Gates Foundation Plots A Fresh Metric For Market Access: Lives Saved

In Vivo visits Gates Medical Research Institute CEO Dr. Penny Heaton to review its first pipeline of drugs and vaccines to attack four of the world’s biggest killers: TB, malaria, enteric diseases and other conditions affecting maternal, newborn and child health.

True to form, the Foundation has invested heavily in the money (more than $200 million annually over the next 15 years) and the talent (recruiting top experts in clinical operations and project management, as well as in new fields like quantitative science modeling and AI) to achieve this vision of moving new treatments seamlessly from bench to bedside. Leading the effort is Dr. Penny Heaton, a 55-year-old physician with one of the more distinctive backgrounds in medicine and public health, as an infectious disease expert in academia and the US government and more recently as a vaccine developer at Merck & Co., Novartis AG and the start-up biotech Novavax Inc. As the CEO of Gates MRI, Heaton is also intimately familiar with the working culture of the Seattle-based Foundation, where she helped develop the group’s current strategy targeting major diseases with a disproportionate impact on vulnerable populations, especially women, infants and young children.

Heaton thus brings to her new assignment a diverse set of career experiences touching virtually every aspect of the health care landscape. It began with an early introduction to tuberculosis – the world’s most deadly infectious disease – when her father, a minister in rural Kentucky, contracted it two years before Heaton was born. “I spent my first years in a household under siege, as my father’s eventual recovery left him in constant fear the bacillus might return and infect us all.”

The one positive was it drew me into the mystery of how something so small could wreak such havoc on human civilization. Even before high school, I knew I wanted to devote my life to the study and treatment of infectious diseases.”

Pathogens Pointed The Way

Indeed, Heaton’s fascination with bugs led her to the University of Louisville Medical School, where she received an MD in pediatric medicine, followed by an additional research fellowship in infectious diseases funded by a local charity. More important, it showed me that progress against endemic infectious diseases could benefit from the active involvement of stakeholders outside government, such as the private sector. At the CDC, we knew that simple, remedial measures like boiling water and hand washing could lower the incidence of disease. But I wanted so much more, such as the ability to introduce vaccines and other innovative technologies to prevent these conditions – a goal that publicly-funded efforts could never achieve on their own.”

Industry’s Calling Card: The Rotavirus Vaccine

It may have been serendipitous but recruiters for big pharmaceutical firms began contacting Heaton as the science advanced on new vaccines for major killers, including for her own specialty in pediatric diarrheal disease. Merck &

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MARKET ACCESS: Innovation

BY WILLIAM LOONEY

As a drug developer, Gates Medical Research Institute will apply to the FDA for an IND just like any biotech. Last month, it launched its first clinical trial, in South Africa, for a booster vaccine against TB; it is also exploring novel options like applying monoclonal antibodies as a seasonal treatment for malaria when it is most virulent.

CEO Penny Heaton hopes to have 20 product candidates in the pipeline by 2025, with half of these in trials.

What it means to be a drug company has begun to change in recent years, as societal expectations of performance extend beyond investor returns and NGOs and governments claim medicines as a universal public good, accessible to all. Adjacent industries are entering the drugs business while non-commercial actors like patient advocates and philanthropists fund their own R&D programs for medicines to address conditions with high unmet need. Perhaps the most prominent of these emerging players is the Bill and Melinda Gates Foundation, which last year established its own non-profit biotechnology enterprise, the Gates Medical Research Institute (MRI), to develop drugs and vaccines targeting major neglected diseases of poverty like tuberculosis (TB) and malaria.

The Gates MRI initiative is representative of a strategic shift among major private health donors from passive funding to hands-on doing. Interest is high in using the integrative, results-oriented practices of translational medicine to better manage disease etiology in vulnerable populations and increase the speed in which new treatments reach patients on the ground.

What is unique about the Gates MRI is its focus on learnings from the private-sector – including big pharma and biotechs – in moving drugs and vaccines from proof of principle to clinical proof of concept, followed by clinical trials, and ending with registration and uptake in the marketplace. Every Gates MRI project is evaluated on a simple, two-word metric of performance: lives saved. The charge looks simple – deceptively so. The fact is Gates MRI was launched out of the awareness that it is not enough to develop a new life-saving technology; you also have to create the expertise to execute around it, with the organization, logistics, information, policy and partnering skills to ensure that the drug or vaccine can be delivered safely to the market. And, most important, be widely used.

So what? The MRI is testing an unusual proposition: can generous, hassle-free financing be combined with a business mindset to treat life-threatening conditions whose persistence is historically associated with market failure? Watch and wait – its an early portent for global market access in the next decade.

By providing a simple but powerful metric of performance, the Foundation can—and will—take a quantum leap forward in public health in the years ahead. It is a profound and welcome initiative, and the MRI’s mission is one that could define the domain of the 21st century in public health and translational medicine. It is an honor to be a part of a project that challenges so many to do things they didn’t think were possible. The Gates MRI is one of the most promising initiatives to emerge in the field of global health in recent years. I can’t wait to see what they will achieve in the years ahead.”

