

Snowballing research preps avalanche to bury COVID-19

By Karen Carey

Research focused on finding viable solutions to counter the COVID-19 pandemic continues at an explosive pace with a total of 588 potential [therapeutics and vaccines](#) at the forefront of scientific efforts launched by industry, academia and government.

The number of options now in the pipeline are a 36% increase above what was seen only [a month ago](#). Likewise, global deaths due to the circulating coronavirus have risen by 37% since June 1, according to the World Health Organization. Global confirmed cases, by contrast, have jumped 70% in the last month. The rise is largely attributed to an increase in diagnostic testing, although society re-opening, no doubt, also plays a part. *BioWorld MedTech* has tracked about [330 diagnostics](#) that are available or in development for COVID-19, including a third of which are immunoassays and two-thirds of which are molecular assays. A total of 157 of them – 35% more than at the beginning of June – have the FDA's emergency use authorization (EUA). To put that into perspective, there were only 23 diagnostics that had an EUA by the end of March.

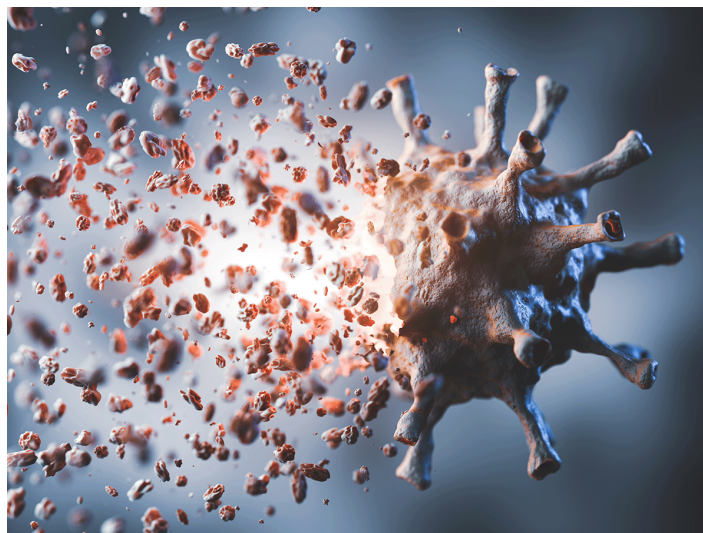
The U.S., where a substantial amount of COVID-19 research is being conducted, accounts for about a quarter of both the world deaths and confirmed cases. As of July 1, the numbers were 126,573 and 2.57 million, respectively.

Click here: [COVID-19 timeline for biopharma development work](#)

The disruptive pandemic continues to affect every aspect of the biopharma industry. In May, nearly [28%](#) of the licensing, collaborations and joint ventures were focused on COVID-19 therapeutics and vaccines. While the SARS-CoV-2 virus has led to many [clinical trial delays](#), it also is consuming much of the phase I through phase III news flow, accounting for about [30%](#) of the data tracked in May.

Throughout June, 155 new therapeutic and vaccine research projects have come to light. Although some of those projects originated in the earlier stages of the pandemic, they are added to the *BioWorld* COVID-19 tracker following confirmation through company statements or clinical trial registrations. Nevertheless, the growing number of efforts are clear evidence that the industry is intensely focused on taking down the deadly virus and targeting it from all directions.

While there are three times as many therapeutics in development



than there are vaccines, the window of opportunity for the therapeutics may begin to close once effective vaccines become available, pressuring biopharma companies to provide affordable, effective drugs, while still recouping investments. Many have put their lead programs on hold to focus on COVID-19.

Nevertheless, an unprecedented amount of money continues to flow into the industry, which is moving at a frantic pace. Industry leaders are organizing simultaneous trials at different phases and ramping up manufacturing capabilities well ahead of an approval. Biopharma money raised so far in the first half of 2020, at \$62 billion, is nearing the industry record of \$68.4 billion collected for the entire year of 2015. Recent [large financings](#) by developers include \$6.07 billion raised by Sanofi SA; and \$1.34 billion, the largest traditional follow-on offering to date, raised by Moderna Inc.

