

# Monitoring International Trends

## March- April 2021

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.

Highlights include:

Interest continued in new treatments for blood disorders, including haemophilia (page 3), sickle cell disease and thalassemia (page 3) and hereditary angioedema (page 4). Although Bluebird bio received European approval for its gene therapy for severe beta thalassemia in June 2019, it has failed to agree a price with German authorities, and it has withdrawn from that market.

In safety and patient blood management, a study found that 42-day old red blood cells deliver oxygen as well as 7-day old red blood cells (page 4), a study suggested that “larger randomized clinical trials comparing restrictive and liberal transfusion thresholds in patients with myocardial infarctions are needed” (page 4) and new anaemia treatments are in trials (pages 4 and 5).

With respect to the COVID-19 pandemic, concerns have included variant strains of the virus (page 6), use of immunoglobulin in vaccine induced thrombosis and thrombocytopenia (page 12), vaccine supply shortages and advice following developing experience with adverse events (from page 13). By the end of the month, India’s overwhelming infections and deaths were dominating global discussion (page 17).

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# 1. Treating blood disorders

## Haemophilia

- Swedish Orphan Biovitrum (Sobi™) announced dosing of the first patient in the phase III, open-label, interventional XTEND-Kids study of efanesoctocog alfa (BIVV001) in paediatric subjects with severe haemophilia A<sup>1</sup>.
- The European Medicines Agency accepted for filing a marketing authorisation application from LFB for its recombinant Factor VIIa, eptacog beta (activated)<sup>2</sup>.
- Sanofi introduced lower dosing of its haemophilia drug fitusiran in clinical trials to reduce the risk of blood clots<sup>3</sup>.
- A review study has found, not surprisingly, that “women who are haemophilia carriers are at a higher risk of experiencing heavy bleeding after giving birth, particularly those who are not on a prophylactic, or preventive, treatment regimen<sup>4</sup>.

## Sickle cell disease and thalassemia

- Vertex and CRISPR Therapeutics have upgraded their agreement concerning a new gene editing therapy for sickle cell disease and transfusion-dependent thalassemia, CTX 001<sup>5</sup>.
- Bluebird bio received European approval for its gene therapy, Zynteglo, for severe beta thalassemia in June 2019. It then set a price of \$US 1.8 million. It has failed to agree a price with German authorities, and it is withdrawing from that market. Negotiations continue with other European countries<sup>6</sup>.
- Imara opened higher dose arms in its two Phase IIb trials assessing the safety and efficacy of its investigational therapy for sickle cell disease<sup>7</sup>.
- A new multi-centre Phase III trial of Poloxamer 188 did not find that it shortened painful vaso-occlusive crises in adult and paediatric patients with sickle cell disease<sup>8</sup>. Poloxamer 188 is a purified form of the non-ionic block copolymer that is designed to decrease blood viscosity and facilitate microvascular blood flow.

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<sup>1</sup> [First patient dosed in phase 3 XTEND-Kids study with efanesoctocog alfa in children with haemophilia A | Sobi](#)

<sup>2</sup> <https://pipelinereview.com/index.php/2021030177552/Proteins-and-Peptides/LFB-Announces-that-the-European-Medicines-Agency-EMA-Has-Accepted-for-Filing-the-Marketing-Authorization-Application-for-eptacog-beta-activated-a-Recombinant-Coagul.html>

<sup>3</sup> [Sanofi Revises Fitusiran Dosing Regimen to Mitigate Risk of Vascular Thrombosis | National Hemophilia Foundation](#) and <https://hemophilianewstoday.com/2021/03/01/fitusiran-dosing-phase-3-trials-reduced-to-lower-risk-of-blood-clots/>

<sup>4</sup> <https://hemophilianewstoday.com/2021/04/05/hemophilia-carriers-at-high-risk-for-heavy-bleeding-after-childbirth-review-finds/>

<sup>5</sup> <https://www.fiercebiotech.com/biotech/vertex-takes-lead-crispr-therapeutics-partnership-900m-upfront>

<sup>6</sup> <https://www.biopharmadive.com/news/bluebird-withdraw-zynteglo-germany-price/598689/>

<sup>7</sup> <https://sicklecellanemianews.com/2021/03/30/imara-opens-higher-dose-arms-in-phase-2b-trials-testing-imr-687-sickle-cell-disease-scd-beta-thalassemia/>

<sup>8</sup> <https://www.medpagetoday.com/hematologyoncology/hematology/92178> and [Effect of Poloxamer 188 vs Placebo on Painful Vaso-Occlusive Episodes in Children and Adults With Sickle Cell Disease: A Randomized Clinical Trial | Hematology | JAMA | JAMA Network](#) and [Purified Poloxamer 188 for Treatment of Acute Vaso-occlusive Crisis of Sickle Cell Disease: A Randomized Controlled Trial | Hematology | JAMA | JAMA Network](#) and [Poloxamer 188 for Sickle Cell Disease | Hematology | JAMA | JAMA Network](#)

- Data from the Phase III HOPE clinical trial showed that dosing with oral voxelotor leads to “rapid and sustained rises in haemoglobin levels, reduces red blood cell destruction (haemolysis), and improves overall health in adolescents and adults with sickle cell disease”<sup>9</sup>.
- Scientists at the US Institutes of Health say they have discovered how DNA fragments can trigger inflammation in sickle cell disease<sup>10</sup>.

### Hereditary Angioedema

- The US Food and Drug Administration (FDA) announced a clinical hold on KalVista Pharmaceuticals’ planned Phase II trial of its prophylactic drug for hereditary angioedema, KVD824. The FDA is seeking further information and analysis of preclinical studies<sup>11</sup>.
- BioCryst Pharmaceuticals announced that the Committee for Medicinal Products for Human Use of the European Medicines Agency had recommended the approval of ORLADEYO™ (berotralstat) for routine prevention of recurrent attacks of hereditary angioedema in patients aged 12 years and older<sup>12</sup>.

## 2. Safety, patient blood management and blood products

- *Transfusion News* reports that a study has found that 42-day old red blood cells deliver oxygen as well as 7-day old red blood cells<sup>13</sup>.
- The UK government has reduced its long-standing ban on the use of local blood plasma to manufacture plasma-based therapies<sup>14</sup>.
- AABB has published an article drawing attention again to hospital-acquired anaemia, under the title “Blood belongs in the patient, not in a tube”<sup>15</sup>.
- A non-inferiority trial of restrictive transfusion thresholds for people with acute myocardial infarction concluded that its non-inferiority margin “may have been too large, thus potentially masking a clinically important harm for patients in the liberal group. Additional larger randomized clinical trials comparing restrictive and liberal transfusion thresholds in patients with myocardial infarctions are needed, as this trial was also not powered to determine superiority”<sup>16</sup>.
- Akebia Therapeutics submitted a new drug application to the US FDA for vadadustat, its oral hypoxia-inducible factor prolyl hydroxylase inhibitor developed to treat anaemia in adult patients whether or not they are on dialysis<sup>17</sup>.

