Q3 2019 Earnings Call

Company Participants

- Lavina Talukdar, Head of Investor Relations
- Lorence Kim, Chief Financial Officer
- Stephane Bancel, Chief Executive Officer
- Tal Zaks, Chief Medical Officer

Other Participants

- Alan Carr
- Alec Stranahan
- Cory W. Kasimov
- Edward Tenthoff
- Hartaj Singh
- Matthew Harrison
- Salveen Richter
- Yasmeen Rahimi

Presentation

Operator

Good morning, and welcome to the Moderna's Third Quarter 2019 Conference Call. At this time, All participants are in a listen-only mode. Following the formal remarks, we will open up the call for your questions. Please be advised that this call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head of Investor Relations at Moderna. Please proceed.

Lavina Talukdar {BIO 19691239 <GO>}

Thank you, operator. Good morning, and welcome to Moderna's third quarter 2019 conference call, to discuss business updates and financial results. You can access the press release, issued this morning, as well as the slides that we'll be reviewing, by going to the Investor section of our website. Today on this call, we have Stephane Bancel, our Chief Executive Officer; Tal Zaks, our Chief Medical Officer, Stephen Hoge, our President, and Lorence Kim, our Chief Financial Officer.

Before we begin, I would like to remind everyone that this conference call will include forward-looking statements. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk factors that could cause our actual performance and results

to differ materially from those expressed or implied in these forward-looking statements. We undertake no obligation to update or revise the information provided on this call, as a result of new information or future developments or update.

I will now turn the call over to Stephane.

Stephane Bancel {BIO 15174250 <GO>}

Thank you, Lavina, and good morning, everyone. We are committed to building mRNA as a new class of medicines, with Moderna positioned to remain the leader in the field. As you know, we believe that mRNA since has a potential to help patients by addressing large unmet medical needs and treating diseases that are not addressable by recombinant proteins or small molecules. Through the platform nature of mRNA, we believe mRNA medicines provide a higher probability of technical success and faster time lines to clinical trials compared to traditional medicine.

We also believe that the manufacturing capacity intensity of mRNA is materially lower than recombinant protein, and the cost of manufacturing at commercial scale will be similar to small molecule injectables. We continue to focus on managing risk across the portfolio, especially technology and biology risk. In the quarter, we were proud to share positive Phase 1 data for two important milestones of CMV vaccine and our antibody against the chikungunya virus-delivered IV. We show that we successfully immunized seronegative subjects with CMV and boosted seropositives. We plan to start a Phase 2 study very soon. The GMP material has already been made, and the study protocol has been submitted to the FDA. As a frame of interim results of our Phase II trial, we should be able to make a decision for Phase 3 dose. The team is already spending a lot of energy to plan for a Phase 3 study. We believe our CMV vaccine could, if approved, change the future of thousands of children around the world by preventing birth defects. Moderna owns the global commercial rights to the CMV vaccine.

We also presented data from the first-ever mRNA-encoded antibody in a human study. We are very proud of this major scientific achievement, and we are eager to move forward with the MMA and PA clinical studies soon. Both of these strategies, programs use the same delivery technology as the one in the antibody program.

If we step back and look at the body of clinical data over the last three and a half years, we have come a long way. We started 16 Phase 1 trials. We dose and maintained 1,400 subjects and patients. We repeat dose up to eight doses of mRNA up to three weeks apart in our OX40 ligand and PCV trials. Additionally, across the five modalities for which we have human data, we have consistently shown that our mRNA medicines are well tolerated, results in consistent protein expression in humans, encode for protein that are functional in humans and translate from preclinical models into humans. These findings are very important. They assure that our technology investments are paying off. We believe we are at an important inflection point in the company's history. Five out of the first five modalities have found success in the clinic. That was not easy.

Nobody is obvious as is would be the case. Two critical factors explained it for me: one, the quality of our science; two, the quality of our CMC, including manufacturing, technical development and quality. One of my mentors at Eli Lilly, the late Dr.Gus Watanabe, who was President of Lilly Research Labs once told me, "Stephane, it takes great science to make important medicines. With okay science, well, good luck." We are very humbled to be named for the fifth year in a row among the best employers around the world by Science. To be a Science 2019 top employers speaks loudly of a culture we have established in our scientific teams, among the platform or drug discovery and also process development in manufacturing. We are more than ever committed to be the best mRNA company in the world. It requires the right culture. And being named to this list five years in a row by our Moderna colleagues seems to signal we are on the right path. mRNA science is not easy. It requires great collaboration from many disciplines with the right capabilities around the table.

We think that with more than 300 scientific colleagues, we have scale. We believe it is very hard to be a great mRNA science with a much smaller team. We, of course, also recognize that great science is being done outside of our walls. As such, a key part of our strategy is to collaborate on research with leading academic and medical centers around the world. We have, over the years, established over 15 collaborations. Our more recent research collaboration with Harvard is centered around developing new medicines for immunonological diseases.

On Slide 9, you see our current European pipeline. Three important milestones in Q3 to note. The PCV Phase 1 randomized trial has begun. We reported positive CMV Phase 1 data. We reported positive result from our antibody program. The first subject has been dosed in the age de-escalation cohort of a Phase 1b of the hMPV+PIV3 vaccine. Zika received fast track designation by the FDA, PA has an open IND by the FDA and recently got fast track designation as well.

Let me now turn to Tal to review our clinical progress.

Tal Zaks {BIO 19987702 <GO>}

Thank you, Stephane. We're advancing our pipeline of medicines in 6 different modalities. So let me start with the prophylactic vaccines, where we have treated over 1,000 healthy volunteers across seven programs to-date. We're pleased with the emerging consistent safety and tolerability profile, and of course, with the repeated demonstration of peptide immunogenicity, which we had expected based both on the fundamentals of expressing of arlant and using our body's own cells and the wealth of preclinical data that continued to translate well in the clinic. The CMV Phase 1 success is the latest addition here. These data have exceeded our expectations. But before I review them, let me first briefly update you on other progress.

