Q1 2021 Earnings Call

Company Participants

- Corinne Le Goff, Chief Commercial Officer
- David Meline, Chief Financial Officer
- Lavina Talukdar, Head of Investor Relations
- Stephane Bancel, Chief Executive Officer
- Stephen Hoge, President

Other Participants

- Cory Kasimov, Analyst
- Edward Tenthoff, Analyst
- Gena Wang, Analyst
- Geoffrey Meacham, Analyst
- Hartaj Singh, Analyst
- Joseph Stringer, Analyst
- Mani Foroohar, Analyst
- Matthew Harrison, Analyst
- Michael Yee, Analyst
- Salveen Richter, Analyst
- Simon Baker, Analyst

Presentation

Operator

Good morning, my name is D Tamara and I will be your operator today. Welcome to Moderna's First Quarter Earnings Call. At this time, all participants are in a listen-only mode. Following the formal remarks, we will open the call up for your questions. Please be advised that the call is being recorded.

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

Lavina Talukdar {BIO 19691239 <GO>}

Thank you D Tamara. Good morning, everyone. Thank you for joining us on today's call to discuss Moderna's First Quarter 2021 financial results and business update. 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 {BIO 15174250 <GO>}

Thank you, Levina. Good morning or good afternoon everyone, Thank you for taking the time to join our Q1 2021 conference call. We'll start by quick business review of the quarter before going over Q4 commercial update. David will then walk you through the key financials. Stephen will provide a clinical update, especially new human data about two of our COVID-19 booster candidates -- mRNA-1273, the currently authorized vaccine and mRNA-1273.351, the virus specific booster to B.1.351 first adopted by in South Africa,. We will then come back to growth.

The Moderna COVID-19 vaccine is now available and protecting people in 37 countries around the world and we've a WHO authorization last Friday night, the number of countries where vaccine would 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. Twelve months ago in Q1 2020, Moderna had never run a Phase 3 clinical study, never got 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 and most importantly, I am very thankful for their impact on the world and the incredible personal sacrifices that our team has made to well protect fellow human beings around the world. This is very humbling and I am fortunate to lead Moderna in this moment. I'm also thankful for Moderna's 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 these (inaudible). 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 many 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 are still aiming for 1 billion doses for the year. The total advanced purchase agreement 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 2/3TeenCOVE study of mRNA-1273 showed vaccine efficacy against COVID-19 of 96%, and mRNA-1273 was generally well tolerated with no serious safety concerns identified to date.

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

One of the things that I'm most excited about is where we're going. The Q1 results highlighted above of the consequence of 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, we invest to scale Moderna. Just two numbers for some color. In Q1 2021, our R&D investment were approximately four times higher than the R&D investments in Q1 of last year.

Not 4% not 40%, four times 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 three times 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 six months at the southern hemisphere and it's fall and winter, we could see more variants of concern emerge. We have set for a while now that we believe booster shots will be needed as we believe that the virus is not going away. We also believe from a scientific standpoint that the highest efficacy booster over time will be provided by multivariant specific booster.

Second, the market has changed quite a lot versus what we knew six months ago. First, mRNA vaccines have emerged as a best-in-class vaccines, high efficacy, good tolerability profile, having to scale manufacturing and speed to chase the virus in the clinic. Many companies are still in the clinic with their first generation vaccine where we are in the clinic with variant specific boosters. More importantly, as we are talking to governments around the world, in the West and in the East, in the North, and in the south, we're hearing loud and clear from the market. Supply us with more mRNA vaccine for primary

studies 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 end of the pandemic. We believe it has become an mRNA market for COVID-19 vaccine.

Third, is on our pipeline. We believe we will bring to market several more products in the next few years, that will add to the market demand. For COVID-19 boosters (inaudible), flu vaccine, as we discussed in our Vaccine Day and our goal is to have a seasonal flu vaccine combined with COVID variant booster in a single dose product, with a strong clinical data for RSV vaccine and CMV vaccine.

Plus, we have seven programs in clinical studies in three 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 serve both the North and the South, we're doubling our drug substance supply in Europe and increasing by 50% of drug substance supply in the US. We are of course adding filling capacity in the US and Europe at our existing partners, but also adding new ones as we speak, more to come. Another piece of feedback we're hearing from the market is that Moderna has the best-in-class mRNA vaccine, shipment of minus 20 Celsius in storage, not minus 70 Celsius, small cartons of $100, storage up to 6 month in standard freezer and four weeks in regular refrigerated temperatures.

