FINAL

Bloomberg Transcript

Q4 2018 Earnings Call

Company Participants

- Lorence H. Kim, Chief Financial Officer
- Stephen Hoge, President
- Stéphane Bancel, Chief Executive Officer & Director
- Tal Zaks, Chief Medical Officer
- Unverified Participant

Other Participants

- Alan Carr, Analyst
- Geoff Meacham, Analyst
- Hartaj Singh, Analyst
- Matthew K. Harrison, Analyst
- Salveen Richter, Analyst
- Ted Tenthoff, Analyst
- Ying Huang, Analyst

MANAGEMENT DISCUSSION SECTION

Operator

Good morning and welcome to the Moderna Corporate Update and 2018 Financial Review 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 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.

Unverified Participant

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 that we plan to discuss 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 the 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 and we open up for Q&A at the end. Before we begin, I would like to remind everyone 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 and 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 of development.

I will now pass the call over to Stéphane.

FINAL

Stéphane Bancel

Thank you, Laura, and good morning everyone. Welcome to Moderna's first quarterly conference call as a public company. As you know, we believe that Moderna (01:49) has the potential to become a new class for medicines. And since Moderna's inception, we have worked hard to build a company that could become the leader in the field.

(02:02) is a potential to make new medicines for intricate diseases, medicines which cannot technologically be made (02:08) molecules. We believe that over time, it can go beyond our current therapeutic areas of infectious disease, oncology, (02:16) diseases and cardiovascular diseases.

Because mRNA is an information-containing molecule, we believe that this new class of medicine and the company we have built around it may have many advantages. First, we're able to use similar technology components across programs. As a result and over time, as we de-risk the use of those components, successive mRNA medicine 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 our next small molecule (02:44) technologies, every time we make a product at every scale, we intend to use similar manufacturing processes, accelerating timelines, for both the discovery of new development candidate as well as a scale-up for clinical trials. And finally because we make mRNA in a liquid-phase (03:09) solution, we believe that over time, our cost of goods would be similar to small molecule injectable commercial products.

With the possibility to build a new class of medicines, while helping many patients and creating value for shareholders along the way, we focus on managing four different type of risk; technology risk, biology risk, execution risk, financing risk.

As you can see on slide 4, it has always been our goal to de-risk each of our modalities by beginning with a development candidate that could allow us to systemically 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 (03:58) vaccine to see if we could safely demonstrate in a Phase 1 trial a defined level of antibodies in healthy volunteers not previously exposed to the virus.

Bloomberg Transcript

FINAL

Bloomberg Transcript

At the time of our IPO, we had advanced programs across (04:15) modalities in the clinic; cancer vaccines, intratumoral immuno-oncology and localized regenerative therapeutics. Already in 2019, we have initiated human dosing in a fifth modality, systemic secreted therapeutics, with mRNA-1944 and mRNA encoding and antibody against the Chikungunya virus. This program uses the same delivery technology as our full rare genetic disease programs, MMA, PA, PKU and Fabry as well as our Relaxin (04:43) 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 also focus on growth and therefore as a subset of our team, focus on creating new development candidates, within our existing six modalities. Given that these new development candidates use the same technology component as those already in the clinic, we're able to significantly reduce technology risk and move swiftly from a drug concept to development candidates.

Our third area of focus is on the long term, meaning inventing new modalities which can deliver mRNA to new issues and/or cell types. On slide 6, our planning (05:30), you can see our pipeline has advanced in the 90 days since our IPO. Let me spend a minute on these from right to left. We are planning a Phase 2 study for PCV and the Phase 2 cohort of OX40 Ligand in ovarian cancer. We reported positive interim Phase 1 hMPV plus PIV3 vaccine data, supporting the move into Phase 1b HD escalation study in children. We have begun dosing in Phase 1 studies from 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 three distinct activities on the slide. First, we manufacture clinical material. Since the site opening, we have successfully manufactured clinical-grade mRNA and then to formulation and went to filling and finally labeling of our virus.

We are now actively working towards vertical integration of critical raw materials like DNA plasmids used as template to mRNA, (06:48) and other raw materials. We have also successfully transferred the second capability to Norwood for personalized cancer vaccine of PCV.