Pathogens Pointed The Way

Indeed, Heaton’s fascination with bugs led her to the University of Louisville Medical School, where she received an MD in pediatric medicine, followed by an additional research fellowship in infectious diseases funded by a local charity. But, coming as it did just as large-scale health maintenance organizations were depersonalizing the physician-patient relationship, Heaton began to question whether a license to practice medicine was enough to make a difference in people’s lives. Looking for opportunities...
Tox Box - a product that works for patients. Combined with my earlier roles in the medical device and government service, it put me in the best possible position to lead this new hybrid institution inspired by Bill Gates’s vision combining public service and private know-how to generate great medicines for the greatest unmet medical needs.”

Heaton’s attention red to the Gates Foundation after she was approached in 2013 by Dr. Trevor Mundel, President of the Foundation’s Global Health Division, to discuss a specific concept and then adding a specific product development component to the group’s baseline strategies to fight disease.

Shortly after, Heaton joined the Foundation with the charge to apply her experience in industry to lay out an approach to vaccine development in resource-constrained settings. “A lot of what I did was introduce the processes used in private industry, starting with that living document called the target product profile, laying out all the upfront work necessary to conduct the clinical trials and everything thereafter, especially the regulatory protocols and manufacturing/distribution logistics that are critical to vaccines but weren’t really part of the Foundation skill set at the time.”

Opportunity Knocks: Origins Of Gates MRI Thus, when Bill Gates decided in 2017 to create a new unit of the Foundation to develop new drugs and vaccines – just like big pharma, but with a broader access footprint – Heaton was the logical choice to run it. It would work in the manner of a nimble biotech start-up, focused on products to prevent, treat, and cure the diseases of the poor. It would open a new chapter in the Foundation’s evolution from a grant-making philanthropy to a hands-on enterprise guided by a business plan relevant to conditions on the ground.

The Gates MRI was launched in January 2018 with a $70m grant from the Foundation, an office in the Cambridge MA biotech hub, and Heaton as CEO. Backed by a staff now totaling 65 professionals from diverse backgrounds in science, clinical practice and commercial operations, the group reports to a board chaired by the Foundation’s global health lead Mundel, and which also includes the Foundation CEO, Dr. Sue Desmond-Hellmann, herself a drug industry veteran as the physician oncologist behind Genentech’s breakthrough drug for breast cancer, Herceptin.

In addition to the Cambridge office, there is a satellite office in Seattle WA, at the University of Washington campus.

Running a non-profit that emulates the mindset of a for-profit enterprise has been a liberating experience for Heaton. “Six weeks in, I felt like a bird let out of the cage, fighting infectious disease while reaping the psychic benefits of giving something back to a world consumed by want. Moreover, I no longer had to worry about finding the financial resources to justify a business plan and the marketing logistics around it, activi-
ties that in the private-sector took three quarters of my time. We had the funding to do what we needed to do.”

From the start, Gates MRI has observed the simple work rule: the Foundation strategy to projects showing promise the greatest threat to global health. These are:

- tuberculosis;
- malaria;
- enteric and diarrheal disease, particularly in children under age five; and
- other conditions that lead to adverse maternal, newborn and child health outcomes (MNH).

Global health statistics bear this out. The TB bacillus is present in one quarter of the world’s population, with 10 million new cases a year and 1.3 million deaths reported by the World Health Organization in 2018. It is a leading co-morbidity factor in deaths from HIV, with more than 250,000 deaths linked to TB in 2018. Malaria accounts for nearly 500,000 deaths annually, out of a case burden now totaling more than 200 million in 87 countries, mostly in Africa. The third pri-
ter, enteric diseases like shigella, one of the leading causes of diarrhea in infants and young children, kills more than 2,000 children under age five die every day. Added to this are other diseases affect-
ing nursing mothers and young children. One, respiratory syncytial virus (RSV) is the current focus of Gates MRI activities for this vulnerable public health cohort. The big takeaway is all four of these disease areas are preventable – and the technology and expertise already exist to make their eradication feasible, with an equally big payoff in terms of fighting poverty and advancing the Foundation’s operative premise that “all lives have equal value.”

Shortening The Time From Idea To Impact

Getting organization and process in line with this objective dominated the Gates MRI’s first year. “It had to build a group of people who can make a difference. It’s difficult to foster the kinds of ideas from many quarters into a few specific solutions, aiming to apply the Foundation strategic direction and showing a measurable outcome,” Heaton tells In Vivo. “In practical terms, my charge is to invoke the principles of translational medicine, marrying the efficiency of new drugs and vaccines with partners that we either contract with ourselves or leverage through the Foundation, progressing to clinical proof of concept and then work-
ing with others to pursue market access for the product, including manufacturing and distribution at scale.”

The Gates MRI does not expect to do all the heavy lifting, all the time; in many cases, a partner will take the lead in con-
ducting a clinical trial or other milestones required to move the asset into the mar-
et. There are plans to work with CROs on the conduct of clinical trials. In fact, one of Heaton’s priorities is to find local companies in low-income countries that can manage commercialization, which has the added advantage of giving them the know-how to stimulate the growth of a strong market for life sciences investment.