The only authorized mRNA vaccine that does not require onsite dilution. We believe this unique and even more important feature today, this will be more in the future in '21 and '22 and '23 as we move to a booster market decentralized in pharmacies and at doctor's office. We believe we have the best mRNA vaccine authorized and we continue to improve our product, continue to have the best-in-class products of the mRNA market. We are delighted to announce this morning the start of the dosing of our first patient in a Phase 1/2 study with propionic acidemia disease. The study is called Paramount. It's yet another milestone for Moderna. Not only do we have, I believe, the most innovative infectious disease vaccine in clinical pipeline, but we also have therapeutics candidate in clinical studies in oncology, in cardiology and now in a rare genetic disease.

Let me close my remark on this final slide. We now have 1,500 employees. We've recently incorporated Moderna Japan with Takeda and we continue to build a commercial network. We have pushed to Asia-Pacific in 2021 and given the 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 a broad mRNA platform with as many people as we can. Let me share our perspective on yesterday afternoon announcement, by the United States Trade Ambassador that the US government will ship both waiving 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 a 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, analytical 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 statements, issued October 8, 2020 that during the pandemic Moderna will not impose 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're 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 dose of authorized mRNA vaccine for 2022, 2023 and beyond. And third, to continue to adapt the vaccine to have highest efficacy vaccine with variant specific booster for which we announced very encouraging clinical results yesterday.

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

Corinne Le Goff {BIO 18937282 <GO>}

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 of 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 deliveries of 34 million doses in the fourth quarter of 2021. COVAX will have an option for additional 456 million doses in 2022. We are grateful to all the collaborated efforts of Sabin, Gavi, UNICEF, the World Health Organization and the Moderna commercial teams in making this important supply agreements a reality.

Moving now to the additional supply agreements signed for both 2021 and 2022, 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 2023.

We have also signed new deals for '21 delivery with Botswana Rene, and in addition, we have also signed an agreement with Zulich 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 through the countries that are listed here on this slide, and we continue to have discussions with countries both 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 variants.

Let me now turn to product sales. Our first -- our product sales for the first quarter of this year were 1.73 billion and we've recorded for the delivery of 102 million doses. Product sales in the US were approximately 1.4 billion and sales outside of the US to the EU, Canada, Switzerland. Israel and Singapore were approximately 400 million for the 14 million doses delivered in the first quarter. In the US, we have successfully completed the delivery of the first 100 million doses to the US 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 US production started earlier and is roughly one quarter ahead in production ramp as such in the second quarter of 2021, we expect the ex-US ramp to be similar to that of the US ramp in the first quarter.

To close, I want to reiterate that as we continue to produce and rollout 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 Meline {BIO 6397419 <GO>}

Okay, thank you. Corinne. Today as with our last earnings call, we are presenting our results primarily on the US GAAP basis. In some cases, we also provide additional detail to provide good -- 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, variants, 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 utilization of our net operating loss carry forward 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 two distinct supply chains, one in the US and one outside the US for rest of world markets.

Our supply chain scale up in the US was roughly one quarter in advance of our ex-US supply chain, which is reflected in the geographic sales mix in Q1. As we move forward in Q2, the ex-US 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 expense $242 million of prelaunch inventory costs in 2020 and started 2021 with the remaining balance of $187 million of zero 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 US 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 was 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 billion at the end of December 2020 to $5.6 billion at the end of Q1 2021.

Lastly, let me comment on tax-related items on Slide 23. The significant investments in our research, development and startup activities to develop the mRNA platform over the last decade have resulted in net operating loss carry forwards with the 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 perform 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 pro-rated based on the cadence of our expected pretax quarterly earnings. We also recorded two 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 advance purchase agreements for expected delivery in 2021 reflect the 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 carry-forward, expected global sales mix and the mentioned discrete benefits in Q1, we now expect our all in 2021 tax rate to be in the above teens. This compares to our previous forecast in the mid-teen range, this forecast is based on current US 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 29th. This concludes my remarks concerning financial performance and I now turn the call over to Stephen.

Stephen Hoge {BIO 17925815 <GO>}

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 2 booster vaccine 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 three different mRNA vaccines, 50 micrograms of mRNA-1273, 50 micrograms of mRNA-1273.351, both of which have data available today and 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-1273.35. Data from the multivalent booster and the 20 microgram booster of 351 will be shared when available now with that backdrop, let's move to the data. Starting with safety, local and systemic adverse events within seven 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 2 study and our Phase 3 COVE Study.

