Company Name: Moderna
Company Ticker: MRNA US
Date: 2020-04-02
Event Description:

Market Cap: 12238.9325936
Current PX: 33.2
YTD Change($): 13.64
YTD Change(%): 69.734

Bloomberg Estimates - EPS
Current Quarter: -0.383
Current Year: -1.537
Bloomberg Estimates - Sales
Current Quarter: 19.443
Current Year: 83.06

Company Participants

- Ben Weintraub, President
- Karin Lore, Professor
- Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Other Participants

- Cinney Zhang, Analyst
- Marc Engelsgjerd, Equity Research Analyst

Presentation

Cinney Zhang, Analyst

Good morning and good afternoon. Thank you for joining our Webinar with two experts, to discuss the latest Coronavirus Vaccine Landscape. This webinar is co-hosted by Bloomberg Intelligence and inThought Research. My name is Cinney Zhang, I'm an Analyst at Bloomberg Intelligence. With me on the line today are Marc, our Senior Biotech Analyst and Ben, President of inThought Research.

Just a couple of housekeeping items before we get started. Today's webinar is being recorded. You can access a replay later by clicking on the link in your registration confirmation e-mail. Also you could ask questions by submitting them online. We'll try to address your questions with experts as we go along.

Very briefly about Bloomberg Intelligence, yeah it's the research arm of Bloomberg. We have about 300 analysts across the globe, covering over 1,900 companies. Our research is available on the Bloomberg Terminal, you could access by BI Goals. The dashboards that are dedicated for the pharma and biotech sector are BI Pharm and BI (inaudible). Lastly, I just wanted to mentioned that we'll have another webinar on COVID-19 focusing on the therapeutic, so stay tuned and look out for details.

With that I'm going to pass it to Ben, to introduce our speakers.

Ben Weintraub, President

Thank you, Cinney. I'm Ben Weintraub, President of InThought Research. InThought is a small group of subject matter experts that help pharmaceutical companies and investors understand the details of drug discovery, my PAC is in immunology, so that arms me just enough to scratch the surface of understanding what our two experts are going to speak today. We are incredibly lucky to have Karin Lore and Michael Diamond with us today to discuss vaccines for the novel Coronavirus. I'm going to give you a very brief introduction to each of them and ask them to tell us more about their research.

Karin Lore is a professor at the Karolinska Institutet in Sweden. She's been studying the immune mechanisms to vaccine responses over the last 15 years, working both at the Karolinska Institutet and at the NIH in the United States. Her work includes both preclinical and clinical work, often in collaboration with the Gates Foundation. Over the last few years, her Group has published several articles on mRNA vaccines to the influenza virus. Professor Lore, thank you very for joining us and please tell us a little bit more about your research.

Karin Lore, Professor

So my research group is -- were involved in clinical trials of new vaccines as you mentioned and also clinical trial testing co-administration of already licensed vaccines to see if you have better efficiency. We also do preclinical work in monkeys primarily right before you go into human trials. And using monkey we can address many more mechanistic questions of how vaccines work. And we use the monkey model to study mRNA vaccines in particular.

Ben Weintraub, President

Excellent. Perfect, thank you so much and thanks again for being here.

Karin Lore, Professor

Thank you.

Ben Weintraub, President

Our second figure is Michael Diamond. He is the Herbert S. Gasser Professor at the Department of Medicine Molecular Microbiology Pathology and Immunology at Washington University in St. Louis. His lab focuses on post immune response to six pathogens, the West Nile, Encephalitis, Dengue fever, Zika virus, Venezuelan equine encephalitis, hepatitis C and he's recently been publishing about mRNA vaccine against Zika virus. Dr. Diamond, thanks so much for joining.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Thank you. So my laboratory is more of a basic laboratory. I'm a viral immunologist and we study emerging RNA viruses. And we've been interested in understanding how viruses cause pathogenesis, how the immune system controls viruses, how the viruses evade immune systems and how this relates to preclinical development of vaccines of different platforms including mRNA platforms and virus based platforms and sub-unit platforms. And we've studied different viruses in terms of vaccine development whether they're flaviviruses, alphaviruses, well, more recently work in my laboratory is focused on COVID-19, SARS COVID-2 viruses.

Ben Weintraub, President

Perfect, thank you so much and thanks to both of you for joining. Let me turn it back over to Cinney to start the questions.

Marc Engelsgjerd, Equity Research Analyst

Ben, it's Marc. I think Cinney was temporarily disconnected, so maybe you could kick it off.

Ben Weintraub, President

Great. I'm sure, she should be right back.

Cinney Zhang, Analyst

Sorry. I'm back on.

Ben Weintraub, President

Okay. Go ahead, Cinney.

Cinney Zhang, Analyst

Sorry for the (multiple speakers). Thanks, Ben and also thank you Professor Lore and Michael Diamond for being here with us today. So let's start the conversation with basic science. So why are some viruses were difficult to immunize against others. Importantly, is it easy or difficult to develop a vaccine for the novel Coronavirus?

Karin Lore, Professor

Could I start?

Cinney Zhang, Analyst

Yeah, sure.

