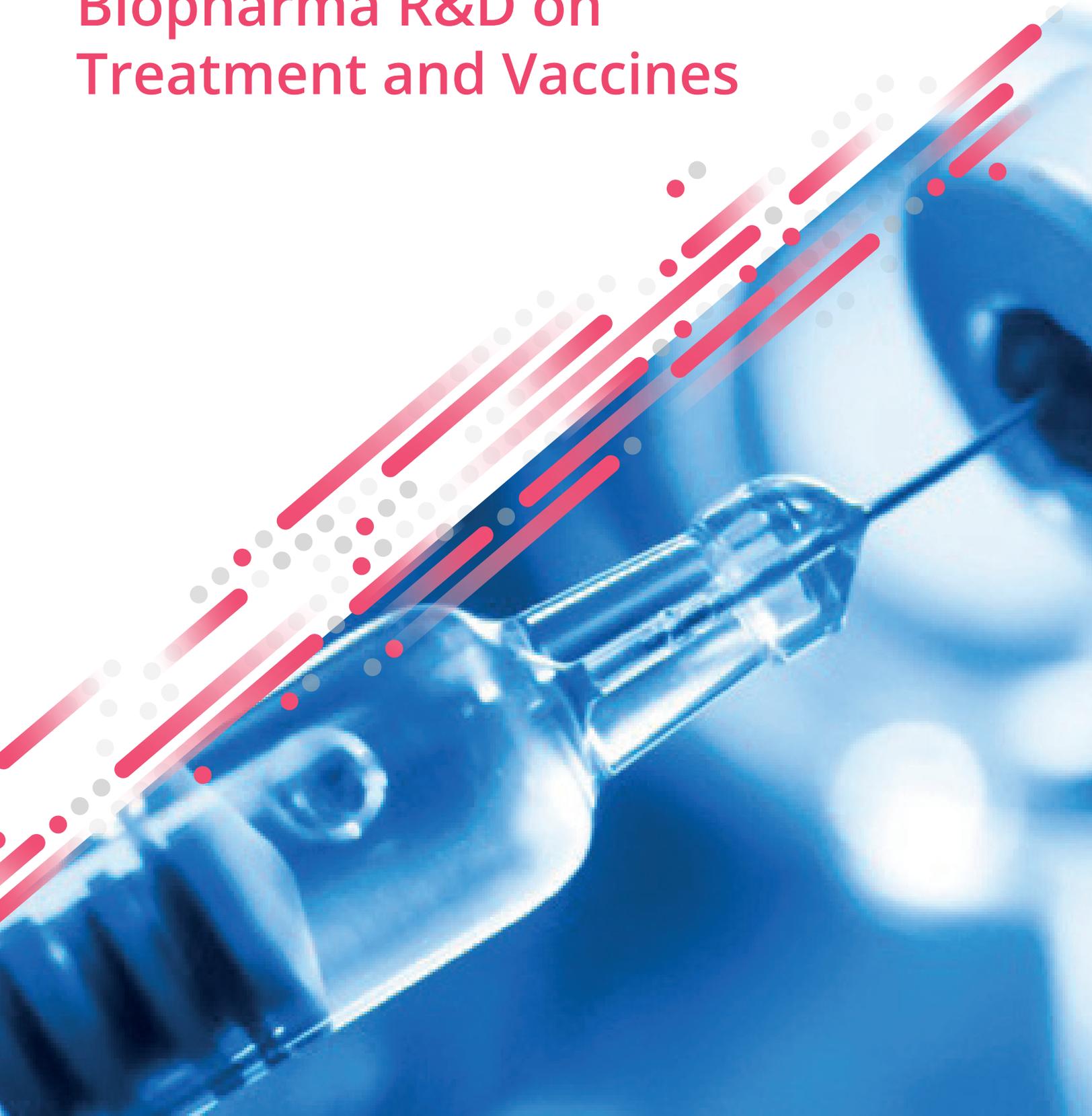


Biopharma R&D on Treatment and Vaccines



Coronavirus: Gilead Readies For Remdesivir Ramp Up, Questions On Profit Motive

Demand Could Be High For Antiviral

Executive Summary

If clinical trials prove it effective against COVID-19, remdesivir could potentially help millions of patients - which raises big questions about funding and access.

