

Monitoring International Trends

July 2020

The NBA monitors international developments that may influence the management of blood and blood products in Australia. Our focus is on:

- Potential new product developments and applications;
- Global regulatory and blood practice trends;
- Events that may have an impact on global supply, demand and pricing, such as changes in company structure, capacity, organisation and ownership; and
- Other emerging risks that could put financial or other pressures on the Australian sector.

In the period covered by this posting, the emphasis within the health sector worldwide has been on the COVID-19 pandemic. Clinical trials for non-related treatments have in many cases been paused, launches of recently approved drugs have been postponed, and the emphasis of research and product development in both the public and private sectors has been on COVID-19 testing, vaccine development and identification of potential therapies. Clinical discourse too has been extensively refocused on how best to manage COVID-19 patients. Some items of interest are reported below.

Table of contents

| | | |
|----|--|----|
| 1. | TREATING BLOOD DISORDERS | 3 |
| 2. | PATIENT BLOOD MANAGEMENT AND OTHER BLOOD MATTERS | 4 |
| 3. | CLINICAL EXPERIENCE WITH COVID-19..... | 5 |
| | Respiratory and cardiovascular concerns | 5 |
| | Neurological symptoms | 5 |
| | The cytokine storm..... | 5 |
| | Suggested disease modifying factors | 6 |
| | COVID-19 in paediatric patients | 6 |
| | Other issues in clinical management | 7 |
| | COVID-19 and its antibodies | 8 |
| 4. | DEVELOPING VACCINES FOR COVID-19 | 9 |
| | Vaccine trials..... | 9 |
| | Vaccine research | 11 |
| | Vaccine manufacture and distribution..... | 12 |
| | Impact of mutation of the SARS-CoV-2 virus | 14 |
| 5. | POTENTIAL TREATMENTS FOR COVID-19 | 14 |
| | Hyperimmune immunoglobulin; immunoglobulin | 14 |
| | Remdesivir | 15 |

| | |
|--------------------------------------|-----------|
| Other therapies | 15 |
| 6. MANAGING THE PANDEMIC..... | 17 |
| Individual country experience | 17 |
| Transmission..... | 18 |
| Origins of the pandemic..... | 19 |
| Other effects of the pandemic | 19 |
| 7. OTHER NEWS..... | 19 |

1. Treating blood disorders

- At the International Society on Thrombosis and Haemostasis Virtual Congress¹, **Sobi reported further data on the efficacy and safety of Elocta®** (efmoroctocog alfa for haemophilia A) **and Alprolix®** (eftrenonacog alfa for haemophilia B), as well as pharmacokinetic data on BIVV001 (rFVIII Fc-VWF-XTEN). Also reported were data for Doptelet® (avatrombopag) to treat thrombocytopenia in chronic liver disease and chronic immune thrombocytopenia (ITP).²
- **Spark Therapeutics**, a member of the Roche Group, announced updated data from three dose cohorts of the ongoing Phase I/II clinical trial of investigational **SPK-8011 in hemophilia A**. The data were presented at the International Society of Thrombosis and Hemostasis (ISTH) 2020 Virtual Congress.³ Spark plans to begin a key haemophilia gene therapy trial next year.⁴
- The US FDA is to decide shortly whether to approve the first **gene therapy for haemophilia A, BioMarin's Roctavian**.⁵
- Researchers who studied 187 Ugandan children with sickle cell anaemia found that **increasing the dose of hydroxyurea** by half significantly **decreased the risk of sickle-cell complications**.⁶

¹ 12 – 14 July 2020

² All abstracts can be accessed via [the official ISTH website](#):

Final Results of PUPs B-LONG Study: *Evaluating Safety and Efficacy of rFIXFc in Previously Untreated Patients with Haemophilia B*. Poster presentation # PB0956. (Joint with Sanofi); A French Multicentre Prospective, Non-Interventional Study (B-SURE) Evaluating Real-World Usage and Effectiveness of Recombinant Factor IX Fc Fusion Protein (rFIXFc) in People with Haemophilia B: Baseline Data. Poster presentation # PB0889; *Rationale and Study Design for a Prospective, Low-Interventional Study to Investigate whether Systematic Joint Examination Impacts Haemophilia Treatment Management Decisions in Patients with Haemophilia A in France: The A-MOVE Study*. Poster presentation # PB0910; *No Relapse in Patients with Previous Inhibitors Switched to rFVIII Fc in Ongoing Observational Phase 4 Studies*. Poster presentation # PB0936; *Females with Haemophilia in Nordic Countries Have a Higher Risk of Developing Pain, Anxiety and Depression Based on Treatment Patterns as Compared to Matched Controls: Data from a Registry Study over a Period of 11 Years*. Poster presentation # PB0951; *First Interim Analysis of a 24-Month, Prospective, Non-Interventional, Multicentre Study in Germany Evaluating the Real-World Usage and Effectiveness of rFVIII Fc and rFIXFc in Patients with Haemophilia A or B (PREVENT)*. Poster presentation # PB0952; *Treatment-Based Risk Assessment of Developing Pain, Anxiety, and Depression as Compared to Matched Controls in People with Haemophilia. A Nordic Registry Study Over a Period of 11 Years*. Poster presentation # PB0955; *Population pharmacokinetic (PK) analysis of BIVV001 (rFVIII Fc-VWF-XTEN), a new class of factor VIII (FVIII) replacement*. Poster Presentation # PB0949. (Joint with Sanofi); *Achieving Clinically Relevant Platelet Count Response Thresholds with Avatrombopag (AVA) in Immune Thrombocytopenia (ITP)*. Poster presentation # PB1335; *Response to Avatrombopag (AVA) in Chronic Immune Thrombocytopenia: Alternative Efficacy Measures*. Poster presentation # PB1349; *Pharmacokinetic/Pharmacodynamic (PK/PD) Modeling Providing Guidance for Selecting Avatrombopag (AVA) Dose When Switching from Eltrombopag in Chronic Immune Thrombocytopenia (ITP)*. Poster presentation # PB1350; *Pooled Safety Analysis of Avatrombopag (AVA) from Clinical Trials*. Poster presentation # PB1352; *Stability of Crushed Avatrombopag Tablets Demonstrated in Multiple Food Vehicles*. Poster presentation # PB1353; *Corticosteroid Reduction or Discontinuation after Initiation of Avatrombopag Treatment in Patients with Chronic Immune Thrombocytopenia (ITP)*. Poster presentation # PB1378

³ <https://pipelinereview.com/index.php/2020071375275/DNA-RNA-and-Cells/Spark-Therapeutics-Announces-Updated-Data-on-SPK-8011-from-Phase-1/2-Clinical-Trial-in-Hemophilia-A-at-ISTH-2020-Virtual-Congress.html>

⁴ <https://www.biopharmadive.com/news/spark-hemophilia-gene-therapy-phase-3/581490/>

⁵ <https://www.biopharmadive.com/news/fda-approval-decisions-third-quarter-2020/581169/>

⁶ <https://www.medscape.com/viewarticle/932935>

- The first **ISTH Guidelines for Treatment of Thrombotic Thrombocytopenic Purpura** (TTP) were presented at the ISTH 2020 Virtual Congress and published in the [Journal of Thrombosis and Haemostasis](#).⁷

2. Patient Blood Management and other blood matters

- The American College of Cardiology updated its **guidance on managing bleeding in patients taking oral anticoagulants**.⁸
- Donated **lungs have been revived** for transplant after being connected to the blood supply of a live pig.⁹
- GlaxoSmithKline's Duvroq and Akebia Therapeutics' Vafseo have been approved in Japan to treat **anaemia due to chronic kidney disease**.¹⁰
- A blood test developed at Massachusetts General Hospital —called iCoagLab— reports several **coagulation metrics within minutes**.¹¹
- Researchers reported that **trauma patients** who underwent emergency general surgery appeared to **have a higher risk for venous thromboembolism** (VTE) than patients whose surgery was elective.¹² They suggested that more aggressive VTE chemoprophylaxis should be considered for these patients.
- AMAG Pharmaceuticals announced data from two Phase II randomized, placebo-controlled, dose ranging studies which showed safety and efficacy of ciraparantag **reversing the effects of apixaban and rivaroxaban** in healthy adults age 50-75 years. Ciraparantag is being developed for patients taking direct oral anticoagulants or low molecular weight heparin when reversal of the anticoagulant effect becomes necessary for emergency surgery, urgent procedures or due to life-threatening or uncontrolled bleeding.¹³
- Researchers have discovered **how to target platelet activation** (pathological clumping) **without interfering in normal processes that prevent uncontrolled bleeding**.¹⁴
- A small imaging device has been developed to **explore inside blood vessels** to understand the causes of heart disease and heart attacks.¹⁵
- Grifols is acquiring a Montreal-based **plasma fractionation facility and two purification facilities**, along with 11 US-based plasma collection centres.¹⁶
- **Grifols** has acquired 10 per cent of the **cloud-based marketplace Bloodbuy**, which facilitates sales and purchases of blood components in the US.¹⁷