Both the RSV and Zika programs continued to dose patients in their respective Phase 1 studies. For Zika, we also presented preclinical data at the International Society for Vaccines conference in late October, where vaccination with mRNA-1893 was shown to be fully protective at the lowest dose tested. On the hMPV+PIV3 program, I'm pleased to report that the age de-escalation study as to file notice has started with the first subject

dosed. We also presented seven-month immunogenicity data at Infectious Disease Week in October. And finally, with our chikungunya vaccine program, we continued to see good durability with 78.6% of the subjects seropositive to chikungunya virus at 12 months post vaccination.

So let's get back to CMV. CMV is a common pathogen that is a member of the herpes family of viruses. And like other herpes viruses, it's a lengthened virus, which means once we're infected, it's for life. The largest associated with CMV is birth defects and disease in babies born to mothers who are infected during pregnancy. The burden of disease is significant, with approximately 25,000 newborns infected each year and is infected each year in the U.S. Currently, there aren't any vaccines against CMV on the market despite repeated attempts over the last 50 years. Now we believe that a reason for prior failures has been the inadequate immunization against the pentameric complex, which the virus uses to infect epithelial cells, either the cells that line body surfaces, and so are the first port of entry for the virus. This pentamer is made of five distinct proteins that have to assemble inside the cell before they are transported to the membrane. So trying to make this structure of one protein at a time using traditional recombinant technologies is obviously challenging.

However, this challenge can be overcome with our mRNA-based vaccine because our technology enables a simultaneous translation of five components. As shown on the bottom half of this slide, mRNA-1647 actually contains 6 mRNA sequences, five of which encode for this pentamer and one that encodes for gB. Now gB is a relatively simple single-protein receptor. And the important thing is that prior studies with the recombinant vaccine that only included gB already showed prevention of half the cases of CMV infection, which provides us with a very good starting point for demonstrating efficacy.

So let me frame the next two data slides. Every one of us has either been infected with CMV in the past or not. And if we have, we're lifelong carriers, and our immune system is constantly fighting this chronic infection. So we have antibodies in the serum of our blood, and that is called seropositive. If we've never been infected, we're seronegative. Now both seropositive and seronegative subjects were enrolled in our Phase 1 study. So we'll be looking at the levels of neutralizing antibody titers for each. mRNA-1647 encodes for the two antigen, the pentamer and the gB, that in general, mediate the ability of the virus to infect two different cell types, the epithelial cells and fibroblast. So we will look at titers in the blood of subject that can neutralize the virus' ability to infect either type of cell. And it is important because we're talking about a functional readout. So all in all, we are looking at four data set from this trial.

Let's start with the seronegative subjects on Slide 13. The top half of the table shows neutralizing antibody titers against epithelial cell infection. I'm going to draw your attention to two rows in the top half of the table. The fourth row down labeled GMT post second vaccination, where you will see the titer levels for placebo in each dose tested, which were basically zero for the placebo group and roughly 3,000 -- 15,000 and 31,000 for the 30, 90 and 180-microgram dose levels. The second row to focus on is the sixth row that shows the CMV seropositive titer level of 5,588. This is the level of neutralizing titers seen in the people who have been previously infected by CMV, the seropositives. The row right above shows the ratio between the neutralizing antibody levels achieved with our

vaccine relative to that level seen from seropositive subjects in the trial. At the 90 and 180-microgram doses, mRNA-1647 elicited an immune response against epithelial cell infection that is 2.7 and 5.5 fold higher than what is seen in seropositive subjects with natural infection. The reason why this is an important point is that because of the CMV seropositive pregnant women have been observed to have a lower rate of CMV transmission to their unborn children. So these results are striking, and that previous vaccines have not exceeded seropositive levels, and it demonstrates the strong immunological potency of our mRNA vaccine platform.

The bottom half of the table shows a similar comparison for neutralizing antibody titers against fibroblast. Here, we see our vaccine-induced neutralizing antibody titer levels similar to levels in seropositive subjects. So we've achieved the goal here as well. Taken together, these interim data shows that mRNA-1647 effectively immunizes seronegative subjects to level at/or well above seropositive individuals.

Slide 14 shows the same representation of the data, only this time for the seropositive subjects in the trial. Here, placebo subjects started off with neutralizing antibody titers. The average level with, as I described, was 5,588. After both the first and second vaccination, we see marked increases in neutralizing antibody titers. So both vaccinations boost the neutralizing antibody levels well above the baseline. And this is true for epithelial cells as well as fibroblast. With epithelial cells, we see a 10 to 19 fold increase above the CMV-seropositive benchmark. And with fibroblast, we see a two to four fold increase. It's worth noting that this boosting of seropositive individuals has not been observed with prior vaccines.

In terms of safety and tolerability, the vaccine was generally safe and well tolerated, without serious adverse events. Local adverse events included pain, redness and swelling at the injection site. And the most common systemic adverse events were flu-like symptoms of fatigue, fever, chills and myalgia. The adverse events seem to be more common and tend to be more severe in seropositive subjects in after more than one vaccination. In other words, they tend to correlate with the potency of this vaccine to elicit a specific immune response. That said, the adverse events are of a type that one expects to see in a healthy volunteer vaccine trial and are consistent with the safety and tolerability profile that we've seen in our other vaccine trials.

As a reminder, the data I've described thus far, the interim data as analyzed one month after the second dose. Our regimen is a three dose regimen at zero, two and six months. And on this slide, you can see preliminary results from a small cohort of seronegative subjects for which we have data out to a year following the three dose regimen. The solid gray line is the level of seropositive-neutralizing titers against epithelial cell infection. And you can see that everyone starts at zero, gets to the level I previously described by month three and are further boosted at month six, so that they remain at/or above the level of seropositive at least out to a year with a relatively shallow decline over time. My expectation is that this durability is a function of eliciting strong T cell help, which we know is an inherent feature of our mRNA vaccine platform.

So in summary, we're very pleased with these CMV data. We've shown seronegative subjects who were successfully immunized to generate neutralizing titers, while

seropositive subjects were boosted to level above their baseline, something that I don't believe the vaccine community has seen before. mRNA-1647 was generally safe and well tolerated, and we have early evidence of durability out to a year. We're excited by these results and are quickly moving to start a Phase 2 dose confirmation study. Phase 3 preparations are well underway. And importantly, FDA feedback suggests a regulatory path to approval using prevention of primary infection in a population that would include women of childbearing age as a basis for licensure, as opposed to a licensure that would be based only on demonstrating the prevention of infection in newborns. We believe a Phase 3 trial with this endpoint is achievable with less than 8,000 subjects.

