University of Dundee**. There, he will be trained in bioassay-guided fractionation, a technique that will enable him to isolate anti-leishmanial compounds from his plant extracts. Through this experience, Dr. Ekuadzi will acquire the expertise necessary to continue his drug discovery program.

Indigenous Cameroonian Flora and an Ingenious Research Project

Prof. Fabrice Boyom, University of Yaoundé I



Dr. Bill Baker, University of South Florida

Over three billion people worldwide are at risk for malaria. The most common and effective treatment options – quinine and artemisinin – are derived from natural products: quinine from cinchona tree bark (*Cinchona succirubra*) and artemisinin from sweet wormwood (*Artemisia annua*). However, the emergence of drug-resistant parasites has rendered such therapies ineffective in some regions and stimulated research into new natural product-derived antimalarial agents.

Prof. Fabrice Boyom at the **University of Yaoundé I** in Cameroon—a country rich in diverse flora—previously identified indigenous fungi and medicinal plants with promising antimalarial activity. He asked BVGH for help in finding a natural product drug development expert to move his project forward.

After much searching through the WIPO Re:Search consortium for a partner who could provide the precise expertise that Prof. Boyom needed, BVGH found Dr. Bill Baker, a chemist at the **University of South Florida**. Dr. Baker had the know-how to develop natural products into potential drugs by isolating, characterizing, and elucidating the chemical structures.

The collaborators determined that the natural product extracts had good antiplasmodial activity and are now isolating the active compounds. BVGH continues to support the collaboration by identifying relevant funding opportunities. The researchers co-published their findings in May 2018 in the *Journal of Parasitology Research*—a significant accomplishment that helps provide the scientific validation needed to attract funders and partners.

This Cameroonian-American partnership not only showcases WIPO Re:Search's robust and far-reaching global network, but also exemplifies the benefits of breaking down geographic silos.

WIPO Re:Search Drives Point-of-Care Diagnostic Development

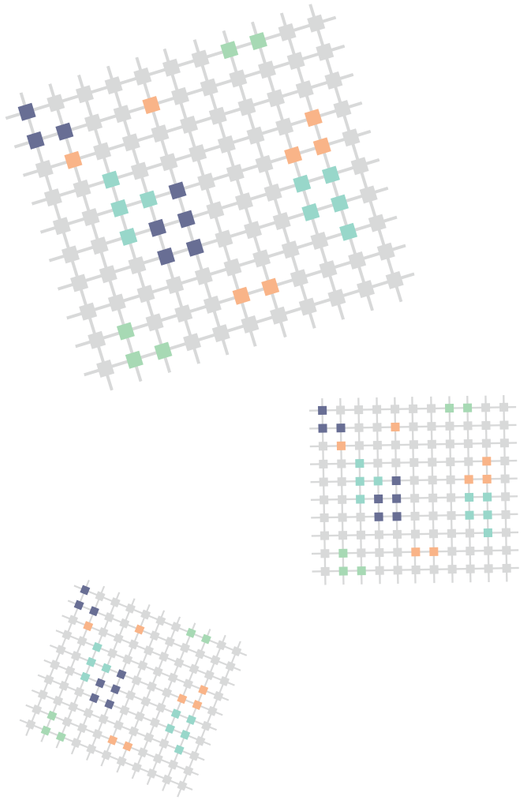
While drugs and vaccines are vital for eliminating neglected infectious diseases, so too are low-cost, high-quality diagnostics. Diagnostics are essential for accurately identifying the cause of a patient's illness, enabling appropriate care, and tracking infection levels over time to guide public health interventions.

BVGH facilitates partnerships around the world with researchers dedicated to developing better diagnostics for neglected infectious diseases.

A Powerful New Tool in Diagnostics Shared Through WIPO Re:Search

Dr. Jose Gomez-Marquez at the **Massachusetts Institute of Technology** and Dr. Kimberly Hamad-Schifferli at the University of Massachusetts, Boston are transforming the standard approach to diagnostic development with their Ampli Blocks—a set of 40 building blocks that researchers around the world can easily assemble in a multitude of configurations to produce diagnostic devices. By engineering a multi-purpose platform for diagnostic development, Ampli Blocks allow researchers to focus on the biochemistry of detection and promote independent development of diagnostic devices. Further removing barriers for their use, the blocks are inexpensive (costing only about six cents for four blocks), do not require refrigeration or special handling, and can be sterilized and reused.

At the request of Dr. Gomez-Marquez and Dr. Hamad-Schifferli, BVGH has established collaborations that are leveraging the pragmatic and versatile Ampli Block technology to improve disease diagnosis in low-resource settings.



U Ibadan
UBC
U Buea

Schistosomiasis

Diagnosis of schistosomiasis is limited to two methods. Microscopy cannot be used in field settings due to the need for electricity, while point-of-care circulating cathodic antigen testing has only 60% sensitivity in detecting one common worm species. Due to the shortcomings of current diagnostics, entire communities are often treated with the drug praziquantel for both prevention and treatment of schistosomiasis, without first identifying which individuals are actually infected. Dr. Chiaka Anumudu at the **University of Ibadan** in Nigeria has identified 54 human proteins as potential biomarkers of schistosomiasis infection and, through WIPO Re:Search, is using Ampli Blocks to develop a device to detect those proteins in blood samples.

Onchocerciasis

An eye and skin disease caused by the parasitic worm *Onchocerca volvulus*, onchocerciasis is the second leading cause of infection-related blindness worldwide. The World Health Organization estimates that at least 25 million people are infected with *O. volvulus* and an additional 123 million people are at risk for infection.Onchocerciasis is currently treated using the microfilaricide ivermectin, which has little effect on the adult worm. As a result, in high-risk areas such as Cameroon, patients may take the drug for over ten years, depending on the lifespan of the adult worm. There are no diagnostic tests sensitive enough to determine if a patient is completely "adult worm-free." The development of sensitive diagnostic tools to detect adult worms and thus define treatment endpoints for onchocerciasis is therefore imperative.

Dr. Stephen Ghogomu at the **University of Buea** in Cameroon has identified two antigens that are produced specifically by adult *O. volvulus* and released into the bloodstream of infected human hosts. He aims to create point-of-care diagnostic tests that can accurately detect the presence of the two proteins in bodily fluids and thus indicate whether a person is infected with adult *O. volvulus*. Individuals who are infected can then continue treatment, while those who are no longer infected can discontinue therapy. BVGH introduced Dr. Ghogomu to Dr. Horacio Bach at the **University of British Columbia**, an antibody engineering expert who is developing antibodies that bind to the two adult *O. volvulus* proteins with high affinity. Dr. Ghogomu will next incorporate the antibodies into the Ampli Block platform to create prototype diagnostic tests.

The collaboration between Dr. Ghogomu and Dr. Bach, and the follow-on partnership between Dr. Ghogomu and the Ampli Block developers, exemplify BVGH's strategic support for WIPO Re:Search product R&D programs across multiple stages of development.

