Monitoring International Trends

**posted January-February 2019**

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.

Some recent matters of interest appear on pages 5 to 17. Highlights are listed below:

**Safety and Patient Blood Management (begins page 6)**

* A study in the US has concluded that universal screening of donated blood for the Zika virus, by individual donation nucleic acid testing (a practice implemented in 2016) “was cost-effective only in the high mosquito season in Puerto Rico, and no evaluated screening policy was cost-effective in the 50 states. During periods with lower rates of Zika-infectious donations, the cost-effectiveness of screening will be even less favourable.”
* Scientists have found that frequent donation and associated iron loss may alter the quality of stored red blood cell components.
* Cerus Corporation enrolled the first patient in a Phase III study of the INTERCEPT Blood System for red blood cells in patients undergoing complex cardiac surgery.
* Nu-Med Plus has applied for a patent to revitalize stored blood with nitric oxide.
* Scientists say that “centrifugation-based processing may be inadequate when transfusing to immunocompromised patients, neonatal and infant patients, or patients susceptible to transfusion-related allergic reactions. Cell separation and volume reduction techniques that employ centrifugation have been shown to damage blood cells.” The authors say that newly developed centrifugation-free methods for washing and volume reducing blood components should become mainstream processing.
* An estimate concluded that “areas of north‐eastern Australia could sustain local transmission of Zika Virus…. understanding the epidemic potential of ZIKV may assist in the assessment and management of threats to blood transfusion safety.”
* After three probable cases of transfusion‐transmitted (TT) parvovirus B19 (B19V) were identified in Australia between 2014 and 2017, a study attempted to estimate the B19V DNA prevalence among blood donors and the risk to recipients of fresh blood components; and to assess options for managing risk. It found that “among vulnerable recipient groups, the risk was higher than 1 in 15,000 patients, but the risk from community exposure far exceeded the transfusion risk for all patient and age groups”. The authors noted the “significant costs that would be incurred by any strategy to reduce the risk”, concluding: “TT‐B19V is a tolerable risk to blood safety, despite being high for some vulnerable recipient groups”.
* US researchers found that screening blood donations for *Babesia microti* in endemic areas eliminates transfusion-transmitted babesiosis effectively.
* A US study concluded that the data supported “the long-term safety of a restrictive red blood cell transfusion approach for most adult patients”, but the researchers suggested further study of particular categories of patients may be advisable.
* Researchers have evaluated the performance of cobas CHIKV/DENV, a qualitative RNA detection assay for use on the cobas 6800/8800 systems to reduce the risk of transmitting chikungunya and dengue through blood transfusions. They concluded the test had demonstrated its suitability for blood donation screening.
* Researchers have found that “the routine use of an additional filter for transfusion of salvaged blood is unlikely to show important additional benefits”.
* A randomized trial showed that a higher platelet transfusion threshold appeared to increase risk for death and major bleeding among preterm infants with severe thrombocytopenia.
* A study has found that orthopaedic surgeons are more likely to encounter perioperative bleeding requiring transfusion, during posterior cervical decompression and fusion, than are neurosurgeons.
* Newer blood thinners have been recommended over warfarin for people with atrial fibrillation, in updated treatment guidelines issued by three major US heart groups.
* Treating iron deficiency anaemia with intravenous iron therapy may reduce blood coagulability, resulting in changes in thrombin generation and factor VIII activity levels.
* Alydia Health is working with the US Food and Drug Administration (FDA) to complete a clinical trial to evaluate its device intended to stop postpartum haemorrhage.
* Some years ago, blood from a donor who had recently consumed a large quantity of peanuts caused a major reaction in a recipient allergic to peanuts. Now Aimmune Therapeutics, a biopharmaceutical company developing treatments for potentially life-threatening food allergies, has initiated POSEIDON, an international Phase III clinical trial of AR101 in peanut-allergic children ages 1–3 years. AR101 is Aimmune’s investigational biologic oral immunotherapy for desensitization of patients with peanut allergy.
* A UK [study](https://www.bmj.com/content/364/bmj.k5222) has shown that a relatively common genetic disorder is associated with much higher levels of haemochromatosis than previously thought. Scientists from the University of Exeter reported that people with an HFE C282Y gene mutation are up to 400 times more likely to develop haemochromatosis than those without the mutation. The mutation is thought to be present in around one in 150 Australians.
* The use of tranexamic acid compared with placebo in patients who underwent surgery for adolescent idiopathic scoliosis decreased blood loss by 27 per cent.
* Ambrosia, the chain of clinics offering transfusions of young people’s blood, opened in five US cities: Los Angeles, San Francisco, Tampa, Omaha, and Houston. On 19 February, the FDA issued a statement saying there was “no proven clinical benefit’ to the transfusions, after which the clinics were reportedly shut down.

#### **Products and Treatments (begins page 10)**

* At the end of 2018, uniQure continued to enrol patients in for its global open-label Phase III HOPE-B trial testing its gene therapy [AMT-061](http://www.uniqure.com/gene-therapy/hemophilia.php) in men with severe or moderately severe haemophilia B.
* At its R and D day in New York in November, uniQure introduced **AMT-180,** an intravenously administered AAV5-based gene therapy for the one-time treatment of haemophilia A which the company says has, in preclinical testing, shown the ability to circumvent FVIII inhibitors.
* [Sangamo Therapeutics](https://www.sangamo.com/)has dosed the first patient in its Phase I/ II clinical trial of its genome-editing therapy, [SB-FIX](https://www.sangamo.com/pipeline/proprietary-programs), in severe haemophilia B. Sangamo says its molecular technology enables a recipient’s liver to produce a stable and continuing supply of factor IX. The therapy is administered through a single injection.
* [Catalyst Biosciences](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=YMocQkxFp1h0tH3esF5nK5qZ9RXcGDON0hSBO2XXGT4%3D&reserved=0)  announced updates on two of its lead compounds — [Factor VIIa (FVIIa) marzeptacog alfa (activated) (MarzAA)](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2Fpipeline%2Fhemostasis%2Ffactor-viia%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=oOgrFtNI86HAh9ssX8Ag%2BoNutb0U8Exvi%2BEf24pKUrQ%3D&reserved=0) and [Factor IX (FIX) dalcinonacog alfa (DalcA)](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2Fpipeline%2Fhemostasis%2Ffactor-ix%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=1mCpRc3roxVkgYoABySCKpb7cXqAJ32GmIwwagjZcdg%3D&reserved=0) — for treatment of haemophilia.
* A Phase IIIb extension trial has shown that long-term treatment with [Novoeight](https://www.novoeight.com/) ([turoctocog alfa](https://www.drugbank.ca/drugs/DB09109)) is safe and effective in preventing bleeding episodes in haemophilia A patients of any age who had already received prior treatment.
* A study has found that administering low doses of Feiba, or activated prothrombin complex concentrate (aPCC), prophylactically after acute bleeding events reduces the risk of relapse in patients with [acquired haemophilia A](https://hemophilianewstoday.com/types-of-hemophilia/acquired-hemophilia/).
* A study in mice has indicated that cell therapy with endothelial progenitor cells and stem cells genetically engineered to produce a functional clotting factor VIII (FVIII) may provide a stable and long-term treatment for haemophilia A.
* A retrospective study has suggested that combining the bypassing agents Novoseven and Feiba, with an increased interval between doses, could be both successful and cost-effective in managing bleeding episodes in haemophilia A patients with inhibitors.
* Protagonist Therapeutics has dosed the first patient in a Phase II trial of PTG-300 for the treatment of patients with beta thalassemia.
* The Bill & Melinda Gates Foundation donated $US1.5 million to Boston Children’s Hospital to develop a gene therapy for sickle cell disease.
* Positive results of the Phase III HERCULES trial of Sanofi’s Cablivi (caplacizumab) in adults with acquired thrombotic thrombocytopenic purpura (aTTP) have been published in the *New England Journal of Medicine.*
* Global Blood Therapeutics announced that data from its Phase I/ II trial of voxelotor in patients with sickle cell disease (SCD) had been published online in *Blood*.
* Orchard Therapeutics announced that the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) had published encouraging results from a clinical trial of OTL-300, an autologous *ex vivo* lentiviral gene therapy program being trialled in patients with transfusion-dependent beta-thalassemia.
* Acceleron Pharma announced the publication of results from the Phase II study of luspatercept in patients with red blood cell transfusion-dependent and non-transfusion-dependent beta-thalassemia.
* Momenta Pharmaceuticals announced the dosing of the first patient in its Phase I/ II trial of M254, hypersialylated Immunoglobulin G (hsIgG). The trial is enrolling normal healthy volunteers and patients with immune thrombocytopenic purpura (ITP).
* Researchers suggest that mini-pools of immunoglobulin incorporating as few as 20 donations are as satisfactory for treating paediatric immune thrombocytopaenia (ITP) as standard high IVIG doses.
* *Oxygem* is a “smart” ring developed by New York designer Hussain Almossawi which allows people with sickle cell disease to detect low levels of oxygen in their blood, by monitoring the levels of red and infrared light that pass through the finger.