⁷ <https://thelimbic.com/haematology/first-ttp-guidelines-released-at-isth-2020/>

⁸ <https://www.medpagetoday.com/cardiology/prevention/87558>

⁹ <https://www.newscientist.com/article/2248535-damaged-human-lungs-revived-for-transplant-by-connecting-them-to-a-pig/>

¹⁰ <https://www.fiercepharma.com/pharma-asia/gsk-s-duvroq-akebia-s-vafseo-win-global-first-nods-japan-to-challenge-astellas-anemia>

¹¹ <https://medicaldialogues.in/laboratory-medicine/news/new-inexpensive-bedside-test-to-detect-bleeding-risk-after-surgery-67078>

¹² <https://www.healio.com/news/hematology-oncology/20200707/emergency-surgery-linked-to-higher-risk-for-venous-thromboembolism>

¹³ <https://pipelinereview.com/index.php/2020071375272/Small-Molecules/AMAG-Announces-Presentation-of-Ciraparantag-Data-at-the-International-Society-on-Thrombosis-and-Haemostasis.html>

¹⁴ <https://www.fiercebiotech.com/research/preventing-heart-attack-by-changing-how-platelets-respond-to-blood-flow-stress>

¹⁵ <https://7news.com.au/news/health/smallest-blood-vessel-imaging-device-made-c-1181285>

¹⁶ <https://seekingalpha.com/news/3592489-grifols-to-acquire-plasma-facilities-in-montreal-and-u-s-for-460m>

¹⁷ <https://seekingalpha.com/news/3594252-grifols-makes-investment-in-digital-healthcare-space>

3. Clinical experience with COVID-19

Respiratory and cardiovascular concerns

- Researchers say that the **ischemic stroke** rate appears more than seven times higher in coronavirus patients than in flu patients.¹⁸
- Australian haematologist Dr James McFadyen¹⁹, his haematology colleague Dr Hannah Stevens and cardiologist Professor Karlheinz Peter have co-authored a [review](#) of **thrombosis in COVID-19**²⁰ in a paper in *Circulation Research*.
- US researchers have found that so far COVID-19 patients have **not often been co-infected with other respiratory viruses**.²¹
- The [International Society on Thrombosis and Haemostasis \(ISTH\) annual congress](#) concentrated on the **cardiovascular complications** of COVID-19.²²
- A Chinese study found **CT scans could not distinguish between pneumonia from COVID-19 and from influenza**.²³
- In the US, the FDA issued a new emergency authorization to the Centers for Disease Control and Prevention for a **combined influenza and COVID-19 diagnostic test**, which identifies which of the two viruses is responsible for respiratory symptoms.²⁴

Neurological symptoms

- Reviewers have recommended a three-stage classification of the impact of COVID-19 on the central nervous system. They **suggest all patients hospitalised with the virus be given an MRI** to identify neurologic damage and guide follow-up monitoring.²⁵

The cytokine storm

- Researchers from China reported that **therapeutic plasma exchange** was an effective treatment for the cytokine storm in three patients.²⁶
- An observational study showed that in patients with COVID-19-associated **cytokine storm**, intensive **immunosuppression with glucocorticoids then interleukin-6**, if required, speeded respiratory recovery and reduced mortality.²⁷

¹⁸ <https://www.medpagetoday.com/infectiousdisease/covid19/87386>

¹⁹ from the Atherothrombosis and Vascular Biology Program at the Baker Heart and Diabetes Institute

²⁰ Published in *Circulation Research*. See also <https://thelimbic.com/haematology/covid-19-and-thrombosis-repurposing-old-drugs-and-finding-new-targets/>

²¹ <https://www.medpagetoday.com/infectiousdisease/covid19/87483>

²² <https://www.medpagetoday.com/meetingcoverage/additionalmeetings/87594>

²³ <https://www.medpagetoday.com/infectiousdisease/covid19/87526>

²⁴ <https://www.fiercebiotech.com/medtech/to-prepare-for-complicated-flu-season-fda-greenlights-cdc-s-combined-influenza-covid-19-test>

²⁵ <https://www.medscape.com/viewarticle/933131>

²⁶ <https://transfusionnews.com/2020/07/01/therapeutic-plasma-exchange-in-patients-with-severe-covid-19/>

²⁷ <https://www.bmj.com/content/370/bmj.m2935>

Suggested disease modifying factors

- A study has suggested that **stress level** (measured as an increased cortisol level at hospital admission for individuals with COVID-19) may prove to be an independent predictor of mortality.²⁸
- A literature review suggests that **low serum testosterone levels** may predispose older men to worse COVID-19 outcomes.²⁹
- A study has found that **proton pump inhibitor use** increases the risk of COVID-19³⁰.
- A case in Spain of late stent thrombosis in a hospitalised COVID-19 patient underlined the importance of **antithrombotic therapy for those with coronary artery disease**.³¹
- Researchers reported that **patients with HIV** who were hospitalised in New York City with COVID-19 (during the spring peak in numbers) fared no worse than hospitalised patients without HIV.³²
- Researchers found that almost half of hospitalized COVID-19 patients with no prior diabetes diagnosis have **hyperglycaemia**, and that this is an independent predictor of mortality at four weeks.³³
- A new study reported that **blood type is not a predictor of COVID-19 severity** but could be **linked with testing positive for the disease**.³⁴

COVID-19 in paediatric patients

- Public health surveillance in New York State for **multisystem inflammatory syndrome in children** suggested that case definitions may hide less clear disease.³⁵
- A European study found that: "Although COVID-19 affects children less severely than adults overall, **there are severe cases in all age groups**. Those who have pre-existing health issues and children under one month of age were more likely to be admitted to intensive care".³⁶
- A UK case-series study suggests that children with COVID-19-related paediatric multisystem inflammatory syndrome may develop **neurologic symptoms involving both the central and peripheral nervous systems**.³⁷
- The American Academy of Pediatrics has issued **guidance on identifying and treating** children with multisystem inflammatory syndrome.³⁸

²⁸ <https://www.healio.com/news/endocrinology/20200629/cortisol-level-may-predict-mortality-risk-in-covid19>

²⁹ <https://www.healio.com/news/endocrinology/20200702/low-testosterone-may-impair-immune-response-in-men-with-covid19>

³⁰ <https://www.healio.com/news/gastroenterology/20200707/proton-pump-inhibitor-use-doubles-risk-for-covid19>

³¹ <https://www.medpagetoday.com/cardiology/pci/87460>

³² <https://www.healio.com/news/infectious-disease/20200713/in-nyc-covid19-outcomes-not-worse-among-patients-with-hiv>

³³ <https://www.medscape.com/viewarticle/933787> and <https://www.healio.com/news/endocrinology/20200714/fpg-at-hospital-admission-predicts-covid19-complications-death-in-those-without-diabetes>

³⁴ <https://www.medscape.com/viewarticle/934313>

³⁵ <https://www.medpagetoday.com/infectiousdisease/covid19/87341>

³⁶ <https://www.physiciansbriefing.com/infectious-disease-8/coronavirus-1008/factors-linked-to-severe-covid-19-in-children-identified-758992.html>

³⁷ <https://www.medscape.com/viewarticle/933311>

³⁸ <https://www.healio.com/news/pediatrics/20200716/aap-issues-guidance-on-multisystem-inflammatory-syndrome-in-children>

- In New York, where 237 patients appear to have suffered **Multisystem Inflammatory Syndrome in Children**, state officials **continue to track their progress**.³⁹