Prevention of CMV in women of childbearing age is a very significant unmet need, which we expect will translate into a large commercial opportunity. Currently, there aren't any vaccines on the market for CMV. And we're targeting a highly motivated population, with clear opportunities down the road for label expansion. The sales effort should be focused, calling on OB/GYNs and pediatricians and assuming pricing similar to other innovative vaccines, one can quickly get to a multibillion-dollar annual sales potential.

Moving to the cancer vaccines modality. Recall that both we and NCI demonstrated at ASCO the ability of our personalized cancer vaccine to induce T cells against the new antigens that we encode. The NCI has now completed enrollment of five subjects in their trial. They used our personalized cancer vaccine as a single agent in an attempt to further boost the expansion of tumor-infiltrating lymphocytes that they had given to a heavily pretreated patient population. They have not seen any responses to the vaccine as a single agent in these five patients.

In contrast, our PCV program is designed primarily towards testing the ability of a personalized cancer vaccine to work in synergy with a PD-1 inhibitor and in earlier stages of disease. And to that end, we're actively enrolling patients with melanoma in the randomized Phase 2 trial, where we will compare our personalized cancer vaccine in combination with KEYTRUDA versus KEYTRUDA alone for the treatment of patients in the adjuvant setting. The Phase 1 PCV trial also continues to enroll. And finally, KRAS as a target is getting a lot of attention these days. And our approach is to use the four most prevalent KRAS mutations as a cancer vaccine. The trial for our cancer -- for our KRAS vaccine in combination with KEYTRUDA is being run by our partner, Merck. And the Phase 1 targeting pancreatic, colorectal and lung cancer is ongoing.

Moving to the intra-tumoral modality. We have three programs in this sphere, with OX40 ligand, the Triplet and interleukin 12. Starting with mRNA-2416, which encodes OX40 ligand, a potent co-stimulator of immune activation. The Phase 1 is completing the monotherapy arm and currently dosing patients with a combination of OX40 ligand and durvalumab. We're no longer moving forward with just monotherapy of OX40 ligand, but we'll focus our efforts on the combination with durvalumab, which we intend to move into a Phase 2 cohort in patients with advanced ovarian cancer once the dose escalation and confirmation cohort is complete.

The Phase 1 trial for mRNA-2752, which encodes for OX40 ligand and two pro-inflammatory cytokines, IL-23 and IL-36, is ongoing. We intend to test the combination of this triplet with durvalumab in several tumor specific cohorts. Finally, our IL-12 program

partnered with AstraZeneca based on a similar rationale is also ongoing. In our localized regenerative modality, the Phase 2 VEGF trial is ongoing. Recall that our partner, AstraZeneca, has opened additional sites in Europe with the goal of increasing enrollment here.

So let me spend the last few minutes on our systemic therapeutics, starting with recent data we shared at the R&D Day. As a reminder, mRNA-1944 encodes for an antibody against chikungunya virus. Antibodies are complex proteins, consisting both of a heavy and a light chain that come together. So mRNA-1944 includes two mRNAs; one that encodes for the heavy chain and one that encodes for the light chain. Once formed, we would expect the antibody to be secreted in the bloodstream where we can measure it. So here are the Phase 1 data. We saw a translation of CHKV-24, the antibody in a dose-dependent manner, meaning the more mRNA-1944 you gave, the more CHKV-24 antibody was made. Administering mRNA-1944 at the middle and high doses show protein production well in excess of the 1 microgram per ml level that we had pre-specified as the level predicted to be protective against the chikungunya virus. And the half-life behavior of the protein is exactly as predicted such that the amount of antibody is expected to stay above the 1 microgram level for at least four months at the 0.3 mg per kg dose.

As you can see in the inset, protein production starts within hours. This is relevant as we think of using this delivery technology to direct the synthesis of intracellular enzymes in liver cells of children born with rare genetic disease, as is the case in methylmalonic acidemia and propionic acidemia. The final point to make on this slide is the remarkably low inter-subject variability, as measured by the coefficient of variance in the range of 20% to 40%. This is similar to what is seen with recombinant proteins. In other words, our delivery technology can direct protein expression without apparent increase in the variability between subjects, which is important as it relates to our ability to define a dose response relationship, not just within a given subject, but within the population as a whole. We also show that the antibody made using mRNA-1944 is active as expected. Here, the antibody is collected from the serum of subjects and tested against virus in an assay. And it is shown here, as the proportion of patients in whom you can dilute the blood at least a hundredfold and still be able to neutralize the virus.

Let me review the safety information. Based on the preclinical toxicology, we were able to test mRNA-1944 without steroid premedications, though of course, the investigator had the option of using steroids if needed. For the low and middle doses, we could not distinguish a difference between the drug arm and placebo as it relates to safety. And recall that at the middle dose, we reached potentially therapeutic levels of protein. And at the high dose, we started to see infusion-related reactions that are typically associated with lipid nanoparticles, and in fact, with recombinant proteins at large. These were anticipated in the protocol. They occurred within hours of the infusion, were clinically resolved by the time the subject went to sleep or got up in the morning and did not require medical intervention. We did not see any serious adverse events and we did not see changes in liver or kidney function tests.

To understand the performance of our technology, I'd ask our clinical pharmacology team to model the exposure that we would expect in humans based on the preclinical animal

model experience. So here in the shaded areas, you can see the 90% confidence intervals for where we would expect human protein levels to fall at each dose level. And the solid dots are the individual clinical data, landing exactly where expected. Our deliberate technology, in other words, translates from preclinical species to human with no loss of potency. And this is important because it increases our confidence in the predicted activity of the 0.2 mg per kg dose level for MMA, our first rare disease program, because it is using the same delivery, lipid nanoparticle.

Given that we explicitly did not include steroid premedication in the first part of the study, the question is whether we can add steroids to the 0.6 mg per kg dose and further reduce or completely eliminate the infusion-related reactions that we've seen. So we're continuing to explore the pharmacology of mRNA-1944 at the 0.6 mg per kg dose level and intend to do so with both the inclusion of steroid premedication as well as by splitting the dose and giving two doses of 0.3 mg per kg one week apart without steroids. So I look forward to continuing to show the data as it emerges from this trial.