<sup>9</sup> <https://sicklecellanemianews.com/2021/04/13/oxbryta-trial-data-hemoglobin-hemolysis-adults-adolescents-sickle-cell-disease/>

<sup>10</sup> <https://www.nih.gov/news-events/news-releases/nih-scientists-discover-how-dna-fragments-can-trigger-inflammation-sickle-cell-disease>

<sup>11</sup> <https://www.biospace.com/article/fda-places-hold-on-kalvista-s-hereditary-angioedema-trial/>

<sup>12</sup> <https://pipelinereview.com/index.php/2021022677525/Small-Molecules/BioCryst-Receives-Positive-CHMP-Opinion-for-ORLADEYO-berotralstat-an-Oral-Once-daily-Therapy-to-Prevent-Attacks-in-Patients-with-Hereditary-Angioedema.html>

<sup>13</sup> <https://transfusionnews.com/2021/03/29/42-day-old-rbcs-deliver-oxygen-as-well-as-7-day-old-rbcs/?>

<sup>14</sup> <https://thelimbic.com/haematology/mad-cow-curbs-on-blood-plasma-lifted-by-uk>

<sup>15</sup> <https://www.aabb.org/docs/default-source/default-document-library/resources/blood-belongs-in-the-patient.pdf>

<sup>16</sup> <https://transfusionnews.com/2021/02/24/randomized-noninferiority-trial-of-restrictive-transfusion-thresholds-for-patients-with-acute-myocardial-infarction>

<sup>17</sup> <https://www.healio.com/news/nephrology/20210414/akebia-files-new-drug-application-for-anemia-drug>

- BioAge commenced a Phase IIa study of BGE-117 for unexplained anaemia of aging. The drug is administered orally and activates hypoxia signalling<sup>18</sup>.
- Fibrogen and AstraZeneca had hoped the US Food and Drug Administration would quickly approve their new drug application for their investigational anaemia therapy roxadustat, but the FDA announced it is constituting an advisory committee of external experts<sup>19</sup>.
- Two recent studies<sup>20</sup> found that donor body mass index is positively correlated with red blood cell haemolysis<sup>21</sup>.
- While there is some uncertainty about whether tick-borne Lyme disease can be transmitted by blood transfusion<sup>22</sup>, Lyme disease bacteria are known to be able to live in donated blood being stored prior to transfusion. The US Centers for Disease Control says that people being treated for Lyme disease should not donate blood<sup>23</sup>. Now a polymerase chain reaction (PCR) test under investigation has been found to indicate the presence of a gene of the spirochete *Borrelia burgdorferi* which causes Lyme disease. This allows scientists to distinguish between early and late infection<sup>24</sup>.
- Opinions vary on whether Lyme disease is present in Australia. NSW Health says: “Although locally-acquired Lyme disease cannot be ruled out, there is little evidence that it occurs in Australia. There is a continuing risk of Lyme disease for overseas travellers”<sup>25</sup>. The Lyme Disease Association of Australia says: “The first Australian-acquired case of Lyme disease was reported in New South Wales in 1982. Current and accurate figures of Lyme cases in Australia are unknown because Lyme disease is not a notifiable disease in Australia and patients are not formally counted. Many patients with Lyme disease are not properly tested and are often diagnosed with other conditions in the early stage of their illness”<sup>26</sup>.
- In 2015 researchers from Murdoch University, the University of Sydney and Curtin University said they had found organisms in one tick that could trigger an illness similar to Lyme disease<sup>27</sup>.
- In developed nations, Kawasaki disease is seen as the primary trigger for acquired heart disease in children, and it is known to have the potential to cause coronary artery lesions in paediatric patients. An association between these lesions and resistance to intravenous immunoglobulin has been suspected, and a meta-analysis is reported to confirm this<sup>28</sup>.

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<sup>18</sup> <https://pipelinereview.com/index.php/2021022577515/Small-Molecules/BioAge-Initiates-Phase-2a-Trial-of-BGE-117-in-Elderly-Patients-with-Unexplained-Anemia.html>

<sup>19</sup> <https://www.biospace.com/article/last-minute-fda-advisory-panel-puts-a-kink-in-approval-hopes-for-anemia-drug/>

<sup>20</sup> <https://transfusionnews.com/2021/03/03/higher-donor-body-mass-index-is-associated-with-increased-rbc-hemolysis>

<sup>21</sup> The rupture of red cells and the release of their contents into plasma.

<sup>22</sup> Although untreated Lyme disease during pregnancy can lead to infection of the placenta, and occasionally the disease is spread to the foetus.

<sup>23</sup> [Transmission | Lyme Disease | CDC](#)

<sup>24</sup> <https://www.medscape.com/viewarticle/949349>

<sup>25</sup> [Lyme disease fact sheet - Fact sheets \(nsw.gov.au\)](#)

<sup>26</sup> [About Lyme disease - Lyme Disease Association of Australia](#)

<sup>27</sup> [Researchers find bacteria in tick that may cause Lyme disease-like symptoms - ABC \(none\) - Australian Broadcasting Corporation](#)

<sup>28</sup> [Novel Inflammation Marker May Predict Coronary Artery Lesions in Kawasaki Disease - Rheumatology Advisor](#) and [Is there an association between intravenous immunoglobulin resistance and coronary artery lesion in Kawasaki disease?—Current evidence based on a meta-analysis \(plos.org\)](#)

- South Korea's GC Pharma<sup>29</sup> submitted its biologics licence application for GC5107 (Immune Globulin Intravenous (Human) 10% Liquid) to the US FDA<sup>30</sup>.

#### 4. Variant strains of COVID-19

- The head of COVID-19 Genomics UK says the world is going to need booster doses for its COVID-19 vaccines, to deal with future variants<sup>31</sup>.
- Researchers in the UK said the UK variant B.1.1.7 has a significantly higher death rate<sup>32</sup>. However, two studies have suggested there is no evidence that the UK variant causes more severe disease, although it may be more easily transmitted than other strains<sup>33</sup>.
- A study found the South African variant to be much more resistant to COVID vaccines from Pfizer and Moderna than was thought to be the case<sup>34</sup>.
- Moderna announced that it had produced clinical trial material for its variant-specific vaccine candidate, mRNA-1273.351, against the SARS-CoV-2 variant B.1.351 first identified in South Africa. It had shipped doses for a Phase 1 clinical trial that will be led and funded by the US National Institute of Allergy and Infectious Diseases<sup>35</sup>.
- Pfizer and BioNTech announced they had begun evaluating the safety and immunogenicity of a third dose of their COVID-19 vaccine to determine the effect of a booster on immunity against COVID-19 caused by known and possibly emerging SARS-CoV-2 variants. The study will approach participants from the previous Phase 1 study in the US and offer them the opportunity to receive a 30 µg booster of the current vaccine 6 to 12 months after receiving their initial two-doses<sup>36</sup>.
- Researchers say the Brazil variant can reinfect people who have recovered from COVID-19<sup>37</sup>.

