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PRESENTATION

Operator

Good morning, and welcome to the Moderna Corporate Update and 2018 Financial Review Conference Call. (Operator Instructions) Please be advised that the call is being recorded.

At this time, I would like to turn the call over to Laura Schneck, Investor Relations at Moderna. Please proceed.

Laura Schneck - *Moderna, Inc. - IR & Associate Director*

Thank you, operator. Good morning, and welcome to the Moderna Corporate Update and 2018 Financial Review Conference Call.

This morning, we issued a press release that outlines the topics of events discussed today. You can access the press release as well as the slides that we'll be reviewing by going to the Investors section of our website at modernatx.com.

Today, on this conference call, we have Stéphane Bancel, our Chief Executive Officer; Tal Zaks, our Chief Medical Officer; and Lorence Kim, our Chief Financial Officer. Stephen Hoge, our President, will also join us when we open up for Q&A at the end.

Before we begin, I would like to remind everyone that this conference call will include forward-looking statements. Slide 2 of the accompanying presentation and our SEC filings have 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 results and developments.

I will now pass the call over to Stéphane.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Laura, and good morning, everyone. Welcome to Moderna's first quarterly conference call as a public company.

As you know, we believe at Moderna, that mRNA has a potential to become a new class of medicines. And since Moderna's inceptions, we have worked hard to build the company that could become the leader in the field. What that drives in us is a potential to make new medicines for untreated diseases, medicines which cannot technologically be made using small or large molecules.

We believe that, over time, this can go beyond our current strategic areas of infectious disease: oncology, rare genetic diseases and cardiovascular diseases. Because mRNA is an information-containing molecule, we believe that this new class of medicines and the company we have built around it may have many advantages. First, we are able to use similar technology components across programs. As a result and over time, as we derisk the use of those components, successive mRNA medicines should have a higher probability of technical success than traditional medicines.

Second, by investing in automation, robotics and IT, we should be able to move very quickly on our small molecule or large molecule technologies. Every time we make a product at every scale, we intend to use similar manufacturing processes, accelerating time lines for both the discovery of new development candidate as well as the scale-up for clinical trials. And finally, because we make mRNA in a liquid-phase sulfur solution, we believe that over time, our costs of -- would be similar to small molecule injectable commercial products. With the possibility to build the new class of medicines while helping many patients and creating value for our shareholders along the way, we focus on managing 4 different type of risks: technology risk, biology risk, exception risk, financing risk.

As you can see on Slide 4, it has always been our goal to derisk each of our modalities by beginning with a development candidate that could allow us to systematically and separately address the biology risk and the technology risk. Early on, we determined that vaccines presented the least technology risk and, therefore, decided to pursue this modality first.

From a biology risk perspective, we started with influenza vaccine to see if we could safely demonstrate in the Phase I trial a defined level of antibodies in healthy volunteers not previously exposed to the virus. At the time of our IPO, we had advanced programs across 3 of our modalities in the clinic: cancer vaccines, intratumoral immuno-oncology and localized regenerative therapeutics.

Already in 2019, we have initiated human dosing in our fifth modality, systemic secreted therapeutics with mRNA-1944, an mRNA encoding antibody against the Chikungunya virus. This program uses the same delivery technology as the 4 rare genetic disease programs: MMA, PA, PKU and Fabry as well as our Relaxin cardiology program.

On Slide 5, you can see our 2019-2020 priorities. As we build the company, our top priority is to advance our development pipeline to get these important innovative medicines to patients. We're also focused on growth. And therefore, other subsets of our team focus on creating new development candidates within our existing 6 modalities. Given that these new development candidates use the same technology component that's also already in the clinic, we're able to significantly reduce technology risk and move swiftly from a drug concept to a development candidate. Our further real focus is on the long term, meaning inventing new modalities, which can deliver mRNAs to new tissues and/or cell types.

On Slide 6, outlined in red, you can see our pipeline has advanced in the 90 days since our IPO. Let me spend a minute on this from right to left. We are planning a Phase II study for PCV and the Phase II trial for OX40L ligand in ovarian cancer. We reported positive interim Phase I hMPV+PIV3 vaccine data, supporting the move into a Phase Ib HD escalation study in children. We have begun dosing in Phase I studies for mRNA encoding an antibody against Chikungunya virus and for the immuno-oncology Triplet. INDs are now open for MMA and IL12.

On Slide 7, let me give you a quick update about the manufacturing site in Norwood, Massachusetts. We have 4 distinct activities on the site. First, we manufacture clinical material. Since the site opening, we have successfully manufactured clinical-grade mRNA and then moved to formulation and then to filling and finally, labeling of our vials. We are now actively working toward vertical integration of critical raw materials like DNA plasmid used as templates to our mRNA, [buffers] and other raw materials.