**Regulatory matters (begins page 14)**

* Grifols has received FDA approval for its fully automated benchtop analyser which performs pretransfusion compatibility testing.
* Amgen submitted a Supplemental Biologics License Application to the FDA for Nplate (romiplostim) to include the treatment of adult patients with immune thrombocytopenia (ITP) who have had ITP for 12 months or less and an insufficient response to corticosteroids, immunoglobulins or splenectomy.
* The FDA released new guidance for stored platelets, including storage and labelling guidelines as well as reporting instructions for manufacturing and labelling changes:
* The FDA will permit the "broad commercial launch in the United States" of the reversal agent andexanet alfa (Andexxa, Portola Pharmaceuticals). Andexxa was [approved](https://www.medscape.com/viewarticle/896182) in May 2018 under the FDA's accelerated approval pathway and is the only agent to specifically reverse the anticoagulation effects of the factor Xa inhibitors [rivaroxaban](https://reference.medscape.com/drug/xarelto-rivaroxaban-999670) (Xarelto, Bayer/Janssen Pharmaceuticals) and [apixaban](https://reference.medscape.com/drug/eliquis-apixaban-999805) (Eliquis, Bristol-Myers Squibb).
* Alexion Pharmaceuticals announced that the FDA had approved Ultomiris for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria.
* Fresenius Kabi received 510(k) clearance from the FDA for the Fenwal Amicus Red Blood Cell Exchange system.

**Company news (begins page 14)**

* Takeda Pharmaceutical closed its $US62 billion purchase of Shire in January.
* bluebird bio wants to sell its genetic therapy through a five-year pay-as-you-go model.
* Biotest AG has exclusive rights for haemophilia on the use of Affibody's technology to prolong the half -life of biopharmaceuticals.

**Country news (begins page 16)**

* The US FDA is establishing an office of drug development science to reduce the cost and increase the speed of bringing new medicines to patients.
* The US Preventive Services Task Force has suggested that pregnant women be screened for hepatitis B virus infection at the first prenatal visit to prevent infection in newborns.
* In the US, the Government Accountability Office spent more than a year investigating the FDA's orphan drug program. It reported that the FDA had not ensured that drugs awarded rare disease status and economic incentives met the intent of the law and that "challenges continue".
* In the US, 12 patients in three states — Florida, Texas and Arizona —developed bacterial infections after injections of stems cells (derived from umbilical cord blood).
* Scientists from the National Institute of Agricultural Innovations in Lima have bred an iron and zinc rich potato.
* An Iranian company is now manufacturing oral iron chelator, deferasirox, domestically.
* Hospitals in Portugal will this year receive their first ever plasma-derived medicinal products from local voluntary blood donations.
* In Bahrain, the Sickle Cell Anaemia Patient Care Society plans to pursue with the government a proposal that Bahrain become the first Arab country to manufacture plasma products.
* An extended donor vigilance data linkage study in Australia has found that, compared with non- donors, “current donors were younger, more highly educated, more likely to be in paid employment, more likely to be a non‐smoker, consumed more alcohol and were more physically active”.
* NSW health experts are warning of bat attacks following a spike in people being bitten or scratched by flying foxes with the rabies-like virus Australian bat lyssavirus.
* Abbott and the Japanese Red Cross will together screen blood and plasma donations.

**Research not included elsewhere (begins page 17)**

* The World Health Organization (WHO) on 14 February announced the formation of an international committee aimed at establishing uniform guidelines for editing human DNA.
* A study demonstrated a new method to measure single red blood cell deformability.
* Researchers have grown human blood vessels from stem cells in the lab.

**Infectious diseases (begins page 18)**

* A study in Nicaragua found that children with a history of previous dengue infection had a significantly lower risk of being symptomatic when infected by Zika.
* Valneva announced positive Phase I interim results for its chikungunya vaccine.
* The world’s first malaria diagnostic test for saliva can detect subclinical infection.
* Takeda’s Phase III trial of its dengue vaccine found it prevented infections with four different serotypes of the dengue virus.
* Influenza vaccine stored up to twelve years as part of the US Department of Health and Human Services’ pandemic readiness plan is still safe and immunogenic.
* A Chinese study found that people infected by influenza A were sicker than those with influenza B and recovered more slowly.
* The FDA approved new flu drug baloxavir marboxir under the product name of Xofluza in October 2018.
* A new Ebola-related virus in bats has been found in Yunnan Province, China. It can lead to fatal disease in humans.
* Early data show that mAB114, a monoclonal antibody treatment for Ebola, is safe and well-tolerated in human adults.
* Researchers at the University of Hong Kong say they have identified a chemical that could kill viruses causing potentially fatal respiratory diseases, including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).
* Officials from the US National Institutes of Health say those living with HIV who achieve and maintain an undetectable viral load by taking and adhering to antiretroviral therapy as prescribed cannot sexually transmit the virus to others.
* Identification of three new strains of hepatitis C virus (HCV) genotype (GT) 7 in Africa, together with [GT 8](https://academic.oup.com/jid/article-abstract/218/11/1722/5047409?redirectedFrom=fulltext%20&rel=0) which was earlier identified in India, may block achievement of the World Health Organization goal of eradicating HCV worldwide by 2030.
* In Victoria, the rate of Buruli ulcer infection has almost quadrupled in four years.
* Victoria has had a resurgence of Hepatitis A.

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# Safety and patient blood management

*We follow current issues in patient safety and achieving favourable patient outcomes.*

## Appropriate Transfusion

* + An article in the journal of the American College of Physicians[[1]](#footnote-1) examined the cost-effectiveness of universal screening of donated blood for the Zika virus, by individual donation nucleic acid testing (ID-NAT), a practice implemented in US states and territories in 2016. The study referred to the first year of screening compared with alternatives for the fifty states and separately for Puerto Rico. It concluded: “Screening was cost-effective only in the high mosquito season in Puerto Rico, and no evaluated screening policy was cost-effective in the 50 states. During periods with lower rates of Zika-infectious donations, the cost-effectiveness of screening will be even less favourable.”
  + A study[[2]](#footnote-2) has found that red blood cells collected from frequent donors with low ferritin have altered susceptibility to haemolysis[[3]](#footnote-3). Therefore, frequent donation and associated iron loss may alter the quality of stored red blood cell components. The researchers concluded that further investigation is needed to assess post-transfusion safety and efficacy in patients receiving these products.
  + Researchers found in a retrospective study[[4]](#footnote-4) that in patients receiving an intraoperative plasma transfusion, higher transfusion volumes were associated with inferior clinical outcomes. Yet greater improvements in INR[[5]](#footnote-5) were associated with better outcomes. They concluded that future prospective trials are needed to clarify these relationships and to explore plasma transfusion triggers beyond the limitations of INR.
  + Cerus Corporation announced the first patient enrolment in ReCePI[[6]](#footnote-6), a randomized, double-blinded, controlled, parallel group, non-inferiority, Phase III study to evaluate the efficacy and safety of the INTERCEPT Blood System for red blood cells in patients undergoing complex cardiac surgery. The first patient was enrolled at Houston Methodist Hospital in Houston, Texas. A total of 600 patients are expected to be enrolled in up to 20 participating sites in the US.
  + Nu-Med Plus, headquartered in Salt Lake City, has applied for a patent for a product it has developed which pre-treats stored blood with nitric oxide, revitalizing its durability.
  + A recent article[[7]](#footnote-7) drew attention to the fact that there are numerous methods for washing and volume reducing blood components, but that most use centrifugation-based processing of some sort. The authors say: “there is evidence that centrifugation-based processing may be inadequate when transfusing to immunocompromised patients, neonatal and infant patients, or patients susceptible to transfusion-related allergic reactions. Cell separation and volume reduction techniques that employ centrifugation have been shown to damage blood cells, contributing to these adverse outcomes”. They express the opinion that newly developed centrifugation-free methods for washing and volume reducing blood components will soon be part of mainstream blood cell processing.
  + A recent estimate[[8]](#footnote-8) has concluded that “areas of north‐eastern Australia could sustain local transmission of Zika Virus, ZIKV. This early contribution to understanding the epidemic potential of ZIKV may assist in the assessment and management of threats to blood transfusion safety.”
  + After three probable cases of transfusion‐transmitted (TT) parvovirus B19 (B19V) were identified in Australia between 2014 and 2017, a study[[9]](#footnote-9) attempted to estimate the B19V DNA prevalence among blood donors and the risk to recipients of fresh blood components; and to assess options for managing risk. It found that “among vulnerable recipient groups, the risk was higher than 1 in 15,000 patients, but the risk from community exposure far exceeded the transfusion risk for all patient and age groups”. The authors noted the “significant costs that would be incurred by any strategy to reduce the risk”, concluding: “TT‐B19V is a tolerable risk to blood safety, despite being high for some vulnerable recipient groups”.
  + US researchers found[[10]](#footnote-10) that screening blood donations for *Babesia microti* in endemic areas eliminates transfusion-transmitted babesiosis effectively.
  + That restrictive approaches to red blood cell (RBC) transfusion are safe for patients in the short term has been demonstrated in a number of randomized clinical trials, but less is known about whether withholding RBC transfusions from patients with moderate anaemia has adverse consequences in the long term. Now Californian researchers have studied retrospectively[[11]](#footnote-11) data on close to 450,000 adult, non- obstetric patients discharged from hospital[[12]](#footnote-12) from January 2010 to December 2014, during which time restrictive RBC transfusion practices were introduced. During the period, the prevalence of moderate anaemia increased while RBC transfusions decreased[[13]](#footnote-13). Researchers reported that “while moderate anemia was less likely to resolve within 6 months, patients with moderate anemia also received fewer RBC transfusions and were less likely to be re-hospitalized or to die within the same time-frame”.  They concluded that the data supported “the long-term safety of a restrictive RBC transfusion approach for most adult patients”, but they suggested further study of particular categories of patients may be advisable.
  + Dengue (DENV) and chikungunya (CHIKV) viruses are primarily transmitted by mosquitoes, but transmission through transfusion occurs for dengue, and is thought to be likely for chikungunya. Without commercially available screening assays, blood collection agencies have used a variety of strategies during outbreaks to minimise risk to transfusion recipients. Now researchers have evaluated[[14]](#footnote-14) the performance of cobas CHIKV/DENV, a qualitative RNA detection assay for use on the cobas 6800/8800 systems. They concluded that “the high sensitivity and specificity of the cobas CHIKV/DENV test, as demonstrated in these evaluations, indicate its suitability for blood donation screening”.
  + When cell salvage devices are used, should processed blood receive additional filtering before transfusion? Researchers compared the clinical outcome and the biochemical effects of cell salvage where additional filtering was in place and where it was not[[15]](#footnote-15). They concluded that “the routine use of an additional filter for transfusion of salvaged blood is unlikely to show important additional benefits”.
  + Results of a randomized trial[[16]](#footnote-16) published in *The New England Journal of Medicine* showed that a higher platelet transfusion threshold appeared to increase risk for death and major bleeding among preterm infants with severe thrombocytopenia.
  + A study[[17]](#footnote-17) has found that orthopaedic surgeons are more likely to encounter perioperative bleeding requiring transfusion, during posterior cervical decompression and fusion, than are neurosurgeons.
  + Ambrosia, the chain of clinics offering transfusions of young people’s blood, has opened in five US cities: Los Angeles, San Francisco, Tampa, Omaha, and Houston. On 19 February, the FDA issued a statement saying there was “no proven clinical benefit’ to the transfusions, after which the clinics were reportedly shut down.