#### 5. Clinical experience in COVID-19

- Some children and teenagers who have been infected with SARS-CoV-2 seem to suffer long-lasting symptoms, as adults do<sup>38</sup>.

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<sup>29</sup> Previously known as Green Cross Corporation

<sup>30</sup> <https://pipelinereview.com/index.php/2021022677527/Antibodies/GC-Pharma-Submits-Biologics-License-Application-to-US-FDA-for-Immune-Globulin-GC5107.html>

<sup>31</sup> [Exclusive: Regular booster vaccines are the future in battle with COVID-19 virus, top genome expert says | Reuters](#)

<sup>32</sup> [UK COVID-19 variant has significantly higher death rate, study finds \(yahoo.com\)](#)

<sup>33</sup> <https://www.medscape.com/viewarticle/949163> and [Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study - The Lancet Infectious Diseases](#) and [Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study - The Lancet Public Health](#)

<sup>34</sup> [This is the worst news we've seen about coronavirus vaccines and the South African variant – BGR](#) and <https://www.nature.com/articles/s41586-021-03398-2> reference.pdf

<sup>35</sup> <https://pipelinereview.com/index.php/2021022577511/Vaccines/Moderna-Announces-it-has-Shipped-Variant-Specific-Vaccine-Candidate-mRNA-1273.351-to-NIH-for-Clinical-Study.html>

<sup>36</sup> <https://pipelinereview.com/index.php/2021022577513/Vaccines/Pfizer-and-BioNTech-Initiate-a-Study-as-Part-of-Broad-Development-Plan-to-Evaluate-COVID-19-Booster-and-New-Vaccine-Variants.html>

<sup>37</sup> <https://www.medscape.com/viewarticle/946698> and <https://www.medscape.com/viewarticle/946746> and <https://www.medscape.com/viewarticle/946641>

<sup>38</sup> <https://www.the-scientist.com/news-opinion/kids-may-suffer-from-long-covid-but-data-are-scarce-68511>

- Scientists reported<sup>39</sup> that in hospitalised patients, seizures were common, and mortality was higher amongst patients who had seizures.
- Preliminary data from a US study suggests that multiple sclerosis patients treated with ocrelizumab had a weaker antibody response after COVID-19 than MS patients not on the drug, but T cell levels were similar between the two groups<sup>40</sup>.
- A study suggests that people suffering from what has been called “long COVID” are at greater risk of dying within six months of contracting the disease<sup>41</sup>.
- A study published in *The Lancet* suggests that reinfection with COVID-19 within six months is rare, but more likely to occur in those aged over 65<sup>42</sup>.
- US scientists say that when testing for natural infection amongst vaccinated people it is preferable to use an antibody test measuring host reactivity to the nucleocapsid protein of SARS-CoV-2 than to rely on an assay that measures reactivity to the viral spike protein<sup>43</sup>.
- Case reviews suggested to researchers that only a minority of paediatric patients had reported illness with prior SARS-CoV-2 when they developed multisystem inflammatory syndrome (MIS-C)<sup>44</sup>.
- A study found that in some paediatric patients COVID-19 or MIS-C resulted in kidney injury<sup>45</sup>.
- A US study found that almost a third of patients hospitalised in the US with COVID-19 needed ICU treatment, and 28 per cent of them died<sup>46</sup>.
- New-onset atrial fibrillation and atrial flutter are observed with similar frequency in hospitalised patients with COVID-19 and with influenza, with clinicians suggesting the connection between the arrhythmias and the infections is related to the general inflammatory state<sup>47</sup>.
- Researchers report that COVID-19 patients presenting with gastrointestinal symptoms have reduced mortality<sup>48</sup>.

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<sup>39</sup> [Electroencephalographic Abnormalities are Common in COVID-19 and are Associated with Outcomes - Lin - 2021 - Annals of Neurology - Wiley Online Library](#) and <https://www.the-scientist.com/news-opinion/seizures-common-in-hospitalized-covid-19-patients-68659>

<sup>40</sup> <https://www.medpagetoday.com/meetingcoverage/aan/92165>

<sup>41</sup> [COVID-19: Study reveals fears over Long COVID sufferers \(news.com.au\)](#)

<sup>42</sup> [COVID Reinfection Rare, but Those Over 65 at High Risk: Lancet \(thequint.com\)](#) and <https://health.economicstimes.indiatimes.com/news/industry/uncertainty-looms-on-how-frequently-covid-reinfection-occurs/81625016>

<sup>43</sup> <https://www.news-medical.net/news/20210421/Seroprevalence-studies-monitoring-SARS-CoV-2-among-vaccinees-require-more-than-spike-assays.aspx>

<sup>44</sup> <https://www.the-scientist.com/news-opinion/most-kids-with-mis-c-report-few-or-no-covid-19-symptoms-study-68646> and <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2778429> and [Kids' Severe COVID-19 Reaction Bears Unique Immune Signature | The Scientist Magazine® \(the-scientist.com\)](#)

<sup>45</sup> <https://www.the-scientist.com/news-opinion/some-children-with-covid-19-or-mis-c-face-kidney-injury-study-68536> and [Acute kidney injury in pediatric patients hospitalized with acute COVID-19 and multisystem inflammatory syndrome in children associated with COVID-19 - Kidney International \(kidney-international.org\)](#)

<sup>46</sup> [https://www.upi.com/Health\\_News/2021/03/04/coronavirus-hospitalization-icu-death-study/1771614869103/](https://www.upi.com/Health_News/2021/03/04/coronavirus-hospitalization-icu-death-study/1771614869103/) and <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777028>

<sup>47</sup> <https://www.healio.com/news/cardiology/20210304/af-atrial-flutter-in-covid19-may-be-tied-to-inflammation>

<sup>48</sup> <https://www.healio.com/news/gastroenterology/20210304/patients-presenting-with-covid19-gi-symptoms-have-reduced-mortality>

- In 2020, a woman in Michigan died following the transplant of lungs not known at the time to be infected with COVID-19. A report on the medical experience gained through that incident has now been published<sup>49</sup>.
- Researchers at Brigham and Women's Hospital found that SARS-CoV-2, the virus responsible for COVID-19, may be attracted to the blood group antigen A found on the lining of the lungs<sup>50</sup>.
- A US study found children and teenagers hospitalised with COVID-19 frequently had neurologic symptoms<sup>51</sup>.
- A survey of recovered patients discharged from hospital found respiratory symptoms could persist for six months<sup>52</sup>.
- A report has associated overweight populations with more severe COVID\_19 and higher mortality<sup>53</sup>.
- Researchers say that while cytokine storms can happen in influenza and other coronavirus infections, in COVID-19 they are triggered in a different way and have the potential to be more severe<sup>54</sup>.
- Some patients with "long COVID" symptoms have reported improvement after one dose of vaccine<sup>55</sup>.

