

Monitoring International Trends

December 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.

The emphasis within the health sector worldwide has continued to be on the COVID-19 pandemic, and the search for suitable treatments and vaccines. Of note, regulatory approval was given to the Pfizer/BioNTech mRNA vaccine in the UK, USA, Canada, Europe and Singapore, and to the Moderna mRNA vaccine in the USA (pages 13-15); additional treatment options in development include monoclonal and polyclonal antibodies, as well as a virus-specific T cell therapies (pages 7-10); the US continues to suffer a high death toll from COVID-19 and Russia has admitted its death toll is three times higher than previously reported (page 17); new variants of the virus have been reported and are said to be more contagious (page 18).

Among items of interest in this month's edition which are unrelated to the COVID-19 pandemic are that: the American Society for Hematology (ASH) held its annual meeting virtually and scientists reported on new developments in the use of gene therapies to treat blood disorders; there are promising early results for patients with haemophilia A coming from the phase 1/2 Alta study, and for patients with haemophilia B from the B-AMAZE and the HOPE-B gene therapy trials (pages 4-5); there are exciting new preliminary results using investigational CRISPR/Cas9-based gene editing therapy for patients with sickle cell disease or thalassemia (pages 5-6); and the US FDA has approved berotralstat, an oral, once-daily drug to prevent attacks in hereditary angioedema patients (page 6).

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1. Treating blood disorders

Haemophilia

- Freeline updated data from its phase 1 / 2 B-AMAZE trial evaluating FLT180a, an AAV gene therapy candidate for people with severe haemophilia B. Study results show sustained factor IX (FIX) activity for nearly three years, with no bleeds reported to require FIX supplementation. The data support selection of a dose and immune management regimen with the potential to produce FIX activity in the normal range.¹
- Pfizer and Sangamo announced updated results from their phase 1 / 2 Alta study which showed that factor VIII activity levels were sustained in one cohort for a year after receiving gene therapy for haemophilia A.²
- The US FDA placed a clinical hold on CSL and uniQure's haemophilia B gene therapy etranacogene dezaparvovec³, after a trial participant developed liver cancer.
- uniQure reported initial data from its pivotal phase 3 HOPE-B gene therapy trial of etranacogene dezaparvovec, an investigational adeno-associated virus five (AAV5)-based gene therapy for patients with severe and moderately severe haemophilia B.⁴ To date, this is the first data set to be reported from a phase 3 gene therapy study into haemophilia B and the largest number of patients ($n=54$) to receive a single gene therapy investigational product. Steven Pipe⁵, the principal investigator of the HOPE-B pivotal trial, said: "These initial data on etranacogene dezaparvovec are encouraging, because thus far in these patients, severe haemophilia B appears to have been transformed into a functionally curative state following administration of this one-time gene therapy, providing cessation in bleeding for a majority of patients and no need for ongoing, chronic replacement therapy. Importantly, these data also show that those patients in the trial who may not have been eligible for other gene therapies because they had pre-existing neutralizing antibodies (NAbs) have achieved results with etranacogene dezaparvovec that are comparable to the results of patients who did not have pre-existing NAbs. This is an important distinction as this is the only known clinical trial that has maximized patient eligibility in this way. The initial data also show that etranacogene dezaparvovec has been generally well tolerated to date."⁶

¹ <https://pipelinereview.com/index.php/2020121476891/DNA-RNA-and-Cells/Freeline-Reports-Updated-Data-From-Phase-1/2-B-AMAZE-Trial-in-Hemophilia-B.html>

² <https://pipelinereview.com/index.php/2020120876791/DNA-RNA-and-Cells/Pfizer-and-Sangamo-Announce-Updated-Phase-1/2-Results-Showing-Sustained-Factor-VIII-Activity-Levels-in-3x1013-VG/KG-Cohort-Through-One-Year-Following-Hemophilia-A-Gene.html>

³ <https://www.fiercebiotech.com/biotech/uniqure-csl-hit-by-fda-clinical-hold-for-hem-b-gene-therapy-program-after-liver-cancer-find> and <https://www.biopharmadive.com/news/uniqure-gene-therapy-clinical-hold-cancer-hemophilia/592545>

⁴ <https://pipelinereview.com/index.php/2020120976831/DNA-RNA-and-Cells/uniQure-Presents-Late-Breaking-Data-from-the-HOPE-B-Pivotal-Trial-of-Etranacogene-Dezaparvovec-Gene-Therapy-in-Patients-with-Hemophilia-B-at-the-62nd-Annual-Meeting-of.html>

⁵ Professor of paediatrics and pathology and paediatric medical director of the hemophilia and coagulation disorders program at the University of Michigan

⁶ <https://pipelinereview.com/index.php/2020120976831/DNA-RNA-and-Cells/uniQure-Presents-Late-Breaking-Data-from-the-HOPE-B-Pivotal-Trial-of-Etranacogene-Dezaparvovec-Gene-Therapy-in-Patients-with-Hemophilia-B-at-the-62nd-Annual-Meeting-of.html> and

<https://www.fiercebiotech.com/biotech/ash-uniqure-csl-hem-b-gene-therapy-curbs-bleeding-phase-3-even-patients-anti-aav-antibodies> and

<https://www.medpagetoday.com/meetingcoverage/ashhematology/90087> and

<https://www.biopharmadive.com/news/uniqure-ash-hemophilia-gene-therapy-hope-b/591733> and [Paper: First Data from the Phase 3 HOPE-B Gene Therapy Trial: Efficacy and Safety of Etranacogene Dezaparvovec \(AAV5-Padua hFIX variant; AMT-061\) in Adults with Severe or](#)

- The FDA has granted fast track status for Catalyst Biosciences' Marzeptacog alfa (activated) or MarzAA, a subcutaneously administered, engineered coagulation factor VIIa to be used, with inhibitors, for the treatment of episodic bleeding in subjects with haemophilia A or B.⁷ The company is initiating a 60 patient Phase III study.⁸
- Pfizer announced that the first dose of marstacimab (PF-06741086), an anti-tissue factor pathway inhibitor (anti-TFPI), has been given in the phase 3 BASIS study for people with severe haemophilia A or B.⁹

Sickle cell disease and thalassemia

- Graphite Bio has been cleared to begin a clinical trial for its next-generation gene editing therapy GPH101 in patients with sickle cell disease.¹⁰
- CRISPR Therapeutics and Vertex Pharmaceuticals have announced, at the annual ASH Meeting on 6 December, new data on 10 patients treated with the investigational CRISPR/Cas9-based gene-editing therapy CTX001 showing a consistent and sustained response to the treatment.¹¹ Seven patients with beta thalassemia, who had been receiving a median of 15 blood transfusions annually, were able to avoid transfusion for between 3 and 20.5 months after receiving CTX001. Three patients with sickle cell disease had a median of seven painful vaso-occlusive crises, annually, before receiving CTX001, but after treatment were crisis-free for between 3 and 17 months. CTX001 is being investigated in these two ongoing phase 1 /2 clinical trials as a potential one-time curative therapy for patients suffering from TDT and severe SCD.¹²
- Two other studies reported at the December ASH meeting indicate promising results for sickle cell patients:¹³
 - a. One uses a virus to introduce RNA into extracted bone marrow and turns off *BCL11A*, a gene that normally suppresses foetal haemoglobin production.
 - b. The second uses CRISPR-Cas9 gene editing to switch off *BCL11A*.