## Other

* + A trial[[18]](#footnote-18) has found that Apixaban therapy resulted in a significantly lower rate of venous thromboembolism than did placebo among intermediate-to-high-risk ambulatory patients with cancer who were starting chemotherapy. The rate of major bleeding episodes was higher with apixaban than with placebo.
  + Newer blood thinners[[19]](#footnote-19) have been recommended over warfarin for people with atrial fibrillation, in updated treatment guidelines issued by three major US heart groups[[20]](#footnote-20).
  + A study[[21]](#footnote-21) has found that treating iron deficiency anaemia with intravenous iron therapy may reduce blood coagulability, resulting in changes in thrombin generation and factor VIII activity levels.
  + Alydia Health is working with the FDA to complete a clinical trial to evaluate its device intended to stop postpartum haemorrhage. The device is a simple lasso-shaped silicone loop attached to a low-pressure vacuum that helps compress a woman's uterus when she is bleeding after childbirth. The trial is expected to run for 12 to 18 months.
  + A Japanese study of kidney transplant recipients found that achieving high haemoglobin concentrations of 12.5–13.5 g/dL with erythropoiesis-stimulating agents resulted in longer graft survival. It appeared it could delay progression of chronic allograft nephropathy by more than three years compared with targeting lower Hb levels[[22]](#footnote-22), according to new study findings published in *Nephrology Dialysis Transplantation.*
  + Some years ago, blood from a donor who had recently consumed a large quantity of peanuts caused a major reaction in a recipient allergic to peanuts. Now Aimmune Therapeutics, a biopharmaceutical company developing treatments for potentially life-threatening food allergies, has initiated POSEIDON, an international Phase III clinical trial of AR101 in peanut-allergic children ages 1–3 years. AR101 is Aimmune’s investigational biologic oral immunotherapy for desensitization of patients with peanut allergy. Brian Vickery, associate professor of pediatrics at Emory University, founding director of the Food Allergy Center at Children’s Healthcare of Atlanta and principal investigator for the POSEIDON trial, said: “Food allergies are a growing, potentially life-threatening condition with no approved treatments, and peanut allergy, which is often diagnosed in the first or second year of life, is one of the most common food allergies, affecting more than six million people in the United States and Europe. This trial represents the critical next step not only in validating that early immunotherapy in young peanut-allergic children is safe and highly effective, but in generating evidence that, pending approval, AR101 can be smoothly incorporated into allergists’ practices to address the needs of children who can benefit.”
  + A UK [study](https://www.bmj.com/content/364/bmj.k5222) has shown[[23]](#footnote-23) that a relatively common genetic disorder is associated with much higher levels of haemochromatosis than previously thought. Scientists from the University of Exeter reported that people with an HFE C282Y gene mutation are up to 400 times more likely to develop haemochromatosis than those without the mutation. The mutation is thought to be present in around one in 150 Australians[[24]](#footnote-24).
  + Recently published data[[25]](#footnote-25) showed that the use of tranexamic acid compared with placebo in patients who underwent surgery for adolescent idiopathic scoliosis significantly decreased blood loss (by 27 per cent).

# Products and treatments

*Here the NBA follows the progress in research and clinical trials that may, within a reasonable timeframe, either make new products and treatments available or may lead to new uses or changes in use for existing products.*

## Treating haemophilia

* + At the end of 2018, uniQure continued to enrol patients in its global open-label Phase III HOPE-B trial([NCT03569891](https://clinicaltrials.gov/ct2/show/NCT03569891)) testing its gene therapy [AMT-061](http://www.uniqure.com/gene-therapy/hemophilia.php) in men with severe or moderately severe haemophilia B[[26]](#footnote-26). The trial includes a six-month phase to collect baseline data, with patients serving as their own controls while on their standard-of-care therapy. This will be followed by treatment with a single intravenous administration of AMT-061. Dosing is expected to begin in the first quarter 2019. uniQure had announced that three patients included in a Phase IIb trial (dose confirmation) ([NCT03489291](https://clinicaltrials.gov/ct2/show/NCT03489291?recrs=abc&cond=blood+disease&cntry=US&lupd_s=11%2F12%2F2017&lupd_d=360)) of AMT-061 had already been treated[[27]](#footnote-27). While the primary goal of the HOPE-B trial is to assess FIX activity levels following administration of AMT-061, other variables to be analysed are annual bleeding rate, annualized factor IX replacement therapy use rate, and adverse events. Pfizer/ Spark also has a potential gene therapy for haemophilia B which is in late-stage trials.
  + At its Research and Development day in New York in November, uniQure introduced **AMT-180,** an intravenously administered AAV5-based gene therapy for the one-time treatment of haemophilia A which the company says has, in preclinical testing, shown the ability to circumvent FVIII inhibitors.
  + [Sangamo Therapeutics](https://www.sangamo.com/)has dosed the first patient in its Phase I/ II clinical trial of its genome-editing therapy, [SB-FIX](https://www.sangamo.com/pipeline/proprietary-programs), in severe haemophilia B. The trial is being conducted by [Georgetown University](https://www.georgetown.edu/) and [MedStar Georgetown University Hospital](https://www.medstargeorgetown.org/). Participants are being recruited at nine sites across the US and the UK[[28]](#footnote-28). Sangamo says its molecular technology enables a recipient’s liver to produce a stable and continuing supply of factor IX, the clotting protein which is defective or absent in haemophilia B patients. The therapy is administered through a single injection. SB-FIX received [orphan drug](https://www.fda.gov/forindustry/developingproductsforrarediseasesconditions/howtoapplyfororphanproductdesignation/default.htm) and [fast track](https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm)designations from the FDA in [2016 and 2017](https://hemophilianewstoday.com/2017/05/08/fda-grants-sangamo-special-designations-for-hemophilia-gene-therapies/) respectively. In 2018 the [Medicines and Healthcare Products Regulatory Agency (MHRA)](https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency)granted clinical trial authorization(CTA) in the UK. The UK CTA allows assessment of SB-FIX not only in adults, but also in paediatric patients older than 12.
  + [Catalyst Biosciences](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=YMocQkxFp1h0tH3esF5nK5qZ9RXcGDON0hSBO2XXGT4%3D&reserved=0)  announced updates on two of its lead compounds — [Factor VIIa (FVIIa) marzeptacog alfa (activated) (MarzAA)](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2Fpipeline%2Fhemostasis%2Ffactor-viia%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=oOgrFtNI86HAh9ssX8Ag%2BoNutb0U8Exvi%2BEf24pKUrQ%3D&reserved=0) and [Factor IX (FIX) dalcinonacog alfa (DalcA)](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.catalystbiosciences.com%2Fpipeline%2Fhemostasis%2Ffactor-ix%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087816159&sdata=1mCpRc3roxVkgYoABySCKpb7cXqAJ32GmIwwagjZcdg%3D&reserved=0) — for treatment of haemophilia.
    1. MarzAA is a next-generation recombinant factor VIIa designed for long-term prophylaxis of patients with haemophilia A or B who develop blood-clotting factor inhibitors. After the promising [interim results](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fhemophilianewstoday.com%2F2018%2F08%2F20%2Fcatalyst-announces-positive-interim-results-from-phase-2-3-clinical-trial-of-marzaa%2F&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087972410&sdata=JXTkM4uoLgcn8JiwVNTA5UtlCCV06w3sFfOJyp%2FvWt4%3D&reserved=0) of the ongoing open-label, multi-center Phase II/ III trial ([NCT03407651](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fclinicaltrials.gov%2Fct2%2Fshow%2FNCT03407651&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087972410&sdata=kWQ6hWwpcBlymf99xJOF77IbO9XJYdNZjiKF5uSeUEY%3D&reserved=0)) for MarzAA, the company announced new data from the Phase II portion of the study. Of the nine patients enrolled in the study to date, five had completed the trial with significant reductions in the annualized bleed rate (ABR). Up until that time, no anti-drug antibodies had been found in any of the participants and only one adverse reaction at the injection site had occurred, and this without long-term consequences. Catalyst plans to launch a global Phase III trial to evaluate ABR reductions in a group of 20-40 hemophilia patients receiving daily subcutaneous injections of MarzAA for six months.
    2. DalcA is a synthetic factor IX prophylactic therapy designed to prevent acute bleeding episodes in haemophilia B. It can be administered by subcutaneous injection. During Catalyst’s Research & Development Day on 18 December 2018 in New York[[29]](#footnote-29), the company announced the completion of the  immune reaction risk assessment for DalcA on the sixth cohort of patients enrolled in the ongoing proof-of-concept, open-label, multi-center Phase I/ II trial ([NCT03186677](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fclinicaltrials.gov%2Fct2%2Fshow%2FNCT03186677&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087972410&sdata=%2F565aVnd3FMafQTC6EYvaA4JwNdRjWSyo8rKCKDX3Vw%3D&reserved=0)). According to the new data, the immunogenicity risk and drug quality of DalcA were identical to those of other factor IX products currently on the market. Nassim Usman, CEO fficer of Catalyst, said: “We plan to initiate a Phase IIb trial that will include 28 days of daily subcutaneous dosing in the first quarter of 2019”.
  + A Phase IIIb extension trial[[30]](#footnote-30) has shown that long-term treatment with [Novoeight](https://www.novoeight.com/) ([turoctocog alfa](https://www.drugbank.ca/drugs/DB09109)) is safe and effective at preventing bleeding episodes in haemophilia A patients of any age who had already received prior treatment[[31]](#footnote-31).
  + Clinical [symptoms](https://hemophilianewstoday.com/symptoms-of-hemophilia/) of [acquired hemophilia A](https://hemophilianewstoday.com/types-of-hemophilia/acquired-hemophilia/) in elderly patients can vary, and researchers suggest patients should be managed individually[[32]](#footnote-32).
  + A study[[33]](#footnote-33) has found that administering low doses of Feiba, or activated prothrombin complex concentrate (aPCC), prophylactically after acute bleeding events reduces the risk of relapse in patients with [acquired hemophilia A](https://hemophilianewstoday.com/types-of-hemophilia/acquired-hemophilia/).
  + A study in mice[[34]](#footnote-34) has indicated that cell therapy with endothelial progenitor cells and stem cells genetically engineered to produce a functional clotting factor VIII (FVIII) may provide a stable and long-term treatment for haemophilia A.
  + A study[[35]](#footnote-35) found that a [Bleeding Assessment Tool](https://cdn.ymaws.com/www.isth.org/resource/resmgr/ssc/isth-ssc_bleeding_assessment.pdf) (BAT) created by the [International Society on Thrombosis and Hemostasis](https://www.isth.org/) (ISTH) is useful to identify and assess disease severity in people with haemophilia, whether they are newly diagnosed patients or have had a prior diagnosis.
  + A retrospective study[[36]](#footnote-36) has suggested that combining the bypassing agents Novoseven and Feiba, with an increased interval between doses, could be both successful and cost-effective in managing bleeding episodes in haemophilia A patients with inhibitors.