Karin Lore, Professor

Right. So, some real challenge in vaccine research or to develop a vaccine to a virus is whether the virus is mutating like HIV, for example, then it's really hard to come up with a vaccine. With the Coronavirus, that we have problems with now, the mutation rate is relatively low. So from that point of view, this is not a large challenge, we should be able to tackle it.

Other problems in vaccine development can be, for example, if you're dealing with a pathogen, that is latent, that infect cells and establishes latencies also like HIV for example and like viruses, that is a real challenge to them -- develop vaccines against them. Again Coronavirus -- with Coronavirus we don't have that problem. Another challenge can be if the virus impact cells of the immune system, that can also disturb the pattern. Do you want to add anything, Michael, too?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Yeah, sure, I just wanted to give you a chance because I completely agree with the concepts that you've outlined. The few other things to perhaps add are the challenges could be associated with the antigen itself and how to present that antigen and whether the antigen is better presented just as a soluble protein or on the cell surface or as part of a viral particle.

And so for certain vaccine you can actually generate virus like particles, so the viral protein or antigen, which is the target of let's say neutralizing antibodies is displayed in a way that looks more like the virus. And so there may be particular antibodies that you raise that recognize the antigen only on the particl and not actually in the soluble protein, so that can be a challenge for some viral vaccine. We don't know yet for the COVID-19 virus, SARS COVID-2 whether the antibody responses to the spike -- sizable spike which is really targeted by many of the vaccine platforms

how they'll be relative to the ones that are generated in the context of natural infection, so that remains to be something seen and monitored over time.

One other issue with vaccine of course is the challenge is safety and whether we will have safety issues that are inherently related to immune responses to the vaccine and this is going to be very different for different types of vaccines. So I think that, there are the usual challenges here. One additional one I think is, it's always easier to make a vaccine against the family member which you already have a vaccine that's approved. For example, if this was a virus that was very closely related to flu or was very closely related to one of the flaviviruses like yellow fever virus, we have vaccines, we said we know what the cohorts or protection are. For new viruses or viruses that we don't have approved vaccines, that's a little bit more of a challenge as well.

Ben Weintraub, President

So Dr. Diamond, maybe you could tell us for Coronavirus -- other Coronavirus like SARS and MERS, have we had any success with vaccines?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Well, I think we've had some preclinical success with vaccine, certainly that there is evidence that some of the immunizations have been productive, but they've never really be gone into expanded human clinical trials. And I think that is -- I think clearly preclinical studies are valuable and important, but and being one that actually conducts them, I can tell you, I think we get good information from them, but they are not a substitute from advanced clinical trials, because the immune responses in humans may be different than immune response in a mouse certainly and even in a monkey as well.

So we have learned what are the targets that we probably should be getting, what are the types of antibodies we mark, perhaps recognizing receptor binding domain and also the other regions outside the receptor binding domain on the spike. We know a little about the trimmer of the spike and how these antibody should recognize the prefusion trimmer for example. But still it remains to be seen whether for this particular virus is immune response going to respond to it in appropriate way.

We also don't know a lot about the balance of the T-cell response with the B-cell response that something that I think needs to be done in higher animals, monkeys and then ultimately human trial. So there are lot of unanswered questions, we do have some information from the prior SARS and MERS work, but I still think there's many, many questions to answer.

Karin Lore, Professor

Yeah, I agree. And for SARS, 17 years ago, it was actually two products, two vaccines that reached clinical trial in China I believe, at least one of them was in 2004. But by the time the clinical -- this was a Phase 1 trial and by the time the trial was over, the epidemic was over and other products would get priority, so this one was shelved. But still I think we can learn a lot by all this work that was done as an effort to SARS and MERS and there are outbreaks and we really get a head start on the vaccine development here. If we look at the companies that were in the game at the time, studying SARS and MERS, they also had headway and started early on their vaccine development for SARS COVID-2.

For example Moderna did work with the NIH already for MERS and SARS and there is also an inactivated whole virus particle that was tested in China, in one of these trials, that they now -- the same company is now produced an inactivated virus vaccine again based on the current stream and is pursuing that. But I think all the preparatory work

that was done a long time ago is very important now. And I definitely agree with Michael that all this preclinical work is critical, is especially when we are in the situation when we are pushing products forward quite quickly that we have to understand how they work, so that we're not finding our self in a difficult situation. So I think in parallel with already ongoing clinical trial that preclinical models need to be used.

For example, we are -- with this virus we can infect monkeys, so rhesus macaque monkeys and (inaudible) monkeys that are most common thesis for laboratory research and they are susceptible and not only susceptible they also develop disease. And this is a large advantage that we have and that we should utilize not only to test safety and also -- whether you induce vaccine responses, but also protection and also whether there is vaccine enhanced pathology after infection. And I think this is really something critical that we have to look into that could be detrimental if we could see this effect.

Ben Weintraub, President

Yeah, so that's -- we're going to dig into all of those topics in a few minutes. I think that one thing that we want to ask you about -- you both about is the main types of vaccines that are being developed. We're going to cover in detail in this call the mRNA vaccines, the DNA vaccines and more traditional types of vaccines. And so I'm interested in your views on the particular challenges of each of those three types. Professor Lore, maybe you can start on -- oh, sorry, go ahead.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Either one, Dr. Lore can start, if she wants time.