As vaccines will take around 12 months to develop, companies with antiviral treatments are now been pushed to the front line in the battle against coronavirus, and Gilead Sciences Inc.'s remdesivir is currently the biggest hope of a drug to treat infected patients.

The company had big news to talk about on 2 March at the Cowen Health Care conference, as it had announced earlier in the day the acquisition of oncology firm Forty Seven for \$4.9bn. (Also see "Gilead Calls Forty Seven Buyout Complementary To Kite, Other IO Efforts" - Scrip, 2 Mar, 2020.)

Speaking at the investor conference, Gilead's chief commercial officer Johanna Mercier was also questioned about the company's developing role in the fight against the coronavirus.

"It is not about creating a business around remdesivir," said Mercier. "It has always been, can Gilead be part of the solution to this incredible pandemic?"

Mercier said the company had demonstrated its intent by donating supplies of the drug to anyone who required it (through US and Chinese government channels). It is also ramping up its manufacturing of the intravenously administered drug 'at risk', ahead of initial safety and efficacy results from two newly initiated clinical trials.

"All of that is at risk in not knowing if the drug works or not - and that is really not with an eye to commercial," she added.

Mercier said the company was spending more time on considering issues of access to the drug once its safety and efficacy is established - especially in regions of the world with less developed healthcare systems.

Nevertheless, Gilead is contemplating a possible commercial future for the drug.

"I have to be honest, commercial opportunity might come if this becomes a seasonal disease or if stockpiling comes into play, but that is much later down the line," concluded Mercier.

One precedent for a big commercial hit for an antiviral product is Roche's Tamiflu (oseltamivir). The drug achieved peak revenues of \$3bn in 2009, largely down to stockpiling in response to that year's H1N1 flu pandemic. While Tamiflu was a moneyspinner for Roche, it also brought with it scrutiny of Roche's patent, and the drug's clinical efficacy.

For COVID-19, public health officials and governments around the world are warning that it may be inevitable that the disease officially reaches pandemic status, where it has spread to all regions across the globe.

As of 2 March, there were 88,948 cases worldwide, with a rapid increase in confirmed cases in the US and Europe causing particular concern. A total of 3,043 deaths from the infection have been recorded, with all but 128 of these in China.

Despite its alarming spread, the World Health Organization is nevertheless stressing that containment measures will help minimize the impact of COVID-19, and give health systems time to build up their capacity for dealing with thousands of serious cases.

Gilead launched two Phase III clinical trials of remdesivir for the treatment of COVID-19 in adults last week.

The open-label, multicenter studies will assess the safety and efficacy of the drug in nearly 1,000 patients. A five-day and ten-day dosing regimen of an intravenous formulation of remdesivir will be tested.

The drug is a nucleotide analog, and was originally developed to treat the Ebola virus, but has also shown efficacy against the coronavirus family, including the earlier SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) viruses.

One of the trials will enrol around 400 patients with severe clinical manifestations of the infection, while the second trial will look to recruit 600 patients with moderate clinical manifestations.

The trials will mainly be conducted at sites in Asian countries worst hit by the coronavirus outbreak. The company says new sites will be added in other countries where high numbers of confirmed cases emerge.

Moderna Marches First Coronavirus Vaccine To US Test

Enters Clinic In Just 42 days

Executive Summary

The first vaccine for the new coronavirus has entered the clinic, with US firm Moderna leading the race.

The first vaccine for the new coronavirus is officially out of lab and being put to the clinical test, as the outbreak originating from Wuhan in China continues its spread around the world with hundreds of new cases being reported in South Korea, Italy and Iran.

The vaccine, from US biotech firm Moderna Inc., using a novel technology called messenger RNA (mRNA), has been made ready for testing on humans in just 42 days, and is the first to reach this stage of development.

