REFINITIV STREETEVENTS

EDITED TRANSCRIPT

MRNA.OQ - Q1 2021 Moderna Inc Earnings Call

EVENT DATE/TIME: MAY 06, 2021 / 12:00PM GMT

OVERVIEW:

Co. reported 1Q21 total revenue of $1.9b and net income of $1.2b.

REFINITIV

CORPORATE PARTICIPANTS

Corinne M. Le Goff *Moderna, Inc. - Chief Commercial Officer*

David W. Meline *Moderna, Inc. - CFO & Principal Accounting Officer*

Lavina Talukdar *Moderna, Inc. - Senior VP & Head of IR*

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

Stephen Hoge *Moderna, Inc. - President*

CONFERENCE CALL PARTICIPANTS

Cory William Kasimov *JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst*

Edward Andrew Tenthoff *Piper Sandler & Co., Research Division - MD & Senior Research Analyst*

Geoffrey Christopher Meacham *BofA Securities, Research Division - Research Analyst*

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

Huidong Wang *Barclays Bank PLC, Research Division - Research Analyst*

Joseph Robert Stringer *Needham & Company, LLC, Research Division - Associate*

Mani Foroohar *SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst*

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

Michael Jonathan Yee *Jefferies LLC, Research Division - Equity Analyst*

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

Simon P. Baker *Redburn (Europe) Limited, Research Division - Head of Pharmaceutical Research*

PRESENTATION

Operator

Good morning. My name is Dee Tamara, and I will be your operator today. Welcome to Moderna's First Quarter Earnings Call. (Operator Instructions)

Please be advised that the call is being recorded.

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

Lavina Talukdar - *Moderna, Inc. - Senior VP & Head of IR*

Thank you, Dee Tamara. Good morning, everyone. Thank you for joining us on today's call to discuss Moderna's First Quarter 2021 Financial Results and Business Updates. You can access the press release issued this morning as well as the slides that we'll be reviewing by going to the Investors section of our website.

On today's call are Stephane Bancel, our Chief Executive Officer; David Meline, our Chief Financial Officer; Stephen Hoge, our President; Tal Zaks, our Chief Medical Officer; Corinne Le Goff, our Chief Commercial Officer; and Juan Andres, our Chief Technical and Operations Officer.

Before we begin, please note that this conference call will include forward-looking statements made pursuant to the safe harbor provision of the Private Securities Litigation Reform Act of 1995. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk factors

that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements. We undertake no obligation to update or revise the information provided on this call as a result of new information or future results or developments.

On Slide 3, please see the important indication and safety information for our COVID-19 vaccine. which has been authorized for emergency use in the United States and many other countries around the world.

I will now turn the call over to Stephane.

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

Thank you, Lavina. Good morning or good afternoon, everyone. Thank you for taking the time to join our Q1 2021 conference call.

We'll start by a quick business review of the quarter before Corinne walks you through commercial update. David will then walk you through the key financials. Stephen will provide a clinical update, especially new human data about 2 of our COVID-19 booster candidates, mRNA-1273, the currently authorized vaccine; and mRNA-1273.351, the variant specific booster to B.1.351 first identified in South Africa. I will then come back to close.

The Moderna COVID-19 vaccine is now available and protecting people in 37 countries around the world. And with the WHO authorization last Friday night, the number of countries where our vaccine will be available, will go up significantly.

In the first quarter alone, 102 million doses have been shipped and many tens of millions of people have been fully vaccinated or received their first dose. 12 months ago, in Q1 2020, Moderna had never ran a Phase III clinical study, never gotten a product authorized by a regulator and never made 100 million doses in a single quarter, not even 10 million, not even 1 million doses.

I am very proud of what the Moderna team has achieved, but most importantly, I am very thankful for their impact on the world and the incredible personal sacrifices that our team has made towards protect fellow human beings around the world. This is very humbling, and I'm fortunate to lead Moderna in this moment.

I'm also thankful for Moderna scientists, engineers, doctors and team members who have worked relentlessly over the last 10 years now to be ready for when the virus emerged in late 2019. We invented technology to produce safe, well-tolerated mRNA vaccines, which made it possible for us to chase the SARS.

The company achieved revenues of $1.9 billion in Q1 2021 of which $1.7 billion were COVID-19 vaccine product sales. The net income for the period was $1.2 billion. This marks the company's first GAAP profitable quarter in its history after 9 years of operating losses.

At the end of 2021, we had cash and cash investments of $8.2 billion. David will give you more details in a few minutes.

We increased our 2021 supply forecast once again. We now believe that we should be able to supply 800 million doses in 2021, and we're still aiming for 1 billion doses over the year. The total advanced purchase agreements signed for delivery in 2021 have been increased to $19.2 billion.

We are happy to report this morning an interim update to our TeenCOVE study. The initial interim analysis of our Phase II/III TeenCOVE study of mRNA-1273 showed the vaccine efficacy against COVID-19 over 96% and mRNA-1273 was generally well tolerated with no serious safety concern identified to date.

We're also on track to start this month the filing of our rolling BLA to the FDA for COVID-19 vaccine mRNA-1273, a type of COVID, we added another first as a company. And that gives the dosing of our first patient with an mRNA for our therapeutics candidate against a rare genetic disease, propionic acidemia a genetic deficiency in the liver with a candidate mRNA-3927.

One of the things that I'm the most excited about is where we are going. The Q1 results highlighted above of the consequence of the last year work and decisions we made. So as I look to where Moderna is going, I get very excited by the level of our increased investments across the board. Using our strong balance sheet to invest to scale Moderna. These 2 numbers, awesome color. In Q1 2021, our R&D investments were approximately 4x higher than the R&D investments in Q1 of last year. Not 4%, not 40%, 4x higher.

For all of you who have known us for many years, Moderna has been built as a digital enterprise since the early days. But we now have the opportunity to do much more and to build new functions like clinical trial operations, pharmacovigilance, commercial, digitally from the get-go. So looking at the next 5 to 10 years, we're investing intensively in digital, automation and AI. Our plan for 2021 is to invest 3x more in digital than in fiscal year 2020.

We announced last week that we have decided to invest to increase our 2020 supply to up to 3 billion doses. Let me share with you why we decided to recommend to our Board to invest at that scale. First, let's talk about the science of SARS-CoV-2 virus. New variants of concern continue to emerge around the world. And we believe that over the next 6 months as the southern hemisphere enter its foreign winter, we could see more variants of concern emerge. We have said for right now that we believe booster shots will be needed as we believe that the virus is not going away. We also believe from the scientific standpoint, that the highest efficacy booster over time will be provided by multivalent variant-specific booster.

Second, the market has changed quite a lot versus what we knew 6 months ago. First, mRNA vaccines have emerged as the best-in-class vaccines, high efficacy, good tolerability profile, having to scale manufacturing and speed to chase the variants in the clinic. Many companies are still in the clinic with their first-generation vaccine, where we're in a clinic with variant-specific boosters.

More importantly, as we are looking to throw our nets around the world, in the West and in the East, in the North and in the South, we are hearing loud and clear from the market, supply us with more mRNA vaccine for primary series and supply us with more mRNA vaccine in the future for boosters for 2022 and 2023. There is a big shift versus what the market perceived 6 or 9 or 12 months ago, when protein vaccine or adeno vaccines were thought to be the answer to the pandemic. We believe it has become an mRNA market for COVID-19 vaccine.

Third is rollout pipeline. We believe we will bring to market several more products in the next few years as we add to this market demand for COVID-19 boosters vials, flu vaccine as we discussed at the Vaccine Day. And our goal is to have a seasonal flu vaccine combined with COVID variant booster in a single-dose product.

We saw strong clinical data for RSV vaccine and CMV vaccine. Plus we have 7 programs in clinical studies in 3 therapeutics area and more programs to move from preclinical development to clinical studies in the months to come.

So we decided to build capacity to deliver up to 3 billion dose of supply in 2022 to share both the North and the South. We are doubling our drug substance supply in Europe and increasing by 50% of drug substance supply in the U.S. We are, of course, adding filling capacity in the U.S. and Europe at our existing partners, but also adding new ones as we speak, more to come.