We have also successfully transferred the second capability to Norwood for personalized cancer vaccine, or PCV. We started our PCV clinical trial in 2017 by making a PCV vaccine as a contract manufacturer in the U.S., using Moderna manufacturing process and the robotics we invented to

be able to make one lot personalized for one patient. I am pleased to report that we are now capable of making all our PCVs in Norwood for patients in the remainder of Phase I as well for Phase II.

The third capability transferred to Norwood, which will enable us to reduce costs, is our preclinical robotics that makes all of our research-grade mRNA and formulations.

Let me close my introduction by saying that I'm very proud of the progress our team made in 2018 and in 90 days since our IPO. Momentum and growth are very important to Moderna's success, and it is exciting to see significant progress across the business.

I would like now to turn to Tal.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you, Stéphane.

Let me now review our progress by modality. If you go ahead to Slide 9 and 10, I'll start with the prophylactic vaccines. A few weeks ago, we reported the Phase I data for our combination vaccine against 2 respiratory viruses, human Metapneumovirus and Parainfluenza Virus 3, or hMPV and PIV3. These are 2 important causes of respiratory tract infections in children and can lead to viral pneumonia and hospitalization, particularly in children under 2 years old. There are currently no approved vaccines against either hMPV or PIV3.

Now on Slide 11, as we had disclosed, the top line interim data from the study showed that a single vaccination with mRNA-1653 boosted the titers of neutralizing antibodies against both hMPV and PIV3 and that the magnitude of the boost was similar at all dose levels tested. As you would expect, all study participants had some level of baseline neutralizing antibodies against both viruses, yet 1 month after a single mRNA-1653 vaccination, neutralizing titers against hMPV rose to approximately sixfold baseline and those against PIV3 rose to approximately threefold baseline. A second vaccination 1 month later did not further boost antibody titers, suggesting that a single vaccination is already achieving a plateau in the generation of neutralizing antibodies in this pre-exposed population. mRNA-1653 was found to be generally well tolerated. No serious adverse events, adverse events of special interest or adverse events leading to withdrawal were reported. Injection site pain was the most commonly reported adverse event and the most common grade 3 adverse event. The magnitude of responses that we observed is sufficient for us to advance mRNA-1653 to a Phase Ib trial in toddlers, a trial that we are currently designing. I look forward to a further discussion of this point and other aspects of our clinical data in a future medical meeting.

Let me move to our congenital CMV vaccine on Slide 12. This is a vaccine against cytomegalovirus, which is the most common congenital viral infection impacting close to 40,000 infants annually in the United States. Congenital CMV infection can severely affect infant brain development, and it's an important cause of childhood hearing loss. There's currently no approved vaccine to prevent CMV.

Our vaccine, mRNA-1647, has enrolled the initial 3-dose levels in the Phase I trial. While we have not yet seen any immunogenicity data, the safety and tolerability data, both in this trial and across our other infectious disease vaccines, suggest that we should be able to dose escalate above 180 microgram. So we are expanding the trial to enroll 2 additional dose levels at higher doses in the range of 300 micrograms. As a reminder, 300 microgram was the top dose that we tested in the hMPV+PIV3 study.

Reviewing our overall progress on Slide 13, we have, to date, dosed approximately 950 healthy volunteers enrolled across 7 Phase I trials at doses up to 300 microgram. The emerging safety and tolerability profile has been consistent with that of marketed adjuvanted vaccines. And with a positive readout for hMPV+PIV3, we have now shown promising data from 5 Phase I programs within our prophylactic vaccines modalities, and we continue to make progress. I spoke about our plans for hMPV+PIV3 and CMV.

On Zika, we previously disclosed data for mRNA-1893, which has the potential to be a much more potent follow-on to mRNA-1325. We're in the process of writing the IND for it, and so we'll not be further developing mRNA-1325. Overall, our development of a vaccine against Zika continues to be funded by BARDA under the grant award of approximately $125 million. Lastly, our partners at Merck are preparing to initiate a Phase IIa trial of mRNA-1777, our RSV vaccine.

Let me now talk about our cancer vaccine programs. And if you advance to Slide 15, you can clearly see the immunogenicity data from the patient in the Phase I trial of our personalized cancer vaccine. As we previously disclosed, at the second dose level of 0.13 milligram, we were able to show that we elicited new antigens specific T cell responses. To date, we have dosed over 30 patients. At the top dose of 1 milligram, we have not seen any dose-limiting toxicities either for the vaccine alone or in combination with KEYTRUDA. And so we have selected this as the dose to move forward into Phase II.

On Slide 16, you can see the design of this Phase II study. It is designed to assess whether post-operative adjuvant therapy with mRNA-4157 and KEYTRUDA can improve the recurrence-free survival for melanoma patients when compared to KEYTRUDA alone. We will be testing this in patients who remain at high risk of recurrence despite having had their tumors resected. So the primary endpoint for the study will be recurrence-free survival. And we're planning to have the primary analysis done 12 months after the last subject is enrolled. This protocol has been submitted to FDA.

As an aside, I would note that we are increasing the neoantigen count in our personalized cancer vaccines from 20 to 34 neoantigens, all still encoded on a single mRNA chain. And we intend to apply this advance to the Phase II study.