We started our PCV clinical trial in 2017 by making the 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 dose personalized for one patient. I am pleased to report that we are now capable of making all our PCVs in Norwood operations in the remainder of Phase 1 as well for Phase 2.

The third capability transferred to Norwood which will enable us to reduce cost is or 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 process our team made in 2018 and in 19 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 {BIO 19987702 <GO>}

Thank you, Stéphane.

Let me now review our progress my 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 1 data for our combination vaccine against two respiratory viruses, human metapneumovirus and parainfluenza virus 3 or hMPV and PIV3. These are two 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.

And on slide 11, as we had disclosed, the top line interim data from this 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 both 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, one month after a single mRNA-1653 vaccination, neutralizing titers against hMPV rose to approximately six-fold baseline and those against PIV3 rose to approximately threefold baseline.

A second vaccination one month later did not further boost the antibody titers, suggesting that a single vaccination is already achieving its 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 1b trial in toddlers, a trial that we are currently designing. I look forward to further discussion of this point and other aspects of our clinical data at a future medical meeting.

Let me move to our congenital CMV vaccine on slide 12. This is the vaccine against cytomegalovirus, which is the most common congenital infection impacting close to 40,000 infants annually in the United States. Congenital CMV infection can severely affect infant brain development and is an important cause of childhood hearing loss. There is currently no approved vaccine to prevent CMV. Our vaccine mRNA-1647 has enrolled the initial three dose levels in the Phase 1 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 micrograms. So we are expanding the trial to enroll two 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.

FINAL
Bloomberg Transcript

FINAL

Bloomberg Transcript

Reviewing our overall progress on slide 13, we have to-date dosed approximately 950 healthy volunteers enrolled across seven Phase 1 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 read-out for hMPV/PIV3, we have now shown promising data from five Phase 1 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 will 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 2a 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 a patient in the Phase 1 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 antigen-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 2.

On slide 16, you can see the design of this Phase 2 study. It is designed to assess whether post-operative adjuvant therapy with mRNA-4157 in 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 this 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 new antigen count in our personalized cancer vaccines from 20 to 34 neoantigens, all still encoded on a single mRNA and we intend to apply this advance (13:00) to the Phase 2 study.

Let me now turn to our intratumoral immuno-oncology programs, which you can see on slide 18. We continued to advance the Phase 1 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 OX40 Ligand protein expression in certain injected lesions and have observed regression of injected lesions in two patients with advanced ovarian cancer, although these regressions did not meet RECIST criteria. These observations have motivated us to trigger the Phase 2 cohort in patients with ovarian cancer. The top dose tested in the Phase 1 trial, 8 milligram, is currently in the dose conformation stage and this is the dose we intend for the Phase 2 cohort in ovarian cancer. Let me talk about mRNA-2752, which encodes the throughput 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

FINAL

Bloomberg Transcript

both injected and distant un-injected 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 1 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 have now begun to treat patients at the second dose level. Finally, there has 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 anti-cancer agent. In the past, the clinical development of systemically administered recombinant IL12 has been hampered by systemic toxicity. We've demonstrated preclinically that intratumoral doses of mRNA encoding IL12 can be delivered safely and induced a complete response of 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 2a trial of AZD8601, which is an mRNA encoding for VEGF-A. As a reminder, the Phase 1 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 encoding 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 two 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 anti-viral 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? And this relationship would be of obvious relevance to our pipeline of mRNA medicines for rare diseases, particularly because 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 1 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 one day we may be able to offer people 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 eight subjects in the first cohort of healthy volunteers in this Phase 1 study and I look forward to sharing more about

FINAL

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 MUT enzyme missing in children with this disease. We're now preparing to begin the Phase 1/2 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 this 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.

Bloomberg Transcript

Lorence H. Kim {BIO 18670491 <GO>}

Thank you, Tal. Let me turn to slide 28. In today's press release, we've 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 at 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 two cash flow metrics which provide a better view on cash use 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

FINAL

Bloomberg Transcript

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 studies of mRNA-1893 or 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 $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 and increase in consulting and outside services and an increase in facility and equipment-related costs.