Another clinical feedback we're hearing from the market is that Moderna has a best-in-class mRNA vaccine. Shipment of minus 20 Celsius in storage, not minus 70 celsius. Small cartons of 100 doses. Storage up to 6 months in standard freezer and 4 weeks in regular repurchase temperatures. The only authorized mRNA vaccine that does not require on-site dilution. We believe this is an even more important feature today, but will be more in the future in '21 and '22 and '23 as we move to a booster market decentralized in pharmacies and in a doctor's office.

We believe we have the best mRNA vaccine authorized, and we continue to improve our product to continue to have a best-in-class product of the mRNA market.

We were delighted to announce this morning the start of a dosing of our first patient in our Phase I/II study with propionic acidemia disease. The study is called Paramount. It is yet another milestone for Moderna. Not only do we have, I believe, the most innovative infectious vaccine clinical pipeline, but we also have therapeutic candidates in clinical studies in oncology, in cardiology and now in a rare genetic disease.

Let me close my remarks on this familiar slide. We now have 1,500 employees. We have recently incorporated Moderna Japan K.K. And we'll continue to build our commercial network. We will push to Asia Pacific in 2021.

And given our strong balance sheet of $8.2 billion, we're going to continue to accelerate and invest to allow Moderna to scale and maximize the impact of our broad mRNA platform to help as many people as we can.

Let me share our perspective on yesterday afternoon announcement by the United States Trade Ambassador that the U.S. government will ship off waving intellectual property protection for COVID-19 vaccines. We believe this will not help supply more mRNA vaccines to the world any faster in 2021 or in 2022, which is the most critical time of the pandemic. There is no idle mRNA manufacturing capacity in the world. There is no industry of talented individuals who are skilled in the art of making high-quality and high-purity GMP-grade mRNA vaccines. There are no companies who have developed manufacturing processes, purification processes and medical processes that would allow them to quickly run a clinical trial. And if approved by regulators around the world, then provide hundreds of millions or billions of supply of mRNA vaccine.

We have announced in the company's statement issued October 8, 2020 that during the pandemic, Moderna will not enforce COVID-19-related patents. You can find that statement on our website. We believe that the best way to end the pandemic is what we are currently doing. First, to maximize supply in 2021 to protect as many people as we can.

Second, to build additional capacity, which we have announced last week to get up to $3 billion of authorized mRNA vaccines for 2022, 2023 and beyond. And third, to continue to adapt the vaccine to have a highest efficacy vaccine with variant-specific booster for which we announced a very encouraging clinical results yesterday.

Let me now turn to Corinne to give you a commercial update. Corinne?

Corinne M. Le Goff - *Moderna, Inc. - Chief Commercial Officer*

Thank you, Stephane and good morning or good afternoon, everyone. As all of you already know, Moderna's COVID-19 vaccine is our first authorized product. And on the back of it, we have turned into a commercial company very quickly. So today, I'm delighted to give you an update on the commercial progress in the first quarter.

I will start with our most recently signed supply agreements, those that occurred in the first quarter and at the beginning of the second quarter this year. I am particularly happy to announce our agreement with COVAX, which will provide access to our vaccine to millions of people in low- and middle-income countries and is in keeping with our global access principles.

In total, our COVAX agreement is for 500 million doses for delivery in the 2021 and 2022 period. Specifically, in 2021, Moderna will begin delivery of 34 million doses in the fourth quarter of 2021. COVAX will have an option for an additional 466 million doses in 2022. We are grateful to all the collaborative efforts of CEPI, Gavi, UNICEF, the World Health Organization and the Moderna commercial teams in making this important supply agreement a reality.

Moving now to the additional supply agreements signed for both 2021 and '22. We have signed additional supply agreements with Israel for 5.3 million doses in 2022 with an additional option of 17.3 million doses for '22 and '23. And with Switzerland for 7 million doses in 2022 and options for an additional 7 million in late 2022 and '23.

We have also signed new deals for '21 delivery with Botswana, Brunei. And in addition, we have also signed an agreement with Zuellig Pharma, our distribution partner,in Southeast Asia, Hong Kong, Macau and Taiwan.

In total, we announced advanced purchase agreements totaling 845 million doses to be delivered in 2021 to the countries that are listed here on the slide. And we continue to have discussions with countries, who those we have already contracted with and new countries for supply in 2022 and beyond.

In our discussions, as Stephane said, we are hearing consistently from governments that in their view, there is no other technology that provides the high efficacy of mRNA vaccines and the speed necessary to adapt to variants, while at the same time, allowing reliable scalability of manufacturing. We are grateful for the trust placed in us from the various governments we have signed agreements with, and we look forward to supplying the vaccine to other countries and helping end the pandemic and getting ahead of variance.

Let me now turn to product sales. Our first -- our product sales for the first quarter of this year were $1.73 billion and were recorded for the delivery of 102 million doses. Product sales in the U.S. were approximately $1.4 billion and sales outside of the U.S. to the EU, Canada, Switzerland, Israel and Singapore were approximately $400 million for the 14 million doses delivered in the first quarter.

In the U.S., we have successfully completed the delivery of the first 100 million doses to the U.S. government within 100 days of emergency use authorization. And we expect to complete the delivery of the second 100 million doses to the United States government before the end of the second quarter.

As you know, the U.S. production started earlier and is roughly 1 quarter ahead in production ramp. As such, in the second quarter of '21, we expect the ex-U.S. ramp to be similar to that of the U.S. ramp in the first quarter.

To close, I want to reiterate that as we continue to produce and roll out vaccines into the global market, we are humbled and proud to be part of the solution.

I will now turn the call over to David Meline.

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Okay. Thank you, Corinne. Today, as with our last earnings call, we are presenting our results primarily on a U.S. GAAP basis. In some cases, we also provide additional detail to provide greater clarity on underlying trends. With this background, we are providing an analysis of actual 2021 first quarter results, along with an updated view of key drivers of financial performance going forward.

Turning to Slide 18. Total revenue was $1.9 billion in the first quarter of 2021 compared to $8 million in Q1 of last year. Following our first-ever product sales of $200 million in December 2020, we recorded product sales of $1.7 billion for our COVID-19 vaccine in the first quarter of 2021.

Grant and collaboration revenue increased to $204 million in Q1, primarily due to increases in grant revenue from BARDA to accelerate development of our COVID-19 vaccine.

Cost of sales were $193 million in the first quarter, benefiting substantially from previously expensed pre-commercial inventory costs, which I will discuss in more detail on a later slide.

Research and development expenses were $401 million for Q1 2021 compared to $115 million for the same period in 2020. The higher spend was driven by increased COVID-19 vaccine clinical development activities, including our announced efforts around booster, variant-specific and multivalent vaccine candidates. Headcount increases as well as pharmacovigilance activities related to our COVID-19 vaccine also contributed to the year-on-year expense increase.

Selling, general and administrative expenses were $77 million for Q1 2021 compared to $24 million for the same period in the prior year. The growth in spending was driven by increases in personnel, outside services and costs associated with commercialization of our COVID-19 vaccine globally.

Our provision for income taxes was $39 million in Q1 2021, reflecting a benefit from the utilization of our net operating loss carryforward as well as discrete items. I will provide further context on the following slides.

We recorded net income of $1.2 billion for Q1 of this year compared to a net loss of $124 million in the same period of last year. Earnings per share on a diluted basis was $2.84. Please note that our share count on a diluted basis now also includes the effect of outstanding options and RSUs as we began to be profitable. Previously, when we were in a net loss position, basic and reported diluted number of shares were the same.

Turning to cash and selected cash flow information on Slide 19. We ended Q1 2021 with cash and investments of $8.2 billion compared to $5.2 billion at the end of Q4 2020. The increase is driven by our commercial sales and additional customer deposits received in the first quarter for future purchases of our COVID-19 vaccine. Net cash provided by operating activities was $2.97 billion in Q1 of this year compared to net cash used in operating activities of $106 million in Q1 of last year. The reversal from net operating cash outflow to cash inflow was driven by our commercial market entry for the entire quarter.

Similar to last quarter, before providing an updated financial framework for the remainder of 2021, let me summarize a few areas from our Q1 results that are important to keep in mind when modeling expected 2021 financial performance.