Karin Lore, Professor

So you're meaning that virus-like particle inactivated and the mRNA vaccine or you mentioned three different vaccine --

Ben Weintraub, President

Yeah, the mRNA -- yeah the mRNA vaccines, the DNA vaccines and the more traditional inactivated virus particles, yeah.

Karin Lore, Professor

So with the challenges where the DNA and mRNA vaccines, I mean, there are many benefits and we can go through them. The challenge to help that there is not yet the licensed vaccine. So we have nothing to fall back on that, we know work. So there are unknowns here and -- but there are multiple benefits and prospects of scaling up production, rapid production to size antigen production and prospects of having an affordable vaccine.

So I assume most people know that what DNA and mRNA vaccines you inject a piece of genetic material that is including for the antigen of interest and antigen of the virus for example the spike protein that we discussed. So you inject that in self, will start to produce protein from that -- the DNA or mRNA. So you will produce the antigen yourself after vaccination which is different from all other vaccines where you inject -- a pro thing or an inactivated whole virus or in some circumstances a live attenuated vaccine. So with that, you inject the protein and you induce the new response to that.

I don't know if you wanted more specific information.

Ben Weintraub, President

Well, one particular question that I had -- one particular question that I had is with the entire inactivated virus particle you would presumably have many antigens. And as far as I'm aware with the mRNA and the DNA vaccines, you only have one antigen. What are the consequences of that difference?

Karin Lore, Professor

Not necessarily, so Moderna's clinical trial that is started based on the spike, so, yes that is one antigen, but it looks like in our view pursues DNA that is encoding for multiple antigens. But with this technology, you have the potential of adding several sequences, so you can add on other antigens as well. So I think that that is critical. We should not put all our eggs in the same basket and induce bed on the spike protein because maybe in this case it's important for example to induce T-cell responses that would clear infected cells. So and they may recognize something else, some other protein of the virus than just to fight protein. It's also possible that it is despite protein that is causing vaccine and hence pathology after infections, there is one paper last year in February that show this in monkeys that they got enhanced lung pathology and after receiving a vaccine based on the Spike protein. So this is something that could be done -- more research should be done on this issue.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Yeah.

Ben Weintraub, President

Dr. Diamond, what could we know about that -- yeah, go ahead. I was going to ask about the immune response to Coronavirus or particularly this novel Coronavirus, what do we know about it and what does that tell us about the different types of vaccine approaches?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

We're still learning about the -- certainly about the human response. One thing that does appear at least I have heard sort of you know, there is a big movement now to perhaps use immune plasma as an early therapy and I guess we're going to talk about therapies in other times, I'm not going to go into it, except to say that there has been screening of samples done as part of this and questions remain how quickly people generate robust adaptive immunity, what's the role of adaptive immunity in clearance here, these are still which part of the arm is it really the early antibody response and via ADCC, Antibody-dependent cytotoxicity or other mechanisms, whereas Lore alluded to -- Dr. Lore alluded to, there could be robust T-cell response which is absolutely required.

And so I completely agree that in terms of the vaccine platforms, there is flexibility in the mRNA and the DNA platforms, that said they've already sort of chosen what they're doing initially, but they can't respond at multiple levels. One of them is at the sequence level for example if there was a need to change the sequence because there were viral variance emerged which is possible under new selection pressure, although these viruses don't mutate at the same rate that let's say flu or HIV or HCV does because they actually have proofreading enzyme called Xon in one of their

non-structural protein, so they can actually correct errors.

That said, they certainly can't escape antibody responses. So these mRNA and DNA platforms could make variance and then they could bundle them if you will, as some of them already are starting to do but not all of them put multiple antigens in. One question is, which antigens? And we don't exactly know that we certainly know spike is important, where people are defining the T-cell dominant ones for different HLA haplotype, those studies are ongoing in the field. And then there's all of these other open reading frames which we think probably have some immunization activity which probably wouldn't prevent you from getting infected, but might if those were very important for immunomodulatory activity prevent you from getting very sick. And so there's a lot of interest in studying at the basic level, some of these other open reading frames and then they could be easily integrated into second generation mRNA or DNA vaccines.

The inactivated vaccine when you inactivate it oftentimes you may decrease it's immunogenicity inherently because you may inactivate some epitopes, most of those are focused likely on the outside protein, it depends if you use Formalin or if you use some other mechanism of inactivation. They tend to get more dominant T-cell responses and weaker T-cell responses because of the reasons that that Dr. Lore outlined is that the mRNA and DNA vaccines are being made inside the cell translated from DNA or from mRNA directly. And then as you make your proteins, you're also then able to load peptides onto MHC and then a listed good T-cell responses. And so they're generally speaking can make reasonable ones especially the mRNA vaccine.

One other vaccine that's not mentioned which I think also is moving towards clinical trial is the Adenovirus vectored vaccine I believe Janssen may be the one that is developing that, they have platforms. And I think it's scheduled to start Phase 1 trial at some point a lighting factor know when. It's similar -- it has a -- they're targeting spike also, they have a little bit more constraints in terms of the size of the inserts they can put in, I mean how many different genes they could put in because they would be putting in one adenovirus if you will probably not multiple ones, but those also would be translated within the cell and therefore the host would be making there the proteins and therefore also get more balanced B and T-cell responses.