[Moderate-Severe Hemophilia B Treated Irrespective of Pre-Existing Anti-Capsid Neutralizing Antibodies \(confex.com\)](#)

⁷ [Catalyst Bio Factor VIIa variant Fast Track'd in U.S. for hemophilia \(NASDAQ:CBIO\) | Seeking Alpha](#)

⁸ <https://clinicaltrials.gov/ct2/show/NCT04489537>

⁹ <https://pipelinereview.com/index.php/2020112376640/Antibodies/Pfizer-Doses-First-Participant-in-Phase-3-Study-Evaluating-anti-TFPI-Investigational-Therapy-Marstacimab-for-People-With-Severe-Hemophilia-A-and-B-With-or-Without-Inhibitors.html>

¹⁰ <https://pipelinereview.com/index.php/2020121476887/DNA-RNA-and-Cells/Graphite-Bio-Receives-IND-Clearance-to-Initiate-Clinical-Trial-for-Next-Generation-Gene-Editing-Therapy-GPH101-in-Sickle-Cell-Disease.html>

Both CRISPR-Cas9 gene editing and lentiviral gene therapy are in early trials for treatment of these β -globin hemoglobinopathies; preliminary results have been published in *The New England Journal of Medicine*, see <https://transfusionnews.com/2020/12/15/crispr-cas9-gene-editing-and-lentiviral-gene-therapy-hold-promise-to-treat-transfusion-dependent-%CE%B2-globin-hemoglobinopathies> and <https://www.medpagetoday.com/meetingcoverage/ashvideoparlsrbd/90345>

¹¹ <https://pipelinereview.com/index.php/2020120676750/DNA-RNA-and-Cells/CRISPR-Therapeutics-and-Vertex-Present-New-Data-for-Investigational-CRISPR/Cas9-Gene-Editing-Therapy-CTX001-at-American-Society-of-Hematology-Annual-Meeting-and-Exposit.html> *The New England Journal of Medicine (NEJM)* published an independently peer-reviewed article entitled "CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β Thalassemia".

¹² <https://www.biopharmadive.com/news/crispr-vertex-sickle-cell-thalassemia-ash-2020/591657/>

¹³ <https://consumer.healthday.com/12-5-could-gene-therapy-or-crispr-cure-sickle-cell-disease-2649124930.html>

Other blood disorders

- Swedish Orphan Biovitrum reported that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) arrived at a positive opinion of Doptelet® (avatrombopag) as a therapy for primary chronic immune thrombocytopenia (ITP) in adults who are refractory to other treatments, such as corticosteroids and immunoglobulins.¹⁴
- A late-breaking abstract submitted to the ASH meeting,¹⁵ *A Multicentre Randomised Trial of First Line Treatment Pathways for Newly Diagnosed Immune Thrombocytopenia: Standard Steroid Treatment Versus Combined Steroid and Mycophenolate: the Flight Trial*,¹⁶ suggests that mycophenolate combined with corticosteroid may be considered as an effective first line treatment option for some patients with ITP.
- Results from the phase 3 PEGASUS trial¹⁷ suggest that the targeted C3 inhibitor pegcetacoplan improves haemoglobin levels, more so than eculizumab, in patients with paroxysmal nocturnal haemoglobinuria.
- BioCryst announced the US FDA has approved berotralstat, an oral, once-daily drug to prevent attacks in hereditary angioedema patients.¹⁸

2. Safety and Patient blood management

- Researchers say natriuretic peptide levels may help diagnose transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI)¹⁹.
- Researchers reported that they found direct oral anticoagulants to be effective and safe alternatives to warfarin at preventing stroke in patients with atrial fibrillation who also had type 2 diabetes mellitus.²⁰
- The US FDA moved its decision date for the AstraZeneca / FibroGen anaemia drug Roxadustat from 20 December 2020 to 20 March 2021.²¹
- Scientists²² report²³ a new method to generate large quantities of red blood cells from induced pluripotent stem cells, cells that have been reprogrammed from a differentiated state back to an embryonic-like state.

¹⁴ [Doptelet® \(avatrombopag\) receives positive opinion from CHMP for treatment of ITP](#)

¹⁵ <https://thelimbic.com/haematology/ash-2020-late-breaking-abstracts-a-preview/>

¹⁶ [Paper: A Multicentre Randomised Trial of First Line Treatment Pathways for Newly Diagnosed Immune Thrombocytopenia: Standard Steroid Treatment Versus Combined Steroid and Mycophenolate. the Flight Trial \(confex.com\)](#)

¹⁷ [Paper: Categorized Hematologic Response to Pegcetacoplan Versus Eculizumab in Patients with Paroxysmal Nocturnal Hemoglobinuria: Post Hoc Analysis of Data from a Phase 3 Randomized Trial \(PEGASUS\)](#) and <https://www.medpagetoday.com/meetingcoverage/ashvideoppearlsrbd/90429>

¹⁸ <https://pipelinereview.com/index.php/2020120476743/Small-Molecules/BioCryst-Announces-FDA-Approval-of-ORLADEYO-berotralstat-First-Oral-Once-daily-Therapy-to-Prevent-Attacks-in-Hereditary-Angioedema-Patients.html>

¹⁹ <https://transfusionnews.com/2020/12/09/nt-probnp-levels-may-help-diagnose-taco-and-trali/>

²⁰ <https://www.medscape.com/viewarticle/942906>

²¹ <https://www.fiercepharma.com/pharma/az-fibrogen-s-roxadustat-decision-delayed-by-fda-but-approval-still-likely-analysts>

²² Steve Oh, Director of the Stem Cell Bioprocessing group at the Agency for Science, Technology and Research (A*STAR) in Singapore, and his colleagues

²³ [A Scalable Suspension Platform for Generating High-Density Cultures of Universal Red Blood Cells from Human Induced Pluripotent Stem Cells](#) and <https://www.the-scientist.com/news-opinion/new-protocol-advances-toward-lab-made-universal-red-blood-cells-68296>

- Researchers found rivaroxaban to be “non-inferior to warfarin in terms of efficacy and safety in the management of patients with atrial fibrillation and a bioprosthetic mitral valve”.²⁴
- The US FDA has approved Cerus’ INTERCEPT Blood System for cryoprecipitation.²⁵
- An Australian study²⁶ investigated trends in the co-prescribing of direct oral anticoagulants and drugs which have known pharmacokinetic or pharmacodynamic interactions with them.²⁷ A recommendation was made to lower the risk of co-prescribing.
- Researchers from the University of Chicago investigated whether red blood cell transfusions reduced exhaustion in hospitalised patients with anaemia. They recommended that measures of exhaustion and tiredness should be included in any further research on the effects of red blood cell transfusions on quality of life.²⁸

3. Antibodies, T cells and COVID-19

- Vir Biotechnology and GSK announced the beginning of a clinical trial, sponsored by the US National Institutes of Health to evaluate VIR-7831 in adults hospitalised with COVID-19. The candidate is a fully human anti-SARS-CoV-2 investigational monoclonal antibody selected to neutralise the virus, kill infected cells, and achieve high concentrations in the lungs.²⁹
- Two monoclonal antibodies BRII-196 and BRI-198, from Bria Biosciences, are being tested in randomized controlled phase 3 clinical trials for their safety and efficacy in treating patients hospitalised with COVID-19.³⁰
- Research has suggested that healthcare workers who have had COVID-19 are unlikely to be re-infected for at least six months.³¹
- US scientists reported that over 25 per cent of health care workers who were positive for SARS-CoV-2 antibodies were seronegative about 60 days later.³²
- US National Institutes of Health researchers have isolated a set of promising, tiny antibodies, or ‘nanobodies’ against SARS-CoV-2 that were produced by a llama.³³

²⁴ https://thelimbic.com/haematology/reassurance-on-doacs-in-af-patients-with-bioprosthetic-valves/?mc_cid=cdfc6b06e0&mc_eid=7872445fe3 and [Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve | NEJM](#)