## Treating beta thalassemia and sickle cell disease

* + Protagonist Therapeutics has dosed the first patient in a Phase II trial of PTG-300[[37]](#footnote-37) for the treatment of patients with beta thalassemia. President and CEO Dinesh Patel said: “In addition to beta thalassemia, PTG-300 has broad potential in the treatment of other disorders, including hereditary hemochromatosis and the myeloproliferative neoplasms polycythemia vera and myelodysplastic syndrome”. Initial results of the Phase II trial are expected to be reported in the second half of 2019.
  + The Bill & Melinda Gates Foundation donated $US 1.5 million to Boston Children’s Hospital to develop a gene therapy for sickle cell disease, with the goal of making the drug technology more widely available in regions of the world with high rates of the condition[[38]](#footnote-38).
  + Positive results of the Phase III HERCULES trial of Sanofi’s Cablivi[[39]](#footnote-39) (caplacizumab) in adults with acquired thrombotic thrombocytopenic purpura (aTTP) have been published in the *New England Journal of Medicine* (NEJM)[[40]](#footnote-40). Marie Scully, professor of haematology at University College London Hospitals, and lead author of the HERCULES study, commented: "aTTP is a life-threatening disease, and the current treatment options do not fully halt the extensive clot formation in small blood vessels throughout the body, leaving patients at risk for significant morbidity and early death. These results demonstrate that Cablivi has the potential to address a major unmet medical need and to help those facing the potentially devastating consequences of this disorder." In the trial, treatment with Cablivi was associated with a 74 per cent decrease in aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event, compared with placebo.
  + Global Blood Therapeutics announced at the end of January that data from its Phase I/ II trial of voxelotor in patients with sickle cell disease (SCD) had been published online in Blood*[[41]](#footnote-41)*. The drug is being developed as a disease-modifying treatment for SCD. The company plans to submit a New Drug Application for voxelotor under an accelerated approval pathway to the FDA later this year.
  + Orchard Therapeutics announced on 22 January that the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) had published encouraging results from a clinical trial of OTL-300, an autologous ex vivo lentiviral gene therapy program being trialled in patients with transfusion-dependent beta-thalassemia. The paper, published in Nature Medicine, provides an interim analysis of long-term efficacy outcomes in seven of the nine treated patients with more than one year of follow up from this ongoing trial.
  + Acceleron Pharma announced the publication of results from the Phase II study[[42]](#footnote-42) of luspatercept in patients with red blood cell (RBC) transfusion-dependent and non-transfusion-dependent beta-thalassemia. Luspatercept is subject to a global collaboration between Acceleron and Celgene. Antonio Piga, Professor, Department of Clinical and Biological Sciences at Turin University and lead author of the study, said: “Current treatment options for patients with beta-thalassemia are essentially limited to supportive therapy, including red blood cell transfusions, which leads to iron overload. Luspatercept has demonstrated an ability to improve hemoglobin levels and reduce transfusion burden through apparent restoration of the late-stage red blood cell maturation process, which is known to be inhibited in these patients. Based on these results and those of subsequent studies, luspatercept has the potential to address significant unmet medical needs for patients suffering from beta-thalassemia.”

## Other products

* + Momenta Pharmaceuticals on 29 January announced the dosing of the first patient in its Phase I/ II trial of M254, hypersialylated Immunoglobulin G (hsIgG). The trial is enrolling normal healthy volunteers and patients with immune thrombocytopenic purpura (ITP). The multi-part study includes single and multiple dose parts, and a placebo-controlled, randomized double-blinded cross-over study comparing M254 with intravenous immunoglobulin (IVIg). Santiago Arroyo, Senior Vice President of Development and Chief Medical Officer of Momenta Pharmaceuticals, said: “Our aim for this study is to show clinically what we have observed in extensive preclinical models, which is that hypersialylated IgG is substantially more potent than intravenous immunoglobulin G (IVIg) in ITP and other inflammatory disorders. We look forward to obtaining initial clinical data in the first half of 2020.”
  + Researchers suggest[[43]](#footnote-43) that mini-pools of immunoglobulin (incorporating as few as 20 donations) are as satisfactory for treating paediatric immune thrombocytopaenia (ITP) as standard high IVIG doses.
  + *Oxygem* is a “smart” ring developed by New York designer Hussain Almossawi which allows people with sickle cell disease to detect low levels of oxygen in their blood, by monitoring the levels of red and infrared light that pass through the finger.

# Regulatory

*The NBA monitors overseas regulatory decisions on products, processes or procedures which are or may be of relevance to its responsibilities.*

* + Grifols has received approval from the FDA for Erytra Eflexis, which is a fully automated benchtop analyser which performs pretransfusion compatibility testing.
  + Spectrum Pharmaceuticals submitted a biologics license application to the FDA for Rolontis eflapegrastim, successfully trialled for low white blood cell levels caused by a specific type of chemotherapy in breast cancer patients.
  + Amgen submitted a Supplemental Biologics License Application to the FDA for Nplate (romiplostim) to include the treatment of adult patients with immune thrombocytopenia (ITP) who have had ITP for 12 months or less and an insufficient response to corticosteroids, immunoglobulins or splenectomy.
  + The FDA released new guidance for stored platelets, including storage and labelling guidelines as well as reporting instructions for manufacturing and labelling changes: [Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion](https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM627407.pdf)**.** The FDA reported that platelets, which are stored at room temperature, are associated with a higher risk of sepsis and fatality than other transfusable blood components; and bacterial contamination of platelets is a leading risk of infection from blood transfusion.
  + The FDA will permit the "broad commercial launch in the United States" of the reversal agent andexanet alfa (*Andexxa*, Portola Pharmaceuticals). Andexxa was [approved](https://www.medscape.com/viewarticle/896182)in May 2018 under the FDA's accelerated approval pathway and is the only agent to specifically reverse the anticoagulation effects of the factor Xa inhibitors [rivaroxaban](https://reference.medscape.com/drug/xarelto-rivaroxaban-999670)(*Xarelto*, Bayer/Janssen Pharmaceuticals) and [apixaban](https://reference.medscape.com/drug/eliquis-apixaban-999805) (*Eliquis*, Bristol-Myers Squibb). Access to the drug, however, was limited to about 40 hospitals, pending approval of Portola's next generation manufacturing process.
  + Alexion Pharmaceuticals announced that the FDA had approved Ultomiris for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria, an ultra-rare blood disorder characterized by destruction of the red blood cells. The company noted that regulatory authorities in the EU and Japan were also reviewing applications for the approval of the drug.
  + Fresenius Kabi received 510(k) clearance from the FDA for the Fenwal Amicus Red Blood Cell Exchange (RBCx) system. This system allows for the automated removal of the patient’s red blood cells (eg in sickle cell disease) and replaces them with a prescribed replacement fluid.[[44]](#footnote-44)

