

# Monitoring International Trends

## October 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. Of note, this month's edition provides updates on the use of convalescent plasma to treat COVID-19 (pages 6-7) and trials of manufactured antibodies to treat COVID-19 (pages 12-14). Among items of interest in this month's edition which are unrelated to the COVID-19 pandemic are that: Australian scientists have engineered a single-chain antibody that recognises the pathological form of the Von Willebrand Factor blood protein (page 3); the US Food and Drug Administration has approved Ultomiris 100mg/mL formulation for the treatment of adults with paroxysmal nocturnal hemoglobinuria and for atypical haemolytic uremic syndrome (page 4); and Lifeblood has removed the four-month deferral period for plasma donations and has been calling on newly tattooed individuals to donate plasma (page 5).

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## 1. Treating blood disorders

- Scientists from the Australian Centre for Blood Diseases have engineered a single-chain antibody that recognises the pathological form of the Von Willebrand Factor (VWF) blood protein. It selectively blocks thrombus formation while maintaining normal haemostasis.<sup>1</sup>
- Haemophilia Australia welcomed the decision to make emicizumab (Hemlibra) available by December 2020 to people with haemophilia A. It will be provided without charge to patients, funded under the National Blood Agreement. Haemophilia Australia said: “This is a very significant step forward. It will provide as much protection for people with haemophilia from the risk of bleeding as current treatments and it will be much easier to administer, without the need for regular intravenous injections”.<sup>2</sup>
- The US National Institutes of Health awarded the [DNA Medicine Institute \(DMI\)](#) \$US 1.5 million to advance rapid monitoring of Factor VIII (FVIII) and [Hemlibra](#) (emicizumab) blood levels in people with haemophilia A. DMI is developing a device to analyse within fifteen minutes a blood sample taken by finger prick.<sup>3</sup>
- Cycleron Therapeutics announced results from its STRONG-SCD trial of olinciguat, an orally-administered drug for the potential treatment of sickle cell disease (SCD). The drug was well tolerated across all dose ranges, but results did not merit further internal clinical development. Peter Hecht, CEO of Cycleron, said: “While we are disappointed that we won’t be contributing a much-needed new treatment option for SCD, we are continuing to analyse the data to understand several potential biomarker signals, including inflammation, as we explore partnership options for this program”.<sup>4</sup>
- Fulcrum Therapeutics has US Food and Drug Administration (FDA) approval to proceed with a Phase I trial in healthy adults of its drug FTX-6058 for SCD. FTX-6058 is a small molecule designed to increase expression of foetal haemoglobin.<sup>5</sup> The company is also advancing FTX-6058 for the treatment of beta thalassemia into Phase 1 clinical development.<sup>6</sup>
- Imara announced that the first patient had been dosed in the Forte Phase IIb clinical trial of IMR-687 for patients with beta-thalassemia. Perla Eleftheriou<sup>7</sup>, national lead investigator in the UK on the Forte trial, said: “There are currently no approved oral therapies to increase foetal haemoglobin in beta-thalassemia, a rare inherited red blood cell disorder which if left untreated, causes severe anaemia, enlarged spleen, skeletal abnormalities, organ failure and early death. We believe there is a clear rationale to expand development of IMR-687 to include beta-thalassemia”.<sup>8</sup>
- [Alexion Pharmaceuticals, Inc.](#) announced the US FDA had approved Ultomiris (ravulizumab-cwvz) 100 mg/mL formulation for the treatment of adults with

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<sup>1</sup> <https://haematologica.org/article/view/haematol.2020.250761>

<sup>2</sup> <https://thelimbic.com/haematology/emicizumab-to-be-funded-for-people-with-haemophilia-a/>

<sup>3</sup> <https://hemophilianewstoday.com/2020/10/12/nih-awards-1-5-million-to-advance-hemophilia-a-finger-blood-test-fviii-helimbra-levels/>

<sup>4</sup> <https://pipelinereview.com/index.php/2020101476175/Small-Molecules/Cycleron-Announces-Phase-2-STRONG-SCD-Study-Results-in-Patients-with-Sickle-Cell-Disease.html>

<sup>5</sup> <https://seekingalpha.com/pr/18030453-fulcrum-therapeutics-to-initiate-phase-1-trial-ftxminus-6058-for-sickle-cell-disease>

<sup>6</sup> <https://seekingalpha.com/news/3619731-fulcrum-therapeutics-on-go-early-stage-study-ftxminus-6058-for-sickle-cell>

<sup>7</sup> Consultant Haematologist in the Red Cell Hematology department at University College London Hospitals NHS Foundation Trust and Honorary Clinical Senior Lecturer at University College London

<sup>8</sup> <https://pipelinereview.com/index.php/2020101676206/Small-Molecules/Imara-Announces-First-Patient-Dosed-in-Forte-Phase-2b-Clinical-Trial-of-IMR-687-in-Beta-Thalassemia.html>

paroxysmal nocturnal hemoglobinuria (PNH) and for atypical haemolytic uremic syndrome (aHUS). Ultomiris 100 mg/mL reduces average annual infusion times by approximately 60 per cent compared with Ultomiris 10 mg/mL but delivers comparable safety and efficacy.<sup>9</sup>

- BioCryst Pharmaceuticals announced new data from treatment-naïve paroxysmal nocturnal hemoglobinuria patients receiving doses up to 400 mg of its oral Factor D inhibitor, BCX9930, as monotherapy. The company says the drug is “driving rapid and dose-dependent reductions in key biomarkers” and increasing haemoglobin levels in all participants. Improved haemoglobin levels were maintained without transfusions.<sup>10</sup>
- [Vertex Pharmaceuticals Incorporated](#) updated news on its clinical program in alpha-1 antitrypsin deficiency (AATD). Carmen Bozic<sup>11</sup> said: “Based on the liver enzyme elevations observed, along with the determination that we would not be able to safely achieve targeted exposure levels with VX-814, we are discontinuing further development of this molecule. We remain committed to transforming the treatment of this disease. We look forward to continuing clinical study of VX-864 and other molecules targeting the underlying cause of AATD.” A Phase II trial of VX-864, which is structurally distinct from VX-814, began in July 2020. This study is randomized, double-blind, and placebo controlled. Being conducted in around 40 patients, it is designed to evaluate the safety and pharmacokinetics of VX-864, and its capacity to increase functional levels of alpha-1 antitrypsin over 28 days of dosing. Enrolment is continuing, and clinical data from this study are expected in the first half of 2021.<sup>12</sup>
- Harbour BioMed began dosing patients in two separate Phase II clinical trials of batoclimab (HBM 9161), a fully human monoclonal antibody the company hopes will prove safe and effective in treating immune thrombocytopenia in adults, and myasthenia gravis.<sup>13</sup>

## 2. Safety and Patient blood management

- The American Red Cross tested all blood donations from 15 June 2020 to 23 August 2020 for anti-SARS-CoV-2 IgG. Of the 953,926 donations 1.82 per cent were positive for SARS-CoV-2 antibodies. Almost 3 per cent of first-time donors were seropositive compared with almost 2 per cent of repeat donors. Donors aged 18-24 years were more likely to be seropositive compared with those aged 55 years or older. Seroprevalence in donations increased between June and August.<sup>14</sup>
- In the US, the RESPONSE (REDS-IV-P Epidemiology, Surveillance and Preparedness of the Novel SARS-CoV-2 Epidemic) Study aims to screen blood donations and monitor SARS-CoV-2 infections in key metropolitan areas. The study

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<sup>9</sup> <https://pipelinereview.com/index.php/2020101276148/Antibodies/Alexion-Receives-FDA-Approval-for-New-Advanced-Formulation-of-ULTOMIRIS-ravulizumab-cwvz-with-Significantly-Reduced-Infusion-Time.html>

<sup>10</sup> <https://pipelinereview.com/index.php/2020093076047/Small-Molecules/BioCrysts-Oral-Factor-D-Inhibitor-BCX9930-Shows-Clinical-Benefit-as-Monotherapy-Through-400-mg-bid-in-Treatment-naive-PNH-Patients.html>

<sup>11</sup> Executive Vice President, Global Medicines Development and Medical Affairs, and also Chief Medical Officer at Vertex

<sup>12</sup> <https://pipelinereview.com/index.php/2020101576182/Small-Molecules/Vertex-Provides-Update-on-its-Clinical-Programs-Targeting-Alpha-1-Antitrypsin-Deficiency.html>