The vehicle to make all this happen...
**Market Access: Innovation**

**砜 Gates Mri CEO Penny Heaton Speaks on Progress in Global Health**

“When I look back and think about what things were like in 2000, the big multibilateral donor institutions we took for granted today did not exist. There was no Gavi for vaccines; no Global Fund for AIDS, TB and malaria; no PEPFAR to prevent the spread of HIV in Africa; the Bill and Melinda Gates Foundation was in its infancy. This concerted institutional response has cut child mortality from infectious disease by more than half, from 10 million deaths annually to less than six million. Deaths from malaria have also been cut by half, with 80% of sub-Saharan Africans diagnosed with HIV are now on life-saving anti-retroviral drugs.”

**...And the Challenges that Remain**

“Too many people—especially women, infants and children—continue to die of diseases that are largely preventable. I worry about maintaining our progress in improving health status, for two reasons. One is that, from a technological and logistical perspective, what we have left to do is really hard. Having clocked so many ‘wins,’ the complexities involved in delivering health solutions on the ground—that ‘last mile’ to the patient—are daunting. The second is public health interventions still need more support from private-sector players like big pharma and biotech. They have the product development know-how to help us succeed. But, as investor pressure on the whole line bottom, keeping them involved has become tougher than ever.”

**Why She’s an Optimist at Heart**

“We are at a special time in history, with new science that has enormous potential in saving and extending lives. The tools are within our grasp to confront the pathogenic and immunologic roots of infectious diseases that have plagued humankind since the dawn of civilization. Insights derived from the oncology and rare disease space are capable of being translated into interventions with even broader impact on the neglected diseases of poverty that kill millions—if we get the access and affordability issues right.”

**With a Clear Vision on the Future**

“I can envision a time when the potential of every woman, man and child is unleashed by good evidence and unbiased information. Can we use the cloud and the cell phone to overcome the absence of a reliable data collection and retrieval infrastructure in low income communities? I think we can—and it’s a logical step from there to introduce, without the barriers imposed by legacy systems, the latest real world evidence (RWE) technologies to inform our clinical trials and support development of a new generation of vaccines to improve health standards in communities where the unmet medical need is greatest.”

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The Potential Of Monoclonal Antibodies In Malaria
Gates MRI Accelerating an active learning program based on the clinical history of RTS,S. According to Heaton, “We’ve already learned a lot from RTS,S about the immune response to malaria. What’s really exciting is now we have monoclonal antibodies – a treatment platform first identified in a rational approach to an effective and powerful bridge in treatment until a more durable vaccine with longer efficacy in patients can be brought forward. So it’s not long-acting but less efficacious vaccine to induce that antibody response, we could focus on a more important seasonal approach, giving the antibody forms before the rainy season when carrier mosquito proliferate and prevent malaria until the dry season when the threat of infection diminishes. Right now, we know the antibody approach works in animal tests, so the goal is to do human studies, including children, the most vulnerable victims of the disease.”

The plan calls for toxicology studies to begin on a selected candidate in late 2020, followed by a phase Ia study in third quarter 2021 and a Phase Ib to commence in late 2022, continuing to the end of 2023. At that point, a decision will be made to proceed with human trials leading to full development and eventual commercialization. Another payoff from this effort could be reducing the cost of manufacturing monoclonals so they become more affordable to low income countries. On its own, the Foundation has been considering this for some time.

A Wider Template For TB Vaccines
The pipeline is also primed for new opportunities – both drugs and vaccines – to help fight TB. The most important is last month’s start of Gates MRI’s first sponsored clinical trial on the Bacillus Calmette-Guérin (BCG) vaccine, which was first tested in humans in 1921 and has long been vetted as a potential prophylactic against TB when given to infants. The trial, funded by the Foundation, will see if boosting BCG when those infants become adolescents and young adults can confer lifetime immunity against TB. The trial will be conducted in South Africa. Heaton said, “This trial is big for us, as it provides the opportunity to see if the 40-year-old BCG MRI partnering model is as proficient as industry or government in driving so many moving parts to a successful, timeline-uncertain two years worth of work. Despite that, we are excited and we are grateful that this is going to be the biggest demographic in employ. And we are a window on emerging country markets of the future, with their enormous untapped demand for better health and wellbeing, including access to good medicines and vaccines. I wish biopharma CEOs had a better appreciation of that latent desire for a better tomorrow. It’s universal among today’s poor.”

How Heaton Measures Success
Putting all this together, how does the MRI define success? Heaton notes, “I think our normal four year planning cycle? Heaton responded immediately in stressing that here is an assignment that is going to take longer. He said, “It’s going to be the biggest demographic in employ. And we are a window on emerging country markets of the future, with their enormous untapped demand for better health and wellbeing, including access to good medicines and vaccines. I personally wish biopharma CEOs had a better appreciation of that latent desire for a better tomorrow. It’s universal among today’s poor.”

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