²⁵ <https://www.medicaldevice-network.com/news/fda-approval-cerus-system/>

²⁶ [JCM | Free Full-Text | Five-Year Trends in Potential Drug Interactions with Direct-Acting Oral Anticoagulants in Patients with Atrial Fibrillation: An Australian-Wide Study \(mdpi.com\)](#)

²⁷ [Co-prescribing study shows need to lower risk of drug interactions with DOACs \(thelimbic.com\)](#)

²⁸ <https://transfusionnews.com/2020/12/01/rbc-transfusions-reduce-fatigability-in-hospitalized-patients-with-anemia/> and [The effect of red blood cell transfusion on fatigability after hospital discharge | Blood Advances | American Society of Hematology \(ashpublications.org\)](#)

²⁹ [Vir Biotechnology and GSK announce start of NIH-sponsored ACTIV-3 trial evaluating VIR-7831 in hospitalised adults with COVID-19 | Antibodies | News Channels](#) and [After Lilly's failure, NIH tests GSK/Vir and Bria COVID-19 drugs in hospitalized patients](#)

³⁰ <https://www.nih.gov/news-events/news-releases/investigational-covid-19-therapeutics-be-evaluated-large-clinical-trials>

³¹ [Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers](#) and <https://www.medscape.com/viewarticle/943154>

³² <https://consumer.healthday.com/decline-in-sars-cov-2-antibody-response-seen-over-60-days-2649040076.html> and [Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network — 12 States, April–August 2020 | MMWR \(cdc.gov\)](#)

³³ <https://www.nih.gov/news-events/news-releases/nih-neuroscientists-isolate-promising-mini-antibodies-against-covid-19-llama> and [Esparza, T.J. et al., High affinity nanobodies block SARS-CoV-2 spike receptor binding domain interaction with human angiotensin converting enzyme. Scientific Reports, December 22, 2020 DOI: 10.1038/s41598-020-79036-0.](#)

- Regeneron is investigating whether its infusible antibody-based treatment for COVID-19 may protect against coronavirus infections when given intranasally. The company is collaborating with gene therapy pioneer James Wilson of the University of Pennsylvania.³⁴
- SmartPharm Therapeutics, a wholly-owned subsidiary of Sorrento Therapeutics, has been awarded a contract by the US Defence Advanced Research Projects Agency and the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defence to develop a rapid countermeasure to COVID-19. The contract provides SmartPharm up to \$US 34 million for development of a gene-encoded antibody that could quickly protect from and/or treat SARS-CoV-2 infection.³⁵
- Celltrion Group has completed enrolment of 327 patients with mild-to-moderate symptoms of COVID-19 in the global phase 2 clinical trial of its monoclonal antibody CT-P59. Depending on trial outcomes, Celltrion expects to apply to the Korean Ministry of Food and Drug Safety for emergency use authorisation.³⁶
- Twist Bioscience Corporation announced preclinical data for three of its proprietary antibodies against the S1 protein in SARS-CoV-2.³⁷
- A Singaporean woman who had COVID-19 during the first trimester of her pregnancy is reported to have delivered a healthy baby who has antibodies against the virus.³⁸
- AbbieVie has been developing an experimental antibody with Harbour BioMed. It has begun dosing patients in a 24-participant phase 1 trial and is paying a licence fee for global development and commercialization rights.³⁹
- SAB Biotherapeutics announced that as part of Operation Warp Speed, the US Biomedical Advanced Research and Development Authority and the Department of Defence Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defence have awarded the company \$US 57.5 million. This will enable the manufacturing of SAB-185, the company's clinical stage, therapeutic candidate for COVID-19.⁴⁰
- AlloVir reported that preclinical data, presented at the 62nd ASH Annual Meeting, demonstrated selective antiviral activity of ALVR109 –a virus-specific T cell therapy designed to combat SARS-CoV-2. The therapy was able to produce effector molecules which selectively kill viral antigen-expressing targets, while leaving non-infected targets intact. There may be potential for using these cells to treat COVID-19 in hospitalised patients to prevent the development of severe disease.⁴¹

³⁴ [Penn Medicine Collaborates with Regeneron to Investigate Delivery of COVID-19 Antibody Cocktail via Gene Therapy Platform – PR News](#) and <https://www.biopharmadive.com/news/regeneron-upenn-coronavirus-antibody-nasal-spray/589905/>

³⁵ <https://pipelinereview.com/index.php/2020112876671/DNA-RNA-and-Cells/DARPA-and-JPEO-Award-Contract-to-SmartPharm-a-Subsidiary-of-Sorrento-for-Development-of-Rapid-Countermeasure-Against-COVID-19-Using-Gene-Encoded-Neutralizing-Antibodies.html>

³⁶ <https://pipelinereview.com/index.php/2020112676661/Antibodies/Celltrion-completes-enrolment-for-global-Phase-II-clinical-trial-with-COVID-19-treatment-candidate-CT-P59.html>

³⁷ <https://pipelinereview.com/index.php/2020112376639/Antibodies/Twist-Bioscience-Announces-Positive-Preclinical-Data-for-SARS-CoV-2-Antibodies.html>

³⁸ [Singapore woman gives birth to baby with coronavirus antibodies, report says - ABC News](#)

³⁹ <https://endpts.com/abbvie-pulls-the-trigger-on-a-covid-19-antibody-going-all-in-on-a-drug-discovered-by-research-alliance/>

⁴⁰ [https://pipelinereview.com/index.php/2020120176679/Antibodies/SAB-Biotherapeutics-Awarded-\\$57.5M-from-BARDA-and-U.S.-Department-of-Defense-for-Manufacturing-of-SAB-185-for-the-Treatment-of-COVID-19.html](https://pipelinereview.com/index.php/2020120176679/Antibodies/SAB-Biotherapeutics-Awarded-$57.5M-from-BARDA-and-U.S.-Department-of-Defense-for-Manufacturing-of-SAB-185-for-the-Treatment-of-COVID-19.html)

⁴¹ <https://pipelinereview.com/index.php/2020120676756/DNA-RNA-and-Cells/Preclinical-Data-Demonstrate-Anti-Viral-Activity-of-AlloVir-ALVR109-an-Allogeneic-Off-the-Shelf-SARS-CoV-2-Specific-T-Cell-Therapy.html>

- Scientists report that the monoclonal antibody HB27 has two distinct ways of inhibiting the virus-host cell interaction and subsequent infection with SARS-CoV-2.⁴²
- Other companies working in the antibody space include
 - Inovio⁴³
 - Eureka Therapeutics⁴⁴
 - Harbour BioMed and Utrecht University⁴⁵
 - Abpro⁴⁶
 - Ology Bioservices⁴⁷
 - Boehringer Ingelheim⁴⁸
 - Eli Lilly/AbCellera⁴⁹

4. Use of convalescent plasma in COVID-19

- At the ASH Annual Meeting, a small study in one health system was reported to have found that more than 40 per cent of patients with severe COVID-19 improved within a week of having convalescent plasma infusion, and more than 50 per cent were alive and discharged from hospital within 28 days.⁵⁰
- In the US, blood collection agencies wrote to the Biden-Harris transition COVID-19 Advisory Board⁵¹ advising members that by 7 December they had supplied 400,000 doses of convalescent plasma to hospitalised patients. They also encouraged the incoming administration to:
 - a. raise awareness of the ongoing need for donation of convalescent plasma;
 - b. maintain Biomedical Advanced Research and Development Authority payments directly to blood collectors for convalescent plasma;
 - c. vaccinate blood collection workers as a priority; and
 - d. support clinical trials evaluating the efficacy of convalescent plasma and determining appropriate dosing.