Let me now turn to our intratumoral immuno-oncology programs, which you can see on Slide 18. We continue to advance the Phase I study of mRNA-2416, which encodes for the OX40 ligand membrane protein and have dosed over 30 patients on this study, some for as many as 10 cycles at doses of up to 8 milligram. We have not seen any dose-limiting toxicities. We have shown that OX40 ligand protein expression in certain injected lesions and have observed regression of injected lesions in 2 patients with advanced ovarian cancer, although these regressions did not meet resist criteria. These observations have motivated us to trigger the Phase II cohort in patients with ovarian cancer.

The top dose tested in the Phase I trial, 8 milligram, is currently in the dose confirmation stage. And this is the dose we intend for the Phase II cohort in ovarian cancer.

Let me talk about mRNA-2752, which encodes the Triplet combination of OX40 ligand interleukin 23 and interleukin 36 gamma. In January, we published new preclinical data in Science Translational Medicine showing that local delivery of the Triplet induced a broad immune response and caused tumor regressions in both injected and distant uninjected lesions in murine models. Additionally, when combined with checkpoint inhibitors, this Triplet was able to induce responses in tumor models that are otherwise unresponsive to checkpoint inhibitors. So these data provide the scientific basis for the Phase I study of mRNA-2752. We initiated dosing late last year, and we have not seen any dose-limiting toxicities in the first dose level and are now began to treat patients at the second dose level.

Finally, there's always -- there's also been progress with MEDI1191 and mRNA encoding interleukin 12. IL12 is a potent immune modulator whose preclinical profile has generated much interest as a potential anticancer agent. In the past, the clinical development of systemically administered recombinant IL12 has been hampered by systemic toxicity. We have demonstrated preclinically that intratumoral doses of mRNA encoding IL12 can be delivered safely and induced a complete response in multiple murine models, providing the scientific foundation for our partners at AstraZeneca to advance MEDI1191 into the clinic. So indeed, I'm happy to report that AstraZeneca has filed the IND for MEDI1191, and this IND is now open. This trial is designed to evaluate safety and efficacy in patients with solid tumors in combination with a checkpoint inhibitor.

On Slide 19, I want to briefly mention the modality of localized regenerative therapeutics. AstraZeneca continues to enroll patients in the randomized Phase IIa trial of AZD8601, which is an mRNA encoding for VEGF-A. As a reminder, the Phase I showed that AZD8601 was well tolerated and led to the translational of functional VEGF-A protein, which caused the dose dependent increase in blood flow where it was injected. These data were recently published in Nature Communications.

Moving next to our systemic secreted therapeutics, let me provide some context on our first program in this modality. On Slide 21, you can see that as we were assessing the biology risk for our systemic secreted therapies, we began the development efforts by including a monoclonal antibody with the goal of inducing transient passive immunity in the recipient. An antibody would represent a complex protein as it requires the co-translation of 2 separate mRNAs and the correct intracellular folding and eventual secretion to the blood of a formed antibody.

From a safety perspective, we would expect an antiviral monoclonal antibody to be safe, and we should be able to measure its blood levels. This would then allow us to quantify the PK/PD relationship, in other words, how much mRNA is required to produce how much protein in a relatively straightforward manner. Now this relationship would be of obvious relevance to our pipeline of mRNA medicines for rare diseases, particularly because the lipid nanoparticle delivery system is shared with our rare disease programs as well as with Relaxin. And so we chose an antibody against the Chikungunya virus encoded as mRNA-1944.

On Slide 22, you can see the Phase I design for this study. We're conducting it in healthy volunteers. So it should give us a read on the safety and tolerability of the formulation. The pharmacological goal is to determine how much antibody we can produce as a result of systemically administered mRNA and whether 1 day we may be able to offer people with passive immunity against infection by this virus, which today has neither vaccine nor specific therapies available.

On Slide 22, you can see our progress overall in systemic secreted therapeutics. We recently completed dosing of all 8 subjects in the first cohort of healthy volunteers in this Phase I study. And I look forward to sharing more about this study once we have a complete picture of the data. In addition, we're continuing to move our Fabry and Relaxin programs forward into clinical trials.

Finally, let me turn to our systemic intracellular therapeutics. On Slide 25, I'm happy to share today that FDA has given us fast track designation for our methylmalonic acidemia program and has allowed us to open the IND for mRNA-3704, which encodes the mute enzyme missing in children with this disease. We're now preparing to begin the Phase I2 study, and I'll come back to this in just a moment. In addition to mRNA-3704, we continue to progress the preclinical development for both propionic acidemia and phenylketonuria programs with the goal of bringing them into the clinic.

