Center for Strategic and International Studies

TRANSCRIPT

Online Event

"A Conversation with Dr. Anthony Fauci on the Antiviral Program for Pandemics"

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FEATURING

Anthony Fauci

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Director, National Institute of Allergy and Infectious Diseases

CSIS EXPERTS

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J. Stephen Morrison: Good afternoon, good evening, good morning to everyone who's joining us here. I'm J. Stephen Morrison, senior vice president at the Center for Strategic and International Studies in Washington, D.C., where I direct the Global Health Policy Center.

We're thrilled today to be joined by Dr. Tony Fauci. He's a longstanding friend, director of the National Institute of Allergy and Infectious Diseases, and chief medical advisor to President Joe Biden. Welcome and thank you, Tony, for joining us today.

Anthony Fauci, M.D.: Thank you, Steve. Thank you for having me. It's always a pleasure to be with you.

Dr. Morrison: And congratulations; you've crossed the 70 percent line of adults with at least one vaccine. You've crossed the 110 million line in terms of donations to our external partners. Congratulations on that.

Dr. Fauci: Thank you.

Dr. Morrison: We're here today to discuss the new $3.2 billion Antiviral Program for Pandemics launched by the Biden administration on June 17th.

Before we start, two things. First, thanks to our – to my colleagues Amith Mandavilli and Samantha Chivers; and to our production team: Margaret Rogers, John Monts, Dhanesh Mahtani, and Graham MacGillivray. From NIH, David Awwad – special thanks to David – and to Patricia Conrad and Greg Folkers.

A few brief comments on this topic before we get to our first question for Dr. Fauci. Recently, the urgency of prioritizing therapies has intensified and become more visible. It's become clear that the pandemic is a long war. It may become a – it may become endemic. And the proliferation of dangers by variants are fundamentally changing the nature of the pandemic, including our understanding of what vaccine protection will truly mean and how long it will last.

While vaccines, including boosters, remain vitally important, we increasingly recognize that therapies – safe, effective, scalable, affordable – are no less essential to any lasting solutions to the pandemic for all populations in America and across the full spectrum of countries – rich, poor, and in between. The demand for therapies will remain urgent and strong, including those deployed early in infection to – (audio break) – replication of the virus and those that can be administered to address extreme illness. Looking out into the future, we can anticipate it will be months, even years, before large segments of the global population are fully vaccinated. There are

populations who will remain hesitant or outright refuse to be vaccinated. Many others will seek vaccinations but face situations in which there's a shortage of vaccines, of adequate financing and delivery mechanisms.

So we've arrived at a moment of greater consciousness of the centrality of therapies. We also have to be conscious of the chronic barriers. Therapies for SARS-CoV-2 are inherently problematic, and the recent record is sobering. Across therapies, we face a pattern of neglect and underinvestment, a lack of private-sector interest to carry forward from this initial discovery phase through clinical trials to production and distribution through the valley of death in product development.

As we'll talk about, much of that is beginning to change in significant ways. In the case of MERS and SARS, interest in coronavirus therapies faded earlier as outbreaks declined. There's potentially a similar risk here with SARS-CoV-2. We've seen the development of promising monoclonal antibodies and the antiviral remdesivir, but these remain infusions. They're expensive. They're often not available outside large hospitals. And they apply often to high-risk patients. With remdesivir, its value has been the subject of much debate.

Some monoclonals did not deal very well with variants. Two of Eli Lilly's candidates, the Regeneron cocktail and GSK's monoclonal candidates, do look quite promising. We've seen false starts and politicized options – hydroxychloroquine, convalescent plasma. Ivermectin is the latest case of controversy. And we've seen systemic problems in the American health system, which has difficulties enrolling infected patients in the clinical trials and getting promising therapies to those who need them. And we've had problems with the research infrastructure that needs more coordination and prioritization.

Antivirals, a pill to drop replication early, are complicated and they take time to develop. It's scientifically challenging to develop a pill that stops replication and does no harm to the infected human cell. HIV drug cocktails took a long time to develop. They've become essential, as we'll hear from Dr. Fauci.

We may have a similar experience of needing time to create an antiviral cocktail for COVID-19, which brings us to today's conversation – the launch of the Antiviral Program on Pandemics. It's a major step forward in attempting to prioritize antivirals, overcome challenges and accelerate change in both the immediate and the long term. And it's a major effort to use the influence of the federal government to drive forward new partnerships with industry and academic centers.

