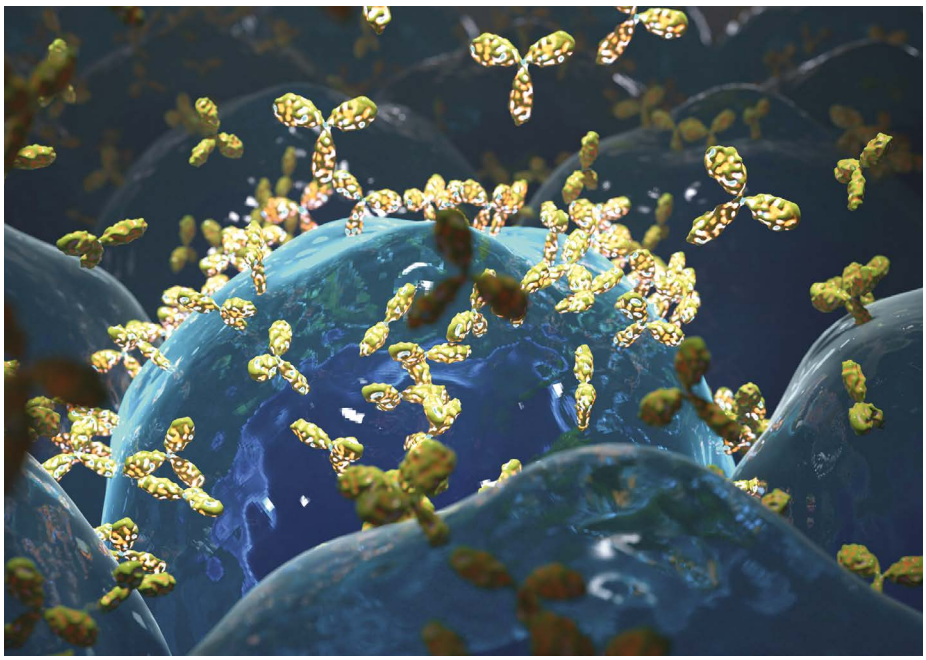

NANOCLUSTERING/SPL

Molecules called monoclonal antibodies (artist's impression) could treat COVID-19.

CORONAVIRUS: WILL THE WORLD BENEFIT FROM ANTIBODY THERAPIES?

Monoclonal antibodies are expensive to produce, meaning poor countries might be priced out.

By Heidi Ledford

As the race to develop a vaccine against COVID-19 rages on, some researchers are focused on a short-term way to treat people with the disease: monoclonal antibodies. Rather than wait for vaccines to coax the body to make its own antibodies, these scientists want to inject designer versions of these molecules to directly disable the SARS-CoV-2 coronavirus. But mass-produced antibodies, routinely used to treat diseases such as cancer, are complex to manufacture and come with a hefty price tag. That risks placing them beyond the reach of poor countries.

That warning comes from a report released on 10 August by two leading charities: the International AIDS Vaccine Initiative (IAVI), a non-profit research organization in New York City, and Wellcome, a research funder in London. It calls for boosting the global availability of therapeutic antibodies against COVID-19 and other diseases by developing regulatory pathways, business models and technologies to lower the cost of the pricey medicine (see go.nature.com/30vwb5b).

It is a tall order, acknowledges Mark Feinberg, president of IAVI. "But COVID-19 really forces the issue in a major way," he says. "The pandemic demands that this dialogue take place."

Compelling science

A vaccine against COVID-19 is probably still months away, and it will be months after that before many people are able to receive it. Even then, some people, including older individuals, might not respond strongly to immunization, and others might refuse it altogether.

Those factors make it important to develop therapies against COVID-19. Physicians still don't have many ways to treat the disease. The antiviral drug remdesivir has been shown to shorten hospital stays for some patients, but it is expensive and in short supply. And a cheap steroid called dexamethasone has been shown to benefit only people with severe infections.

So scientists are increasingly focusing on monoclonal-antibody drugs in the hope that they will harness the immune system's natural response to viral invaders, says Jens Lundgren, an infectious-disease physician at the University of Copenhagen and Rigshospitalet, one of the city's hospitals. "The science around this has been exploding," he says. "It's very compelling." Lundgren is leading a large, multinational trial of an antibody developed by Eli Lilly in Indianapolis, Indiana; AbCellera in Vancouver, Canada; and the US National Institutes of Health (NIH).

In this approach, researchers isolate antibodies from recovering patients and identify those that best 'neutralize' the virus by binding to it and keeping it from replicating. They then produce these antibodies in bulk in the laboratory. If the treatment is found to be effective, companies will scale up production, using cells grown in giant bioreactors.

This differs from 'convalescent plasma' treatments, composed of a complex mixture of antibodies and molecules taken directly from the blood of people recovering from COVID-19 and used to treat other patients. The effects of both of these approaches are short term: neither type of treatment will produce a long-lasting immune response.

Access gap

IAVI estimates that more than 70 antibody therapies are being developed to treat and prevent COVID-19, and several clinical trials are under way.