## 6. Potential treatments for COVID-19 not mentioned elsewhere

- Israel's Kamada and Italy's Kedrion Biopharma are progressing with their development of an anti-COVID therapy derived from convalescent plasma sourced in the US. The therapy is being used in Israel<sup>56</sup>.
- The US National Institutes of Health stopped a clinical trial evaluating the safety and effectiveness of COVID-19 convalescent plasma in patients with mild to moderate symptoms. Following its interim analysis of the Clinical Trial of COVID-19 Convalescent Plasma of Outpatients (C3PO), an independent data and safety monitoring board "determined that while the convalescent plasma intervention caused no harm, it was unlikely to benefit this group of patients"<sup>57</sup>.
- Brisbane biotech company Implicit Bioscience has developed an anti-inflammatory drug which is being tested in the US as a potential treatment for severely ill COVID-19 patients. Professor Ian Frazer said: "it's also a treatment... potentially for any disease that causes severe long-lasting inflammation... It switches off one part of the immune pathway which causes trouble rather than benefit ... anywhere where chronic damage is produced by inflammation. It's an antibody so it's infused into the bloodstream and basically it targets the molecule on the surface of one of the white

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<sup>49</sup> [Donor To Recipient Transmission Of SARS-CoV-2 By Lung Transplantation Despite Negative Donor Upper Respiratory Tract Testing - Kaul - - American Journal of Transplantation - Wiley Online Library](#) and <https://www.medpagetoday.com/special-reports/exclusives/91464>

<sup>50</sup> <https://www.healio.com/news/hematology-oncology/20210304/study-suggests-link-between-covid19-blood-group-a-and-ancient-protein-family>

<sup>51</sup> <https://www.medpagetoday.com/infectiousdisease/covid19/91509>

<sup>52</sup> <https://www.healio.com/news/pulmonology/20210304/respiratory-symptoms-persist-6-months-after-hospitalization-for-covid19-survey>

<sup>53</sup> <https://www.washingtonpost.com/world/2021/03/04/coronavirus-overweight-global-report>

<sup>54</sup> <https://www.medscape.com/viewarticle/946900>

<sup>55</sup> <https://www.medpagetoday.com/special-reports/exclusives/91476>

<sup>56</sup> [Israel's Kamada forges ahead with development of new anti-Covid immunoglobulin therapy in partnership with Kedrion Biopharma of Italy \(prnewswire.com\)](#)

<sup>57</sup> <https://www.healio.com/news/primary-care/20210303/another-covid19-convalescent-plasma-trial-ends-prematurely> and <https://www.the-scientist.com/news-opinion/nih-halts-outpatient-covid-19-convalescent-plasma-trial-68514>

blood cells, that particular target is a key regulator of inflammation and if we block that pathway then the inflammation dies down”<sup>58</sup>.

- Eli Lilly and Incyte’s baricitinib did not meet its primary endpoints in a Phase III trial in hospitalised patients<sup>59</sup>.
- Eli Lilly said it had a revised agreement with the US government for its antibody drug, bamlanivimab, which will now be sold in combination with another therapy<sup>60</sup>. The company agreed to provide 100,000 doses of the bamlanivimab-etesevimab combination for \$US 210 million by the end of March, and the government has the option to purchase 1.1 million more doses before 25 November<sup>61</sup>.
- Eli Lilly announced that the European Medicines Agency’s Committee for Medicinal Products for Human Use issued a positive opinion for bamlanivimab alone and bamlanivimab administered together with etesevimab. The opinion advised that bamlanivimab alone and bamlanivimab in combination with etesevimab can be used for the treatment of confirmed COVID-19 in patients aged 12 or more who are not receiving supplemental oxygen and who are at high risk of progressing to severe disease. The scientific opinion of the European Medicines Agency’s human medicines committee can be considered by the EU member states when making decisions on the use of the therapies before a formal marketing authorization is issued<sup>62</sup>.
- The US FDA cleared Sorrento to proceed with its Phase I safety and pharmacokinetic trial of its intranasal COVIDROPS in healthy volunteers and in patients newly diagnosed with mild COVID-19<sup>63</sup>.
- Roche confirmed that the European Medicines Agency’s Committee for Medicinal Products for Human Use supported the use of the investigational antibody cocktail, casirivimab and imdevimab, in COVID-19 patients who do not require oxygen supplementation and who are at high risk of progressing to severe COVID-19. Roche is collaborating with Regeneron to develop, manufacture and distribute casirivimab and imdevimab worldwide, with the aim of having over two million doses available this year<sup>64</sup>. In the US, Regeneron had earlier announced changes to the Phase III trial of REGEN-COV™ (casirivimab with imdevimab) in outpatients with COVID-19. The Independent Data Monitoring Committee noted clinical efficacy in decreasing hospitalisation and mortality with both the 1,200 mg and 2,400 mg doses of REGEN-COV compared with placebo. It recommended ceasing enrolment into the placebo group<sup>65</sup>.

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<sup>58</sup> <https://www.abc.net.au/news/2021-04-16/queensland-covid-19-us-drug-trial-treatment-covid-patients/100070558>

<sup>59</sup> [http://www.pharmatimes.com/news/lilly\\_incytes\\_olumiant\\_fails\\_in\\_covid-19\\_trial\\_1366598](http://www.pharmatimes.com/news/lilly_incytes_olumiant_fails_in_covid-19_trial_1366598)

<sup>60</sup> <https://www.reuters.com/business/healthcare-pharmaceuticals/eli-lilly-ends-supply-agreement-with-us-govt-covid-19-antibody-drug-2021-04-12/>

<sup>61</sup> <https://www.fiercepharma.com/pharma/lilly-scores-210m-supply-deal-for-newly-authorized-coronavirus-antibody-cocktail>

<sup>62</sup> <https://pipelinereview.com/index.php/2021030777596/Small-Molecules/EMA-issues-advice-on-Lillys-bamlanivimab-LY-CoV555-alone-and-administered-together-with-etesevimab-LY-CoV016-for-the-treatment-of-confirmed-COVID-19-in-the-European-Union.html> and [http://www.pharmatimes.com/news/chmp\\_issues\\_positive\\_opinion\\_for\\_lillys\\_covid-19\\_antibodies\\_1364767](http://www.pharmatimes.com/news/chmp_issues_positive_opinion_for_lillys_covid-19_antibodies_1364767)

<sup>63</sup> <https://pipelinereview.com/index.php/2021030377573/Vaccines/Sorrento-Receives-US-FDA-Clearance-to-Proceed-With-Phase-1-Study-for-STI-2099-Intranasal-COVIDROPS-in-Healthy-Volunteers-and-Outpatient-Treatment-for-Newly-Diagnosed-COVID-19-Po.html>

<sup>64</sup> <https://pipelinereview.com/index.php/2021022877540/Antibodies/EMA-issues-advice-on-casirivimab-and-imdevimab-antibody-cocktail-for-the-treatment-of-mild-to-moderate-COVID-19.html>