So Dr. Fauci, thank you so much for being with us. Why don't we start; if you could just explain why the administration, why the Biden administration, took the step of launching the APP. And describe both its immediate priorities with respect to molnupiravir, a Merck – the Merck candidate; Atea-Roche and Pfizer products; and also the longer-term strategy of building up new academic centers.

Thank you.

Dr. Fauci: Well, thank you very much, Steve, for that introduction, which was really quite good, about where we stand with all of this.

But let me start by saying that this pandemic is 20 months old. And, in fact, medications have been a priority all along. But when you had to move very quickly, we really had to focus on the medications for the most people in dire need, and namely the hospitalized patients, people who were advanced in their disease. And we had to look at repurposed medications.

You mentioned quite correctly that monoclonal antibodies turned out to be an early success. But they have their vulnerabilities, particularly when you deal with the variants that we've had to face.

But the approach that we are taking right now is really what we call a two-tiered approach, two fundamental pillars. And the fundamental pillars address what you had alluded to in that the drugs that are already out there, the molnupiravir, the protease inhibitor, the Atea-Roche product, and even others that have not gotten as much visibility but are still somewhere along the early pipeline.

That falls into what we are referring to as the developmental pillar of the APP, which is the Antiviral Pandemic Preparedness Program. Those drugs have already gotten a head start with the companies that were involved – you know, Merck and Pfizer and Roche-Atea, and others. We will partner with those pharmaceutical companies to further the advanced development of those products, number one; number two, to be available for other companies, biotech as well as pharma, who might have similar products.

But the one part of the two-pillared approach that I think looks in the long term as part of – and I want to take the opportunity, Steve, to mention this – that this is all part of a comprehensive pandemic preparedness plan that is associated with an even broader and larger pandemic preparedness plan for vaccines, which I know we'll get a chance to talk about at another time in another setting, namely the prototype pathogen approach for the development of vaccines rapidly against any pathogen of any family. That program, together with this antiviral program, together with an extension of the diagnostics program, is part of the broader comprehensive plan to

prepare for pandemics. Just wanted to mention that it isn't in a vacuum with antivirals.

But let's get back to the antivirals. You know, because we've spoken about this over the years multiple times, Steve, of the extraordinary and, in fact, spectacular success of the targeted antiviral program that we have had with HIV, which we'll get a chance to talk about a little bit later. But that same approach of developing molecules right from the beginning by using the replication cycle of, in this case, the SARS coronavirus to identify vulnerable targets, that program we're putting FOAs out right now – funding opportunity announcements – to get people stimulated and interested in doing that from the ground-up development of molecules together and simultaneously with the developmental component of this two-pillared process. So we're very excited about it.

And I think that we are going to get both, as you said, early wins easy on. Hopefully, one of the candidates that you mentioned will turn out to be as good if not better than the monoclonal antibodies in remdesivir, which are the two approaches that we have right now. And then, hopefully, as we go on into 2022, when we'll start putting out some money for the discovery component of this two-pillared process, we're going to start seeing some long-term action and results.

So I'll stop there and happy to continue.

Dr. Morrison: Thank you. Thank you. I mean, I'm struck by two things, two steps that have been taken as part of this effort. One, the prepurchase of 1.7 million doses of the Merck molnupiravir if it is approved and reports that we could get an emergency-use authorization by the end of the year or early next year. That changes the landscape. The other thing that I found really significant was the decision by the CEO, Bourla, of Pfizer to put a – commit a billion dollars towards the development of protease inhibitors. Those are pretty significant steps. So do you anticipate we'll have quick wins and the landscape will begin to change so that we do arrive with pills in our hands that can disrupt replication?

Dr. Fauci: Yes. I don't know whether it's going to be the home run that we got with HIV when we, in 1996 – the transforming year when we had the triple combination and we went from modest suppressant of virus to complete durable suppression of virus with HIV, which totally changed the landscape. But you know, I want some of the listeners if not all of them – because I know many of them already appreciated it – why it's so important and a bit different than what we faced with HIV, Steve. And the reason is with HIV we're talking about lifelong therapy for an individual to keep the virus suppressed to below detectable, to get the person to return to some form of normality. And we have been spectacularly successful.