The majority of the events were mild or moderate in severity and Grade III events occurred with the 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 IV events reported.

On the next slide, our figures from two papers, the figure on the left hand side were published in New England Journal of Medicine and show the difference in neutralization of SARS-CoV-2 pseudo viruses in serum samples one week after vaccination with the primary series of mRNA-1273, recall that there was a six fold decrease in neutralization titers against the B1351 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 one 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 this slide is a figure from the pre-print manuscript of our initial results from our Phase 2 study posted yesterday to bio archive, the figures show the neutralization tighter levels of the participants in our Phase 2 booster study immediately before their booster vaccinations.

A reminder that these individuals were previously vaccinated with the primary series of mRNA-1273 in either our Phase 2 or Phase 3 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 P.1 the variance of concern were much lower. In fact, approximately half of participants had titers below the assay's limit of quantification at this time point.

So, it is clear that waning of titer -- titers is apparent both with time and that lower titers against variance of concern lead to more rapid loss of neutralizing activity. Turning to the next slide, the data shows that two weeks after booster vaccines of either mRNA-1273 or 1273.351 neutralizing titer levels increased against both the wild-type virus as well as the B.1.351 and P.1 variants of concern. In fact, following boost geometric mean titers against the three 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 GMT's of the different strains, we achieved levels of 1400 after booster vaccination with mRNA-1273.351 against the 351 variant. This compares against the GMT of 864 when that--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 and 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 1 study and there are neutralizing titers against ancestral strain following primary vaccination series with mRNA1273. GMT is achieved in the Sasser approximately 1500. 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 the 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 1400 in this 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 3 study in 2021. our Zika vaccine is expected to begin a Phase 2 study also in 2021.

Our hMPV/PIV3 respiratory combo vaccine is currently enrolling in toddlers and in our Vaccine Day last month we announced positive interim Phase 1 data from our RSV vaccine and mRNA-1345. This continues in pediatric and older adult cohorts of that Phase 1 study are still enrolling. Finally, within our flu vaccine program, we expect a Phase 1 study of mRNA-1010 to begin in 2021.

Outside of vaccines, we have seven clinical proof of concept trials ongoing across four modalities. Our VEGF program partnered with AstraZeneca is enrolling in a Phase 2. Our personalized cancer vaccine program partnered with Merck is also enrolling in the Phase 2 trial and KRAS our second program partnered with Merck is ongoing in a Phase 1 study, within intra-tumoral immuno-oncology, our Phase 2 dose expansion OX40 ligand, Phase 1 triplet and Phase 1 IL-2 study which is partnered with AstraZeneca are also ongoing.

Finally, as Stephane mentioned, we are pleased to have started dosing in the Paramount study in propionic academia. On slide 33, you can see our full development pipeline. In addition to our large portfolio of infectious disease vaccines, we now have seven therapeutic programs in the clinic. I'll now turn the call over to Stephane, to take us on.

Stephane Bancel {BIO 15174250 <GO>}

Thank you. Stephen, Corinne and David. Our 2021advanced purchase agreement signed have now been increased to $19.2 billion. As we look in 2022 we're investing to be 3 billion dose of 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 additional prime series for children, but also for variant specific boosters, Israel last week and Switzerland this morning. If you recall they were some of the first countries who signed APS in 2020 and again these countries are head of the game for 2022 and 2023.

Second, we've COVAX partnership announced Monday, we anticipate to supply up to 466 million doses in 2022. Third, we are 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 are having numerous discussions with government that do not have 2021 APAs with Moderna because we cannot supply them in 2021 fortunately. 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 three specific areas, oncology, cardiology and rare disease and soon, we should be in the clinic in autoimmune disease as well.

We're continuing to innovate and invest in science, that for example for delivering mRNA in the lung with our partner Vertex. As we continue to prepare Moderna to scale and that's 10 times more impact we're investing aggressively. We are accelerating our investment in digital, automation and AI. From a spend of $27 million in 2019, we invested

around $60 million in 2020 in digital. We are planning to almost triple that to $170 million in 2021. We're investing across the board in R&D to ensure high quality to accelerate the pace of learning and to ensure we can transform clinical operations.

We are 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 mRNA academy, Today we have some exciting pockets of excellence in the AI across the company, but AI is not yet part of our DNA. The result is simple, most companies don't do AI. So as we grow and hire new talent,they have great skills in their up [ph], 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 the manufacturing, quality commercial in HR and finance everywhere. It is a check -- the same change in management evolution as 20-40 years ago when personal computers entered the workforce.

