A health worker carries a tray of Pfizer-BioNTech vaccine vials at a vaccination center in Naples, Italy, last week. SALVATORE LAPORTA/IPA VIA ZUMA PRESS VIA NEWSCOM

'A question of choices.' Pfizer vaccine leader on confronting new coronavirus variants

By **Meredith Wadman** | Feb. 3, 2021 , 1:40 PM

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Philip Dormitzer led Pfizer's successful coronavirus vaccine research effort, which yielded a vaccine with a stunning **95% efficacy** in interim results from a clinical trial last year. That vaccine, developed with the German firm BioNTech, relies on a new technology employing messenger RNA (mRNA). It was the first to win emergency use authorization from the Food and Drug Administration for use against COVID-19 in the United States.

However, **recent lab studies** and **new clinical trial results** have **suggested** recently emerged variants of SARS-CoV-2, the pandemic coronavirus, have evolved resistance to vaccines, including Pfizer's. The company's vaccine,

which requires two doses 3 weeks apart, is now being administered in more than 50 countries, including the United States. Pfizer says it is on track to supply 200 million doses to the United States by the end of May and aims to ship 2 billion doses globally this year.

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Dormitzer, who has an M.D. and Ph.D. from Stanford University, has a history with pandemics. He was U.S. research chief at Novartis Vaccines, where he steered that company's work creating—in what is still record time—a successful vaccine against the 2009 H1N1 pandemic flu. He has been at Pfizer since 2015.

Dormitzer spoke with *Science*Insider about how the company is responding to the new variants and what challenges it foresees as SARS-CoV-2 continues to evolve in unpredictable ways. This interview has been edited for brevity and clarity.

Q: The pandemic is moving into a new phase as vaccination campaigns gear up while viral variants, or strains, proliferate. What keeps you up at night?

A: Things were supposed to get much, much calmer after we had the vaccine authorized. But things just don't hold still. The virus throws out new variants and we need to evaluate those and be prepared to respond. And there are

many other things: … How will the vaccine work in special populations? What reactions are people having? How do we improve things like temperature stability? The vaccine's authorized. It's wonderful to see it being used. But it's not the end of the process.

Q: Last week, researchers published a preprint looking, in the lab, at how well antibodies from the blood of Pfizer vaccinees attacked two of the new coronavirus strains—one first identified in South Africa and a highly contagious strain first identified in the United Kingdom. They found a 6.5-fold reduction in antibodies that neutralize the variant identified in South Africa, and a twofold reduction in the levels, or titers, of these neutralizing antibodies against the other variant. Should Pfizer vaccinees be concerned about these results?

A: I don't know if I would use the word concerned exactly. These laboratory findings don't of themselves tell us that a strain change [in the vaccine] is necessary. But we need to be prepared for the possibility that there could be some reduction in effectiveness. We see no evidence of that yet. We know [from our trial results] that we see protection—not full protection, but protection—starting at 12 to 14 days after that first dose. At that time [12 to 14 days out from the first dose] there are almost no neutralizing antibodies [that our tests detect in the blood of vaccinees]. There must be something other than high neutralizing antibody titers that can protect. Whether it's cell-mediated immunity, whether it's low neutralizing antibody titers, we don't know.

Q: Do you intend to run a comprehensive lab analysis of how your vaccine works against the suite of mutations seen in the new variants?

A: We already have. I can say broadly that our findings are very similar to others', in that you do see more reduction in neutralization with the South African variant than with the U.K. variant. We are also running similar tests against [a concerning variant first identified in Brazil]. We are hoping to get both the South African and the Brazilian

data out very soon. At the rate that this virus is spinning out variants, we will be continuing to do this for quite some time.

Q: What do you expect will be the effectiveness of your vaccine in human beings exposed to the new viral strains?

A: The fact that we see protection by means other than high neutralizing antibody [levels] makes me optimistic that we are going to see preserved protection. But nothing trumps the data. There are two main kinds of clinical data we might expect. First, we ran our phase 3 trial at sites including in Brazil and South Africa. At the time … these new variants … had not become dominant. But continuing to monitor what goes on in those clinical trial participants will give us some idea [if anyone who has been vaccinated gets sick with a new variant].

Second, the pattern of epidemiological findings could give us information, [for example whether] the instance of disease simply falls with immunization, or falls [but then] starts to increase.

Q: What is Pfizer doing to tailor its vaccine to be effective against these variants?

A: The work started well before the variants had emerged … through basic scientific research [on potential mutations]. … We are now at the point where we are routinely making the DNA templates for variants. And we are having discussions, internally and with regulators, about how far we progress each of these.

Q: Do you need to change your vaccine now to beat the new variants?

A: No. Simply seeing a reduction in a lab neutralization test does not tell you that you need to change [the vaccine]. You just have to be prepared. You have to do the work to prepare for a [vaccine] change regardless of whether you actually need to execute one or not.

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The other observation we have from pandemic flu is that after a couple of priming doses, a boosting dose months later gives not only very strong immunity but very broad immunity. So, one possibility is you do a [vaccine] change. The other possibility is you simply boost. And a rising tide lifts all boats. This is why you need to do the clinical studies. We need to understand what a SARS-CoV-2 booster looks like and what kind of immune response it gives you.

Q: What hurdles would an adapted vaccine face with regulators? Would you need to do animal studies or big clinical trials?

A: Those are key questions. For flu, since we have been doing it for decades, the rules are very clear: A fourfold reduction in hemagglutination inhibition titers [a measure of the level of antibodies against the virus in the blood of vaccinees] suggests you need to change the [vaccine]. But we know that something is very different between the flu and COVID-19. For flu, in a good year with a good strain match, you see about 60% [vaccine] efficacy. Here we see about 95% efficacy. We—the companies, the regulators, everybody—now need to figure out the rules of the game for COVID-19 vaccines. That's what we're working through right now.

Q: Do you need additional manufacturing plants to make an adapted vaccine?

A: We have tremendous manufacturing capacity. Our goal for the current vaccine is 2 billion doses in 2021. So, I don't think it's a question of having the resources. It's more a question of choices. If you are going to switch [the vaccine] to a new strain, it means you are going to have to reduce production of the current [vaccine]. There are real decisions to make.

Q: Other vaccinemakers have said changing the mRNA construct to target a new variant can be done in 6 weeks or less. Is that right, in Pfizer's case?

A: I have been working in pandemic response for a very, very long time. I have learned that what most people say about how fast they can do something—you have to examine those statements very carefully.

The part that's done in the lab, switching one mRNA to another, is very quick. … But the biggest question is what laboratory, animal, or clinical testing you need to do. And of course, an efficacy study would be almost impossible now because you would need to deny vaccine to people in the placebo group.

Q: Would you be interested in doing a human challenge study?

A: Personally, I would not. I think it's imposing a risk that's not necessary because we can get the information in other ways. I don't have an objection to human challenge studies in general—we are doing one right now with respiratory syncytial virus … but we are still learning about all the consequences of COVID-19 disease.

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