D&A expenses for full year 2013 were approximately $94 million compared to $65 million dollars 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 and 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 Stephan. As noted in our press release, we're pleased that we are going to be added to the Russell 1000 and Russell 3000 industries effective March 2018. 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 audio and a long career on the buy side.

Now let me turn it over to Stephen.

Stephen Hoge {BIO 17925815 <GO>}

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 central to both our culture and omission. Three priorities. Number one, advancing the development pipeline and getting to clinical readouts as fast as we can with high quality. Number two, investing new development candidates in the six existing modalities and moving them to our development pipeline. Number three, inventing new modalities.

FINAL

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 1 readouts and multiple Phase 2 starts and readouts.

Turning to slide 31, we would like to announce two 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 Stephen Hoge and we'll host an 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, a large development pipeline continues to progress based on the data we are generating. We have now four programs in or planning for Phase 2, six positive Phase 1 readouts, five ongoing Phase 1 trials, three open INDs. If you look at the pipeline by (25:09) area, I'm very proud that we now have five immuno-oncology programs, OX40 ovarian and PCV preparing for Phase 2. (25:16) is continuing dose escalation in Phase 1 and two open INDs, KRAS, with Merck and (25:20). 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 who are committed to leading mRNA (25:40), a 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, a strong balance sheet with $1.7 billion of cash. This provides multi-year of financing for operations and investments in our future.

On slide 33, our mission. We know that we have a special opportunity and we're committed to delivering on the promise of our science and going 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?

Q&A

Operator

Thank you. And our first question comes from the line of Matthew Harrison of Morgan Stanley. Your line is open.

Q - Matthew K. Harrison {BIO 17603148 <GO>}

Great. Good morning. Thanks for taking the question. I guess two for me. Can you talk about first for PCV, why you chose that specific indication and just maybe I'm not familiar with, but what's 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 with the PCV combination versus that? And then second question, just given the fact you pushed OX40 Ligand into a Phase 2 study (27:30), how should we think about that program versus the triple and is there a point at which you have to pick one? Thanks.

Bloomberg Transcript

FINAL

A - Tal Zaks {BIO 19987702 <GO>}

Thank you. This is Tal. Let me answer them in sequence. So let's start with the adjuvant trial for PCV. The reason to pick this indication is because I think it's generally true across anti-cancer drugs that when the drug is effective, the magnitude of effect tends to be higher 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 and 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 and 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, in recent studies, I think the recurrence-free survival of patients with advanced melanoma that have been resected has been around 33% to 40% if you look at recent studies. Our underlying assumptions, since we're taking a slightly higher risk patient population, was that the baseline rate should be about 45%. The trial is powered at about 85% power with a one-sided alpha of 0.1 as is typical for Phase 2 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 this study has a 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 3 trials in the 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 the 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 triplets. 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 (30:33) want to do for the benefit of patients.

Q - Matthew K. Harrison {BIO 17603148 <GO>}

And Tal, can I just ask a follow-up on the triplet. I mean 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 OX40 Ligand alone?

A - Tal Zaks {BIO 19987702 <GO>}

Not necessarily. So I think, yes, we are starting it at a somewhat lower dose than we started with OX40 Ligand alone because OX40 Ligand is a membrane-bound protein, you'd expect less risk. And of course when you've got locally secreted cytokines, you want to dose them at a dose that has the local activity (31:12) 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.

Bloomberg Transcript

FINAL

Bloomberg Transcript

Q - Matthew K. Harrison {BIO 17603148 <GO>}

Great. Thanks very much.

Operator

Thank you. Our next question comes from the line of Salveen Richter of Goldman Sachs. Your line is open.

Q - Salveen Richter {BIO 15151450 <GO>}

Good morning. Two questions for me as well. With regard to the PCV program, you mentioned that you've increased the neoantigen count of 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'll look to multiple doses. How should we think about the safety profile in the context of de-risking this program based on the re-dosing aspect and then the second systematic therapeutic question is when can we see M&A data? Thank you.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you for those. Let me start in the sequence that you asked. The neoantigen number. So look, what we know from immuno-oncology is that, it really only takes one antigen, if you have a sufficiently potent immune response to lead to cancer regression. 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 protein, depending on the tumor type, you can have up to typically in the order of a couple of hundred is sort of 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 encoded 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 a safety profile would be. And so that's why we started with a single ascending dose in healthy people for a protein 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 them, (35:30) 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 is 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 and so you'll see us give you regular updates on our progress.