In summary, we're really happy with the results of our chikungunya antibody program, mRNA-1944. We saw a dose-dependent increase in levels of antibodies against the chikungunya virus. The antibodies were functional, with a predicted translation profile from species to species and no loss of potency when we bring it into humans. mRNA-1944 was also well tolerated in a healthy volunteer population at a dose where we saw therapeutic levels of antibodies being produced. And importantly, these results bode well for our rare disease programs like MMA that use the same LNP delivery technology as mRNA-1944.

So this brings me to the intracellular therapeutics. And in this modality, let me provide you a quick update on MMA and PA. These are similar diseases caused by inborn error of protein metabolism and are caused by MUT enzyme deficiency or PCC deficiency, both of which act intracellularly. Our MMA and PA programs aim to replace these proteins and bring the protein metabolism and the associated acidemia levels closer to normal. From a regulatory standpoint, mRNA-3704 and mRNA-3927 have similar designations. Both compounds have FDA orphan drug designation, EMA orphan disease status, FDA fast-track status and FDA rare pediatric disease designation, which upon approval, will qualify the two programs for rare pediatric disease vouchers. The Phase 1 study for MMA is currently active recruiting patients, and the PA program recently had its IND open. And we're preparing to start a Phase 1/2 trial there shortly.

Now regarding MMA, the initial cohort was limited by FDA to adolescents between the ages of 12 and 18. And during the summer, we had gone back to the agency, and they allowed for the expansion of this age bracket to include patients older than eight. While we're continuing the dialogue with FDA regarding further modification to the enrollment criteria, in the past few weeks, this amended protocol has been approved by the IRBs of the first few institutions. So I look forward to updating you on our progress soon. PA has a similar design and similar initial age restrictions. And following the opening of the IND and subsequent fast track designations, we have begun start-up activities at the leading academic centers.

Let me close with Slide 32, which lists the anticipated next steps and upcoming clinical catalysts. And I'll focus you on the CMV Phase 2 start as well as the eventual readout and on the MMA and PA Phase 1/2 trials.

With that, let me turn the call over to Lorence.

Lorence Kim {BIO 18670491 <GO>}

Thank you, Tal. In today's press release, we reported our third quarter 2019 financial results. Please note, these results are unaudited.

We ended Q3 2019 with cash, cash equivalents and investments of $1.34 billion. This compares to $1.69 billion at the end of 2018. Net cash used in operating activities was $363 million for the first nine months of 2019 compared with $240 million in 2018. And cash used for repurchases of property and equipment was $25 million for the first nine months of 2019 compared to $92 million in 2018, which was the first year that we put our Norwood manufacturing facility into service.

Now recall that on January 1, 2019, we adopted the mandated revenue recognition standard, ASC 606, using the modified retrospective transition method applied to those contracts which were not completed as of January 1, 2019. And so the decreases in total revenue for Q3 and for the first nine months of 2019 compared to 2018 were mainly attributable to the adoption of this new revenue standard. Revenue for Q3 2019 was $17 million as compared to $42 million for Q3 of 2018. And for the first nine months of 2019, revenue was $46 million compared to $100 million in 2018. Total revenue under the previous revenue recognition standard would have been $25 million for Q3 2019 and $80 million for the first nine months of 2019.

R&D expenses for Q3 2019 were $120 million compared to $109 million for Q3 2018. For the first nine months of 2019, R&D expenses were $379 million compared to $304 million in 2018. The increase in Q3 and for the first nine months of 2019 compared to prior year was mainly driven by an increase in personnel-related costs, including stock-based compensation, with additional increases for the first nine months of 2019 being driven by higher clinical trial, manufacturing costs and increase in lab supplies and materials, and an increase in consulting and outside services.

G&A expenses for Q3 2019 were approximately $28 million compared to $19 million in Q3 2018. And for the first nine months of 2019, G&A expenses were $84 million compared to $56 million in 2018. The increases in Q3 and the first nine months of 2019 compared to the prior year were mainly due to the additional costs of operating as a publicly traded company, including an increase in personnel-related costs and stock-based compensation, consulting and outside services, legal and insurance costs.

Let me now drill down on our balance sheet strength. We ended Q3, as I mentioned, with cash, cash equivalents and investments of $1.34 billion. That balance sheet is augmented by our access to a number of grants. We are fortunate to have established strategic alliances with government-sponsored and private organizations, including DARPA,

BARDA and the Bill & Melinda Gates Foundation. And so as of September 30, 2019, we've recognized $59 million in revenue to-date, while we have a total additional available funding of $187 million, comprising $99 million of committed funding and another $88 million of non-committed funding that we can tap into.

I'll turn now to where we expect to end 2019. We ended 2018 with $1.69 billion in cash, cash equivalents and investments. And early this year, we guided to a year-end 2019 cash balance of $1.15 billion to $1.20 billion. We've reiterated that guidance on subsequent quarterly calls. And today, we are guiding the year-end cash at the high end of that range. That is, we expect to have approximately $1.2 billion at the end of 2019. This works out to a change in cash of less than $500 million for 2019.

I also want to highlight two specific cash flow line items, our cash used in operating activities and purchases of property and equipment by quarter. In Q1, we used $152 million of cash in these two items. That number included $22 million of in-licensing payments, but we have no further in-licensing payment obligations to these entities going forward. And then you can see the decline in our quarter-over-quarter cash used for these items and a year-to-date number of $388 million. And so when we look ahead to the full year on these cash flow metrics, we can expect 2019 net cash used in operating activities and purchases of property and equipment to total approximately $500 million. As we've said in the past, this reflects our ongoing focus on allocation of our shareholders' capital toward value-driving investments in our portfolio and platform.

Lastly, as we look at 2020, we are issuing guidance now for next year around these same cash flow metrics. I'll start by noting that we actually expect the trend to be relatively flat year-over-year. This trend is really due to a combination of factors. First, we had nonrecurring costs, such as the $22 million of in-licensing payments in 2019. Also at this time, with Norwood operating well, our need for significant new facilities and associated capital expenditures is limited. And our pipeline, while it's advancing well, is actually not burdened with very large trials in 2020. For instance, while we are planning for a substantial Phase 3 CMV vaccine study, that program only requires pre-investment in 2020. And lastly, I'll note that our partners fund significant development costs for programs such as RSV, Zika, KRAS, IL-12, VEGF and chikungunya antibody. And so for these reasons, we do not expect growth in our cash needs for next year, while being able to fund significant pipeline advancement and ongoing platform development.