On Slide 26, let me describe the design of the MMA study. The primary objective is to evaluate the safety, pharmacodynamics and pharmacokinetics of mRNA-3704 in patients with methylmalonic acidemia. We intend to enroll pediatric patients with elevated plasma MMA levels. And the first dose level will begin with adolescents aged 12 to 18. Once we assess the safety and tolerability of this age group, we then intend to enroll patients who are between the ages of 1 and 18 years old. Following dose escalation, we anticipate the study will move into a dose expansion phase. As a reminder, we have an ongoing natural history study underway for both methylmalonic acidemia and propionic acidemia, which we call the MaP Study. As of the end of February, we have 32 patients enrolled in the study, 20 with MMA and 12 with PA.

Let me close on Slide 27 with our pipeline, which illustrates the breadth of our development programs. We're proud of our ability to advance multiple programs in parallel across many different treatment modalities and for different diseases. I look forward to updating you further as we continue to progress our programs.

With that, I will now turn the call over to Lorence to walk through the financials.

Lorence H. Kim - *Moderna, Inc. - CFO*

Thank you, Tal.

Let me turn to Slide 28. In today's press release, we reported our fourth quarter and full year 2018 financial results. Please note, these results are unaudited. We ended 2018 with cash, cash equivalents and investments of $1.7 billion. This compares to $902 million at the end of 2017. This increase was due primarily to financing proceeds, approximately $563 million in net proceeds from our initial public offering in December 2018, approximately $661 million in net proceeds from our preferred stock issuances earlier in 2018 and a $13 million premium associated with the 2018 amended and restated PCV agreement with Merck. All of this was offset partially by the cash used in 2018 to fund operations and for purchases of property and equipment.

In further discussing our financial results, let me then focus on 2 cash flow metrics, which provide a better view on cash used given the quantity of deferred revenues, stock-based compensation and depreciation embedded in our operating income. Net cash used in operations was approximately $331 million for the full year 2018, which was comparable to 2017. Secondly, cash used for purchases of property and equipment was $106 million

for the full year 2018 compared to $58 million for the full year 2017. Of that, cash used specifically related to our Norwood manufacturing facility was $95 million in 2018 compared to $41 million in 2017.

Revenue for the full year 2018 was $135 million as compared to $206 million for 2017. The decrease was mainly attributable to the termination of the Alexion strategic alliance arrangement in October 2017, which caused an accelerated recognition of deferred revenue in 2017. Also, there was a decrease in grant revenue from the BARDA contract, primarily due to revisions in the Zika program leading to a focus on preclinical study of the mRNA-1893, our follow-on to mRNA-1325. The decreases were partially offset by increases in collaboration revenue from AstraZeneca and Merck.

R&D expenses for full year 2018 were approximately 404 -- $454 million compared to $410 million for 2017. The increase was primarily due to an increase in personnel-related costs, including stock-based compensation, mainly driven by an increase in the number of employees supporting our R&D programs, an increase in consulting and outside services and an increase in facility and equipment-related costs.

G&A expenses for full year 2018 were approximately $94 million compared to $65 million in 2017. This increase was mainly attributable to increases in personnel-related costs, including stock-based compensation, driven by an increase in the number of employees and consulting an outside services, all of which were in support of our public company readiness.

I'll finish this slide with our expectations for our cash use in 2019. Currently, we expect that we will finish the year with between $1.15 billion and $1.2 billion in cash, cash equivalents and investments. Our use of cash is rising from 2018 driven by our advancing pipeline and the associated development and supply costs, offset by a decline in our expected capital expenditures after last year's completion of Norwood.

Two last points before I hand the call back over to Stéphane. As noted in our press release, we're pleased that we are to be added to the Russell 1000 and Russell 3000 indices effective March 18. And lastly, I'm very excited to welcome Lavina Talukdar to our team as Head of Investor Relations effective April 1. Lavina joined us from ADIA and a long career on the buy side.

Now let me turn it over to Stéphane.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Lorence.

Moving to Slide 29. To close our remarks, I would like to reiterate that the company is very focused on execution. I hope our recent progress gives you a sense for that focus, which is essential to both our culture and our mission. Three priorities. Number one, advancing the development pipeline and getting to clinical readouts as fast as we can with high quality. Number two, investing in new development candidates in the 6 existing modalities and moving them to our development pipeline. Number three, investing in new modalities.

If you can turn to Slide 30, which shows our anticipated clinical next steps. 2019 and 2020 are going to be important for Moderna. We expect additional Phase I readouts and multiple Phase II starts and readouts.

Turning to Slide 31. We would like to announce 2 important investor events for Moderna this year that we hope you can join. We will host the Science Day in Cambridge on May 7, led by Dr. Stephen Hoge; and we'll host the R&D Day in New York City on September 12, led by Dr. Tal Zaks.

On Slide 32, you have an update of Moderna. I believe that Moderna is operating from a place of tremendous strength. Enabled by our mRNA platform, our large development pipeline continues to progress based on the data we are generating. We have now 4 programs in or planning for Phase II, 6 positive Phase I readouts, 5 ongoing Phase I trials, 3 open INDs.