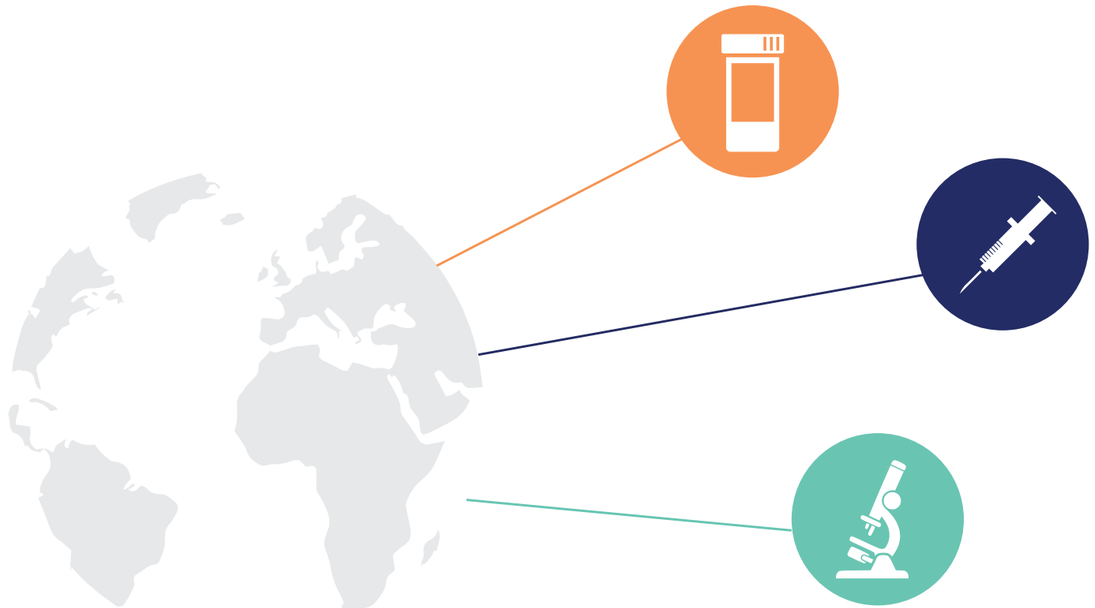
Dr. Chiaka Anumudu, University of Ibadan

Dr. Stephen Ghogomu, University of Buea

Dr. Horacio Bach, University of British Columbia

Value Driver 2:
Optimizing Collaborative R&D
for Diseases of the World's Poor

One billion. Over one *billion* people are currently suffering or dying from neglected infectious diseases. Because they disproportionately afflict the poor in low- and middle-income countries, these diseases have historically — and tragically — not received the investment that would save lives and families.



A Sustainable, Shared Solution for Diseases of the World's Poor

Today, through WIPO Re:Search, global health companies and research institutions have access to a well-established, sustainable research and development (R&D) model that flips the old paradigm of neglected infectious disease investment. By uniting public- and private-sector assets in an innovative resource-matching model specifically designed to help the poorest of the poor, companies and researchers have a cost-effective, risk-reducing platform to target these diseases.

Buruli ulcer

Mycobacterial skin lesions primarily afflicting children — if treated late, they result in permanent disfigurement and disability.

Discovering new treatments without debilitating side effects
Stories on pages 35, 50

Chagas disease (American trypanosomiasis)

Insect-borne parasite infecting 6+ million, primarily in Latin America — curable if caught early, otherwise chronic and potentially deadly. Current drugs have limitations.

Facilitating timely diagnosis and developing improved therapies
Stories on pages 35, 51

Cysticercosis

Tapeworm larvae (from undercooked pork) that spread beyond the human intestine with devastating health effects.

Dengue

Mosquito-borne viral, flu-like infection putting 40% of the global population at risk with potentially lethal complications.

Echinococcosis

An ingested larval parasite that can go undetected for years in the lungs and liver — potentially deadly if diagnosed too late.

Dracunculiasis (Guinea-worm disease)

A water-borne, 24- to 31-inch parasitic worm nearly eradicated from humans worldwide through prevention efforts.

Leishmaniasis

An asymptomatic parasitic infection from sandfly bites can turn disfiguring and deadly if it progresses to the disease phase — 1 billion people at risk.

Exploring alternative drugs without life-threatening side effects
Stories on pages 21, 40, 47

Lymphatic filariasis (elephantiasis)

A mosquito-borne roundworm disease — preventable with treatment — that otherwise leads to disfigurement.

Foodborne trematodiases*

A group of ingested parasitic flatworms affecting the liver or lungs of 40 million people, primarily children.

Human African trypanosomiasis (sleeping sickness)

A parasite transmitted by the tsetse fly causes sleep disturbances, mental deterioration, and, if untreated, death. Current drugs can be toxic.

Developing novel, safer drugs
Story on page 40

Leprosy

A curable mycobacterial disease that, if untreated, can cause permanent damage to skin, nerves, limbs, and eyes.

*Clonorchiasis, fascioliasis, opistorchiasis, and paragonimiasis

WIPO Re:Search:
Advancing Product Development for Neglected Infectious Diseases

Since 2011, BVGH has catalyzed **155** innovative intellectual property-sharing collaborations.

10 ongoing collaborations have advanced critical solutions for neglected infectious diseases at least one step along the product development pathway; **7** drug development collaborations are highlighted below and in the companion publication, **WIPO Re:Search: Advancing Product Development for Neglected Infectious Diseases through Global Public-Private Partnerships.**

Schistosomiasis

MSD*
UC San Diego
• *Dr. Conor Caffrey*
Seattle Children's Research Institute
SSGCID

Cholesterol-lowering medications prime pump as schistosomiasis treatment leads
(story on page 16)

Tuberculosis

Johnson & Johnson
WUSTL
• *Dr. Christina Stallings*

Targeting an unexploited vulnerability in *M. tuberculosis* to combat drug-resistant infections
(story on page 46)

Tuberculosis

Johnson & Johnson
National Institutes of Health
• *Dr. Clif Barry, Dr. Helena Boshoff*

Helping the human immune system win the battle against tuberculosis
(story on page 47)

Onchocerciasis

Merck KGaA, Darmstadt, Germany
University of Buea
• *Prof. Fidelis Cho-Ngwa*

Fighting onchocerciasis, a leading cause of infectious blindness, through Global North/South collaborations
(story on page 39)

Malaria

Johnson & Johnson
WEHI
• *Prof. Alan Cowman, Dr. Brad Sleebs*

Developing an antimalarial drug with a novel mode of action to circumvent growing resistance
(story on page 45)

Tuberculosis

Takeda Pharmaceutical Company Limited
University of British Columbia
• *Dr. Yossef Av-Gay*

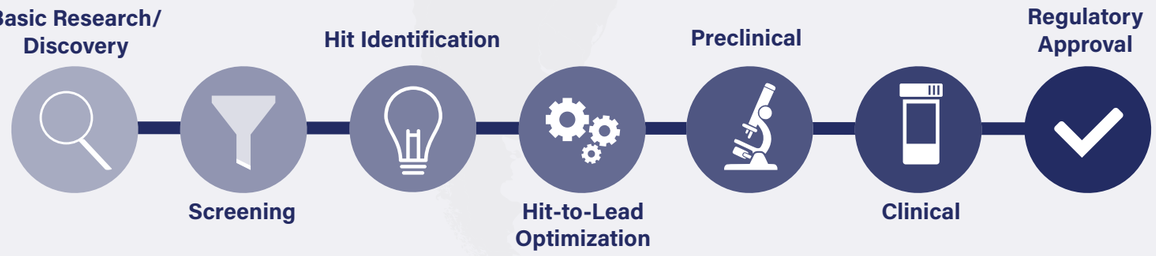
Protecting human immune cells from the ravages of tuberculosis
(story on page 18)

Malaria

MSD*
WEHI
• *Prof. Alan Cowman, Dr. Justin Boddey, Dr. Brad Sleebs*

Disrupting malaria parasite replication via a novel target
(story on page 36)

Product Development Pathway



SSGCID Seattle Structural Genomics Center for Infectious Disease
UC San Diego University of California, San Diego
WEHI Walter and Eliza Hall Institute of Medical Research
WUSTL Washington University in St. Louis

*MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA

Malaria

A life-threatening mosquito-borne parasitic infection affecting hundreds of millions with fever and possible organ failure.