Other issues in clinical management

- A small study found that although **loss of smell and taste** could be associated with COVID-19 infection it did not appear to persist for more than a month.⁴⁰
- Previously, researchers showed that patients with mild forms of COVID-19 have circulating T cells that respond to the virus. Now, scientists have found that **COVID-19 patients in the intensive care unit also make SARS-CoV-2-reactive T cells**. Both research teams identified a subset of healthy, unexposed people who also had T cells that react to the virus.⁴¹
- Dr Christine Ko⁴² told the virtual annual meeting of the American Academy of Dermatology that there are at least **five dermatologic patterns in patients who are suspected or confirmed of having COVID-19** and that new studies are coming out daily.⁴³ Meanwhile, two small studies have questioned suggestions of “COVID toes” as symptoms of coronavirus infection.⁴⁴
- Researchers have recommended collaborative research to improve understanding of **acute kidney injury secondary to COVID-19**, to obtain adequate evidence to support clinical approaches, and to develop new approaches to monitoring and management.⁴⁵
- The Asia-Pacific Working Group for Liver Derangement during the COVID-19 Pandemic has issued 36 recommendations on the use of **drug therapy for COVID-19 in the case of liver dysfunction**.⁴⁶
- Doctors have reported evidence that a baby was infected in the womb in the last weeks of gestation.⁴⁷ However another study found that the **placenta lacks the major molecules used by SARS-CoV-2 virus to cause infection**.⁴⁸
- Spanish researchers say that a **rash in the mouth** can be a symptom of COVID-19.⁴⁹
- Researchers reported that **intensive care mortality has fallen by one-third** since the pandemic began.⁵⁰
- A study found that recovered patients discharged from acute care **need extended monitoring**.⁵¹

³⁹ <https://www.medscape.com/viewarticle/934148> and <https://coronavirus.health.ny.gov/childhood-inflammatory-disease-related-covid-19>

⁴⁰ <https://www.medpagetoday.com/infectiousdisease/covid19/87405>

⁴¹ <https://www.the-scientist.com/news-opinion/sars-cov-2-reactive-t-cells-found-in-patients-with-severe-covid-19-67695>

⁴² Professor of Dermatology and Pathology at Yale University

⁴³ <https://www.medscape.com/viewarticle/933240>

⁴⁴ <https://www.medpagetoday.com/dermatology/generaldermatology/87335>

⁴⁵ [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30229-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30229-0/fulltext)

⁴⁶ <https://www.medscape.com/viewarticle/933617>

⁴⁷ <https://www.news.com.au/lifestyle/parenting/babies/coronavirus-in-pregnant-women-baby-infected-with-covid19-in-womb/news-story/181f2c6d8d4c75d526b41416a4812152>

⁴⁸ <https://www.nih.gov/news-events/news-releases/placenta-lacks-major-molecules-used-sars-cov-2-virus-cause-infection>

⁴⁹ <https://www.medpagetoday.com/infectiousdisease/covid19/87584>

⁵⁰ <https://www.bmj.com/content/370/bmj.m2882>

⁵¹ <https://www.medscape.com/viewarticle/933835> and <https://www.bmj.com/content/370/bmj.m2815>

- Some COVID-19 patients are taking a **long time to recover** (“long COVID”)⁵², and there are also suggestions that SARS-CoV-2, like some other viruses, may **trigger chronic disease** in some people.⁵³
- Researchers found that in a New York City hospital people **presenting with higher viral loads** were less likely to require admission.⁵⁴
- The CDC found that although a wide range of symptoms can be caused by COVID-19, **most patients have at least one out of fever, cough and shortness of breath.**⁵⁵
- A report in *thebmj* said there are **six “types” of COVID-19**, each distinguished by a cluster of symptoms. These types could predict the need for respiratory support in severe disease.⁵⁶

COVID-19 and its antibodies

- A small Australian study of plasma of recovering patients found antibodies, memory B cells, and circulating follicular helper T cells against the SARS-CoV-2 spike glycoprotein. However there was a **range of certain B and T cell responses and frequency** amongst the 41 substantial variations in patients convalescing from COVID-19.⁵⁷
- A UK study in people who had recovered from COVID-19 found that **levels of antibodies peaked about three weeks after infection** and declined after as little as two to three months.⁵⁸
- WHO officials said recovered patients may be able to be reinfected because of **waning immunity.**⁵⁹
- A Chinese study found that where people developed antibodies when infected with COVID-19 these **may not last long**, particularly if they were asymptomatic.⁶⁰
- **SAB Therapeutics**, which has developed the technology to produce **fully human polyclonal antibodies without the need for human plasma donors**, has closed a funding round. One of its new investors is Merck. SAB-185, a fully-human polyclonal antibody therapeutic candidate for COVID-19, is being developed with initial funding up to \$US 9.4 million supported by the US Biomedical Advanced Research Development Authority (BARDA).⁶¹
- While the world awaits a vaccine, **Regeneron is beginning a Phase III trial of its antibody cocktail** to see if it can prevent infection in people exposed to COVID-19.⁶² Regeneron signed a \$US 450 million **supply deal with the US government**⁶³, which

⁵² <https://www.medscape.com/viewarticle/934287>

⁵³ <https://www.the-scientist.com/news-opinion/could-covid-19-trigger-chronic-disease-in-some-people-67749>

⁵⁴ <https://www.medscape.com/viewarticle/934147>

⁵⁵ <https://edition.cnn.com/2020/07/16/health/patient-symptom-cdc-study-wellness/index.html>

⁵⁶ <https://www.bmj.com/content/370/bmj.m2911>

⁵⁷ <https://www.medpagetoday.com/infectiousdisease/covid19/87544> and

<https://www.nature.com/articles/s41591-020-0995-0>

⁵⁸ <https://www.abc.net.au/news/health/2020-07-16/how-long-does-our-immunity-to-coronavirus-last/12460724>

⁵⁹ <https://www.cnn.com/2020/07/13/who-officials-say-coronavirus-antibodies-may-wane-after-several-months.html>

⁶⁰ <https://www.nature.com/articles/s41591-020-0965-6> and

<https://www.medscape.com/viewarticle/932671>

⁶¹ <https://www.finsmes.com/2020/07/sab-biotherapeutics-raises-14m-in-series-b-funding.html>

⁶² <https://www.fiercebiotech.com/biotech/regeneron-kicks-off-prevention-trial-for-covid-19-antibody-cocktail>

⁶³ <https://www.fiercepharma.com/manufacturing/regeneron-bags-450m-deal-u-s-government-for-covid-19-antibody-cocktail>

(through DOD and BARDA) will pay Regeneron to scale up manufacturing of its experimental COVID-19 antibody-based drug, allowing the US to claim 300,000 doses by this autumn. Regeneron said if REGN-COV2 is used preventively, rather than as a treatment for diagnosed patients, the supply would represent 1.3 million individual doses.⁶⁴

- **Boehringer Ingelheim's** collaboration with academic researchers to develop COVID-19 treatments has led to the discovery of **28 antibodies that might neutralize the virus**.⁶⁵
- **Celltrion** Group announced the launch of a Phase I human clinical trial of its **antiviral antibody treatment**.⁶⁶
- IDBiologics announced the publication of results demonstrating the ability of **ultra-potent monoclonal antibodies** to neutralize the SARS-CoV-2 virus.⁶⁷
- Adagio Therapeutics launched with a \$US 50 million Series A financing to advance its portfolio of coronavirus **antibodies as both therapeutics and prophylactics** against SARS-CoV-2 and future coronavirus outbreaks.⁶⁸
- **Junshi Biosciences** announced the completion of enrolment in a Phase I trial of its SARS-CoV-2 **neutralizing monoclonal antibody** injection, developed jointly with the Institute of Microbiology, Chinese Academy of Sciences.⁶⁹

4. Developing vaccines for COVID-19

Vaccine trials

- In the US, the National Institutes of Health's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Vaccines Working Group have discussed using **controlled human infection models for challenge studies**.⁷⁰
- **Vaxart is testing its experimental oral COVID-19 vaccine on monkeys**, funded by "Operation Warp Speed" the Trump administration's vaccine-acceleration program.⁷¹

⁶⁴ <https://www.biopharmadive.com/news/regeneron-coronavirus-antibody-manufacturing-supply-deal/581144/>

⁶⁵ <https://www.fiercebiotech.com/research/boehringer-ingelheim-backed-covid-researchers-identify-new-antibodies-to-fight-virus> and ⁶⁵ <https://www.cell.com/action/showPdf?pii=S0092-8674%2820%2930821-7>