<sup>65</sup> <https://pipelinereview.com/index.php/2021022577519/Antibodies/Independent-Data-Monitoring-Committee-Finds-Clear-Efficacy-for-REGEN-COV-casirivimab-with-imdevimab-in-Phase-3-COVID-19-Outpatient-Outcomes-Trial.html>

- According to a research report not yet peer-reviewed<sup>66</sup>, Regeneron's cocktail of two monoclonal antibodies sometimes fails to bind to antigens produced by the B.1.351 (South African) variant of SARS-CoV-2. In the laboratory, scientists found that nine times fewer antibodies within the cocktail bind to B.1.351's antigens than to antigens from the most common circulating version of the virus. Treatment for B.1.351 would need to be nine times larger to produce the same level of viral neutralization<sup>67</sup>.
- The US National Institutes of Health launched the third of its Phase III trials evaluating the safety and effectiveness of anticoagulants in adults with COVID-19<sup>68</sup>.
- Merck announced preliminary results from Ridgeback's Phase IIa randomized, double-blind, placebo-controlled trial to evaluate the safety, tolerability, and efficacy (in eliminating SARS-CoV-2 viral RNA) of molnupiravir, an investigational oral antiviral agent. Findings on one secondary objective showed a reduction in time to negativity of infectious virus isolation in nasopharyngeal swabs from participants with symptomatic SARS-CoV-2 infection, as determined by isolation in Vero cell line culture<sup>69</sup>. Findings from the primary efficacy and safety endpoints and other secondary objectives will be presented later.
- The ACTIV-3 trial, sponsored by the US National Institutes of Health and evaluating the safety and efficacy of investigational therapeutics for COVID-19 in hospitalised patients, stopped enrolment in sub-studies examining respectively the investigational monoclonal antibody therapy VIR-7831, and the investigational combination monoclonal antibody therapy containing BRII-196 and BRII-198. The closure followed an interim review and recommendation from an independent data and safety monitoring board<sup>70</sup>.

## 7. Developing vaccines for COVID-19

### Approved or close to submission for approval

#### General comments

- The Royal College of Emergency Medicine, the Society for Acute Medicine, and the Royal College of Physicians have advised that a person presenting with symptoms suggestive of COVID-19 vaccine induced thrombosis and thrombocytopenia (VITT) should have their platelet level checked through a full blood count. They regard VITT as unlikely if the platelet count exceeds  $150 \times 10^9/L$ . If it is less than this, then a clotting and d-dimer test should be carried out. VITT should be suspected if fibrinogen is low (d-dimer >2000). If the patient also has a headache, investigation should proceed to cerebral venous imaging with computed tomography or magnetic resonance venography. The British Society for Haematology advises that patients with suspected VITT should at once be given intravenous immunoglobulin and non-

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<sup>66</sup> [Decreased neutralization of SARS-CoV-2 global variants by therapeutic anti-spike protein monoclonal antibodies | bioRxiv](#)

<sup>67</sup> <https://www.the-scientist.com/news-opinion/regeneron-cocktail-stumbles-against-sars-cov-2-variant-in-vitro-68503>

<sup>68</sup> <https://www.nih.gov/news-events/news-releases/statement-nih-starting-enrollment-third-trial-blood-clotting-treatments-covid-19>

<sup>69</sup> Preliminary findings were presented during Science Spotlights™ at the 2021 Conference on Retroviruses and Opportunistic Infections. [Ridgeback Biotherapeutics and Merck Announce Preliminary Findings from a Phase 2a Trial of Investigational COVID-19 Therapeutic Molnupiravir | Business Wire](#)

<sup>70</sup> <https://www.nih.gov/news-events/news-releases/nih-sponsored-activ-3-clinical-trial-closes-enrollment-into-two-sub-studies> and <https://www.fiercebiotech.com/biotech/gsk-vir-hit-as-covid-drug-hopeful-halted-possible-weak-efficacy-key-nih-phase-3>

heparin based anti-coagulants therapies, but that platelet transfusions should be avoided<sup>71</sup>.

- With data uncertain as to how long immunity via vaccination will last, there are expectations that booster shots may be necessary<sup>72</sup>. The US is expecting that vaccinated people will require an immune-boosting shot within twelve months of their first dose, and that regular supplementary shots may be needed thereafter to cope with variants<sup>73</sup>. Moderna says protection from its vaccine is still strong after six months<sup>74</sup>.
- The UK's Medicines and Healthcare products Regulatory Agency (MHRA) announced that approved COVID-19 vaccines that are modified to deal with new variants will not require large and lengthy trials before being authorised<sup>75</sup>.
- A US study reinforces the view that people who have had COVID-19 need only one dose of a two-dose vaccine<sup>76</sup>.
- Breakthrough infections after vaccination are regarded as normal where vaccines are less than 100 per cent effective<sup>77</sup>. Having recovered from COVID-19 also does not necessarily prevent another infection<sup>78</sup>.
- A UK trial on mixing vaccines for individual patients has added the Novavax and Moderna vaccines<sup>79</sup>.
- Data from Public Health England showed that one shot of either the AstraZeneca vaccine or the Pfizer vaccine reduced the chance, after three to four weeks, of needing hospital treatment by 80 per cent<sup>80</sup>.
- A study in the UK is examining vaccine responses in immune-compromised patients<sup>81</sup>.
- The American Academy of Allergy, Asthma and Immunology's virtual Annual Meeting heard that allergic reactions to COVID-19 vaccines are rare, but some uncertainty persists<sup>82</sup>.
- Researchers say response to vaccines can be affected by body mass index, age and gender<sup>83</sup>.
- Scientists say the vector vaccines such as the AstraZeneca and Johnson & Johnson's products, Sputnik V, and some Chinese vaccines may be at a disadvantage if annual

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<sup>71</sup> [Covid-19: Colleges publish guidance after patients attend emergency departments with vaccine concerns | The BMJ](#)

<sup>72</sup> <https://www.the-scientist.com/news-opinion/pharma-us-government-plan-for-covid-19-booster-shots-68677> and <https://www.medscape.com/viewarticle/948283>

<sup>73</sup> <https://www.reuters.com/business/healthcare-pharmaceuticals/us-preparing-1-year-covid-19-booster-shots-pfizer-chief-sees-need-2021-04-15/>

<sup>74</sup> <https://www.reuters.com/business/healthcare-pharmaceuticals/moderna-says-protection-its-covid-19-vaccine-still-strong-six-months-2021-04-13/>

<sup>75</sup> [http://www.pharmatimes.com/news/modified\\_covid-19\\_vaccines\\_can\\_avoid\\_lengthy\\_clinical\\_studies\\_says\\_mhra\\_1364671](http://www.pharmatimes.com/news/modified_covid-19_vaccines_can_avoid_lengthy_clinical_studies_says_mhra_1364671)

<sup>76</sup> <https://consumer.healthday.com/b-4-5-another-study-suggests-folks-whove-had-covid-only-need-1-dose-of-vaccine-2651323896.html>