Addressing stalled progress in controlling malaria
Stories on pages 19, 22, 36, 40, 41, 45, 48

Onchocerciasis (river blindness)

The second-leading cause of blindness due to infection — transmitted near rivers by the bite of the blackfly.

Removing the risk of a potentially fatal treatment
Stories on pages 24, 39

Podoconiosis (non-filarial elephantiasis)

A soil-triggered inflammatory response — affecting some who go barefoot — leads to swelling and disfigurement in the legs.

Rabies

Endemic in 150 countries, 15 million people annually require post-dog bite treatment for this vaccine-preventable virus.

Adapting a rabies vaccine for tropical heat
Story on page 34

Schistosomiasis (snail fever)

An acute and chronic water-borne parasitic-worm disease with 100 million people treated annually.

Proactively targeting the risk of emerging drug resistance
Stories on pages 16, 24

Snakebite

Venomous snakebites are highly treatable, yet lack of access to antivenoms results in severe paralysis leading to disability, amputation, or death.

Soil-transmitted helminthiases

Easily treated, these intestinal worms nevertheless infect 1.5 billion people, causing malnutrition and physical impairments.

Trachoma

A bacterial infection that, if untreated, causes the eyelashes to turn inward, scrape the eye, and over time, cause blindness.

Tuberculosis

A top-10 cause of death worldwide, this once easily treatable and curable disease is facing greater and greater antimicrobial resistance.

Solving urgent multifaceted treatment challenges
Stories on pages 18, 46, 47

Yaws (endemic treponematoses)

One of a group of curable bacterial infections — primarily in children — that causes disfigurement and debilitation if neglected.

Through WIPO Re:Search, companies can complement their internal R&D and bolster their portfolios with promising collaborations to address antimicrobial resistance and other unmet medical needs for neglected infectious diseases.

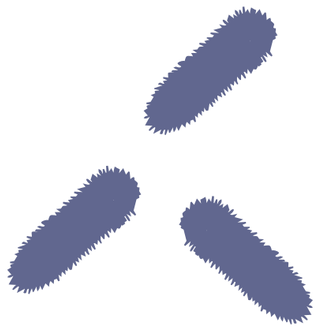
Diversifying Disease Portfolios

WIPO Re:Search opens new opportunities for companies and researchers around neglected infectious diseases. With a unique model that encourages promising research across geographic and institutional borders, BVGH targets and connects the experts who are driving innovation in these disease areas. The result: new pathways to solving otherwise neglected diseases.

The vast network of research collaborations fostered by BVGH yields centers of expertise, assets, and excellence that WIPO Re:Search Members can draw from. For companies, this means savings in time and funding in gaining access to expert collaborators in specialized or remote locations. For researchers, this means gaining access to valuable resources that will spur their work forward.

Adapting a Rabies Vaccine for Tropical Heat

Rabies is invariably fatal without intervention. Due to lack of affordability, there is a scarcity of rabies vaccines in the countries that need them most. Further, current rabies vaccines require cold storage — making distribution to field locations without refrigeration difficult, if not impossible. BVGH connected Dr. Héla Kallel at the **Institut Pasteur Tunis** with the **U.S. National Institute of Allergy and Infectious Diseases (NIAID)**, part of the **National Institutes of Health (NIH)**, to help overcome these challenges. Dr. Kallel utilized NIAID's suite of preclinical services for the development of a thermostable formulation, and she is adapting this formulation to her more affordable and more accessible vaccine.



Did you know?

Once clinical symptoms appear in a person, rabies is almost always fatal.

Partnering on a Novel Biomarker for Chagas Disease

Not caught early, Chagas disease can lead to serious heart, neurological, and digestive tract complications. Dr. Momar Ndao at **McGill University** identified a novel biomarker that could facilitate timely and accurate diagnosis as well as assessment of cure after treatment. Dr. Ndao joined forces with Dr. Horacio Bach at the **University of British Columbia** through a BVGH-coordinated WIPO Re:Search partnership to develop antibodies against the biomarkers that could potentially be incorporated into a simplified point-of-care diagnostic assay.

Dr. Momar Ndao, McGill University

Did you know?

More than 300,000 people with Chagas disease live in the United States.

Accessing Buruli Ulcer Clinical Strains from Cameroon

In treating Buruli ulcer, antibiotics are a vast improvement over former options, which involved surgery, skin grafting, hospitalization, higher costs, and a higher reoccurrence rate. Yet current medications can cause serious side effects such as hearing loss. BVGH linked Dr. Tianyu Zhang at **Guangzhou Institutes of Biomedicine and Health** to Prof. Fabrice Boyom at the **University of Yaoundé I** to test Dr. Zhang's late-stage antibiotic candidate TB47 against Buruli ulcer strains from infected patients from multiple parts of Cameroon. By facilitating the testing of these additional strains, WIPO Re:Search is helping to advance a new treatment through preclinical assessments in preparation for moving into clinical trials.

Did you know?

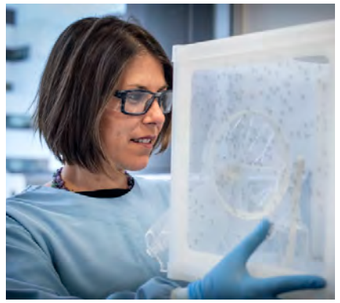
Buruli ulcer is in the same family of organisms that cause leprosy and tuberculosis.

Diversifying Collaboration Strategies

Leveraging Assets to Fuel Antimalarial Drug Discovery

As resistance emerges to frontline antimalarials, the development of novel therapies is urgently required.

When creating new antimalarials, researchers may target specific stages of the malaria parasite's lifecycle. One such stage, and a trademark of malaria infection, involves the parasite invading and replicating within human red blood cells. Plasmepsin V (PMV), a *Plasmodium* aspartyl protease enzyme that plays a key role in the parasite's evasion of the human immune response, is a promising drug target. Importantly, PMV has been validated as a drug target for both *P. falciparum* and *P. vivax* — the two most virulent malaria parasites capable of infecting humans.



Dr. Paola Favuzza, Walter and Eliza Hall Institute of Medical Research

MSD* was interested in identifying collaborators who could evaluate its chemical libraries of protease inhibitors for antimalarial drug discovery. With assistance from BVGH, MSD identified Prof. Alan Cowman, Dr. Justin Boddey, and Dr. Brad Sleebs at the **Walter and Eliza Hall Institute of Medical Research (WEHI)** in Australia. Having worked on the validation of PMV as an antimalarial drug target, the team was well positioned to screen MSD's aspartyl protease inhibitor libraries to identify compounds that target plasmepsins in both *P. falciparum* and *P. vivax.* Established through WIPO Re:Search, this collaboration has now identified novel drug-like hit compounds that are active against the malaria parasite.