⁴² <https://www.news-medical.net/news/20201127/Monoclonal-antibody-HB27-shows-potent-neutralizing-activity-against-SARS-CoV-2.aspx>

⁴³ <https://pipelinereview.com/index.php/2020121676902/DNA-RNA-and-Cells/INOVI0-to-Develop-DNA-encoded-Monoclonal-Antibody-dMAb-Candidates-to-Treat-COVID-19-with-Funding-from-the-Defense-Advanced-Research-Projects-Agency-DARPA-and-the-Depart.html>

⁴⁴ <https://pipelinereview.com/index.php/2020121476885/Antibodies/Eureka-Therapeutics-Announces-Successful-Preclinical-Results-of-InvisiMask-Human-Antibody-Nasal-Spray-Against-SARS-CoV-2-Infection.html> and <https://www.fiercebiotech.com/research/covid-19-nasal-spray-by-eureka-therapeutics-protects-mice-from-coronavirus-infection>

⁴⁵ <https://pipelinereview.com/index.php/2020121676905/Antibodies/Harbour-BioMed-and-Utrecht-University-Announce-License-Agreement-with-AbbVie-and-Initiation-of-COVID-19-Antibody-Clinical-Trial.html>

⁴⁶ <https://pipelinereview.com/index.php/2020121676911/Antibodies/Abpro-Announces-Initiation-of-Phase-2/3-Registrational-Studies-of-its-Neutralizing-Antibody-Therapeutic-ABP-300-for-the-Treatment-of-COVID-19.html>

⁴⁷ <https://pipelinereview.com/index.php/2020121876935/Antibodies/Ology-Bioservices-Enters-Phase-1-Clinical-Trial-for-Anti-COVID-19-Monoclonal-Antibodies.html>

⁴⁸ <https://pipelinereview.com/index.php/2020121876953/Antibodies/New-SARS-CoV-2-Neutralizing-Antibody-enters-Clinical-Phase.html>

⁴⁹ <https://www.nih.gov/news-events/news-releases/results-nih-sponsored-activ-3-trial-published>

⁵⁰ <https://www.healio.com/news/hematology-oncology/20201206/convalescent-plasma-transfusion-shows-encouraging-covid19-results-at-one-institution>

⁵¹ <https://www.aabb.org/docs/default-source/default-document-library/positions/joint-letter-to-the-biden-harris-transition-covid-19-advisory-board-on-ccp.pdf>

5. Clinical experience with COVID-19

- An analysis of records for 8,000 patients who had heart failure and COVID-19 showed 1 in 4 dying in hospital.⁵²
- A study of the first wave of the pandemic suggested vitamin D deficiency quadrupled the death rate.⁵³
- Doctors in Brazil found that increasing vitamin D levels in critically ill COVID-19 patients did not reduce their hospital stay, their likelihood of being admitted to ICU and/or requiring mechanical ventilation, or their mortality.⁵⁴
- Researchers say that a scoring system based on 10 parameters in a complete blood count can predict which COVID-19 patients will become critically ill.⁵⁵
- A new study supports an earlier finding that people with type O or Rh negative blood may be at slightly lower risk from COVID-19.⁵⁶
- COVID-19 is known to produce symptoms relating to the central nervous system. A recent study has found that the SARS-CoV-2 spike protein can enter the brain in mice.⁵⁷
- A brain-imaging study has found that children may develop mild to severe neurological complications from COVID-19.⁵⁸
- A study found that COVID-19 can damage children's blood vessels.⁵⁹
- In the US, the National Institutes of Health are funding 8 studies to identify risk factors for COVID-19-related inflammatory syndrome in children.⁶⁰
- Three large international trials found that pre-emptive therapeutic level heparin was useless and possibly unsafe for COVID-19 patients and the trials were halted.⁶¹
- Researchers have confirmed that ocular symptoms such as conjunctivitis may occur in COVID-19.⁶²
- In the UK, the National Institute for Health and Care Excellence has issued guidelines for managing the long-term effects of COVID-19.⁶³
- Researchers analysed sputum and swab samples from 20 immunosuppressed cancer patients infected with SARS-CoV-2. Three were contagious for more than 3 weeks after their symptoms began, and one was contagious for 61 days.⁶⁴

⁵² [COVID-19 Mortality in HF Patients: Nearly 1 in 4](#) and [Clinical Outcomes in Patients With Heart Failure Hospitalized With COVID-19](#)

⁵³ <https://www.medscape.com/viewarticle/942497>

⁵⁴ [Vitamin D Fails to Help in Severe COVID-19](#) see also ['Not Enough Evidence' to Recommend Vitamin D for COVID-19 Treatment \(medscape.com\)](#)

⁵⁵ [A novel haemocytometric COVID-19 prognostic score developed and validated in an observational multicentre European hospital-based study](#) and <https://www.medscape.com/viewarticle/943326>

⁵⁶ <https://www.medscape.com/viewarticle/943243> and [Association Between ABO and Rh Blood Groups and SARS-CoV-2 Infection or Severe COVID-19 Illness: A Population-Based Cohort Study](#)

⁵⁷ [The S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice](#) and <https://www.genengnews.com/news/sars-cov-2s-spike-protein-can-enter-the-brain-in-mice/>

⁵⁸ <https://www.medscape.com/viewarticle/943198>

⁵⁹ <https://www.medscape.com/viewarticle/942600>

⁶⁰ <https://www.nih.gov/news-events/news-releases/nih-funds-eight-studies-uncover-risk-factors-covid-19-related-inflammatory-syndrome-children>

⁶¹ <https://www.medpagetoday.com/infectiousdisease/covid19/90351> and <https://www.nih.gov/news-events/news-releases/nih-activ-trial-blood-thinners-pauses-enrollment-critically-ill-covid-19-patients> and <https://www.medscape.com/viewarticle/943085>

⁶² <https://www.healio.com/news/optometry/20201214/ocular-manifestations-may-be-seen-in-patients-with-covid19>

⁶³ <https://www.medscape.com/viewarticle/942893> and [Overview | COVID-19 rapid guideline: managing the long-term effects of COVID-19](#)

⁶⁴ <https://www.reuters.com/article/us-health-coronavirus-cancer/covid-19-patients-on-some-cancer-therapies-may-be-contagious-for-months-study-idUSKBN28B5S1>

- Researchers from Spain reported that hyperglycaemia at hospital admission, independent of diabetes status, predicted COVID-19 severity and mortality among non-critical patients.⁶⁵
- Other researchers report that improved glycaemia within the first 2 or 3 days of hospitalisation is a better predictor of outcomes in COVID-19 patients than glycaemia at the time of non-ICU hospital admission.⁶⁶

6. Potential treatments for COVID-19 not mentioned elsewhere

- A phase 3 study of ruxolitinib (Novartis) in hospitalised COVID-19 patients did not meet its primary endpoint.⁶⁷
- Dexamethasone is regarded by some hospital physicians as the most reliable drug for COVID-19. It is cheap and has been around for decades.⁶⁸
- Researchers say that tocilizumab may reduce the need for mechanical ventilation in patients hospitalized with COVID-19 pneumonia, but it does not reduce their risk of dying.⁶⁹
- Japanese health authorities have concluded that the efficacy of antiviral drug Avigan in COVID-19 is inconclusive.⁷⁰
- Researchers reported that icosapent ethyl reduced levels of inflammatory biomarkers and improved symptoms in patients with COVID-19.⁷¹
- In a study of four alternative drugs for hospitalised COVID-19 patients (remdesivir, hydroxychloroquine, lopinavir, or interferon-beta-1a), the World Health Organisation said none reduced in-hospital mortality, decreased the need for ventilation, or shortened hospital stay.⁷²
- A recent study using artificial intelligence has identified baricitinib as having antiviral and anticytokine efficacy in COVID-19 patients.⁷³
- A Melbourne COVID-19 patient with sepsis was reported to have responded rapidly to a mega dose of vitamin C.⁷⁴
- The COVID-19 R&D Alliance, a cooperative of over 20 pharma and life sciences companies, has begun testing existing therapeutic drugs from Amgen, UCB and

