WIPO Re:Search
Advancing Product Development for Neglected Infectious Diseases through Global Public-Private Partnerships
Over one billion people currently suffer from neglected tropical diseases (NTDs), malaria, and tuberculosis (TB). Because these diseases disproportionately affect the poor in low- and middle-income countries, there has historically—and tragically—been a lack of investment in much needed Research and Development (R&D).

In 2011, BIO Ventures for Global Health (BVGH), an industry-engaging non-profit organization, and the World Intellectual Property Organization (WIPO), a specialized agency of the United Nations, joined forces to create a market-based model to foster investments in drug, vaccine, and diagnostic R&D for these disease categories.

We launched the WIPO Re:Search Consortium to unite public and private market forces around an organizing framework that enables the sharing of intellectual property across sectors and geographies, thereby advancing science and scientific networks to address NTDs, malaria, and TB. To date, WIPO Re:Search has catalyzed over 150 R&D collaborations and managed capacity-building fellowships for scientists across sub-Saharan Africa and other low- and middle-income regions. This publication highlights seven exciting collaborations that are advancing solutions to some of the world’s most pernicious diseases.

The foundational success and market sustainability of WIPO Re:Search have been made possible by a membership model whereby companies contribute funding annually. This innovative, public-private partnership demonstrates that coupling industry-driven commitments with international scientific expertise efficiently accelerates R&D. Scientists working on critical solutions gain access to industry assets and expertise. Companies, in turn, gain insights into new applications of their existing assets, knowledge about rapidly expanding new markets, and goodwill—both internal and external to the company.

We call on new partners to join WIPO Re:Search to help address the significant unmet needs in the prevention, diagnosis, and treatment of these devastating diseases. Your commitment will support the human ingenuity needed to transform the lives of people and communities throughout the world.

Sincerely,

Jennifer Dent
President & CEO
BIO Ventures for Global Health

Francis Gurry
Director General
World Intellectual Property Organization
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*MSD is a trademark of Merck & Co., Inc., Kenilworth, NJ, USA
**WIPO Re:Search**

**Overview**

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 that unite the:

- 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

**Neglected Infectious Diseases Covered by WIPO Re:Search**

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* Clonorchiasis, fascioliasis, opistorchiasis, and paragonimiasis

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

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.
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.

BVGH’s Unique Partnering Approach
Optimizes Collaborative R&D for New Products

BVGH proactively coordinates cross-sector collaborations in alignment with WIPO Re:Search Member priorities. By providing Members with end-to-end alliance management support, BVGH advances and de-risks product development to help ensure successful partnership outcomes.

Membership

141 Organizations
133 Academics, Non-Profit, Government Institutions
41 Countries
8 Companies
6 Continents

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Since 2011, BVGH has catalyzed 155 innovative WIPO Re:Search R&D collaborations. Of those, 10 ongoing collaborations are advancing critical solutions for neglected infectious diseases along the product development pathway. The pathway for drug products is depicted below; the pathways for diagnostics and vaccines are similar.

**Screening:** Testing of compounds for desired activity (e.g., inhibition of a specific drug target) in laboratory assays.

**Hit:** A compound that exhibits the desired activity in a screening assay.

**Hit-to-Lead Optimization:** Chemical modification of hit compounds to improve their potency, selectivity, and pharmacokinetics (PK; including absorption, distribution, metabolism, excretion, and toxicity), as well as in vitro and in vivo validation studies to identify a small number of compounds (leads) to take forward to preclinical development.

**Preclinical:** Critical in vitro and in vivo (animal) studies of lead compound toxicity, efficacy, dosing, and PK, conducted to demonstrate to regulatory bodies (such as the US Food and Drug Administration [FDA]) that the compound is ready to proceed to clinical testing.

**Clinical:** Testing of drug candidates in human volunteers to determine safety, tolerability, dosing, and efficacy prior to regulatory approval. Sometimes classified as Phases 0 through III.

**Regulatory Approval:** Determination by a government authority (e.g., US FDA) that a drug candidate has met certain standards (defined by each authority) for therapeutic use and may be sold within the relevant jurisdiction.

The seven promising drug development collaborations featured in this publication have achieved key R&D milestones and have been advanced and de-risked through WIPO Re:Search.
**The Disease**

In 2017, an estimated 219 million cases of malaria occurred worldwide. Fifteen countries in sub-Saharan Africa and India bear almost 80% of the global malaria burden.

**The Challenge**

The World Health Organization sounded an alarm in 2018, noting that progress against malaria has stalled after years of unprecedented successes. Resistance to current medicines is a major threat to malaria control.

**The Solution**

Change the narrative by developing new drugs with novel modes of action that bypass resistance mechanisms.

Target an aspartyl protease enzyme required for malaria parasite replication.

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

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**MSD**

Interested in repurposing its aspartyl protease inhibitor libraries for antimalarial drug discovery, MSD asked BVGH to help identify the best partners for the job.