Dr. Manuel de Lera Ruiz, MSD

> ***Working on a WIPO Re:Search-enabled public-private collaboration to discover drug candidates for malaria is an amazing experience. The teamwork, energy, and inventive spirit within the program are infectious. Alan Cowman and his team are dedicated discovery scientists that make breakthrough science exciting.***
>
> **— Dr. Manuel de Lera Ruiz, Associate Principal Scientist, Medicinal Chemistry Lead, MSD**

*MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA

MSD
WEHI

Diversifying funding sources

BVGH encouraged the MSD and WEHI team to pursue funding opportunities from the Wellcome Trust aimed at stimulating promising public-private partnerships such as theirs. Of the two Wellcome Trust awards the team has received, the most recent endowed the team with over US $3.5 million to accelerate their collaborative research program. Having met ambitious first-year milestones, the team will continue their work in year two toward increasing drug potency and selectivity against malaria parasites.

Prof. Alan Cowman, Dr. Justin Boddey, and Dr. Brad Sleebs, Walter and Eliza Hall Institute of Medical Research

> ***The MSD/WEHI collaboration has made some great progress identifying potent chemical matter that has also provided useful tools to decipher some important malaria biology. We are hopeful that our research will lead to a drug that will benefit those who suffer from the deadly effects of this horrible parasite.***
>
> **— Prof. Alan Cowman, Walter and Eliza Hall Institute of Medical Research**

Repurposing to Reduce Time, Cost, and Risk

One of the key ways WIPO Re:Search accelerates the drug discovery process is by promoting the repurposing of existing drug compounds. Throughout history, drugs intended for one purpose have been found — often through serendipity and side effects — to have efficacy in other areas. Because such drugs have undergone safety testing, the potential time to market for new purposes can be shortened on the order of years, saving considerable development costs and resources.

BVGH maintains the WIPO Re:Search Asset Repurposing Database, which tracks hundreds of compound classes available on a case-by-case basis from company Members with repurposing potential for neglected infectious diseases. Through WIPO Re:Search, BVGH facilitates the sharing of company compounds to drive drug discovery for those diseases.

Excerpts from the WIPO Re:Search Asset Repurposing Database

Compound Class	Original Indication	Potential for Repurposing
Acetylcholinesterase inhibitors	Alzheimer's, urinary incontinence	Human African trypanosomiasis, leishmaniasis, malaria, rabies, schistosomiasis, snakebite, soil-transmitted helminthiases
Calcium channel blockers	Angina, hypertension, insomnia	Chagas disease, fascioliasis, human African trypanosomiasis, leishmaniasis, malaria, schistosomiasis, tuberculosis
Dihydrofolate reductase inhibitors	Cancer, bacterial infections	Chagas disease, human African trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, malaria, tuberculosis

Repurposing Compounds to Target Onchocerciasis

Current treatments for onchocerciasis are ineffective against adult *Onchocerca volvulus* worms and can lead to the death of patients co-infected with *Loa loa*, a parasite commonly found in West and Central Africa. Through WIPO Re:Search, BVGH connected Prof. Fidelis Cho-Ngwa at the **University of Buea** with **Merck KGaA, Darmstadt, Germany** — a company committed to fostering Global North/South collaborations to accelerate neglected infectious disease R&D — to develop a medication with activity against both adult and juvenile *O. volvulus* but not *Loa loa*.

With support from BVGH, the team received a Wellcome Trust Pathfinder Award for US $184,000 to support the initial screening. Prof. Cho-Ngwa identified several promising hits in a screen of over 5,500 company compounds. BVGH assisted the partners in identifying a medicinal chemistry expert to collaborate on hit-to-lead optimization, and they are co-preparing a grant proposal to fund this work. Merck KGaA, Darmstadt, Germany will contribute corporate affairs, patents, global health, and medicinal chemistry expertise to support the advancement of this drug development program.

Prof. Fidelis Cho-Ngwa, University of Buea

Dr. Frédérique Santerre, Merck KGaA, Darmstadt, Germany

> ***Through our Open Innovation Initiative, Merck KGaA, Darmstadt, Germany is committed to addressing access challenges around affordability by sharing our proprietary knowledge to accelerate early discovery for disease areas where we do not have competencies or expertise, such as onchocerciasis or Buruli ulcer. Our aim is to contribute to a vibrant pipeline for these diseases as well as capacity building and health system strengthening in the countries where many of these diseases are endemic.***
>
> **— Dr. Frédérique Santerre, Global Head, Access to Health, Merck KGaA, Darmstadt, Germany**

Repurposing Compounds to Target Parasites

Drs. Alexis Kaushansky and Bart Staker at the **Seattle Children's Research Institute (SCRI)** are working to further anti-parasitic drug discovery. They have previously demonstrated the efficacy of cancer drugs — specifically Bcl-2 family inhibitors — in parasitic infections such as malaria and toxoplasmosis. Through WIPO Re:Search and BVGH, **Takeda Pharmaceutical Company Limited** provided the investigators with compounds of this class to support the expansion of their screening efforts to include other neglected parasitic infections. The SCRI researchers are currently screening the compounds to identify strong candidates for further development.

Dr. Alexis Kaushansky, Seattle Children's Research Institute

Prof. Fabrice Boyom, University of Yaoundé I

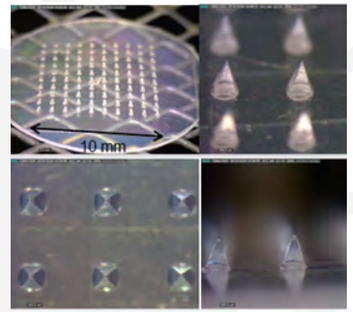
Prof. Fabrice Boyom at the **University of Yaoundé I** aims to develop novel drugs for human African trypanosomiasis, leishmaniasis, and malaria by targeting critical parasite metabolic pathways. With assistance from BVGH, Prof. Boyom applied for funding from Medicines for Malaria Venture (MMV) and the African Academy of Sciences' Grand Challenges Africa. After he expressed interest in obtaining compounds that may inhibit metabolic pathways of interest, BVGH connected him through WIPO Re:Search to **Eisai Co., Ltd.**, which supported his funding proposals by sharing dihydrofolate reductase inhibitors and potassium channel blockers. As a result, Prof. Boyom received both the MMV and the Grand Challenges Africa awards. He has since identified promising hits and is working with collaborators to conduct further tests.

Collaborating on Vaccine Technology for Malaria

Through WIPO Re:Search, **Takeda Pharmaceutical Company Limited** and the **National Institute of Allergy and Infectious Diseases (NIAID) at NIH** have entered into a research collaboration to examine the feasibility of using Takeda's microneedle patch technology to administer a transmission-blocking malaria vaccine developed by Dr. Patrick Duffy and Dr. Puthupparampil Scaria at NIAID's Laboratory of Malaria Immunology and Vaccinology. Transmission-blocking vaccines are novel among malaria vaccine approaches, targeting the parasite's life cycle in the mosquito vector, rather than preventing infection within the human host. While transmission-blocking vaccines do not directly prevent infection, they rely on herd immunity to interrupt continued transmission of parasites, thereby reducing infections across the community with the ultimate goal to eliminate malaria.

As its name suggests, microneedle patches comprise a series of minute needles much smaller than the needles used to administer standard vaccines. The patches are composed of materials that can help improve the encased vaccine's stability in hot climates such as those found in malaria-endemic regions.