<sup>77</sup> <https://thehill.com/policy/healthcare/547696-fauci-no-vaccine-100-percent-effective-breakthrough-covid-19-infections> and <https://edition.cnn.com/2021/04/14/health/breakthrough-infections-covid-vaccines-cdc/index.html>

<sup>78</sup> [https://www.upi.com/Health\\_News/2021/04/15/coronavirus-young-adults-reinfection-study/7161618510951/](https://www.upi.com/Health_News/2021/04/15/coronavirus-young-adults-reinfection-study/7161618510951/)

<sup>79</sup> <https://www.reuters.com/world/uk/uk-trial-switching-covid-19-vaccines-adds-moderna-novavax-shots-2021-04-13/>

<sup>80</sup> [Covid vaccines cut risk of serious illness by 80% in over-80s - BBC News](#)

<sup>81</sup> [COVID-19: New study to examine vaccine responses in patients with impaired immune systems | UK News | Sky News](#)

<sup>82</sup> <https://www.healio.com/news/pulmonology/20210303/allergic-reactions-to-covid19-vaccines-rare-but-a-lot-of-uncertainty-remains> and <https://www.medscape.com/viewarticle/946832>

<sup>83</sup> <https://www.medscape.com/viewarticle/946765>



of pulmonary embolism, deep vein thrombosis (DVT) or thrombocytopenia"<sup>96</sup>. The company said "the number of clotting cases in vaccinated people was no higher than in the general population"<sup>97</sup>. Dr Anthony Fauci, head of the US National Institute of Allergy and Infectious Diseases, said: "the blood clotting issue that has been reported in some cases of people who have been dosed with the vaccine developed by AstraZeneca and Oxford University are at the same level as in the general population"<sup>98</sup>. The European Medicines Agency said it had not found any quality or batch issues with the vaccine. It decreed that the product "was not linked to an overall increased risk of blood clots, and that the benefits of use outweighed the risks"<sup>99</sup>.

- Spain decided to mix two different vaccines after deciding to limit the use of AstraZeneca's vaccine to people over 60. A trial will involve 600 people of all ages to see if a dose of Pfizer's vaccine can be given 28 days after a person's first AstraZeneca dose. A similar study led by the Oxford Vaccine Group is being undertaken in the UK<sup>100</sup>.
- Denmark ceased to use the Astra Zeneca vaccine<sup>101</sup>.
- The family of an Italian woman who died some weeks after receiving the AstraZeneca vaccine launched legal action<sup>102</sup>.
- The University of Oxford paused the trial of the vaccine in children.<sup>103</sup>
- The Australian Government announced that the AstraZeneca vaccine is no longer the preferred vaccine in adults less than 50 years of age, following reports in Australia and overseas of "vaccine induced prothrombotic immune thrombocytopenia" (VIPIT) following its administration<sup>104</sup>.
- Questions have been asked if the particular concern about prevalence of blood clots in women 18 to 48 is related in any way to the blood clot risk from taking the contraceptive pill, but current thinking seems to be that it is a distinct risk<sup>105</sup>.

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<sup>96</sup> <https://www.9news.com.au/world/coronavirus-ireland-suspends-astrazeneca-vaccine/94d1ad6b-6c98-4750-9b52-0473d8b0a5ad> and <https://7news.com.au/lifestyle/health-wellbeing/ireland-germany-italy-france-suspend-astrazeneca-covid-19-vaccine-over-blood-clot-fears-c-236162> and [Germany, Italy, France and Spain suspend AstraZeneca vaccine rollout amid blood clot concerns - ABC News](https://www.abc.net.au/news/2021-03-12/denmark-norway-iceland-suspend-astrazeneca-covid-shots-vaccine/13240984) and <https://www.abc.net.au/news/2021-03-12/denmark-norway-iceland-suspend-astrazeneca-covid-shots-vaccine/13240984>

<sup>97</sup> <https://www.9news.com.au/national/coronavirus-astrazeneca-vaccine-blood-clots-side-effects-countries-explainer/f8827b7a-8332-4bec-a93a-31c3926b0115> and [AstraZeneca responds after European countries suspend use of COVID vaccine over clotting fears | 7NEWS.com.au](https://www.7news.com.au/health-wellbeing/ireland-germany-italy-france-suspend-astrazeneca-covid-19-vaccine-over-blood-clot-fears-c-236162)

<sup>98</sup> <https://www.marketwatch.com/story/white-house-coronavirus-team-says-90-of-american-adults-will-be-eligible-for-vaccine-by-april-19-2021-03-31>

<sup>99</sup> [AstraZeneca vaccine not linked to overall increased risk of blood clots, benefits outweigh risks, says Europe's drug regulator - ABC News](https://www.abc.net.au/news/2021-03-12/denmark-norway-iceland-suspend-astrazeneca-covid-shots-vaccine/13240984)

<sup>100</sup> [Spain to trial mixing COVID-19 vaccines after restricting AstraZeneca shot | Reuters](https://www.reuters.com/article/health-covid19-spain-trial-mixing-vaccines/Spain-to-trial-mixing-COVID-19-vaccines-after-restricting-AstraZeneca-shot-idKCN270001)

<sup>101</sup> <https://www.medscape.com/viewarticle/949249>

<sup>102</sup> [COVID-19: Family of Italian woman who died after Oxford-AstraZeneca vaccine launch legal action | World News | Sky News](https://www.sky.com/news/health/covid-19/family-of-italian-woman-who-died-after-oxford-astrazeneca-vaccine-launch-launches-legal-action)

<sup>103</sup> [Oxford/AstraZeneca jab trial in children paused \(yahoo.com\)](https://www.yahoo.com/health/oxford-astrazeneca-jab-trial-in-children-paused-121500000.html)

<sup>104</sup> [What's VIPIT, the rare blood condition possibly linked to AstraZeneca? - ABC News](https://www.abc.net.au/news/2021-03-12/denmark-norway-iceland-suspend-astrazeneca-covid-shots-vaccine/13240984) and [https://thelimbic.com/haematology/australia-well-positioned-to-respond-to-covid-vaccine-induced-thrombotic-thrombocytopenia/?mc\\_cid=bbee1dfcc4&mc\\_eid=7872445fe3](https://thelimbic.com/haematology/australia-well-positioned-to-respond-to-covid-vaccine-induced-thrombotic-thrombocytopenia/?mc_cid=bbee1dfcc4&mc_eid=7872445fe3)

<sup>105</sup> [Your questions on AstraZeneca, blood clots and coronavirus vaccines answered by experts - ABC News](https://www.abc.net.au/news/2021-03-12/denmark-norway-iceland-suspend-astrazeneca-covid-shots-vaccine/13240984) and <https://health.clevelandclinic.org/yes-your-birth-control-could-make-you-more-likely-to-have-a-blood-clot/> and <https://www.bbc.com/news/uk-wales-56749387> and <https://theconversation.com/blood-clot-risks-comparing-the-astrazeneca-vaccine-and-the-contraceptive-pill-158652> and <https://www.verywellhealth.com/johnson-and-johnson-birth-control-blood-clots-5179341>

- The US is reported to have told the EU not to expect any exports of US-manufactured Astra Zeneca vaccines for the moment<sup>106</sup>.
- A study<sup>107</sup> involving more than 17,000 participants showed the AstraZeneca vaccine had an 81 per cent efficacy rate when the second dose was given three months after the first<sup>108</sup>.