If we look at the pipeline by prophylactic area, I'm very proud that we now have 5 immuno-oncology programs: OX40 ovarian and PCV preparing for Phase II, then Triplet is continuing dose escalation in Phase I and 2 open INDs, KRAS with Merck and IL12 with AstraZeneca. Four rare disease programs: MMA, PA, PKU and Fabry. Three vaccines for large unmet medical needs: RSV, CMV and the combo, hMPV+PIV3.

More than 750 talented employees, we are committed to leading a modern science. The 200,000 square foot manufacturing site in Norwood, which is a strategic asset for Moderna. This capability will enable us to scale and provide an important competitive advantage to Moderna to keep executing and accelerating. The strong balance sheet with $1.7 billion of cash, this provides multiyears of financing for operations and investments in our future.

On Slide 33, our mission. We know that we have a special opportunity. And we are committed to delivering on the promise of our science and bringing forward a new class of medicines for patients in need. I'd like to end our remarks by thanking the many people who participate in our clinical studies, including patients, healthy volunteers and physicians.

With that, we'll now be happy to take any questions. Operator?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) And our first question comes from the line of Matthew Harrison of Morgan Stanley.

Matthew Kelsey Harrison - *Morgan Stanley, Research Division - Executive Director*

I guess two from me. Can you talk about first for PCV, why you chose that specific indication? And just -- because maybe I'm not familiar with, what's the typical recurrence-free survival for patients that you're enrolling here? And maybe you could just talk about how the study is powered or what you're hoping to achieve at the PCV combination versus that. And then, a second question. Just given the fact that you've pushed OX40 ligand into a Phase II study on, I mean, how should we think about that program versus the triple? And is there a point in which you have to pick one?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you. This is Tal. Let me answer them in sequence. So let's start with the adjuvant trial for PCV. The reason we picked this indication is because I think it's generally true across anticancer drugs that when a drug is effective, the magnitude of effect tends to be higher and lower in earlier lines of treatment and even more so in the adjuvant setting. And you would expect this to be true for melanoma and for immunotherapy, specifically because you need some time in a healthy immune system for the patient to be able to react. It is also notable, I think, that most, if not all, of the data to date in similar approaches has been developed in adjuvant melanoma. So it's a place where I think, overall, the likelihood of success is highest. In terms of this patient population, the -- in recent studies, I think the recurrence-free survival of patients with advanced melanoma that has been resected has been around 33% to 40%, if you look at recent studies. Our underlying assumptions since we're taking a slightly high-risk patient population was that the baseline rate should be above 45%. The trial is powered at about 85% power with a one-sided alpha of 0.1 as is typical for Phase II PoC studies to show a hazard ratio of about 0.5. So I think typical stats, more or less, for a proof-of-concept study. I would note that the study has randomization of 2 to 1. And the reason that we're enrolling more patients on the treatment arm with the vaccine is because there is a good body of recent evidence on how patients perform in terms of just KEYTRUDA alone. And our partners, Merck, have all that experience at hand from their recent Phase III trials in this setting, which led to the approval of KEYTRUDA in the setting. So we should be able to leverage not just the control arm on this study, but a wider body of data as a comparator for this study, helping us overall with the sense of power here. So that's on PCV. For the OX40 ligand, it's a good question and one that obviously we wrestle with as well. Like any cancer doc, when you see a signal of activity, you feel compelled to go and see if there's real benefit there for patients. Ultimately, OX40 ligand is ahead of the Triplet in terms of the clinical trials. Time will tell what is the magnitude of activity that we see in this trial and what type of activity we can see with the Triplet. So I think it's too early to predict how this will play out. I think for now, we are following the clinical signals where we see them as one is -- wont to do for the benefit of patients.

Matthew Kelsey Harrison - *Morgan Stanley, Research Division - Executive Director*

And Tal, can I just ask a follow-up on the Triplet? I mean, I assume the dosing strategy there is to go a little bit slower given some of the cytokines you have involved as well. I mean, will that one maybe even take longer to potentially catch up or have similar data to that OX40 ligand alone?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Not necessarily. So I think yes, we are starting it at a somewhat lower dose than we started with 0X40 ligand alone because OX40 ligand is a membrane-bound protein, you would expect less risk. And of course, when you've got locally secreted cytokines, you want to dose them at a dose that has a local activity without spillover to systemic toxicity. So there's probably a couple more dose cohorts in that study, but I don't think it's going to be a significant delay relative to our experience with OX40 ligand.

Operator

Our next question comes from the line of Salveen Richter of Goldman Sachs.