We're looking at a different type of a profile now. We're looking at an orally administered maybe seven to 10 days, given to person who is early on in the course of their infection before you get to the cascade of events that lead to the aberrant activation, inflammatory response that kills people, because we know now from a lot of experience with the care of these individuals that if you can keep that virus from going to the upper airway, from going down into the lung and other organ systems, you can change what can be a devastating disease and make it an upper airway common cold type approach, which is really what we need to do. We only need to knock out that virus for about seven to 10 days, rather than lifelong, what we have to do with HIV.

Now, you mentioned monoclonals and remdesivir. You're absolutely correct. One of the reasons why monoclonals, which are really very good if you give them early enough and appropriately enough, is the logistics of getting somebody into a situation where you can hook them up to an IV and observe them as they're getting an IV infusion. As simple as that sounds that has been a major stumbling block in the more wide use of what is otherwise a very effective antiviral, namely monoclonal antibodies.

Dr. Morrison: I'd ask you, you know, being able to intervene effectively in the first seven days, time is of the essence. The patience has to know he or she is ill. That patient has to be tested to know that he or she is ill. And our testing has fallen off to under a half a million tests per day across this country. Does this imply we're going to – if we're going to move in this direction of cocktails of antivirals to come in fast and disrupt replication, are we going to have to rethink our whole national testing strategy?

Dr. Fauci: Absolutely yes. And the reason is, particularly if you get into the flu season where people present with very similar symptomology, that you're going to want a test that'll tell you immediately: Is this flu? Is this SARS-CoV-2? Or is this something else – whatever that might be? RSV, parainfluenza, rhinovirus, whatever. If you are going to effectively implement an antiviral program, you have to get accurate and ready to use, easily implementable diagnostics. Just the same way, Steve, if you think about it, would you ever institute triple combination of an antiviral to an HIV-infected person if you didn't know they were HIV-infected? It's the same thing. So they go hand in hand. You've got to get a diagnostic before you do that.

Dr. Morrison: So are there plans funded through the ARP – are there plans underway right now to massive expand testing?

Dr. Fauci: Yes, particularly, you know, the RAD program, the RAD diagnostic program that the NIH has initiated is looking now at just that product profile that you're talking about, of getting something that's flooding the system, easily

administered, highly sensitive, and highly accurate, so that if you wind up getting a symptomatology that's suggestive of SARS-CoV-2, you can get a test almost immediately. And if, in fact, you're – (audio break).

Dr. Morrison: Thank you. Let's turn to – can you – let's turn to – (audio break) – variants figures in the strategy for the APP?

Dr. Fauci: You know, Steve, you technically got cut out about 80 percent of what you said. I only heard "variants." I didn't hear what the question was, sorry.

Dr. Morrison: The question is – I'm sorry. We have a bad connection. I may drop off and come back in. The question is, how do variants – current and future variants figure in the strategy for this antiviral program?

Dr. Fauci: OK. So this is important because variants, as we all know, have emerged because of the pressure that the human immune system has put on the virus, very likely from people who are immunosuppressed, wound up getting infected, and had virus in them for days and days and days before they cleared it and/or died, and then essentially led to the emergence of a variant. We feel that's very likely what happened with B.1.1.7 and what happened now with the current Delta variant that we're dealing with.

As soon as we start treating COVID-19 with new antivirals, we need to plan for and anticipate the emergence of drug resistance. And that's the reason why we are in the process of doing the same approach, perhaps even of combination therapies, in case we do wind up getting variants. We're partnering with BARDA to help to get new agents through discover into development and, ultimately, procurement. Part of that is going to be with the active program that you know that we're very actively using right now, because you know, the APP – the Antiviral Pandemic Preparedness program – doesn't have an established clinical arm. So we're going to have to rely on the drug network programs that we are now successfully using with active 2A and active 2B and others because we're using that as part of the – as part of our capability to test the existing antivirals that we have right now.

But it's the same approach. When you have variants, you've got to be – it isn't going to be where you have one pathogen and one drug that's the knockout, home-run drug. You always have to be ready to continue to develop alternatives that could keep up with the variants.

Dr. Morrison: Thank you.