As a result, our guidance is that we expect net cash used in operating activities and for purchases of property and equipment to total $490 million to $510 million for 2020, very similar to where we will end 2019. As I hand it back to Stephane, I'll close again with our pipeline, which reiterated my last point on the number of programs that we've highlighted that our partner-funded. Stephane?

Stephane Bancel {BIO 15174250 <GO>}

Thank you, Lorence. To close, I would like to spend a couple of minutes on the development products and why we are so excited about them and what they can do for patients. Let's start with our innovative vaccines. We now have in the clinical studies four important innovative vaccines; the CMV vaccine, RSV vaccine, a combo hMPV+PIV3

vaccine and the Zika vaccine. There are no approved vaccines to protect humans from these five viruses. The morbidity and mortality costs around the world by these five viruses is devastating. We believe CMV, RSV and our hMPV+PIV3 combo are each multibillion dollar annual fixed sales opportunities and Zika is a several hundred million-dollar annual fixed sales opportunity. We know that our vaccine translates well from preclinical models to Phase 1 data. And it is well documented in the pharmaceutical industry that vaccines, once they show a positive Phase 1, have the highest probability to launch across any therapeutic area.

We have five immuno-oncology programs in the clinic that is a remarkable pipeline. For all of five oncology programs, our aim is the same. Can we add an innovative mRNA medicine to a commercial PD-1 or PD-L1 to improve the response rate of these patients? Checkpoints are wonderful medicines, but unfortunately, most patients do not respond to checkpoint inhibitors. We believe there is a large commercial opportunity to improve the complete response rate of checkpoint inhibitors, and we have five opportunities to try to do that.

And finally, in rare diseases. Here too, we have five important medicines in development. Three of these are designed to treat devastating diseases for which there are no approved medicine on the market; MMA,PA, GSD1a; and two of them are designed to improve the standard of care for patients for PKU and Fabry. Our priorities for 2019, 2020. Priority number one is to execute on our pipeline. I am pleased with the progress across the board in 2019, especially with clinical data, more CMV vaccine and our antibody against chikungunya virus programs as well as our PCV program now in Phase 2. Priority two was named new development candidate in our existing modalities. We then have new DC for GSD1a earlier this year. And priority number three is to create new development candidate in new modalities. We are continuing to make good progress in several new modalities, and we look forward to sharing some updates in 2020.

In summary, we are pleased with the pace of execution. The key highlights of our third quarter are the positive Phase 1 data for CMV and the antibody drug, chikungunya. We have up to $1.5 billion to invest in the business with enough cash, balance and occurrence. We invest approximately $500 million in our company in 2019 and also approximately $500 million in 2020. We intend to continue to do new partnership with biopharma companies and to apply for new grants.

We know that we have a special opportunity, and we are committed to delivering on the promise of our science and bring forward a new class of medicines for patients. I would like to end our remarks by thanking the many people who participate in our clinical studies, including patients, healthy volunteers and physician. I would also like to thank the great team at Moderna, working hard every day to make this vision a reality.

With that, we are now happy to take any question. Operator?

Questions And Answers

Operator

(Question And Answer)

Thank you. (Operator Instructions) And our first question comes from the line of Matthew Harrison with Morgan Stanley. Your line is now open.

Q - Matthew Harrison {BIO 17603148 <GO>}

Great. Good morning. Thanks for taking the question. Thanks for the detail on the updates here. I guess two parts for me. So first, could you just talk about progress and being able to enroll patients in MMA? I think you've had sites open for a bit of time here and now you've been able to expand the age group, but it doesn't sound like you've enrolled a patient yet. So maybe you can just talk about, what's going on there? And then second on chikungunya, maybe just talk about when we should expect to see some information about dosing profile, you're able to drive those higher with premedication or split dosing?

A - Tal Zaks {BIO 19987702 <GO>}

Thank you, Matthew. This is Tal. Let me address both of your questions. You're right on MMA, we have not yet dosed our first subject. We -- as noted initially, FDA had requested that we limit the first three subject to ages 12 and above, and before we can proceed to the children that are young -- as young as one-year old where the highest unmet need is.

And I think, we've found in opening the sites and trying to enroll this that there are several factors that come into play, but the time somebody gets to be an adolescent, if their disease has been severe they've often had a liver transplant. In fact, liver transplants in the U.S. are recommended between the age of a year in preschool, and when a kid with MMA shows up for a liver transplant, they move to the top of the queue, so there's not much waiting.

Those who don't get a liver transplant often suffer from kidney deterioration, and we can't do a Phase 1 trial with really abnormal kidney function. So we've gone back into summer as noted to discuss with FDA lowering the age criteria, they had agreed to take it down to the ages of eight and above, and while we're still in dialogue with them about that the amendment to enable us to do that has just recently opened at some of the leading institutions.

And I look forward to enrolling the first subject soon. It is -- it has been a challenge for all those factors, that I alluded to. But I think, between lowering the age and now being open at some of the select institutions we should see progress soon.

Now you'd asked me about the chikungunya. And when do you expect to see data? The -- this is a healthy volunteer trial. So we had gone back to the safety monitoring committee aligned with them on the next steps, and were actively working with the site to get the next cohorts enrolled, so as soon as data will become available and we understand what it is. We have we'll be sharing it with you, being a healthy volunteer trail it should move relatively quickly.

Operator

Thank you. And our next question comes from the line of Ed Tenthoff with Piper Jaffray. Your line is now open.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Great. Thank you very much. Thanks for the update and all of the great -- on all of the great progress. I want to ask about the CMV vaccine, really just kind of little bit better clarity on what you see is the path forward here appreciating a Phase 2, dose conformation start next year. Can you give us a sense of the size of that study? And maybe how long it would take? And then looking kind of forward, how soon do you think you could actually initiate pivotal studies, in women of childbearing age? Thank you.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you, Ed. This is Tal, I'll take that question.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Hey, Tal.