<sup>13</sup> <https://pipelinereview.com/index.php/2020100176057/Antibodies/Harbour-BioMed-Announces-Dosing-of-First-Patients-in-Two-Phase-II-Clinical-Studies-of-Batoclimab-HBM9161-for-the-Treatment-of-Myasthenia-Gravis-and-Immune-Thrombocytopenia.html>

<sup>14</sup> <https://transfusionnews.com/2020/09/22/less-than-2-of-u-s-blood-donations-positive-for-sars-cov-2-antibodies/>

screened 1000 blood donations each month in New York City, San Francisco, Seattle, Los Angeles, Minneapolis, and Boston from March or April through to the end of June 2020. Seroreactivity for anti-SARS-CoV-2 spike-1 protein increased most in New York City. All other sites experienced modest increases in seroreactivity, with seroprevalence in June ranging from 0.6 per cent in San Francisco to 1.8 per cent in Boston. Approximately 147,000 donations from these same locations were also screened for SARS-CoV-2 RNA using nucleic acid testing (NAT) on mini-pooled samples. One mini-pool sample (in San Francisco) was found to be SARS-CoV-2 RNA positive. These results were interpreted to mean that SARS-CoV-2 RNA is rare in blood donations and that transfusion-transmission is unlikely.<sup>15</sup>

- Researchers at OneBlood in Florida reviewed over 250,000 donations collected from May to June in 2018, 2019, and 2020. Despite cancelled blood drives in 2020, there was still a significant increase in total donations during the pandemic for both males and females compared with 2018 and 2019. Mean donor age increased from 45 in 2018 and 2019 to 50 in 2020, largely due to a decrease in donors 16-29 years.<sup>16</sup>
- In Australia, Lifeblood has been calling on newly-tattooed donors to donate plasma. While a four-month deferral still applies for donations of whole blood, a study by Lifeblood and researchers from the University of New South Wales found that people tattooed in an Australian-licensed parlour are safe to donate plasma.<sup>17</sup>
- Cerus has signed an \$US 11.1 million contract with the FDA for the development of compounds for optimizing pathogen reduction treatment of whole blood, reducing the risk of transfusion-transmitted infections.<sup>18</sup>
- A UK study reported that "a randomised controlled trial has found no evidence of clinical benefit in giving intravenous iron preoperatively to patients undergoing major abdominal surgery".<sup>19</sup>
- Behnood Bikdeli<sup>20</sup> said in late September: "As of now there are more than 20 ongoing or registered randomized studies to address the questions of optimal anticoagulation in various subgroups of patients with COVID-19 -- from outpatients to inpatients or critically-ill patients".<sup>21</sup>
- New guidelines from the American Society of Hematology recommend a standard prophylactic anticoagulant dose over higher doses to prevent clotting in patients who have been hospitalised with COVID-19, including those in intensive care.<sup>22</sup>
- Baxter International announced observational data from the OxirisNet Registry that supported the rationale for using its Oxiris filter set for extracorporeal blood purification in cases of severe COVID-19.<sup>23</sup>

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<sup>15</sup> <https://transfusionnews.com/2020/10/07/serosurveillance-of-sars-cov-2-from-blood-donations-across-the-u-s/>

<sup>16</sup> <https://transfusionnews.com/2020/10/07/covid-19-pandemic-impacts-blood-donation-trends/>

<sup>17</sup> <https://www.abc.net.au/news/2020-10-08/inked-up-aussies-called-on-to-donate-plasma-as-rules-ease/12745812>

<sup>18</sup> <https://seekingalpha.com/article/4379349-cerus-inks-fda-contract-and-news-good-bad-and-ugly-of-biopharma>

<sup>19</sup> <https://thelimbic.com/haematology/preoperative-iv-iron-should-not-be-recommended-for-anaemia-study/> and [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31539-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31539-7/fulltext)

<sup>20</sup> Of Brigham and Women's Hospital and Harvard

<sup>21</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/88825>

<sup>22</sup> <https://www.hematology.org/newsroom/press-releases/2020/ash-releases-clinical-practice-guidelines-on-anticoagulation-in-patients-with-covid-19> and <https://thelimbic.com/haematology/preventive-anticoagulation-in-covid-19-should-be-given-at-a-standard-dose-ash/>

<sup>23</sup> <https://seekingalpha.com/pr/18059453-baxter-supports-new-study-showing-blood-purification-oxiris-filter-set-can-play-role-in> and <https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03322-6> and <https://seekingalpha.com/news/3626439-baxter-blood-filter-shows-potential-benefit-in-severely-ill-covidminus-19-patients>

- Philips has launched a single-use device for clearing clots from peripheral blood vessels.<sup>24</sup>

### 3. Plasma Products

- Takeda is working with drug delivery specialist Elektrofi to investigate whether that company's microparticle formulation technology could simplify delivery of plasma-derived therapies.<sup>25</sup>

### 4. Use of convalescent plasma in COVID-19

- Michael Joyner, principal investigator for the Expanded Access Program at the Mayo Clinic said: *"the largest study to date on convalescent plasma provides robust evidence that transfusion is safe in hospitalized patients with COVID-19"*.<sup>26</sup>
- Researchers profiled plasma samples from convalescent donors, finding "wide variability in the SARS-CoV-2 antibody response in terms of magnitude of response and antigens recognized".
- Doctors transfused a nine-week old baby, who had cardiopulmonary failure associated with COVID-19, with two units of convalescent plasma. She had not responded to remdesivir, but she recovered after the plasma transfusion.<sup>27</sup>
- In the second update of the systematic Cochrane review on use of convalescent plasma and hyperimmunoglobulin for COVID patients, authors analysed 19 studies including two completed randomized controlled trials on the use of convalescent plasma. They remained unclear as to whether convalescent plasma was of benefit to patients hospitalised with COVID-19. Without a control group, the relative safety of convalescent plasma therapy could not be assessed.<sup>28</sup>
- A randomized Phase II clinical trial of convalescent plasma in COVID-19 patients found it had no effect on progression to severe disease or all-cause mortality.<sup>29</sup>
- The US Defense Department collected more COVID-19 convalescent plasma in fiscal 2020 than they targeted. Their collection was "to support advanced illness within the force."<sup>30</sup>

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<sup>24</sup> <https://www.fiercebiotech.com/medtech/philips-launches-small-push-button-blood-clot-removal-system>

<sup>25</sup> <https://www.fiercepharma.com/drug-delivery/takeda-taps-elektrofi-s-microparticle-platform-for-potential-plasma-pairing>

<sup>26</sup> [https://mayoclinicproceedings.org/pb/assets/raw/Health%20Advance/journals/jmcp/jmcp\\_ft95\\_6\\_8.pdf](https://mayoclinicproceedings.org/pb/assets/raw/Health%20Advance/journals/jmcp/jmcp_ft95_6_8.pdf) and <https://www.medpagetoday.com/infectiousdisease/covid19/88863>

<sup>27</sup> <https://transfusionnews.com/2020/09/30/covid-19-convalescent-plasma-provides-more-than-neutralizing-antibodies/>

<sup>28</sup> <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013600.pub3/full>

<sup>29</sup> <https://www.fiercebiotech.com/biotech/convalescent-plasma-fails-phase-2-moderate-covid-19-patients> and <https://www.bmj.com/content/371/bmj.m3939>

<sup>30</sup> <https://www.airforcemag.com/esper-military-exceeded-covid-19-convalescent-plasma-collection-goal/>

- Researchers who conducted a Phase II trial on 400 hospitalised patients with moderate COVID-19 in India found that convalescent plasma may not block development of severe disease or reduce mortality risk. They wrote: "Evidence suggests that convalescent plasma collected from survivors of COVID-19 contains receptor binding domain specific antibodies with potent antiviral activity. However, effective titres of antiviral neutralizing antibodies, optimal timing for convalescent plasma treatment, optimal timing for plasma donation, and the severity class of patients who are likely to benefit from convalescent plasma remain unclear."<sup>31</sup> In an accompanying editorial<sup>32</sup>, Elizabeth B Pathak suggested the results should be interpreted with caution. She referred readers to a recent safety analysis in 20,000 US patients which had concluded: "These updated data provide robust evidence that transfusion of convalescent plasma is safe in hospitalized patients with COVID-19, and support the notion that earlier administration of plasma within the clinical course of COVID-19 is more likely to reduce mortality".<sup>33</sup>