# Market structure and company news

*The NBA’s business intelligence follows company profitability, business forecasts, capital raisings or returns, mergers and takeovers, arrangements for joint research and/or development, contracts for supply of manufacturing inputs, and marketing agreements. Companies considered include suppliers, potential suppliers and developers of products which may be of interest.*

* + Takeda Pharmaceutical closed its $US 62 billion purchase of Shire at the end of the first week of January, and said it was then seeking to divest itself of $US 10 billion in assets. Takeda says it will focus on five core areas: oncology, gastrointestinal conditions, neuroscience, rare diseases and plasma-derived therapies.
  + Takeda later announced that in late March it will sell a set of 21 assets, including a building that houses its Osaka headquarters, to decrease the debt it incurred to acquire Shire PLC. Takeda will transfer the ownership of all 21 assets to a new subsidiary which it will then sell to a private buyer.
  + A report at the end of January said Takeda was also planning the biggest single-tranche Japanese corporate yen bond sale following its purchase of Shire. Takeda was said to be desirous of extending its debt maturities. It reportedly has some maturities as early as 2020 on euro- denominated debt it committed to last November.
  + **Emmaus Life Sciences’ commercial lead product is its L-glutamine oral powder, Endari, approved by the FDA for reducing the acute complications of sickle cell disease. MYnd Analytics has now entered into a stock-for-stock merger agreement with Emmaus.**
  + bluebird bio wants to sell its genetic therapy through a five-year pay-as-you-go model within the next few years. Patients would pay annual instalments instead of a lump sum. Patients could cancel if the gene replacement therapy didn’t work. bluebird plans to launch a gene-replacement therapy to treat beta thalassemia where a faulty gene prevents a patient’s body from making enough haemoglobin. bluebird hopes to begin selling its gene-replacement therapy in the European Union in 2019, pending government approval.
  + On 20 December Novartis announced an offer to acquire French company Cell*for*Cure from LFB. Cell*for*Cure is a contract development and manufacturing organization producing cell and gene therapies in Europe.
  + On 7 January 2019 Cerus Corporation announced that its unaudited preliminary product revenue for the fourth quarter of 2018 was $US 16.5 million compared with $US 16.2 million during the same period in 2017. Including the fourth quarter unaudited preliminary product revenue, the Company expected full year 2018 product revenue to be $US 60.9 million, ahead of the top end of the range of the Company’s most recent guidance of $US 58 million to $US 60 million. Cerus expects 2019 product revenue to grow 15 to 20 per cent on the 2018 figure.
  + Biotest AG has exercised its option and received exclusive rights for haemophilia on the use of Affibody's Albumod technology to prolong the half-life of biopharmaceuticals.
  + Rigel Pharmaceuticals announced that it had entered into an exclusive license and supply agreement with Grifols, to commercialize fostamatinib disodium hexahydrate in all potential indications in Europe and Turkey. Fostamatinib is commercially available in the US under the brand name Tavalisse. It is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. Raul Rodriguez, President and CEO of Rigel, said: "Grifols has a broad presence in Europe and an established position in the hematology commercial landscape, which supports our goal of bringing fostamatinib to patients in these countries. Our marketing authorization application for fostamatinib in chronic ITP is currently under review by the European Medicines Agency, and we anticipate a decision by the end of 2019. This provides a potential opportunity for fostamatinib to begin generating revenue in the European market in 2020."
  + [Sight Diagnostics](https://www.sightdx.com), an Israeli medical devices startup that’s using AI technology to speed up blood testing, has raised $US 27.8 million in a funding round.

# Specific country events

* + In the US, the Sickle Cell Disease and Other Heritable Blood Disorders Research, Surveillance, Prevention, and Treatment Act of 2018 (S. 2465), became law on 18 December 2018. It provides grants for research, surveillance, prevention, and treatment.
  + The FDA is establishing an office of drug development science to reduce the cost and increase the speed of bringing new medicines to patients.
  + The US Preventive Services Task Force has suggested that pregnant women be screened for hepatitis B virus infection at the first prenatal visit to prevent infection in newborns.
  + In the US, the Government Accountability Office spent more than a year investigating the FDA's orphan drug program. It reported that the FDA had not ensured that drugs awarded rare disease status and economic incentives met the intent of the law and that "challenges continue". The FDA issued a statement saying it agreed with the report recommendations regarding documentation and that the agency was streamlining its processes.
  + In the US, 12 patients in three states — Florida, Texas and Arizona —developed bacterial infections after injections of stems cells (derived from umbilical cord blood) for problems like joint and back pain. All 12 were hospitalized, three of them for a month or longer.
  + In Peru, it is estimated that around 44 per cent of children suffer from anaemia. Scientists from the National Institute of Agricultural Innovations in Lima (INIA) have now bred an iron and zinc rich potato. Officially designated INIA 328, it is unofficially called the “lilac potato” because of its colour.
  + In Canada, the CBC will screen an eight -part miniseries, titled “Unspeakable”, which follows two families affected by the country’s tainted blood scandal.
  + An Iranian company is now manufacturing oral iron chelator, deferasirox, domestically. Its main use is to reduce chronic iron overload in patients who are receiving long-term blood transfusions for conditions such as beta-thalassemia and other chronic anaemia.
  + Hospitals in Portugal will this year receive their first ever plasma-derived medicinal products from local voluntary blood donations.
  + In Bahrain, Sickle Cell Anaemia Patient Care Society chairman Zakreya Al Kadhem says the Society plans to pursue with the government a proposal that Bahrain become **the first Arab country to manufacture plasma products.** Mr Al Kadhem said this would save Bahrain millions of dinars and help Bahrain reach the status of a regional support centre for not only sickle cell disease but for other medical conditions as well.
  + An extended donor vigilance data linkage study in Australia[[45]](#footnote-45) has found that, compared with non- donors, “current donors were younger, more highly educated, more likely to be in paid employment, more likely to be a non‐smoker, consumed more alcohol and were more physically active. Compared to lapsed donors, current donors were younger, had fewer comorbidities and better self‐reported health, consumed more alcohol and were more physically active”.
  + In Australia, teatment with [Aplidin](https://myelomaresearchnews.com/plitidepsin-aplidin/) ([plitidepsin](https://myelomaresearchnews.com/plitidepsin-aplidin/)) in combination with dexamethasone has been approved for [multiple myeloma](https://myelomaresearchnews.com/?s=multiple+myeloma) patients who have failed or are resistant to other therapies. Myeloma patients in Australia will be the first to have access to this medication. Jeff Szer, who is a haematologist at the [Peter MacCallum Cancer Centre](https://www.petermac.org/) and [Royal Melbourne Hospital](https://www.thermh.org.au/), was the Australian principal investigator on the Phase III trial of Aplidin, ([NCT01102426](https://clinicaltrials.gov/ct2/show/NCT01102426)). He spoke of the good efficacy and tolerability results of the study that enrolled more Australian patients “than anywhere else in the world.”
  + NSW health experts are warning of bat attacks following a spike in people being bitten or scratched by flying foxes withthe rabies-like virus Australian bat lyssavirus.
  + Extended half-life (EHL) recombinant Factor VIII and Factor IX will be added to the [National Blood Authority list](https://www.blood.gov.au/national-product-list) of clotting factor concentrates in 2019. This follows the 2018 assessment by the Medical Services Advisory Committee (MSAC). MSAC recommended that the EHL products would replace standard half-life (SHL) Factor VIII and Factor IX for the prevention of bleeding in patients with haemophilia A or B. The Committee’s Public Summary Document said: “However, MSAC noted that for on-demand use and surgical prophylaxis, there is insufficient evidence to support a clinical claim for EHL relative to SHL products.”
  + Abbott announced on 17 January that it had been selected by the Japanese Red Cross Society as its partner in screening Japan’s blood and plasma donations. The 8-year contract is for the exclusive supply of serological instrumentation, tests and consumables.

# Research not included elsewhere

*A wide range of scientific research has some potential to affect the use of blood and blood products. However, research projects have time horizons which vary from “useful tomorrow” to “at least ten years away”. Likelihood of success of particular projects varies, and even research which achieves its desired scientific outcomes may not lead to scaled-up production, clinical trials, regulatory approval and market development.*

* + The World Health Organization (WHO) on 14 February announced the formation of an international committee aimed at establishing uniform guidelines for editing human DNA in ways that can be passed down to future generations. The [announcement](https://www.who.int/ethics/topics/human-genome-editing/committee-members/en/) said that the 18-member committee "will examine the scientific, ethical, social and legal challenges associated with human genome editing."
  + Researchers at Yale University have suggested that a “drinkable cocktail of designer molecules” has restored memories in mice engineered to have an Alzheimer’s-like condition[[46]](#footnote-46).
  + Researchers at Purdue University have produced a diagnostic tool they say can identify blood infections in twenty minutes[[47]](#footnote-47).
  + Alkahest, the biotech firm co-founded by Stanford researcher Dr Tony Wyss-Coray, is beginning testing on 90 human patients with Parkinson's disease to see if blood or some of its components from young people could have protective effects on their brains. The first injection was administered on 4 December 2018. If the trial shows promise, and the parallel study successfully identifies the key component in blood, the research team hopes it may have the basis for making a synthetic.
  + The short-term pasteurization of breast milk from mothers with cytomegalovirus (CMV) significantly decreased CMV infections in very preterm infants, according to data published in *Clinical Infectious Diseases[[48]](#footnote-48)* ([clinicaltrials.gov](http://clinicaltrials.gov) identifier: [NCT01178905](https://clinicaltrials.gov/ct2/show/NCT01178905)).
  + Many haematologic conditions present with red blood cells of altered deformability. A recent study published in the *American Journal of Hematology* demonstrated a new method to measure single cell (red blood cell) deformability[[49]](#footnote-49).
  + Researchers announced[[50]](#footnote-50) they had grown human blood vessels from stem cells in the lab that look and behave like the ones in human bodies.
  + The interactions between von Willebrand factor and its cleaving protease ADAMTS-13 have been identified as risk factors for neonatal thromboembolism[[51]](#footnote-51).
  + Research from Regenexx shows potential for treating osteoarthritis of the knee with cell-based therapies. The study[[52]](#footnote-52) was a randomized controlled trial of patients’ own bone marrow concentrate and platelet-rich plasma products versus an exercise therapy regimen for patients with moderate knee osteoarthritis, with clinical outcomes documented over a two-year period. While exercise or physical therapy improve function and reduce pain, this study showed cell-based therapy to be more effective.