Starting with product sales on Slide 20. We started last year to build 2 distinct supply chains, one in the U.S. and one outside the U.S. for rest of world markets. Our supply chain scale up in the U.S. was roughly 1 quarter in advance of our ex U.S. supply chain, which is reflected in the geographic sales mix in Q1. As we move forward in Q2, the ex U.S. supply chain is also ramping up toward full capability.

Turning to Slide 21. Cost of sales includes the cost of goods manufactured, logistics and warehousing costs as well as third-party royalty costs. We began capitalizing our COVID-19 vaccine inventory costs in December of 2020, following the COVID-19 vaccine emergency use authorization based upon our expectation that these inventory costs would be recoverable through commercialization of the vaccine. Prior to the authorization of our COVID-19 vaccine, inventory costs were recorded as research and development expenses in the period incurred. We expensed $242 million of prelaunch inventory costs in 2020 and started 2021 with the remaining balance of $187 million of 0 cost inventory. Almost the entire balance, or $184 million was sold and benefited our cost of sales in Q1 of this year, and hence, will not further impact future quarters in a material way. If inventory sold during the first quarter was valued at actual cost, our cost of sales would have been $377 million or 22% of our product sales somewhat favorable to what we expected, driven by favorable yields in our U.S. production facilities.

Now turning to our cash and investment position on Slide 22. The cash and investment balance reported as of March 31 was $8.2 billion, up from $5.2 billion as of December 31, 2020. The increase is primarily driven by the net increase in customer deposits for future product supply of COVID-19 vaccine. The net balance of cash customer deposits increased from $2.8 million at the end of December 2020 to $5.6 billion at the end of Q1 '21.

Lastly, let me comment on tax-related items on Slide 23. The significant investments in our research, development and start-up activities to develop the mRNA platform over the last decade have resulted in net operating loss carryforwards, with a balance of $2.3 billion at the end of 2020. As of December 31, 2020, we maintained a full valuation allowance against our deferred tax assets related to these loss carryforwards. We performed a valuation allowance assessment during each reporting period based on the latest available financial information and outlook.

After considering the weight of available evidence, both positive and negative, we concluded that as of March 31, it is more likely than not that the company will be able to realize the substantial majority of its net deferred tax assets. This analysis included not only our strong first quarter results, but also our April activity. The majority of the valuation allowance will flow through the P&L over the course of 2021 in our effective tax rate prorated based on the cadence of our expected pretax quarterly earnings.

We also recorded 2 discrete benefits in our tax provision in Q1, which lowered our first quarter tax rate. The first benefit related to the valuation allowance release for the portion of deferred tax assets, which we expect to utilize in future years. The second related to the excess tax benefits associated with stock-based compensation.

Turning now to the 2021 updated financial framework on Slide 24. Signed advanced purchase agreements for expected delivery in 2021 reflect a current full year total of $19.2 billion in anticipated product sales including doses that have been delivered and recognized as revenue in Q1.

Based on continuous progress to ramp up available supply capacity in our network, we have raised the lower end of our global manufacturing plan for 2021 from 700 million to 800 million doses at the 100-microgram dose level. Our manufacturing team and our partners are still working to supply up to 1 billion doses for 2021. Further, we continue to expect a range of deliveries in Q2 2021 of 200 million to 250 million doses.

Our total cost of sales includes the cost of manufacturing, logistics and warehousing and third-party royalties. For 2021, we continue to model average total cost of sales as a percent of product sales to be approximately 20% for the full year with some variation quarter-by-quarter largely driven by average selling price going forward.

Now let me comment on planned R&D and SG&A expenses. Q1 expenses of approximately $0.5 billion were stable compared to the underlying Q4 2020 expense run rate on a like-for-like basis.

In Q1, our actual expenses were lower than the internal forecast primarily driven by the timing of clinical development and commercial activities and related costs. We now expect a notable expense trend increase starting in Q2 on a quarter-over-quarter basis for the remainder of this year.

Based on better visibility of the utilization of our accumulated net operating loss carryforward, expected global sales mix and the mentioned discrete benefits in Q1, we now expect our all-in 2021 tax rate to be in the low teens. This compares to our previous forecast in the mid-teen range. This forecast is based on current U.S. tax policy in effect and does not include any future potential discrete benefits related to stock-based compensation. We will update this view as our business evolves further.

Finally, regarding capital investments, we are raising our forecast for capital investment from our previous range of $350 million to $400 million for 2021 to $450 million to $550 million, including the planned capacity expansion investments as announced on April 29.

This concludes my remarks concerning financial performance, and I now turn the call over to Stephen.

Stephen Hoge - *Moderna, Inc. - President*

Thank you, David. I'll begin with an overview of our COVID-19 strategy against variants of concern and the initial data from our Phase II booster vaccination study before ending with a summary of the rest of our pipeline. And before I go into the data, a reminder that our booster strategy is evaluating single-dose booster vaccinations with 3 different mRNA vaccines: 50 micrograms of mRNA-1273; 50 micrograms of mRNA-1273.351, both of which have data available today and what I will discuss in just a moment; and a multivalent booster vaccine candidate, which combines a 50-50 mix of mRNA-1273 and mRNA-1273.351 in a single vaccine.

In addition, we're also evaluating a lower 20-microgram dose of mRNA-1273.351. Data from the multivalent booster and the 20-microgram booster of 351 will be shared when available.

And with that backdrop, let's move to the data. Starting with safety, local and systemic adverse events within 7 days after a booster dose of either -1273 or -1273.351 were generally comparable to those observed after the second dose of -1273 in our previously reported Phase II study and our Phase III COVE study. The majority of the events were mild or moderate in severity and grade 3 events occurred with a frequency of approximately 15% in participants who received -1273 and approximately 10% in participants who received -1273.351. The most commonly reported solicited local events were injection site pain and the most commonly reported systemic events were fatigue, headache, myalgia and arthralgia. There were no grade 4 events reported.

On the next slide, are figures from 2 papers. The figure on the left-hand side were published in the New England Journal of Medicine and show the difference in neutralization of SARS-CoV-2 pseudoviruses in serum samples 1 week after vaccination with a primary series of mRNA-1273. Recall that there was a sixfold decrease in neutralization titers against the B.1.351 variant, the variant first identified in the Republic of South Africa; and a three-fold drop in titers against P.1, the variant first described in Brazil. And again, as a reminder, these neutralizing titer levels were from serum samples 1 week after the second dose of the primary vaccine series of mRNA-1273. So essentially, these titers are close to peak levels.

On the right-hand side of the slide is a figure from the preprint manuscript of our initial results from our Phase II study posted yesterday at Bio Archive. The figures show the neutralization titer levels of the participants in our Phase II booster study immediately before their booster vaccinations.

A reminder that these individuals were previously vaccinated with a primary series of mRNA-1273 in either our Phase II or Phase III studies, roughly 6 to 8 months prior to enrolling in this booster study.

At this time point, titers against wild-type SARS-CoV-2 remained high with almost all participants having detectable titers. But titers against B.1.351 and P1, the variants of concern were much lower. In fact, approximately half of participants had titers below the assays limit of quantitation at this time point.

So it is clear that waning of titers is apparent, both with time and that lower titers against variants of concern lead to more rapid loss of neutralizing activity.

Turning to the next slide. The data shows that 2 weeks after booster vaccines of either mRNA-1273 or -1273.351 neutralizing tighter levels increased against both the wild-type virus as well as the B.1.351 and P1 variants of concern. In fact, following boost, geometric mean titers against the 3 variants tested increased to levels similar to or higher than previously reported peak titers against the ancestral strain following primary vaccination.

When looking specifically at the GMTs of the different strains, we achieved levels of 1,400 after booster vaccination with mRNA-1273.351 against the 351 variant. This compares against the GMT of 864 when boosting with mRNA-1273.

Vaccination with mRNA-1273.351 was more effective at narrowing the gap in neutralizing titers between wild-type and B.1.351 viruses relative to boosting with mRNA-1273.

Now we're encouraged by this initial data, and we're excited to see additional data over time from these arms as well as the data from the multivalent arm and a lower dose arm of mRNA-1273.351.