The Cambridge, MA-based company said it had shipped its mRNA-1273 vaccine to the National Institute of Allergy and Infectious Diseases (NIAID) on 24 February for use in the US Phase I study. It targets a pre-fusion stabilized form of the Spike protein, selected by the firm in collaboration with investigators at the NIAID's Vaccine Research Center, Moderna said.

Upon the announcement, the company's shares jumped by over 20% overnight in after-hours trading.

With funding from the Coalition for Epidemic Preparedness Innovations (CEPI), Moderna was able to take the vaccine from sequence identification to delivery in only 42 days, said Juan Andres, the company's Chief Technical Operations and Quality Officer, who emphasized the capability at its existing facilities. "This would

not have been possible without our Norwood manufacturing site, which uses leading-edge technology to enable flexible operations and ensure high quality standards are met for clinical-grade material."

mRNA Approach

Manufacturing of the initial batch of mRNA-1273 was funded by CEPI, and Andres praised the collaboration with it and the NIAID as behind the speed to the clinic. To date, the Cambridge firm has produced and released more than 100 batches from the Norwood site for human clinical trials.

Messenger RNA is increasingly becoming a leading technology in fighting virus outbreaks and Moderna has developed six vaccines that have entered clinical studies using the technology - a respiratory syncytial virus vaccine for older adults, an RSV vaccine for young children, a metapneumovirus vaccine, influenza H7N9 vaccine and the coronavirus vaccine.

Industry insiders see the potential mRNA vaccine technology as a tool to speed up the coronavirus fight in the least amount of time. "Normally, vaccine is given in the form of a viral antigen (a protein), which needs to be expressed, purified and fully characterized. Moderna technology gives it in the form of mRNA which will translate to a protein antigen on site in humans.

"Thus it only requires a very small amount of material (mRNA) and does not need the tedious process development," Jim Wu, CEO of Shanghai-based antiviral drug developer Ark Biosciences Inc., told Scrip in a written response.

"The Moderna technology only speeds the

process, without coming up with any new idea or innovation on how to make a vaccine work," he noted.

More Vaccines Coming

Multiple other vaccine developers are accelerating their programs for the coronavirus, known as SARS-CoV-2. US biotech Inovio Pharmaceuticals Inc. has said it is preparing its vaccine INO-4700 for clinical studies as early as this summer. The Nasdaq-listed firm recently partnered with Beijing Advaccine for tests on patients with COVID-19 disease in China, Inovio CEO Joseph Kim told Scrip. (Also see "Coronavirus Notebook: China Focuses On Antivirals As Death Toll Passes SARS" - Scrip, 10 Feb, 2020.)

UK-based GlaxoSmithKline PLC is also partnering with Chinese firm Clover Corp. Ltd. to develop a novel protein-based COVID-19 S-Trimer vaccine, developed by Clover. GSK will provide the company with its pandemic adjuvant system to evaluate the candidate in preclinical studies, and Clover is readying its cGMP facilities in China for scale-up and mass production. (Also see "Coronavirus Pipeline: GSK And Clover Add To Collaborations" - Scrip, 24 Feb, 2020.)

Johnson & Johnson and Sanofi Pasteur meanwhile are partnering with the US Department of Health and Human Services to develop vaccines against the outbreak, which has now affected more than 77,000 people in China, with a death toll of 2,660.

Sanofi To Test Arthritis Drug Kevzara For Coronavirus

'Scientific Rationale' Behind Regeneron-partnered IL-6 Inhibitor

Executive Summary

The French giant is already working on a vaccine to combat COVID-19 and is now evaluating whether its rheumatoid arthritis drug Kevzara could treat pulmonary complications related to the coronavirus.

Sanofi and Regeneron Pharmaceuticals Inc. are moving swiftly to start trials to see whether their rheumatoid arthritis drug Kevzara could treat the symptoms of coronavirus.