**BVGH**

Encouraged MSD and WEHI to co-apply for two Wellcome Trust awards - totaling US $3.6 million altogether.

**MSD/WEHI**

MSD and WEHI researchers are optimizing potency and selectivity of lead compounds.

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**Basic Research/Discovery**

**Screening**

**Hit Identification**

**Hit-to-Lead Optimization**

**Preclinical**

**Clinical**

**Regulatory Approval**

WIPRe:Search Advances Solutions Along the Product Development Pathway

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The Disease

Onchocerciasis (river blindness) is the second-leading cause of blindness due to infection globally.

Caused by worms transmitted near rivers by the bite of the blackfly.

The Current Drug Treatment

The current drug treatment kills young onchocerciasis worms but not adult worms.

Patients must take the drug for 15 years – the lifespan of adult worms.

Fatal side effects of the drug may occur in patients co-infected with Loa loa worms.

The Solution

Develop a medication with activity against onchocerciasis adult and juvenile worms but not Loa loa worms.

Prevent patients with Loa loa from experiencing the devastating side effects associated with the current treatment.

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

WPO 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
Johnson & Johnson and National Institutes of Health
Tuberculosis
Helping the human immune system win the battle against tuberculosis

The Disease
Tuberculosis is the leading infectious disease killer, taking more lives than HIV and malaria combined.

*Mycobacterium tuberculosis* has been successfully co-evolving with *Homo sapiens* almost as long as humans have walked the earth.

The Challenge
*M. tuberculosis* has become adept at surviving and reproducing inside human macrophages (immune cells), killing the cells and impairing the body’s ability to fight the disease.

A trademark feature of *M. tuberculosis* is its ability to survive nutrient-starved conditions within immune cells.

The Solution
Defeat tuberculosis by developing a drug that is active against the pathogen residing inside immune cells, but not toxic to the cells.

Johnson & Johnson and National Institutes of Health
Tuberculosis
Helping the human immune system win the battle against tuberculosis

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**JIJ**
Shared the Jump-stARter library — a chemically and functionally diverse set of 80,000 compounds.

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**NIH**
The NIH researchers screened the Jump-stARter library using a special assay designed to simulate the nutrient-starved environment that *M. tuberculosis* encounters in human immune cells.

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**NIH**
Dr. Barry and Dr. Boshoff prioritized a subset of hits with the most promising drug-like properties to pursue further.

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**BVGH**
Coordinated a collaboration between Dr. Clif Barry and Dr. Helena Boshoff at the National Institutes of Health (NIH) and Johnson & Johnson.

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**NIH**
Dr. Barry and Dr. Boshoff identified multiple hits that killed *M. tuberculosis* but not human immune cells.

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**NIH**
The NIH researchers are screening the analogs to identify more potent hits to serve as starting points for lead optimization.

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**J&J**
Supplied additional compounds with similar structures as the prioritized hits (analsogs).
Takeda Pharmaceutical Company Limited and University of British Columbia

Tuberculosis

Protecting human immune cells from the ravages of tuberculosis

The Disease

Tuberculosis is the world’s deadliest infectious disease.

In 2017, approximately 500,000 people developed tuberculosis that was resistant to rifampicin, the most effective first-line drug.

The Challenge

Current treatment regimens are lengthy and complicated, often involving multiple drugs taken on varying schedules, for up to two years.

Multidrug-resistant and extensively drug-resistant tuberculosis are on the rise.

The Solution

Develop new medications with different mechanisms of action (to outpace resistance) and shorter periods of administration.

Dr. Yossef Av-Gay, University of British Columbia

UBC

Dr. Yossef Av-Gay at the University of British Columbia (UBC) identified a target protein that helps *M. tuberculosis* survive in human macrophages (immune cells).

Takeda

Shared inhibitors of the target protein—originally developed to treat other diseases.

UBC

Dr. Av-Gay identified several hits with good activity against *M. tuberculosis* and relatively low toxicity toward human immune cells.

UBC

Dr. Av-Gay is preparing to test hit activity and toxicity in animal studies, which will help guide lead optimization efforts.

Takeda

Connected Dr. Av-Gay with Takeda Pharmaceutical Company Limited to develop inhibitors of the target protein.

UBC

Dr. Av-Gay screened Takeda’s compounds in his high-throughput screening assay.

UBC

Filed a provisional patent application covering the use of inhibitors of the target protein as tuberculosis drugs.

WIPO Re:Search Advances Solutions Along the Product Development Pathway

Basic Research/Discovery

Hit Identification

Preclinical

Hit-to-Lead Optimization

Clinical

Regulatory Approval

Screening
The Disease
Malaria is one of the world's most devastating diseases, causing over 430,000 deaths in 2017 alone. Children under five years old are the most vulnerable — in 2017, they accounted for over 60% of malaria deaths worldwide.