On the next slide, I would like to highlight one last comparison from the manuscript. On the left hand is a sample of participants from the Phase I study and they're neutralizing titers against ancestral strain following a primary vaccination series with mRNA-1273. GMT is achieved in this assay approximately 1,500.

On the right-hand side is a reproduction of the data we just spoke through, looking at neutralizing titers, and I'm specifically highlighting the neutralizing titers against the B.1.351 variant of concern. A booster dose of 50 micrograms of mRNA-1273, the top bar, was able to increase titers to a level of 864 in this study. That compares with a booster dose of 50 micrograms of 1273.351, which was able to get to titers against the variant of concern as high as 1,400 in the study. We'll continue to closely watch this data, and as I mentioned a moment ago, look forward to subsequent updates and time points.

On Slide 31 is a snapshot of our vaccine development candidates that are in or entering the clinic. I'll highlight a few. Our CMV vaccine is on track to start a pivotal Phase III study in 2021. Our Zika vaccine is expected to begin a Phase II study also in 2021. Our hMPV/PIV3 respiratory combo vaccine is currently enrolling in toddlers. And at our Vaccines Day last month, we announced positive interim Phase I data from our RSV vaccine, mRNA-1345. This continues in pediatric and older adult cohorts of that Phase I study are still enrolling.

Finally, within our flu vaccine program, we expect a Phase I study of mRNA-1010 to begin in 2021.

Outside of vaccines, we have 7 clinical proof-of-concept trials ongoing across 4 modalities. Our VEGF program partnered with AstraZeneca is enrolling in a Phase II. Our personalized cancer vaccine program partnered with Merck is also enrolling in a Phase II trial. And KRAS, our second program partnered with Merck is ongoing in a Phase I study.

Within intratumoral immuno-oncology, our Phase II dose expansion in OX40 ligand, Phase I Triplet and Phase I IL-2 study, which is partnered with AstraZeneca, are all still ongoing.

Finally, as Stephane mentioned, we are pleased to have started dosing in the Paramount study in propionic acidemia.

On Slide 33, you can see our full development pipeline. In addition to our large portfolio of infectious disease vaccines, we now have 7 therapeutic programs in the clinic.

I'll now turn the call over to Stephane. Thank you so much.

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

Thank you, Stephen, Corinne and David. Our 2021 advanced purchase agreement signed have now been increased to $19.2 billion. As we look into 2022, we're investing to distribute and dose supply capacity because we believe the market need -- could be greater in 2022 than in 2021.

First, we already have countries signing APAs for 2022 for prime series for children but also for variant-specific boosters. Israel last week and Switzerland this morning.

If you recall, there were some of the first countries who signed APAs in 2020. And again, these countries are ahead of the game for 2022 and 2023.

Second, with the COVAX partnership announced Monday, we anticipate to supply up to 466 million doses in 2022.

Third, we're having active discussions with all the governments that have signed 2021 APAs with Moderna. For new APAs for 2022 deliveries, again, prime series but also boosters.

Fourth, we're having numerous discussions with government that do not have 2021 APAs with Moderna because we cannot supply them in 2021 unfortunately. But many of these governments are already asking us to enter into 2022 APAs because they want high efficacy mRNA vaccines that are easy to store. This is why we decided to invest for more supply in 2022. We believe from our current deals and current discussions that the market wants more supply from us in 2022 than we can supply in 2021.

As we look at the next 5 to 10 years, we have the most innovative vaccine pipeline in the industry. And we're investing more in research to increase our impact by bringing to the clinic, more innovative vaccines against viruses that hurt humans. We are now in the clinic in 3 therapeutic areas: oncology, cardiology and rare disease and soon, we should be in the clinic in autoimmune disease as well. We are continuing to innovate and invest in science, like, for example, for delivering mRNA in the lung with our partner, Vertex.

As we continue to prepare Moderna to scale and to have 10x more impact, we're investing aggressively. We are accelerating our investments in digital, automation and AI.

From a spend of $27 million in 2019, we invested around $60 million in 2020 in digital. We're planning to almost triple that $170 million in 2021. We're investing across the world in R&D to ensure high quality to accelerate the pace of learning and to ensure we can transform clinical operations. We're investing in digital to ensure high-quality, high scalability for manufacturing. We are building commercial so that we can commercialize our pipeline in a highly efficient and effective manner. We want to change the big pharma paradigm of large, inefficient and expensive sales force and advertising spend to promote me-too drugs. Our pipeline is first-in-class medicine that patients and doctors are waiting for.

We want to enable our corporate functions, HR, legal, finance and so on to scale without creating large corporate organization.

I'm also excited that we are launching an AI Academy. Today, we have some exciting pockets of excellence in AI across the company. But AI is not yet part of our DNA. The reason is simple, most companies don't do AI. So as we grow and hire new talent, they have great skills in their heart, but few have been exposed to AI in their previous company. We want AI to be how we run the business in science, in clinical development, in manufacturing quality in commercial, in HR and finance, everywhere.

It is the same change management revolution as 20 to 30 years ago when personal computers entered the workforce. We want everything at Moderna to understand and use AI in everything we do. AI will become part of our DNA.

As many of you know, we have built integrated digital system connected to each other. And as we have more systems, we get more data. As we get more data, we learn faster. And we keep building and creating a network cycle. Between our strong balance sheet, our mRNA platform, our team, our culture and our digital infrastructure, I believe our belief to scale Moderna is unique in the biopharmaceutical industry.

As part of scaling Moderna, there is software, better so very value added. Many of you were at the opening of a Norwood manufacturing site in July 2018 or you came to visit after the opening. Our building is around 200,000 square feet. We call it Moderna Technology Center South or MTC South.

In 2020, we added the building next to it and added around 245,000 square feet and called it MTC North. We are pleased to announce this week that we now have access to a new building, MTC East, which will start welcoming Moderna employees later this year after some maybe investment and renovation to the building. That is another 240,000 square feet.

So we're now having in MTC access to around 650,000 square feet. We now hold the building on this campus, and we can also add more buildings and build them now that we have the entire campus.

We are deeply committed about building a company that has a strong sense of responsibility. We want Moderna to be a positive force in the world, not only for our medicines, but also by who we are as a company.

We are very committed to belong, inclusion and diversity. We recently published or expanded workforce diversity figures for the first time. Last year, we signed the CEO Action for Diversity & Inclusion pledge. And we have also reiterated our ongoing commitment to increasing diversity in our clinical trials.

We are deeply committed to the environment. We have decided to source our Norwood and Cambridge site with renewable energy and will offset any energy that is not from renewable sources, and we will be working on our target as to when we should be a net-zero carbon company.

We also encouraging our employees with a positive impact on the communities in which we live and volunteer, from cleaning the Charles River in Cambridge, to feeding the homeless and stem education and much more. You can find a lot of resources online on our website.

As I close, I want to convey how thankful we are at Moderna to have a chance to do what we do. Every day, we come to work to make innovative medicine using the first information platform of a biopharmaceutical industry. My colleagues and I work and collaborate to make more medicines to protect or treat people.

I am proud of what the team has done over the last 10 years to get us to this stage. Over the last 14 months, since we started chasing SARS-CoV-2 virus. And in Q1, as we continue to execute relentlessly.

But as I look at the future of Moderna, I believe we have a chance over the next 5, 10, 20 years to transform medicines potentially like no other company has ever changed medicine. This is just the beginning.

Before taking your questions, I would like to remind you that we will be hosting our Annual Science Day in a few weeks on May 27. You are going to work to connect this event as Stephen and his team have some very cool new things to share with you.

And later at the end of the summer, on September 9, our annual R&D Day for holistic clinical update.

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

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Your first response is from the line of Salveen Richter with Goldman Sachs.

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

I have a couple here. So firstly, with regard to, if the U.S. supports the WHO waiver of COVID-19 vaccine IP, what does that mean for Moderna? I mean if you could just walk us through that.

Secondly, if you could just discuss contract dynamics for the vaccine in 2022 as you look to address variants and kind of you see them move towards an endemic market.

And third, it's nice to see the PA program move forward. It would be great to kind of understand whether we'll see data from that program this year and what else we might see from the ex COVID pipeline?