## 5. Use of hyperimmune immunoglobulin in COVID-19

- Companies in the [CoVlg-19 Plasma Alliance](#), including CSL Behring and Takeda, began commercial manufacturing of coronavirus hyperimmune immunoglobulin. Manufacturing relies on donations of convalescent plasma.<sup>34</sup> The US National Institute of Allergy and Infectious Diseases (NIAID) is running a Phase III clinical trial. The batches of the drug used in the clinical trial were produced by CSL Behring in Bern and Takeda in Georgia. Patient enrolment continues in the trial, called Inpatient Treatment with Anti-Coronavirus Immunoglobulin (ITAC). It is evaluating the safety, tolerability and efficacy of hyperimmune intravenous immunoglobulin for preventing serious complications of COVID-19. The international multicentre, double-blind, placebo-controlled, randomised trial is in 500 adults (at almost 60 sites in 18 countries) who have had symptoms for 12 days or fewer, without life-threatening organ dysfunction or end-organ failure. Patients will receive remdesivir as well. Dr Bill Mezzanotte, co-leader of the CoVlg-19 Alliance and Chief Medical Officer, CSL Behring, said: "Thanks to the unprecedented collaboration from the CoVlg-19 Plasma Alliance members, commitment from those who have recovered from the virus and generously chosen to donate their plasma, as well as the strong support from the US National Institutes of Health, we are hopeful that data from the clinical trial will be available before the end of the year."

## 6. Clinical experience in COVID-19

- Two studies have found that a large proportion of asymptomatic people with COVID-19 go on to develop symptoms.<sup>35</sup>
- Brian Garibaldi<sup>36</sup> and colleagues have developed the [COVID-19 Inpatient Risk Calculator](#) with 24 variables associated with COVID-19 severity, including symptom

<sup>31</sup> <https://www.medscape.com/viewarticle/939662> and <https://www.bmj.com/content/371/bmj.m3939> and <https://www.msn.com/en-us/health/medical/convalescent-plasma-did-not-reduce-covid-19-deaths-or-keep-patients-from-severe-illness-in-new-study/ar-BB1ajdcp?ocid=uxbndblng>

<sup>32</sup> <https://www.bmj.com/content/371/bmj.m4072>

<sup>33</sup> <https://pubmed.ncbi.nlm.nih.gov/32861333/>

<sup>34</sup> <https://www.fiercepharma.com/manufacturing/takeda-led-alliance-starts-manufacturing-covid-19-plasma-therapy-as-phase-3-kicks-off>

<sup>35</sup> <https://www.medscape.com/viewarticle/938195> and <https://journals.plos.org/plosmedicine/article> and <https://thorax.bmj.com/content/early/2020/08/28/thoraxjnl-2020-215042>

<sup>36</sup> associate professor of medicine at the Johns Hopkins University School of Medicine in Baltimore

severity at the time of admission, underlying conditions, vital signs, age, and body mass index.<sup>37</sup>

- The COVID Human Genetic Effort is a project covering more than 50 sequencing hubs and many more hospitals. Its first results show that “more than 10 per cent of healthy people who develop severe COVID-19 have misguided antibodies that attack the patient’s own immune system, rather than the invading virus”. Furthermore, there are “at least another 3.5 per cent carrying genetic mutations that impair their immune response to the virus”.<sup>38</sup>
- A study has compared the difference between the different immune response in adults from that in children, and suggested that in the latter “a branch of the immune system that evolved to protect against unfamiliar pathogens rapidly destroys the coronavirus before it wreaks damage on their bodies”.<sup>39</sup>
- Researchers reported that stroke may be the presenting symptom of COVID-19 in patients under the age of 50.<sup>40</sup>
- A study has shown “the spectrum of cardiac manifestations among paediatric patients during the SARS-CoV2 pandemic, allowing for better detection and preparation for treatment in clinical settings”.<sup>41</sup>
- Researchers reported that a sometimes fatal COVID-19 complication reported occasionally in children, multisystem inflammatory syndrome (MIS-C), is distinct from both Kawasaki disease and severe adult cases of COVID-19.<sup>42</sup>
- In the US, the Biomedical Advanced Research and Development Authority (BARDA) has awarded a contract to Beckman Coulter to develop a rapid diagnostic test for children with COVID-19 to provide early warning of the development of MIS-C.<sup>43</sup>
- MIS-C is now being reported in adults.<sup>44</sup>
- A study found that babies born to mothers with COVID-19 are not usually adversely affected by the virus.<sup>45</sup>
- Researchers have reported that autopsies on COVID-19 patients found heart damage to be common, but more from clotting than from inflammation.<sup>46</sup>
- New research published in the *Journal of the American College of Cardiology* shows one in four people hospitalised with COVID-19 suffer heart damage<sup>47</sup> while a series of review papers<sup>48</sup> summarise what is known so far, and why patients who have existing heart disease have an elevated risk of severe COVID-19.

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<sup>37</sup> <https://www.medscape.com/viewarticle/938201>

<sup>38</sup> <https://labonline.com.au/content/life-scientist/article/the-missing-link-behind-severe-cases-of-covid-19--217276414>

<sup>39</sup> <https://www.theage.com.au/world/north-america/research-shines-light-on-how-children-fight-off-the-coronavirus-20200928-p55zsd.html>

<sup>40</sup> <https://www.medscape.com/viewarticle/938344> and <https://n.neurology.org/content/early/2020/09/15/WNL.000000000010851>

<sup>41</sup> <https://www.2minutemedicine.com/covid-19-associated-with-a-wide-range-of-cardiac-manifestations-in-pediatric-patients/>

<sup>42</sup> <https://www.the-scientist.com/news-opinion/kids-severe-covid-19-reaction-bears-unique-immune-signature-67996>

<sup>43</sup> <https://www.fiercebiotech.com/medtech/barda-taps-beckman-coulter-to-develop-a-blood-test-for-mis-c-severe-childhood-illness>

<sup>44</sup> <https://7news.com.au/lifestyle/health-wellbeing/a-rare-covid-19-complication-was-reported-in-children-now-its-showing-up-in-adults-c-1402226> and <https://www.healio.com/news/infectious-disease/20201002/sarscov2-causes-inflammatory-syndrome-in-adults-that-resembles-misc>

<sup>45</sup> <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/most-newborns-of-covid-19-infected-moms-fare-well-761508.html>

<sup>46</sup> <https://www.medpagetoday.com/meetingcoverage/tct/89143>

<sup>47</sup> <https://www.onlinejacc.org/content/76/17/2011> and <https://www.abc.net.au/news/health/2020-10-21/coronavirus-covid-19-effects-on-the-heart/12795726>

<sup>48</sup> <https://www.onlinejacc.org/content/76/17>

- Researchers have reported that elderly people are not necessarily more likely to contract COVID-19, but if they do contract it they are at higher risk of dying.<sup>49</sup>
- The journal *Blood Advances* on 27 October carried articles reporting that:
  - a. blood group O is associated with a decreased risk for contracting SARS-CoV-2 infection<sup>50</sup>; and
  - b. COVID-19 patients with blood group A or AB are at increased risk for requiring mechanical ventilation compared with those with blood group O or B; and they also appear to exhibit a greater disease severity than patients with blood group O or B.<sup>51</sup>
- Researchers reported that in patients hospitalised for COVID-19, admission levels of a specific protein predict the development of acute kidney injury and the need for dialysis.<sup>52</sup>

## 7. Developing vaccines for COVID-19

### Vaccine trials and research

- Paul A Offit, director of the Vaccine Education Center at Children’s Hospital of Philadelphia, told the American Academy of Pediatrics National Conference that children should be included in COVID-19 vaccine trials.<sup>53</sup> Pfizer’s COVID-19 vaccine is being tested in children as young as 12.<sup>54</sup>
- Hong Kong researchers will in November begin Phase I trials of a vaccine against both influenza and COVID-19.<sup>55</sup>
- LabCorp released a COVID-19 antibody test for measuring vaccine efficacy.<sup>56</sup>
- The US FDA allowed AstraZeneca to restart its COVID-19 vaccine trial in the US.<sup>57</sup> This large, late-stage US trial had been placed on hold from 6 September, after a study participant in the UK fell ill. While the UK trial was permitted to restart quickly, as was the trial in Japan, the US FDA broadened its investigation.
- The Brazilian health authority Anvisa allowed a clinical trial of the AstraZeneca to continue despite the death of a volunteer.<sup>58</sup>
- Johnson & Johnson paused its 60,000- person Phase III trial of its COVID-19 vaccine because of an unexplained illness in a participant.<sup>59</sup> Johnson and Johnson had begun a Phase III trial in late September of its COVID-19 vaccine with a single-injection regimen.<sup>60</sup>