The Challenge
Novel drugs with different mechanisms of action are urgently needed, as current therapeutics are becoming less effective due to emerging resistance.

The Solution
Develop a new drug that attacks malaria parasites in a different way than existing therapies, in order to bypass resistance mechanisms.

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

J&J
Shared the Jump-stARter library—80,000 compounds with a wide array of targets and mechanisms of action.

WEHI
The WEHI team identified several highly active hits that killed malaria parasites through novel molecular pathways.

BVGH
Connected Prof. Alan Cowman and Dr. Brad Sleebs at Walter and Eliza Hall Institute of Medical Research (WEHI) with Johnson & Johnson.

WEHI
The WEHI researchers screened the Jump-stARter library.

J&J/WEHI
WEHI and Johnson & Johnson scientists are chemically modifying the hits to improve their potency and drug-like properties.

Researchers will validate the optimized highly active hits in animal models to inform selection of lead compounds for preclinical development.

Johnson & Johnson and Walter and Eliza Hall Institute of Medical Research

Malaria
Developing an antimalarial drug with a novel mode of action to circumvent growing resistance

WIPO Re:Search Advances Solutions Along the Product Development Pathway
**The Disease**

Schistosomiasis is an acute and chronic water-borne parasitic-worm disease, with 100 million people treated annually.

Infection occurs when larvae, having been released by freshwater snails, breach the skin during contact with infested water.

**The Challenge**

Praziquantel is the only available treatment.

Reliance on a single drug increases the risk that resistance will develop.

**The Solution**

Develop a new drug with a novel mechanism of action.

Repurpose medicines used for other conditions as starting points, to bypass the many time-consuming and risky stages of early drug discovery.

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**WIPO Re:Search Advances Solutions Along the Product Development Pathway**

**Basic Research/Discovery**

**Hit Identification**

**Hit-to-Lead Optimization**

**Screening**

**Preclinical**

**Clinical**

**Regulatory Approval**

**UC San Diego**

Dr. Conor Caffrey at UC San Diego discovered that statins kill schistosome worms and prevent them from producing eggs by inhibiting an enzyme called SmHMGR.

**MSD**

Shared selected statin compounds with specified chemical characteristics.

**UC San Diego**

Dr. Caffrey identified hits with promising activity against schistosome worms.

**SCRI/SSGCID**

Encountered issues producing SmHMGR protein. Identified a specialized technology called codon-optimized gene constructs as a potential solution.

**BVGH**

Presented Dr. Caffrey’s project to MSD, a leading statin manufacturer.

**UC San Diego**

Dr. Caffrey screened MSD’s statin compounds.

**BVGH**

Connected Dr. Caffrey with crystallization experts at SCRI and SSGCID to pursue structure-based drug design.

**MSD**

Provided codon-optimized gene constructs and technical input on protein expression.

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Johnson & Johnson and Washington University in St. Louis

Tuberculosis: Targeting an unexploited vulnerability in M. tuberculosis to combat drug-resistant infections

The Disease

In 2018, tuberculosis caused an estimated 1.5 million deaths around the world.

Globally, approximately 500,000 new cases of multidrug-resistant and extensively drug-resistant tuberculosis were reported in 2018.

The Challenge

Multidrug resistance is on the rise. Only one in three people with drug-resistant tuberculosis were enrolled in treatment in 2018, with an infected person able to transmit their infection to 15 more people.

Nearly half of patients with drug-resistant tuberculosis are treated unsuccessfully with existing drugs, potentially leaving them both ill and able to transmit the disease.

The Solution

Develop medicines targeting proteins that are not found in humans (reducing the risk of serious side effects) and are not affected by current tuberculosis drugs (decreasing the likelihood that resistance has already developed).

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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

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

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WIPO Re:Search Advances Solutions Along the Product Development Pathway

- **WUSTL**
  - Dr. Christina Stallings
  - Identified a promising drug target
  - Essential for M. tuberculosis growth and virulence

- **J&J**
  - Shared the Jump-stARter library
  - Collection of 80,000 small molecules with diverse structures and functions

- **WUSTL**
  - Dr. Stallings
  - Identified several hits that inhibited the target enzyme

- **J&J**
  - Resupplied hundreds of compounds with similar structure as hits
  - Johnson & Johnson will chemically modify the initial hits to produce lead compounds

- **WUSTL**
  - Dr. Stallings
  - Identified several hits
  - Tested inhibitory activity with additional compounds from J&J

- **BVGH**
  - Connected Dr. Stallings with Johnson & Johnson

- **WUSTL**
  - Dr. Stallings
  - Screened the Jump-stARter library in a high-throughput assay

- **J&J/WUSTL**
  - Guided by additional screens
  - Johnson & Johnson will chemically modify the initial hits to produce lead compounds for preclinical development
Developed in cooperation with our funding Members:

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