#### Moderna, Pfizer/ BioNTech and CureVac (mRNA vaccines)

- Researchers found that in some people who received the Pfizer mRNA vaccine, immune structures were induced that could lead to long-lasting immunity<sup>109</sup>.
- A study suggested that both the Pfizer and Moderna vaccines are safe and effective in pregnancy<sup>110</sup>.
- A report from Israel suggests that shingles may follow the Pfizer/BioNTech vaccine in some patients with autoimmune/inflammatory diseases<sup>111</sup>.
- France has extended to six weeks the period between first and second injections of mRNA vaccines to extend coverage<sup>112</sup>.
- An Israeli study (not yet peer reviewed) has suggested the South African variant may evade the Pfizer vaccine<sup>113</sup>.
- The US National Institutes of Health have begun evaluating a vaccine Moderna is developing to protect against the South African variant in case this is required<sup>114</sup>.
- The US National Institutes of Health is studying why some people have developed severe allergic reactions to the Pfizer and Moderna vaccines<sup>115</sup>. They will investigate whether anyone who is highly allergic or has a mast cell disorder is subject to a higher risk for an immediate, systemic allergic reaction to the Moderna or Pfizer-BioNTech mRNA vaccines<sup>116</sup>.
- Moderna says supply problems have caused it to reduce supply to countries such as the UK and Canada<sup>117</sup>.
- Scientists at Stanford University have reverse engineered the mRNA sequence of the Moderna vaccine, using residual drops in discarded vials<sup>118</sup>.

<sup>106</sup> <https://www.abc.net.au/news/2021-03-12/us-reportedly-tells-europe-to-not-expected-vaccine-any-time-soon/13241362>

<sup>107</sup> [Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 \(AZD1222\) vaccine: a pooled analysis of four randomised trials - The Lancet](#)

<sup>108</sup> [AstraZeneca COVID-19 vaccine doses have better efficacy when given 12 weeks apart, study finds - ABC News](#)

<sup>109</sup> [SARS-CoV-2 mRNA vaccines induce a robust germinal centre reaction in humans | Research Square](#) (not yet peer reviewed) and <https://www.the-scientist.com/news-opinion/pfizer-vaccine-induces-immune-structures-key-to-lasting-immunity--68594>

<sup>110</sup> [Pfizer, Moderna Covid vaccines safe and effective in pregnancy, according to new data | Health24 \(news24.com\)](#)

<sup>111</sup> <https://www.medpagetoday.com/infectiousdisease/covid19vaccine/92106>

<sup>112</sup> <https://www.medscape.com/viewarticle/949123>

<sup>113</sup> <https://www.medscape.com/viewarticle/949111>

<sup>114</sup> <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-evaluating-moderna-covid-19-variant-vaccine-begins>

<sup>115</sup> [https://www.upi.com/Top\\_News/US/2021/04/07/NIH-to-study-allergic-reactions-to-Pfizer-and-Moderna-COVID-19-vaccines/6521617811189/](https://www.upi.com/Top_News/US/2021/04/07/NIH-to-study-allergic-reactions-to-Pfizer-and-Moderna-COVID-19-vaccines/6521617811189/)

<sup>116</sup> <https://www.nih.gov/news-events/news-releases/nih-begins-study-allergic-reactions-moderna-pfizer-biontech-covid-19-vaccines>

<sup>117</sup> <https://www.fiercepharma.com/pharma/moderna-cuts-covid-19-vaccine-deliveries-to-canada-u-k-amid-european-supply-struggles>

<sup>118</sup> <https://www.the-scientist.com/news-opinion/scientists-reverse-engineer-mrna-sequence-of-moderna-vaccine-68640>

- Pfizer identified fake versions of its vaccine in Mexico and Poland<sup>119</sup>.
- Pfizer began testing its vaccine in children under 12<sup>120</sup>. Pfizer/BioNTech has already sought emergency use authorisation for the vaccine in adolescents aged 12 to 15<sup>121</sup>.
- Germany's CureVac has begun production of its mRNA vaccine and has begun a rolling review process with the European Medicines Agency. It is a two-dose vaccine<sup>122</sup>. The company expanded its vaccine trial protocol to determine effectiveness against new variants<sup>123</sup>.
- The Serum Institute of India CEO has warned that a US move to control supplies for manufacturing the Pfizer vaccine could hamper production by other manufacturers<sup>124</sup>.
- Victoria announced a \$A 50 million fund to encourage mRNA vaccine manufacture<sup>125</sup>.

#### Novavax

- Novavax has an agreement to supply Australia with 51 million doses of its vaccine beginning in mid-2021, but says it is now facing supply shortages in production materials and will face production delays<sup>126</sup>. Australia's vaccine purchase is subject to product approval by the Therapeutic Goods Administration<sup>127</sup>.
- Novavax completed enrolment in its pivotal Phase III study in the US and Mexico to evaluate the efficacy, safety and immunogenicity of the company's COVID-19 vaccine. Of around 30,000 trial participants, 20 per cent are Latino, 13 per cent are African American, 6 per cent are Native American and 5 per cent are Asian American. NVX-CoV2373 contains purified protein antigen. It cannot cause COVID-19 and it cannot replicate. In a Phase III trial in the UK, the vaccine demonstrated 95.6 efficacy against the original virus strain, while in a Phase IIb trial in South Africa it demonstrated 50 to 60 per cent efficacy against emerging variants<sup>128</sup>. Novavax hopes to have its vaccine approved in the US by May<sup>129</sup>.
- Takeda, which has a licence agreement with Novavax, began a Phase II trial in Japan of immunogenicity and safety of the Novavax vaccine<sup>130</sup>. Takeda announced it had completed dosing in the Phase I/ II trial of the Moderna vaccine in Japan<sup>131</sup>.