<sup>49</sup> <https://www.nature.com/articles/s41598-020-73777-8> and <https://www.medscape.com/viewarticle/939210>

<sup>50</sup> <https://doi.org/10.1182/bloodadvances.2020002657>

<sup>51</sup> <https://doi.org/10.1182/bloodadvances.2020002623>

<sup>52</sup> <https://www.medscape.com/viewarticle/939052>

<sup>53</sup> <https://www.healio.com/news/infectious-disease/20201004/time-to-include-children-in-covid19-vaccine-trials-experts-say>

<sup>54</sup> <https://edition.cnn.com/2020/10/26/health/covid-vaccine-pfizer-trial-kids/>

<sup>55</sup> <https://bgr.com/2020/10/09/coronavirus-flu-vaccine-hong-kong-spray-phase-1-trial-november/>

<sup>56</sup> <https://www.fiercebiotech.com/medtech/labcorp-launches-quantitative-covid-19-antibody-test-for-measuring-vaccine-effectiveness>

<sup>57</sup> <https://www.abc.net.au/news/2020-10-24/astrazeneca-johnson-and-johnson-coronavirus-vaccine-trials/12810090> and <https://www.fiercepharma.com/pharma/coronavirus-tracker-novavax-boasts-billion-plus-shot-capacity-by-2021-russia-s-world-first>

<sup>58</sup> <https://www.reuters.com/article/health-coronavirus-brazil-vaccine/update-4-astrazeneca-covid-19-vaccine-trial-brazil-volunteer-dies-trial-to-continue-idUSL1N2HC1O6> and <https://www.medscape.com/viewarticle/939534>

<sup>59</sup> <https://www.fiercebiotech.com/biotech/j-j-hits-pause-covid-19-vaccine-trial-for-unexplained-illness>

<sup>60</sup> <https://www.biopharmadive.com/news/johnson-johnson-coronavirus-vaccine-first-data/585910/>

- A Phase 1 trial in 40 adults over the age of 55 suggests that Moderna's vaccine elicits an immune system response that's equal to that seen in younger recipients. Researchers said vaccine side effects "were predominantly mild or moderate in severity" and included fatigue, chills, headache or ache or discomfort at the injection site.<sup>61</sup> A study in adults over 75 would perhaps be of more interest, given the concentration of COVID-19 deaths in that age group.
- Ose Immunotherapeutics will enrol up to 400 patients for Phase I and Phase II clinical trials of an experimental coronavirus vaccine. Ose believes a subgroup of Tcells ("killer cells") can be programmed to attack cells infected by a virus and recognise multiple coronavirus proteins.<sup>62</sup>
- German company CureVac is conducting a Phase IIa trial of its COVID-19 vaccine in Peru and Panama. It plans to begin a global trial in 30,000 patients before the end of the year.<sup>63</sup>
- COVAXX began its Phase 1, open-label, dose-escalation study of the UB-612 vaccine candidate for COVID-19 in Taiwan.<sup>64</sup>
- Altimmune reported on its intranasal COVID-19 vaccine and therapeutic programs at the World Vaccine Congress.<sup>65</sup>
- [Medigen Vaccine Biologics Corporation \(MVC\)](#) and [Dynavax Technologies Corporation](#) announced that MVC had been awarded a Taiwan government subsidy for initiating a Phase I clinical trial in Taiwan. The first participant was dosed with MVC's COVID-19 vaccine combined with Dynavax's CpG 1018 adjuvant at National Taiwan University Hospital in early October. The grant received by MVC was for purposes of research and development of a locally produced COVID-19 vaccine.<sup>66</sup>
- Sanofi Pasteur and Translate Bio announced the preclinical results for MRT5500, an mRNA-based vaccine candidate against SARS-CoV-2, the virus that causes COVID-19. They said that MRT5500 demonstrated a favourable immune response profile against SARS-CoV-2. A Phase I/ II clinical trial is following.<sup>67</sup>
- ImmunityBio announced it had received authorization from the US FDA to commence a Phase I clinical trial of hAd5-COVID-19, its COVID-19 vaccine candidate that "targets both the inner nucleocapsid (N), engineered to activate T cells, and outer spike (S) protein, engineered to activate antibodies against SARS-CoV-2. These dual constructs (bivalent sequences) of SARS-CoV-2 offer the potential for the hAd5

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<sup>61</sup> <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/early-results-show-moderna-s-covid-vaccine-safe-effective-in-older-people-761713.html> and <https://www.healio.com/news/infectious-disease/20200929/earlystage-covid19-vaccine-data-provides-good-news-for-older-adults> and

<https://www.nih.gov/news-events/news-releases/investigational-covid-19-vaccine-well-tolerated-generates-immune-response-older-adults>

<sup>62</sup> <https://www.reuters.com/article/us-health-coronavirus-vaccines-oseimmuno/frances-ose-to-enrol-up-to-400-for-t-cell-coronavirus-vaccine-trials-idUSKBN2742DT>

<sup>63</sup> <https://in.reuters.com//article/idINKBN26L098> and <https://pipelinereview.com/index.php/2020093076040/Vaccines/CureVac-Initiates-Phase-2a-Clinical-Trial-of-COVID-19-Vaccine-Candidate.html>

<sup>64</sup> <https://pipelinereview.com/index.php/2020092876017/Vaccines/COVAXX-Initiates-Phase-1-Clinical-Trial-of-COVID-19-Vaccine-UB-612-in-Taiwan.html>

<sup>65</sup> <https://pipelinereview.com/index.php/2020092976028/Vaccines/Altimmune-Presents-Highlights-of-Intranasal-COVID-19-Vaccine-and-Therapeutic-Programs-AdCOVID-and-T-COVID-at-the-World-Vaccine-Congress.html>

<sup>66</sup> <https://pipelinereview.com/index.php/2020101476169/Vaccines/Medigens-COVID-19-Vaccine-Combined-with-Dynavaxs-CpG-1018-Adjuvant-Receives-Taiwan-Government-Subsidy-with-First-Participant-Dosed-in-Early-October.html>

<sup>67</sup> <https://pipelinereview.com/index.php/2020101576187/Vaccines/Sanofi-and-Translate-Bio-mRNA-COVID-19-Vaccine-Candidate-Induced-High-Antibody-Levels-in-Preclinical-Studies.html> and <https://www.biorxiv.org/content/10.1101/2020.10.14.337535v1>

vaccine to provide recipients with durable, long-term cell-mediated immunity with potent antibody stimulation against both the S and N proteins”.<sup>68</sup>

- Vaxart’s CEO said that the company’s “room temperature stable oral tablet vaccine has the potential to ease many of the problems associated with distribution and administration of cold chain dependent injectable vaccines and may make herd immunity more achievable by making it much easier to vaccinate more people faster.” Vaxart has begun early-stage testing of VXA-CoV2-1 in 48 healthy volunteers aged between 18 and 54.<sup>69</sup>
- Merck began Phase I/ II testing of a COVID-19 vaccine, after acquiring Themis and partnering with the International AIDS Vaccine Initiative (IAVI). It is a live attenuated vaccine that could be given orally, and the company hopes it will be a one-dose vaccine.<sup>70</sup>
- Novavax began a Phase III trial of its vaccine in the UK.<sup>71</sup>

### Vaccine approval, manufacture and distribution

- Moderna began a rolling submission to Health Canada for mRNA-1273, its COVID-19 vaccine.<sup>72</sup> The company said it did not expect to file in the US for emergency use authorization for its vaccine until late November.<sup>73</sup>
- BARDA (see above) has contracted with Cytiva to expand capacity to assist vaccine manufacturing e.g. cell culture and bioreactors.<sup>74</sup>
- The European Medicines Agency’s Committee for Medicinal Products for Human Use began the first ‘rolling review’ of the COVID-19 vaccine being developed by AstraZeneca in collaboration with the University of Oxford.<sup>75</sup>
- The Australian Government said it might take a year to roll out a COVID-19 vaccine, depending on which candidates succeed.<sup>76</sup>
- Sanofi and GlaxoSmithKline agreed with the Canadian Government to supply up to 72 million doses of their adjuvanted COVID-19 vaccine, starting in 2021.<sup>77</sup>
- Inovio faced additional questions from the US FDA about its planned Phase II/ III trial of its vaccine candidate INO-4800, including its delivery device to be used in the trial.<sup>78</sup> Delivery requires small electrical pulses to open pores in cell walls large