We want every team at Moderna to understand and use AI in everything we do. AI would become part of our DNA. As many of you know, we have 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 by mRNA platform our team our culture and digital infrastructure I believe our to scale Moderna is unique in the biopharmaceutical industry.

As part of scaling Moderna there is software, but there is also various hardware[ph]. Many of you are aware of 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 called it Moderna Technology Center, South, or MTC South. In 2020, we added a 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 we will start welcoming Moderna employees later this year after so much in investment and innovation to the building. That is another 240,000 square feet, So we now have in MCC access to around 650,000 square feet. We now have both [ph] 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 medicines, but also by who we are as a company. We are very committed to belong, inclusion and diversity. We recently published or expected a workforce diversity figures for first time. Last time we signed a CEO action for diversity and Inclusion pledge and we have also reiterated our ongoing commitment to including 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 would offset any energy that is not from renewable sources, and would be working on the target as to when we should be a net zero carbon company. We're also encouraging our employees with to have 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's, we have a chance to do what we do. Everyday 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 shaping 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'll be hosting our Annual Science Day in a few weeks on May 27, you are going to want to connect with this event as Stephen and his team has some very cool new things to share with you and later, at the end of the summer. on September 9th, our annual R&D Day for holistic clinical update.

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

Questions And Answers

Operator

Thank you, (Operator Instructions) Your first response is from the line of Salveen Richter with Goldman Sachs. Please go ahead.

Q - Salveen Richter {BIO 15151450 <GO>}

Good morning, thanks for taking my questions. I have a couple here. So firstly, with regard to, if the US supports WHO waiver of COVID-19 Vaccine IP. What does that mean from Moderna? I mean, if you could just walk us through that. Secondly, if you could just discuss contract dynamics for the vaccine, and 2022 as you look to address variants and kind of, we see the 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. Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Salveen. Good morning, its Stephane. Let me start with your first questions and then some of the question to Stephen. So on the IP right now, what does it mean. I believe it doesn't change anything for Moderna as I said, you know we had said last October that we will

not enforce our COVID-19 related patents during the pandemic, and as I've said in my remarks, there is no mRNA in a manufacturing capacity in the world, this is a new technology. You cannot go hire people who know to make mRNA, those people don't exist and then even if all those things were available, whoever wants to do mRNA vaccines will have to buy the machine, invest in manufacturing process, invest purification processes, analytical processes and then they will have to go run the clinical trial, get the data, get the product approved and scale manufacturing.

These doesn't happen in 6, 12 or 18 months, we have been working at this for years and as you know we have some smaller mRNA companies that that are still clinic trying to get the products with finish line, and so we saw the news last night and I didn't lose a minute of sleep over the news during the night. Our 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 I know, 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 kin of mRNA contract came later just in case and then the clinical data came along.

And the speed to get through approval and so, and then you had the fact the proteins are still not authorized anywhere in the West and then you the low efficacy of adenos and other safety questions on the adenos, manufacturing, scale-up issues that adenos companies have had and the big question that scientists (inaudible) actually boost adeno -- with more adeno 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 you look at the marketplace, which were governments are doing again given you know many government, I think last time I believe the pandemic will be going quickly, trust me a few governments were 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 virus specific boosting is 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 contracts with us, are calling for more and we're in active discussion with all of them to supply most of 2022 and 2023 both prime series and specific variant booster. The beauty about the technology is we can agree right now in the contracts to give them next year, but that we are having to choose what they want, based on the clinical data and that's an incredible competitor advantage and this we can do, because as you know, the manufacturing process is the same for 1273 or 1273.351 or 1273.211, or our new1273 dot something that is a new variant. And we can set up on a very short notice because it's the same equipment in the same room with the same people, with same raw materials. And then all those governments, which is more exciting to me that never called before or that they called before but we couldn't supply them because we are in a unfortunate position to say, look we're very sorry, we have no more supply for you in 2021which is, of course, a very difficult discussion to have given the suffering on happening around the world, but the great news we've -- investments we've announced to get up to 3 billion next year, we now can have

those discussions with those government and Corinne and her team are having a lot of discussions with them.

So that's kind of give you a sense for the dynamic Stephen on PN?