⁶⁵ <https://www.medscape.com/viewarticle/941716>

⁶⁶ <https://www.medscape.com/viewarticle/942928> and [Association Between Achieving Inpatient Glycemic Control and Clinical Outcomes in Hospitalized Patients With COVID-19: A Multicenter, Retrospective Hospital-Based Analysis](#)

⁶⁷ <https://pipelinereview.com/index.php/2020121476880/Small-Molecules/Novartis-provides-update-on-RUXCOVID-study-of-ruxolitinib-for-hospitalized-patients-with-COVID-19.html>

⁶⁸ <https://www.medpagetoday.com/infectiousdisease/covid19/90327> and [COVID-19 preprint data led to 'immediate, dramatic change' in critical care practice](#)

⁶⁹ <https://www.healio.com/news/primary-care/20201217/tocilizumab-may-lower-risk-for-covid19-progression-but-not-mortality> and [China turns Roche arthritis drug Actemra against COVID-19 in new treatment guidelines](#)

⁷⁰ <https://www.medscape.com/viewarticle/942820>

⁷¹ <https://www.healio.com/news/cardiology/20201216/icosapent-ethyl-appears-to-reduce-inflammation-improve-symptoms-in-covid19>

⁷² <https://www.cidrap.umn.edu/news-perspective/2020/12/who-trial-finds-no-benefit-4-drugs-hospital-covid-patients>

⁷³ [JAK inhibition reduces SARS-CoV-2 liver infectivity and modulates inflammatory responses to reduce morbidity and mortality | Science Advances \(sciencemag.org\)](#)

⁷⁴ [COVID patient with sepsis makes 'remarkable' recovery following megadose of vitamin C - ABC News](#)

Takeda which may have the potential to suppress or control the immune response and resulting inflammation in patients with severe COVID-19.⁷⁵

7. Developing vaccines for COVID-19

In late stage of development

- Pfizer/BioNTech included children in US trials of its vaccine in September. Moderna has now begun a phase 2 /3 trial in adolescents.⁷⁶ AstraZeneca also expects to produce US trial results for children. One area of interest is dosage levels. While children may be less affected than adults by COVID-19, vaccinating them is seen as important in achieving community immunity⁷⁷.
- The Oxford University COVID-19 vaccine was reported to give a better immune response with a regimen of two full doses rather than a full dose with a half-dose booster.⁷⁸ AstraZeneca's CEO has said the vaccine should provide protection for a year.⁷⁹
- Pfizer and BioNTech reported data from a phase 1/ 2 I/II study in Germany further characterising the immune response after vaccination with BNT162b2.⁸⁰
- Moderna has confirmed 94.1 per cent efficacy for its vaccine.⁸¹
- Trials of the University of Queensland vaccine were abandoned after some participants falsely tested positive for HIV in the phase 1 trials. CSL will instead make another 20 million doses of the AstraZeneca/ Oxford University vaccine, in addition to the 30 million doses already agreed with the Australian government.⁸² Co-leader of the project Professor Paul Young said that the "molecular clamp" vaccine had elicited a robust response to the virus and had a strong safety profile". He added: "We're not going to progress this particular vaccine approach... but the underlying platform should be applicable to a wide range of virus threats".⁸³

Regulatory approval, sales and distribution

- On 10 December the US FDA's expert panel concluded that the benefits of the Pfizer/ BioNTech vaccine outweigh the risks for people 16 and older and

⁷⁵ http://www.pmlive.com/pharma_news/joint_covid-19_trial_begins_testing_drugs_from_amgen_ucb_and_takeda_1358778

⁷⁶ <https://www.fiercebiotech.com/biotech/moderna-doses-adolescents-covid-19-vaccine-study-setting-it-up-to-target-2021-2022-school> and [Moderna Announces First Participants Dosed in Phase 2/3 Study of COVID-19 Vaccine Candidate in Adolescents](#)

⁷⁷ <https://www.wsj.com/articles/covid-19-vaccine-makers-turn-toward-testing-children-11607688001>

⁷⁸ <https://www.medscape.com/viewarticle/942843> and [Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses](#)

⁷⁹ <https://www.fiercepharma.com/vaccines/astrazeneca-s-covid-19-to-protect-for-about-one-year-ceo-says>

⁸⁰ <https://pipelinereview.com/index.php/2020121476893/Vaccines/Pfizer-and-BioNTech-Provide-Data-from-German-Phase-1/2-Study-Further-Characterizing-Immune-Response-Following-Immunization-with-Lead-COVID-19-Vaccine-Candidate-BNT162b2.html> and [BNT162b2 induces SARS-CoV-2-neutralising antibodies and T cells in humans](#)

⁸¹ <https://pipelinereview.com/index.php/2020113076673/Vaccines/Moderna-Announces-Primary-Efficacy-Analysis-in-Phase-3-COVE-Study-for-Its-COVID-19-Vaccine-Candidate-and-Filing-Today-with-U.S.-FDA-for-Emergency-Use-Authorization.html>

⁸² [Australia's CSL ends COVID-19 vaccine trial, to focus on AstraZeneca's shots |](#) and [No homegrown coronavirus vaccine, but CSL inoculated against failure](#)

⁸³ [It won't be rolled out for COVID-19, but technology developed for UQ vaccine might help fight future viruses](#) and <https://www.abc.net.au/news/2020-12-12/coronavirus-queensland-vaccine-uq-trial-cancellation-setback/12973724>

recommended emergency use authorisation. The panel discussed allergic reactions experienced by two UK healthcare workers who received the vaccine.⁸⁴

- After emergency use authorisation Pfizer began shipping the vaccine in dry ice within the US.⁸⁵
- The company plans to file in the US for full FDA approval for its mRNA vaccine by April 2021.⁸⁶
- The US government signed a deal to acquire 100 million further doses of the Pfizer/BioNTech vaccine.⁸⁷ Each person vaccinated requires two doses. The FDA has said most Americans with allergies should be safe to receive the Pfizer/BioNTech vaccine.⁸⁸
- The Pfizer/BioNTech vaccine being delivered across the US is in vials holding at least five doses. The US FDA says that any extra full doses can be used, but that leftovers from different vials should not be combined.⁸⁹
- On 2 December the Medicines & Healthcare Products Regulatory Agency in the UK, granted Pfizer/ BioNTech a temporary authorization for emergency use of their COVID-19 mRNA vaccine and rollout followed quickly.⁹⁰ A variant mutant strain of COVID-19 was identified but experts said it need not necessarily render the vaccine ineffective.⁹¹
- On 9 December Canada authorised Pfizer and BioNTech's mRNA vaccine. Pfizer will supply Canada with up to 76 million doses. Early delivery of 249,000 doses allowed vaccination efforts to begin before Christmas.⁹²
- The European Medicines Agency approved the Pfizer/ BioNTech vaccine,⁹³ as did Singapore.⁹⁴
- In Germany there have been some concerns about whether the Pfizer/BioNTech vaccine transit temperature was maintained.⁹⁵