⁶⁶ <https://pipelinereview.com/index.php/2020071775321/Antibodies/Celltrion-Launches-Human-Clinical-Trial-of-Potential-COVID-19-Antiviral-Antibody-Treatment-Following-Positive-Pre-Clinical-Results.html>

⁶⁷ <https://pipelinereview.com/index.php/2020071675318/Antibodies/IDBiologics-Announces-Nature-Publication-Highlighting-Preclinical-Results-of-Ultra-Potent-Monoclonal-Antibodies-Against-SARS-CoV-2.html>

⁶⁸ <https://pipelinereview.com/index.php/2020071675310/Antibodies/Adagio-Therapeutics-Launches-With-%2450M-Series-A-Financing-to-Advance-the-Development-of-Best-in-Class-Broadly-Neutralizing-Antibodies-for-Coronavirus-Treatment-and-Prophylaxis.html>

⁶⁹ <https://pipelinereview.com/index.php/2020071375274/Antibodies/Junshi-Biosciences-Announces-Completion-of-Enrollment-in-Phase-I-Trial-of-SARS-CoV-2-Neutralizing-Antibody-JS016-in-China.html>

⁷⁰ <https://www.nih.gov/news-events/news-releases/nih-activ-vaccine-working-group-weighs-role-human-challenge-studies-sars-cov-2-vaccine-development> and Deming, M., Michael, N., Robb, M., Cohen, M., Neuzil, K. [Accelerating Development of SARS-CoV-2 Vaccines —The Role for Controlled Human Infection Models](#). *N Engl J Med*. DOI:10.1056/NEJMp2020076 (2020).

⁷¹ <https://www.reuters.com/article/us-health-coronavirus-vaxart/vaxart-says-potential-covid-19-vaccine-picked-for-operation-warp-speed-idUSKBN23X1PA>

- A 45-patient study showed that a BioNTech **messenger RNA vaccine candidate for COVID-19 could elicit an immune response**.⁷² Pfizer and BioNTech are developing four mRNA vaccine candidates.⁷³ The US FDA granted Pfizer and BioNTech **Fast Track Designation** for two mRNA vaccine candidates.⁷⁴ Pfizer and BioNTech have reported phase I/II data suggesting their COVID-19 vaccine triggers **stronger CD8 T-cell responses than Moderna's candidate**.⁷⁵
- **Moderna** announced **publication of interim results** from its Phase I study of its mRNA vaccine in the *New England Journal of Medicine*.⁷⁶
- Achieving **herd immunity depends on both vaccine efficacy and whether people accept vaccination**.⁷⁷ Dr. Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases, told CNN he would "settle" for a Covid-19 vaccine that's 70 per cent to 75 per cent effective. However he said a level such as this could be insufficient to halt the outbreak, since a survey suggested one-third of the population were resistant to accepting the vaccination.⁷⁸ The *Wall Street Journal* reported that the US FDA would require 50 per cent efficacy for COVID-19 vaccines.⁷⁹
- Professor Sarah Gilbert of the University of Oxford told a UK parliamentary hearing that its vaccine candidate **AZD1222, licensed to Astra Zeneca, is producing "the right sort of immune response that will give protection"**.⁸⁰ Phase I human trials of the Oxford University vaccine showed it generated both antibodies and T cells. T cells remain in the body longer than antibodies.⁸¹
- Astra Zeneca has been working with **Daiichi Sankyo** to develop a deal to supply its vaccine candidate **AZD1222 in Japan**.⁸²
- **Imperial College London's COVID-19 vaccine** candidate was administered to the first volunteer on 25 June, in a trial to test for safety and efficacy.⁸³
- The European Commission has approved Johnson & Johnson's Ebola vaccine, part of a regimen with a Bavarian Nordic vaccine. The **Johnson & Johnson** platform is the same as it is using in its COVID-19 candidate.⁸⁴ The company began enrolling 1000 adult participants in a Phase I/IIa study of its vaccine.⁸⁵

⁷² <https://xconomy.com/europe/2020/07/01/biontechs-mrna-covid-19-vaccine-shows-early-signs-of-sparking-immunity/> and <https://www.fiercepharma.com/pharma/after-positive-early-data-pfizer-biontech-ceos-sound-off-vaccine-timelines>

⁷³ <https://www.biopharmadive.com/news/pfizer-biontech-coronavirus-vaccine-phase-1-results/580877/>

⁷⁴ <https://pipelinereview.com/index.php/2020071375281/Vaccines/Pfizer-and-BioNTech-Granted-FDA-Fast-Track-Designation-for-Two-Investigational-mRNA-based-Vaccine-Candidates-Against-SARS-CoV-2.html>

⁷⁵ <https://www.medrxiv.org/content/10.1101/2020.07.17.20140533v1.full.pdf> and

<https://www.fiercebiotech.com/biotech/pfizer-reports-strong-t-cell-response-to-covid-19-vaccine>

⁷⁶ <https://pipelinereview.com/index.php/2020071575301/Vaccines/Moderna-Announces-Publication-in-The-New-England-Journal-of-Medicine-of-Interim-Results-From-Phase-1-Study-of-Its-mRNA-Vaccine-Against-COVID-19-mRNA-1273.html>

⁷⁷ <https://www.healio.com/news/infectious-disease/20200714/vaccine-hesitancy-could-make-it-difficult-to-achieve-herd-immunity-for-covid19>

⁷⁸ <https://edition.cnn.com/2020/06/28/health/fauci-coronavirus-vaccine-contact-tracing-aspen/>

⁷⁹ <https://www.fiercepharma.com/vaccines/fda-to-require-at-least-50-efficacy-for-covid-19-vaccines-wsj>

⁸⁰ <https://www.medscape.com/viewarticle/933255>

⁸¹ <https://www.9news.com.au/world/coronavirus-vaccine-oxford-university-breakthrough-tcells/8ebff6c8-cfcc-46eb-9aa6-3f60188f1961>

⁸² <https://www.fiercepharma.com/manufacturing/astrazeneca-and-daiichi-sankyo-working-japanese-supply-deal-for-covid-19-vaccine>

⁸³ http://www.pharmatimes.com/news/imperial_covid-19_vaccine_begins_human_testing_1342891

⁸⁴ <https://www.fiercepharma.com/vaccines/j-j-amid-covid-19-race-scores-ebola-vaccine-approval-europe>

⁸⁵ <https://www.fiercepharma.com/vaccines/j-j-to-start-human-testing-covid-19-vaccine-next-week-exec>

- **Shanghai Fosun Pharmaceutical Industrial Development Co., Ltd.** has received the acceptance notice of its clinical trial application for its vaccine candidate BNT162b1.⁸⁶
- **IMV Inc.** says the design of the phase I clinical study of its vaccine candidate DPX-COVID-19 has been agreed with **Health Canada** and includes **two age cohorts**: (1) adults between 18-55 years old inclusive and (2) 56 and above.⁸⁷
- At a US congressional hearing, drug companies provided assurances that the larger clinical trials to come would include **a diversity of volunteers** e.g. in terms of race, gender and age.⁸⁸
- Data has been published on trials of **CanSino's coronavirus vaccine**.⁸⁹
- **Brazil** has agreed to human **trials** of a third vaccine, this time from **Pfizer/BioNTech**.⁹⁰

Vaccine research

- [Meissa Vaccines](#) has begun preclinical studies and manufacturing for the development of MV-014-210, **a live attenuated vaccine candidate** to induce immunity against SARS-CoV-2.⁹¹
- **Sorrento Therapeutics** announced selection of a **novel targeted protein vaccine** candidate (T-VIVA-19) against COVID-19.⁹²
- **Medicago** has begun testing its **plant-based vaccine**.⁹³
- **Applied DNA Sciences** announced that linear-DNA forms of COVID-19 vaccine candidates under development by partner Takis Biotech and manufactured by the company yielded **strong antibody and T-cell responses**.⁹⁴
- **ZYUS Life Sciences** says it has reached a positive milestone in the development of COVID-19 vaccine components by achieving **plant-based expression, isolation, and purification of a potential antigen** for a SARS-CoV-2 vaccine - providing proof of concept for plant-based COVID-19 antigen production.⁹⁵
- Zydus announced that the Adaptive Phase I/ II human clinical trials of its **plasmid DNA vaccine**, ZyCoV-D had commenced.⁹⁶

