

RAJ MANCHANDA ON MRI'S MISSION, SCOPE, AND BIOMANUFACTURING GOALS



At the Biomanufacturing Summit organized by UMass Lowell in September 2018, Gates MRI Innovation Portfolio Leader Raj Manchanda, as part of his presentation, addressed the mission and scope of Gates MRI and the role of biomanufacturing innovation in meeting the institute's goal of expanding access to needed medicines in the developing world. Formatting changes and other minor edits have been made by IPQ for clarity and readability. The normal disclaimer that the presentation represents the views of the speaker and not necessarily that of his/her organization is not included.

The Mission of Gates MRI

I will just give you a little history of how Gates MRI came about.

Gates Foundation, which sits in Seattle, has been funding a lot of research in disease areas that are not the focus of the Western world. These include HIV, malaria, TB, enteric and diarrheal diseases. It also includes Alzheimer's, but primarily the focus was on tropical diseases. In these disease areas, the focus was on research.

How do we come up with better drugs, better animal models, and better clinical studies that can be done in the endemic areas? This was not in the US or in the Western world. And they give out around \$4 billion a year to fund these.

But what was missing was, with all this research, how do you actually make drugs that are available and ready as the next innovative drugs for these diseases in the rest of the world? So, Gates MRI was founded in January of 2018. I have been there for two weeks. The mission is to really focus on three disease areas and act as a biotech company.

So, we have a fully integrated biotech company funded by the foundation. We will have a portfolio of vaccines, drugs, and antibodies that we will develop to the proof of concept stage in the clinic, and then we will look for partners who can commercialize them.

What that means is that as part of this development of vaccines, antibodies, and small molecules, we have to keep the cost and the utilization sized so that it can be affordable in Africa and Southeast Asia. That is why we are looking for innovation from all different areas that exist. And how do we bring all that in so that we can actually come up with a vaccine, antibody, or a drug that will be applicable in these areas?

MRI's Focus and Strategies

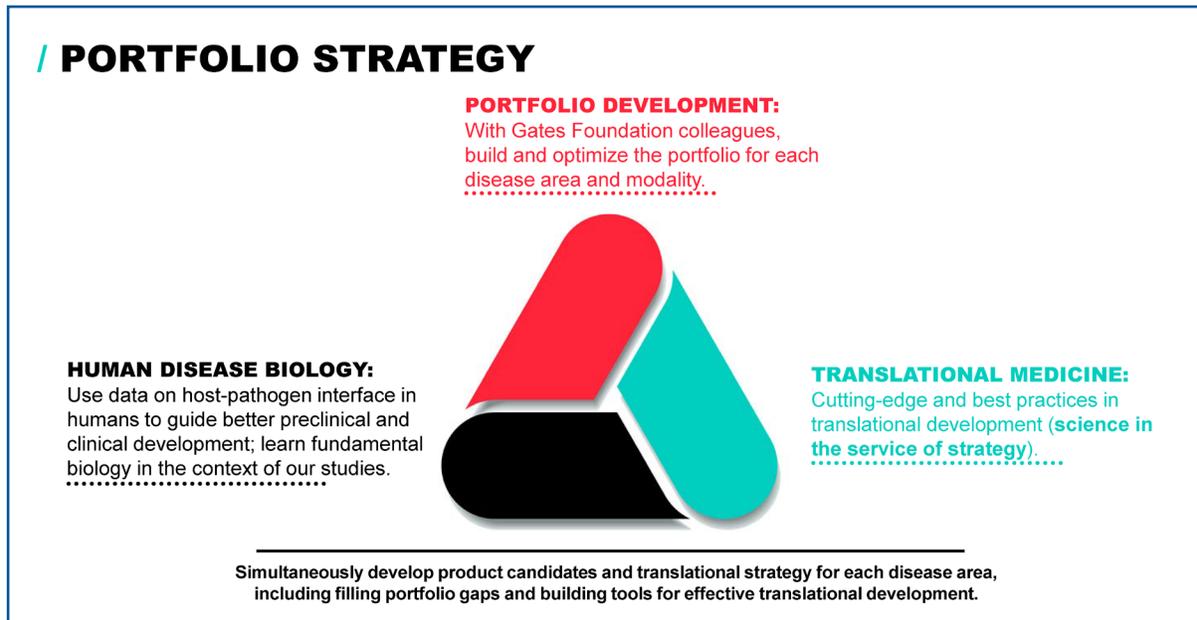
As I said, we are not limited by the modality. We will be looking at three disease areas: • small molecules • antibodies – antibody vaccines, vaccines that are, you know, wild in nature, any kind of vaccine – and then • biologics, it could be nucleic acids, could be antibodies, could be anything.