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<sup>68</sup> <https://pipelinereview.com/index.php/2020101676191/Vaccines/FDA-Authorizes-Phase-1-Trial-of-ImmunityBios-Novel-COVID-19-Vaccine-Candidate-hAd5-Dual-Construct-is-Designed-to-Drive-Both-T-Cell-and-Antibody-Immunity.html>

<sup>69</sup> <https://www.reuters.com/article/health-coronavirus-vaxart/update-1-vaxart-begins-early-stage-trial-of-oral-covid-19-vaccine-candidate-idUSL4N2H42XQ>

<sup>70</sup> <https://www.fiercepharma.com/pharma/merck-advancing-single-dose-and-oral-coronavirus-vaccines-could-still-make-warp-speed>

<sup>71</sup> <https://www.fiercebiotech.com/biotech/novavax-kickstarts-u-k-phase-3-covid-vaccine-u-k-as-cases-surge-across-country>

<sup>72</sup> <https://www.pharmaceutical-technology.com/news/moderna-rolling-submission/>

<sup>73</sup> <https://www.fiercepharma.com/pharma/moderna-s-coronavirus-vaccine-won-t-be-ready-for-before-late-november-ceo-says-ft>

<sup>74</sup> <https://www.fiercepharma.com/manufacturing/contract-manufacturer-cytiva-tasked-covid-19-vaccine-work-as-part-31m-us-government>

<sup>75</sup> <https://pipelinereview.com/index.php/2020100276074/Vaccines/EMA-starts-first-rolling-review-of-a-COVID-19-vaccine-in-the-EU.html>

<sup>76</sup> <https://www.abc.net.au/news/2020-10-26/covid-19-vaccine-rollout-will-take-time-but-how-long/12811364> and <https://www.abc.net.au/news/2020-10-25/the-logistics-of-lab-to-jab-covid-19-vaccine/12808914>

<sup>77</sup> <https://medicaldialogues.in/news/industry/pharma/gsk-sanofi-ink-covid-19-vaccine-supply-deal-with-canada-69916>

<sup>78</sup> <https://pipelinereview.com/index.php/2020092876015/Vaccines/INOVIIO-reports-FDA-partial-clinical-hold-for-planned-Phase-2-/-3-trial-of-COVID-19-vaccine-candidate-INO-4800.html>

enough to permit passage of the DNA plasmid which encodes production of the coronavirus' characteristic "spike" protein'.<sup>79</sup>

## 8. Potential treatments for COVID-19

### Antibodies

- Initial data for Regeneron's COVID-19 antibody cocktail shows that the highest dose reduced virus levels and relieved symptoms more quickly than did the placebo in patients infected with COVID-19 but not hospitalised.<sup>80</sup>
- US President Donald Trump, having tested positive for COVID-19, received the Regeneron antibody cocktail, remdesivir, and steroids.<sup>81</sup>
- Former FDA Commissioner Scott Gottlieb said that as Regeneron pursues an emergency use authorization for its antibody cocktail (following the President's endorsement), companies are already "too late" to scale up production to meet the potential US demand for antibody doses in 2020. He said between 300,000 and 400,000 antibody treatment courses would be needed nationally each month during a "difficult fall and winter".<sup>82</sup>
- The US National Institutes of Health has been testing antibody treatments in COVID-19 patients.<sup>83</sup>
- The independent data safety monitoring board of the ACTIV-3 clinical trial paused enrolment in the study, which was evaluating Eli Lilly's investigational SARS-CoV-2 neutralizing antibody bamlanivimab (LY-CoV555) as a treatment for COVID-19 in hospitalised patients. The study was sponsored by NIAID.<sup>84</sup> It was discontinued in hospitalised patients when investigators found LY-CoV555 was unlikely to improve outcomes in that patient population.<sup>85</sup> The company hoped the antibody might prove useful for non-hospitalised patients. Eli Lilly planned to seek an emergency use authorization from the US FDA for its antibody treatments, but the FDA raised concerns about a manufacturing site.<sup>86</sup>

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<sup>79</sup> <https://www.biopharmadive.com/news/inovio-coronavirus-vaccine-FDA-hold/585990/>

<sup>80</sup> <https://www.fiercebitech.com/biotech/regeneron-s-covid-19-antibody-cocktail-curbs-virus-speeds-recovery-early-data> and <https://www.biopharmadive.com/news/regeneron-antibody-coronavirus-study-results/586105/> and

<https://pipelinereview.com/index.php/2020093076039/Antibodies/Regenerons-REGN-COV2-Antibody-Cocktail-Reduced-Viral-Levels-and-Improved-Symptoms-in-Non-Hospitalized-COVID-19-Patients.html>

<sup>81</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/88943>

<sup>82</sup> <https://www.fiercepharma.com/manufacturing/amid-regeneron-s-emergency-use-bid-former-fda-chief-says-u-s-too-late-mass>

<sup>83</sup> <https://www.reuters.com/article/us-health-coronavirus-nih/nih-starts-clinical-trial-testing-antibody-treatments-in-covid-19-patients-idUSKBN26Y2F1>

<sup>84</sup> <https://pipelinereview.com/index.php/2020101576184/Antibodies/Lilly-Statement-on-the-NIAID-Decision-to-Pause-Enrollment-in-ACTIV-3-Clinical-Trial.html> and <https://www.fiercepharma.com/manufacturing/eli-lilly-hot-water-fda-for-manufacturing-issues-at-plant-handling-covid-19-antibody>

<sup>85</sup> <https://www.fiercebitech.com/biotech/lilly-s-covid-19-antibody-fails-trial-hospitalized-patients> and <https://www.niaid.nih.gov/news-events/statement-nih-sponsored-activ-3-trial-closes-ly-cov555-sub-study> and <https://www.cnbc.com/2020/10/13/us-pauses-eli-lillys-trial-of-a-coronavirus-antibody-treatment-over-safety-concerns.html>

<sup>86</sup> <https://www.fiercepharma.com/manufacturing/eli-lilly-could-face-warning-letter-after-follow-up-fda-inspection-at-covid-19>

- Merck has partnered with non-profit scientific research organisation IAVI and Serum Institute of India to develop monoclonal antibodies for COVID-19. Scientists from IAVI's Neutralizing Antibody Center based at Scripps Research helped identify antibodies from convalescent plasma that can neutralise SARS-CoV-2.<sup>87</sup>
- Aridis Pharmaceuticals is developing an inhaled neutralizing antibody for COVID-19, AR-711. It was reported to have cleared signs of SARS-CoV-2 virus from infected hamsters using a lower dose than for other experimental monoclonal antibodies.<sup>88</sup>
- Sorrento Therapeutics released preclinical data reporting on COVI-GUARD™ (STI-1499) and COVI-AMG™ (STI-2020; Affinity Matured COVI-Guard) neutralizing antibodies (nAbs) against SARS-CoV-2 as well as a D614G virus variant infection.<sup>89</sup> Both STI-1499 and STI-2020 demonstrated potent neutralizing activities against SARS-CoV-2 virus infection in preclinical models. STI-1499 nAb has been cleared by the FDA for a Phase 1 clinical trial in hospitalised COVID-19 patients.<sup>90</sup>
- IONTAS and FairJourney Biologics announced the discovery of potent SARS-CoV2 neutralizing antibodies. Their efficacy in viral neutralization was, the companies reported, independently verified by the National Institute for Biological Standards and Control (NIBSC).<sup>91</sup>
- Impact BioMedical formed a new wholly owned subsidiary, Innate Immune, to initiate efficacy testing of a pancoronavirus vaccine, designed to protect against multiple coronaviruses.<sup>92</sup>
- The Gates Foundation has awarded Evotec funds to develop antibody treatments for COVID-19 in low-income countries.<sup>93</sup>
- Two reports in *ScienceImmunology* suggest that people with COVID-19 develop antibodies that last at least three months.<sup>94</sup>
- New research shows that antibody levels in the blood of coronavirus patients fall rapidly after the body clears the virus.<sup>95</sup>
- AstraZeneca has concluded a \$US 486 million deal with the US government to provide up to 100,000 doses of its experimental COVID-19 antibody treatment, if it receives regulatory approval.<sup>96</sup> The grant will fund two Phase III trials of the antibody cocktail AZD7442. The larger study will investigate whether the antibodies can prevent infection for up to a year, as a result of Astra Zeneca's use of half-life extension technology.<sup>97</sup>