Q - Salveen Richter {BIO 15151450 <GO>}

All right. Thank you.

Operator

Thank you. Your next question comes from the line of Cory Kasimov of JPMorgan. Your line is open.

Hey guys, thanks for taking my questions and this is Matthew (36:08) on for Corey. 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 2 trial specifically at the 1 mg dose cohort?

A - Tal Zaks {BIO 19987702 <GO>}

Yeah. 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 one patient, the rest we'll disclose when there's a body of evidence that's sufficient to really, ahead of 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 2.

In terms of what it takes to plan your Phase 2, 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 2 study. We will be continuing to expand the Phase 1 experiment with additional cohorts to further characterize both the immunogenicity and the potential for benefits in a single-arm sense. But if you want a definitive result, you run a randomized Phase 2 and that's what we're doing here.

FINAL
Bloomberg Transcript

FINAL

Q - Operator

Great. Thanks. And then just quickly on the CMV vaccine program. Does the opening of the 300 micrograms dose cohort affect timelines for when we should expect to see initial immunogenicity and safety data?

A - Tal Zaks {BIO 19987702 <GO>}

Yeah. So I think that's a fair question and I would anticipate it will delay somewhat the timeline. We have made great progress to-date. We've completed enrollment in the first three cohorts. It is a healthy volunteer study. So our ability to accrue, recruit patients on time and analyze the data has been exactly where we'd wanted. But I think the nature of these studies is that you first get a sense of tolerability and only later immunogenicity. So I'd hate to come to the end of this study and figure that I've under-dosed, 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.

Q - Operator

Great. Thanks for taking my question.

Thank you. Our next question comes from the line of Ying Huang of Bank of America Merrill Lynch. Your line is open.

Q - Ying Huang {BIO 16664520 <GO>}

Hi, good morning. Thanks for taking my questions. The first one is on the PCV program. Tal, can you comment whether you observed any epitope spreading in the Phase 1 portion? And also can you comment on your manufacturing needle-to-needle timeline 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 to go to a higher dose for OX40 Ligand or do you think maybe ultimately you need a combination of the triplet to achieve meaningful clinical activity here? Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you for those. Let's start with antigens spreading. I think that's a tough one. We are not, to be fair, the majority of the (39:42) translational experiments has been to ascertain whether we can actually elicit the immunogenicity against the new (39:47) 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 1. Really the goal of the Phase 1 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 the data as we get a sufficient body of evidence to be able to share 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 timeline, but this will be a continuous evolution over time

Bloomberg Transcript

as we look. Everyday 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 a 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.

Q - Ying Huang {BIO 16664520 <GO>}

Thank you.

Operator

Thank you. Our next question comes from the line of Geoff Meacham of Barclays. Your line is open.

Q - Geoff Meacham {BIO 21252662 <GO>}

Hey, guys. Good morning and thanks for the question and contracts on your first public call. 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 the pivotal or large scale studies in all your disclosed programs or do you think ultimately you need to expand even more down the road? Thank you.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you. Let me take the first question in terms of active comparator 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 a single arm and everybody agrees that yes, you are bringing benefit to patients. Traditionally, one expects at some point a randomized trial. 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 a more prevalent indication. 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.

FINAL
Bloomberg Transcript

FINAL

A - Stéphane Bancel

Yeah. 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 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 and build Norwood, from a utility standpoint, it can accommodate Phase 3 and launches. It is not launch-ready today for commercial, but we have roadmaps and timelines that have been developed by our team, so that if we were to decide to get ready for Norwood for launches we could do that. We have 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 (44:30), we could decide to have a rapidly enabled Norwood for first few launches or use the contract manufacturer. In the long term, our goal will be to build a commercial plan, but for obvious reason of managing risk, we do not want to do that until we have 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.

Q - Geoff Meacham {BIO 21252662 <GO>}

Okay. Thanks.

Operator

Thank you. Our next question comes from the line of Ted Tenthoff of Piper Jaffray. Your line is open.