But to your question, what do we know about the protective call it right now for the virus is still underway from the prior one, it's -- there is clearly evidence that antibody responses can protect if you passively administer antibodies and there is clearly evidence that T-cell responses can be involved as well. But the balance -- the exact balance that would be optimal that would prevent adverse pathogenic reaction is still not known for this virus certain.

Cinney Zhang, Analyst

Dr. Diamond, I have a question on my side, oh, sorry, Professor Lore, go ahead.

Karin Lore, Professor

No, I mean (multiple speakers) just fill, sorry just fill in that most if not all vaccines via production antibody. So that is the history. But I think we have to rethink some of the infections that we're dealing with now. And also I believe that Inovio has worked on the MERS vaccine for a couple of years and they have found in their preclinical studies that it was a better correlate of immunity was the T-cell response, not antibodies.

Cinney Zhang, Analyst

Okay. I was going to ask, do we need to worry about the antibody dependence enhancements with COVID-19 vaccine, if so, how do we mitigate that?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

You asked a challenging question and I'm going to hedge and say, I don't know the answer to be honest. I work in a field where antibody enhancement is a major problem and an established problem, that's flavivirus and that's dengue. And there is really good epidemiologic data and also good animal model data to show that isolated antibody responses that are cross-reactive, but not particularly neutralizing can lead to enhancement in vitro and in vivo.

You can also see this phenomenon in vitro for many viruses, HIV, you can see it for Coronavirus as you can see it for a wide swath of viruses. It's not clear that it matters in vivo for any of those other viruses except flavivirus even though there may be scattered reports suggesting it, but in terms of human epidemiology, sequential infection or otherwise there even vaccination is not really been clear.

The Coronavirus is complicated because there is a little bit more literature on that, there's literature in the fee line, infectious peritonitis virus. There is old literature where they used spike DNA-based vaccines in some of these other model Coronavirus and saw enhanced infection. And then there is not only enhancement to well call the Canonical -- you had an antibody, it doesn't neutralize, it binds the virus, at least enhance internalization and infections in cells expressing C receptor. But there are also some evidence that maybe there are antibodies to Coronavirus that you generate and they can buy themselves have pathogenic effects independent of Fc receptor activity.

So there is a couple of different mechanisms by which antibodies could be pathogenic. The question is, if you had a balanced response and a robust response both T-cells and B-cells would this actually matter or not? And that's what we don't know. And the question is, is Spike only going to be an issue relative to let's say if you had a more broad larger number of antigens, but we don't really know to be honest. And I think that's what preclinical data would help with and that's what ultimately we're going to figure out in early clinical trial, it is a concern, it's going to have to be addressed I think but for the FDA and it's one of the reasons why we cannot just ship out a vaccine in three months to a 100 million people, because we really need to know is there going to be a safety issue or not. So this is why it's going to take some time, not just the manufacturing issue, but I think we need to do the analysis in the early human trials to make sure these are going to be safe.

Karin Lore, Professor

Yeah, I couldn't agree more, very critical.

Ben Weintraub, President

So give us a sense of you do have some people have the opposite of the intended effect that they get more sensitive that sort of goes to how frequently that happen, goes to how many people you have to test in. So this is something you would expect to see one in 10 people, one in 100 or one in 10,000 people. And so how would you design the trial to make sure that you were -- but that risk is low enough?

Karin Lore, Professor

That's very hard to know too and also you can only see that if that person first get vaccinated and then exposed, infected to the virus, so that must mean that the virus must be around. And right now, that's not going to be a challenge, but later on when this pandemic is hopefully over, it's hard to measure that successfully in humans.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I completely agree as well. There's two issues here, one of them is, I guess more solo and one of them is more logistic, one of them is when we're measuring relative to the time they got vaccinated. Obviously, if you want to introduce a vaccine, we want it now and we want to be able to see that they get protection immediately because we don't know if this virus will go away or not like SARS. I'm going to guess it won't go away, just because of its transmission patterns and its potential to a notice, but whether it does or not, I don't know. But if it just stay around for some period of time and you vaccinate what happens if you don't get boosted and it's a year, two years three years as your titre vein, do you still have enough of an adaptive memory response, memory B-cell response, memory T-cell response to actually have a inducive rapidly protective response -- well, that be a problem then, so there is one issue over durability.

And then the second issue comes to this logistic issue, if you look at the dengue vaccines, which is really the best case that we have for this for the Sanofi vaccine, that's the tetravalent Live-attenuated dengue vaccine. In Phase 3 trials, they went and did sizes of 30,000 or more vaccinations to try to capture this enhanced disease phenotype. And they really didn't see it in the Phase 3. There were some hints perhaps that there might be under certain serotypes slightly more symptomatic cases, but they didn't reach statistical significance.

But in the post-marketing Phase 4 study, this is where in the Philippines and a few other places where it became more clear that this event could occur and this resulted in a change and the indication for this vaccine to only be used in people who are already immune to one dengue -- at least one dengue serotype. So it may take large numbers to be able to pick it up going forward. So the question would be, what's the risk benefit if it's one -- if it's one in 10, it's a problem, if it's one in 100, it's a problem, it's one in 1000 a problem, whether if it's one in 100,000. And so then what's the risk benefit for immediate protection versus

Somebody who might get enhanced and this is a challenging question. And I think one that will -- the regulators are going to have to grapple with based upon what the data shows, but we may not know until large scale clinical trials for actually before.