Public markets are doing well, too. The Biopharma Stock Index, despite the sharp dip following the U.S. lockdown in March, is up 33% since the beginning of the year, while the Nasdaq Biotechnology Stock Index is up about 12%.

Hot and cold data

As of July 1, there were 442 therapeutics in development for COVID-19 and its complications. As several are added every day to the *BioWorld* watch list, disappointments continue to surface.

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The FDA revoked an EUA issued March 28 for [chloroquine and hydroxychloroquine](#), drugs used to treat malaria, lupus and rheumatoid arthritis, following Recovery trial data that showed no significant difference with hydroxychloroquine and standard of care in terms of death (25.7% vs. 23.5%) or length of hospital stay.

Likewise, the Recovery trial nixed hopes for Abbvie Inc.'s HIV combination drug [lopinavir-ritonavir](#), showing no beneficial effect in hospitalized COVID-19 patients. A total of 1,596 patients randomized to the treatment vs. 3,376 patients randomized to standard of care showed no significant difference in the primary endpoint of 28-day mortality (22.1% vs. 21.3%, respectively).

Therapeutics with the best data reported in the past month are remdesivir, lenzilumab and dexamethasone.

Gilead Sciences Inc. recently priced [remdesivir](#), which has emergency use authorization from the FDA, at \$390 per vial for all developed countries and it is expected to cost \$2,340 for a five-day course of treatment. RBC Capital Markets analyst Brian Abrahams said the price could generate \$2.3 billion in global revenue this year. The pricing followed data in which hospitalized COVID-19 pneumonia patients receiving the treatment for five days were 65% more likely to have clinical improvement at day 11 vs. standard of care.

Humanigen Inc., however, reported in June that its Humaneered anti-human-GM-CSF monoclonal antibody [lenzilumab](#) led to a median time to improvement and recovery in 12 patients of five days vs. the 10 to 11 days with remdesivir. Although it is a small victory as part of a compassionate use program, all eyes will be on the company's phase III trial currently enrolling 238 hospitalized COVID-19 pneumonia patients.

Another celebration followed with [dexamethasone](#) showing a one-third reduction in deaths in COVID-19 patients on ventilators, compared with a 15% reduction in 28-day mortality in patients receiving oxygen therapy in the U.K. Recovery trial.

Accumulating research

A total of 97 therapies are currently in late-stage trials, including 37 in phase II/III, 47 in phase III and 13 in phase IV. Similarly, a total of 94 therapies are in phase II trials. At the earlier stage, 46 are in either phase I or phase I/II, while 157 are still preclinical and 41 other projects are at the discovery stage.

A number of potential therapies are entering phase III studies, including Regeneron Pharmaceuticals Inc.'s monoclonal antibodies, REGN-10933 plus REGN-10987, and Genentech Inc.'s acute ischemic stroke treatment alteplase, (Activase), a tissue plasminogen activator, for atypical acute respiratory distress syndrome related to COVID-19. Following an interim analysis, the Montreal Heart Institute is continuing with its Colcorona trial to see if colchicine may prevent inflammatory storm; and Immodulon Therapeutics Ltd. is starting its COV-IMMUNO phase III trial of IMM-101 to prevent severe respiratory and COVID-19-related infections in cancer patients. Others entering phase III

include Fulcrum Therapeutics Inc.'s losmapimod in higher-risk hospitalized adults, Oncoimmune Inc.'s CD24Fc, Eli Lilly and Co. and Incyte Corp.'s baricitinib, and CTI Biopharma Corp.'s pacritinib.

Entering phase II/III trials are Edesa Biotech Inc.'s EB-05; Evelo Biosciences Inc.'s EDP-1815; Fibrogen Inc.'s pamrevlumab; Neurorx Inc. and Relief Therapeutics Holding SA's Aviptadil (RLF-100), which gained FDA fast track designation in June to treat acute lung injury/acute respiratory distress syndrome associated with COVID-19; PTC Therapeutics Inc.'s PTC-299; Kiniksa Pharmaceuticals Ltd.'s mavrilimumab; and Algernon Pharmaceuticals Inc.'s NP-120 (ifenprodil).

Going for the gold

As of July 1, there were 146 vaccines in development for COVID-19.

