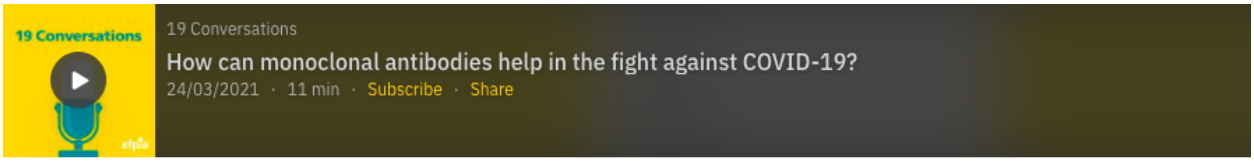

19 Conversations - Ep. 19

How can monoclonal antibodies help in the fight against COVID-19?

INTRO: Who decides medicine prices? How are vaccines made?

SUE: Do you have questions about the health care industry? Welcome to 19 Conversations! Today, we're asking Dr. Janelle Sabo, Lilly Global Platform Leader for COVID Therapeutics, how can monoclonal antibodies help in the fight against COVID-19. I'm Sue Saville. Thank you for joining the conversation. Janelle, welcome. Tell me, firstly, what are monoclonal antibodies? How do they work?

JANELLE: When you're sick and the virus enters your body, what happens is your immune system makes these antibodies, normally to fight it off. But it takes time for your body to make these antibodies to a new virus because it's never seen it before. And in the meantime you can get pretty sick. So neutralizing antibodies are similar to these antibodies you would normally make in your body but they are taken from patients who had recovered from COVID-19. So these treatments are based on a blood sample from an early COVID-19 survivor and they're isolated from some of the most potent antibodies that were found in their blood. And then they are administered and at the time what happens is these neutralizing antibodies limit the amount of virus in your body because they target the virus attached to it, and essentially allow your body to quickly clear it, allowing your normal immune system to begin to work and fight it off.

SUE: Of course, monoclonal antibodies have been used in the fight against cancer before. How big a challenge has it been to focus them on COVID?

JANELLE: Not as difficult as it may sound but it does take really great science and we were doing it on a very accelerated pace. What we did is we targeted the spike protein … many people have probably seen the little round sphere with spikes coming off of it. Those spikes are made of protein and we were able to actually target and attach to those so that it attaches to the neutralizing antibody instead of to your body and enters it to make you sick.

SUE: And they are of course rather complex, they are biologics, it's not that easy to make them. How difficult is it to actually produce these monoclonal antibodies?

JANELLE: These treatments which were designed specifically to treat COVID-19, need to have dedicated lines in order to really scale up very quickly at large scale and they require specialized people, both scientists and engineers. Just to manufacture one of them is about 300,000 square feet of manufacturing space, 40 miles of piping at 50 processing vessels and lots of controlled clean rooms. It takes about 90 days to manufacture a single batch of both the active ingredient, which is the neutralizing antibodies, as well as the drug product. So this process is pretty complex and has carefully controlled conditions and lots of numerous quality and safety checks. But it's an important one that we were able to invest in quite early, which is why we were able to get so many doses very quickly.

SUE: What about the pace of accelerated change and development? You referred there to the work you put in as a company, the investment in time, space and research. How has it been ramped up so quickly to turn this around?

JANELLE: Innovation and investment at risk are probably the two most important aspects that really fueled the acceleration here. And if you think about the overall timeline of development, typically these are measured in years. You know, say ten years from the time of discovery until the time it's on the market. If we think about innovation, one really innovative approach was thinking about how we might actually do clinical development very differently. So in this particular case what we did is we realized that patients are quarantined at home. You really have to meet patients where they are, they're not able to come back into the traditional health care system and go to traditional healthcare sites for clinical studies so we did two important things. So we did two important things. Number one is we designed the study so that they could largely be done remotely in the comfort in the home with a remote and digital technology. The second thing is in many cases we actually went to the patient. So when our nursing home study, we retrofitted RVs and actually drove RVs to nursing homes bringing the entire clinical trial site to the nursing home. These innovations allowed for quicker enrollment of patients who were the exact type of vulnerable high-risk patients that are being targeted by these therapies. And then of course we invested at risk. One of the major examples across the industry is investing in manufacturing and scaling quickly without having all the clinical data. Where we would traditionally wait to see proof of concept data, and start to see that replicate in phase 3 prior to major investments in scale up, and here we really made those investments very early on in the discovery process.