Salveen Jaswal Richter - *Goldman Sachs Group Inc., Research Division - VP*

Two questions from me as well. With regard to the PCV program, you mentioned that you've increased the neoantigen count at the cassette from 20 to 34. Just wanted to get your thoughts around that and whether you think that's a broad enough sample set. And then secondly, on the systemic therapeutic modalities. Can you help us understand with regard to the Chikungunya program, you're looking at a single dose right now but at one point, you looked to multiple doses. How should we think about the safety profile in the context of derisking this program based on the redosing aspect? And then a second level or the second systemic therapeutic question is, when could we see MMA data?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you for those. Let me start in the sequence of that you asked. The neoantigen number, so look, it -- what we know from immuno-oncology is that it really only takes 1 antigen if you have a sufficiently potent immune response to lead to cancer aggression. The question is, how do you increase the probability of getting the right one? If you look at the average number of mutations that occur within coding sequences and then get expressed in proteins, depending on the tumor type, you can have up to, typically, in the order of a couple of a hundred is sort the number at the median range. So increasing the number, I think, overall, should increase the probability of success. Now you have to do it within the context of what you think is feasible for the technology. One of the benefits of having it all included in mRNA is that going from 20 to 34 in this case doesn't materially affect our complexity of either process or cost of goods. It just took us some optimization of the mRNA and what we're doing. So I think it's a step in the right direction in terms of how one thinks about eliciting the most potent immune response possible. It will be obviously difficult to nail down what is the right number. We're trying to give this vaccine the best possible opportunity to succeed for patients here. In terms of how to think about single dose versus multiple doses and the safety, it's a good question. The place for us to start is at a place where we can have the clearest understanding of what the safety profile would be. And so that's why we started with a single ascending dose in healthy people for approaching that should be innocuous in and of itself. And that's why I think the Chikungunya, we view it as a very informative first step. It's a good question on the safety of single versus repeated doses. If I look at the totality of our preclinical models, I don't think we have a sense that giving multiple doses should give you a different safety profile than giving a single dose. And if you look at typical adverse event profiles for injected medicines, whether they be antibodies or lipid nanoparticles, the sort of acute reactogenicity or hypersensitivity reactions, should you see them, don't necessarily increase over time. In some cases, they decrease over time. In some cases, it just happens sporadically. So I'm not sure that I expect a different safety profile on repeat dose versus single dose. And that's how we think about the relevance of this first program to the rest of our rare disease repeat dose programs. Your last question on when can we expect data from MMA? Look, we're not forward guiding. Obviously, this is a very rare patient population. We have to start in a place that balances the age of the patients and the age of where actually disease is prevalent, which -- what led us to this adolescent group. What we are committed to is being transparent at every stage of the way, where we are in terms of enrollment until you'll see us give you regular updates on our progress.

Operator

Our next question comes from the line of Cory Kasimov of JPMorgan.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

This is Matthew on for Cory. Just a follow-up on the PCV program. I'm curious if you can help us better understand what informs your decision from an efficacy perspective to move ahead to the Phase II trial specifically at the 1-mg dose cohort.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Yes. It's a great question. We are talking about cancer vaccines, which obviously are a tough place to predict efficacy, historically. I think it's a combination of two things. Our sense of the totality of the immunogenicity data that we've seen to date in our program, we've disclosed for 1 patient; the rest we'll disclose when there's a body of evidence that's sufficient to really -- had a scientific discourse at a medical meeting. But the totality of our data combined with our sense of the tolerability and safety profile at the 1 milligram dose, I think has given us and our partners, Merck, the confidence that we are ready to go to Phase II. In terms of what went -- what it takes to plan your Phase II, we've always been committed to ensuring that we test this personalized cancer vaccine in a way that is as definitive as possible, which is why you see us launch relatively early a randomized Phase II study. We will be continuing to expand the Phase I experiment with additional cohorts to further characterized both the immunogenicity and the potential for benefit in a single arm sense. But if you want a definitive result, you run a randomized Phase II. And that's what we're doing here.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Great. And then just quickly on the CMV vaccine program. Does the opening of the 300-microgram dose cohort affect time lines for when we should expect to see initial immunogenicity data?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Yes. I think that's a fair question. And I would anticipate it will delay somewhat the time line. We have made great progress to date. We've completed enrollment in the first 3 cohorts. It is a healthy volunteer study. So our ability to accrue or recruit patients on time and analyze the data has been exactly where we wanted. But I think the nature of these studies is that you first get a sense of tolerability and only later of immunogenicity. So I'd hate to come to the end of the study and figured that I'd underdosed, which is why we've decided to take a little bit longer and make sure we're exploring the full range of doses that we think is appropriate.

Operator

Our next question comes from the line of Ying Huang of Bank of America Merrill Lynch.