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

Salveen, it's Stephane. Let me start with your first questions and then turn few questions to Stephen.

So on the IP, what does it mean? I believe it doesn't change anything for Moderna. As I said, we had said last October that we will not enforce our COVID-19-related patents during the pandemic. And as I said in my remarks, there is no mRNA in manufacturing capacity in the world. This is a new technology. You cannot go hire people who know how to make the mRNA. Those people don't exist.

And then even if all those things were available, whoever who wants to do mRNA vaccines will have to buy the machine, invent the manufacturing process, invest verification processes, analytical processes. And then they will have to go run a clinical trial, get the data, get the product approved and scale the manufacturing. This doesn't happen in 6 or 12 or 18 months. We have been working at these for years.

And as you know, there are some smaller mRNA companies that are still in the clinic, trying to get the products to a finish line. And so we saw the news last night and I didn't lose a minute of sleep of the news during the night.

On 2022 contract, the dynamic is, as I just described it, which is, the market has tremendously changed. Since the pandemic started last year, before clinical data, many countries as you know, didn't want to move, especially because of mRNA being a new technology. They moved first on protein contracts, on adenos contracts. And then the kind of mRNA contracts came later, more just in case. And then the clinical data came along and the speed to get to approval.

And so -- and then you have the fact that the proteins are still not authorized anywhere in the West. And then you had the low efficacy of the adenos in over the safety questions around the adenos, manufacturing scale-up issues that adenos companies have had. And the big question that scientists advising governments are which is, can you actually really boost adenos with more adenos products because, by definition, you give again the same virus vector to somebody that we believe over time will get less and less response from it.

So as we look at the marketplace, which what governments are doing, and given many governments, I think last year, believe the pandemic will be gone quickly. Trust me, every governments we're talking to believe this is going to stay for a long time. They have got massively educated by the scientists and the clinician, and they believe this virus is not going away. They believe boosting is going to be critical. They believe variant-specific boosting is going to be the right way to do the science. And as you saw from Stephen's presentation, this is what the clinical data are showing as well.

And so the dynamic is that current governments that have already contracted us are calling for more, and we're in active discussion with all of them to supply more for '22 and '23, both prime series and specific-variant booster. The beauty about this technology is, we can agree right now in the contracts to give them next year to be able to choose what they want based on the clinical data. And that's an incredible competitive advantage. And this we can do because, as you know, the manufacturing process is the same for -1273 or -1273.351 or -1273.221 or new 1273 dot something is a new variant. And we can change that on a very short notice because it's a same equipment, in the same room, with the same people, with same raw materials.

And then -- all those governments, which is almost more exciting to me that never called before -- that we called before, but we couldn't supply them because we are in the unfortunate position and we're very sorry. We have no more supply for you in 2021, which, of course, a very difficult discussion to have given the suffering happening around the world.

But the great news with the investments we've announced to get up to 3 billion next year. We now can have those discussions with those governments. And Corinne and the team are having a lot of discussions with them. So that kind of give you a sense on the dynamics.

Stephen, on PA?

Stephen Hoge - *Moderna, Inc. - President*

Sure. Salveen, thanks for the question. So as you know, the program, the Paramount study for propionic acidemia is going to be looking at biomarkers as a part of its dose optimization. And so it's possible that we'll be seeing very early indicators of impact there. But we are going to -- there's no guarantee that the first dose level and the first cohort that we're looking at will be the correct one. And we're going to make sure that we develop a cogent and consistent data set before we bring that forward. It is a dose optimization study, and we will perhaps be looking at multiple dose levels. So while I think it's possible that we would see data this year, it's dependent upon many things that are well beyond our control.

Now you asked a more general question also about our broader portfolio. And if you look at the programs more generally, VEGF, as we mentioned, is a Phase II program that's been enrolling for a while. It's possible we could see data from that. Our PCV and KRAS programs, again, as open-label programs will continue to track those closely as they enroll. And then similar intratumoral programs that we highlighted, many of them are ongoing and producing data. And of course, when we have a complete and cogent data set, we will bring it forward.

Operator

Your next response is from Matthew Harrison with Morgan Stanley.

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

Great. I guess two from me. One, on the sort of next-generation COVID vaccine where you think it might be refrigerator stable. Can you just talk about the regulatory path for that vaccine given that it's not the full spike. Do you think you might have to run an actual efficacy study? Or do you think a neutralization titer study with safety might be enough for that?

And then the second question, Stephen, if I can just follow up on PA. I know in the past, right, one of the struggles has been enrollment. Obviously, it's great to see that you've gotten a patient into the study. Can you just talk about now that you've gotten a patient in what your sort of view is around enrollment and if you think you've gotten through some of those hurdles?

Stephen Hoge - *Moderna, Inc. - President*

Sure. Thank you, Matt, for both questions. So first on -- I believe you're referencing our second-generation vaccine candidate, which is mRNA-1283. It is a shorter construct that we think could have a much longer refer through its stability profile.

As we announced previously, we started enrolling in the Phase I in that study. And it's probably a little bit premature to comment on what we think the regulatory path will look like for that until we get some of that initial data and have conversations, obviously, with regulators. But I would highlight that it's possible that -1283 may not go into a full primary series vaccination study. It could impact in the future function as a booster. But again, that's probably too early to say. We will have to wait until we see that data and ultimately, it would be dependent upon conversations with regulators in the future.

As it relates to PA enrollment, yes, as you mentioned, we've been working very hard on that over the coming -- over the past years, and we're quite pleased to have enrolled the first participant, the first patient in that study. And the team is working hard to enroll additional patients as quickly as possible. I think time will tell whether we've actually broken through here and addressed any of the issues that we previously had in terms of enrollment. And so hopefully, we'll be able to provide subsequent updates on expanding enrollment in the near term that will demonstrate that we've made that progress.

Operator

Your next response is from Ted Tenthoff with Piper Sandler.

Edward Andrew Tenthoff - *Piper Sandler & Co., Research Division - MD & Senior Research Analyst*

Great. Thank you for all of the detailed updates. including running through the financial analysis. So detailed, David. Congrats on all the success. Stephen, I wanted to pick up on the booster data that you've shown. And maybe you can kind of take us a step forward. What is the booster strategy going to look like. Do We actually need to maybe do redose or revaccinate sooner than 8 to 6 months because of where the levels were? And maybe you can just tell us what you see as sort of the potential timing in queue for when we would be getting boosters.

Stephen Hoge - *Moderna, Inc. - President*

Thank you for the question, Ted. Look, I think we have to start by saying we don't know. We do not have data on when to expect waning immunity leading to breakthrough infections. But we do know that there is a raging pandemic that reinfections will happen at some point. And the best way to ensure that we do not have renewed outbreaks in well vaccinated countries is to boost and maintain the highest possible levels of neutralizing immunity.

We, as Moderna, also believe that, that means we want to maintain the broadest neutralizing immunity against the largest number of than circulating variants of concern.

If you look at the data that we have posted today as well as some of our published data and others reports, it does feel like immunity to a primary vaccination series or a previous infection seems to weigh in over the 6- to 12-month time horizon, at least as measured by neutralizing titers. Again, we don't know whether that's a clinical cohort or not, but it certainly is an indication of that waning immunity.

And if you look at the data that we -- that I presented earlier, approximately half of the participants in our booster studies, no longer have detectable neutralizing immunity against the variants of concern. They have neutralizing immunity against the ancestral strain that they were vaccinated against.

So the logical thing we think to do is to boost their immunity against those variants of concern. If you will vaccinate them against those to both increase those titers right now, but also give them a longer duration of protection, perhaps long enough, that we can see our way through the pandemic. That probably looks like boosting on a 9 to 12 months after primary series as an annual booster for now. At least while we're continuing to see the evolution of the virus.

Now the last point was about our strategy more generally here. And we do believe that the virus is not going to follow one path of evolution. That we are going to see many variants of concern, that there may be divergent paths. And therefore, the best way to ensure that we can protect against the broadest number of variants of concern will be a multivalent vaccine.