# Infectious diseases

*The NBA takes an interest in infectious diseases because: the presence of disease in individual donors (e.g. influenza), or potential disease resulting from travel (e.g. malaria) means a donor must be deferred; temporary disease burden within a community (e.g. dengue in North Queensland) may limit blood collection in the community for a time; and some people may not be permitted to donate at all (e.g. people who lived in the UK for a period critical in the history of vCJD). Blood donations are tested for a number of diseases (e.g. HIV and Hepatitis B), but there are also emerging infectious diseases for which it may become necessary to test in the future (e.g. Chagas disease, Zika virus and the tick-borne babesiosis and Lyme disease).*

## Mosquito-borne diseases

* + India asked the US Centres for Disease Control and Prevention (CDC) to “withdraw or modify” its 13 December alert warning pregnant women against travelling to India lest they risk a Zika infection. The alert notified that “an outbreak of Zika has been reported in India” and that the disease is “endemic” in the country. The Indian government objected to the use of the term “endemic” because, it argued, Zika infections had so far been contained within specific areas such as Gujarat and Rajasthan.
  + A study[[53]](#footnote-53) in Nicaragua of more than 3,000 children found that children with a history of previous dengue infection had a significantly lower risk of being symptomatic when infected by Zika.
  + A finding[[54]](#footnote-54) that [hydroxychloroquine](https://d.docs.live.net/topic/hydroxychloroquine) (HCQ), a drug commonly prescribed for treating malaria, reduces ZIKV transmission from mother to foetus, has been followed by the identification of the target viral protein on which HCQ acts[[55]](#footnote-55).
  + Valneva announced positive Phase I interim results for its chikungunya vaccine candidate VLA1553. This is a monovalent, single dose, live-attenuated vaccine.
  + Erada Technology Alliance will market the world’s first malaria diagnostic test for saliva, able to detect subclinical infection.
  + A new approach to protecting against malaria uses a cytomegalovirus-based platform already in use in vaccines being developed against HIV and tuberculosis. This new vaccine is reported[[56]](#footnote-56) to have decreased the malaria-causing parasite's release from the liver and into the blood of infected rhesus macaques by 75 to 80 per cent.
  + Takeda’s Phase III trial of its dengue vaccine tested TAK-003 in 20,000 children across eight dengue-endemic countries in Latin America and Asia. The company says its candidate prevented infections with four different serotypes of the dengue virus. The trial, which enrolled children aged 4 to 16, is ongoing, with more data expected later this year.

## Influenza

* + In Canada, the flu shot is working better than it has in years, especially for the young children at greatest risk of being made seriously ill by H1N1. Official estimates of the vaccine’s performance found the shot was 68-per-cent effective at preventing all types of influenza, and 72 per cent effective at warding off H1N1, the prevalent strain. The vaccine protected 91 per cent of children between the ages of 1 and 8 from H1N1, according to the BC Centre for Disease Control. Over all, the 2018-2019 vaccine is a big improvement over the previous four seasons. Last year’s version was only 17-per-cent effective against the dominant H3N2 strain of the virus at midseason. Allison McGeer, the medical director of infection control at Toronto’s Sinai Health System said this year’s vaccine is effective because the prevailing strain is H1N1. She said H1N1 strains mutate slower than other types of influenza A, making it easier for vaccine designers to keep up. Also, the vaccine seems able to build on the immunity that adults – especially seniors – have built over time against H1N1. However, H1N1 tends to take a higher toll on children, as it has this season. Influenza has sent twice as many children to hospital and three times as many to the intensive-care unit compared with this time last season, according to the twelve paediatric hospitals that report flu statistics to the Public Health Agency of Canada (PHAC).
  + In the US the [2018-2019 influenza season](https://www.cdc.gov/flu/weekly/index.htm) is also well underway. As in Canada, influenza A(H1N1) pdm09 viruses have been predominating, except in the Southeast, which is seeing mostly influenza A(H3N2) viruses.
  + The CDC reported on 14 February that the flu vaccine’s success had varied according to the age of the recipient. For people up to 17 years of age, overall effectiveness against the flu appeared to be 61 per cent, while for people aged 50 or more, only 24 per cent of those vaccinated were protected from infection.
  + The FDA has approved the use of the 0.5ml dose of Sanofi’s Fluzone quadrivalent vaccine for children aged 6 months to 35 months. It will be available in the US for the 2019-20 season.
  + A human challenge study using seasonal H3N2 flu virus found that it can be administered to produce mild-to-moderate disease, a necessary step in developing and evaluating better and more broadly protective flu vaccines[[57]](#footnote-57).
  + Greek research[[58]](#footnote-58) suggests that Roche's antiviral Tamiflu (oseltamivir) reduced mortality in severely ill patients with influenza A/H3N2. The 1330 patient study from the Hellenic Centres for Disease Control and Prevention concluded: “Severely ill patients with suspected influenza should be promptly treated with oseltamivir, particularly when A/H3N2 is circulating. The efficacy of oseltamivir should not be assumed to be equal against all types of the disease.”
  + A [study](https://www.sciencedirect.com/science/article/pii/S0264410X18316323) has found that influenza vaccine stored up to twelve years as part of the US Department of Health and Human Services’ pandemic readiness plan is safe and immunogenic[[59]](#footnote-59).
  + A Chinese study[[60]](#footnote-60) found that people infected by influenza A were sicker than those with influenza B and recovered more slowly.
  + The FDA approved new flu drug baloxavir marboxir[[61]](#footnote-61) under the product name of Xofluza in October 2018. Now the Korean government has approved a Phase III clinical trial in patients hospitalized with severe influenza.
  + Avian flu outbreaks (various strains) have continued to occur in a range of locations. H5N1 was reported on two poultry farms in India on 17 December, and at around the same time was reported in house crows and in peacocks at a zoo. Iran reported outbreaks of H5N8 in ducks and chickens, beginning 24 and 25 December.
  + On 15 February, China reported another H9N2 avian flu illness, involving a boy aged eight from Yunnan province. China reported seven cases in 2018.

## Ebola virus disease – and a newly described relative

* + A study[[62]](#footnote-62) has found a new Ebola-related virus in bats in Yunnan Province, China. It can lead to fatal disease in humans [according to findings](https://www.nature.com/articles/s41564-018-0328-y). Researchers said this new genus of filovirus fits in between the Ebola and Marburg viruses on the evolutionary scale. It was a partnership between scientists at Singapore’s Duke-NUS medical school and researchers from China which identified the new strain[[63]](#footnote-63).
  + Columbia University scientists[[64]](#footnote-64) have found “genetic material from the ebola virus, and ebolavirus antibodies,” in a greater long-fingered bat located in the Nimna District of Liberia. This is the first time the virus has been found in a bat in West Africa, although it has previously been found in bats in Central Africa.
  + A stream of refugees crossing from the Democratic Republic of Congo into Uganda have fuelled concerns about the spread of Ebola, despite efforts by Ugandan health officials to screen arrivals for Ebola.
  + On 23 January 2018 Merck said it was preparing to ship another 120,000 doses of its Ebola vaccine on top of 100,000 doses already shipped to WHO.
  + On 25 January health authorities announced that the number of deaths from Ebola in the DR Congo had reached 443.
  + The Ministry of Health of South Sudan, with support from WHO, the Vaccine Alliance, UNICEF and the CDC amongst others, on 28 January began vaccinating health workers and other front-line responders against Ebola.
  + Early data show that mAB114, a monoclonal antibody treatment for Ebola, is safe and well-tolerated in adults, according to the results from the first human trial of the drug published in The Lancet*[[65]](#footnote-65)*.
  + Doctors Without Borders (MSF) announced on 18 February that an ongoing trial of four experimental Ebola treatments would now start enrolling participants in the current hotspots in the Democratic Republic of Congo. The four treatments are Remdesivir, mAb114, REGN-EB3, and ZMapp.
  + Scientists have developed a combination of monoclonal antibodies that protected animals against the three Ebola viruses known to cause disease in humans[[66]](#footnote-66).
  + Nine vaccine and treatment units funded by the US National Institute of Allergy and Infectious Diseases will test the safety of two experimental Ebola vaccines and their ability to generate an immune response in healthy volunteers. Previous research has shown that the ChAd3-EBO-Z vaccine and the MVA-BN-Filo vaccine together generate “potentially protective anti-Ebola responses.”