A - Stephen Hoge {BIO 17925815 <GO>}

Sure Salveen. Thanks for the question. So, as you know the program, the Paramount study of 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 -- if there is no guarantee that the first dose level in 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 in this year it's dependent on 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 we're generally VEGF, as we mentioned, is a Phase 2 program that's been enrolling for a while, it's possible we could see data from that, our PCV and KRAS programs again is open label programs we will continue to track those closely as they enroll.

And then similarly the intra-tumoral programs that we highlighted, many of them are ongoing and producing data and of course, when we have a complete and cogent dataset, we will bring it forward.

Q - Salveen Richter {BIO 15151450 <GO>}

Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you, Salveen.

Operator

Thank you. Your next response is from Matthew Harrison with Morgan Stanley. Please go ahead.

Q - Matthew Harrison {BIO 17603148 <GO>}

Great. Good morning, thanks for taking the questions. I guess two from me, one on the sort of next generation COVID vaccine where you think it might be a 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 PPA. I know in the past rate. 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 and -- what your

sort of view is around enrollment and if you think you've gotten through some of those hurdles.

A - Stephen Hoge {BIO 17925815 <GO>}

Sure. Thank you, Matthew, 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 refrigerants stability profile. As we announced previously, we've started enrolling in the Phase 1 in that study, and it's probably a little bit premature to comment on what we think the regulatory pathway will look like for that until we get some of the additional 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 -- it's probably too early to say we will have to wait until we see that data and ultimately it will 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

Thank you, your next response is from Ted Tenthoff with Piper Sandler. Please go ahead.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Great, thank you very much and thank you for all of the detailed updates including running through the financial balances, so detailed David. Congrats on all the success. Stephen, I wanted to pick up on the booster data that you've shown, and maybe can kind of take us a step forward, what is the booster strategy going to look like. Do we actually need to maybe re-dose or re-vaccinate 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, thank you for when we'll be getting boosters.

A - Stephen Hoge {BIO 17925815 <GO>}

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 re-infections 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 at Moderna also believe that means we want to maintain the broadest neutralizing immunity against the largest number of then 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 correlate 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 variant 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, and right now, we're still waiting to see our multivalent vaccine data, which is a combination as you know of ancestral and 351 of 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 are 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 widest range of variants.

Q - Edward Tenthoff {BIO 1880164 <GO>}

Incredibly helpful thank you guys for all the work you're doing.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you, Ted.

Operator

Thank you, your next response is from Michael Yee with Jefferies. Please go ahead.

Q - Michael Yee {BIO 15077976 <GO>}

Hi, thank you. Good morning. Appreciate -- 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 etcetera. 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, I don't think, we can have 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. Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Thanks, Michael. Stephen. Let me start on the raw material and IP, going back to what I said, you know if that if somebody was to start from scratch, because again there is no mRNA player that's with idle capacity out there, one we'll not stop by focusing on large scale raw material to supply. well we have to first figure out how to make your money and you cannot find patents which, as you all know on the on the US, but focus this website.

And so one must figure out what method you need. How do you make mRNA, what purification methods you need, What analytical methods you need and once you're going to figure out all those things, which trust me is going to take you time, it is not easy, in us and our companies that on the market were mRNA vaccine that (inaudible) how to get to the finish line And so, I really believe that this is not the issue. I really believe the IP topic is mostly (inaudible), and this is not the issue. It might impact over technology that had in (inaudible) could not comment on, as for mRNA I think this is a wrong question, Stephen you want to take about.

A - Stephen Hoge {BIO 17925815 <GO>}

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 then 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 are presented those 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 is a -- 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 current bivalent vaccine. But because we think we're going to go down the path of multivalent vaccine 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 is going to be trivalent maybe quadrivalent. It will keep happening in the time ahead. We have completed GMP manufacturing of all of those vaccines 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.

A - Stephane Bancel {BIO 15174250 <GO>}

Yes, just a point to add to Stephen on the multivalent, which I think a lot of people don't have (inaudible), it is not easy to do a multivalent mRNA GMP product from an analytical QC standpoints because those mRNAs are the same size. They look mostly similar because we just ended a few -- I mean a few nucleic acid and that takes time to and is where the platform comes to have so much value as you all know, we have a CMV vaccine on its Phase 3 where we developed a very complex product 6 mRNA and the same variant, so if you think about what the multivalent vaccine for COVID is going to look like it's not going to be easier. So for people who have not done, multivalent in GMP setting before trust me the regulators because we had these discussion with regulators over CMV over year. They don't want to see a lot of analytical methods 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. Thank you, Mike.

