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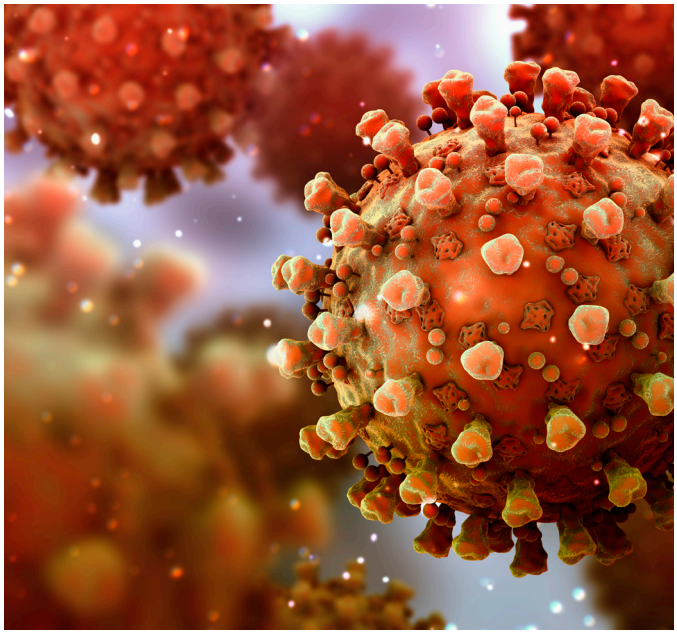
COVID-19: Super-charging Drug Development in the Race for a Cure

IQVIA Pipeline Intelligence



The magnitude of the 2019-2020 coronavirus (COVID-19) pandemic has led to an unprecedented concerted and collaborative effort of scientific researchers internationally to develop vaccines and treatments as quickly as possible to contain the virus. Recent scientific breakthroughs include the publication of the complete genome sequence of SARS-CoV-2 isolated from infected patients and the atomic structure of the spike protein of the virus (a promising target for COVID-19 vaccines), and the identification of the membrane protein ACE2 as the host cell entry receptor for the virus.[1-3].

The race to develop COVID-19 treatments

Since the first COVID-19 vaccine candidate entered clinical trials on 16 March 2020,[4-5] rapid progress has been made to develop and clinically test vaccines and drugs in patients with COVID-19. According to the World Health Organization, there are currently 70 vaccines in development, four of which are in clinical trials and the other 66 under preclinical evaluation.[6-7] Researchers are also investigating three main drug types to treat COVID-19; antivirals to inhibit replication of SARS-CoV-2, anti-inflammatories including IL-6 inhibitors, which reduce hyperinflammation (lowering production of cytokines) in patients with respiratory distress syndrome due to COVID-19 infection, and antibody-based treatments derived from recovered patients or developed in laboratories.[8-9]

As of 21 April 2020, IQVIA Pipeline Intelligence, which is a proprietary drug pipeline database covering drug development from discovery phase to approval and launch, listed 122 clinical programs in active development for COVID-19. Table 1 summarizes several vaccines, experimental and repurposed drugs under development that may emerge as key candidates in the fight to treat and prevent COVID-19, as sourced from IQVIA Pipeline Intelligence:

Table 1: Key vaccine and therapeutics in development for COVID-19

INNOVATOR COMPANY	DRUG NAME	MODE OF ACTION OR PLATFORM	DESCRIPTION/TYPE	PHASE / STATUS
Moderna	mRNA 1273	RNA	LNP-encapsulated mRNA vaccine	Phase I
Inovio Pharmaceuticals	INO 4800	DNA	DNA plasmid vaccine	Phase I
Cansino Biological/ Beijing Institute of Biotechnology	Ad5 nCoV	Non-replicating vector	Adenovirus type 5 vaccine	Phase II
University of Oxford	ChAdOx1 nCoV-19	Non-replicating vector	Simian adenovirus vaccine	Phase I/II
Novavax	NVX-CoV2373	Protein subunit	VLP recombinant protein nanoparticle vaccine + Matrix-M adjuvant	Preclinical
Gilead Sciences	Remdesivir	Nucleoside RNA polymerase inhibitor	Antiviral nucleotide analog	Experimental/ repurposed
Fujifilm Toyama Chemical	Favipiravir	RNA polymerase inhibitor	Pyrazine derivative	Experimental/ repurposed
Sanofi	Hydroxychloroquine	ACE2 terminal glycosylation inhibitor	Anti-malarial agent	Repurposed
Ascletis Pharma	ASC 09 + ritonavir	Protease inhibitors	Antiviral fixed-dosed combination	Phase III
Roche	Tocilizumab	IL-6 inhibitor	Monoclonal antibody	Repurposed
Sanofi/Regeneron	Sarilumab	IL-6 inhibitor	Monoclonal antibody	Repurposed
InflaRx	IFX 1	C5 inhibitor	Monoclonal antibody	Phase II/III
Novartis/Incyte	Ruxolitinib	JAK1/JAK2 inhibitor	Small molecule	Repurposed
Apeiron Biologics	APN 01	Angiogenesis inhibitor	rhACE2	Phase II

Source: IQVIA Pipeline Intelligence

Selected key vaccine candidates for COVID-19

MRNA 1273

Moderna, in collaboration with the US National Institute of Allergy and Infectious Diseases (NIAID), is developing a lipid nanoparticle (LNP)-encapsulated mRNA vaccine mRNA 1273, encoding the spike S protein of SARS-CoV-2, for the prevention of COVID-19 infection. mRNA 1273 was the first COVID-19 vaccine candidate to enter human clinical testing when dosing began in a phase I trial in March of this year. The trial will evaluate the safety and immunogenicity of three dose levels of mRNA 1273 (25, 100 and 250 mcg) administered on a two-dose vaccination schedule and is expected to complete in June 2020.

INO 4800

Inovio Pharmaceuticals' INO 4800 is a DNA plasmid vaccine, currently in a phase I trial to assess its safety, tolerability and immunogenicity for COVID-19 in healthy volunteers. INO 4800 is designed for administration intramuscularly or intradermally utilizing the company's proprietary hand-held smart device CELLECTRA, which uses an electrical pulse to open small pores in the host cells reversibly to enable the plasmids to enter. The plasmids are used by the cells to generate specific coded antigens, which then stimulate an immune response. Preliminary data from this trial is expected by late summer, according to the company.

AD5 NCOV

Cansino Biological and the Beijing Institute of Biotechnology's Ad5 nCoV is a non-replicating vaccine

with the replication-defective adenovirus type 5 vector to express the SARS-CoV-2 spike protein. A phase II trial to test the safety and immune responses generated by the recombinant vaccine is under way with completion anticipated in January 2021.

CHADOX1 NCOV-19

Researchers at the University of Oxford (UK) have begun testing a non-replicating simian adenovirus vector vaccine ChAdOx1 nCoV-19, which encodes the spike S protein antigen of SARS-CoV-2 in a phase I/II trial for prophylaxis against COVID-19. The trial will assess the safety and immunogenicity of one or two doses of the vaccine and is expected to complete in May 2021.

NVX-COV2373

Novavax is developing a Matrix-M protein subunit vaccine utilizing its proprietary recombinant nanoparticle technology platform. The vaccine candidate NVX-CoV2373 comprises antigens derived from the spike S protein of SARS-CoV-2 and is expected to enter testing in a phase I trial in mid-May 2020.

Selected antivirals in development for COVID-19

REMDESIVIR

Gilead Sciences' nucleotide analogue prodrug remdesivir is currently being evaluated in two company-sponsored phase III trials for the treatment of COVID-19. The antiviral drug, which inhibits viral RNA polymerases, was originally being developed for treating Ebola virus infection. Data from a compassionate use program demonstrated that 68% of hospitalized patients with severe COVID-19 that were treated with remdesivir had a clinical improvement based on oxygen support.