If NIAID's studies of the patch prove successful, this collaboration has the strong potential to result in a malaria vaccine that is truly suited to the healthcare needs of malaria-endemic low- and middle-income countries. In particular, the patches could eliminate the need for vaccine storage in freezers or refrigerators; healthcare professionals trained on the proper use of needles; and control of contaminated needle disposal. Since children comprise the majority of malaria illnesses and deaths globally, microneedle patches could also improve coverage in this population by offering a less-painful alternative to conventional, injectable vaccines.



Microneedle patch

Dr. Patrick Duffy, National Institute of Allergy and Infectious Diseases/ National Institutes of Health

Dr. Puthupparampil Scaria, National Institute of Allergy and Infectious Diseases/National Institutes of Health

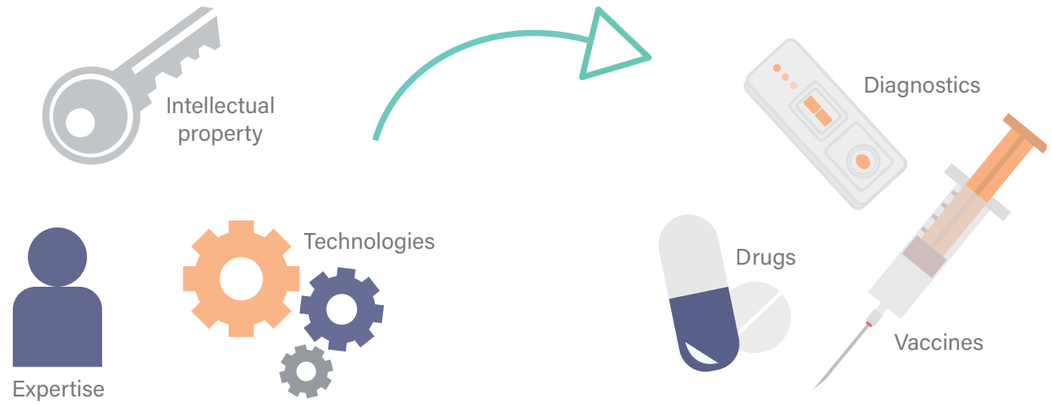
Value Driver 3:

Harnessing Open Innovation to Improve Global Health

Today, leading pharmaceutical companies are embracing open innovation as an urgently needed solution to diseases endemic in low- and middle-income countries. More than just a buzzword, open innovation represents a company's commitment to sharing its greatest strengths—its intellectual property, technologies, and expertise—outside its walls to drive the development of life-changing products. Open innovation is particularly important for neglected infectious diseases, which affect one-seventh of the world's population but benefit from only a small fraction of global research and development (R&D) resources.

Through WIPO Re:Search, BVGH connects academic and non-profit global health researchers to industry assets that they might not otherwise have been aware of, or been able to access. This section showcases the combined power of BVGH's strategic partnering approach (described on pages 12-15) and industry open innovation to advance neglected infectious disease R&D around the world.

Transforming Company Assets into Life-Changing Products

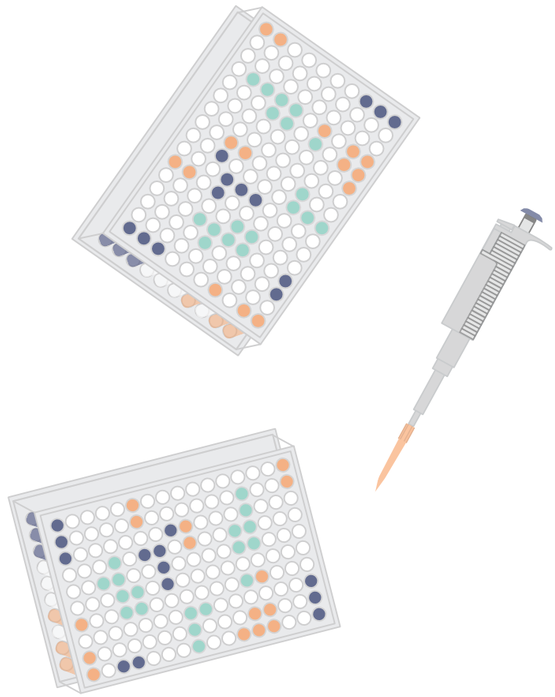


"Jump-stARt"ing Drug Development for Deadly Diseases

Sharing Molecular Libraries to Fight Neglected Infectious Diseases and Pandemic Threats

As part of **Johnson & Johnson**'s global public health commitment, Janssen has made available its Jump-stARter library through WIPO Re:Search. Johnson & Johnson medicinal chemists reviewed millions of proprietary molecules and voted on those with the greatest potential for drug development. This resulted in a diverse collection of 80,000 high-quality drug-like small molecules and compound fragments created to "jump-start" collaborations with a broad array of drug discovery researchers to identify and advance promising drug candidates.

To help get those compounds into scientists' hands as quickly as possible, the company created a material transfer agreement template to expedite negotiations with recipients and established processes for efficient preparation and shipment of the library. When drug discovery researchers identify compounds (or hits) within the library that have interesting activity in their assay systems, Johnson & Johnson divulges the structures of those hits to inform and enable follow-on R&D. On a case-by-case basis, Johnson & Johnson also provides in-kind support to help move particularly promising compounds closer to the clinic.



Through WIPO Re:Search, BVGH has connected us with outstanding scientific partners around the world, uniting their expertise and Johnson & Johnson's resources to catalyze neglected infectious disease R&D with the aim of creating new drugs. Without the Consortium, we would not have had the opportunity to share our Jump-stARter library and other assets so broadly, to potentially develop better solutions for these devastating diseases.

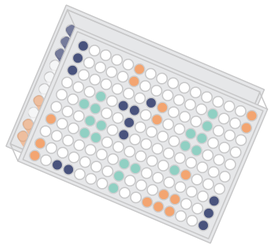
— Dr. Paul Jackson, Scientific Director, Johnson & Johnson

BVGH has coordinated the sharing of the Jump-stARter library across the WIPO Re:Search network to combat diseases that cause millions of deaths each year and for which better drugs are urgently needed. Those diseases include:

Malaria

The World Health Organization sounded an alarm in its *World Malaria Report 2018*, noting that progress against the disease has stalled after years of unprecedented successes. The Report called parasite resistance to antimalarial medicines a major threat to malaria control. Through WIPO Re:Search, Prof. Alan Cowman and Dr. Brad Sleebs at the **Walter and Eliza Hall Institute of Medical Research (WEHI)** are partnering with **Johnson & Johnson** to develop a new drug that attacks malaria parasites in a different way than existing therapies, in order to bypass resistance mechanisms. The WEHI team identified several hit compounds in their initial screens that not only had excellent antimalarial activity, but also appeared to kill the parasites through novel molecular pathways. Building on those exciting results, the WEHI researchers and Johnson & Johnson are chemically modifying the hits to improve their potency and drug-like properties in preparation for preclinical testing.