⁸⁴ [Pfizer/BioNTech COVID-19 shot sails through FDA panel after staffers sing its praises | FierceBiotech](#) and <https://www.biopharmadive.com/news/fda-pfizer-coronavirus-vaccine-emergency-approval/591933/> and [Pfizer coronavirus vaccine receives expert panel endorsement for US Food and Drug Administration to approve emergency use - ABC News](#)

⁸⁵ [United States Pfizer vaccine shipments begin after emergency authorisation](#)

⁸⁶ [Pfizer plans to file for full FDA approval of COVID-19 vaccine in April 2021](#)

⁸⁷ <https://www.biopharmadive.com/news/us-pfizer-coronavirus-vaccine-supply-deal-more-doses/592706>

⁸⁸ <https://www.reuters.com/article/us-health-coronavirus-vaccines-allergies/most-americans-with-allergies-should-be-safe-to-get-pfizer-biontech-vaccine-fda-idUSKBN28MOSU>

⁸⁹ <https://www.bloomberg.com/news/articles/2020-12-17/extra-doses-in-pfizer-vaccine-vials-can-be-used-fda-says> and [Pfizer's COVID-19 vaccine data raise some flags, analysts say, but not enough to scuttle an FDA nod](#)

⁹⁰ <https://pipelinereview.com/index.php/2020120276699/Vaccines/Pfizer-and-BioNTech-Achieve-First-Authorization-in-the-World-for-a-Vaccine-to-Combat-COVID-19.html> and [UK approves first COVID-19 vaccine, roll-out begins in days \(newatlas.com\)](#)

⁹¹ [New COVID-19 variant identified in the UK but experts say coronavirus vaccines should still be effective](#) and [Coronavirus: US scientists examine UK mutant strain to check vaccine resistance](#) and <https://uk.reuters.com/article/health-coronavirus-britain-variant/new-coronavirus-strain-spreading-in-uk-has-key-mutations-scientists-say-idUKKBN28P15E> and [New variant of coronavirus identified in the UK](#)

⁹² [Canada Authorizes Covid-19 Vaccine From Pfizer and BioNTech - WSJ](#)

⁹³ <https://www.medscape.com/viewarticle/942973> and [Pfizer/BioNTech's Covid-19 vaccine authorised by EU](#) and <https://pipelinereview.com/index.php/2020120176686/Vaccines/Pfizer-and-BioNTech-Submitted-Application-for-Conditional-Marketing-Authorization-for-COVID-19-Vaccine-to-the-EMA.html> and [Hackers breach Pfizer/BioNTech COVID-19 vaccine data in cyberattack targeting EMA | and Pfizer/BioNTech weren't alone: Moderna COVID-19 vaccine data targeted in EMA cyberattack](#)

⁹⁴ <https://www.medscape.com/viewarticle/942569>

⁹⁵ [German states raise concerns over consistency of COVID-19 vaccine temperature during transit](#)

- Moderna announced US FDA authorization of its vaccine for use on an emergency basis.⁹⁶ The US government had earlier signed a deal to purchase another 100 million doses of the Moderna vaccine.⁹⁷
- Moderna applied for EU approval for its vaccine.⁹⁸
- Researchers reported that the vaccine developed by Moderna and the US National Institutes of Health provided protection which remained elevated three months after the second dose.⁹⁹
- The American College of Allergy, Asthma, and Immunology (ACAAI) has issued advice regarding risks of allergic reactions to new mRNA COVID-19 vaccines (by Moderna and by Pfizer/BioNTech): "The new vaccines should be given in health care settings where reactions can be treated, and patients must be observed for at least 15-30 minutes...to monitor for any adverse reaction." ACAAI says patients who experience a severe allergic reaction to the first injection should not be given the second. It advises that anyone with allergies to medications, foods, insects and latex is no more likely than the general public to be allergic to the mRNA COVID-19 vaccines¹⁰⁰. A doctor in Boston who had a severe reaction to the Moderna vaccine was reported to have a shellfish allergy.¹⁰¹ The US Centers for Disease Control issued this guidance¹⁰²: "mRNA COVID-19 vaccines may be administered to people with underlying medical conditions provided they have not had a severe allergic reaction to any of the ingredients in the vaccine".
- Australia signed deals to distribute COVID-19 vaccines around the nation.¹⁰³

Earlier stage of development

- Interim data from a trial in Turkey of Sinovac's COVID-19 vaccine suggests it is 91.25 per cent effective, a much higher figure than was announced from a trial in Brazil.¹⁰⁴
- Stanley C. Erck, President and CEO of Novavax, reported the company was continuing to make meaningful progress as it worked to test, manufacture and

⁹⁶ <https://pipelinereview.com/index.php/2020121976954/Vaccines/Moderna-Announces-FDA-Authorization-of-Moderna-COVID-19-Vaccine-in-U.S.html> and <https://www.fiercebiotech.com/biotech/moderna-covid-19-vaccine-gets-fda-panel-s-backing-despite-concerns> and [US Food and Drug Association to approve Moderna's COVID-19 vaccine on emergency basis](https://www.usfoodanddrug.org/press-releases/2020/12/19/moderna-covid-19-vaccine-passes-fda-reviewers-test-but-shares-drop-anyway) and [Moderna COVID-19 vaccine passes FDA reviewers' test, but shares drop anyway](https://www.usfoodanddrug.org/press-releases/2020/12/19/moderna-covid-19-vaccine-passes-fda-reviewers-test-but-shares-drop-anyway) | and <https://pipelinereview.com/index.php/2020121876923/Vaccines/Moderna-Receives-FDA-Advisory-Committee-Vote-Supporting-Emergency-Use-for-Modernas-Vaccine-Against-COVID-19-in-the-United-States.html> and

<https://www.nih.gov/news-events/news-releases/statement-nih-barda-fda-emergency-use-authorization-moderna-covid-19-vaccine> and [US Food and Drug Administration authorises Moderna's COVID-19 vaccine for emergency use](https://www.fda.gov/oc/2020/12/19/moderna-covid-19-vaccine-authorized-emergency-use) and

<https://www.medpagetoday.com/infectiousdisease/covid19/90242>

⁹⁷ <https://thehill.com/policy/healthcare/529897-trump-administration-to-purchase-another-100m-doses-of-moderna-vaccine>

⁹⁸ <https://www.bmj.com/content/371/bmj.m4709>

⁹⁹ <https://www.healio.com/news/primary-care/20201204/protection-from-modernas-covid19-vaccine-remains-elevated-after-first-3-months>

¹⁰⁰ <https://www.medscape.com/viewarticle/943212> and

<https://www.medpagetoday.com/infectiousdisease/covid19/90331>

¹⁰¹ <https://www.medscape.com/viewarticle/943228>

¹⁰² <https://www.medscape.com/viewarticle/943254> and [CDC issues guidelines on COVID-19 vaccination after allergic reactions](https://www.cdc.gov/media/releases/2020/s1218-covid-19-vaccine-allergy.html)

¹⁰³ [Australia signs deals to distribute tens of millions of coronavirus vaccine doses around the country](https://www.abc10.com.au/news/2020-12-19/australia-signs-deals-to-distribute-tens-of-millions-of-coronavirus-vaccine-doses-around-the-country)

¹⁰⁴ [COVID-19 vaccine from China's Sinovac 91.25 per cent effective, Turkey says after trial involving 7,000 volunteers](https://www.abc10.com.au/news/2020-12-19/covid-19-vaccine-from-china-s-sinovac-91-25-per-cent-effective-turkey-says-after-trial-involving-7-000-volunteers) and <https://www.medscape.com/viewarticle/94316>

ultimately deliver its vaccine NVX-CoV2373.¹⁰⁵ Its plans for a phase 3 trial of the vaccine were delayed as the US FDA queried its arrangements for manufacturing vaccine.¹⁰⁶