⁸⁶ <https://pipelinereview.com/index.php/2020071475293/Vaccines/Fosun-Pharma-Announces-its-Licensed-COVID-19-Vaccine-Product-Receives-Acceptance-Notice-of-Clinical-Trial-Application-by-NMPA.html>

⁸⁷ <https://pipelinereview.com/index.php/2020071475291/Vaccines/IMV-Updates-Rapid-Progress-on-COVID-19-Vaccine-Program.html>

⁸⁸ <https://www.reuters.com/article/us-health-coronavirus-usa-vaccines/coronavirus-vaccine-developers-vow-diversity-in-clinical-trials-idUSKCN24M1UZ>

⁸⁹ <https://www.biopharmadive.com/news/coronavirus-vaccine-cansino-china-phase-2/581946/> and [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31605-6/fulltext#supplementaryMaterial](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31605-6/fulltext#supplementaryMaterial)

⁹⁰ <https://www.medscape.com/viewarticle/934352>

⁹¹ <https://pipelinereview.com/index.php/2020063075178/Vaccines/Meissa-Vaccines-Provides-a-Pipeline-Update-on-Vaccine-Candidates-for-COVID-19-and-RSV.html>

⁹² <https://pipelinereview.com/index.php/2020070275200/Vaccines/Sorrento-Announces-Selection-of-T-VIVA-19-as-Targeted-Protein-Vaccine-Candidate-for-SARS-CoV-2.html>

⁹³ <https://www.reuters.com/article/us-health-coronavirus-medicago-vaccine/canadas-medicago-begins-human-trials-of-plant-based-covid-19-vaccine-idUSKCN24F1EN>

⁹⁴ <https://pipelinereview.com/index.php/2020071775322/Vaccines/Applied-DNA-and-Takis-Report-Positive-Preclinical-Results-from-LineaDNA-Vaccine-Candidates-for-COVID-19.html>

⁹⁵ <https://pipelinereview.com/index.php/2020071575302/Vaccines/ZYUS-Announces-Positive-Milestone-in-Plant-Based-COVID-19-Vaccine-Antigen-Production.html>

⁹⁶ <https://pipelinereview.com/index.php/2020071575298/Vaccines/Zydus-starts-human-dosing-of-its-vaccine-ZyCoV-D.html>

- Altimmune and the University of Alabama at Birmingham announced encouraging preclinical results for AdCOVID, their **investigational intranasal vaccine**.⁹⁷
- **Tonix Pharmaceutical and Kansas State University** have agreed to develop a COVID-19 vaccine.⁹⁸

Vaccine manufacture and distribution

- The **World Health Organization** and its partners aim to distribute globally to high-risk groups **two billion doses** of coronavirus vaccines by the end of 2021.⁹⁹
- Dr Francis Collins, **Director of the US National Institutes of Health**, told a [hearing held by the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies](#) that it took only 63 days from when scientists were given the virus's DNA sequence to a volunteer being injected with Moderna's vaccine candidate in its Phase I trial. Phase II began 29th May, and Phase III is expected to begin this month. He said: "We are all optimistic that the goal we've set, to have a vaccine that's safe and that works by the end of 2020, will be met by one of the vaccines, and **we would then have, by early 2021, 300 million doses of a vaccine that would be safe and effective.**"¹⁰⁰
- Tesla CEO **Elon Musk** said the company had agreed with **CureVac** to make **portable molecular RNA printers** to help produce doses of the German vaccine maker's COVID-19 candidate.¹⁰¹
- **Johnson & Johnson and Emergent BioSolutions** signed a five-year work order worth at least \$US 480 million to produce COVID-19 vaccine. J&J is beginning a Phase I/ II human trial of Ad26.COVS-2-S.¹⁰²
- **GlaxoSmithKline and Sanofi** are close to a \$US 625million deal with the UK government for 60 million doses of their COVID-19 vaccine candidate if it is approved. The UK government has signed with the Astra Zeneca- Oxford University partnership for 100 million doses.¹⁰³ The UK also signed deals for 60 million doses with the French group Valneva and 30 million with the Pfizer-BionTech partnership.¹⁰⁴
- **GlaxoSmithKline, with its adjuvant**, has signed a vaccine deal with **Canada-based Medicigo** whose recombinant coronavirus virus-like particles mimic the structure of SARS-CoV-2, and can be recognized by the immune system. GSK says that its adjuvant "can be of particular importance in a pandemic situation as it may boost the

⁹⁷ <https://pipelinereview.com/index.php/2020071375284/Vaccines/Altimmune-and-the-University-of-Alabama-at-Birmingham-UAB-Announce-Positive-Preclinical-Results-for-Intranasal-COVID-19-Vaccine-Candidate-AdCOVID.html>

⁹⁸ <https://pipelinereview.com/index.php/2020071375283/Vaccines/Tonix-Pharmaceuticals-Enters-into-Research-and-Exclusive-License-Option-Agreement-with-Kansas-State-University-to-Develop-Vaccine-Against-COVID-19.html>

⁹⁹ <https://www.biopharmadive.com/news/coronavirus-vaccine-who-2-billion-doses/580637/>. See also <https://www.fiercepharma.com/manufacturing/4-billion-covid-19-vaccine-doses-it-s-possible-cepi-official-tells-reuters> and <https://www.fiercepharma.com/vaccines/who-global-partners-launch-18b-covid-19-vaccine-initiative> Details on progress with a number of vaccines can be found at <https://www.biopharmadive.com/news/coronavirus-vaccine-pipeline-types/579122/>

¹⁰⁰ <https://www.medpagetoday.com/infectiousdisease/covid19/87407>

¹⁰¹ <https://www.fiercepharma.com/manufacturing/curevac-teaming-up-tesla-to-make-rna-microfactories-for-covid-19-shot>

¹⁰² <https://www.fiercepharma.com/manufacturing/johnson-johnson-emergent-ink-480m-work-order-for-covid-19-vaccine-hopeful>

¹⁰³ <https://www.fiercepharma.com/vaccines/sanofi-glaxosmithkline-near-625m-covid-19-vaccine-supply-deal-u-k-government-report>

¹⁰⁴ <https://www.abc.net.au/news/2020-07-20/uk-government-secures-90-million-coronavirus-vaccine-doses/12474814>

immune response and reduce the amount of antigen required per dose, allowing more vaccine doses to be produced".¹⁰⁵

- **Novavax** has a new \$US 1.6 billion **deal with the US government** to fund Phase III testing of its COVID-19 vaccine candidate and support its manufacturing.¹⁰⁶
- **SiO2 Materials Science is expanding and upgrading its packaging plant in Auburn, Alabama** to produce vials and syringes for COVID-19 vaccines and treatments. It has received financial assistance from the US Biomedical Advanced Research and Development Authority (BARDA) and the US Department of Defense.¹⁰⁷
- **The CEO of Merck said that people talking up the prospect of vaccine availability by the end of 2020 could be inhibiting the fight against COVID-19.**¹⁰⁸ A senior official in the Trump administration said on 13 July that at least one vaccine maker would be "actively manufacturing" within the next four to six weeks.¹⁰⁹ Moderna, which is launching its Phase III trial for its mRNA vaccine during July, is preparing doses to make available quickly if the US FDA approves the vaccine.¹¹⁰ Its vaccine, which was developed in partnership with the US National Institute of Allergy and Infectious Diseases, generated immune responses in all participants in its Phase I trial.¹¹¹ Pfizer's CEO said FDA approval could occur as early as October.¹¹²
- **Beijing is reportedly supplying doses of COVID-19 vaccine candidates to staff at state-owned companies and the armed forces** ahead of full trial results.¹¹³
- **Astra Zeneca** confirmed it had signed a licensing deal with **Russian drug-maker R-Pharm** to produce and distribute doses of its University of Oxford-partnered adenovirus-based vaccine, AZD1222.¹¹⁴
- In the US, pharma company executives told a House subcommittee that vaccines in development may require **two doses to be effective.**¹¹⁵
- Vaccitech is a spinout from the University of Oxford's Jenner Institute, working alongside Astra Zeneca on its COVID-19 vaccine. Its CEO has said that two doses

¹⁰⁵ <https://www.fiercepharma.com/manufacturing/regeneron-bags-450m-deal-u-s-government-for-covid-19-antibody-cocktail>

¹⁰⁶ <https://www.fiercepharma.com/pharma/novavax-inks-1-6b-warp-speed-deal-to-support-covid-19-vaccine-phase-3-testing-manufacturing>