So, we are not limited by the foundation. We are limited by our own capacity and what we can take from different sources – institutes, academia, biotech companies, pharma companies that have given up on these programs – and we will take those and develop those.

Our approach, as I mentioned, is:

- To develop this **portfolio of different drugs** in these three disease areas. The foundation has a whole portfolio of drugs that they have funded across the globe. We are tapping into that portfolio right now, selecting what fits in with our mandate and then taking it through.

The portfolio includes drugs that are already in the clinic, the commercial drugs as well that we can repurpose and either increase the dosing, so it is more effective, or redo the clinical trials to look at other indications as well. So that is one source of developing the portfolio.



Then we are setting up partnerships with biotechs, big pharma, and academic institutes that have these focus areas and trying to bring those in as well.

- We are focused very heavily on **human disease biology**. To understand malaria and TB it is not really straightforward. A lot of the work that has been done is scattered all over the globe, so we are trying to bring all that data into the Gates MRI. We will be using quantitative tools to really understand the biology of these drugs and where and how to attack to get the maximum benefit for the patients.
- And then **the translational side**, as I mentioned: As a fully integrated biotech we will be doing a lot of CMC development. We will be doing a lot of pre-clinical testing, and we will be doing clinical trial design, and running these trials across the globe to really translate the research and come up with paradigms that will be suitable.

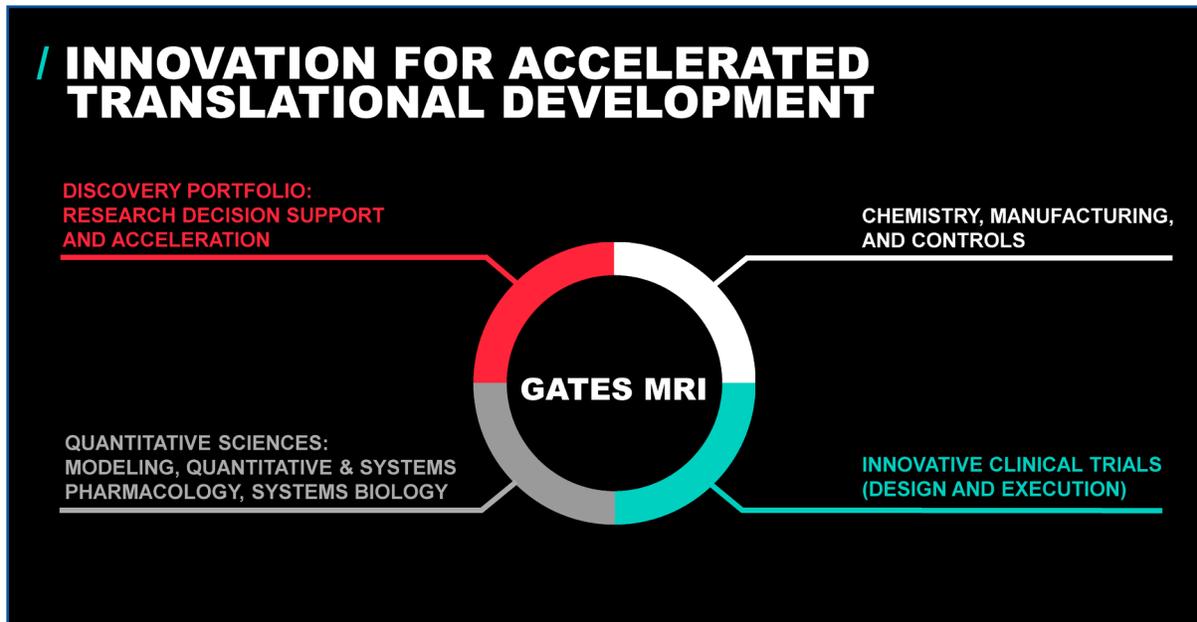
So, our sweet spot then becomes the translational development. A lot of research will come in. It will have drugs from all different sources. But where we add value is truly the red circle, where we put in a lot of tools, a lot of partnerships and collaborations to translate the research and the drugs into the clinic. **[A link to Manchanda's full slide deck is included below. See slide 25 for the graphic referenced here.]**