Let's talk about industry and the relationship with industry, because this is intended – this 3.2 billion (dollars) is intended to change the incentives and calculations of industry. You're committing 2 billion (dollars) of that for the

acceleration of these promising candidates we talked about, 300 million (dollars) for research and labs, a billion (dollars) for clinical trials, and 700 million (dollars) for the production and distribution. So tell us a bit about what is the interface going to look like with industry in this moment.

Dr. Fauci: Well, Steve, it's really an easy answer to the question because we really have in the past, together with fundamentally our relationship with BARDA – which the APP is going to be very closely interacting with BARDA – it is absolutely essential to have a very good partnership with industry in any program that talks about the development of a product, particularly in this case a drug. It will be very much the same as we've done with all of the pharmaceutical and biotech companies that we have partnered with in the development of drugs for HIV. It's absolutely essential. We do that with direct collaborations.

For example, we are collaborating in our clinical trial process with each of the ones that you mentioned early on – with Pfizer, with Merck, and with Roche and Atea – in a partnership that involves – right now, since they've already developed the product, we're involved in the clinical trial testing of that. The same will hold true as new products come along. It will be a very close collaboration with industry. I don't think it would be possible at all to have any success without doing that.

Dr. Morrison: So do you think that 3.2 billion (dollars) is going to be enough to change calculation, change the picture and the orientation of industry? You think it's going to be enough?

Dr. Fauci: Steve, you've known me a long time – (laughs) – and you know what my answer is. It's a good start. I'm very pleased that the – that the program and President Biden allowed us to use money from the American Rescue Plan to get that 3.2 billion (dollars) as really a good start. I think that success will breed greater enthusiasm for more support, and that's exactly what happened with the HIV program. Nothing convinces the source of resources to give more resources than success. So if we come up with success, I think we will get more. Obviously, if you want to have a program that's sustainable over a period of time, you're going to want more money. But 3.2 (billion dollars) is very generous and we're very pleased with it.

Dr. Morrison: Thank you.

Now, tell us a bit about what you see as the ideal or optimal product profile. What does a product have to look like in order to be a winner in your view, when you take into consideration use, equity considerations, access? What are you telling people is the optimal profile?

Dr. Fauci: OK. The optimal profile – we're comfortable with this, because we've developed product profiles for so many other drugs, including with HIV. So, first of all, I want a pill that blocks a specific viral function. I want to give it once a day if possible. I want it to be low in toxicity. And I want it to have very minimal drug-drug interactions. So orally administered, single pill, given for seven to 10 days, little drug-drug interaction, and low toxicity; give me that and I'll be really happy.

Dr. Morrison: And what about scalability, ease of use, and access to populations?

Dr. Fauci: Well, yeah. I mean, obviously, we want to do with this what we did with PEPFAR. I mean, that's the model, that you get a product that you can make, give it. I mean, the companies are going to be involved with us. I mean, I hope that we can get arrangements, given the investment that the federal government has made, that we could have reasonable pricing so that we can make it available throughout the world, the same as we're trying to do with the vaccines.

We don't want to have a situation where people in low- and middle-income countries don't have access to this. So it's got to be able to be scalable, not something that has a process of development that has 25 separate steps in it, that you can't translate that to being done in other parts of the world.

Dr. Morrison: So you build that into the initial agreements with industry partners in terms of creating a pathway to reach all Americans who need this, but also to reach low- and middle-income countries down the road.

Dr. Fauci: That has always been an important part of everything we do. If you look at what we built into the vaccine program, equity has been the most – one of the most important aspects of it, both domestic equity and now international equity. And that's the reason why, as you know, the Biden program has already committed a half a billion (dollars) plus 80 million (dollars) that's going out right now.

I'm pleased – I want to say this because I think the listeners should hear that I'm pleased to see that we already have millions and millions of doses that have already gone out to Africa. Just this past week we sent 5 million doses to South Africa. We're sending doses to other African countries. You want to do the same thing when you're dealing with therapy. We want to make sure we have international accessibility, as well as domestic equity.

Dr. Morrison: You talked earlier about the antiviral program fits within a comprehensive strategy that addresses both vaccines, diagnostics, and therapies. So are we going to see sometime soon a kind of formal rollout of a pandemic preparedness strategy that sort of embeds the development of therapies as a

vital element of that and sets sort of targets in terms of trying to create the kind of ever-warm capacities and stockpiles that we're going to need?