- Clover Biopharmaceuticals announced data from its phase 1 trial demonstrating that its protein-based COVID-19 S-Trimer vaccine candidates, in combination with adjuvants from either GSK or Dynavax, induced strong immune responses, including neutralizing antibodies and cell-mediated immunity, as well as favourable safety and tolerability profiles, in 150 adult and sometimes elderly participants.¹⁰⁷
- Providence Therapeutics submitted a clinical trial application to Health Canada for its mRNA vaccine PTX-COVID-19-B.¹⁰⁸
- AstraZeneca plans to trial its Oxford University vaccine in combination with Russia's Sputnik V, hoping that by combining the two adenovirus vaccines, AstraZeneca's candidate can demonstrate improved efficacy.¹⁰⁹
- Sanofi and GlaxoSmithKline's vaccine candidate achieved an adequate immune response in people aged 18 to 49 years, according to interim phase 1/2 trial data; but the vaccine failed to achieve a comparable response in older people. The companies suggested the problem may have been due to insufficient concentrations of Sanofi's adjuvant. A revised antigen formulation will be used from February.¹¹⁰
- Researchers from City of Hope and Biovaxys Technology have reported positive data for their experimental COVID-19 vaccine products in animals. The vaccines are designed to induce both antibody and T-cell immune responses. Some scientists think they may offer longer-lasting protection against COVID-19 than the first vaccines to be approved.¹¹¹
- COVAXX, which is developing a multipeptide-based vaccine to fight COVID-19, announced advanced purchase commitments of more than 140 million doses, and will deliver vaccines to multiple countries, including Brazil, Ecuador and Peru.¹¹²

¹⁰⁵ <https://pipelinereview.com/index.php/2020120176692/Vaccines/Novavax-Announces-COVID-19-Vaccine-Clinical-Development-Progress.html>

¹⁰⁶ <https://www.fiercepharma.com/manufacturing/novavax-swamped-fda-s-manufacturing-questions-hopes-for-us-trial-within-year>

¹⁰⁷ <https://pipelinereview.com/index.php/2020120476730/Vaccines/Clover-Biopharmaceuticals-Announces-Positive-Phase-1-Data-for-its-Adjuvanted-S-Trimer-COVID-19-Vaccine-Candidates.html>

¹⁰⁸ [Providence Therapeutics Submits Clinical Trial Application \(CTA\) to Health Canada for the mRNA COVID vaccine |](#)

¹⁰⁹ [AstraZeneca hitches ride with Russia's Sputnik in vaccine race](#) and [AstraZeneca teams up with Russia's Sputnik V vaccine for COVID-19 trials](#)

¹¹⁰ [Weak clinical data force Sanofi, GSK to delay COVID-19 vaccine](#) and <https://www.theguardian.com/world/2020/dec/11/gsk-sanofi-covid-vaccine-delayed-end-next-year>

¹¹¹ <https://www.fiercebiotech.com/research/covid-19-vaccines-based-novel-platforms-show-early-promise-mice> and

<https://pipelinereview.com/index.php/2020112476651/Vaccines/City-of-Hope-Initiates-Phase-1-Clinical-Trial-to-Test-Its-First-SARS-CoV-2-Investigational-Vaccine.html> and

<https://pipelinereview.com/index.php/2020120176678/Vaccines/City-of-Hope-COVID-19-Investigational-Vaccine-Produces-Strong-Immunity-in-Preclinical-Research.html> and [Development of a multi-antigenic SARS-CoV-2 vaccine candidate using a synthetic poxvirus platform | Nature Communications](#)

¹¹² [https://pipelinereview.com/index.php/2020112676659/Vaccines/COVAXX-Announces-\\$2.8-Billion-in-Advance-Purchase-Commitments-to-Deliver-More-Than-140-Million-Vaccine-Doses-to-Emerging-Countries.html](https://pipelinereview.com/index.php/2020112676659/Vaccines/COVAXX-Announces-$2.8-Billion-in-Advance-Purchase-Commitments-to-Deliver-More-Than-140-Million-Vaccine-Doses-to-Emerging-Countries.html)

- Altimmune submitted an investigational new drug application to the US FDA to commence a phase 1 clinical trial of its single-dose intranasal COVID-19 vaccine candidate.¹¹³
- Other companies working in the vaccine space include
 - ImmunoPrecise/ LiteVax¹¹⁴
 - Codagenix/ Serum Institute of India¹¹⁵
 - Valneva¹¹⁶
 - CureVac¹¹⁷
 - Enesi Pharma/ Imperial college, London¹¹⁸
- Hackers have targeted COVID-19 vaccine and drug developers and cold chain suppliers.¹¹⁹
- A nasal spray said to protect against the SARS-Cov-2 virus has been developed at the University of Birmingham's Healthcare Technologies Institute.¹²⁰

8. Managing the pandemic

Individual country experiences

- Spain's Supreme Court has ordered an investigation into the mortality of elderly people in nursing homes during the pandemic, and also the lack of protective gear for health workers.¹²¹
- By the end of 2020, the US had recorded close to 318,000 deaths from coronavirus.¹²²
- Brazil has used genome sequencing to see whether cases of apparent reinfection with COVID-19 were caused by a different strain.¹²³

¹¹³ <https://pipelinereview.com/index.php/2020112676665/Vaccines/Altimmune-Announces-Submission-of-Investigational-New-Drug-Application-for-AdCOVID-a-Single-dose-Intranasal-COVID-19-Vaccine-On-Track-to-Commence-Phase-1-Clinical-Study-in-Decem.html>

¹¹⁴ <https://pipelinereview.com/index.php/2020121476882/Vaccines/ImmunoPrecise-and-LiteVax-Advance-SARS-CoV-2-Vaccine-Candidate.html>

¹¹⁵ <https://pipelinereview.com/index.php/2020121476889/Vaccines/Codagenix-and-Serum-Institute-of-India-Announce-Commencement-of-First-in-Human-Trial-of-COVI-VAC-A-Single-Dose-Intranasal-Live-Attenuated-Vaccine-for-COVID-19.html> and <https://www.fiercepharma.com/drug-delivery/codagenix-serum-institute-take-nasal-covid-19-vaccine-into-clinic>

¹¹⁶ <https://pipelinereview.com/index.php/2020121676915/Vaccines/Valneva-Initiates-Phase-1/2-Clinical-Study-of-Inactivated-Adjuvanted-COVID-19-Vaccine-Candidate.html> and http://www.pharmatimes.com/news/valneva_starts_uk-based_early-stage_covid-19_vaccine_trials_1360160

¹¹⁷ <https://pipelinereview.com/index.php/2020121776921/Vaccines/CureVac-Commences-Global-Pivotal-Phase-2b/3-Trial-for-COVID-19-Vaccine-Candidate-CVnCoV.html>

¹¹⁸ <https://pipelinereview.com/index.php/2020121876940/Vaccines/Enesi-Pharma-and-Imperial-College-London-Collaborate-to-Develop-Thermostable-RNA-Vaccines-with-Potential-to-Eliminate-Cold-Chain-and-Transform-Global-Vaccination-Logistics-for-C.html>

¹¹⁹ www.fiercepharma.com/pharma/not-just-astrazeneca-north-korean-hackers-targeted-5-other-covid-drug-developers-wsj and [North Korean Hackers Are Said to Have Targeted Companies Working on Covid-19 Vaccines - WSJ](#)

¹²⁰ <https://www.labonline.com.au/content/consumables/news/nasal-spray-developed-to-protect-against-sars-cov-2-150974940>