Q - Michael Yee {BIO 15077976 <GO>}

Got it. Thank you, guys.

Operator

Thank you, your next response is from Gena Wang of Barclays. Please go ahead.

Q - Gena Wang {BIO 18848097 <GO>}

Thank you for taking my questions. I also have two one also related to the IP question. So, wanted to ask differently just wondering, Stephen. How many contracts 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 was a little surprised that differences between 1273, versus 1273.35 was less, narrow than initially I would expect it seems like 1273 should be also sufficient to protect from variant stream.

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 just single shot that was due should be sufficient for the protection.

A - Stephen Hoge {BIO 17925815 <GO>}

Thanks, Gena. I'll -- maybe I'll take the 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, the level of titers as you suggested there is little bit less than twofold difference between them and you are but you are seeing substantially higher titers on the order of 1400 when you give the very specific booster mRNA-1273.351. Now, I would note that this is happening already at day 15. All right, this is an early time point that we're looking at this point, we will also be looking at day 29 and in this case we are effectively, it is a prime with 1273.351 I think is the first dose of the strain first identified in South Africa.

And so, it's actually, there's two 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 two variants, were 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 suggest that that is also a useful strategy. But if you had to choose between the two, 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 even at day 15, even after a priming dose that there is going to be an advantage to some strain matching of the antigen.

And that's what has us continued to be excited about the multiple dose strategy, Stephane?

A - Stephane Bancel {BIO 15174250 <GO>}

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

Q - Gena Wang {BIO 18848097 <GO>}

Thank you.

Operator

Thank you, your next response is from Geoff Meacham with Bank of America. Please go ahead.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Hi, good morning guys. Thanks so much for the question. 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 that the need for annual boosters versus minimal breakthroughs thus far and higher 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.

Thank you.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you, Jeff those are both the 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 are still only months away into our -- 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 nine 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 in 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, 10s 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 breakthrough a year from after vaccination in the real world setting and let that start to guide re-vaccination decisions. At that point, it's almost too late. And so I think at this 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 and pandemic phase that we're in with this variant evolution into the years beyond that. 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 re-infections and as we shared with 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, and you still see re-infections mortality, substantial healthcare -- more cost 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 re-infect. And when they do, they can really have a devastating effect in high-risk populations particularly older immunocompromised.

We think that's a real 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 and whether the multivalency continues to add more and more valencies,. I don't think anybody can say it, but it's certainly a situation we're preparing for.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Stephane just on the second question on the different modalities, will Stephen.

A - Stephen Hoge {BIO 17925815 <GO>}

Yes, yes, I apologize. And this is your second question on different modalities and different parts of the antigen. So I think what is pretty clear from all of vaccines If you look across them, but certainly the focus on the messenger RNA vaccines is that the high degree of efficacy, we're seeing in vaccines right now is based on the spike protein immunogenicity. That is the antigens 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, you would, you would be remiss to look past the multiple large Phase 3 trials that provide pretty conclusive evidence of after spike protein trying to prevent COVID-19. So I think you would probably if you went down that route how to have to re-demonstrate 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. Yes, even theoretically.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Okay, great, thank you so much.

Operator

Thank you, your next response is from Cory Kasimov with JP Morgan. Please go ahead.

Q - Cory Kasimov {BIO 3009346 <GO>}

Hey, good morning guys. Thanks for taking the questions. I want to go back to the topic of the future contracts. I know this is kind of been asked in a couple of different ways, but based on discussions and negotiations that are currently taking place. How much confidence do you have that there is going to be demand to fill up to 3 billion doses and anticipated supply that you think you could have next year, especially if people are getting to 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 want to see if we should be assuming stable pricing for modeling purposes, for 22. Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

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 our customer this is becoming an mRNA markets looking markets 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 even the (inaudible) vaccinate adults, all others are 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, the boosting. So when you add all those pieces, we're going to -- we are building up to 3 billion of supplies, as a mix between prime service 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 set up than what it was a year ago. A year ago, you hear people saying, I'm going to get now a cheap [ph] adenovirus vaccine because (inaudible) supply at cost. This is not a discussion anymore today. The discussion is I want mRNA vaccine for multiple, I want variant booster specific, I want anti variant, I want the best thing because I don't want the second and the third and the fourth (inaudible).

Am I correct Cory.

Q - Cory Kasimov {BIO 3009346 <GO>}

Yeah, yeah. No. And on the pricing question for modeling.