<sup>87</sup> [http://www.pharmatimes.com/news/merck\\_kgaa\\_iavi\\_and\\_serum\\_institute\\_link\\_up\\_to\\_develop\\_covid-19\\_mabs\\_1354671](http://www.pharmatimes.com/news/merck_kgaa_iavi_and_serum_institute_link_up_to_develop_covid-19_mabs_1354671)

<sup>88</sup> <https://www.fiercebiotech.com/research/inhaled-antibody-drug-for-covid-19-clears-coronavirus-animals> and <https://www.biorxiv.org/content/10.1101/2020.10.14.339150v1>

<sup>89</sup> <https://biorxiv.org/cgi/content/short/2020.09.27.316174v1>

<sup>90</sup> <https://pipelinereview.com/index.php/2020092976025/Antibodies/Sorrento-Releases-Preclinical-Data-for-STI-1499-COVI-Guard-and-STI-2020-COVI-AMG-Potent-Neutralizing-Antibodies-Against-SARS-CoV-2.html>

<sup>91</sup> <https://pipelinereview.com/index.php/2020092876011/Antibodies/IONTAS-and-FairJourney-Biologics-Discover-SARS-CoV2-Neutralizing-Antibodies-with-Picomolar-Potency.html>

<sup>92</sup> <https://pipelinereview.com/index.php/2020100276075/Vaccines/Impact-BioMedical-to-Begin-Efficacy-Testing-of-Pan-Coronavirus-Vaccine-Under-New-Wholly-Owned-Subsidiary-Innate-Immune-Inc.html>

<sup>93</sup> <https://www.fiercebiotech.com/biotech/evotec-nabs-bill-and-melinda-gates-foundation-cash-for-low-income-countries-covid-antibody>

<sup>94</sup> <https://immunology.sciencemag.org/content/5/52/eabe5511> and <https://immunology.sciencemag.org/content/5/52/eabe0367>

<sup>95</sup> <https://mbio.asm.org/content/11/5/e02590-20> and <https://www.medscape.com/viewarticle/939372>

<sup>96</sup> [https://www.upi.com/Top\\_News/US/2020/10/12/AstraZeneca-US-govt-sign-deal-for-COVID-19-antibody-treatment/1641602500260/](https://www.upi.com/Top_News/US/2020/10/12/AstraZeneca-US-govt-sign-deal-for-COVID-19-antibody-treatment/1641602500260/)

<sup>97</sup> <https://www.fiercebiotech.com/biotech/astrazeneca-gets-486m-to-test-if-covid-19-antibodies-can-provide-12-months-protection>

- Experts from the Infectious Diseases Society of America (IDSA) reportedly told a media briefing “that while manufacturers of monoclonal antibody treatment, Regeneron and Eli Lilly, both applied for emergency use authorization (EUA) from the FDA to treat COVID-19, the data on both so far have yet to demonstrate any impact on patient care”.<sup>98</sup>

### Remdesivir

- The US FDA approved Gilead Sciences' antiviral drug remdesivir (Veklury) for treating patients hospitalised with COVID-19.<sup>99</sup>
- A placebo-controlled double-blinded study (led by Dr John Beigel from NIAID) found that on average patients on remdesivir for COVID-19 recovered five days faster than those on placebo. Patients who were severely ill recovered seven days faster on average.<sup>100</sup>
- Gilead is now directly responsible for seeing remdesivir distributed to US hospitals, ending a five-month period when the US Department of Health and Human services was responsible for allocating it.<sup>101</sup>
- A World Health Organization (WHO) study found that remdesivir did not help hospitalised COVID-19 patients.<sup>102</sup>
- The final report from the Adaptive COVID-19 Treatment Trial (ACCT-1), published in *The New England Journal of Medicine*, supported the view that remdesivir shortens recovery in hospitalised patients, although “researchers said antiviral treatment alone is probably not sufficient for all patients”.<sup>103</sup>
- An international Phase III clinical trial investigating the safety, tolerability, and efficacy of remdesivir plus hyperimmune intravenous immunoglobulin has begun. It is sponsored by NIAID.<sup>104</sup>

### Other therapies

- Merck is working with Ridgeback Bio on the antiviral drug molnupiravir.<sup>105</sup>
- A large WHO trial concluded that patients prescribed any of four antivirals (remdesivir, hydroxychloroquine, lopinavir-ritonavir, and interferon) were not any

<sup>98</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/89065> see also [https://www.bmj.com/content/371/bmj.m3937?=&utm\\_source=adestra&utm\\_medium=email&utm\\_campaign=usage&utm\\_content=daily&utm\\_term=text](https://www.bmj.com/content/371/bmj.m3937?=&utm_source=adestra&utm_medium=email&utm_campaign=usage&utm_content=daily&utm_term=text)

<sup>99</sup> <https://www.abc.net.au/news/2020-10-23/gilead-remdesivir-gets-us-fda-approval-for-hospitalised-covid-19/12806434> and [http://www.pharmatimes.com/news/gileads\\_covid-19\\_drug\\_remdesivir\\_bags\\_us\\_approval\\_1354674](http://www.pharmatimes.com/news/gileads_covid-19_drug_remdesivir_bags_us_approval_1354674) and <https://www.fiercepharma.com/pharma/gilead-scores-full-fda-approval-for-covid-19-drug-veklury-as-cases-spike-again>

<sup>100</sup> <https://www.fiercepharma.com/pharma/gilead-sciences-remdesivir-reduces-covid-19-mortality-new-analysis> and <https://www.nejm.org/doi/full/10.1056/NEJMoa2007764> and <https://consumer.healthday.com/infectious-disease-information-21/coronavirus-1008/remdesivir-speeds-recovery-for-covid-patients-762034.html>

<sup>101</sup> <https://www.fiercepharma.com/pharma/gilead-takes-back-remdesivir-distribution-after-drop-demand-confusing-government-allocation>

<sup>102</sup> <https://www.abc.net.au/news/2020-10-17/world-health-organization-remdesivir-not-useful-for-coronavirus/12778296>

<sup>103</sup> <https://www.healio.com/news/infectious-disease/20201008/final-trial-results-continue-to-show-benefit-from-remdesivir-for-covid19>

<sup>104</sup> <https://www.pharmacytimes.com/> and <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-testing-hyperimmune-intravenous-immunoglobulin-plus-remdesivir-treat-covid-19-begins>

<sup>105</sup> <https://www.fiercepharma.com/pharma/merck-looks-ahead-to-a-covid-drug-and-vaccine-and-a-gardasil-recovery-as-pandemic-takes-a-2>

more likely to survive than those who did not receive one of them. Nor were their hospital stays any shorter.<sup>106</sup>

- The randomized RECOVERY trial found that treatment with lopinavir-ritonavir did not reduce 28-day mortality or the risk of moving to mechanical ventilation in hospitalised patients with COVID-19.<sup>107</sup>
- Johns Hopkins researchers say that it may be possible to prevent COVID-19 from causing severe complications by blocking a specific protein.<sup>108</sup>
- A nasal treatment called INNA-051, designed to boost the immune system to fight common colds and flu, has reduced COVID-19 viral replication. INNA-051 is being developed by Australian company, Ena Respiratory.<sup>109</sup>
- New studies of Roche's Actemra in treating COVID-19 have given mixed results.<sup>110</sup>
- In the US, the National Institutes of Health launched a Phase III clinical trial investigating the safety and efficacy of three immune modulators against the "cytokine storm" that can accompany COVID-19: infliximab and abatacept, both already used as therapies in rheumatoid arthritis, and an investigational late-stage drug developed by AbbVie.<sup>111</sup>
- Scientists reported that genetically engineered cells can be used as decoys to bind and neutralize SARS-oV-2 *in vitro*.<sup>112</sup>
- In the US, a small clinical study led by researchers from the National Cancer Institute suggested that the blood cancer drug acalabrutinib might assist patients with breathing difficulties in severe COVID-19.<sup>113</sup>
- NIAID began a study to identify which therapies or investigational drugs show sufficient promise against COVID-19 to justify their advancement into larger clinical trials. The ACTIV-5 Big Effect Trial will enrol adult volunteers across around 40 US hospitals. It is being conducted with the National Institutes of Health's public-private partnership program, Accelerating COVID-19 Therapeutic Innovations and Vaccines (ACTIV).<sup>114</sup>
- A trial in the UK is testing whether the anti-tumour necrosis factor (TNF) drug adalimumab is effective for treating COVID-19 patients in non- hospital settings (including aged care facilities).<sup>115</sup>