A - Tal Zaks {BIO 19987702 <GO>}

So a couple of points, first in terms of size and timing, the Phase 2 is about 250 subjects or so, the design is really meant to confirm the dose and give us more color on both immunogenicity and safety and tolerability, so that we are able to pick the right dose for Phase 3. That being said, the time should be relatively quickly, because the -- we'll make a decision based on a three-month endpoint once everybody has been dosed similar to what the interim data that we've shown in the Phase 1. By then, we will have the further follow-up post the third dose in the Phase 1. So we'll have overall more data to be able to share and substantiate that decision.

Now the path to Phase 3, I think the big change here for me has been the fact that FDA has provided guidance that speaks of the potential for licensier based on the prevention of primary infection. And that's very significant because that means that it is eminently doable with the trial of the side that we've discussed. In terms of launching that, I would say the two gating factors, I think to actually launching that study are going to be the Phase 2 data, and some regulatory discussions, this was just a very preliminary initial guidance, of course, before one launches a Phase 3 trial here, we need to have those more deep discussions with FDA and other agencies to make sure we're launching the right study.

Now once we get their agreement, I think the design is fairly straightforward one would expect an incident rate of about 1.5% a year. So hopefully with a couple of years of follow-up once everybody is enrolled. You could see the effect that you're looking for and wrapped it up. So that gives you a rough sense of the overall timeline here.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Great, it's super helpful. And then if I may just ask a second question, appreciating that it's with Merck. When could we get data from the enhanced RSV vaccine? Thanks so much.

A - Tal Zaks {BIO 19987702 <GO>}

Yes, that's a great question. I asked it as well. The truth is that they're pretty efficient in running these trials, they've got a long track record of running healthy volunteer vaccine trials, and of analyzing data quickly. So as soon as they have something material to share with us, we'll of course, share it with you.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Awesome. Thanks so much guys.

Operator

Thank you. And our next question comes from the line of Salveen Richter with Goldman Sachs. Your line is now open.

Q - Salveen Richter {BIO 15151450 <GO>}

Good morning. Thanks for taking my questions. Maybe a first question here, and how your chikungunya vaccine clinical development plan, reflects the guidance that was provided by the FDA? And then a second question on the chikungunya antibody program here, could you just walk us through your plans for evaluating repeat dosing, recognizing that you do have this cohort study coming up with two doses about a week apart?

A - Tal Zaks {BIO 19987702 <GO>}

Thank you, Salveen. This is Tal, I'll take that. So the plan to develop a chikungunya vaccine is a great the great question. It's true that FDA is giving a potential path, in fact, there's a big discussion in a couple of days time down at FDA, where our team is presenting alongside others to flush out what that could look like. To date it hasn't been clear how one could develop it, and do it in a commercially viable setting, to the degree that the discussions with the agency in the near term will actually paint a path where it would be worth our capital and time to go there will obviously be looking at it carefully.

So I don't have a clear answer because I think this is a work in progress. To date, we've not seen a commercial path. I'm happy with the recent agency guidance, and we'll see how the conversations go. Your question on repeat dosing for the monoclonal antibody program. The goal here is to substantiate our ability to stack pharmacology.

In other words to show that the antibody level, the protein level production of two doses given a week apart behave as expected in the clinic. We have seen that in the preclinical toxicology in the non-human primate, but I think being able to show that and leveraging the fact that the adverse event profile seems to be a very quick infusion related reactions that come on quickly -- and come up come up quickly. We would expect that there would -- there should not be any stacking in terms of safety, while there would be stacking in terms of pharmacology. And that's the rationale of doing two doses one week apart at a

dose where we actually have not seen any significant adverse events. Do that answer the question.

Q - Salveen Richter {BIO 15151450 <GO>}

Yes, that was helpful. Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you.

Operator

Thank you. And our next question comes from the line of Cory Kasimov with JP Morgan. Your line is now open.

Q - Cory W. Kasimov {BIO 3009346 <GO>}

Hey, good morning, guys. Thanks for taking my questions. So two as well, so first is just following up on CMV. And as you get the Phase 2 sites up and running and plan for your Phase 3. Are there any additional processes or challenges, we should be thinking about giving the new modality or introducing or is this something that, you think you can go pretty quickly from a patient accrual point of view?

And then my second question, is regarding your natural history studies for MMA and PA. What's the age range you have there for the natural history? And do you think that provides any read through to how enrollment might go once you have a broader age range introduced for your clinical trials 87 subjects at this stage seems like a pretty decent number for rare diseases? Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you, Cory. It's Tal, let me take those two in sequence. I don't foresee any additional challenge for enrolling the CMV out of Phase 2 or Phase 3 that are platform dependent, and I'll sort of give you the two reasons for that. The first is the totality of safety and tolerability data that we've seen across the portfolio are consistent with one -- with what one would expect. We haven't seen anything surprising. There's no scientific reason to expect anything untoward, and we hadn't seen anything untoward in preclinical.

So I think, this is going to be a vaccine platform that will behave as such, in fact, the CMV data suggest that is the more prudent vaccine is, the more adverse event you get the flu like symptoms, but the adverse event, the type of adverse events as I've noted is what you'd expect. I think the other reference point is the fact that this is the platform, as a platform is no longer considered as an adjuvanted vaccine by agency, and I think that is also reassuring in that respect. So I don't see any hurdles that are function of the platform to enrolling CMV or getting itto market frankly.

Your question about the natural history study is a good one, you're right, I was pleased by the rate of enrollment and the numbers that we've gotten there to-date. The age

distribution is pediatric. We are seeing I think a median age of around five to eight roughly speaking, looking at the totality of the data so far. It is providing us I think good information as it relates to the variability that biomarkers clinical endpoints all the things we've expected to see. And I think it is substantiating our sense that the older the children are at least those that are found at any given time points in terms of prevalence. Certainly in the U.S., tend to have either undergone transplant or have deteriorated kidney function. So it all -- it is very coherent I would say overall with what we're seeing in starting up sites now, and trying to enroll the first subjects into the MMA trial.

Q - Cory W. Kasimov {BIO 3009346 <GO>}

Okay, that's helpful. Thanks, Tal.

Operator

Thank you. And our next question comes from the line of Alec Stranahan with Bank of America. Your line is now open.