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<sup>119</sup> [Pfizer Identifies Fake Covid-19 Shots Abroad as Criminals Exploit Vaccine Demand - WSJ](#) and [First counterfeit Pfizer COVID-19 vaccines surface in Poland and Mexico | FiercePharma](#)

<sup>120</sup> <https://www.nytimes.com/2021/03/25/health/coronavirus-children-vaccinations-pfizer.html>

<sup>121</sup> <https://www.reuters.com/world/pfizer-biontech-request-expanded-emergency-use-covid-19-vaccine-adolescents-2021-04-09/>

<sup>122</sup> <https://www.fiercepharma.com/pharma/europe-s-vaccine-rollout-slagging-after-j-j-and-az-holdups-curevac-readies-doses-for>

<sup>123</sup> [http://www.pmlive.com/pharma\\_news/curevac\\_expands\\_covid-19\\_vaccine\\_trial\\_protocol\\_to\\_include\\_variant\\_specification\\_1365731](http://www.pmlive.com/pharma_news/curevac_expands_covid-19_vaccine_trial_protocol_to_include_variant_specification_1365731)

<sup>124</sup> <https://www.fiercepharma.com/manufacturing/u-s-focus-pfizer-production-could-delay-manufacturing-other-covid-19-vaccines-serum>

<sup>125</sup> [Victoria announces \\$50m to fund mRNA COVID-19 vaccine production in Australia, paving way for Pfizer-style manufacturing - ABC News](#)

<sup>126</sup> [Novavax COVID-19 vaccine production set back due to supply shortages - ABC News](#)

<sup>127</sup> [Australia's vaccine agreements | Australian Government Department of Health](#)

<sup>128</sup> <https://pipelinereview.com/index.php/2021022277493/Vaccines/Novavax-Completes-Enrollment-of-PREVENT-19-COVID-19-Vaccine-Pivotal-Phase-3-Trial-in-the-United-States-and-Mexico.html>

<sup>129</sup> <https://www.fiercebiotech.com/biotech/novavax-targets-may-approval-for-covid-19-vaccine-u-s>

<sup>130</sup> <https://pipelinereview.com/index.php/2021022877538/Vaccines/Novavax-and-Takeda-Finalize-License-Agreement-for-Novavax-COVID-19-Vaccine-Candidate-in-Japan-Takeda-Initiates-Phase-1/2-Trial-in-Japan.html>

<sup>131</sup> <https://pipelinereview.com/index.php/2021022477503/Vaccines/Takeda-Provides-Updates-on-Phase-1/2-Clinical-Trials-of-Novavax-and-Modernas-COVID-19-Vaccine-Candidates-in-Japan.html>



- The Director of the US Centers for Disease Control said that contagious variants were threatening to fuel a “potential fourth surge of cases”<sup>143</sup>.
- Investigators in North Carolina found secondary transmission to be less common in schools than in the community more generally<sup>144</sup>.
- Modelling showed that mandating mask wearing in Victoria’s “second wave” of the pandemic was the most important factor in limiting case numbers<sup>145</sup>.
- In the week ending 16 March, Brazil beat its previous record of daily COVID deaths, with a total approaching 13,000 and nearly 465,000 new cases<sup>146</sup>.
- Germany experienced slow uptake of the AstraZeneca vaccine. By 1 March only one-third of its 1.45 million doses had been administered<sup>147</sup>. By 28 February, France’s administration rate of its AstraZeneca stock was 24 per cent<sup>148</sup>. France approved the AstraZeneca vaccine for those aged over 65, who had not been included in the original approval<sup>149</sup>.
- A screening program in Luxembourg showed that asymptomatic carriers are a “significant risk for transmission”<sup>150</sup>.

### Transmission

- A new review found that the evidence of predominantly airborne transmission of COVID-19 is incontrovertible<sup>151</sup>.
- The Fraunhofer Institute for Ceramic Technologies and Systems IKTS and the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM have developed a system that filters pathogens (including SARS-CoV-2) from ambient air and destroys them through cold combustion<sup>152</sup>.
- Scientists say older, heavier people may be “super spreaders” of COVID-19 because they exhale more respiratory droplets<sup>153</sup>.

### Other

- In the *New York Times*<sup>154</sup> 24 scientists and researchers from Europe, the US, Australia and Japan called for a full investigation into the origins of COVID-19. They said the report of the previous study involving WHO “was tainted by politics”<sup>155</sup>.

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<sup>143</sup> [Covid-19 variants pose 'real threat' to vaccine progress, CDC warns - BBC News](#)

<sup>144</sup> <https://www.healio.com/news/primary-care/20210304/study-finds-limited-sarscov2-transmission-in-nc-school-districts>

<sup>145</sup> [Modelling shows mandatory face masks during Victoria's COVID-19 second wave helped 'save thousands' - ABC News](#)

<sup>146</sup> <https://www.9news.com.au/world/coronavirus-brazils-covid19-resurgence-is-pushing-hospitals-to-the-brink/030a49f3-802e-4e6e-b089-24ca51ac4025>

<sup>147</sup> <https://www.bmj.com/content/372/bmj.n619>

<sup>148</sup> <https://www.medscape.com/viewarticle/946687>

<sup>149</sup> [Covid: France approves AstraZeneca vaccine for over-65s - BBC News](#)

<sup>150</sup> [https://www.thelancet.com/journals/lanpep/article/PIIS2666-7762\(21\)00033-8/fulltext](https://www.thelancet.com/journals/lanpep/article/PIIS2666-7762(21)00033-8/fulltext)

<sup>151</sup> [Ten scientific reasons in support of airborne transmission of SARS-CoV-2 - The Lancet](#) and <https://newatlas.com/health-wellbeing/covid19-sars-cov-2-airborne-transmission-aerosol-evidence-study/>

<sup>152</sup> <https://www.labonline.com.au/content/lab-design-fit-out-services/article/ventilation-system-filters-and-destroys-sars-cov-2-1083164018>

<sup>153</sup> <https://www.medscape.com/viewarticle/946599> and [Exhaled aerosol increases with COVID-19 infection, age, and obesity | PNAS](#)

<sup>154</sup> [full.pdf \(nyt.com\)](#)

<sup>155</sup> <https://www.medscape.com/viewarticle/948963>

- There had earlier been calls for the World Health Organisation to withdraw its interim report on the investigation of the origins of the pandemic, since data on early COVID-19 cases was withheld by China. One group of scientists had at that time urged a new investigation<sup>156</sup>.

## 9. Miscellaneous news

### Diseases other than COVID-19

- Australian researchers have identified a new strain of Hendra virus and equine vets are urging owners to vaccinate<sup>157</sup>.
- By 1 March, there had already been nine cases in the Northern Territory of leptospirosis, associated with the wettest summer for a decade<sup>158</sup>.

### Other

- Biogen announced it will spend \$US200 million to build a gene therapy manufacturing facility in North Carolina<sup>159</sup>.
- Grifols has purchased 25 US plasma collection centres from BPL<sup>160</sup>.

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<sup>156</sup> <https://www.medscape.com/viewarticle/946881> and [COVID OPEN LETTER FINAL 030421 \(1\).pdf \(wsj.net\)](#)

<sup>157</sup> [Vets urge horses, owners to get Hendra virus vaccine as new strain identified - ABC News](#)

<sup>158</sup> <https://www.queenslandcountrylife.com.au/story/7146558/wet-season-spike-in-a-rare-disease-among-cattle-workers>

<sup>159</sup> <https://www.biopharmadive.com/news/biogen-gene-therapy-plant-north-carolina/596137>

<sup>160</sup> [Grifols acquires 25 U.S.-based plasma centers from BPL | Seeking Alpha](#)