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<sup>106</sup> <https://www.forbes.com/sites/williamhaseltine/2020/10/20/massive-covid-19-drug-trial-underscores-the-importance-of-controlled-clinical-studies/#63b516a41681> and <https://labonline.com.au/content/life-scientist/news/disappointing-results-for-who-s-covid-19-therapeutics-trial-118303326>

<sup>107</sup> <https://www.medpagetoday.org/infectiousdisease/covid19/89216>

<sup>108</sup> <https://bgr.com/2020/10/14/coronavirus-cure-factor-d-inhibitor-johns-hopkins-study/>

<sup>109</sup> <https://www.pharmiweb.com/press-release/2020-09-27/preventative-nasal-spray-shown-to-reduce-viral-replication-by-up-to-96-in-covid-19-challenge-study>

<sup>110</sup> <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2772185> and

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2772186> and

<https://www.fiercepharma.com/pharma/does-roche-s-actemra-work-covid-19-new-studies-once-again-depict-mixed-picture>

<sup>111</sup> <https://www.nih.gov/news-events/news-releases/nih-begins-large-clinical-trial-test-immune-modulators-treatment-covid-19>

<sup>112</sup> <https://www.the-scientist.com/news-opinion/decoy-cells-trick-sars-cov-2-reduce-cytokines-in-vitro-68042> and <https://www.pnas.org/content/early/2020/10/05/2014352117>

<sup>113</sup> <https://magazine.medlineplus.gov/article/cancer-medicine-may-help-treat-covid-19-breathing-problems>

<sup>114</sup> <https://www.nih.gov/news-events/news-releases/nih-study-aims-identify-promising-covid-19-treatments-larger-clinical-trials>

<sup>115</sup> <https://www.bmj.com/content/371/bmj.m3847>

- Humanigen, in seeking an emergency use authorization from the US FDA for the use of lenzilumab in COVID-19, will collaborate with Thermo Fisher Scientific to increase manufacturing capacity.<sup>116</sup>
- A patient in the UK has been treated in a new COVID-19 trial investigating the use of GlaxoSmithKline's experimental rheumatoid arthritis drug, otilimab, for severe lung disease.<sup>117</sup>
- Researchers have designed "miniproteins" which in the laboratory bound tightly to the SARS-CoV-2 spike protein so the virus could not infect human cells.<sup>118</sup>

## 9. Managing the pandemic

### Individual country experience

- Sweden's Prime Minister said in late September that the country's resurgence of COVID-19 was "because many people seem to have set aside months of caution in favour of full-on social life once again".<sup>119</sup>
- Scientists have been surprised that Africa's fatality rate from COVID-19 has been lower than expected. Some are testing whether the widely used BCG vaccine against tuberculosis has provided cross-protection.<sup>120</sup>
- The Chinese Center for Disease Control and Prevention said it had detected and isolated living coronavirus on the outer packaging of frozen cod.<sup>121</sup>
- Chinese authorities conducted mass coronavirus testing across the entire city of Kashgar, after a large number of asymptomatic cases were detected.<sup>122</sup>
- COVIDIQ is a text messaging platform that collects self-reported COVID-19 symptoms. It reportedly identified Florida's spike in COVID-19 cases long before it was reported by the state's Department of Health.<sup>123</sup>
- The US had a case in Nevada of reinfection with COVID-19, with differences between the variants confirmed by genomic sequencing.<sup>124</sup>
- A person who tested positive to COVID-19 in Victoria in October had already tested positive in July. The Chief Health Officer said this could be a very rare case of reinfection, or the person could still be shedding non-infectious fragments of the virus from the July infection.
- Safer Care Victoria, the state's healthcare quality and safety agency, has been contacting 243 people whose blood glucose levels were tested while they were in

<sup>116</sup> <https://seekingalpha.com/news/3616446-humanigen-inks-manufacturing-deal-thermo-fisher-for-lenzilumab>

<sup>117</sup> [http://www.pharmatimes.com/news/first\\_uk\\_patient\\_given\\_gsks\\_experimental\\_arthritis\\_drug\\_in\\_covid-19\\_trial\\_1351634](http://www.pharmatimes.com/news/first_uk_patient_given_gsks_experimental_arthritis_drug_in_covid-19_trial_1351634)

<sup>118</sup> <https://www.nih.gov/news-events/nih-research-matters/computer-designed-proteins-may-protect-against-coronavirus>

<sup>119</sup> <https://www.medscape.com/viewarticle/937984>

<sup>120</sup> <https://www.medscape.com/viewarticle/938238>

<sup>121</sup> <https://7news.com.au/lifestyle/health-wellbeing/china-claims-frozen-food-could-spread-covid-19-c-1406254>

<sup>122</sup> <https://www.abc.net.au/news/2020-10-27/china-to-test-whole-city-in-xinjiang-after-coronavirus-cluster/12816224> and <https://7news.com.au/lifestyle/health-wellbeing/mystery-mass-infection-chinas-symptomless-covid-cases-surge-c-1459423>

<sup>123</sup> <https://www.healio.com/news/infectious-disease/20201023/text-message-platform-beats-health-department-in-identifying-covid19-spike>

<sup>124</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/89077> and [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3680955](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3680955) and [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30764-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30764-7/fulltext) and [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30783-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30783-0/fulltext)

hotel quarantine, over concerns about the "potential risk of cross-contamination and infection" through the use single blood glucose monitors for multiple patients.<sup>125</sup>

- A cargo ship anchored off the Queensland coast was suspected of carrying a previously undetected strain of COVID-19.<sup>126</sup>

## Transmission

- A randomized trial, stopped early when judged futile, found there was no clinical benefit in using hydroxychloroquine for COVID-19 pre-exposure prophylaxis among a small sample of hospital-based healthcare staff.<sup>127</sup>
- A CSIRO study found the SARS-CoV-2 virus may be able to survive up to 28 days on glass, stainless steel and even banknotes. Both the researchers and commentators have emphasised the need for caution over how these results are interpreted as "they do not translate to conditions influencing real-world transmission".<sup>128</sup>
- An open letter in *The Lancet* from over 80 biomedical experts said that the "renewed interest in a so-called herd immunity approach" for COVID-19 is a "dangerous fallacy unsupported by scientific evidence."<sup>129</sup>
- A new study published in the journal *Nature* says humidity and temperature do not seem to have an impact on the coronavirus as much as other viruses, so COVID-19 does not appear to be seasonal.<sup>130</sup>

## Testing

- The US FDA has approved a COVID-19 antibody test designed for use at point-of-care.<sup>131</sup>
- US scientists reporting on a study of more than 5,000 genetic sequences of the SARS-CoV-2 virus confirmed that the virus is continually mutating.<sup>132</sup>
- From 15 October, United Airlines offered COVID-19 tests to passengers flying from San Francisco International Airport to Hawaii.<sup>133</sup>
- The IDSA has issued new guidelines in the journal *Clinical Infectious Diseases* on when to test for COVID-19 antibodies. The Society says that "antibodies to the novel coronavirus do not show up in the blood for quite a while after someone becomes infected, so serology tests are unreliable for diagnosing COVID-19 unless a patient has been sick for weeks".<sup>134</sup>
- The US FDA has approved a "rinse and spit" test for COVID-19.<sup>135</sup>

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<sup>125</sup> <https://www.abc.net.au/news/2020-10-19/hotel-quarantine-residents-infection-blood-glucose-monitors/12782910>

<sup>126</sup> <https://www.abc.net.au/news/2020-10-21/ship-with-mystery-covid-19-strain-anchors-off-sunshine-coast/12796842>

<sup>127</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/88883> and <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771265>

<sup>128</sup> <https://newatlas.com/health-wellbeing/coronavirus-study-survive-28-days-surfaces-banknotes/>

<sup>129</sup> <https://www.medscape.com/viewarticle/939161>

<sup>130</sup> <https://www.nature.com/articles/s41598-020-74089-7> and [https://www.medscape.com/viewarticle/939137?nlid=137831\\_5404&src=wnl\\_dne\\_201015\\_mscpedit&uac=239431PV&implID=2620677&faf=1](https://www.medscape.com/viewarticle/939137?nlid=137831_5404&src=wnl_dne_201015_mscpedit&uac=239431PV&implID=2620677&faf=1)

