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Eleven clinical trials that will shape medicine in 2026

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Nature Medicine asks leading researchers to name their top clinical trial for 2026, from long-awaited vaccines for infectious diseases to new treatments for advanced cancers and long COVID.

From next-generation vaccines to gene editing and stem-cell therapies, scientists are testing bold new ideas to tackle some of the world's toughest diseases. These clinical trials — from tuberculosis and Lassa fever to cancer and autoimmune disorders — offer a glimpse into a future in which precision medicine, innovation and persistence could transform global health (Table 1).

A longer-lasting tuberculosis vaccine

Lee Fairlie: The reason this tuberculosis (TB) trial was developed is because the current Bacillus Calmette–Guérin (BCG) vaccine only works well in young children, and its protection fades pretty quickly with age, especially during adolescence and adulthood. As that is the group most likely to get TB and spread it, we really need something better. TB is still a massive problem worldwide — about 10.8 million people became ill with TB and around 1.25 million died in 2023 — so there is a huge need for a new vaccine.

The vaccine we are testing, called M72/AS01E, showed some very promising results in an earlier phase 2b study. It reduced progression to pulmonary TB by about 50% in people who had evidence of TB infection. This large phase 3 trial includes about 20,000 participants across South Africa, Kenya, Malawi, Zambia and Indonesia. Most participants are IFN-γ release assay (IGRA)-positive, meaning they have had prior TB infection (18,000), and people living with HIV (1,000) and people who are IGRA-negative (1,000) are also included.

The trial enrolled 11 months faster than expected, mostly because the communities we work with have very high TB rates (disease awareness is high), as well as the great work of the sites. The main goal is to see how well the vaccine prevents progression to lab-confirmed TB disease. We expect data in about three years' time. The trial is sponsored by the Gates Medical Research Institute, with funding from the Gates Foundation and

Table 1 | Clinical trials to watch in 2026

Treatment	Organization	Description	Phase	Indication
M72/AS01E-4	Gates Medical Research Institute	A vaccine against *Mycobacterium tuberculosis* in people never infected with TB, previously infected or living with HIV	Phase 3	Tuberculosis
3BNC117-LS and 10-1074-LS	Rockefeller, Imperial and Oxford Universities	Two HIV-specific, long-acting broadly neutralizing antibodies on post-treatment viral control	Phase 2	HIV
Loratadine, famotidine and colchicine	University College London	Open label, adaptive platform, randomized drug trial	Phase 3	Long COVID
LASSARAB	University of Maryland	An inactivated rabies-based vaccine using the full Lassa glycoprotein	Phase 1	Lassa fever and rabies
Ziltivekimab	Novo Nordisk A/S	Efficacy of inhibiting IL-6 in patients with atherosclerosis, chronic kidney disease and residual inflammatory risk	Phase 3	Cardiovascular events
Daraxonrasib	Revolution Medicines	Comparing an oral RAS inhibitor to standard chemotherapy	Phase 3	Metastatic pancreatic cancer
CAR T cells	Cartesian Therapeutics	Safety and preliminary efficacy of autologous T cells expressing a chimeric antigen receptor directed to B cell maturation antigen	Phase 2b	Myasthenia gravis
Stem cells	Prime Medicine	Safety and efficacy of a patients' edited stem cells	Phase 1/2	Chronic granulomatous disease
Bria-IMT	BriaCell Therapeutics Corporation	Cell-based immunotherapy plus an immune checkpoint inhibitor	Phase 3	Metastatic breast cancer
Autologous bone marrow-derived stem cells	MD Stem Cells	Delivering a patient's bone-marrow stem cells intravenously and nasally	Human clinical study	Neurological diseases and damage
Pelacarsen	Novartis Pharmaceuticals	Antisense-oligonucleotide drug to reduce cardiovascular risk in patients with heart disease and high Lp(*a*)	Phase 3	Major cardiovascular events

Wellcome. It is a long process, but honestly, this is the most promising TB vaccine work we have seen in nearly a century.

Lee Fairlie is the director of maternal and child health at the University of the Witwatersrand, Wits RHI, Johannesburg, South Africa.

Testing long-acting antibodies against HIV

Sarah Fidler: The RIO trial is testing a new kind of HIV treatment that uses long-acting antibodies instead of daily pills. Current HIV medicines, called antiretroviral therapy, work incredibly well to stop the virus from multiplying, but they do not remove the tiny pool of infected cells that stays hidden in the body. That is why, when someone stops their medication, the virus almost always comes back.

Our question was: could these special antibodies keep the virus under control even when people stop their regular treatment? The trial is called RIO because it is a collaboration between three universities: Rockefeller, Imperial and Oxford, funded by the Gates Foundation. We worked with people who started HIV treatment very early after first becoming HIV-positive, since their immune systems were still strong. They received one infusion of placebo or long-lasting antibodies, which stay in the body for about six months.

Participants made a huge commitment, because they stopped their daily medicine and came in every week for blood tests to check when the virus returned. The main result was exciting: after five months, 75% of people given the antibodies still had not needed to restart HIV medicines, compared with just 11% in the placebo group. Some even stayed off treatment for nearly two years.