Q - Alec Stranahan {BIO 20630524 <GO>}

Hey guys. Thanks for taking my question. So on the ongoing follow-up from the Phase 1 trial of the personalized cancer vaccine. I appreciate that the objective of the Phase 1 is primarily to assess safety and immunogenicity. But do you intend to present any outcomes type data from the study beyond immunogenicity, say with the next six months or will we need to wait on the Phase 2 study for this sort of analysis? And then on the KRAS vaccine, is this something that Merck will report, since they are the ones leading the study?

A - Tal Zaks {BIO 19987702 <GO>}

Hi, Alec. It's Tal. So yes, yes to both questions. The Phase 1 PCV data we will share that data, once we've got sort of a cogent totality of it every Phase 1 or every clinical trial that we do as a matter of policy and ethics in the company. We will publish and this is no different. So at the next opportune moment when we have a body of evidence there, we will share it including the totality of the clinical data.

And, in fact, I think it is the clinical data that is important to me. And I think the rest of the world to assess activity here. In that regard, recall that one of the cohorts there is testing patients with previously refractory to PD1 inhibitor. And so I think, that will be meaningful data once we have it. KRAS you are correct, Merck is running it. And so Merck will be I think the party reporting out the data, and I look forward to that as well.

Q - Alec Stranahan {BIO 20630524 <GO>}

Okay. great. Thanks. And I had one more question, if I may. So I noticed that the follow on Phase 1b for the hMPV+PIV3 vaccine was posted CT.gov last week, and looks like you dose the first patient in the study. So a few questions. What kind of safety metrics are required for gating between the adult and pediatric cohort? What dose levels of the vaccine will be included in the study? How quickly do you foresee the study completing?

And from your conversations with the FDA, do you have a sense of potential registration path following the study? Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

Those are great questions. Let me answer them in turn. So the safety metrics are your typical vaccine safety metrics. So you look for safety tolerability, and we have a safety monitoring and independent safety monitoring committee, that reviews that and we've actually had our recent inaugural meeting with them. And so it won't be just us making that, we've got some of the world's experts in this actually looking over our shoulders and helping make those decisions. The dose level honestly on the top of my mind. I don't remember is the honest truth. I happy to get back to you. If it's not in clinical trial, double check that.

The path to approval, that's a great question. I think as we had disclosed in the past, we had an initial interaction with the agency. We had a type C meeting in response, and we had a line of sight to the possibility to have a pivotal trial, that would test both viruses together.

So roughly speaking the path there is demonstrate safety in the seropositive toddlers and then go on to a larger Phase 3 study that would demonstrate efficacy and seronegative toddlers, because remember, we're trying to establish immunogenicity from before anybody has been exposed. So I can't give you a clear time to completion and as with CMV, before one dose into the Phase 3 trial, we're going to have to have more in depth discussion with the regulatory authorities before we do this.

Q - Alec Stranahan {BIO 20630524 <GO>}

Great. Thanks for the color.

Operator

Thank you. And our next question comes from the line of Hartaj Singh with Oppenheimer. Your line is now open.

Q - Hartaj Singh {BIO 18796450 <GO>}

Great. Thank you for the questions. I just want to ask one question about an asset that you've got the furthest along AZD-8601. I know that's in partnership with AstraZeneca. The Cabot study, I mean that's including patients for almost about a year and a half now. Just any thoughts there, and could -- with the readout of this Phase 2 basically a study could AZ move that along faster or into a pivotal clinical trial. So any thoughts there? And then I've got a couple of quick follow-ups.

A - Tal Zaks {BIO 19987702 <GO>}

Hi, Hartaj. It's Tal, let me take that. Two points on that trial, It is, I mean I've to give AZ credit, they've designed a very informative pharmacology trial, because they're using sort of state of the art as you may recall oxygen label test imaging to really very finely map the

heart and the areas at risk. Now the challenge for them has been that they the half-life of that isotope is extremely short, and so you have to find a hospital that basically has a cyclotron next door. And so what they've done I think in this past year has been to go and find additional sites where they can launch that trial. So they're now open, not just in Finland as they were, but actually, in Germany and in the Netherlands and are actively looking for patients. The good thing about that trial is, at the endpoint, once they enroll the subject should be relatively quickly because it a six-months endpoint. And the trial overall is not very large. I think that's as much insight as I have in terms of enrollment. Could they move faster? I think there are other ways that one could think of how you would develop an intra-cardinally injected molecule. They've got a ton more expertise in this space than I do, and they're actively thinking and working along those fronts. But frankly, I'd have to defer to them to give you more color on what that could look like.

Q - Hartaj Singh {BIO 18796450 <GO>}

Great. Thank you, Tal.

A - Tal Zaks {BIO 19987702 <GO>}

I think you have a few follow-ups. Yes.

Q - Hartaj Singh {BIO 18796450 <GO>}

Yes. A quick one. I'll just mention them quickly. I know you had mentioned that the seropositive patients, there's -- the data seen in those in the CMV trial, that had not been seen previously in other trials. For your Phase 2 and your Phase 3, will your stratify by seropositives? And could those be a group that you could get approval just on their own? Just any thoughts there?

A - Tal Zaks {BIO 19987702 <GO>}

Yes. So a couple of thoughts. I think the fact that one sees this effect on seropositives, I think, is really scientifically interesting, and I've got a deep curiosity to try and figure out whether it could translate to benefit. That being said, in terms of enrolling on the Phase 3 and the eventual label, I'd make two points. One, I think the Phase 3 will be focused on seronegatives because that's where you can see the obvious effect of preventing infection. It's hard if not impossible to actually demonstrate a clinical benefit in the seropositive, although, of course, I remain intensely curious about that. The second point to note is that FDA in their response had told us that they understand that one is not expect to demonstrate the benefit initiatives seropositives, but in order for this vaccine to be viable in terms of access to patients and having an impact on the population, you would need a label that would encompass both population. So the expectation is that we would demonstrate immunogen -- I'm sorry, prevention of primary infection in the seronegatives, but we would demonstrate safety and tolerability in the entire population that is all-inclusive of seropositives, and that could lead then to a label irrespective of sero status. Does that answer?

Q - Hartaj Singh {BIO 18796450 <GO>}

That's great, Tal. Thank you.

Operator

Thank you. And our next question comes from the line of Yasmeen Rahimi with Roth Capital Partners. Your line is now open.