¹⁰⁷ <https://www.fiercepharma.com/manufacturing/sio2-injects-163-million-into-glass-vial-production-plant>

¹⁰⁸ <https://www.fiercepharma.com/vaccines/merck-ceo-frazier-says-covid-19-vaccine-hype-a-grave-disservice-to-public>

¹⁰⁹ <https://www.fiercepharma.com/manufacturing/trump-administration-hopes-for-covid-19-shot-manufacturing-to-start-within-6-weeks>

¹¹⁰ <https://www.fiercepharma.com/pharma/moderna-has-started-producing-commercial-covid-19-vaccines-at-risk-ceo>

¹¹¹ <https://www.9news.com.au/world/moderna-coronavirus-vaccine-shows-promising-safety-and-immune-response-results-more-research-needed/3ad41806-b572-4b8b-97f2-d6fce5a461aa> and <https://www.nih.gov/news-events/news-releases/experimental-covid-19-vaccine-safe-generates-immune-response> and <https://www.medpagetoday.com/infectiousdisease/covid19/87567> and <https://www.fiercebiotech.com/biotech/moderna-s-covid-19-jab-spurs-immune-response-first-published-data>

¹¹² <https://time.com/5864690/pfizer-vaccine-coronavirus/>

¹¹³ <https://www.fiercepharma.com/pharma/coronavirus-tracker-hydroxychloroquine-fails-va-study-fda-approves-at-home-sample-collection>

¹¹⁴ <https://www.fiercepharma.com/pharma/astrazeneca-signs-covid-19-shot-deal-russia-days-after-hacking-accusations-surface>

¹¹⁵ <https://www.medpagetoday.com/infectiousdisease/covid19/87678> and <https://energycommerce.house.gov/committee-activity/hearings/hearing-on-pathway-to-a-vaccine-efforts-to-develop-a-safe-effective-and>

may be required, “**with possible annual or two-yearly vaccinations required thereafter**”.¹¹⁶

- As potential vaccines undergo trials, discussion occurs on how to **encourage public acceptance of vaccination against COVID-19**.¹¹⁷
- **In the UK**, Cell and Gene Therapy Catapult will receive around **\$US 130 million of government funding to construct a manufacturing centre to speed vaccine production**.¹¹⁸
- The US government has committed nearly \$US 2 billion to **secure 100 million doses of a Pfizer/ BioNTech vaccine**.¹¹⁹

Impact of mutation of the SARS-CoV-2 virus

- Dr Paul A Offit¹²⁰ said of the SARS-CoV-2 virus: "Although it is a single-stranded RNA virus, it does mutate to some extent, but it **doesn't look like it's going to mutate away from the vaccine**. So, this is not going to be like influenza virus, where you must give a vaccine every year. I think we can make a vaccine that will last for several years. And we know the protein we're interested in. We're interested in antibodies directed against the spike glycoprotein, which is abundantly present on the surface of the virus. We know that if we make an antibody response to that protein, we can therefore prevent infection."¹²¹

5. Potential treatments for COVID-19

Hyperimmune immunoglobulin; immunoglobulin

- Takeda, CSL Behring and other members of an **alliance of plasma fractionators are working on a hyperimmune globulin for COVID-19 infection**. The [CoVlg-19 Plasma Alliance](#) is pooling knowledge and resources to develop a single medicine, **which it hopes will, along with antivirals, “bridge” the void until the world has one or more effective COVID-19 vaccines**. Chris Morabito, head of Research and Development for Takeda’s Plasma-Derived Therapies unit, called it: “a standard product, a drug produced from pooled plasma. We will know what the batch-to-batch consistency, what the neutralizing titre [of antibodies] is like. It’s a stable, homogeneous mixture, so we can give specific dosing instructions”.¹²²
- Octapharma reports **positive results for Octagam® use in critical COVID-19 patients**.¹²³

¹¹⁶ <https://www.fiercebiotech.com/biotech/conversation-bill-enright-vaccitech-ceo-pandemic-vaccines>

¹¹⁷ <https://www.biopharmadive.com/news/coronavirus-vaccine-public-trust/582190/>

¹¹⁸ <https://www.biopharmadive.com/news/uk-to-spend-almost-130m-more-on-coronavirus-vaccine-manufacturing/582219/> and <https://www.fiercepharma.com/manufacturing/cgt-catapult-nabs-127m-to-supply-u-k-covid-19-vaccines>

¹¹⁹ <https://www.biopharmadive.com/news/pfizer-coronavirus-vaccine-warp-speed-supply/582093/> and <http://www.globenewswire.com/news-release/2020/07/22/2065701/0/en/Pfizer-and-BioNTech-Announce-an-Agreement-with-U-S-Government-for-up-to-600-Million-Doses-of-mRNA-based-Vaccine-Candidate-Against-SARS-CoV-2.html>

¹²⁰ Director of the Vaccine Education Center at the Children's Hospital of Philadelphia

¹²¹ <https://www.medscape.com/viewarticle/933260>

¹²² <https://www.fiercebiotech.com/biotech/covid-closeup-takeda-s-chris-morabito-science-behind-plasma-based-treatments> and <https://ascpt.onlinelibrary.wiley.com/doi/10.1111/cts.12816>

¹²³ <https://pipelinereview.com/index.php/2020071575304/Antibodies/Octapharma-Reports-Positive-Data-from-octagam-Usage-in-Critically-Ill-COVID-19-Patients.html>

Remdesivir

- **The European Medicines Agency's human medicines committee (CHMP) recommended¹²⁴ the use of remdesivir in adults and adolescents from 12 years of age with COVID-related pneumonia who require oxygen support.** The European Commission **then** awarded conditional marketing authorisation for remdesivir in COVID-19.¹²⁵
- **The US has contracted with Gilead for more than 500,000 treatment courses of remdesivir** for American hospitals, representing 100 per cent of Gilead's projected production for July and 90 per cent of production in both August and September, with a further allocation for clinical trials.¹²⁶ Cornering of the market by the US has attracted some unfavourable comment from other countries, and concerns about what may happen if a successful vaccine is developed.¹²⁷
- **Gilead Sciences has signed on multiple partners to manufacture remdesivir,** including India's Cipla and Hetero Labs and Jubilant Life Sciences.¹²⁸
- **Australia's Therapeutic Goods Administration has provisionally approved the use of remdesivir** for use for adult and adolescent patients hospitalised with severe COVID-19.¹²⁹
- A case report from the Netherlands has **suggested that remdesivir may induce liver injury.**¹³⁰
- There has been some **criticism of the claim that remdesivir reduces mortality.**¹³¹
- The Infectious Diseases Society of America is concerned that **developed countries are relying on a single manufacturer for supplies of remdesivir.** Gilead has licensed the drug to generic drug-makers for sales in low income countries.¹³²

Other therapies

- **Anakinra (Kineret, SOBI)** was initially approved as a drug for severe rheumatoid arthritis. It is now **claimed to reduce the need for mechanical ventilation** in patients with COVID-19, as well as their mortality.¹³³
- A UK trial found that the drug **combination lopinavir-ritonavir does not benefit patients** hospitalised with COVID-19.¹³⁴
- Researchers have identified several **molecules that interfere with the polymerase reaction which spreads the infection** through the body.¹³⁵

¹²⁴ <https://www.medscape.com/viewarticle/932954> and <https://bit.ly/3i3O6Ck>

¹²⁵ <https://pipelinereview.com/index.php/2020070375208/Small-Molecules/European-Commission-Grants-Conditional-Marketing-Authorization-for-Gileads-Veklury-remdesivir-for-the-Treatment-of-COVID-19.html>

¹²⁶ <https://www.healio.com/news/infectious-disease/20200702/us-gilead-strike-deal-for-large-supply-of-remdesivir-for-covid19> and Press Release

¹²⁷ <https://www.theguardian.com/us-news/2020/jun/30/us-buys-up-world-stock-of-key-covid-19-drug>

¹²⁸ <https://www.fiercepharma.com/manufacturing/gilead-sciences-inks-licensing-agreements-to-produce-covid-19-therapy-remdesivir-for>

¹²⁹ <https://7news.com.au/lifestyle/tga-approves-use-of-covid-drug-remdesivir-c-1159307> and <https://www.labonline.com.au/content/life-scientist/news/remdesivir-approved-by-tga-to-treat-covid-19-991817605>