The perception that vaccines will be the gold standard for curing COVID-19 persists with 30 potential candidates currently in clinical trials, including two in phase IV, two in phase III, 15 in phase I/II and 11 in phase I. There are also more than 100 potential candidates at the preclinical stage and at least 12 discovery projects underway. Money continues to flow into companies working specifically on those vaccines. Etherna Immunotherapies NV, for instance, raised \$38.2 million in a series B round in June. It expects to enter the clinic with its mRNA vaccine for COVID-19 in 2021. SK Bioscience Co. Ltd. received \$3.6 million from the Bill & Melinda Gates Foundation in May and plans to enter the clinic with its vaccine in September.

In a large vote of confidence, Translate Bio Inc. signed a \$2.3 billion [expansion deal](#) in June with Sanofi to develop mRNA-based vaccines. Also in June, Merck & Co. Inc. completed an [acquisition](#) of Themis Biosciences GmbH, gaining access to its measles vector-based vaccine for COVID-19, and Novavax Inc. was awarded a \$60 million contract by the U.S. Department of Defense (DoD) for the manufacturing of its vaccine, NVX-CoV2373.

Some of the most advanced COVID-19 vaccines come from Astrazeneca plc, Moderna Inc., and Biontech SE and Pfizer Inc., all of which are not only developing them but working on building manufacturing capabilities.

Astrazeneca's AZD-1222 vaccine, formerly ChAdOx1, is on an accelerated path, supported with \$1.2 billion through Operation Warp Speed. Already part of a phase I/II trial with the University of Oxford, it is set to enter a phase II/III at any time. It signed an \$87 million partnership with Emergent Biosolutions Inc. in June and agreed to supply the European Union with [400 million doses](#) with deliveries starting by the end of 2020.

Moderna's mRNA-1273 vaccine is currently part of a phase I and a phase II trial, both of which are recruiting. As of June 11, enrollment of 300 people was completed and company executives have said that [phase III work](#) could begin this

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summer. Moderna signed with Catalent Inc. for the large-scale, commercial fill-finish manufacturing of the vaccine.

Biontech and Pfizer reported positive phase I/II results of their [BNT-162](#) mRNA vaccine on July 1, with participants displaying better immune responses than recovered COVID-19 patients. The companies expect to move into a phase IIb/III study with 30,000 healthy volunteers before the end of July and to manufacture 100 million doses by the end of the year. The trial tested four vaccine candidates, with the preliminary data referring specifically to the BNT-162b1 candidate, which encodes a SARS-CoV-2 receptor binding domain antigen.

A few phase I/II vaccines showing positive results recently include Inovio Pharmaceuticals Inc.'s INO-4800 and Sinovac Biotech Ltd.'s Coronavac. Out of 36 patients enrolled, 34 of them, or 94%, displayed overall immunological response rates after receiving the 1-mg and 2-mg doses of INO-4800 at week six. Coronavac demonstrated favorable immunogenicity and safety profiles, and Sinovac told *BioWorld* it would move into phase III trials outside of China in July.

Other phase I/II trials underway or soon to start include those for BBIBP-CorV, from Sinopharm subsidiary, Beijing Institute of Biological Products Co. Ltd.; COVAC1, from Imperial College; GX-19, from Genexine Inc.; Allostim, from Mirror Biologics Inc. and Immunovative Therapies Ltd.; V-SARS, from Immunitor LLC; Gam-COVID-Vac, from the Gamaleya Research Institute of Epidemiology and Microbiology; and AV-COVID-19, from Aivita Biomedical Inc.

Entering the clinic soon is Janssen Pharmaceuticals' Ad26. COV2-S, a recombinant adenoviral vector vaccine that is part of a \$1 billion agreement with the Biomedical Advanced Research and Development Authority (BARDA). The company is launching a phase I/IIa trial in July and plans to start a phase III immediately thereafter.

Others initiating phase I trials are Genecure Biotechnologies' vaccine; Medicago Inc.'s virus-like particle vaccine; Curevac AG's mRNA vaccine, CVnCoV; and Clover Biopharmaceuticals Inc.'s SCB-2019 vaccine.