But past experience suggests that if such treatments are developed against COVID-19, they might not find their way to much of the world. Monoclonal-antibody therapies are generally more expensive to make than are small-molecule drugs; they must be injected rather than taken orally; and they are difficult for generic-drug makers to duplicate. About 80% of global sales of licensed therapeutic antibodies – which treat autoimmune diseases, among other ailments – are in the United States, Europe and Canada. The median price for antibody therapies in the United States is US$15,000–200,000 per year of treatment, according to the IAVI–Wellcome report.

Feinberg says that the pandemic could spur technological innovation to find easier and cheaper ways to make large quantities of antibodies. It could also prompt business arrangements between the companies that develop therapeutic antibodies and other manufacturers – akin to the makers of generic versions of small-molecule drugs – that could try to copy the process and distribute the drugs more widely. And it might force regulators in low- and middle-income countries to become more familiar with antibody therapies and better able to approve their use.

"I don't know that any one of those will provide the solution," says Feinberg. "But if you combine them, then hopefully you'll have significant synergy."

Unique properties

No one has yet completed a large, randomized study of an antibody therapy against COVID-19, but results from such trials are

expected in the coming months. Lundgren's trial, announced on 4 August, aims to enrol 1,000 people with COVID-19. Another large trial, sponsored by the NIH and Regeneron, a biotechnology company in Tarrytown, New York, launched on 6 July and will test a cocktail of two antibodies against SARS-CoV-2. Results are expected in late September.

Although these antibodies target the same virus, each interacts with SARS-CoV-2 differently: some will bind more strongly to the virus than will others, for example, or will target sites on its surface that shut the virus down more efficiently. And although antibodies are a natural means of defence, there are safety concerns, Lundgren notes. Researchers will be looking out for 'antibody-dependent enhancement', a phenomenon in which some antibodies can help viruses to gain entry into human cells, rather than prevent infection. A large trial is needed to settle the matter convincingly, Lundgren says.

OUTRAGE OVER RUSSIA'S FAST-TRACK CORONAVIRUS VACCINE

Scientists worry about the immunization's safety because it hasn't been tested in large trials.

By Ewen Callaway

Russian President Vladimir Putin announced on 11 August that the country's health regulator had become the first in the world to approve a coronavirus vaccine for widespread use — but scientists globally have condemned the decision as dangerously rushed. Russia hasn't completed large trials to test the vaccine's safety and efficacy, and rolling out an inadequately vetted vaccine could endanger people who receive it, researchers say. It could also impede global efforts to develop quality COVID-19 immunizations, they suggest.

"That the Russians may be skipping such measures and steps is what worries our community of vaccine scientists. If they get it wrong, it could undermine the entire global enterprise," says Peter Hotez, a vaccine scientist at Baylor College of Medicine in Houston, Texas.

"This is a reckless and foolish decision. Mass vaccination with an improperly tested vaccine is unethical. Any problem with the Russian vaccination campaign would be disastrous both through its negative effects on health, but also because it would further set back the acceptance of vaccines in the population," said Francois Balloux, a geneticist at University College London, in a statement distributed by the UK Science Media Centre.

ALEXEI NIKOLSKY/SPUTNIK/EPA-EFE/SHUTTERSTOCK

Russian President Vladimir Putin receives a report about the coronavirus vaccine.

In his announcement, Putin said that the Russian regulator had approved a COVID-19 vaccine developed by the Gamaleya Research Institute of Epidemiology and Microbiology in Moscow, even though phase III trials of the vaccine had yet to be completed. Such trials involve giving thousands of people a vaccine or a placebo injection, and then tracking them to see whether the vaccine prevents disease. The tests also allow researchers to confirm the vaccine's safety and look for rare side effects that might not have been observed in smaller, earlier-stage trials. Russian health-care minister Mikhail Murashko said at a government briefing that the vaccine would be gradually introduced to citizens, starting with health workers and teachers.

More than 200 COVID-19 vaccines are in development worldwide and several are already in phase III trials, with more front runners slated to begin theirs soon. But researchers think that even the earliest of those vaccines will not be approved for months.

Lack of data

The Gamaleya vaccine has been given to 76 volunteers as part of two early-stage trials listed on ClinicalTrials.gov, but no results from those trials or other preclinical studies have been published, and little else is known about the experimental vaccine.

According to the ClinicalTrials.gov listings, the vaccine, which is given in two doses, is made of two adenoviruses — viruses that cause a range of illnesses, including colds — that express the coronavirus's spike protein. The first dose contains an Ad26 virus — the same strain as is used in an experimental vaccine being developed by pharmaceutical company Johnson & Johnson of New Brunswick, New Jersey, and its subsidiary Janssen. The second, 'booster' dose is made of an Ad5 virus, similar to the one in an experimental jab being developed by CanSino Biologics in Tianjin, China.

According to the vaccine's Russian-language registration certificate, 38 participants who received one or two doses of the vaccine had produced antibodies against SARS-CoV-2's spike protein, including potent neutralizing antibodies that inactivate viral particles. These findings are similar to the results of early-stage trials of other candidate vaccines. Side effects were also similar, such as fever, headache and skin irritation at the site of injection.

Hotez expects that the Gamaleya vaccine will elicit a decent immune response against SARS-CoV-2. "The technical feat of developing a COVID-19 vaccine is not very complicated," he says. "The hard part is producing these vaccines under quality umbrellas — quality control and quality assurance — and then