Now right now, we're still waiting to see our multivalent vaccine data, which is a combination, as you know, of ancestral and 351, the strain first identified in South Africa. But we think this is just the beginning, and we think we're going to be unfortunately continuing to fight this pandemic through 2022, at least, globally. And therefore, we're committed as a company to make as many updates to the vaccine, to add as many variants as we think are necessary, to ensure that when people receive a booster, it provides the broadest immune protection against the widest range of variants.

Operator

Your next response is from Michael Yee with Jefferies.

Michael Jonathan Yee - *Jefferies LLC, Research Division - Equity Analyst*

I appreciate the questions. I had two important follow-ups. One was going back to the question about the WTO. Can you just offer some color around the view of loss of raw material supply capacity, et cetera? In other words, shedding some light on any ability to actually increase global capacity even if there were some form of open patents. So maybe just talk about that. Because I don't think that you can just make it. And like it's easy. Can you maybe just offer some color there?

And the second question is also a follow-up on the variant strategy. It sounds like the bivalent strategy might be the best, Stephen. So at what point would you just pull the trigger on beginning to manufacture that and ramp that all up for 2022?

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

Thanks, Michael. It's Stephane. Let me start on the raw material. Going back to what I said is, if somebody was to start from scratch because again there is no mRNA player that's with idle capacity out there. One will not start by focusing on large-scale raw material supply. I mean why will I first figure out how do we make mRNA. And you cannot find that patent, which as you all know are on the founded on the U.S., but they block this website. And so one is going to figure out what machine do you need, how do you make mRNA, what purification method you need, what analytical methods you need. And once you recognize all those things, which trust me is going to take you time, it is not easy. Us and other companies that are in the market we are on a vaccine that we've been building for decades. And even companies that have been working on it for 10 or 20 years are still in a clinic trying to figure out how to get to the finish line.

And so I really believe that this is not the issue. I already believe the IP topic is mostly critically driven. It is not the issue. It might impact other technology that had a role in proteins and this I could not comment on. But for mRNA, I really think this is the wrong question. Stephen, do you want to take the variants?

Stephen Hoge - *Moderna, Inc. - President*

Yes. So thank you, again, Michael, for the question. So on our multivalent strategy, we have -- at this point, we are still waiting for the clinical data to confirm that. And as we expect to have that shortly, as we've mentioned, we previously dosed people with the mRNA-1273.211 variant. The preclinical data that we have published does -- or presented to dose suggest that, that is going to be the winning approach. And as I highlighted, or as is highlighted by the monovalent clinical data we already have, there is a benefit to adding additional antigens and potentially, therefore, benefit with a multivalent approach.

I think it's important to recognize that we view this as an ongoing battle. And so your question about when do we pull the trigger and move forward bivalent manufacturing. We're already on the path of doing that manufacturing, not because we think that we're done with mRNA-1273.211 the bivalent -- current bivalent vaccine, but because we think we're going to go down the path of multivalent vaccines and continue needing to add things.

And so that platform capability, we are already in the process of building and establishing to support multiple updates to a multivalent vaccine.

And we do think that's going to be required because we think the virus is not going to stand still and stop evolving, and we suspect there's going to be trivalent, maybe quadrivalent. It will keep happening in the time ahead. We have completed GMP manufacturing of all of those batches, and we're at sufficient scale, we think, to be able to quickly move into commercial scale distribution if needed. But at this point, we are still waiting for data to come shortly to confirm that performance in clinic.

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

Yes. So just a point to add to Stephen on a multivalent, which I think a lot of people don't appreciate is, it is not easy to do a multivalent mRNA, GMP product from an analytical QC standpoint because those mRNAs are of the same size. They look mostly similar because you just changed a few -- I mean a few nucleic acid. And that expand now. And it's why the platform comes to drive so much value. As you all know, we have a CMV vaccine on its way to Phase III, where we developed and that we find over the years, a very complex product, seeks mRNA in the same guidance.

So if you think about what the multivalent vaccine for COVID is going to look like, it's not going to be easy. And so for people that have not done multivalent in GMP setting before, trust me, the regulators because we had this discussion with regulators around CMV over years. They didn't want to see a lot of analytical method characterization so that you can prove to them that you know what is in the pipe. And that is yet again another big differentiation with Moderna.

Operator

Your next response is from Gena Wang of Barclays.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

I also have two. One also related to the IP question. So wanted to ask differently, just wondering, Stephane, how many contracted global manufacturing sites you have? And how long in general is the contract?

And the second question also regarding the new booster data. This is more for Steve, actually, to me, it was a little bit surprised the differences between -1273 versus -1273.351 was less or narrow than initially I would expect it. It seems like -1273 should be also sufficient to protect from variant strain. So what could be the explanation? And then you did just lay out the plan, you still will be going after the multi-variant approach. But regarding the explanation there, like do you think that, that just a single shot that was should be sufficient for the protection?

Stephen Hoge - *Moderna, Inc. - President*

Thanks, Gena. I'll -- maybe I'll take that question first and then hand it back to Stephane on your IP question. So a couple of things I would note. The first is the level of titers, as you suggested, there's a little bit less than twofold difference between them, and you are -- when you are seeing substantially higher titers in the order of 1,400 when you give the very specific booster, that's mRNA-1273.351.

Now I would note that this is happening already at Day 15, right? This is an early time point that we're looking at, at this point. We will also be looking at Day 29. And in this case, we are -- effectively, it is a prime with the 1273.351, right? It is the first dose of the strain first identified in South Africa. And so it's actually -- there's 2 ways you could look at it. One is obviously that it is -- both look good. I think the other and the way that I'm

still looking at this is, it looks like we can very rapidly direct the immune response to an increased level of neutralizing titers against the variant of concern that was first identified in South Africa 351 in this case.

And if you compare the titers that we've achieved even by day 15, between these 2 variants -- or between the ancestral strain and the 351 strain, it's really only the 351 strain that's getting to the same level that we saw against the ancestral strains in that last comparison. So to levels that are approximately similar amount.

Now that's not to say that mRNA-1273 as a booster couldn't -- wouldn't provide a benefit, and I think you're highlighting that, Gena. There is evidence in this data as well that we can substantially increase neutralizing titers generally across the response with a booster dose of mRNA-1273, our authorized vaccine at 50 micrograms. And that is encouraging. That is good news because I think it suggests that is also a useful strategy. But if you had to choose between the 2, and you were primarily concerned about increasing immunity to a higher level so that it can last longer, particularly in patient populations at high risk of either waning immunity or incomplete immunity, we think this starts to provide very early event, even at Day 15, even after a priming dose, that there's going to be an advantage to some strain matching of the antigen. And that's what has us continue to be excited about a multivalent strategy. Stephane?

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

Sure. Thanks, Stephen. So Gena, on the contract manufacturers, we kind of look at kind of raw material drug substance and drug products. In all of these, we have multiyear contracts. As soon as we got board's authorization to go to 3 billion supply for 2022, we right away, sent a lot of orders and a lot of additional supplies to our suppliers. And not to forget the drug substance actually now, it is the place, it's on Moderna site where we actually have the biggest capacity of a drug substance even in the 3 billion dose 2022 scenario over.

Operator

Your next response is from Geoff Meacham with Bank of America.

Geoffrey Christopher Meacham - *BofA Securities, Research Division - Research Analyst*

Just had two on COVID. The first one is, what does your data tell you with real-world effectiveness of -1273 today as of now with respect to some of the main variants? I'm just trying to reconcile the need for annual boosters versus minimal breakthroughs thus far and high efficacy.

And then the second question is, when the next-gen vaccines for COVID-19, when you have some permutations, what's the potential to leverage the technology to use different parts of the virus versus just modifying the spike protein or do you think this could add regulatory steps that make it difficult, even if it's theoretically possible.

Stephen Hoge - *Moderna, Inc. - President*

Thank you, Geoff. Those are both good questions. So maybe I'll take the first one, first, which is our real-world evidence, the largest amount of it that we've seen has been published by groups like the CDC and continues to reinforce that the efficacy we saw in the clinical trial seems to be translating well into real-world use with very high efficacy against disease, against COVID-19.