Q - Yasmeen Rahimi {BIO 20388907 <GO>}

Hi team. Thank you for taking the questions. Questions are all around PA. Congrats on recently receiving fast track designation. So the first one is for you. Can you tell me when you're thinking about dosing strategy for MA -- I'm sorry, PA, how it will differ from your strategies in 3704? And then when we think about sort of key PD biomarker, what key biomarker, in your view proof, if that is proof of concept? And then part three of the question is, what do we know from the literature in regards to what level of expression of PCC one needs to achieve to provide therapeutic benefit?

A - Tal Zaks {BIO 19987702 <GO>}

Thank you, Yasmeen. Great questions. Let me take them one at a time. The dosing strategy is roughly similar to what we expect to see in MMA. It is based on our translation of the preclinical data. We've done long-term models in animals and have used that to sort of extrapolate. So far, the technology has extrapolated nicely from all the preclinical species in the various modalities. And so I would expect this one to be similar. So I expect the dosing strategy to be once every two or every three weeks. So I think we're going to have to define that and see the effect we have on Phase 1. There is a whole slew of biomarkers here that one looks at, and I think it's premature to specify which one is going to be the one. It is true, I think what you're indirectly alluding to is that the biomarkers on PA are not maybe as clear-cut as they are in MMA. I think that remains to be proven. I think the information we hope to achieve from the natural history study in terms of biomarker levels where we're collecting it should also be informative. So I mean we'll continue to update that as we learn more, I think, our understanding of the literature and -- of our natural history level here is evolving.

In terms of the level of expression needed, I think it's hard to quantify. What we've seen from our preclinical models suggest that it is a similar level that we need of MMA in order to have the effect in the mice, be effective as profound in the PA models as it is in the MMA models. And so we expect a similar dosing level to be required for both. It may be a little bit higher given that, in PA, we are encoding for two proteins, not one, right? So on a molar basis, we would expect similarity on a mg per kg. It may be a tad higher. But it's clearly within the same ballpark.

Q - Yasmeen Rahimi {BIO 20388907 <GO>}

Thank you. And I have -- I may have a quick follow-up in regards to the antibody against chikungunya. And we're excited to see the data from the two doses of 0.3 mg per kg. How far out are you going to assess safety? So what are you planning to do? And what has regulators asked you to do?

A - Tal Zaks {BIO 19987702 <GO>}

Just to clarify the question. You are asking how far are we looking at safety?

Q - Yasmeen Rahimi {BIO 20388907 <GO>}

Yes. Yes. Just monitoring the safety since you're giving for the first time two doses, how far out will you actually monitor these patients, and therefore, will provide for us the safety results?

A - Tal Zaks {BIO 19987702 <GO>}

Several weeks, I would say. I don't think it's going to be much longer than that. The reality is you've seen the adverse event profile to date, it really is a function of the LNP, as I understand it, more than the protein that we make. We'll be continuing to follow these patients -- I'm sorry, these subjects for weeks, but I've not seen anything that leads me to expect that there's a long-term challenge here. I think the safety profile, within a week, we'll describe what it is.

Q - Yasmeen Rahimi {BIO 20388907 <GO>}

Thank you.

Operator

Thank you. And our last question comes from the line of Alan Carr with Needham. Your line is now open.

Q - Alan Carr {BIO 15355437 <GO>}

Hi. Thanks for taking my questions. Can you give us an update on where the other rare disease programs stay? And might those be a little bit easier to enroll? And then also, do you have any update on ACS program with Relaxin? Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

Yes. So this is Tal. Let me take them. They're in their preclinical phases. Once we file the IND and we get rolling, we'll update you accordingly. And I think we don't typically comment on where exactly in the early research space they are. I think the same holds true for Relaxin which is partnered with AstraZeneca.

Q - Alan Carr {BIO 15355437 <GO>}

All right. And then you also mentioned in the press release some interest in more partnerships and that sort of thing. I was wondering if you were getting at more in terms of with academic institutions or talking about partnering programs with pharma and that sort of thing? Thanks.

A - Stephane Bancel {BIO 15174250 <GO>}

Yes. So thank you. This is Stephane. So I mean if you look at the company history, as you know, we have done a lot of partnership. On the last 12 months, you might have observed, we have been quite happy just because we are very busy. We're preparing the IPO and then spending a lot of time on the road as a newly public company. But if you look at what the team has achieved and what we believe a platform can provide in term of new

medicines for patients, we have a prime abundance, which is a wonderful point to have in this industry. And so we think that we cannot take all the drugs that are coming from Stephen's team on the platform into the clinic by ourselves. And so we will continue to have dialogue with biopharmaceutical companies. If you look at the company history, we work around the clock there of our capital since inception of the company through partnerships. And we think this is a wonderful way to tap capabilities that we don't have, to tap capital that we don't have and to just increase the opportunities of getting Moderna's mRNA medicines to patients and to a finish line. And so we anticipate to continue to have new partnership set up in the quarters to come.

Q - Alan Carr {BIO 15355437 <GO>}

And what's the profile of programs that you might partner versus keep in-house when you're looking at this?

A - Stephane Bancel {BIO 15174250 <GO>}

So I mean speaking to what we have done before is looking at where do we have expertise and keep us looking at biology risk. So this is what selling for.

Q - Alan Carr {BIO 15355437 <GO>}

Great. Thanks for taking my questions.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you.

Operator

Thank you. And this concludes today's question-and-answer session. I would now like to turn the call back to Stephane Bancel for any further remarks.

A - Stephane Bancel {BIO 15174250 <GO>}

Yes. Thank you very much for joining us today and for your questions. We look forward to seeing many of you in the coming weeks and at the JPM conference in January. We also wanted to share with you that we are planning to start an Annual Day, focused on manufacturing and digital. This new Investor Day will complement our Science Day, which usually happen in the spring, and the R&D Day, usually in September.

So 2020 manufacturing and digital events will be held at our Norwood plant on the afternoon of March 4, on the back end of Cowen conferencing bottom. Juan Andres, who leads our technical development, manufacturing and quality, as well as Marcello Damiani, our Chief Digital Officer, will host the event. They will share with you what the progress their team has made in 2019 and the new initiatives they will do in 2020. We hope to see many of you on the afternoon March 4 in Norwood. Have a nice day.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.