The French drug-maker told Scrip that "there is scientific rationale that supports the exploration" of Kevzara (sarilumab), its interleukin-6 (IL-6) receptor blocker approved for moderately to severely active rheumatoid arthritis, to treat pulmonary complications related to the COVID-19 infection. Sanofi noted that "given the quickly evolving situation around COVID-19, we are working to leverage the knowledge of both companies in evaluating how Kevzara may be a potential treatment option for some patients."

The company added that the development of any trials would be done together, with Sanofi leading international efforts and Regeneron co-ordinating studies in the US. It will also make Kevzara available to collaborate with interested external partners such as the Biomedical Advanced Research and Development Authority (BARDA) and the US Department of Defense "and is evaluating the best way to explore this further."

Kevzara was one of the drugs, along with the cholesterol-lowering medicine Praluent (alirocumab), at the heart of a revamped agreement announced in December between Sanofi and Regeneron. The restructured

collaboration will see the latter take over the full US rights to the PCSK9 inhibitor, while Sanofi will take over ex-US and global rights to Kevzara; the Paris-headquartered firm told Scrip that the restructured pact was "not yet final and we are in active discussions on how COVID-19 may factor into this." (Also see "Sanofi CEO Hudson Delivers An Ambitious Turnaround Agenda" - Scrip, 10 Dec, 2019.)

As for timing on the trials, Regeneron chief scientific officer George Yancopoulos told the Wall Street Journal that the goal would be "in the next couple of weeks to have the trial up and running, and in weeks to months after that to have the data."

Kevzara was approved in the US and Europe in 2017 but has struggled to make an impact in the rheumatoid arthritis market against the established TNF inhibitors Enbrel (etanercept) and Humira (adalimumab) or Roche's entrenched IL-6 blocker Actemra (tocilizumab). Sales of Actemra in 2019 were CHF2.31bn (\$2.40bn), while Kevzara total revenues were a modest €183m (\$206.1m).

On Sanofi's fourth-quarter conference call on 6 February, CEO Paul Hudson said that the objective for the restructuring of the Kevzara deal was "simplification and accountability." He added, "We are looking at which way to go next; some ideas on the table. But I think, frankly, we have to decide what is actually possible and what is a sensible investment to make when there are other very attractive opportunities in the pipeline."

Roche's Actemra Also In Studies

News of the Kevzara trials comes a week after Chinese authorities recommended Actemra to tackle COVID-19 in patients with damage to both lungs, those with severe symptoms and

an elevated IL-6 level. (Also see “China Taps Roche Antibody, Green Lights Testing Kits For Coronavirus Arsenal” - Scrip, 5 Mar, 2020.)

IL-6 inhibits pro-inflammatory cytokines and so far cytokine release syndrome has been cited by front-line physicians in Wuhan as the leading cause of death in severe coronavirus patients. The China National Clinical Registry shows that a clinical study of Actemra in severe COVID-19 patients started on 13 February.

Kevzara and Actemra are just two of several approved drugs being evaluated to tackle coronavirus. Others recommended by the Chinese authorities include AbbVie Inc.’s antiviral Kaletra (lopinavir and ritonavir) and ritonavir alone, Bayer AG’s antimalarial chloroquine and the flu drug favipiravir from Zhejiang Hisun Pharmaceutical Co. Ltd.

Evaluating Kevzara is the latest initiative taken by

Sanofi to tackle the coronavirus pandemic. Last month (18 February), it unveiled an alliance with BARDA to develop a new vaccine, employing the same technology used to produce its Flublok flu vaccine, of which 70 million doses were supplied to the US market last year.

John Shiver, head of vaccines R&D at Sanofi Pasteur, said its candidate could be in in vitro testing within six months, and in clinical trials within 12-18 months. He noted that the efforts of other companies were welcome, but that Sanofi Pasteur would be unique in bringing its experience of producing flu vaccine in millions of doses to global patient populations.

On the Q4 calls before the BARDA tie-up was unveiled, CEO Hudson noted that the objective for Sanofi was not to grab “a newspaper headline” around COVID-19 but to focus on “real work that will make a difference.”

[For full coverage on Coronavirus from Scrip, please click here](#)