Q - Ted Tenthoff {BIO 1880164 <GO>}

Great. Thank you very much for taking my questions and congratulations on all the progress. My question has to do with MPV+PIV3 and congrats on a good Phase 1 data, (45:19) 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 learn sort of from the immunogenicity curves from the healthies (45:36)? Thanks.

A - Tal Zaks {BIO 19987702 <GO>}

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 zero positives. We have to make sure that because of the history primarily of inactivated RSV back in the day, there is a theoretical concern of disease exacerbation and so one always starts by evaluating safety in zero-positive toddlers. I think the nice thing for the Phase 1 or for the data is because we reached a 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 this zero-positive toddlers. I can't comment further because we're still in the design phases of this study and obviously we would have to sit down with the regulatory authority as well before we can commit to what that is.

Q - Ted Tenthoff {BIO 1880164 <GO>}

Bloomberg Transcript

Great. Excellent. Thank you very much.

Operator

Thank you. Your next question comes from the line of Hartaj Singh of Oppenheimer & Company. Your line is open.

FINAL

Q - Hartaj Singh {BIO 18796450 <GO>}

Great, thank you. Thanks for the questions. I just have a couple of questions, one general, one specific. The general question is you've been having a lot of regulatory interactions now as you're having your programs going to Phase 1 and 2. You've got a lot of different or, I'd call them, orthogonal approaches ongoing interacting with different groups of the FDA. What – do you get a sense that with different groups that there's a potential to accelerate some of the programs, you know oncology for example versus vaccines, et cetera, do you get a sense that some groups are more amenable 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, 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? Thank you.

A - Tal Zaks {BIO 19987702 <GO>}

Thank you for those. I'm just charting a note, so I don't forget the questions. Let me start with your general question on FDA. It is true that we interacting across three 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 track with two 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 has overseen the approval of every new vaccine in this 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 are developing 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 deep insight and help as we move

Bloomberg Transcript

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 talk 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 immuno-confident, I wish I had a way to do that – and I'm open to any ideas. I think it's hard to be – 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 it gives us the best opportunity to immunize the patient whose immune system is as robust as it can be.

Q - Hartaj Singh {BIO 18796450 <GO>}

Great. Thank you so much for those really granular responses. Really appreciate it.

Operator

Thank you. Our next question comes from the line of Alan Carr with Needham. Your line is open.

Q - Alan Carr {BIO 15355437 <GO>}

Hi. Thanks for taking my questions. 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 the CapEx would go down. I'm wondering if can give us a sense, is this something that's going to be substantially lower than the 2017 levels even? Thanks.

A - Stéphane Bancel

Thank you, it's Stéphane. So I'll 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 will do is, either through quarterly calls or through different model events, we will share any new development candidate. The team is working on all of our modalities to advance newly development candidate and when they'll be ready, we will communicate those to investors and analysts. Lorence?

A - Lorence H. Kim {BIO 18670491 <GO>}

Thanks, Alan. On (52:55) by 2019 and the CapEx question, yeah 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 a fact that Norwood is complete and the investment in Norwood, which

FINAL
Bloomberg Transcript

was substantial and well worth it was – 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 guidance here.

Q - Alan Carr {BIO 15355437 <GO>}

Great. Thanks for taking my questions.

A - Tal Zaks {BIO 19987702 <GO>}

Okay.

Operator

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

A - Stéphane Bancel

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. And at the latest, I hope to see you on May 7 time there 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 call. You may now disconnect. Everyone, have a great day.

This transcript may not be 100 percent accurate and may contain misspellings and other inaccuracies. This transcript is provided "as is", without express or implied warranties of any kind. Bloomberg retains all rights to this transcript and provides it solely for your personal, non-commercial use. Bloomberg, its suppliers and third-party agents shall have no liability for errors in this transcript or for lost profits, losses, or direct, indirect, incidental, consequential, special or punitive damages in connection with the furnishing, performance or use of such transcript. Neither the information nor any opinion expressed in this transcript constitutes a solicitation of the purchase or sale of securities or commodities. Any opinion expressed in the transcript does not necessarily reflect the views of Bloomberg LP. © COPYRIGHT 2021, BLOOMBERG LP. All rights reserved. Any reproduction, redistribution or retransmission is expressly prohibited.

FINAL

Bloomberg Transcript