## MERS-CoV

* + Researchers at the University of Hong Kong led by Yuen Kwok-yung say they have identified a chemical substance that could kill viruses causing potentially fatal respiratory diseases, including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)[[67]](#footnote-67). Yuen said the compound, AM580, would block the route that may allow many types of viruses to replicate in the human body. The researchers said they had tested the chemical AM580 on lab rats. It could stop the replication of flu viruses such as H1N1, H5N1, H7N9, the coronaviruses that cause SARS and MERS, the Zika virus and Enterovirus 71, responsible for hand, foot and mouth disease. Yuen said the drug “can be taken by injection, also by the oral route, and also by an intranasal spray. This is very important [because] many emerging infectious diseases, like influenza or SARS or MERS, are respiratory tract infections. If the compound can be administered by inhalation, that is a distinct advantage.” A US provisional patent application has been filed.
  + On 7 January, Saudi Arabia’s Ministry of Health reported the third MERS-CoV case connected to a household cluster in Riyadh. This new case increased the global total since 2012 to 2,283, at least 806 of them fatal.
  + The Saudi Ministry of Health on 21 February confirmed 65 MERS cases since 1 January, with 41 of those cases recorded in Wadi ad-Dawasir. Ten cases were detected in Oman during the same period.

## Other diseases

* + WHO has called for “open and timely” sharing of pathogen data during disease outbreaks. It released a draft code of conduct for comment.
  + Researchers have suggested that over 60 per cent of emerging infectious diseases in humans originated in animals, and more than 70 per cent of those zoonotic diseases come from wild animals.[[68]](#footnote-68)
  + Scientists have discovered[[69]](#footnote-69) new species of antibiotic-resistant bacteria in the blood of two patients in China. They were carrying unidentified species of *Enterobacter huaxiensis* and *Enterobacter chuandaensis* that did not respond to penicillin or the cephalosporin group of antibiotics.
  + Emergent BioSolutions submitted an application to the FDA for potential emergency use of NuThrax (anthrax vaccine adsorbed with CPG 7909 adjuvant) in the event of a public health emergency involving Bacillus anthracis. NuThrax (AV7909), is a vaccine for post-exposure prophylaxis, in conjunction with the recommended course of antimicrobial therapy. The submission will be reviewed by the FDA during the first half of 2019.
  + Officials from the US National Institutes of Health say those living with HIV who achieve and maintain an undetectable viral load by taking and adhering to antiretroviral therapy as prescribed cannot sexually transmit the virus to others. Officials from the National Institute of Allergy and Infectious Diseases (NIAID) reviewed the scientific evidence underlying the “undetectable means untransmissible” principle and discussed the implications[[70]](#footnote-70).
  + Researchers funded by the US National Institutes of Health (through NIAID[[71]](#footnote-71)) have developed a new assay to count the cells that make up the HIV reservoir. This will enable scientists who are trying to eliminate the HIV reservoir to determine whether their strategies are working[[72]](#footnote-72).
  + Identification of three new strains of hepatitis C virus (HCV) genotype (GT) 7 in Africa, together with [GT 8](https://academic.oup.com/jid/article-abstract/218/11/1722/5047409?redirectedFrom=fulltext%20&rel=0) which was earlier identified in India, may block achievement of the World Health Organization (WHO) goal of eradicating HCV worldwide by 2030[[73]](#footnote-73).
  + On 3 January a child became the third person in NSW diagnosed with measles in less than a week.
  + In Victoria, the rate of Buruli ulcer infection has almost quadrupled in four years, with 330 cases in 2018. Cases are reported to be becoming more severe, with larger wounds taking longer than a year to heal. Whereas the most affected area has been the Mornington Peninsula (146 cases), followed by Greater Geelong, Frankston and Bayside Melbourne, an increasing number of cases are being diagnosed in Melbourne's inner suburbs.
  + In Far North Queensland, the flesh-eating ulcer infection is known as the “Daintree ulcer”. Two cases were identified in late November.
  + Victoria has had a resurgence of Hepatitis A. The State’s acting chief health officer, Dr Brett Sutton, reportedly said: “This is the biggest outbreak we would have had since hepatitis A was endemic in Australia, which is really before reticulated sewerage came into being.” Free vaccination for at- risk groups is being continued till mid-year.
  + Valneva has begun a Phase II study of VLA15, at present the only Lyme disease vaccine candidate in active clinical development.
  + The CDC announced in January that [Chronic wasting disease, or CWD](https://d.docs.live.net/story/news/nation/2019/02/14/chronic-wasting-disease-what-know-zombie-deer-ailment/2870843002/), has afflicted free-ranging deer, elk and/or moose in 24 US states and two Canadian provinces. "We are in an unknown territory situation," said Michael Osterholm, director of the Center for Infectious Disease Research and Policy at the University of Minnesota. "It is probable that human cases of chronic wasting disease associated with consumption of contaminated meat will be documented in the years ahead. It’s possible the number of human cases will be substantial and will not be isolated events." No human cases of CWD have been reported, but studies have shown that it can be [transmitted to animals](https://www.cdc.gov/prions/cwd/transmission.html) other than deer, including primates.
  + A measles outbreak in the Philippines had claimed 136 lives by 18 February, half of them children aged between one and four. The outbreak has been partly blamed on vaccination fears. On 3 January a child became the third person in NSW diagnosed with measles in less than a week.

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2. Tamir Kanias et al, “Frequent blood donations alter susceptibility of red blood cells to storage‐ and stress‐induced hemolysis”, *Transfusion,* first published 26 November 2018. [**https://doi.org/10.1111/trf.14998**](https://doi.org/10.1111/trf.14998) [↑](#footnote-ref-2)
3. The rupturing of red blood cells and the release of their contents into the surrounding fluid. The process may occur *in vivo* or *in vitro*. [↑](#footnote-ref-3)
4. Matthew A Warner et al., “Higher intraoperative plasma transfusion volumes are associated with inferior perioperative outcomes”, *Transfusion,* first published 1 November 2018[**https://doi.org/10.1111/trf.14988**](https://doi.org/10.1111/trf.14988) [↑](#footnote-ref-4)
5. International Normalised Ratio, a standardised measurement of the time it takes for blood to clot. [↑](#footnote-ref-5)
6. ReCePI is funded as part of an agreement with the Biomedical Advancement Research and Development Authority (BARDA). BARDA is part of the Office of the Assistant Secretary for Preparedness and Response within the U.S. Department of Health and Human Services. [↑](#footnote-ref-6)
7. # Madeleine Lu, Dalia L Lezzar, Eszter Vörös, Sergey S Shevkoplyas, “Traditional and emerging technologies for washing and volume reducing blood products”, *Journal of Blood Medicine,* 3 January 2019 Volume 2019:10 Pages 37—46 **DOI** <https://doi.org/10.2147/JBM.S166316>

   [↑](#footnote-ref-7)
8. Peter Watson-Brown et al., “Epidemic potential of Zika virus in Australia: implications for blood transfusion safety”, *Transfusion*, First published: 08 January 2019 [https://doi.org/10.1111/trf.150**95**](https://doi.org/10.1111/trf.15095) [↑](#footnote-ref-8)
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10. Tonnetti L, Townsend RL, Deisting BM, Haynes JM, Dodd RY, Stramer SL. [The impact of *Babesia microti* blood donation screening](https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.15043) [published online November 30, 2018]. *Transfusion*. doi: 10.1111/trf.15043 [↑](#footnote-ref-10)
11. # [Roubinian NH, Murphy EL, Mark DG, Triulzi DJ, et al. Long-term outcomes among patients discharged from the hospital with moderate anemia.  *Annals of Internal Medicine* 2018](http://annals.org/aim/article-abstract/2719218/long-term-outcomes-among-patients-discharged-from-hospital-moderate-anemia)

    [↑](#footnote-ref-11)
12. Data from 21 hospitals were included. Some of the patients had multiple hospitalizations. [↑](#footnote-ref-12)
13. Measured in units per 1000 patients [↑](#footnote-ref-13)
14. Susan L Stramer et al, “Duplex nucleic acid test for the detection of chikungunya and dengue RNA viruses in blood donations”, *Transfusion*, published online 4 January 2019. [**https://doi.org/10.1111/trf.15128**](https://doi.org/10.1111/trf.15128) [↑](#footnote-ref-14)
15. Adrianus j de Vries et al., “Additional filtering of blood from a cell salvage device is not likely to show important additional benefits in outcome in cardiac surgery”, *Transfusion*, published online 4 January 2019. [**https://doi.org/10.1111/trf.15130**](https://doi.org/10.1111/trf.15130) [↑](#footnote-ref-15)
16. Anna Curley et al., ‘Randomized Trial of Platelet-Transfusion Thresholds in Neonates”, [January 17, 2019](https://www.nejm.org/toc/nejm/380/3?query=article_issue_link) N Engl J Med 2019; 380:242-251 DOI: 10.1056/NEJMoa1807320 [↑](#footnote-ref-16)
17. Daniel J Snyder et al., Assessing Variability in In-Hospital Complication Rates Between Surgical Services for Patients Undergoing Posterior Cervical Decompression and Fusion, [*Spine*](https://eur03.safelinks.protection.outlook.com/?url=https%3A%2F%2Fjournals.lww.com%2Fspinejournal%2FAbstract%2F2019%2F02010%2FAssessing_Variability_in_In_Hospital_Complication.5.aspx&data=02%7C01%7C%7Ccfde4ae9517c4bcd34ab08d67ea86ecd%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636835659219472669&sdata=aeD%2BjYYO%2FXRW8l7s7Ca2N34IABSZC%2BmM7T2yO3lkltQ%3D&reserved=0)*:* [February 1, 2019 - Volume 44 - Issue 3 - p 163-168](https://journals.lww.com/spinejournal/toc/2019/02010) doi: 10.1097/BRS.0000000000002780 [↑](#footnote-ref-17)
18. Marc Carrier et al., “Apixaban to Prevent Venous Thromboembolism in Patients with Cancer”, [**New England Journal of Medicine**,](https://www.nejm.org/doi/full/10.1056/NEJMoa1814468) Dec. 4, 2018; DOI: 10.1056/NEJMoa1814468 [↑](#footnote-ref-18)
19. Non-vitamin K oral anticoagulants (NOACs) include dabigatran (Pradaxa), rivaroxaban (Xarelto) and apixaban (Eliquis). These do not require the frequent monitoring of blood-clotting levels that warfarin (Coumadin) does; and they do not have the same drug and food interactions as warfarin. [↑](#footnote-ref-19)
20. The new guidelines were published simultaneously on 28 January in *Circulation*, the *Journal of the American College of Cardiology* and the journal *HeartRhythm*. [↑](#footnote-ref-20)
21. Nashashibi J, Avraham GR, Schwartz N, et al. [Intravenous iron treatment reduces coagulability in patients with iron deficiency anaemia: a longitudinal study](https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.15765) [published online January 25, 2019]. *Br J Haematol*. doi: 10.1111/bjh.15765 [↑](#footnote-ref-21)
22. Tsujita M, Kosugi T, Goto N, et al. “The effect of maintaining high hemoglobin levels on long-term kidney function in kidney transplant recipients: a randomized controlled trial”. *Nephrolpgy Dialysis Transplantation* 2018:1–8. DOI:10.1093/ndt/gfy365 [↑](#footnote-ref-22)
23. Luke C. Pilling et al., “Common conditions associated with hereditary haemochromatosis genetic variants: cohort study in UK Biobank”, *BMJ* 2019;364: k5222 published 16 January 2019 doi: <https://doi.org/10.1136/bmj.k5222> [↑](#footnote-ref-23)
24. The researchers recommend screening at a young age for the mutation to prevent consequences such as arthritis. [↑](#footnote-ref-24)
25. [Goobie SM, et al. J Bone Joint Surg Am. 2018; doi:10.2106/JBJS.18.00314.](https://journals.lww.com/jbjsjournal/Abstract/2018/12050/Tranexamic_Acid_Is_Efficacious_at_Decreasing_the.4.aspx?sessionEnd=true) Article title: “