I think it's important to note, though, that this is all happening very acutely, right? We're still only months away into -- we're months into these vaccination campaigns. And the primary concern that we and others have from a public health perspective is really not what's going to happen right after vaccination. But what does this look like in 9 months? What does this look like in 18 months? And I think that the really difficult situation everybody is in is you could say, well, let's wait until it's a year from now, and we see a reemergence of spikes of cases. We see -- maybe it's not as bad, but we see a very big and bad flu season in the winters, tens of thousands, maybe hundreds of thousands of death, that kind of scale. That's not a situation that most are willing to take a risk on because it obviously could be substantially worse than that.

And so we're probably not going to have a chance to wait for data for cases to really break through a year from after vaccination in the real-world setting and let that start to guide revaccination decisions.

At that point, it's almost too late. And so I think at this level, we think for the very near term, the correct and sort of conservative decision is to continue to try and maintain the highest level of broadest immunity in the populations that are well vaccinated already.

Now if you look beyond this sort of epidemic phase or pandemic phase that we're in with this variant evolution, into the years beyond that, so 3, 4, 5 years from now, hopefully, we're well past the current pandemic. We still believe there's going to be SARS-CoV-2 reinfections. And as we shared at the Vaccines Day just a couple of weeks ago, we take that lesson from the previous endemic coronavirus epidemics that have happened, where hundreds of years later, you still see reinfections, mortality, substantial health care costs associated with those viruses. And we don't know whether SARS-CoV-2 is worse than them or the same, but we believe that, that burden of disease that's created by the fact that respiratory viruses continually reinfect. And when they do, they can really have a devastating effect in high-risk populations, particularly older immunocompromised. We think that's a real probability in the future. In fact, it would almost be unprecedented for that not to be the case in the coronavirus context.

And so for that reason, we believe there is going to be a need for continual boosters, whether it's annual or not and whether the multivalency continues to add more and valencies, I don't think anybody can say yet. But it's certainly a situation we're preparing for.

Geoffrey Christopher Meacham - *BofA Securities, Research Division - Research Analyst*

And Stephane, just on the second question on the different modalities or Stephen, either...

Stephen Hoge - *Moderna, Inc. - President*

Yes, Geoff, sorry. I apologize for that. And this is your second question on different modalities and different parts of the antigen. So I think what is pretty clear from all the vaccines, if you look across them, but certainly if you focus on the messenger RNA vaccines is that the high degree of efficacy we're seeing in vaccines right now is based on spike protein immunogenicity. That is the antigen that's being expressed.

Is it theoretically possible that non-spike antigens could have provided the same protection? I think it's definitely possible. So forward-looking possible. But I think you would be remiss to look past the multiple large Phase III trials that provide pretty conclusive evidence of the value of going up for spike protein and trying to prevent COVID-19.

So I think you would probably -- if you went down that route have to redemonstrate that efficacy that may be increasingly difficult in a world where we have so many good choices in terms of vaccines. And so I'm not exactly sure how we go down that path, even theoretically.

Operator

Your next response is from Cory Kasimov with JPMorgan.

Cory William Kasimov - *JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst*

I want to go back to the topic of the future contracts. I know this has kind of been asked in a couple of different ways, but on discussions and negotiations that are currently taking place, how much confidence do you have that there's going to be demand to fill up to 3 billion doses in anticipated supply that you think you could have next year, especially if people are getting a single annual booster in the future?

And then the second question is from really a modeling perspective. Are the price points currently being negotiated on future contracts comparable to what you have on the existing ones for 2021? Just basically wanted to see if we should be assuming stable pricing for modeling purposes for '22.

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

Yes. So let me take a stab at the question, Cory. And if I miss anything, Corinne, just please add some color. So as I said in my remarks, from what we're hearing from customers, this is becoming an mRNA market looking forward. And so there are not so many players in the mRNA market. And if you look at what the future needs across the globe, you're going to see have vaccinate others. All others are not going to get vaccinated this year on the planet. The math doesn't work.

And then you have adolescents and then you have children across the world. And then you are boosting. So when you add all those pieces, the reason we are building up to 3 billion of supply as a mix between the prime series and boosters is because we believe that this is what the world is looking for based on the daily engagements we have with governments around the world. It's a very different setup than what it was a year ago.

A year ago, you get people saying, "Oh, I'm going to get cheap adenovirus vaccine because it means supplied at cost." This is not a discussion anymore today. The discussion is, "I want some mRNA vaccine for my people, I want variant booster specific, I want multi-variant, I want the best thing because I don't want a second and the third and the fourth year with this thing. I need my country to be back on its feet." Did that help, Cory?

Cory William Kasimov - *JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst*

Yes. No, on the pricing question for modeling.

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

No. Look, I think, I'll give you any color, but again, there is no more discussion at all, that your price is this and there's a small company. That company will price at cost at $3, this discussion is gone.

Operator

Your next response is from Hartaj Singh with Oppenheimer & Company.

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

Great. A question I would have is just on the 50-microgram going forward, the booster and against variants. Would you see that potentially becoming your initial kind of prime boost vaccine possibly in the future? Or you think you'll stick with the 100-microgram route, whether it's with 1283 also.

And then just on OpEx, just any kind of color when we think about '22 and '23 for David, what cost of goods sold could look like once these quarterly variations kind of flush out? And then what your adjusted operating margins could start looking like us?

Stephen Hoge - *Moderna, Inc. - President*

Thanks, Hartaj. I'll take a stab at the first one and then hand to David for the other. So on 50 micrograms, obviously, the data we shared today is a small number of subjects. But we've previously shared and published our Phase II data on a slightly larger number of subjects looking at a 50-microgram primary series. That looked quite good and at least as measured by immunogenicity seemed to achieve levels that were consistent with 100-microgram dose.

So it's certainly something we're going to look at as to whether or not we could pursue a 50-microgram primary series. But how we get there will depend upon data that we don't yet have, right? So we will have to look at whether there are clear correlates of protection that we can use to bridge between those doses and/or we'll have to look at different populations in which we started those doses. As an example, this has been shared.

We're evaluating 50 micrograms as a potential primary series even in pediatric populations. As you can imagine, you don't need perhaps as higher dose in younger people than you do in older ones.

So there's a lot of things ahead of us in terms of looking at whether or not a primary series for 50 micrograms is possible. Certainly for a booster series, that is the top dose at which we're looking. And as we look forward, we'll continue to carefully evaluate whether or not we can adopt that as a target dose across all of our applications. But it will depend on data.

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

Great. And then question on the...

Stephen Hoge - *Moderna, Inc. - President*

No. Go ahead, David.

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Yes. So cost of goods and operating expense trends as in '22 and beyond. I guess what I'd say is it's a little early to start giving that kind of guidance for 2022. What I would say is that, if you look at our cost of goods and the cost of goods manufacturing thus far, we've been quite pleased with what we're seeing as we've ramped up production initially here in the U.S. We've seen, as I said, yields have been better than we'd foreseen as we did the initial planning. So that's obviously very helpful.

And we reiterated today We think right now, the right planning assumption continues to be 20% cost of goods. As you move beyond '21, you get into a question of vaccines versus therapeutics. We think cost of goods manufactured will be very competitive for this product. And therefore, margins and gross margins will depend very much on price levels, which I think it's early to comment on.

And then in terms of operating expenses, we are building out the company. We continue to do that. And as I mentioned, we -- while our overall operating expenses were quite stable at $0.5 billion in the first quarter. We do see that trending up as we now move through the year. And we'll continue to invest appropriately to drive the portfolio investment and to build out globally. So I would say we'll continue to do that. And we'll give you better and more precise guidance here as we move closer to '22 and beyond.

Operator

Your next response is from Joseph Stringer with Needham & Company.

Joseph Robert Stringer - *Needham & Company, LLC, Research Division - Associate*

Just another one on manufacturing capacity there. As you potentially move to next-generation COVID vaccines. Just wondering if you could give us a sense, maybe even qualitatively in terms of the -- given the modularity of the technology, what a potential manufacturing ramp would look like for some of the second-gen vaccines in terms of manufacturing capacity and the ramp relative to what we had seen with -1273.

