Coronavirus drugs: Who's doing what, and when they might come

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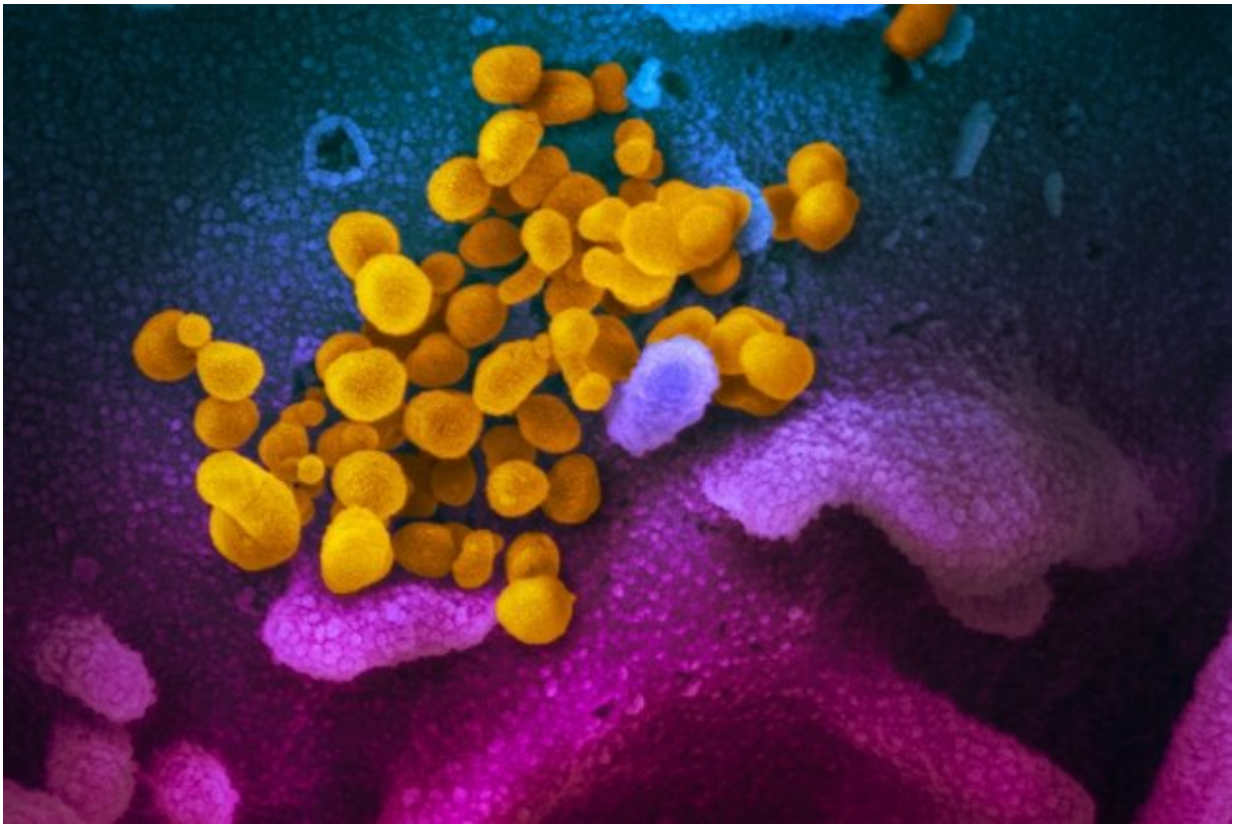

This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient, emerging from the surface of cells (blue/pink) cultured in the lab. Credit: NIAID-RML

Pharmaceuticals and research labs across the world are racing to find

vaccines and treatments for the new coronavirus, using a variety of different technologies.

According to Benjamin Neuman, a virologist at Texas A&M University-Texarkana, immunizing against the pathogen is a long shot: There has never been a very successful human vaccine against any member of the coronavirus family.

"This is going to be a lot of trial, a lot of error, but we have a lot of options to try," Neuman said.

Treatment could come sooner, with antiviral remdesivir showing early promise and already being used on an ad hoc basis before regulatory approval.

US President Donald Trump has urged his scientists and drug companies to speed up the process—but experts say fundamental constraints could leave little wiggle room.

"A vaccine has to have a fundamental scientific basis. It has to be manufacturable. It has to be safe. This could take a year and a half——or much longer," wrote H. Holden Thorp, the editor-in-chief of the journal *Science* in response to the president's calls.

"Pharmaceutical executives have every incentive to get there quickly—they will be selling the vaccine after all—but thankfully, they also know that you can't break the laws of nature to get there."

The United States is funding several companies through the Department of Health and Human Services (HHS) and National Institutes of Health (NIH).

The Coalition for Epidemic Preparedness Innovations (CEPI), a global

organization based in Oslo, is also helping to fund many companies, mostly smaller partners that would lack the capacity to scale-up mass production. It has so far provided about $24 million.

Firm: Gilead sciences

What it is: Treatment

When it might come: Later this year

Of all the drugs linked to the virus that causes COVID-19, Gilead's remdesivir could be the closest to market launch. It's actually not new per se but was developed to fight other viruses including Ebola (where it was shown to be ineffective) and it hasn't yet been approved for anything.