    Tranexamic Acid Is Efficacious at Decreasing the Rate of Blood Loss in Adolescent Scoliosis Surgery: A Randomized Placebo-Controlled Trial” [↑](#footnote-ref-25)
26. Haemophilia B means that the clotting protein factor IX is defective or missing. AMT-061 uses a viral vector to deliver a gene that generates a mutated FIX, called the Padua variant (FIX-Padua), for increased production of FIX. [↑](#footnote-ref-26)
27. In 2017, the US Food and Drug Administration (FDA) awarded breakthrough therapy status to AMT-061 based on [**results**](https://hemophilianewstoday.com/2018/01/15/uniqure-hemophilia-b-gene-therapy-amt-060-shows-long-term-efficacy/)from the Phase I/II study ([**NCT02396342**](https://clinicaltrials.gov/ct2/show/NCT02396342?term=uniQure&rank=1)**)** of gene therapy, AMT-060. This differs from AMT-061 in a variation in the gene sequence for FIX. Across the three patients in the dosing confirmation trial for AMT-061, six-week FIX activity came in at 31 per cent of normal. There was some patient-to-patient variation, but the lowest level of FIX activity at the cut off was the 23 per cent recorded by one person at eight weeks. Activity at cut off in the other two people was 37 per cent and 30 per cent. [↑](#footnote-ref-27)
28. This is an open-label, non-randomized, ascending dose trial  ([**NCT02695160**](https://clinicaltrials.gov/ct2/show/NCT02695160)), in which 12 patients will be given a low, medium or high dose of SB-FIX to evaluate its safety, tolerability and preliminary effectiveness. As a primary goal, therapy-related adverse side effects will be assessed for three years after SB-FIX infusion. Secondary goals include change from baseline in FIX antigen (a molecule that induces an immune response) and activity levels, plus presence of parts of the SB-FIX molecular complex in plasma, saliva, urine, stool and semen. [↑](#footnote-ref-28)
29. a webcast of the event is available [**here**](https://nam02.safelinks.protection.outlook.com/?url=http%3A%2F%2Fir.catalystbiosciences.com%2Fevents%2Fevent-details%2Fcatalyst-biosciences-research-development-day-focused-factor-viia-and-factor&data=02%7C01%7C%7C040a252cb6d54536d5ee08d6777a702a%7C84df9e7fe9f640afb435aaaaaaaaaaaa%7C1%7C0%7C636827765087972410&sdata=QEZscc1%2FdYCpAfiiaB8Mzp1AEslROhpwl8gp6hQSZ2o%3D&reserved=0) [↑](#footnote-ref-29)
30. Stephen R Lentz, , “[Long‐term safety and efficacy of turoctocog alfa in prophylaxis and treatment of bleeding episodes in severe haemophilia A: Final results from the guardian 2 extension trial](https://onlinelibrary.wiley.com/doi/full/10.1111/hae.13617)**,**” published in [*Haemophilia*](https://onlinelibrary.wiley.com/journal/13652516) 6 November 2018 [**https://doi.org/10.1111/hae.13617**](https://doi.org/10.1111/hae.13617) [↑](#footnote-ref-30)
31. Novoeight, NovoNordisk’s third-generation recombinant FVIII is approved by the US Food and Drug Administration (FDA) for the treatment and prevention of spontaneous bleeding in patients with haemophilia A. In two earlier Phase III trials — guardian 1 ([**NCT00840086**](https://clinicaltrials.gov/ct2/show/NCT00840086)) and guardian 3 ([**NCT01138501**](https://clinicaltrials.gov/ct2/show/NCT01138501)**)** — Novoeight achieved positive results in both adults/adolescents and children with severe hemophilia A who had already received prior treatment. The non-randomized, open-label, multicenter Phase IIIb extension study ([**NCT00984126**](https://clinicaltrials.gov/ct2/show/NCT00984126)), called guardian 2, assessed the long-term safety and efficacy of Novoeight in pretreated patients with severe haemophilia A. [↑](#footnote-ref-31)
32. Cases were described in Tomoya Yamaguchi et al., “[Management of Acquired Hemophilia A in Elderly Patients](https://doi.org/10.1155/2018/6757345), in [Case Reports in Hematology](https://www.hindawi.com/journals/crihem/). Volume 2018, Article ID 6757345, 5 pages <https://doi.org/10.1155/2018/6757345> [↑](#footnote-ref-32)
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35. “[Application of the ISTH bleeding score in hemophilia](https://www.trasci.com/article/S1473-0502(18)30030-2/abstract)” was published in [Transfusion and Apheresis Science](https://www.trasci.com/). [↑](#footnote-ref-35)
36. Umit Yavuz Malkan and Salih Aksu, “[Combination of Novoseven and Feiba in hemophiliac patients with inhibitors,](https://www.degruyter.com/view/j/med.2018.13.issue-1/med-2018-0090/med-2018-0090.xml)” published 24 December in [*Open Medicine*](https://www.degruyter.com/view/j/med) “. Volume 13, Issue 1 **DOI:**<https://doi.org/10.1515/med-2018-0090> [↑](#footnote-ref-36)
37. PTG-300 is an injectable hepcidin mimetic peptide [↑](#footnote-ref-37)
38. In the current process, blood stem cells are removed from the patient, treated with a vector to replace or add genes, and then returned to the patient. The multi-step process involves significant time in hospital. The new collaboration wants to develop therapies that could be infused directly into the patient. “We will look at new technologies of non-viral methods for introducing the therapeutic gene into stem cells that could help standardize gene therapies and make them more available and affordable,” said project leader Dr. [David A. Williams](https://d.docs.live.net/0169687de598bd26/Documents/ARC/boston/search/results?q=David%20A.%20Williams), chief scientific officer and senior vice president of Boston Children's Hospital and President of Dana-Farber/Boston Children’s Cancer and Blood Disorders Center. [↑](#footnote-ref-38)
39. Cablivi is an anti- von Willebrand Factor (vWF) Nanobody, which inhibits the interaction between ultra-large vWF multimers and platelets and, therefore, stops the formation and accumulation of the micro-clots that cause the thrombocytopenia, tissue ischemia, and organ dysfunction in aTTP. [↑](#footnote-ref-39)
40. Marie Scully et al., “Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura”. *NEJM,* 9 January 2019 DOI: 10.1056/NEJMoa1806311 [↑](#footnote-ref-40)
41. Published by the American Society of Hematology. [↑](#footnote-ref-41)
42. Antonio Piga et al., “Luspatercept improves hemoglobin levels and blood transfusion requirements in a study of patients with beta-thalassemia”, *Blood* 2019: blood-2018-10-879247; doi: https://doi.org/10.1182/blood-2018-10-879247 [↑](#footnote-ref-42)
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44. [businesswire.com](http://businesswire.com):<https://www.businesswire.com/news/home/20190215005075/en/> [↑](#footnote-ref-44)
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    [↑](#footnote-ref-45)
46. [Read the full Yale study at cell.com.](https://www.cell.com/cell-reports/fulltext/S2211-1247(18)31932-6) [↑](#footnote-ref-46)
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49. Guruprasad P, Mannino RG, Caruso C, et al. [Integrated automated particle tracking microfluidic enables high-throughput cell deformability cytometry for red cell disorders [published online November 12, 2018]](https://onlinelibrary.wiley.com/doi/10.1002/ajh.25345). *Am J Hematol*. doi: 10.1002/ajh.25345 [↑](#footnote-ref-49)
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