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

Yes. It's Stephane. So the -1273 ramp has been constrained by manufacturing capacity. So if you look at this year, the only -- we "only supply 100 million" to those in Q1, which is an extraordinary number is because we are building the capacity. And so the way to think about it is, as Corinne and her team are working out to add new lines and to increase the capacity, the ramps of follow-on products will be much faster because today,

manufacturing is slowing down the ramp. So I anticipate that as you think about the multivalent booster launches, as you think about RSV to CMV launch, we will not be on the back foot.

As you know, as part of our 2020 budget that we did at the end of 2019, we did not plan for pandemic. We were supposed to be commercial several years down the road. And so the team has done a remarkable job to get to this point, but we are -- and we're going to stay for, I would anticipate all over year supply constrained.

Corinne and her team would love to be able to sell more product because trust me, their phone is turning red hot by calls from around the planet and would love to be able to help protect more people, but we just can't because we were not planning a pandemic in 2020. So I anticipate that for variants and for new product launch, we will make sure that we are not capacity constrained, which is why the 3 billion supply volume that some people might think is maybe too aggressive.

As I said in my remarks, the pipeline of the company is also going to pay with this. And so it is just behind the multivalent vaccine. So if you look at a couple of years out, and we're not building manufacturing for 6 months. We're going to be really happy to have that capacity so as we launch product. We can supply the market every single dose that Corinne and her team can make sure that the market wants.

Operator

Your next response is from Mani Foroohar with SVB Leerink.

Mani Foroohar - *SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst*

One quick one sort of on financials. You gave a little clarity on CapEx investments around expanding capacity reduction. Should we think of that level setting CapEx is going to be forward with a modest increase going forward? Or should we be thinking of that as primarily a onetime build-out?

And then secondarily, you've given a little bit of clarity -- and there's a lot of clarity around COGS for this quarter versus rest of the year. Going forward, so we think about the absolute COGS per unit again pretty linearly related to dose. Or are there other attributes, royalties, et cetera, differences in products used between different vaccines, would that suggest if that's not the right way to think about it.

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Yes. So CapEx, if I understand the question is guidance for '22 and beyond on CapEx. And again, unfortunately, it's a bit early to be able to comment. We -- if you look now, we've increased our guidance for this year based on the developments that have occurred over the last couple of months. Is that a steady state going forward into the future?

I think for a company of what will be our size and scope and level of vertical integration, I think it's reasonable to expect that we'll continue to invest in our own capacity. And therefore, you can expect we'll have ongoing CapEx. Is it precisely in this range or somewhat above or below? I really wouldn't want to give you that precision as of yet because we're -- it's not that clear yet. But I think an ongoing CapEx trend will be appropriate for the company.

In terms of the COGS, I think that's the right way to think about the cost of manufacturing this product. It will be impacted at some level by the amount of materials in the product. But when you're talking about micrograms of materials, it's really not that significant. So I think you can -- as the simplest assumption assume, it's a pretty steady cost of manufacture as we're seeing right now.

Mani Foroohar - *SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst*

Great. And a quick follow-up on some of the contracting. I know it's been asked in various forms. You talked about the OUS manufacturing being about 1/4-ish behind U.S. manufacturing. Right now, based on your disclosures on volume dose, those are delivered versus what we have from the other mRNA competitor in duopoly right now.

Market share for you guys is somewhere between 5% and 10% and a lot of these countries until you deliver doses. How do you think about catch-up on manufacturing and deliveries and how that influences the ongoing contracting for next year, i.e., does your stronger incumbent position in the U.S. suggest you are better positioned for U.S. contracting volume?

Or do you think 2021, the results for 2021 contracting have nothing to do with 2022 and every year is a whole new game between you, too?

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

Yes. It's a good question. So as we said, the plan was always -- the plan we're executing on. And so when we spoke to countries and set up those 21 APAs. we managed the quarter delivery to the countries as we knew capacity would come online. We had not anticipated early parts of the year that we will be able to export from the U.S. And the piece we should not forget is, as you know, it's reported in the media daily, the U.S. is going to be having way too many vaccines very, very soon, if not already.

And so the capacity that we are building in the U.S. and we're adding is also going to supply the world. So I think one should anticipate a very big acceleration of shipments to countries outside the U.S. as we go into Q2 and even more in Q3 and Q4 as we meet our obligation to the U.S. government.

Mani Foroohar - *SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst*

Great. That's really helpful. And could you guys comment on where you are -- what you're seeing in the real world in terms of vaccine hesitant/end market demand. There's been a couple of media reports that, that's starting to be more of a limiting factor as opposed to supply, at least in the U.S. currently, certainly not globally.

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

Correct. In the U.S., and you see it on the daily numbers probably by the CDC people, I think, since mid-April roughly, the number of vaccinations per day in the country is going down. And it is not because of supply. If you look at the shipments coming from the companies, they keep increasing exactly as we have been saying.

And so now there's an oversupply of vaccine. It's very demand-driven problem now. So you see some states across the country that are still very active in vaccination. And we are looking -- as we said, that very high rates of vaccination is going up every day. There are other parts of the country, as you know, where they have way too many vaccines. As you have heard that the federal government, I think yesterday or the day before, has announced that they we were going to start to shift products from one state to the other based on actual demand and it really need to vaccinate the [discrepancy].

The U.S. doesn't have a supply of vaccine issue anymore. That was true in January. It is not true anymore.

Operator

Your next response is from Simon Baker with Redburn.

Simon P. Baker - *Redburn (Europe) Limited, Research Division - Head of Pharmaceutical Research*

Firstly, just going back to the debate around IP waivers. Stephane, as you said that the talk of IP waivers rather misses the point about limited global manufacturing capacity. So to sort of support that, given that you announced you would literally waive IP enforcement back in October. To your knowledge, has any company in the following 7 months sought to exercise that freedom to operate?

And also sticking with the vaccine, going back to Slide 28. Do you have data on T cell response over that 6- to 8-month period post primary vaccination for -1273.

And then just a quick question on the financials. David, I think you mentioned that -- in the SG&A in Q1, there were some costs related to effectively start-up of good supply. I just wondered if you could give us any color on the nonrecurring one-off elements of SG&A in Q1 as we think about evolution across the year.

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

Thank you so much. I'll take the first one on IP and Stephen will take the T cell and David the financials.

So I'm not aware of any company of size that is going after [Moderna]. Again, going back to what I described. One would have first to figure out how to make -- managing IP before asking the regulators to start the clinical study. And that doesn't happen quickly. We are monitoring the field very closely as we always have. But at this stage, happy that this is really not the point that will impact. Of course, '21 is possible, but even '22. Stephen, on T cell.

Stephen Hoge - *Moderna, Inc. - President*

So the data we have from today is the initial analysis on the boosters. We are -- as we previously announced, we've been looking at a study ourselves and with the NIH. They are running a primary series vaccination study and also looking at other elements. And so we will perhaps get T cell data in the midterm. But at this point, we do not have any T cell data yet on the boosters. We do have ongoing studies with NIH on -- in general, our Phase I and our own Phase II. And if it becomes important in the future, we can obviously look at T cell responses with waning immunity out 6, 12 months in those studies as well.

We don't have a specific plan to do that at this point. But we are pretty encouraged by the historical correlation between our previously reported T cell data and public T cell data and the neutralizing titers that are obviously much easier to measure over time across a wider range of subjects in T cells. And David?

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Yes. So in terms of the expenses we incurred in the first quarter, including in commercial, yes, we had some onetime expenses to set up businesses around the world. But the preponderance of the total operating expenses, including in commercial, I would say, will continue. And therefore, that's why I gave you some guidance that, if you start at that $0.5 billion spend level in the first quarter and the fourth of last year, we're expecting now to see that trend up notably, as we move forward through the year, which we thought it would start sooner, but we now expect we'll start in the second quarter. So running a business of this size on a global basis, we think that, that spend level is quite reasonable, to be honest.

Operator

I'm showing no further questions at this time. I would now like to turn the conference back over to Stephane Bancel.

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

Thank you so much for participating in to this call and for the great questions. We look forward to seeing you at Times Day on May 27. Stay safe, everybody. Have a nice day. Bye.

Operator

Ladies and gentlemen, this concludes today's conference. Thank you for your participation. You have a wonderful day, and you may all disconnect.