A - Stephane Bancel {BIO 15174250 <GO>}

I think I will give you any color, but again there is no more discussion at all, but your price is this, and there is a small company. The company will price at a cost of $3.This discussion has gone.

Q - Cory Kasimov {BIO 3009346 <GO>}

Okay, all right, perfect. Thank you,, Stephane.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you.

Operator

Okay. Your next response is from Hartaj Singh with Oppenheimer and Company. Please go ahead.

Q - Hartaj Singh {BIO 18796450 <GO>}

Great, thank you. Thanks for the question, all the color. A question I would have is just on the 50 microgram going forward has a boost against variants would you see that potentially becoming your initial kind of prime boost vaccine possibly in the future you think you'll stick with 100 microgram route whether it's with 1283 or so. 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 also. Thank you for the question.

A - Stephen Hoge {BIO 17925815 <GO>}

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 share today is a small number of subjects, but we previously shared and published our Phase 2 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 seem to achieve levels that were consistent with the 100 microgram dose. So it's certainly something we're going to look at as to whether we're

not we could pursue a 50 microgram primary series, but how we get there will depend upon data that we don't yet have.

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 it has been shared, we are evaluating 50 microgram dose as a potential primary series even in pediatric populations as you can imagine, you don't need perhaps a higher dose in younger people than you do. In older once.

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 will continue to carefully evaluate whether or not we can adopt that as a target dose across all of our applications. But it will depend upon data.

Q - Hartaj Singh {BIO 18796450 <GO>}

Great. And then question on the.

A - Stephen Hoge {BIO 17925815 <GO>}

Go ahead David.

A - David Meline {BIO 6397419 <GO>}

Yes, so cost of goods and operating expense trends as in 2022 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 US. We've seen, as I said, yields have been better than we are foreseeing 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 the gross margins will depend very much on the 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.

Q - Hartaj Singh {BIO 18796450 <GO>}

Thank you.

Operator

Thank you, your next responses from Joseph Stringer with Needham and Company. Please go ahead.

Q - Joseph Stringer {BIO 21979666 <GO>}

Hi, good morning. Thanks for taking our questions. Just another one on manufacturing capacity here as you potentially move to next generation COVID vaccines. I was wondering if you could give us a sense maybe even qualitatively, in terms of the, given the modularity of the technology. What are potential manufacturing ramp would look like for some of these second-gen vaccine in terms of manufacturing capacity in the ramp, relative to what we had seen with 1273. Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Yes, it's Stephane. So the 1273 ramp has been constrained by manufacturing capacity. So, if you look at this year, the only " only supplier" 100 million through those in Q1, which is an extraordinary number because we are building the capacity and so the way to think about it is as Juan and his team are working hard to add new lines and to increase the capacity, the ramps of a follow-on products will be much faster because today manufacturing is slowing down the ramp. So I anticipate that, as you think about in over the multi-variant booster launches, as we think about, you know RSV through CMV launch, we will not be on the back foot you as you know, as part of a 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 fall, I would anticipate all of the year supply constraint.

Corinne and her team would love to be able to sell more product because trust me that phone is becoming red hot by calls from around the planet, and we would not be able to help protect more people, but we just can't because we were not planning on the pandemic in 2020.

So I anticipate that for variants and for new product launch, we will make sure that we're not capacity constrained, which is why the 3 million supply volume that some people might think it maybe too aggressive, as I said in my remarks, the pipeline of the companies are still going to pay with these and so this is just behind the multivalent vaccine. So if you look a couple of years out and with opening manufacturing for six months, we're going to be very happy to have that capacity so that as we launch products, we can supply the market every single dose that Corinne and her team can make sure that the market wants.

Q - Joseph Stringer {BIO 21979666 <GO>}

So great, thanks for taking the question.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you.

Operator

Thank you, your next response is from Mani Foroohar of SVB Leerink. Please go ahead.

Q - Mani Foroohar {BIO 20015167 <GO>}

Hey guys, thanks for taking the question. One quick one, the thing on financials, you gave us a little clarity on CapEx investments around expanding capacity for production should we think of that as level setting CapEx going forward, the modest increase going forward or should we think of that as primarily a one-time build on, and then secondarily, you've given a little bit of clarity, there's a lot of clarity around COGS for this quarter versus the rest of the year going forward. So, we think about the absolute COGS per unit again pretty linearly related to dose or the other attributes royalties etcetera, differences in -- differences in product between different vaccines would that suggest that that's not the right way to think about it.