Dr. Fauci: The answer is yes. We are in active discussion right now, sometimes sensitive discussions, about amount of resources. So I would rather not give you granular details of that right now, Steve. But you know me and you know what my intentions are. And to the extent that I could have any influence on it, there will be a broad, comprehensive approach to pandemic preparedness and response at every level.

Dr. Morrison: Thank you.

I want to turn to the international context. You know, when you look at vaccines we have an international entity, CEPI – Coalition Epidemic Preparedness Innovations – which is charged with doing upstream development of vaccines that fall outside of market incentives for dangerous pathogens. We have GAVI, the Vaccine Alliance, at the other end of the spectrum that's there for procurement distribution of vaccines and partnerships with countries. And the COVAX facility, most of it's being run right through GAVI as the principal partner there. We don't have institutions of that kind. We have a collection of different actors at those two ends of the spectrum when we talk about therapies and talk about antivirals. Are we going to need something like CEPI and GAVI when we're looking at therapies into the future, internationally?

Dr. Fauci: The answer is yes, Steve, and I think a good example of what we did with HIV, the HIV model is good. You know, we had the Global Fund, of which the U.S. government is a third of and has been from the beginning. We have the PEPFAR program and that has worked very closely with groups like the Clinton Health Access Initiative.

So that was kind of the CEPI and the GAVI of HIV, namely, of therapy. So I would imagine that I can see something like that falling into place when you're dealing with therapies, something along the lines of what you mentioned, GAVI, CEPI, but some international access organization very similar to what the Clinton Foundation – the Clinton Health Initiative has done for therapies for HIV.

Dr. Morrison: The Global Fund is getting very active across this whole spectrum of things. We've just given them quite a large grant through the ARP funds for nonvaccine response in low and middle income countries. Are you expecting the Global Fund is going to be a big partner as – if we get winners in this process in terms of therapies?

Dr. Fauci: You know, that's a possibility, Steve. I mean, I can't say that that's going to happen. But it, certainly, is a reasonable question to ask and I think it would

be a possibility. Remember, when the Global Fund got set up, it was started off to be the Global Fund for HIV, and then we expanded it to malaria and tuberculosis. I think there's no reason to think that it isn't possible to include in that pandemic preparedness.

Dr. Morrison: Yes. Well, that's a big debate there within their own board and –

Dr. Fauci: Yep. Yep.

Dr. Morrison: – they're expanding. They've expanded some significantly and they've been very nimble and fast in that regard and so I would expect them to play.

What about the Europeans? The EU is pre-purchasing some of these therapies that are, you know, in development. They've announced they're going to set up a new institution, HERA, as a counterpart to our BARDA institution. What role do you see them playing and how does what we're doing link to that?

Dr. Fauci: Well, I'm pleased to say that we are and have been and will continue to be in conversations with each of these players, specifically, you know, with Jeremy Farrar at Wellcome, a good friend and colleague in a lot of what we do. We've been involved in discussions there with Unitaid, with Intrepid, with the Global Fund. So we're trying to define how we can all work together on this because this, obviously, is something that has international implications. So the answer to your question is there will be involvement with those entities that you mentioned.

Dr. Morrison: Thank you.

I want to shift back to some comments you made over the weekend on Sunday, August 1st, on "This Week," ABC. You said – and this – you know, we've entered this new surge. We're in – we're in this new phase. You said things are going to get worse. We're looking to some pain and suffering in the future as infections climb. The focus was on the 93 million unvaccinated.

We've seen multiple pressure points come forward and intensify in trying to get people to accept vaccinations and overcome their resistance or refusals: federal policy in workforce, DOD policy – that's in development – actions by cities, by mayors, governors, employers.

Republican leadership have stepped forward in new ways – faith leadership, media. This has also been joined up with masking – change of masking guidance that's created some – a little bit of anxiety and confusion there. But public patience also, it seems, has worn very thin and we see this polarization between vaccinated and unvaccinated in the characterization of – by the president and others of this is a pandemic of the unvaccinated.

My question to you is, this – we've entered this new phase; it's more uncertain and it's causing some anxiety. But with bringing these pressures again upon populations to re-mask but also, most importantly, to get vaccinated – on that latter point, are we beginning to see results, and are you hopeful that we're going to be able to move rapidly enough to close the gap?