The antibodies have been safe so far, and we are running follow-up studies to see if combining them with vaccines or other approaches could help even more. The big hope is to eventually give people long breaks from daily HIV medicine — maybe even help their own immune systems take over to be able to maintain lasting viral control.

Sarah Fidler is professor of HIV medicine and communicable diseases at Imperial College London, London, UK.

Learning to treat long COVID

Emma Wall: I am an infectious disease physician and research scientist at University College Hospital in London and the Francis Crick Institute. During the pandemic, I was working both in acute-COVID care and in a long-COVID clinic with respiratory colleagues. We were seeing many patients with extreme fatigue, and we talked about which, if any, drugs we should use, but decided instead to do a trial. We joined forces with others and were awarded £6.8 million funding from the National Institute for Health and Care Research, which is like the UK's version of the National Institutes of Health (NIH), to run a major trial testing drugs and other interventions for long COVID[1].

We designed the trial in 2021, when we still knew very little about long COVID. Most of our patients had debilitating fatigue, especially something called post-exertional malaise — basically, when any effort makes people feel like they have run a marathon. We found that even short walks caused abnormal blood changes, suggesting problems in tiny blood vessels. So, we tested drugs in the trial that might reduce inflammation or improve blood flow, including an anticoagulant and anti-inflammatory options.

It has been heartbreaking — many patients were previously healthy young professionals who have been ill for years. We involved patients directly in designing and running the trial, including drug selection and shaping the study design, making it open label because they wanted transparency. The trial is complete, the analysis finished and the manuscript has been submitted — we are planning to present the results later this year in Boston and publish them in 2026.

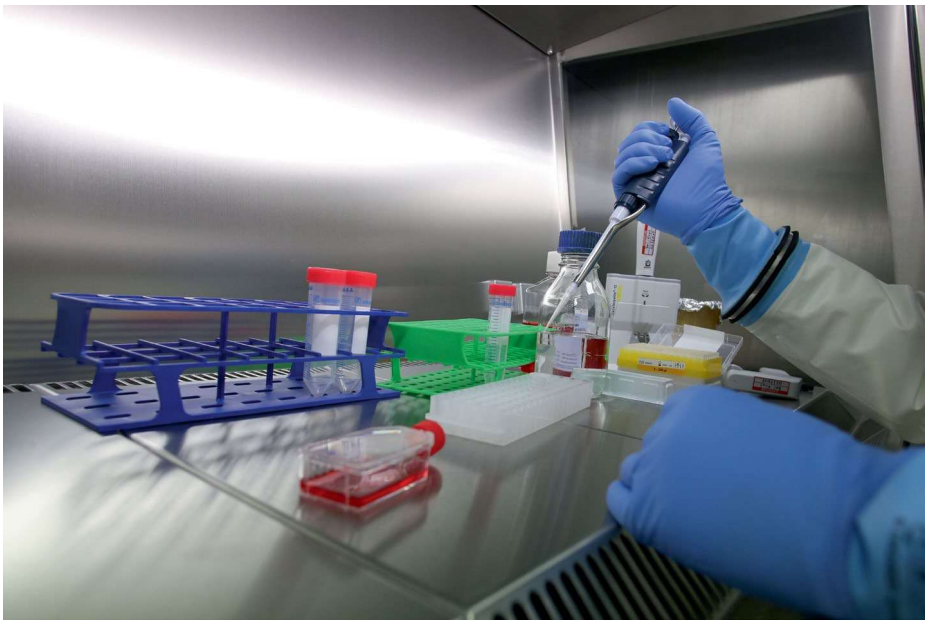
Emma Wall is a clinical research group leader at the Crick and consultant in infectious diseases at University College London Hospitals, London, UK.

Developing a dual Lassa–rabies vaccine

Justin Ortiz: Lassa fever is a viral hemorrhagic illness, similar in seriousness to Ebola and Marburg, caused by the Lassa virus. It is endemic to West Africa and transmitted mainly through contact with rodent excreta or infected individuals, particularly in healthcare settings. The World Health Organization (WHO) identifies Lassa fever as a major public-health threat and a priority disease for research and vaccine development, given its epidemic potential, lack of effective treatments and high mortality.

The WHO estimates 100,000 to 300,000 infections and about 5,000 deaths each year, though actual numbers are probably much higher owing to limited surveillance. The disease is particularly devastating in pregnancy, with over 80% of late-term infections resulting in maternal or fetal death.

The Lassa Fever CVD 1000 trial was created to meet this urgent global health need. Lassa fever persists because of poverty, limited healthcare capacity and under-resourced One Health systems that insufficiently connect animal, human and environmental disease surveillance and response. A vaccine could save lives immediately while long-term improvements continue. Beyond humanitarian



Virologist working in a secure lab that can handle the Lassa virus. Credit: dpa picture alliance / Alamy.

concerns, the USA considers Lassa fever a Category A agent, a major bioterrorism threat as it lacks approved vaccines and treatments.