¹²¹ <https://www.medscape.com/viewarticle/942900>

¹²² <https://www.msn.com/en-us/news/us/us-sets-daily-coronavirus-death-record-for-second-straight-day/ar-BB1cnwqp> and [US deaths in 2020 top 3 million, by far most ever counted](#)

¹²³ <https://www.medscape.com/viewarticle/942534>

- Researchers estimate that 76 per cent of the population of Manaus, the first Brazilian city to be hit hard by SARS-CoV-2, have been infected, based on antibodies present in samples from blood banks.¹²⁴
- Russia admitted its death toll from coronavirus is more than three times higher than was previously reported.¹²⁵
- Virus fragments were found in sewage at Batemans Bay and Liverpool, as testing numbers fall in NSW.¹²⁶
- Victoria's health department says there could be a spike in COVID-19 cases from March as the weather cools and people gather indoors.¹²⁷
- Denmark culled its mink population because of coronavirus concerns. Now there are fears that mass graves may have contaminated the groundwater.¹²⁸
- South Korea has been experiencing a third wave of COVID-19 infections.¹²⁹

Transmission

- A study of four distinct coronaviruses over eight years showed they were highly seasonal, peaking in winter months.¹³⁰
- Britain, South Africa and Nigeria have all reported new variants of the SARs-CoV-2 virus that are said to be more contagious.^{131, 132} BioNTech is confident that its vaccine will be effective against the mutation found in the UK.¹³³
- A study of hospital air reported that viable viruses are typically found close to COVID-19 patients. It supported continued use of surgical masks around most of the hospital, with respirator use reserved for aerosol-generating procedures on patients' respiratory tracts.¹³⁴
- Three old vaccines are being discussed as potential candidates for boosting the immune response, which may be helpful in fighting COVID-19: bacillus Calmette-Guérin against tuberculosis; the measles, mumps, and rubella vaccine; and oral polio vaccine.¹³⁵

¹²⁴ [Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic](#)

¹²⁵ [Coronavirus death toll triples in Russia after government admits to downplaying COVID-19 outbreak](#)

¹²⁶ [Coronavirus Australia live news: Virus fragments found in NSW sewage as authorities warn testing numbers are falling](#)

¹²⁷ [Victorian health authorities eye autumn as potential COVID danger period](#)

¹²⁸ [Concerns mink mass graves in Denmark may have contaminated groundwater -](#)

¹²⁹ [South Korea facing COVID-19 'emergency' with record cases in third wave](#)

¹³⁰ <https://www.healio.com/news/infectious-disease/20200413/8year-study-shows-coronaviruses-have-sharp-seasonality>

¹³¹ <https://www.medscape.com/viewarticle/943186> and <https://www.medscape.com/viewarticle/943280> and [Covid-19: What have we learnt about the new variant in the UK?](#)

¹³² [First case of new COVID-19 variant found in France as cases rise](#) and <https://www.cnbc.com/2020/12/22/cdc-says-new-covid-strain-in-uk-could-already-be-circulating-undetected-in-us.html> and [Singapore and Denmark confirm cases of new COVID-19 variant strain spreading rapidly in the United Kingdom](#) and [First US case of COVID-19 variant found in Colorado as highest number of COVID hospitalisations recorded](#)

¹³³ <https://www.medscape.com/viewarticle/943005> and <https://www.medscape.com/viewarticle/943048>

¹³⁴ [Assessment of Air Contamination by SARS-CoV-2 in Hospital Settings | Infectious Diseases | JAMA Network Open](#) and <https://www.medscape.com/viewarticle/943229>

¹³⁵ [Are Old Vaccines Helpful Against COVID-19](#)

- Scientists say COVID-19 patients are most infectious during the first 2 days of symptoms and for 5 days afterwards.¹³⁶

Testing

- Researchers at the University of California, Davis, have developed a rapid COVID-19 test that gives results in 20 minutes.¹³⁷
- An inventor says he is trialling a remote-controlled robot which can test for COVID-19.¹³⁸

9. Miscellaneous news

Infectious diseases other than COVID-19

- Over 207,000 people worldwide died from measles in 2019 as the number of cases reached a 23-year high.¹³⁹
- Researchers reported on a case of sustained HIV remission without a bone marrow transplant.¹⁴⁰
- Provention Bio initiated a human study of its Coxsackievirus B vaccine PRV-101.¹⁴¹
- Hookipa announced positive interim efficacy results, as well as additional safety and immunogenicity data, for its prophylactic cytomegalovirus vaccine candidate HB-101. This is a non-replicating arenavirus vaccine. It is being investigated for use in patients receiving a kidney transplant from a living donor.¹⁴²
- VBI Vaccines submitted a biologics licence application to the US FDA for its 3-antigen hepatitis B vaccine for adults.¹⁴³
- A potential DNA-based vaccine against infection by Crimean-Congo haemorrhagic fever virus has been shown to protect cynomolgus macaques.¹⁴⁴
- Genetworx Labs launched a diagnostic flu A-B/COVID-19/RSV combination test that requires only one sample.¹⁴⁵

¹³⁶ <https://www.beckershospitalreview.com/infection-control/covid-19-patients-most-infectious-2-days-before-5-days-after-symptoms-emerge-analysis-finds.html> and [SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis - The Lancet Microbe](#)

¹³⁷ <https://www.ktvu.com/news/uc-davis-develops-rapid-covid-test-that-yields-results-in-20-minutes>

¹³⁸ <https://uk.reuters.com/article/health-coronavirus-egypt-robot/egyptian-inventor-trials-robot-that-can-test-for-covid-19-idUKKBN2852F6>

¹³⁹ <https://www.healio.com/news/infectious-disease/20201112/measles-killed-207k-people-in-2019-as-cases-hit-23year-high>

¹⁴⁰ <https://www.healio.com/news/infectious-disease/20200707/man-achieves-longterm-hiv-remission-without-bone-marrow-transplant>

¹⁴¹ <https://pipelinereview.com/index.php/2020121676908/Vaccines/Provention-Bio-Initiates-First-in-Human-Study-of-Coxsackievirus-B-Vaccine-Candidate-PRV-101.html>

¹⁴² <https://pipelinereview.com/index.php/2020120176693/Vaccines/HOOKIPA-Announces-Positive-Phase-2-Interim-Safety-Immunogenicity-and-Efficacy-Data-for-its-Cytomegalovirus-Vaccine-Candidate-HB-101.html>

¹⁴³ <https://pipelinereview.com/index.php/2020120276702/Vaccines/VBI-Vaccines-Announces-Submission-of-Biologics-License-Application-to-FDA-for-3-Antigen-Prophylactic-Hepatitis-B-Vaccine.html>

¹⁴⁴ <https://www.nih.gov/news-events/news-releases/experimental-vaccine-deadly-tickborne-virus-effective-cynomolgus-macaques>

¹⁴⁵ <https://www.massdevice.com/genetworx-labs-launches-covid-19-flu-rsv-diagnostic-test/>

Other

- A study suggests that a new blood-based assay can detect five cancer types up to 4 years earlier than current screening methods.¹⁴⁶
- AstraZeneca has agreed to acquire Alexion Pharmaceuticals, whose products include Soliris and Ultomiris.¹⁴⁷
- Cases of poisoning from swallowing alcohol-based hand sanitizer have increased during the COVID-19 pandemic.¹⁴⁸

¹⁴⁶ [Blood test detects common cancer types 4 years before current screening methods](#)

¹⁴⁷ <https://www.biopharmadive.com/news/astrazeneca-acquire-alexion-rare-disease-deal/592087/>

¹⁴⁸ <https://www.medscape.com/viewarticle/941899>