Dr. Fauci: Well, I think it's going to be complicated, but let me explain what I project will happen. You never can guarantee it's going to be accurate, but I think this is what's going to happen: Since an acceleration of vaccines doesn't give a result until several weeks after, we are already on a trajectory that looks strikingly similar to the sharp incline that the U.K. saw. So remember, we went from an average of about 12(,000) to 15,000 cases a day to 20(,000), 30(,000), 40(,000), 50(,000), 60(,000); we're up to 70(,000) now. We are going to be between 100(,000) and 200,000 cases before this thing starts to turn around.

Now, with regard to vaccines, in order to make sure that by the time we get into the fall we don't continue to accelerate but turn around and start coming down acutely, we've got to get those 93 million people who are eligible to be vaccinated who are not getting vaccinated. What I believe we will see – and interestingly, even in those areas that are accounting for the vast majority of infections – you know, like 40 percent of all the infections in the country are in, like, three states or so; 20 percent are in Florida, more. I mean, that's one state out of 50 states is accounting for, you know, 20 percent or more of the infections. Yet, we're seeing that in those states where you're seeing a lot of infection, the rate of vaccination, as an average, is better than the rest of the country, so that's telling us that the states that are suffering most from the increase are starting to realize that you've got to get vaccinated if you want to get out of this. And we're seeing governors and others from those states who normally were not enthusiastic who are going out and speaking about getting vaccinated. Asa Hutchinson in Arkansas is out beating the bushes asking people to get vaccinated. We have people, even like Governor DeSantis, who doesn't want to have mask mandates, is going out saying people should wind up getting vaccinated. Stephen Scalise, a Republican leader, is saying go out and get vaccinated. So I think we're going to see a turnaround.

The thing that I think is going to be a real somewhat of a game changer, Steve, is as soon as the FDA gives full approval for the vaccines, those people who are hesitant to get vaccinated because they perceive the emergency use authorization as not being proof enough that it's safe and effective, even though we have ample, ample evidence that it's highly effective and highly safe, I think you're going to see more people get vaccinated. And then you're also going to see enterprises feeling much more confident in local mandates for vaccines. You're not going to see a central mandate coming from the

federal government, but you're going to see more universities, colleges, places of business who, once they get the cover of an officially approved vaccine, they're going to start mandating vaccines. So we're going to see an increase in vaccines, and that's going to be the solution to the problem, because if you get the overwhelming majority of people vaccinated, we wouldn't even be having this conversation now.

Dr. Morrison: There's been a lot of reporting lately on the steps taken internally within the FDA to try and sprint towards getting to that point, internal procedures and the like, and, of course, external parties like yourself have to be very respectful of their autonomy and ability to preserve the trust and confidence Americans have in them. It looks to me like we're likely to get something early in the fall, in terms of approval, and you're saying you think that some significant share of those who are hesitant, or refusals, will change their minds on that basis because that concern that this is experimental hangs so heavy on them?

Dr. Fauci: I believe that there will be a proportion. I don't know how large that proportion would be. But going around speaking about vaccines, literally on a daily basis, Steve, there's no doubt that there are a proportion of people – likely not a majority. Likely a relatively small – 10, 15, 20 percent or so – who as soon as this gets approved would say, OK, I'm ready to go get vaccinated.

Dr. Morrison: Yeah. Right now we're vaccinating less than a million people a day, as I understand. What do we need to reach? What the daily target? We hit a peak of, I think, 3.2 million earlier in the year. Where do we need to be, realistically, in order to get the vaccination levels up to a point where we can close this gap most effectively, and not have this just drag on through the winter as a mixed set of outcomes?

Dr. Fauci: Well, I don't want to give a number, Steve. The reason is that, as you know, I say it, it becomes a soundbite, and the next thing you know everybody's arguing about it. But – (laughs) – don't want to go there. But I can dance around it a bit, if you want to use that terminology. (Laughs.) So let's say we have 93 million people who are eligible to get vaccinated. And we really want to get 90 percent of those people vaccinated, if you really want to nail this thing down. I'll settle for 70 or an 80 percent, but I'd love to see 90 percent. So, you know, 90 percent of that – let's say you get 80 – you know, 80 million people that you want to get vaccinated. If you get a million people a day, that's 80 days. That's two and two-thirds months. That's a long time.