Karin Lore, Professor

And also I can just add to the experience we had in Scandinavia, with the swine flu vaccine in 2009, where a small proportion of people developed narcolepsia and which was related to the vaccination. And this would have been impossible to pick that -- pick up in any animal model and also hard because it was a rare event to pickup in clinical trial. So, it's -- the more people you vaccinate the more information you will have and that is hard to achieve sometimes even in a Phase 3 trial.

Cinney Zhang, Analyst

So other --

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

One of the other -- can I just add one other logistic issue that we may have is if the vaccines get into Phase 1 and obviously that's a small number of people Phase 2 not so big, but we're talking Phase 3 trials. When do we expect them to get in Phase 3 trials and will the pandemic be sufficiently slowed by then that it will be hard to find sites that actually are going to be able to show you efficacy. So this is what happened with Zika, there was a rapid rush that was pretty fast, not quite as fast as this one, but pretty fast as well. And by the time the vaccines were made, the epidemic was

gone and it was no place to actually do a vaccination trial and see efficacy. So this is going to be the race of can you get your vaccine into clinical trial -- into large numbers of people while there still is the pandemic going on, so you can actually see efficacy.

Cinney Zhang, Analyst

Okay. So the safety risk of RNA vaccines inherently higher given that they will have -- there hasn't been any approved products in the market.

Karin Lore, Professor

Sorry, what was the question?

Cinney Zhang, Analyst

So the safety risk of RNA vaccines, are they inherently higher given there hasn't been any approved products in the market.

Karin Lore, Professor

If they are safer, you mean than other vaccines?

Cinney Zhang, Analyst

Yeah, they're safer, yeah, also (multiple speakers) we, go ahead.

Ben Weintraub, President

I think she was saying whether there were safety risks or higher or not given that any approved?

Karin Lore, Professor

Yeah, so anything that hasn't been in kind of is not license with no much less about, so that is a risk in itself, but mRNA vaccines have been tested for (inaudible) rabies for example. And the side effects that were reported there were in the range of other regular vaccines, there was nothing that popped up that was extraordinary compared to other vaccines, many people get it in store in the arm after vaccination, many of their side effects were manageable. And as I said just like normal vaccination, a few more severe side effects like Bell's palsy was reported in one case and things like that. But in general, the side effects didn't come across something that was manageable.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

So I would agree with Karin, I would just say and I think she highlighted in her first sentence, if there is no vaccine -- flat vaccine and that platform approved, then there is some inherent risk because we just don't know because it hasn't been administered to 100,000 or 1 million or 10 million people. So we don't know exactly what we're aims forth. But inherently at least in the pre-clinical and the clinical trials that have been done for mRNA vaccine, there has not been

anything substantially different than any of the other vaccines that we've looked at outside of the things you mentioned at very, very small frequencies. So the only -- the real risk I think is the fact that we don't have a vaccine of that platform. And so there -- maybe there are things that we won't know until we have millions of people in, but those are unknowns at this point I think.

Cinney Zhang, Analyst

I have a question coming from online. Can you please clarify how mRNA vaccines given that protein section slate on producing host cell and present in the concept of host and HC that we won't be inducing tolerance to the actual viral protein in step antigen responses.

Karin Lore, Professor

Yeah, so mRNA vaccines are very immunogenic and they turn on the innate immune system very rapidly. So they are good in that, you don't need an adjuvant added to them. So that in itself is a benefit I think with mRNA vaccine. So when you inject an mRNA vaccine, you get a clear type 1 into CRM response and activation -- in it's immune activation many different in itself. So that type of response is not timing tolerance, it's alerting the immune system to induce an immune response and the protein will be produced and recognized as foreign, so that will be what the response will be against.

So there is always a balance with in the modification of the mRNA sequence, so -- because you want to have good translation of the proteins, but you don't want to alert the immune system too much with the mRNA because what can happen then is that the innate immune activation is just too high and that would turn off translation, the translation machinery in the cell.

But the mRNA companies, I mean this is their expertise, they know how to modify the mRNA, so that it has this good balance of inducing a good production of antigen and a good response to the antigen. So I would say that it's very slim, risk that you would get tolerance, it's also saw that antigen production is transom, it doesn't go on for a long time, maybe a week or so and that's -- that is likely to short of a period to induce any robust tolerance.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I would agree, you summed it up. I completely agree.