¹³⁰ <https://www.medscape.com/viewarticle/933529>

¹³¹ <https://www.bmj.com/content/370/bmj.m2839>

¹³² <https://in.reuters.com/article/health-coronavirus-remdesivir/infectious-disease-specialists-ask-u-s-government-to-ensure-remdesivir-supply-idINKBN24J03Q>

¹³³ <https://www.healio.com/news/rheumatology/20200629/anakinra-reduces-ventilation-need-mortality-in-covid19>

¹³⁴ <https://www.bmj.com/content/370/bmj.m2650>

¹³⁵ <https://www.fiercebiotech.com/research/five-fda-approved-antivirals-could-target-covid-19-study>

- Quercetin, a **plant flavonoid** found in capers and green tea is being **suggested as an adjunct therapy** for COVID-19, but it has yet to undergo rigorous trials.¹³⁶
- A trial in Greece found that hospitalized patients with COVID-19 who were given the anti-inflammatory drug **colchicine had improved time to clinical deterioration** compared with standard of care.¹³⁷
- A study yet to be peer reviewed suggested that **women taking the common diabetes drug metformin may be at lower risk for fatal COVID-19**.¹³⁸
- **Aligos Therapeutics** has agreed with KU Leuven and the Rega Institute for Medical Research to develop a **coronavirus protease inhibitor** as a potential therapy for COVID-19.¹³⁹
- **Fujifilm** has signed with India's Dr. Reddy's Laboratories and Dubai-based Global Response Aid to manufacture and sell its **flu drug Avigan** (favipiravir) for COVID-19.¹⁴⁰
- Sanofi and Regeneron halted trialling **Kevezara** in COVID-19 after finding **no benefit for ventilated patients**.¹⁴¹
- **Cancer drugs with anti-inflammatory effects** are being considered as treatments for COVID-19.¹⁴²
- In the US, trials are underway of **radiation as a means of calming the cytokine storm** which may be experienced by some COVID-19 patients.¹⁴³
- An Iranian study found suggested that a **combination of sofosbuvir** (Sovaldi, Gilead Sciences) **plus daclatasvir** (Daklinza, Bristol-Myers Squibb) for 14 days significantly reduced time to recovery and **improved survival** in severe disease.¹⁴⁴
- **Biocon Ltd.** received the Drugs Controller General of India's approval to market **Itozumab** (ALZUMAb®) Injection 25mg/5mL solution for emergency use in India for

¹³⁶ <https://www.medpagetoday.com/infectiousdisease/covid19/87373>

¹³⁷ <https://www.medpagetoday.com/infectiousdisease/covid19/87245>

¹³⁸ <https://www.medscape.com/viewarticle/93138> <https://www.fiercebiotech.com/biotech/covid-closeup-takeda-s-chris-morabito-science-behind-plasma-based-treatments> and <https://ascpt.onlinelibrary.wiley.com/doi/10.1111/cts.12816>

¹³⁸ <https://www.healio.com/news/rheumatology/20200629/anakinra-reduces-ventilation-need-mortality-in-covid19>

¹³⁸ <https://www.medscape.com/viewarticle/932954>

¹³⁸ <https://www.healio.com/news/infectious-disease/20200702/us-gilead-strike-deal-for-large-supply-of-remdesivir-for-covid19> and [Press Release](#)

¹³⁸ <https://www.theguardian.com/us-news/2020/jun/30/us-buys-up-world-stock-of-key-covid-19-drug>

¹³⁸ <https://www.fiercepharma.com/manufacturing/gilead-sciences-inks-licensing-agreements-to-produce-covid-19-therapy-remdesivir-for>

¹³⁸ <https://www.bmj.com/content/370/bmj.m2650>

¹³⁸ <https://www.fiercebiotech.com/research/five-fda-approved-antivirals-could-target-covid-19-study>

¹³⁸ <https://www.medpagetoday.com/infectiousdisease/covid19/87373>
[2881](#)

¹³⁹ <https://pipelinereview.com/index.php/2020070175195/More-News/Aligos-Therapeutics-and-KU-Leuven-Announce-Collaboration-for-the-Development-of-a-Therapeutic-Candidate-Targeting-Coronavirus.html>

¹⁴⁰ <https://www.fiercepharma.com/manufacturing/fujifilm-pairs-dr-reddy-s-global-response-aid-to-make-covid-19-drug-avigan>

¹⁴¹ <https://www.fiercepharma.com/pharma/sanofi-regeneron-s-kevzara-trial-covid-19-comes-to-a-screching-halt-after-no-benefit-found>

¹⁴² <https://www.healio.com/news/hematology-oncology/20200629/cancer-drugs-targeted-antiinflammatory-effects-support-repurposing-for-covid19>

¹⁴³ <https://www.healio.com/news/primary-care/20200708/researchers-look-to-radiotherapy-to-treat-severe-cases-of-covid19>

¹⁴⁴ <https://www.medscape.com/viewarticle/933822>

the treatment of **cytokine release syndrome** in moderate to severe acute respiratory distress syndrome due to COVID-19.¹⁴⁵

6. Managing the pandemic

Individual country experience

- **Scotland's** measured approach to managing the pandemic is referred to as **“Test and Protect.”** It appears to have been a sound choice.¹⁴⁶
- Researchers estimate that only **five per cent of the Spanish population has antibodies** to the SARS-CoV-2 virus.¹⁴⁷
- The **European Union** is trying to secure supply of 24 intensive care drugs, as it faces **shortages of medicines** for COVID-19 patients if a second wave occurs.¹⁴⁸
- Experience in one NSW outbreak suggests that **people who are asymptomatic but have a high viral load can be responsible for significant community transmission.** It also appears that the incubation period for infection can be less than 24 hours, although it is mostly within 5 to 7 days.¹⁴⁹
- **Sweden** has altered its COVID-19 contact tracing guidelines so that **infected people carry more of the burden for tracing.**¹⁵⁰ Sweden's chief epidemiologist said that **Sweden's COVID-19 strategy** of avoiding a hard lock down seemed to be **working.**¹⁵¹
- A **US government report** says more Americans have been infected with COVID-19 than reported case counts suggest. Antibody testing showed that in seven locations there were **ten times as many infections as there were reported cases.**¹⁵² In the US, **long turnaround times in COVID-19 testing** are again hampering the fight against the virus.¹⁵³ The National Institutes of Health reported plans for improved technology and a **significant increase in the number and quality of tests** for SARS-CoV-2.¹⁵⁴ A US study found that **self-swab home testing** for COVID-19 could be as accurate as nasopharyngeal swabbing by healthcare professionals.¹⁵⁵
- A survey in **South Korea** found that **more people had antibodies to SARS-CoV-2 than were known to have been infected.**¹⁵⁶
- Swiss researchers reported that **children did not seem to be driving SARS-CoV-2 transmission.**¹⁵⁷

¹⁴⁵ <https://pipelinereview.com/index.php/2020071375273/Antibodies/Biocons-Breakthrough-Drug-tolizumab-Receives-DCGI-Nod-for-its-Use-in-Moderate-to-Severe-COVID-19-Patients.html>

¹⁴⁶ <https://blogs.bmj.com/bmj/2020/06/30/devi-sridhar-and-adriel-chen-scotlands-slow-and-steady-approach-to-covid-19-may-lead-to-a-more-sustainable-future/>

¹⁴⁷ <https://www.bbc.com/news/world-europe-53315983>

¹⁴⁸ <https://www.medscape.com/viewarticle/933581>

¹⁴⁹ <https://7news.com.au/lifestyle/health-wellbeing/increased-viral-loads-shorter-incubation-periods-the-concerning-aussie-covid-cases-c-1169517>

¹⁵⁰ <https://www.medscape.com/viewarticle/934234>

¹⁵¹ <https://www.medscape.com/viewarticle/934319>

¹⁵² <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/u-s-covid-19-cases-could-be-way-beyond-official-count-study-finds-759685.html>

¹⁵³ <https://thehill.com/policy/healthcare/508432-testing-delays-once-again-hamper-covid-19-response>

¹⁵⁴ <https://www.nih.gov/news-events/news-releases/nih-leadership-details-unprecedented-initiative-ramp-testing-technologies-covid-19> and <https://www.nejm.org/doi/full/10.1056/NEJMSr2022263>

¹⁵⁵ <https://www.medscape.com/viewarticle/934421>

¹⁵⁶ <https://7news.com.au/news/health/undetected-korean-cases-very-high-study-c-1185186>