Still, it has shown early promise in treating some coronavirus patients in China, according to doctors, and Gilead is moving ahead with final stage clinical trials in Asia (known as "Phase 3"). It has also been used to treat at least one US patient so far.

NIH's Anthony Fauci, one of the top government scientists overseeing the coronavirus response, has said it could be available in the next "several months."

"There's only one drug right now that we think may have real efficacy. And that's remdesivir," said Bruce Aylward, a World Health Organization official at a recent press conference in China.

Remdesivir gets modified inside the human body to become similar to one of the four building blocks of DNA, called nucleotides.

Neuman told AFP that when viruses copy themselves, they do it "quickly

and a bit sloppily," meaning they might incorporate remdevisir into their structure—though human cells, which are more fastidious, won't make the same mistake.

If the virus incorporates the remdesivir into itself, the drug adds unwanted mutations that can destroy the virus.

Firm: Moderna

What it is: Vaccine

When it might come: 12-18 months

Within weeks of Chinese researchers making the genome of the virus public, a team at the University of Texas at Austin was able to create a replica model of its spike protein, the part which attaches to and infects human cells, and image it using a cryogenic (cooled) electron microscope.

This replica itself is now the basis for a vaccine candidate because it may provoke an immune response in the human body without causing harm—the classical method for developing vaccines based on principles dating back to smallpox vaccine in 1796.

NIH is also working with Moderna, a relatively new firm founded in 2010, to make a vaccine using the protein's genetic information to grow it inside human muscle tissue, rather than having to inject it in.

This information is stored in an intermediary transient substance called "messenger RNA" that carries genetic code from DNA to cells.

"The advantage is that it's really fast," explained Jason McLellan, who led the UT Austin team, whereas the traditional approach of creating the

protein outside is difficult to scale and takes a long time.

The vaccine began its first human trial on March 16 after being proven effective in mice.

If all goes to plan, it could be available on the market in about a year and a half, ready in case the coronavirus outbreak continues until the next flu season, according to Fauci.

Firm: Regeneron

What it is: Treatment and vaccine

When it might come: Firm timeline not yet provided

Regeneron last year developed an intravenous drug that was shown to significantly boost survival rates among Ebola patients using what are known as "monoclonal antibodies."

To do this, they genetically modified mice to give them human-like immune systems. The mice are exposed to viruses, or weakened forms of them, in order to produce human antibodies, Christos Kyratsous, the company's vice president of research told AFP.

These antibodies are then isolated and screened to find the most potent ones, which are grown in labs, purified and given to humans intravenously.

"If everything goes well, we should know what our best antibodies are within the next few weeks," with human trials to begin by summer, said Kyratsous.

The drug could work as both a treatment and as a vaccine, by dosing up

people before they are exposed—though these effects would be only temporary.

In the near term, they are also trying to repurpose another of their drugs devised using the same platform called Kevzara, which is approved to treat inflammation caused by arthritis.

This could help fight the lung inflammation seen in the severe forms of the COVID-19 disease—in other words fighting a symptom as opposed to the virus itself.

Firm: Sanofi

What it is: Vaccine

When it might come: Time not yet clear

The French drugmaker is partnering with the US government to use a so-called "recombinant DNA platform" to produce a vaccine candidate.

It takes the virus' DNA and combines it with DNA from a harmless virus, creating a chimera that can provoke an immune response.

The antigens it produces can then be scaled up.

The technology is already the basis of Sanofi's influenza vaccine, and believes it has a head start due to a SARS vaccine it developed that offered partial protection in animals.

David Loew, the company's head of vaccines, is reported to have said Sanofi expects to have a research candidate ready for lab testing within six months and for clinical study within a year and a half.

Firm: Inovio Pharmaceuticals

What it is: Vaccine

When it might come: Emergency supplies by end of year?

Inovio, another US biopharmaceutical, has since its founding in the 1980s worked on DNA vaccines—which work in a similar way to RNA vaccines explained above but work at an earlier link of the chain.

As an analogy, DNA can be thought of as a reference book in a library, while RNA is like a photocopy of a page from that book containing instructions to carry out a task.

"We plan to begin human clinical trials in the US in April and soon thereafter in China and South Korea, where the outbreak is impacting the most people," said J. Joseph Kim, Inovio's president and CEO in a statement.

"We plan on delivering one million doses by year end with existing resources and capacity."

Other notable efforts

British drugmaker GlaxoSmithKline has teamed up with a Chinese biotech firm, providing adjuvant platform technology.

An adjuvant is added to some vaccines to enhance the immune response, thereby creating a stronger and longer lasting immunity against infections than the vaccine alone.

Like Moderna, CureVac is working with the University of Queensland on a messenger RNA vaccine. Its CEO Daniel Menichella met with the

White House earlier this month, and announced the company expects to have a candidate within a few months.

American pharma Johnson & Johnson is looking at repurposing some of its existing drugs to see how they might help treat the symptoms of patients already infected with the virus.

It's also working on developing a vaccine involving a deactivated version of the pathogen.

California-based Vir biotechnology has isolated antibodies from SARS survivors and is looking to see if these can treat the new coronavirus. Its platform has previously developed treatments for Ebola and other diseases.

Even the likes of chloroquine—the synthetic form of quinine, used to treat malaria, may have some properties that fight the virus and scientists are calling for more work to investigate.

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