Ben Weintraub, President

Great. So I think it's important next to take this into the sort of practical realm. One question that we've been getting from almost everybody that we work with on this is, there is so many approaches, there is over 50 different vaccines being tried. Dr. Diamond, you outlined the scenario where there's not enough cases left to test this, because the pandemic finishes, that's I think what we would all consider a high level problem for society. But let's talk on the practical side, on the less optimistic scenario where we really do need this vaccine and there is a race to get it, is 50 different approaches too many? And how would you sort of pick the right ones to really accelerate going forward, maybe Dr. Diamond we can start with you.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

So I think at this time, it's a good thing that we have a lot of horses in the race if you will and there is overlap and there may be some redundancy and repetition because we just don't know which one is going to induce the best response. And so we have to actually work in parallel rather than in series here. I think that what most people will do, I would imagine that the manufacturers will want to do is while they may be raising to get into Phase 1 to show safety is in parallel they will be trying to get preclinical data which would assess immunogenicity in parallel and you also get an idea about perhaps mechanism and protection against challenge if they have appropriate models as we heard a little bit about the rhesus macaque model. And there are some mouse models that are being developed, although they are -- they have some challenges because as far as doesn't normally infect wild-type mice.

So my suspicion is that if we have 20 or 30 platforms going forward, some of them will drop out because either they will have a reactogenicity that's not tolerable, they won't have immunogenicity in the Phase 1 or in the preclinical studies, they just won't show an adequate level of protection or immunogenicity such that a commercial entity will want to take a risk with many other vaccines that if they don't feel their vaccine is optimal and some of the data as it gets published they may be able to benchmark their own work.

So I think some of that will follow-up that way. And then we may be left with a few different ones of different platforms that actually begin to progress through advanced clinical trials. And there the issue of safety will come up and will any of them have safety issues either via this immune enhancement effect for other types of problems that come up.

And so I think that maybe a few of them will have problems there and drop at as well which would narrow the field substantially forward. And then I guess the last one that will come up is are they going to be able to finance it appropriately, do they think that they're going to get support from either government agencies or other agencies, is there a market? And again those will be all things which contribute to it as well, so that's my feeling at this point.

Ben Weintraub, President

So Professor Lore, give us a sense of how fast you think all that could happen and what we as interested parties in this process should be looking for in terms of clinical data along the way?

Karin Lore, Professor

The WHO Director says that, we should have a vaccine within 18 months, which is working at a speed that hasn't been seen before in vaccine development. So there is already clinical trials ongoing, there are few more starting later in April, in June. And Moderna and I think Johnson and Johnson said that they could do a large efficacy trial in November and could by January next year, no, if they have a product to put forward. So I think that is really working fast to get a product, in the best case scenario we will have a vaccine then. And along the way there will also be other smaller players pursuing their products and at the end of the day, they may be the lucky ones. So we'll see -- I think it's very important, there are many players in the game from the beginning and that there are many different kinds of vaccines that are being tested and both T-cell based vaccines and B-cell based vaccines are I think, but we will know much more in a year obviously.

Ben Weintraub, President

So what's going to tell you that it's working, is it the animal data showing that they're protected from infection, is that the safety data from human studies, what is it that you think is going to be the most important sort of indicator of which one is going to be successful?

Karin Lore, Professor

So, this is a challenge in vaccine development, because you would know unless you are performing your clinical trial in an area where people are exposed to that pathogen, because that is the real proof. And also you don't have that luxury, sometimes you have infections where you know the level of protection, you know which antibody level you have to be in order to be protected. We don't have that information for this virus.

So without knowing that the people who got vaccinated also didn't get the infection, we wouldn't know for sure. Animal studies will help us a lot and in this case as I said before, we have monkey models, whose immune system closely resembles that of humans and they get infected and sick. So I think we should really utilize that model in parallel with the clinical trials. We try to understand how protection works and potential risks of being infected when you have been vaccinated and things like that. But the ultimate proof is hard to have unless you have -- you can study in human infection.

Ben Weintraub, President

So I know that both of you have been more immersed in the details of the trials that are already underway. So perhaps we can take advantage of your expertise by asking the question. Based on what you've seen so far, is it promising and are there particular approaches that you're the most excited about, Dr. Diamond?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Well, you know it's a hard question because I haven't seen a lot of data yet. It's not like we have Phase 2 data from antibody, we're still at Phase 1 early recruitment stages. And even animal model data there is scant animal amount of data except for some immunogenicity data would suggest that some of these vaccines can induce strong anti-spike responses and moderate to reasonable anti-neutralizing responses. And so some of the issues there are all of the assays are not developed, they're not agreed upon, so then you have variation in the assays from vaccine manufactured -- vaccine manufacturer, which makes it difficult to compare a vaccine unless you have some other clinical outcome where that's pretty much straightforward to understand, in other words, where you make cut off for protection well unless we have a standardized assay it's going to be hard to go from one to the other.

So I would say that we are facing some of the work based on the work that was done with SARS and MERS and also work that is done with other viral vaccines. And so I don't necessarily say have a lead candidate if you will, I think they all have some promising avenues that have based on the past performances and I'm interested to see what happens, but I think it's very difficult at this early stage to say there is a front-runner except that some of them are already in humans just by the nature of the kinetics of development production, introduction in humans, they will be the ones that get the first data back eventually when they go into some sort of either Phase 2b or or Phase 3 study where they can similarly look at efficacy hopefully to see that and then pair that with NHP studies, potentially preclinical studies in smaller animal models, but I think it's too early to call right now.

Cinney Zhang, Analyst

I have a question online related to what you just said. What are your thoughts about the T-cell vaccines, will they work better than the antibody vaccines or any effective T-cell vaccine technology on the market that could be used for the COVID-19?