Prof. Alan Cowman and Dr. Brad Sleebs,
Walter and Eliza Hall Institute of Medical Research

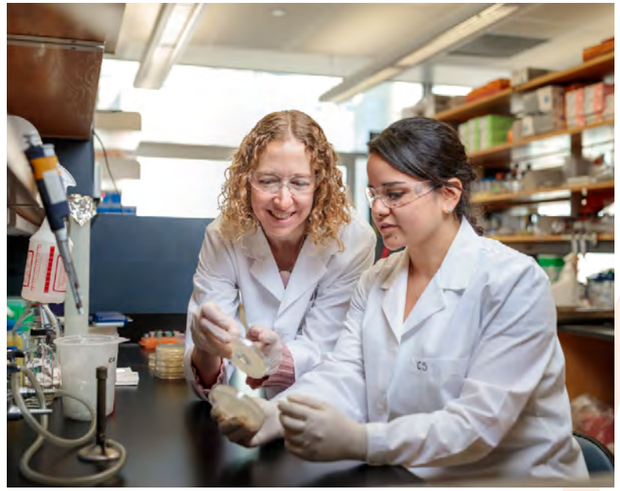


J&J Jump-stARter library

WEHI screening platform

Identification of hit compounds with novel antimalarial activity

Tuberculosis



Dr. Christina Stallings and research scientist Sthefany Chavez, Washington University in St. Louis

Multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB) strikes over 550,000 people each year. Nearly half of patients are treated unsuccessfully with existing agents, potentially leaving them both ill and able to transmit the disease to others. Through WIPO Re:Search, BVGH connected Dr. Christina Stallings at **Washington University in St. Louis** to **Johnson & Johnson** to develop an inhibitor of an enzyme critical for *Mycobacterium tuberculosis* growth and virulence. A drug targeting this enzyme could potentially be a safe and effective treatment for MDR/RR-TB, given that the enzyme is not found in humans (reducing the risk of serious side effects) and is not inhibited by current antitubercular medicines (decreasing the likelihood that *M. tuberculosis* has already acquired resistance).

After identifying multiple hits in her first set of screens, Dr. Stallings is now testing the inhibitory activity of additional Johnson & Johnson compounds with similar chemical structures. The results of those studies will help company scientists chemically modify the initial hits to produce lead compounds with better activity for further development and testing.

> ***I am grateful to BVGH for introducing me to Johnson & Johnson — who might not otherwise have returned my calls! — to take my tuberculosis drug discovery research to the next level. We have received not only high-quality compound libraries for screening, but also scientific expertise and logistical support for our ongoing development of the most promising compounds. I am energized by our successes to date and by the prospect of improving tuberculosis treatment for millions of people worldwide.***
>
> **— Dr. Christina Stallings, Washington University in St. Louis**

BVGH is facilitating a WIPO Re:Search collaboration between **Johnson & Johnson** and tuberculosis researchers at the **National Institutes of Health (NIH)**. *M. tuberculosis* can survive and reproduce inside human macrophages, eventually killing the cells and suppressing the body's immune response to the infection. Dr. Clif Barry and Dr. Helena Boshoff at NIH found several Jump-stARter compounds that inhibited *M. tuberculosis* growth under conditions similar to those within infected macrophages. Using those data, along with the results of ongoing studies of structurally similar compounds, Johnson & Johnson will chemically optimize the most active compounds. The partners will then validate the resultant lead candidates in laboratory and preclinical studies.

Dr. Clif Barry and Dr. Helena Boshoff, National Institutes of Health

Prof. Tanya Parish, Infectious Disease Research Institute

Similarly, Prof. Tanya Parish, a drug discovery scientist at the **Infectious Disease Research Institute (IDRI)**, was connected with **Johnson & Johnson** through WIPO Re:Search and BVGH to target *M. tuberculosis* residing within human macrophages. Her team's novel high-content imaging system permits the identification of compounds that kill *M. tuberculosis* in macrophages without harming the macrophages. Results from the Jump-stARter library screening are expected by the end of 2019.

Leishmaniasis

While the burden of tuberculosis is widely recognized by the global health community, leishmaniasis — which afflicts more than 12 million people worldwide — is often given less attention. The most common form, cutaneous leishmaniasis, causes skin lesions and ulcers leading to scarring, disability, and stigma. Although newer treatments are superior to older medicines, life-threatening side effects are still a major concern. In parallel with their WIPO Re:Search tuberculosis drug discovery activities, Prof. Parish and her group at **IDRI** are using their high-content imaging system to find Jump-stARter compounds with selective activity against *Leishmania donovani* within human cells. They anticipate completing the initial screens by the end of 2019.

Treating Malaria by Sugar Deprivation

GSK established the Tres Cantos Open Lab Foundation in 2010 as a demonstration of its commitment to open innovation and creation of new medicines for diseases of the developing world (including Chagas disease, human African trypanosomiasis, leishmaniasis, malaria, and tuberculosis). The Open Lab is an incubator that provides selected researchers with funding and access to GSK facilities, resources, and expertise to help them advance their own drug discovery projects.

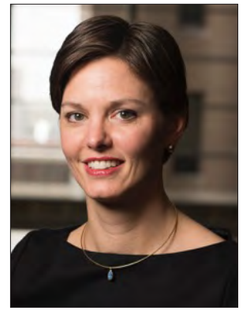
> ***GSK has been active in WIPO Re:Search since its inception, as well as in its predecessor, the Pool for Open Innovation against Neglected Tropical Diseases (POINT) program. It has enabled opportunities for GSK scientists to connect with talented and innovative scientists across the globe to advance our research and partnership goals.***
>
> **— Dr. Mike Strange, Head, Global Catalyst, GSK**

By introducing GSK to WIPO Re:Search investigators with whom they might not otherwise have engaged, BVGH is supporting corporate objectives while also stimulating neglected infectious disease R&D through broader access to the company's assets. Those assets include the Tres Cantos Antimalarial Set (TCAMS), a library of over 13,000 compounds with activity against the blood-stage form of *Plasmodium falciparum*. Over 80 percent of the compounds were new to the malaria research community when GSK compiled the library in 2010.

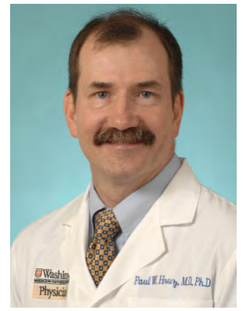
Libraries such as TCAMS, particularly when accompanied by chemical structures and data, are excellent starting points for drug discovery programs – including the work of Dr. Audrey Odom John and Dr. Paul Hruz at **Washington University in St. Louis**.*

In response to growing concern about antimalarial resistance, Dr. Odom John and Dr. Hruz aim to develop a drug that acts through a novel mechanism to which *P. falciparum* remains susceptible. Malaria parasites within the human host rely on sugars taken up from the host's blood to produce energy, suggesting that depriving the parasites of such sugars may be lethal. The researchers have developed a high-throughput screening assay system to identify compounds that prevent *P. falciparum* hexose transporter from importing sugars from the blood, without affecting the activity of similar human transporters. BVGH connected the team to GSK, who agreed to share TCAMS through WIPO Re:Search. Dr. Odom John and Dr. Hruz found several hits in their initial screens, and validation of hit activity is ongoing.

* Dr. Odom John is now at Children's Hospital of Philadelphia.