So I want to see that gap closed so two and two-thirds months from now, you know, is going to be sometime October, maybe even into November – or the end of October. I'd like to see us there before then. So I'd like to see

hopefully between one and two million per day. We may get there when mandates come, but it can't be 250,000, 500,000 a day. Otherwise, it's going to go well into the winter. I want to get there sooner.

Dr. Morrison: And tell us, what can we expect in terms of vaccination of children?

Dr. Fauci: Well, that's a good point, because scientifically we are currently doing the clinical trials in an age de-escalation approach in kids from 11 to nine, nine to six, six to two, and six months to two years. We're already collecting substantial data on the safety and the immunogenicity which would predict effectiveness in children in those age groups. I think we're going to get that information as we get into the fall. Then it becomes a regulatory decision. Is it going to come under an amendment to the EUA? Or is it going to wait for the BLA? Or is it going to be a separate BLA? I'm not sure exactly what it's going to be. But it's going to be a regulatory decision. So that's the thing that's going to hinge on how that rolls out.

Dr. Morrison: And that'll be in the – in the fall?

Dr. Fauci: I hope it's in the fall. I hope it doesn't go beyond the fall.

Dr. Morrison: OK. When you look out now and think about all of these pressure points and exercises and changes in vaccination policy, masking policy, trying to expedite the approval of the vaccines, trying to expedite getting children in the mix, what's the missing pieces right now? What missing pieces are there in terms of scientific unknowns or actions that we need to consider that we've kept in reserve or not thought enough about?

Dr. Fauci: Well, you know, vaccine looms as always the big factor, the overriding factor. As you mentioned, we've got to get that 93-plus million people who are not vaccinated, vaccinated. That is going to require the kinds of things we just mentioned – local mandates, people being convinced that it's OK to get vaccinated now that the vaccine – when it becomes officially approved and we don't have to rely on an EUA. But we also – we really do need a bit more of a uniformity in our approach. And I have to say, you know, I don't want to conflict in any way with the local authorities doing what they feel they need to do, but you know, you have situations where you have governors giving orders that you cannot mandate a mask in a school or in a workplace. We need to mask up until we get to the point where we really have control of this escalation of cases. If everybody got vaccinated, you wouldn't be arguing about masks. You likely – the need for masks would diminish dramatically. But in the meantime, I would think that if we could get everyone to adhere to the CDC recommendations about mitigation, that would be important.

Dr. Morrison: What about boosters? We haven't talked about boosters as a next step here in trying to consolidate our gains. What do you see on the horizon there as we enter this phase?

Dr. Fauci: Well, there's two buckets of booster considerations, Steve. The first is the immunocompromised, those who are transplant, cancer chemotherapy, immunosuppressed because of autoimmune therapy, and others. Giving them an additional shot is almost not considered a booster; it's considered part of what their original regimen should have been, because if you examine them in multiple groups that are doing that, many of them – maybe most of them – have not gotten an adequate immune response to begin with. So I think it's more emergent. And as a physician, as opposed to a public-health authority – but as a physician I feel that's almost medically emergent to have to do that because they are vulnerable. And what we need to do is to get whatever mechanism that is or regulatory mechanism to get them as quickly as we can to get an additional shot.

Then you ask the question, well, putting those people aside, taking care of them, what about the booster for the general population, starting off with the elderly? And then what about people who are otherwise normal, non-elderly? We are – we are gathering in real time, with both the follow up of the clinical trial data, looking at the people that we'll be following over a two-year period, as well as the cohort datas and the cohorts that the CDC are following, that literally on a week-by-week basis we evaluate whether we need it, to whom, and when. And that decision could be made anytime because, you know, we're already starting to see from Israeli studies and others that the duration of immunity, particularly in the context of Delta, is coming down. And other countries – France, Germany, Israel – have already decided. The U.K. will probably implement in September. So we're keeping an eye on that.

The decision was made by the CDC and the ACIP that right now, today, we don't need the general public who's been vaccinated to get a booster. But that could change, and that's the reason why we're following it really carefully on a week-by-week basis.

Dr. Morrison: So that could change on a fast trigger, potentially?

Dr. Fauci: Absolutely. Absolutely.