Karin Lore, Professor

So there are no T-cell vaccines on the market, vaccines worked via antibodies, I mean cancer vaccines are different obviously, but otherwise vaccines against infectious diseases are based on antibodies, in the absolute majority of cases,

sometimes in combination with T-cell responses. So -- but again we don't know the correlate of protection here. And if there is an issue with vaccine enhanced pathology, then we definitely have to look into T-cell based vaccines more. And both with the DNA and mRNA platforms, you have that opportunity, you can switch over to antigens that are T-cell antigens and pursue that.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Yeah, I would agree that we don't have a T-cell vaccine for a viral vaccine. Obviously, there was one trial years ago for HIV and it did not really work that well. I'm a big believer personally and this is my philosophy if you want me to put my two sense in is that getting a balanced B-cell and T-cell response will be helpful, there is data in preclinical studies not with Coronavirus, but with many other viruses that while a very, very robust B-cell response is sufficient to provide protection and you can establish that by taking the antibodies out of the animal and giving it to another animal and establishing protection under conditions where antibodies are inhibiting the virus, but not fully protective, having a T-cell response than matters. And you can tell that because if you have a let's say marginal B-cell response and then you deplete T-cells, CDA T-cell and the animal may not be able to control the infection whereas if they had a T-cell response generated as part of the vaccine, they can show protection.

And in other cases, you can actually adoptively transfer the T-cell response and show protection. So my feeling is personally these vaccines, which generate balanced risk may do quite well. And the ones that are intracellular ones that use the host actually makes the protein, you have a good chance of making a T-cell response as part of that while making the B-cell response as well if there are immuno dominant epitopes within that particular gene.

And if there is not as Karin alluded to, you can just add them in a separate gene. And so then you would get a T-cell response and a B-cell response, but you might be able to get both for one, we just don't know yet. We have to sort of see how the responses are. But my feeling is a balanced response, we give you some protection beyond the B-cell response and maybe good to optimize.

Karin Lore, Professor

And then other challenge in this is also that if you study inspected individuals and learn from them what type of immune response they have with antigens that their immune system is recognizing that is not necessarily the antigens that you want to have in a vaccine that are best for protection, but is protecting yourself from an infection is different from handling an already established infection. So that is always something to -- I mean the HIV vaccine field made this mistake, trying to base vaccine of what good controllers had in terms of their responses, but that didn't work for protecting individuals.

Cinney Zhang, Analyst

Thank you -- thank you Professor Lore. I'm getting a lot of questions on the RNA vaccine development front. Could you comment on Moderna, BioNTech (inaudible) platform, are they different? Is there one that's better than others?

Karin Lore, Professor

That's a hard question, I don't think I know, details of how -- so they differ in terms of how their mRNA is modified, they have their different techniques to do this and this is their proprietary information and they don't reveal details on this. So -- but these secure backed by BioNTech, Moderna they all have their own ways of modifying the RNA, so that is stable and it can be translated and it induces a good balanced immune response. So these are details they have worked for many, many years. I think one thing they have in common is that they all practice their mRNA in lipid nano

particle as used to protect the mRNA and facilitate delivery. So in essence, they are quite I mean they are quite similar.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I agree.

Karin Lore, Professor

We haven't seen the data, so it's hard to pick favorites out of them.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I agree, Karin. The problem is that it is intellectual property for each of these companies. And so they only disclose relatively 30,000 foot information they have in mRNA, they have some basis, they call and optimize in certain way, so that they can optimize protein translation and either minimize the immune response or get a little bit of immune response. We know those are some of the variables that they do, but we don't know exactly how they do it, we don't know how each of them differs from one another.

So even at the mRNA level we don't exactly know what the sequences are and we don't exactly know how they've altered them, that's very difficult as an outsider or to evaluate that a priority, without seeing just what is their immunogenicity data. And then beyond that in the lipid nanoparticle, we don't know if they are different or exactly the same or the same size, do they use the same lipids of the composition, how do they make it all of that is proprietary. And so it is impossible to evaluate at this point in time. So you have both the mRNA and the lipid nanoparticle being potentially different in subtle ways, but important ways maybe they target slightly different cell, maybe they have different test life, maybe they have different amounts of protein levels that they are producing, but there is no way that we can as academics or otherwise evaluate that, we'll have to wait essentially to see the immunogenicity data because that is all their proprietary information.

Cinney Zhang, Analyst

But fact that Moderna has some human data in CMB that said, if you can encounter about their platform?

Karin Lore, Professor

But they have data on Zika influence as well and Mirvac has rabies data. So they all have data, they looking very promising. So, and I have no reason not to say anything that BioNTech will have good data, I mean this is a powerful vaccine platform for sure.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Just hard to know to distinguish at this point.

Marc Engelsgjerd, Equity Research Analyst

This is Marc. I have a quick question on what might be considered another platform or at least another approach. We've started to hear about some companies with plant based production platforms. My understanding this would be used to do kind of large-scale affordable production of inactive viral particles. I don't know if either of you have any familiarity with essentially plant based production vaccines or if you have any thoughts on potential flexibility here?