¹⁵⁷ <https://www.physiciansbriefing.com/infectious-disease-8/coronavirus-1008/children-seem-not-to-be-driving-sars-cov-2-transmission-759357.html>

- A South Korean study found **children aged 10 to 19 can transmit COVID-19 within their households like adults.**¹⁵⁸
- Researchers in the US found that **adults aged 18 to 35 may be at higher risk of severe COVID-19 than they think.**¹⁵⁹

Transmission

- Scientists have extracted a **plant-based antimicrobial compound that could be added to face masks.**¹⁶⁰
- A study has found that **cells infected with SARS-CoV-2 develop tentacle-like protrusions** that spread the virus.¹⁶¹
- After a group of scientists urged the **World Health Organisation** to change its guidance, it has **recognized “evidence emerging” of airborne transmission.**¹⁶²
- Attention has recently turned to the role of **small droplet aerosols in poorly ventilated spaces** as a transmission mechanism for the SARS-CoV-2 virus.¹⁶³
- Meanwhile, one scientist¹⁶⁴ has expressed the view that **the risk of transmission of the SARS-CoV-2 virus through inanimate surfaces** has been exaggerated.¹⁶⁵
- Researchers say that the **coronavirus causing the current pandemic has mutated** and spread from Europe to the US. They estimate while it is **more likely to infect people it does not cause more severe illness.**¹⁶⁶
- Stanford University bioengineers say that, using **CRISPR gene-editing technology**, they **can inhibit 90 per cent of coronaviruses**, including the one which causes COVID-19.¹⁶⁷
- A doctor has criticised **plastic visors for restaurant employees**, saying they give “a **false sense of security**”.¹⁶⁸
- During the pandemic we have been kept informed of the basic reproductive number of the virus, the **average number of people infected by one infectious person.** However, the number appears to have some **limitations as a predictive tool.**¹⁶⁹

¹⁵⁸ <https://www.9news.com.au/world/coronavirus-disease-transmitted-by-older-children-as-much-as-adults-study-finds/919929eb-4634-4e0a-94a7-d2581d5c1937>

¹⁵⁹ <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/young-adults-may-face-higher-risk-for-severe-covid-than-thought-759536.html>

¹⁶⁰ <https://www.labonline.com.au/content/consumables/article/antimicrobial-compound-added-to-face-masks-1301697617>

¹⁶¹ <https://www.the-scientist.com/news-opinion/coronavirus-infected-cells-grow-filopodia-67679>

¹⁶² <https://7news.com.au/lifestyle/health-wellbeing/airborne-coronavirus-spread-evidence-emerging-world-health-organization-says-c-1152145> see also <https://www.9news.com.au/world/coronavirus-airborne-germs-threat-us-government-warned-on-indoor-infection-threat/10a61199-9e98-40a1-a4c4-a6ef9f3df1c4>

¹⁶³ [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30245-9/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30245-9/fulltext)

¹⁶⁴ Emanuel Goldman, Professor of Microbiology, Biochemistry and Molecular Genetics in the New Jersey Medical School at Rutgers University

¹⁶⁵ [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30561-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30561-2/fulltext)

¹⁶⁶ <https://www.9news.com.au/world/coronavirus-world-new-version-of-covid-19-spreads-faster/1d7075e9-3a93-44d0-914d-901d17494a87> and

<https://www.news.com.au/world/coronavirus/health/mutant-coronavirus-strain-can-spread-up-to-nine-times-faster/news-story/3fd3d8e9c61c917ac7b5524b7baf74f>

¹⁶⁷ <https://www.fiercebiotech.com/research/stanford-team-deploys-crispr-gene-editing-to-fight-covid-19>

¹⁶⁸ <https://www.medscape.com/viewarticle/933905>

¹⁶⁹ <https://www.the-scientist.com/features/why-r0-is-problematic-for-predicting-covid-19-spread-67690>

Origins of the pandemic

- **The World Health Organisation is sending experts to China** to investigate the origins of the coronavirus causing the present pandemic.¹⁷⁰
- **Germany has pushed for WHO to speed up review** of how the pandemic was handled in its early days.¹⁷¹

Other effects of the pandemic

- The World Health Organisation says **access to HIV medication has been impacted** negatively by the pandemic.¹⁷²
- Researchers have reviewed publications about COVID-19 and distilled **guidance for blood supply and use during the pandemic**.¹⁷³

7. Other news

- **Takeda** has signed a deal with startup Carmine Therapeutics to target rare diseases using **gene therapies out of Carmine's red blood cell extracellular vesicles platform**.¹⁷⁴
- The **European Commission has approved ULTOMIRIS®** (ravulizumab) for the treatment of some adults and children with atypical haemolytic uremic syndrome.¹⁷⁵
- A Japanese study found that a single dose of the **flu drug baloxavir marboxil** (Xofluza), if given to other family members as soon as a patient is diagnosed, **can prevent 86 per cent of parents and siblings from becoming ill**.¹⁷⁶
- Scientists from the US National Institutes of Health have shown that **neurofilament light chain** (NfL) offered superior diagnostic and prognostic performance compared with other blood tests for **mild, moderate, and severe traumatic brain injury**.¹⁷⁷
- A **Brazilian man, diagnosed with HIV in 2012**, was one of five participants in a clinical trial who received a treatment regimen that included maraviroc and nicotinamide. He has tested **negative for over a year**.¹⁷⁸
- Dynavax Technologies Corporation and the Icahn School of Medicine at Mount Sinai announced they have agreed to develop a **universal influenza vaccine**. The Mount Sinai CIVICs team will evaluate a novel approach they have developed called

¹⁷⁰ <https://www.9news.com.au/world/coronavirus-who-team-to-visit-china-for-virus-investigation/1253ef7a-a412-4d55-bcb8-b52d21e3ad6b>

¹⁷¹ <https://www.medscape.com/viewarticle/934067>

¹⁷² <https://www.who.int/news-room/detail/06-07-2020-who-access-to-hiv-medicines-severely-impacted-by-covid-19-as-aids-response-stalls>

¹⁷³ <https://transfusionnews.com/2020/07/15/practical-guidance-for-blood-supply-and-use-during-the-covid-19-pandemic/>

¹⁷⁴ <https://www.fiercebiotech.com/biotech/takeda-pens-900m-biobucks-pact-carmine-tx-for-non-viral-gene-therapy-work>

¹⁷⁵ <https://pipelinereview.com/index.php/2020062975154/Antibodies/ULTOMIRIS-ravulizumab-Receives-Marketing-Authorization-from-European-Commission-for-Adults-and-Children-with-Atypical-Hemolytic-Uremic-Syndrome-aHUS.html>

¹⁷⁶ <https://www.medscape.com/viewarticle/933632>

¹⁷⁷ <https://www.nih.gov/news-events/news-releases/nfl-outperforms-other-blood-tests-predict-diagnose-traumatic-brain-injury>

¹⁷⁸ <https://www.healio.com/news/infectious-disease/20200707/man-achieves-longterm-hiv-remission-without-bone-marrow-transplant>

chimeric hemagglutinin (cHA) designed to protect against all strains of influenza in combination with Dynavax's CpG 1018™ adjuvant.¹⁷⁹

- **Victoria has reported a spike in congenital syphilis cases**, with 1670 in 2019 compared with 634 in 2014.¹⁸⁰
- A research team based in China says it has developed a **blood test that can detect cancer four years before symptoms appear**.¹⁸¹
- A study supported by the US National Institutes of Health showed that **the pool of available kidneys for people with HIV can safely be expanded by including donors with HIV**.¹⁸²

¹⁷⁹ <https://pipelinereview.com/index.php/2020071675317/Vaccines/Dynavax-and-Mount-Sinai-Announce-Collaboration-to-Develop-a-Universal-Influenza-Vaccine-Candidate-with-CpG-1018-Adjuvant.html>

¹⁸⁰ <https://7news.com.au/lifestyle/health-wellbeing/warning-issued-as-syphilis-rates-surge-in-victoria--c-1186396>

¹⁸¹ <https://www.theguardian.com/science/2020/jul/21/researchers-unveil-test-that-can-detect-cancer-years-before-symptoms>

¹⁸² <https://www.nih.gov/news-events/news-releases/kidney-transplantation-between-people-hiv-safe-nih-study-finds>