Dr. Audrey Odom John, Children's Hospital of Philadelphia



Dr. Paul Hruz, Washington University in St. Louis

Fighting Buruli Ulcer through Global North/South Collaborations

Buruli ulcer, a bacterial disease found mostly in Central and West Africa, destroys skin and soft tissue, resulting in large necrotic ulcers. Primarily affecting children, the disease causes significant long-term functional disability and permanent deformity unless diagnosed and treated early. In addition to requiring frequent visits to health clinics over a period of several weeks — which is not always practical in remote areas — current medicines can also cause severe side effects such as hearing loss.

BVGH recently coordinated a WIPO Re:Search collaboration between Prof. Fabrice Boyom of the **University of Yaoundé I** in Cameroon and **Merck KGaA, Darmstadt, Germany** to develop a safer Buruli ulcer drug that can be administered over a shorter time frame. Prof. Boyom will screen the company's Mini Library — a diverse set of drug-like compounds with a broad range of molecular targets — for activity against *Mycobacterium ulcerans*, with an eye on the ultimate goal of reducing the suffering caused by Buruli ulcer.

"Through WIPO Re:Search, I am collaborating with leading international companies and scientists to repurpose pharmaceutical compounds and Cameroonian medicinal plants as new drugs for Buruli ulcer, human African trypanosomiasis, leishmaniasis, and malaria. Thanks to the Consortium and the partnerships that BVGH has facilitated, I have new scientific publications, additional grant funding to pursue neglected infectious disease R&D, and increased visibility of my research," said Prof. Boyom.

Prof. Fabrice Boyom, University of Yaoundé I

Dr. Arno Hartmann, Merck KGaA, Darmstadt, Germany

> ***The WIPO Re:Search platform provides a great network and excellent opportunities for collaborations in the neglected tropical disease space. We have supported this initiative for many years and were able to start new exciting projects, alongside our existing collaborations, through the use of our Mini Library. This open-source approach contributes a lot to addressing Access to Health (A2H) challenges.***
>
> **— Dr. Arno Hartmann, Vice President, Head, Patents Healthcare, Merck KGaA, Darmstadt, Germany**

Combatting Chagas Disease, a Significant Public Health Problem in Latin America

Drs. Gustavo Fernando Mercaldi (LNBio), Artur Cordeiro (LNBio), Dominick Casalena (Novartis), and Douglas Auld (Novartis). Photo courtesy of Novartis.

Novartis partners to support drug discovery for neglected diseases and to help foster research capabilities in low- and middle-income countries. Novartis' partnership with Dr. Artur Cordeiro at **Laboratório Nacional de Biociências (LNBio)** — the first WIPO Re:Search collaboration for the Brazilian institute — merged those interests to conduct collaborative research focused on Chagas disease. Also known as American trypanosomiasis, Chagas disease affects an estimated eight million people, mainly in Latin America. Dr. Cordeiro previously discovered compounds that inhibit two key *Trypanosoma cruzi* enzymes and are active against the parasite within human cells. To assist Dr. Cordeiro in identifying additional active compounds to move his drug discovery work forward, BVGH introduced him to Novartis.

After securing a grant from São Paulo Research Foundation (FAPESP) to cover his expenses, Dr. Cordeiro traveled to Cambridge, USA, where he screened thousands of proprietary Novartis compounds through the company's Facilitated Access to Screening Technologies (FAST) Lab program. In addition to having access to Novartis' facilities, he also benefited from technical support and mentorship from scientists at the Novartis Institutes for BioMedical Research. Dr. Cordeiro returned to LNBio with data for both drug targets and new chemical structures with good activity.

> ***My time at Novartis was an amazing experience and the two most productive weeks of 2019. Without BVGH, it would have been very difficult to make this important connection to industry.***
>
> **— Dr. Artur Cordeiro, LNBio**

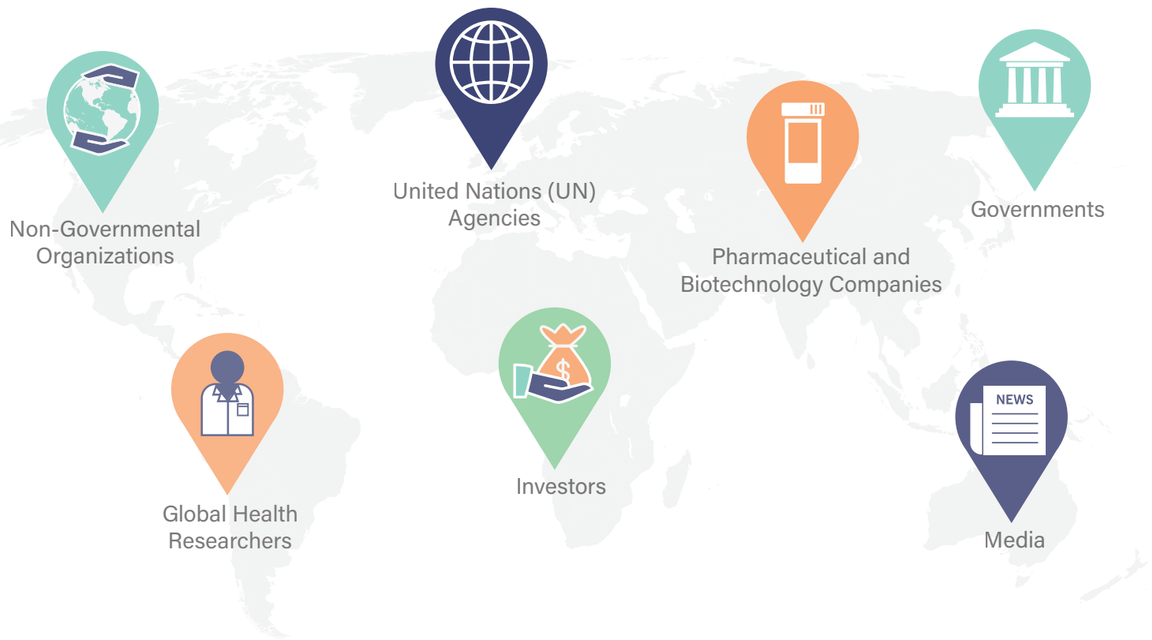
Through WIPO Re:Search, I am collaborating with leading international companies and scientists to repurpose pharmaceutical compounds and Cameroonian medicinal plants as new drugs for Buruli ulcer, human African trypanosomiasis, leishmaniasis, and malaria. Thanks to the Consortium and the partnerships that BVGH has facilitated, I have new scientific publications, additional grant funding to pursue neglected infectious disease R&D, and increased visibility of my research.

— Prof. Fabrice Boyom, University of Yaoundé I

Value Driver 4:
Expanding Global Recognition of Members' Accomplishments

BVGH and WIPO share **WIPO Re:Search accomplishments** with **global audiences** to increase Member visibility, engage prospective collaborators, and open doors to new opportunities.

