Renewing our commitment to neglected tropical disease and malaria elimination

Thierry Diagana and Jonathan Spector from the Novartis Institute for Tropical Diseases (NITD) discuss learnings about their work in Neglected Tropical Diseases (NTDs) and share insights into the factors, which could lead to a resurgence of these diseases.

By Christine Elleboode-Zwaans | Jun 23, 2022

Novartis endorses the Kigali Declaration on Neglected Tropical Diseases (NTDs) #KigaliSummit #100PercentCommitted

On June 23, Novartis endorsed the Kigali Declaration on Neglected Tropical Diseases (NTDs), pledging USD 250 million to advance R&D of new treatments against NTDs and malaria over five years. On the occasion, we spoke to Thierry Diagana, who heads the NITD, and Jonathan Spector, who oversees the NITD's global heath and access strategy, to learn about these diseases that affect 1.7 billion people every year, or more than one in five people alive.

Which NTDs is the Novartis Institute for Tropical Diseases (NITD) focusing on?

Thierry: NTDs are typically distributed across the tropical belt, and they cause devastating health, social and economic consequences among the poorest of the poor in low- and middle-income countries (LMICs). At the NITD, we focus on NTDs caused by kinetoplastid pathogens, such as Chagas disease and visceral leishmaniasis, and viral pathogens such as dengue. More recently, we began work on cryptosporidiosis, which is caused by a protozoan parasite and not classically considered as an NTD – although it is a major cause of diarrhea in young children.

Thierry Diagana, Head of the Novartis Institute for Tropical Diseases (NITD)

For all these diseases, we have identified novel mechanisms of action and targets, and progressed molecules into clinical trials. The breadth and depth of our portfolio, with multiple agents against multiple NTDs and infectious diseases, is unprecedented in the healthcare industry.

What learnings can you draw from your work on NTDs?

Thierry: Maybe the biggest learning is that moving the NTD science forward requires contributions from the entire community. Those pathogens are complex and their biology unique – we therefore need to partner with academia to identify novel mechanisms of action and drug targets, and to develop animal models to test the molecules. Organizations like Wellcome or the Bill & Melinda Gates Foundation have made significant investments in the field. Yet, compared to the global budgets allocated to malaria, HIV/AIDS and TB – NTDs remain neglected.

Jonathan: Two additional learnings worth mentioning. First, over the past 20 years, the NITD has refined its drug discovery approach to NTDs, notably through phenotypic screening. We realized we can apply learnings from one program to another, for instance our work in malaria is relevant to Chagas disease and leishmaniasis. Second, we learned that one drug can treat multiple diseases. As an example, the proteasome inhibitor we discovered for visceral leishmaniasis with the support of Wellcome also showed clinical benefits in Chagas disease as both conditions are caused by kinetoplastid parasites.

Jonathan Spector, Head of Global Health Strategy and Access, Novartis Institute for Tropical Diseases (NITD)

How will the new financial commitment be spent over the next 5 years for NTDs?

Thierry: This investment will first support the evaluation of our novel agents in patient studies and hopefully bring them to proof of concept. Second, we will continue to work with the scientific community to evaluate new targets. It's a long and arduous journey from target to clinical candidate, it takes investment across a vast field of expertise and skills in medicine, chemistry, biology, pharmacology, and safety. Yet it doesn't stop there. Once we achieve proof of concept, we need to work with partners to further develop the compounds – and this is still pretty much uncharted territory for NTDs.

Why is it important for organizations like Novartis to continue to invest in NTDs?

Jonathan: Academic groups, publicly funded research labs, small biotechs typically work on very specific, yet crucial parts of drug R&D – for instance to further reveal the biology and understand potential targets. Only a handful of highly powered laboratories focus on NTDs and have the capability to span across the entire R&D process. If groups like the NITD wouldn't work on these diseases, this would dramatically decrease the odds of finding cures for NTDs.

Thierry: I would add that NTDs have been holding LMICs in a vicious cycle of disease and poverty for centuries, and we need new interventions that put pressure on those pathogens to break this vicious cycle. Therapeutics alone won't be enough, we need the full arsenal of vaccines and medicines, vector control, and other public health measures to combat NTDs effectively.

Could we see a resurgence of NTDs in the near future?

Thierry: The short answer is yes! Two threats in particular are hanging over our heads like a Damocles sword. One is drug resistance, which is particularly worrying, especially when there is only one agent available against a certain pathogen. If we lose it, we're left with nothing. The second threat is climate change, which is changing the distribution of pathogens and the vectors transmitting those pathogens. With that comes an increased risk of disease transmission.

Jonathan: Dengue is a poster child for this concept of changing vector habitats, and we know from modeling exercises and real-world data that climate change causes this. Coupled with human densification in areas where people overlap with the vectors and the pathogens that cause NTDs, this could be a ticking time bomb. We can also anticipate cryptosporidiosis outbreaks because cryptosporidium, the pathogen causing the disease, is transmitted through absorption of contaminated water, and global warming will likely result in increased risk of floods in areas where water sanitation is poor.

How do you include access considerations in drug discovery for NTDs?

Jonathan: We aspire to think about access at the earliest stages of discovery and to anticipate access barriers along the way. We look at the target product profile and favor oral medicines with low pill-burden and short drug treatment regimens. Basically, we want the medicine to be practical for use in the populations it is intended for. There are also other considerations that teams across Novartis assess. For example, medicine adoption at the patient, provider, community, or health system level. Do medicines against a particular disease already exist? If they do, could new medicines be included in existing treatment guidelines? Or if no guideline exists, are health workers even aware they're dealing with the disease? These situations require different approaches to education, training, and stakeholder mobilization.

Thierry: At the discovery level, we already have intense conversations on minimizing the cost of goods, and we are looking early on at simplifying the synthesis of drug candidates – as molecules that are too complex to synthesize would dramatically increase the cost of active pharmaceutical ingredients. We also assess a compound's physical chemical properties to ensure it is stable under humid and hot conditions and doesn't require refrigeration or special formulations that would add to its cost. Also, from a safety perspective, we ensure the drugs we develop don't have special monitoring requirements that would add a huge burden on national disease control programs. Our sole focus is on patients, who they are, where they live, and we try to remove as many barriers as possible to access.

Can you tell us about the work of NITD on malaria specifically?

Thierry: Our ambition is to have a malaria pipeline that's so rich that we eventually work ourselves out of a job! Driving a broad portfolio of new agents with complementary mechanisms of actions is what will enable disease elimination. And we're making great progress. Currently, we have three malaria clinical drug candidates, and our fourth compound against uncomplicated malaria should move into clinical trials by end of year, early next. Importantly, each of these candidates has distinct and novel mechanisms of action. In addition, our inhibitor against the clinically validated drug target PI4K is also nearing candidate stage, and a second agent for severe malaria is further behind. We are also screening for compounds for a radical cure against *Vivax* malaria.

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