Ying Huang - *BofA Merrill Lynch, Research Division - Director in Equity Research*

The first one is on the PCV program. Tal, can you comment whether you observed any epitope spreading in the Phase I portion? And also, can you comment on your manufacturing needle-to-needle time line now that everything is brought in-house? And then I have a second question on the OX40 ligand program. So do you believe that you need go to a higher dose for OX40 ligand? Or do you think maybe, ultimately, you need a combination, the Triplet, to achieve meaningful clinical activity here?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you for those. Let's start with antigen spreading. I think that's a tough one. We are not -- to be fair, the -- majority of the trials for our translational experiments has been to ascertain whether we can actually elicit the immunogenicity against the new epitopes for which we encode. So the magnitude, I think, overall, of data here is not going to be as scientifically I think rewarding as you might want in terms of answering such a multitude of questions in this first Phase I, really. The goal of Phase I was to establish a dose where we believe there is immunogenicity against that which we encode. Some of those questions, we will answer I think later in the program. And you'll see some of that data as we get a sufficient body of evidence to be able to share it with the broader scientific community. The turnaround time, we are currently at around 50 days, I'd say, needle-to-needle. We're continuously looking at ways to improve it. As you would expect, bringing it to Norwood should enable us to tighten the time line. But this will be a continuous evolution over time as we look -- every day matters here and we look at hours and days as a metric to continuously improve there. In terms of the dose for OX40 ligand, I think that to date, we've seen protein expression in the injected lesions. So it's hard to determine what is the optimal dose. I think the fact that we've been able to show some local pharmacology when you actually look at the stained tissue gives us a sense that we are activating the pathway in the way that we hope to. And to your point, I think that -- or from a scientific perspective, you would expect that you would need additional signals, whether they are additional local signals like in the Triplet or potentially, even the additional of the systemic checkpoint inhibitor to see the maximal activity of this type of therapy. And I think that's been borne out for other approaches in this space as well.

Operator

And our next question comes from the line of Geoff Meacham of Barclays.

Geoffrey Christopher Meacham - *Barclays Bank PLC, Research Division - MD & Senior Research Analyst*

Just have a couple. The first one is an active comparator study in PCV, obviously, is a high bar, but it really is the best way to achieve proof-of-concept. The question is philosophically, should this be the template that we should expect going forward in oncology or really wherever you're targeting indications where there is an existing standard of care? And the second question is on manufacturing. I know the Norwood facility is obviously built for scale up. But just given the breadth of the pipeline, is there ample capacity, for example, to get to pivotal or large-scale studies in all your disclosed programs? Or do you think, ultimately, you need to expand even more down the road?

Lorence H. Kim - *Moderna, Inc. - CFO*

Thank you. Let me take the first question in terms of active comparative study. Clinical development remains artisanal. The truth is that it depends on the situation. I think in oncology, in large indications, there are instances where the signal is unquestionable there. And you go on the single arm and everybody agrees that yes, you're bringing benefits to patients. Traditionally, one expects at some point a randomized trial. And I think to make sort of broad statements of what's always applicable is hard certainly for a company that's so early in this stage. And I would further note that if you look across our pipeline, some of the indications we're targeting are extremely rare indications in which it's virtually impossible to conduct a full randomized study as you would for more prevalent indications. So I don't think I can really give you a more satisfactory answer than that. In terms of our manufacturing capacity, let me ask Stéphane to take that one.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. Thanks, Tal. So regarding manufacturing, the thing that is very clear is that the vision and the mission of Norwood is to be a development site for long term. Having said that, as you know, managing risk is really important to the team. And so what we have done as we designed in this Norwood from a utility standpoint, it can accommodate Phase III and launches. It is not a launch probably today for commercial, but we have road maps and time lines that have been developed by the team so that people who have to decide who gets ready for Norwood for launches, we could do that. We have a, also, of course, a second plan that give us full optionality, which is we have enabled a commercial contract manufacturing organization in the U.S., which is doing commercial product, as we speak. They are -- acted as our backup for Norwood. And so as we get closer to launch and to running pivotals, we could decide whether rapidly enable Norwood for our first few launches or use a contract manufacturer. In the

long term, our goal will be to build a commercial plant. But for obvious reason of managing risk, we did not want to do that until our first product approved. And so we have a good path forward of how we manage the next phase of our growth dealing with pivotal and commercial.

Operator

Our next question comes from the line of Ted Tenthoff of Piper Jaffray.

Edward Andrew Tenthoff - *Piper Jaffray Companies, Research Division - MD & Senior Research Analyst*

My question has to do with hMPV+PIV3. And congrats on that good Phase I data, really clean safety profile. What are some of the special considerations or how should we be thinking about this toddler study? Obviously, safety is going to be paramount. But are there anything else we should be considering like when you dose or things like that, that maybe learned sort of from the immunogenicity curves from the healthy?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you for that question. I think there are several relevant considerations here. The first is to note that the first exposure in the pediatric population will still be in 0 positives. We have to make sure that because of the history, primarily of inactivated RCV back in the day, there is a theoretical concern of disease exacerbation. And so one always starts by evaluating safety in 0-positive toddlers. I think the nice thing for the Phase I or for the data is because we reached the plateau so soon, we have a wide margin of doses that we could test that should give us a read on safety and tolerability in these 0-positive toddlers. I can't comment further because we're still in the design phases of the study. And obviously, we will have to sit down with the regulatory authority as well before we can commit to what that is.

Operator

Our next question comes from the line of Hartaj Singh of Oppenheimer & Co.