<sup>131</sup> <https://www.fiercebiotech.com/medtech/fda-green-lights-its-first-coronavirus-antibody-blood-test-for-point-care>

<sup>132</sup> <https://www.washingtonpost.com/health/2020/09/23/houston-coronavirus-mutations/?arc404=true>

<sup>133</sup> <https://www.fiercehealthcare.com/tech/united-airlines-teams-up-color-to-make-covid-19-tests-available-to-passengers>

<sup>134</sup> <https://www.medscape.com/viewarticle/938164> and <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1343/5904785>

<sup>135</sup> <https://www.fiercebiotech.com/medtech/fda-authorizes-oral-rinse-and-spit-test-for-covid-19>

- Caltech researchers have designed a new sensor for at-home diagnosis of COVID-19 infection.<sup>136</sup>
- The American Academy of Pediatrics has updated guidance on how and when to test children for the SARS-CoV-2 virus.<sup>137</sup>
- Doctors from the Royal College of Pathologists of Australasia warned a new rapid coronavirus test, approved by the Therapeutic Goods Administration, “detects the signs of the coronavirus in between 50 and 94 per cent of cases” and is therefore not reliable.<sup>138</sup>
- In regional Victoria, some COVID-19 testing has been based on mouth swabs.<sup>139</sup>
- A Queensland based company says it has developed a test which can detect whether someone is a COVID-19 “super spreader”.<sup>140</sup>
- The WHO hopes to make available to low-income countries 120 million rapid diagnostic tests for the SARS-CoV-2 virus.<sup>141</sup>
- 50 Boots pharmacies in the UK are marketing LumiraDx 12-minute COVID-19 test for consumer use in those without symptoms.<sup>142</sup>

## Masks

- Researchers at Flinders University have tested commonly available fabric face masks. They “found they significantly reduce the number of aerosolised viruses a wearer could be exposed to, with even the poorest-performing mask filtering at least 50 per cent of viruses.”<sup>143</sup>
- Research has emphasised that where cloth masks are in use for infection control, they should be washed appropriately in hot water and soap every day.<sup>144</sup>

<sup>136</sup> <https://www.sciencetimes.com/articles/27559/20201002/new-graphene-based-sensor-rapidly-detects-covid-19-infection.htm>

<sup>137</sup> <https://www.healio.com/news/primary-care/20201016/aap-updates-interim-covid19-guidance>

<sup>138</sup> <https://www.abc.net.au/news/2020-10-02/coronavirus-australia-live-blog-queensland-pubs-clubs/12723430>

<sup>139</sup> <https://www.abc.net.au/news/2020-10-09/bendigo-health-authority-rolls-out-saliva-covid-19-testing/12747126>

<sup>140</sup> <https://www.abc.net.au/news/2020-10-28/could-test-detect-if-someone-is-a-coronavirus-superspreader/12818638> and <https://www.news.com.au/world/coronavirus/health/worldfirst-coronavirus-test-can-detect-superspreaders-infectious-rate/news-story/297a3b4b233fd482523726028946efba> and <https://www.nationalgeographic.com/science/2020/10/why-people-are-coronavirus-superspreaders-how-body-emits-infectious-particles/>

<sup>141</sup> <https://www.abc.net.au/news/2020-09-29/who-unveils-rapid-diagnostic-testing-in-lower-income-countries/12712462>

<sup>142</sup> <https://www.fiercebiotech.com/medtech/british-pharmacy-chain-sells-lumiradx-12-minute-covid-test-for-consumer-use-those-without> and <https://www.fiercebiotech.com/medtech/helix-grabs-boosted-fda-emergency-usage-for-covid-test-can-look-out-asymptomatic-carriers>

<sup>143</sup> <https://labonline.com.au/content/consumables/news/fabric-masks-prove-effective-at-virus-filtration-1195773820> and <https://www.mdpi.com/2076-0817/9/9/762>

<sup>144</sup> <https://blogs.bmj.com/bmj/2020/09/29/raina-macintyre-cloth-masks-should-be-washed-appropriately-everyday/>

## 10. Miscellaneous news

### Infectious diseases other than COVID-19

- Singapore suspended flu vaccination with two of the four products it had approved.<sup>145</sup>
- Scientists have newly identified two antibodies that protect against strains of influenza B. The findings may assist in the development of a broad-spectrum influenza drug.<sup>146</sup>
- Virologists at the university of Wisconsin at Madison have outlined a T-cell-based vaccine strategy that was effective against multiple strains of influenza virus in mice. It is administered through the nose.<sup>147</sup>
- China reported an H9N2 avian influenza case in Guangdong province which had occurred in August.<sup>148</sup>
- The FDA has approved Regeneron's Inmazeb to treat Zaire ebolavirus in adults and children. The drug combines three monoclonal antibodies. Regeneron has been developing Inmazeb since 2015 under a partnership with tBARDA.<sup>149</sup>
- The Western NSW Local Health District has issued a reminder about the effects of Q fever on farmers, and the importance of being vaccinated.<sup>150</sup> A study reported in 2019 on 2,740 blood donations in Queensland and NSW showed the incidence of Q fever in the rural population was higher than expected.<sup>151</sup>
- Researchers report that the bacteria responsible for scarlet fever, *Streptococcus pyogenes*, has been mutating and making a resurgence, after being infected by viruses.<sup>152</sup>
- Scientists have gene-edited the parasite that causes leishmaniasis, so it can be administered as a vaccine to give immunity without infection.<sup>153</sup>

### Other

- Researchers from the US National Institutes of Health reported in the *New England Journal of Medicine* that they have identified a new inflammatory disorder (vacuoles, E1 enzyme, X-linked, autoinflammatory and somatic syndrome or VEXAS), which is caused by mutations in the *UBA1* gene. VEXAS causes symptoms that include venous blood clots, recurrent fevers, pulmonary abnormalities and unusual cavity-like in myeloid cells (vacuoles).<sup>154</sup>

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<sup>145</sup> <https://www.moh.gov.sg/news-highlights/details/temporary-cessation-of-use-of-two-influenza-vaccines> and <https://www.fiercepharma.com/vaccines/sanofi-sk-flu-shots-halted-singapore-as-south-korea-post-vaccination-deaths-climb-to-59>

<sup>146</sup> <https://www.techexplorist.com/two-antibodies-protect-against-influenza-b-virus-strains/35469/>

<sup>147</sup> <https://www.genengnews.com/news/t-cell-based-vaccine-effective-against-multiple-influenza-virus-strains/> and [https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(20\)30121-X](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(20)30121-X)

<sup>148</sup> <http://outbreaknowtoday.com/china-h9n2-avian-influenza-case-reported-in-guangdong-province-71917/>

<sup>149</sup> <https://www.fiercepharma.com/pharma/amid-covid-19-effort-regeneron-wins-first-fda-approval-for-ebola-treatment>

<sup>150</sup> <https://www.parkeschampionpost.com.au/story/6962621/farmers-urged-to-protect-livelihoods-by-vaccinating-against-q-fever/>

<sup>151</sup> <https://www.abc.net.au/news/2019-03-09/q-fever-breakthrough-study-reveals-exposure-risk/10882162>

<sup>152</sup> <https://www.abc.net.au/news/2020-10-08/scarlet-fever-incidence-on-the-rise-bacteria-infected-by-viruses/12740806>

<sup>153</sup> <https://newatlas.com/science/crispr-gene-edited-parasite-leishmaniasis-vaccine/>

<sup>154</sup> <https://www.nih.gov/news-events/news-releases/scientists-use-clues-human-genome-discover-new-inflammatory-syndrome>

- UK correspondents to *Nature* have written that UK departure from EU research "will be 'catastrophic' for COVID-19 and other research".<sup>155</sup>
- The US FDA has approved GlaxoSmithKline's biologic drug Nucala to treat hypereosinophilic syndrome (HES). The syndrome is caused by overproduction of a type of white blood cell.<sup>156</sup>

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<sup>155</sup> <https://www.medscape.com/viewarticle/938053>

<sup>156</sup> <https://www.fiercepharma.com/pharma/glaxosmithkline-s-nucala-earns-fda-nod-for-rare-white-blood-cell-disease-shot-to-rival>