A - David Meline {BIO 6397419 <GO>}

Yes. So CapEx, if I understand the question is guidance for 2022 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 development side of 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 in ongoing CapEx trend will be appropriate for the company.

In terms of 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 a simple assumption assume it's a pretty steady cost of manufacture as we're seeing right now.

Q - Mani Foroohar {BIO 20015167 <GO>}

Great. And a quick follow-up on some of the contracting. I know it's been asked in various forms,you talk about the OUS manufacturing being about a quarter ish behind US manufacturing. Right now based on your disclosures on volume. Does that you delivered, this is what we have from the other mRNA competitor and duopoly right now, market share for you guys somewhere between 5% and 10% there a lot of these countries, which has delivered 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 --does your stronger incumbent position in the US suggest a better position for US contracting volume or do you see 2021, the results for 2021 contracting have nothing to do with 2022 and every year is a whole new game between you two.

A - Stephane Bancel {BIO 15174250 <GO>}

Yes, it's a good question. So as we said the plan was always the plan, we are executing on. And so when we spoke to countries and set of those 21 APAs, we manage the quarter delivery to the countries as we knew capacity will come online. We had not anticipated early part of the year that we will be able to export from the US and the piece we should not forget these, as you know, it's, we put in the media there be the US is going to be. I mean, way too many vaccine very, very soon if not already. And so, the capacity that we are building in the US I think is also going to supply the world.

So I think once we anticipate a very big acceleration of shipments two countries outside the US as we go into Q2 and even more in Q3 and Q4 as we met our obligation to the US government.

Q - Mani Foroohar {BIO 20015167 <GO>}

Great, that's really helpful. And you guys, could you just comment on where you are what you're seeing in the real world in terms of vaccine hesitancy plus end market demand, there's been a couple of year reports. But that's far into be more of a limiting factor as opposed to supply at least in the US currently certainly not globally.

A - Stephane Bancel {BIO 15174250 <GO>}

Correct, in the US and you see it on the the daily in the numbers published by the CDC for I think since mid-April roughly the number of vaccination for the -- 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 is an oversupply of vaccine, it is really demand driven problem now. So you see some states across the country that are still very active in vaccination and we are lucky, but as we said that we are very high rate of vaccination is going up every day, in the Delaware part of the country as you know, where they have way too many vaccine and you have heard that their federal government I think yesterday or before announced that they were going to stopped to ship products from one phase to the other based on actual demand is relating to vaccine (inaudible).

The US, doesn't have a supply of vaccine issue anymore. That was true in January '21.

Q - Mani Foroohar {BIO 20015167 <GO>}

Great, thanks all. I'll get back in the queue (inaudible)

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you.

Operator

Thank you, your next response is from Simon Baker with Redburn. Please go ahead.

Q - Simon Baker {BIO 2415399 <GO>}

Thank you for taking my questions. Firstly just going back to the debate around IP waivers Stephane, as you said that to talk about fee waivers rather misses the point about limited global manufacturing capacity. So, just to support that, given that you announced, you would unilaterally waive IP enforcement back in October to your knowledge was any company in the following seven 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 cost related to effectively start up of supply. I just wondering if you could give us any color on the non-recurring one-off elements of SG&A in Q1 as we think about the evolution across the year. Thanks so much.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you so much. I think the first on and Steven will take the T-cell and David on the financials. So I'm not aware of any company of size that is going after mRNA. Again going back with the described, when we have first we'll figure out how to make mRNA GMP before asking the regret those 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, I think that this is really not the point that will impact, of course, 21impossible but even '22. Stephen on T-cells.

Q - Simon Baker {BIO 2415399 <GO>}

So the data we have from today is an 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 mid term, but at this point, we do not have any T-cell data yet on the boosters. And we do have ongoing studies with NIH on -- in general our Phase 1 and around Phase 2 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.

A - Stephane Bancel {BIO 15174250 <GO>}

And David?

A - David Meline {BIO 6397419 <GO>}

Yes, so in terms of the, the expenses we incurred in the first quarter, including in commercial, yes, we had some one-time 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, but 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 will start in the second quarter.

So I'm running a business of this size, on a global basis, we think that the spend level is quite reasonable, to be honest.

Q - Simon Baker {BIO 2415399 <GO>}

All right, thank you very much.

Operator

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

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you so much for participating into this call and for the great questions. We look forward to seeing you at Science Day May 27, stay safe everybody, have a nice day, Bye.

Operator

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