What all this hinges on is innovation. A lot of work has been done with vaccines, a lot of work has been done on antibodies, and I am not just talking about processing.

Looking at: • How do you design a dosing regimen? • How do you design a clinical trial that is adaptive? • How do you look at the data that you are collective from preclinical and clinical studies? • How are you analyzing the big-data analytics? • How can you then really design a study or simulate a design of the study that will actually give you the end points that you are looking for? • And if not, then how do you quickly adapt the clinical trial on the preclinical studies based on the data as you have seen?

So, the core four pillars of Gates MRI are: • preclinical models that are suitable • quantitative sciences • innovative clinical design, and then definitely • chemistry, manufacturing and controls, looking at bioprocessing or manufacturing, how do we make it affordable, how do we keep the cost of goods down, how do we look at distribution to tropical countries? Is it cold chain? Is it other things that we need to worry about?

So, all that thinking of preclinical, to CMC, to clinical will come together as a package that then can be leveraged through the foundation and then they can find either big pharma partners or some other consortium that can commercialize it.



Altering the Paradigm

It is likely that the current biomanufacturing paradigm will work outside of the developing world. But we are not sure.

Vaccines have been affordable for polio and for pneumonia and meningitis in the global health perspective. But as we are thinking of novel innovative technologies and modalities, how do we make it affordable? How do we make it scalable? And these are not small populations, as we are used to in the rest of the world for most of the diseases. We are talking about tens of millions of patients, and if we are talking about vaccines, you are going to vaccinate every newborn. And that is a huge population in itself.

What did we learn from disruption of other industries? As I have been talking about, how do we bring it together as part of the Gates MRI?

Our request to all of you is we are open. We are open for ideas, we are open for innovation. As you think about gene therapy or think about the next-gen bioprocessing, how does that apply? We are open to having that dialogue, we are open to having funding for such ideas as they fit into our platform.

And then we really want to be innovative and disruptive so that we can make it affordable and make it available for the whole world, not just the Western world.

The way we look at it is: Our only bottom line is lives saved. It is a not-for-profit. We are getting together as Gates MRI with one mission and one mission only: how quickly can we eradicate malaria? How quickly can we plateau the deaths from TB? And how quickly can we reduce the rate of mortality with enteric diseases and diarrhea?

Summary

So, in summary, in the general landscape of biopharmaceuticals, there is no singular view of the future. It is diverging, and it is diverging into many different directions. But there is the need for having platforms – platforms that can be adapted, that can be applied.

Again, for small biotech, for gene therapy, we need to get innovation for first-in-human [clinical trials] as quickly as possible and at affordable rates.

We must learn from other branches of technology like automation, big-data analytics, and how we apply that to our paradigm to really disrupt drug development and vaccine development for the developing world.

Gates MRI, again, I have said it three or four times now already: Our approach is going to be different. It is not just another biotech company. We are fully integrated. We are open to ideas. We are open to innovation. We are open to disruption. Because other than that, if we do it the same way over and over again, I do not think we would be able to succeed.

You are the experts in this field. Come talk to us, and let's make the world a better place.

LINK:

- [Machandra's full set of slides presented at the UMass Biomanufacturing Summit](#)