FAVIPIRAVIR

Fujifilm Toyama Chemical's favipiravir (AVIGAN) is an antiviral pyrazine RNA polymerase inhibitor currently approved in Japan for treating influenza. The agent prevents viral proliferation and is in phase III development for the treatment of COVID-19; a phase III trial is being conducted in Japan and a phase II trial is under way in the USA.

HYDROXYCHLOROQUINE

Hydroxychloroquine (PLAQUENIL), an anti-malarial drug launched by Sanofi in 1949, demonstrated in vitro antiviral activity. In in vitro studies, hydroxychloroquine blocked SARS-CoV-2 entry into cells.

ASC 09 + RITONAVIR

Ascletis Pharma's fixed-dose combination of HIV-1 protease inhibitors ASC 09 and ritonavir is being tested in a phase III trial in China for the treatment COVID-19 pneumonia.

Selected antibodies in development for COVID-19

TOCILIZUMAB

Roche's humanized anti-IL-6 receptor monoclonal antibody tocilizumab is under evaluation in a multinational phase III trial (COVACTA) for the treatment of patients with severe COVID-19 pneumonia. The company has also submitted a clinical trial notification to Japan's Pharmaceuticals and Medical Devices Agency to conduct a phase III trial of tocilizumab for this indication. Tocilizumab is available in many markets worldwide including the USA, the EU, Japan and Canada for rheumatoid arthritis and systemic juvenile idiopathic arthritis.

SARILUMAB

Sanofi and Regeneron Pharmaceuticals' sarilumab (KEVZARA), an IL-6 monoclonal antibody, is in a phase II/III trial for the treatment of patients with severe COVID-19. Sarilumab is available in many major markets including the USA, Canada, Japan and several European countries for rheumatoid arthritis. The antibody is also under phase II evaluation uveitis and juvenile rheumatoid arthritis.

IFX 1

InflaRx's IFX 1, a monoclonal antibody targeting complement activation product C5a, is designed to block a mechanism of inflammation. IFX 1 is in a phase II/III trial (PANAMO) for patients with severe COVID-19 pneumonia and preliminary data are expected in late October 2020. The antibody is also under phase II evaluation for hidradenitis suppurativa, ANCA-associated vasculitis and pyoderma gangrenosum.