Dr. Morrison: Now, the news last – the disclosures last week about breakthrough infections and the ability of those who are fully vaccinated who experience breakthrough infections to transmit, that caused, you know, quite a stir, and it raised a lot of anxiety, certainly, across a spectrum of conversations that I

was part of or witnessed. Do you think that people have overreacted a bit? Because when you do look at the numbers, it's a tiny – 35,000 breakthrough infections in a population of 162 or 163 million people is a – is a miniscule number. What is your – how do you talk to people – this is a real phenomenon and it is a serious phenomenon, but it doesn't – it doesn't fundamentally change the picture, it seems to me.

Dr. Fauci: Well, I do it multiple times a day every day – (laughs) – and I'll do it again now with you. You go through, in a logical way, the steps of what is actually going on. So no vaccine is 100 percent protective. And even the really, really good ones that we have right now, fortunately for us, the ones that are 94 to 95 percent protective against clinical disease, are somewhat less protective against asymptomatic disease.

So the protection against infection is probably, you know, somewhere in the high 70s, the low 80s, depending upon what candidate you have, what product you have. That means that there naturally will be breakthrough infections. The word breakthrough kind of scares people; you know, breakthrough infection.

Dr. Morrison: Right.

Dr. Fauci: You expect that when you don't have 100 percent effective vaccine that some vaccinated people are going to get infected. The good news is that what we are clearly seeing is that the vaccine is doing exactly what you're asking it to do, because it's preventing people from getting seriously ill, because when you look at the breakthrough infections, they almost invariably – not always, but almost invariably are about 96 percent or so percent protective against advanced disease leading to hospitalization.

So even though you're getting breakthrough infections, the fact is, if you're vaccinated, you're prevented from getting severe disease. And the numbers are astounding. If you look at anywhere in the different states and different countries, 99.5 percent of the deaths due to COVID-19 are among unvaccinated people. And a very small, very, very small percentage are among vaccinated people.

So we should be careful. When you hear about breakthrough infections, remember, the more people you get vaccinated, the more breakthrough infections you're going to get, because if you have 90 percent of the people vaccinated and you don't have 100 percent effective vaccine, you're going to get a lot of – you're going to get a lot of people who are vaccinated and infected.

That's what we saw in Provincetown. That's what we recently saw at San Francisco General Hospital and another hospital in San Francisco. But when

you look at the ultimate effect, those people didn't get hospitalized or die. They were protected.

Dr. Morrison: Yes. Well, I do think – and that's very helpful to hear, and I know you've had to say this over and over again. And thank you for going through that with us. It is a confusing situation and it's a very difficult one for communication purposes. And I'm hearing that over and over again also from people that seem somewhat unclear, exactly, how to think about all of this.

Dr. Fauci: Well, absolutely. We're dealing with a highly transmissible, changing virus. And with that, you are going to see modification of recommendations. And I think the thing that got people most shook up is first it was said if you're vaccinated you don't need to wear a mask indoors, and then you say if you're vaccinated you still have to wear a mask indoors if you're in an indoor public place in a region that has a high or substantial transmissibility.

And the reason for that relates to what we were saying about the fact that vaccinated people who get infected, given this Delta variant, have a high degree of virus in the nasopharynx. And even though the vaccine protects them from getting severe disease, they can transmit it. And it has been documented that they do transmit it. So the mask has a lot to do with protecting you so you don't transmit it to someone else.

Dr. Morrison: Yes.

One last – I know we're at the end of your time and you're going to need to move on. Going back to the Antiviral Program for Pandemics, what are you most worried about in terms of achieving – barriers to achieving success? And what gives you the greatest confidence this is going to deliver the returns you're looking for?

Dr. Fauci: I have confidence in the science that will get us there. We did it with HIV. There's absolutely no reason why we can't do it for SARS-CoV-2. What I hope is that we have a sustained commitment, that it becomes, as we are planning, part of a broad, comprehensive pandemic preparedness plan that involves vaccines, therapeutics, diagnostics, and production and distribution. That's what a comprehensive program is.

Dr. Morrison: Dr. Fauci, thank you so much for all the time you've given us, all your candor, and all of the detail and nuance, and for your continued leadership as the chief medical advisor to the president of the United States. So thank you for being with us today.

Dr. Fauci: My pleasure, Steve. Thank you for having me, as always.

(END)