Karin Lore, Professor

I have very little experience with plant based vaccines. So it's hard for me to say, it's an intriguing platform that I think should be explored, it's hard to say again how this will compare against the other platforms.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Yeah, so I have some experience in plant based antibodies. And so people have made those in the flavivirus field, they have made virus-like particles. The corona will be much more challenging I think to make a bio particle and I don't know if you could make a bio particle in a plant. I haven't really seen the data suggesting that you can, I think you certainly could make sizable antigens, then they would have to be likely modified plants where they change their quite constellation patterns, so they have a human like quite constellation pattern, otherwise they may be perceived as foreign and cleared very rapidly or that may also be good and may be cleared rapidly into the appropriate cell and you made enhancements in antigenicity. So I think there would have to be some analysis of what icons you had on the protein. I think the sizable ones are possible. I'm not so clear about a particle in plants, but I haven't seen that data, so I'm not that familiar with it.

Karin Lore, Professor

Just a comment on the different platforms on which ones issues that somebody raised the comment that do you think whole inactivated buyers as a vaccine is a simple technology has been used for many other viruses and work? And that is a technology that many countries could use -- many countries even low-income countries have facilities that would be able to produce that kind of vaccine if needed, which is not the case yet for sophisticated technologies like the mRNA based vaccine for example. So worst case scenario that everybody had to produce their own vaccines that gives us the simple technique is also something that should be taken into the consideration.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I do think that we do have formulated and activated vaccines for several viruses. There are two I think limitations with them, one of them is you have to make sure you inactivate the virus. And so and it seems to voke, but the way they do this to preserve antigenocity is normally they take up huge viral perhaps and they put it at 4 degrees with a low percentage of Formalin and they let it sit for some period of time. But then you have to absolutely QC what you got because you don't want to have live virus in your vaccine prep and if you're using it, let's say a non-attenuated Coronavirus then it could be an issue.

There are other ways to do it, but if you were just going to do the simplest thing which is just to drop a bunch of virus and enact it, that safety issue would have to be a paramount. The second is, this virus doesn't grow that well for whatever reason. So compared to some other viruses which grow at very high titre, this one grows in cell culture at about tenth to the sixth, tenth to the seventh infectious units per mill, which is reasonable, but it's not enormous to the

high. And so that means that you have to actually grow larger cultures that become not they have huge amount of virus that you have to grow at under BSL-3 conditions, Biosafety Level 3 conditions with appropriate protective gear. And so you have the huge amount that you have to grow up and then concentrate and then show that it's inactivated.

So from a logistics issue, it's not as simple perhaps if you could grow hugely titres in a very small theater if you will. So that's a second issue that one would have to sort of address from a scale point of view. And then the third one is, most of these inactivated ones you have to dose repeatedly, they tend to be B-cell dominant with very small T-cell responses, and so this kept -- that the issue of or are we going to have issues with inactivated viruses with enhancement of some sort of another relative to once you have more balanced response. So I think it's possible and it's certainly is worth pursuing, but there are some caveats associated with these particularly that are unique to challenge us for the Coronavirus.

Cinney Zhang, Analyst

Okay. We're getting close to the hour. Anyone willing to put (inaudible) approval in 2021?

Karin Lore, Professor

Sorry, can you repeat the question please?

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Yeah, I didn't hear that either.

Cinney Zhang, Analyst

Sorry.

Ben Weintraub, President

That was -- Cinney's question is similar to what was going to be my final question which is there is a lot of push to a very fast approval of a vaccine and sort of some extraordinary measures to get it into the hands of maybe healthcare professionals, even sooner. So the last question that we have is around, is it possible to have a vaccine in 2021?

Karin Lore, Professor

I think it's possible, but it will come with some risks. We won't know that it is 100% safe or effective.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

I would agree, that's right -- that's what you're hearing from Tony Fauci and others that 2021 is the earliest that we would see it. The issue here is efficacy and safety both and those are high bars to figure out for ones where we don't have pre-existing Coronavirus and so we have to learn more about correlates of protection, we have to learn more about vaccine safety issues for this particular virus. And so that's just going to take introduction into people and it's going to

take time and we have to develop some of the animal models to help us learn more about what we're looking for. And I guess 2021 would be the earliest, but as they say throughout the 18 months, I think is optimistic, it's just very challenging to do in this setting.

Cinney Zhang, Analyst

And Devil's Advocate say that 2021, we have another circulating Coronavirus strain, so the current vaccine will be no good anymore.

Michael Diamond, Professor - Department of Medicine Molecular Microbiology Pathology and Immunology

Let's hope not.

Marc Engelsgjerd, Equity Research Analyst

Before Ben or Cinney wrap up, this is Marc, I just wanted to reiterate that Bloomberg and InThought are working on a Coronavirus therapeutic, all sort of as a companion piece to this, we were getting a number of questions coming in about potential of antivirals and other direct therapeutic measures. We'll be exploring those in great detail in similar events. We're just fine-tuning the details of that, but please look out for an announcement and an invitation hopefully in the coming days.

Cinney Zhang, Analyst

Well, thank you so much Professor Lore; Dr. Diamond. Thank you so much for your time and thanks everyone for joining. Please stay safe. So that's all from our webinar. Thank you.

Karin Lore, Professor

Thank you.

Marc Engelsgjerd, Equity Research Analyst

Thank you.