SUE: Of course, it was back in November last year that in America the FDA approved your monoclonal antibodies for the emergency use authorization and you've just had a similar authorization for the two to work together. What about roll out in Europe? How's that going?

JANELLE: Yes, across the world we prioritized the highest disease burden countries, those that had the largest number of cases and worked with both governments and regulatory agencies across the globe. And today actually have authorizations on most continents in the globe, including in Europe.

SUE: There was always big competition but now there's so much more collaboration between pharmaceutical companies. You're now working in a partnership with other companies GSK and Vir. The very first time that companies producing monoclonal antibodies separately have come together in a trial. How important are these collaborations?

JANELLE: Collaboration is another really important lever that was used to accelerate. One might actually say it's almost unprecedented the types of innovative collaboration, not just across the industry but also with professional organizations, with private organizations and governments and regulatory agencies. Each of these, in some way, have contributed to the acceleration whether it was really sharing best practices or key learnings that we were getting from the scientific efforts. It could have been collaborating in new and innovative ways. One example with the FDA is that we needed to very quickly scale very early on the manufacturing to have material for first-human dose, so we partnered with the FDA to quickly move that treatment into human testing. We even set up these mobile labs in our parking lots and dedicated a pharmacist that would actually sole dedicate this antibody in these new pods that were essentially clean rooms. Normally it would take us three years we were able to turn that around in literally three months. So this important collaboration to look at very different ways of thinking about

manufacturing, and dedicated manufacturing in pods, really created opportunities to really accelerate the timelines for development.

SUE: Some of your partnerships have been truly international, one of them with a Chinese company. How important is that to do cross-border work?

JANELLE: Actually, we've partnered with two different companies on the antibodies. One is Junshi, which is located in China. The second is AbCellera, located in Canada. And in both cases these companies had worked to do some of the earliest work to isolate the monoclonal neutralizing antibodies from blood samples of past survivors. When some of these discoveries were made, we were partnering with them to accelerate it in development to scale it up, and to eventually bring it to patients who need it the most.

SUE: What about the future then? What do you see as the next steps for the company in terms of taking this forward?

JANELLE: I think the next steps for us are … the virus is always under pressure and as with vaccines roll out and additional COVID-19 therapeutics are available, the virus has a desire to survive and so as a result, it will continue to mutate and to change over time. There will be a need for additional changes, potentially both in vaccines as well as additional COVID-19 therapeutics to manage some of these and so we are evaluating additional potent-broad second generation monoclonal neutralizing antibodies. We're also partnering, as you noted previously, with GSK and Vir to bring a second-generation combination into clinical studies as well. These are important to really think about how we can stay ahead of the virus knowing that under pressure these mutations or variants will occur.

SUE: So what do you see then as the main challenges coming up? And what do you see as exciting as we look ahead?

JANELLE: I mean actually I have a very positive outlook. I think that with vaccines now starting to roll out across the globe, I think with multiple COVID-19 therapeutics both on the market, as well as additional ones coming to the market, there's never been more options and they're going to continue to grow in the coming months.

I do think we have to remain diligent and so there are really four important points I would leave with you.

1. Number one is still the very basics of masking up and you know good hygiene will remain important for some time. I know there's a lot of fatigue but I think we have to stick with some of these fundamentals because they are the first layer of protection.
2. And number two is the vaccine rollouts remain incredibly important. We need to increase uptake and the speed at which these are rolling out. For some of the vaccines that you know manufacturers are talking about boosters to manage some of the variants and mutations these two will be important. We need to help make sure that there's global awareness that you need to take all of the shots of the vaccine based on what scientifically was demonstrated in terms of overall effectiveness of them.
3. The third component is really around COVID-19 therapeutics. We need to make sure that there is overall awareness of the COVID-19 therapeutics available not only to treat the earliest stages of the disease that's where the monoclonal neutralizing antibodies work but there are also

treatments that are available for the sickest patients, those that are hospitalized. Making sure that there's keen awareness among the healthcare community but also availability in the hardest hit and most impacted areas of the pandemic.

4. And last but not least is there is continued research and development that is likely necessary to stay pace with the virus until again herd immunity and some of the stabilization occurs in the pandemic.

SUE: Dr. Janelle Sabo, Lilly Global Platform Leader for COVID Therapeutics. Thank you very much for your insights there. And thank you very much for listening to 19 Conversations. If you liked this podcast, please click on the subscribe button to be the first to know when we release our next episode, and please leave a rating and a review. Until our next episode, we invite you to join the conversation on Twitter, with the #QuestionsInspireSolutions. Bye for now.