Hartaj Singh - *Oppenheimer & Co. Inc., Research Division - Research Analyst*

I just have a couple of questions, one general and one specific. The general question is you've been having a lot of regulatory interactions now as you're having your programs go into Phase I and II. You've got a lot of different, or I'd call them, orthogonal approaches ongoing, interacting with different groups at the FDA. What -- do you get a sense that with different groups that there's a potential to accelerate some of the programs, oncology, for example, versus vaccines, et cetera? Do you get a sense that some groups are more amendable to an accelerated approach versus others? And what would those be? And then the more specific question is, just on the PCV, what percent of the patients with their resected melanoma and with a high risk of recurrence actually get KEYTRUDA? And then will you be selecting for patients that have sort of a better immune system status, if that's possible?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Thank you for those. I'm just jotting a note, so I don't forget the questions. The -- let me start with your general question on FDA. It is true that we are interacting across 3 very different disease areas. We've got healthy volunteers in the vaccines division. We've got oncology applications and obviously, rare disease applications. We primarily interact with 2 groups at FDA. It's either the division of vaccines, or OTAT, under which falls both the cancer and rare disease indications. On the vaccine side, I think we're in a very fortunate position. Wellington Sun was the director of that division for the past decade, and he's overseeing the approval of every new vaccine in the space in the U.S. for the past 10 years, has actually joined us a few months back. And he's our Head of Regulatory and Strategy for Vaccines. So I think under his leadership, we have a good sense of what is the best way forward to balance the regulatory risk and the development risk, if you will. In terms of OTAT and are some groups different than others at FDA, I think to give FDA credit, their framework of understanding benefit risk is pretty systemically applied across. I think the hard reality

is that we're talking about very different indications and very different assessments of safety and risk versus potential benefit. So of course, when you go into healthy kids with a vaccine, it's a very different bar of how you develop it versus going after rare diseases with huge unmet needs and no standard of care or oncology, which we're all familiar with. I think the totality of our indication -- of our interactions with FDA today, I think has been very positive. Numerous pre-IND meetings, discussions on changes in clinical design, patient population, CMC. I think we found a very active partner that has really helped us. We're starting our first steps into Europe. We've been to Europe, both us and our partners, in several countries. But I give FDA a lot of credit as providing really a deep insight and help as we move forward. In terms of PCV and KEYTRUDA, I'm not sure what the actual commercial numbers are for KEYTRUDA. Suffice to say that it's a recognized standard of care. They have a label in this indication. And I think it's hard to argue that KEYTRUDA is, if not the best, one of the best checkpoint inhibitors in the space. And so I think we're on very solid footing. Certainly, the investigators that I talked to out there who are treating these patients are all very familiar and very comfortable with using KEYTRUDA in this indication. Selecting for patients who are more immunocompetent, I wish I had a way to do that. And I'm open to any ideas. I think it's hard to -- we, as a scientific community, have not really yet found a way that can parse out who is likely to respond and who isn't. I think by going early or in the life of a patient with cancer, if you will, before they've been extensively treated after basically getting a surgical resection, I think gives us the best opportunity to immunize a patient whose immune system is as robust as it can be.

Operator

(Operator Instructions) Our next question comes from the line of Alan Carr, Needham.

Alan Carr - *Needham & Company, LLC, Research Division - Senior Analyst*

You've obviously got a pretty sizable pipeline as it is, but you have talked about your ability to expand beyond that. Wondering if you can give us a sense of to what extent you expect it to grow this year and how you might disclose new programs as they move forward. And then also, in terms of spend for 2019, you said that CapEx would go down. I'm wondering if you can give us a sense, is this something that's going to be substantially lower than 2017 levels even?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you. It's Stéphane. So I'll take the first question and obviously, Lorence will take the finance question. As we've said in the past, we don't disclose the important work that's happening in research as we go and as we build the business. But what we do is have a few quarterly calls or through different model event, we will share any new development candidate. The team is working on all of our modalities to advance new development candidate. And when they'll be ready, we will communicate those to investors and analysts. Lorence?

Lorence H. Kim - *Moderna, Inc. - CFO*

Thanks, Alan. On our spend for FY '19 and the CapEx question, yes, we're not specifically guiding on CapEx. But what I can say is that when you look at what's driving CapEx down for this year, it's the fact that Norwood is complete and the investment in Norwood, which was substantial and well worth it was what really bridges between 2017 and 2018. And so if you look at the total cash used to purchase property and equipment in 2017, that was $58 million. And again, a big chunk of that, $40-plus million, was Norwood. So I think that gives you a sense for where we're heading without the specificity of that in here.

Operator

And I'm showing no further questions at this time. I'd like to turn the conference back over to Stéphane for any closing remarks.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Well, thank you very much, everybody, for joining us today and for your questions. We look forward to catching up with many of you in the coming weeks. At the latest, I hope to see you on our May 7 Science Day in Boston. Have a nice day. Thank you.

Operator

Ladies and gentlemen, thank you for your participation in today's conference. This does conclude the program. You may now disconnect. Everyone, have a great day.