Global Audiences: Leaders and Decision-Makers on Six Continents



Member Accomplishments

WIPO Re:Search is

- Catalyzing intellectual property sharing and research partnerships to accelerate drug, diagnostic, and vaccine development for neglected infectious diseases
- Driving progress toward the UN Sustainable Development Goals (SDGs)
- Bolstering the capacity of low- and middle-income countries to conduct healthcare research and development (R&D)
- Validating the importance of intellectual property in driving global health innovation

> ***WIPO Re:Search's successes in advancing research and development for the world's neediest populations demonstrate that intellectual property facilitates, rather than hinders, innovation. BVGH, as an independent non-profit, and WIPO, as a prominent UN agency, are powerful and credible voices in the global dialogue on intellectual property policy.***
>
> **— Sharon Reiche, Senior Corporate Counsel, Intellectual Property Policy, Pfizer**

BVGH and WIPO Communications Channels

BVGH and WIPO communications are **amplified** by Members and external stakeholders

International Presentations

IEEE Global Humanitarian Technology Conference
Seattle, USA

European Congress on Tropical Medicine and International Health
Liverpool, UK

ISNTD d³ Meeting
London, UK

UN High-Level Panel on Access to Medicines
London, UK
Panel solicited recommendations from BVGH

BIO International Convention
San Francisco & San Diego, USA
16,000+ global business, government, and academic leaders in attendance

Global Innovation Policy Center
Washington, DC, USA

LES Global Technology Impact Forum
San Diego, USA

TTS Latin America
Medellin, Colombia

WHO, WIPO, WTO Joint Technical Symposia
Geneva, Switzerland
Meetings of government, UN, and NGO leaders to discuss key topics at the intersection of public health, intellectual property, and trade

World Health Assembly (side events)
Geneva, Switzerland
Annual meetings of WHO and Member State leaders to define health policies and action plans

JPMA
Tokyo, Japan

WIPO General Assembly (side event)
Geneva, Switzerland
Collaborators showcased WIPO Re:Search intellectual property-sharing activities to government, UN, and NGO leaders

GHIT Fund
Tokyo, Japan
Leading global health R&D investor (US $170M to date)

EDCTP Forum
Lusaka, Zambia
EDCTP has funded > US $280M in neglected infectious disease R&D to date

Malaria World Congress
Melbourne, Australia
WIPO Re:Search Fellowship Program outcomes presented to researchers, companies, and funders

Publications

Peer-Reviewed Papers

WIPO Re:Search: A Platform for Product-Centered Cross-Sector Partnerships for the Elimination of Schistosomiasis (*Tropical Medicine and Infectious Disease;* reprinted in *Prospects for Schistosomiasis Elimination*)

WIPO Re:Search: Catalyzing Public-Private Partnerships to Accelerate Tropical Disease Drug Discovery and Development (*Tropical Medicine and Infectious Disease*)

Technical Papers

Antimicrobial Resistance and Multidrug Resistance: Overview of Current Approaches, Consortia, and Intellectual Property Issues (WIPO *Global Challenges in Focus* series)

Creating, Managing, and Advancing Collaborations: The Road to Successful Partnerships (*The Cambridge Handbook of Public-Private Partnerships, Intellectual Property Governance, and Sustainable Development*)

Fostering Innovative Product Development for Neglected Tropical Diseases through Partnerships (*Pharmaceutical Patent Analyst*)

How to Accelerate Pharmaceutical R&D: A New Framework for Sharing Intellectual Property with Global Health Researchers (Co-authored with the Access to Medicine Foundation; white paper)

Industry Initiatives to Drive Medical Product Development and Access (Contributions to the UN High-Level Panel on Access to Medicines)

Sharing Innovation and Building Capacity to Fight Neglected Tropical Diseases: A Selection of WIPO Re:Search Fellowship Stories (WIPO *Global Challenges in Focus* series)

Vaccines: Accelerating Innovation and Access (WIPO *Global Challenges in Focus* series)

WHO, WIPO, WTO Joint Technical Symposium on Antimicrobial Resistance: How to Foster Innovation, Access, and Appropriate Use of Antibiotics? (WIPO *Global Challenges in Focus* series)

WHO, WIPO, WTO Joint Technical Symposium on SDGs: Innovative Technologies to Promote Healthy Lives and Wellbeing (WIPO *Global Challenges in Focus* series)

WIPO Re:Search: Advancing Science for Neglected Tropical Diseases, Malaria, and Tuberculosis (WIPO *Global Challenges in Focus* series)

WIPO Re:Search Strategic Plan, 2017-2021

Features

A New Framework for Evaluating – and Encouraging – Industry's Intellectual Property-Sharing Activities for Global Health (*BIOtech Now*)

Behind the Scenes with WIPO Re:Search (*WIPO Wire*)

Changing Global Disease Patterns and the Need for Medical Innovation (*WIPO Magazine*)

Drug Development for Neglected Infectious Diseases (Interview with RxNet)

The Impact of Innovation: WIPO and the SDGs (WIPO interactive web story)

WIPO and the SDGs: Innovation Driving Human Progress (WIPO)

WIPO Global Challenges Division Bolsters Innovation in Global Health, Climate Change, and Food Security (Interview with *INTA Bulletin*, Voice of the International Trademark Association)

WIPO Re:Search – 150 Collaborations and Counting in the Fight Against Neglected Tropical Diseases, Malaria, and Tuberculosis (WIPO)

WIPO Re:Search Supports the Battle Against Malaria (*WIPO Magazine*)

Press Releases

BVGH Calls for More Collaboration between Industry and Governments to Increase Access to Medicines: UN High-Level Panel on Access to Medicines Solicits Recommendations from BVGH

BVGH Responds to UN High-Level Panel on Access to Medicines to Encourage More Partnership and Cooperation

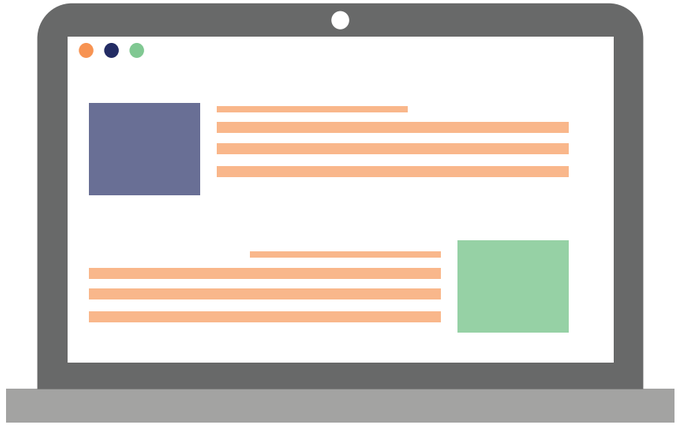
Reports and Newsletters

BVGH Partnership Hub Annual and Mid-Year Reports

BVGH Partnership Hub Snapshot Monthly Newsletters

Social Media Promotion

BVGH and WIPO Websites



> ***Eisai is proud of our engagement in WIPO Re:Search, including drug discovery collaborations with outstanding academic researchers who have been highlighted in publications and presentations by the Consortium leadership. We are honored to be a founding company Member and to share our commitment to improving patients' quality of life, particularly in low- and middle-income countries, through creation and delivery of innovative medicines.***
>
> **— Dr. Katsura Hata, Senior Director, Global Health Research Section, hhc Data Creation Center, Eisai Co., Ltd.**

People are Talking about WIPO Re:Search

Access to Medicine Foundation

BIO

Devex

Genetic Engineering & Biotechnology News

IFPMA

Intellectual Property Watch

International Trademark Association

WIPO Re:Search Members: Websites, social media, presentations, peer-reviewed papers

WIPO | Re:Search

Sharing Innovation
in the Fight Against
Neglected Tropical Diseases

Developed in cooperation with our funding Members:

Eisai

gsk

Johnson & Johnson

Merck KGaA*
Darmstadt, Germany

MSD** INVENTING FOR LIFE

NOVARTIS

Pfizer

Takeda

*Known as EMD in the USA and Canada | **MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA

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