Other agents in development for COVID-19

RUXOLITINIB

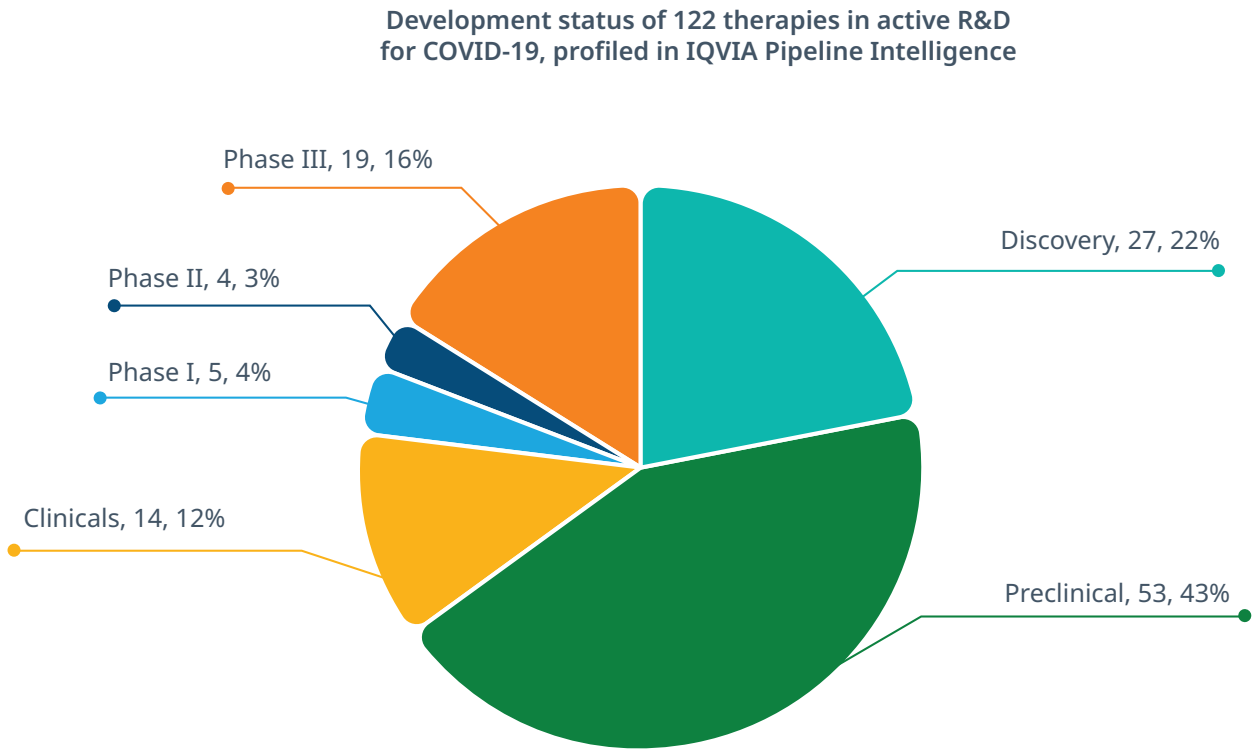
Novartis and Incyte announced plans to conduct a phase III trial to evaluate ruxolitinib (JAKAVI), a selective JAK1/JAK2 inhibitor, for the treatment of respiratory complications associated with cytokine storm in patients with COVID-19. The companies have also established a managed access program in the USA for use of ruxolitinib in severe and very severe COVID-19 disease. Ruxolitinib was previously being developed for the treatment of inflammatory and autoimmune diseases and is available in the USA and other major markets for myelofibrosis, polycythemia vera and thrombocythemia. It is also approved in the USA for graft versus host disease and under phase III evaluation for atopic dermatitis.

APN 01

Apeiron Biologics is conducting a phase II trial of APN 01, a recombinant human angiotensin converting enzyme 2 (rhACE2), for the treatment of COVID-19. APN 01 has the potential to become the first drug approved to treat COVID-19 that specifically targets the SARS-CoV-2 virus. It imitates the human enzyme ACE2 and induces the binding of the SARS-CoV-2 virus to soluble ACE2/APN 01 instead of ACE2 on the surface of host cells, thereby blocking the infection of cells by SARS-CoV-2 and concomitant reduction in inflammation of the lungs to protect against acute lung injury. The agent was previously being developed for pulmonary hypertension and acute lung injury.

Figure 2 displays the phase distribution of the 122 clinical programs in active development for COVID-19 captured in IQVIA Pipeline Intelligence.

Figure 2: Clinical programs in development for COVID-19



Source: IQVIA Pipeline Intelligence

Future directions

As COVID-19 has quickly become a global health crisis, with far-reaching consequences that are unprecedented in the modern era, an urgent scaling up of the international response between drug developers, regulators, policy makers, public health bodies and governments is required to minimize the spread of SARS-CoV-2, protect health systems and mitigate the deleterious effects on worldwide population health. While a safe and effective vaccine is some time away from approval, researchers continue the search for effective treatments, with focus on repurposing existing drugs to bridge this gap.

The implications of the COVID-19 pandemic has put a spotlight on the need for new drugs, diagnostics, antibody tests, patient- and contact-tracing technologies, disease surveillance and other early-warning tools to better tackle future pandemics.

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Sam Lam holds a bachelor's degree in Biotechnology, and has 12 years of experience in competitive intelligence, syndicated analytics, drug forecasting, pharmaceutical regulatory procedures and medical writing. He has been associated with the Pipeline Intelligence team for 2 years.