The CVD 1000 trial uses the LASSARAB vaccine candidate, developed by Matthias Schnell of the Jefferson Center for Vaccines & Pandemic Preparedness in Philadelphia, and it is distinctive in combining protection against both Lassa fever and rabies, two neglected yet deadly diseases prevalent in West Africa. Early data show a well-tolerated vaccine and strong immune responses, with all participants developing antibodies after two doses. The last patient data will be collected around May 2026 in this first-in-human WHO-aligned trial.

Justin Ortiz is a physician scientist at the Center for Vaccine Development and Global Health at the University of Maryland, Baltimore, MD, USA.

Three Greek gods attack heart disease

Paul Ridker: Inhibition of inflammation is a major new target for atherosclerosis. My group's earlier work showed that blocking interleukin-1 (IL-1) significantly reduced heart attacks and strokes, proving that inflammation drives cardiovascular disease independently of cholesterol. But what we noticed was that the biggest benefit from IL-1 inhibition came in people whose downstream IL-6 levels fell the most. So, the next logical step was to target IL-6 directly, and that is where ziltivekimab — a fully human monoclonal antibody that targets IL-6 — comes in.

There are three major ziltivekimab trials ongoing globally. The first is ZEUS, addressing whether IL-6 inhibition can reduce cardiovascular event rates in patients with atherosclerosis, chronic kidney disease and residual inflammatory risk, defined as an elevated level of high-sensitivity C-reactive protein (hsCRP). ZEUS is fully enrolled with around 6,300 patients worldwide and should complete sometime in late 2026. The second is HERMES[2], in which IL-6 inhibition is being tested in the setting of heart failure with preserved ejection fraction, another population in which residual inflammatory risk is known to drive disease progression. The third ziltivekimab trial is ARTEMIS, which starts treatment right when patients arrive at the hospital with an acute heart attack. The idea is to see if blocking inflammation immediately can improve recovery and reduce future events for individuals with acute coronary syndromes.

Doctors will not treat what they do not measure. As just described in an American College of Cardiology 2025 Scientific Statement, we need universal screening for the inflammatory biomarker hsCRP at the same time we screen for LDL cholesterol. The time has arrived for combined lipid-lowering and anti-inflammatory therapies, which are synergistic, and we really need to get past a monolithic sense that the only thing to do is lower cholesterol.

Paul Ridker is a cardiovascular epidemiologist and biomedical researcher at Harvard University and Mass General Brigham Hospital, Boston, MA, USA.

Gumming up the works of pancreatic cancer

Brian Wolpin: Pancreatic cancer is one of the toughest cancers out there — it has limited treatment options, it is very aggressive and survival times are heartbreakingly short. Right now, the standard of care for patients with metastatic disease is multi-agent chemotherapy. It can work, but it has considerable toxicities and is often only modestly effective. The big breakthrough is that nearly 95% of pancreatic cancers are driven by a single mutation — in *KRAS* — something scientists have been trying to target for 40 years.

This new global trial is testing a broad RAS inhibitor, called RMC-6236 or daraxonrasib. Unlike earlier KRAS drugs that only worked for the rare G12C mutation, this one hits the most common ones — G12D, G12R and G12V — covering nearly all patients with pancreatic cancer. It is an oral, once-daily treatment that is easier to administer than intravenous chemotherapy. The trial is enrolling 460 patients worldwide, randomized half to chemotherapy, half to the RAS inhibitor, with dual endpoints of progression-free survival and overall survival. Results are expected around 2026.

Side effects so far are manageable — mostly rash, mouth inflammation, nausea and diarrhea — often less than what is seen with chemotherapy. The drug also uses a really interesting mechanism: it is a molecular glue. Instead of directly blocking KRAS, it binds a helper protein called cyclophilin A and essentially glues it to RAS, stopping the cancer's growth signals.

If this works, it could finally bring a targeted therapy to almost every patient with advanced pancreatic cancer — something that has never been possible before. It is an exciting, hopeful step forward for a disease that desperately needs one.

Brian Wolpin is a medical oncologist and director of the Hale Family Center for Pancreatic Cancer Research at the Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA.

Targeting myasthenia gravis with mRNA

James Howard: Myasthenia gravis is a chronic autoimmune disease that interferes with the communication between nerves and muscles, leading to weakness and fatigue. For decades, treatments were borrowed from transplant medicine — broad immunosuppressants that take months to work and cause major side effects, especially steroids. Then in 2017, we finally saw breakthroughs with immunotherapies that act fast, with more favorable side-effect profiles, but require constant dosing to keep symptoms controlled.

The Descartes-08 trial, led by Cartesian Therapeutics, takes a totally different approach using mRNA chimeric antigen receptor (CAR) T cell therapy. Instead of editing DNA as with cancer CAR T cells, this method programs cells temporarily — reducing long-term risks such as cytokine-release syndrome. Early studies were promising, and the ongoing phase 3 trial aims to confirm that. The treatment involves six short weekly infusions, and some patients have gone a year or more symptom-free afterward.

In the phase 2b trial, about 57% of patients achieved minimal symptom expression — essentially no disease — by month 6, maintaining that through month 12. That is remarkable durability compared with older options. The therapy targets BCMA-expressing plasma cells, a narrow group responsible for producing harmful antibodies. Because it is so specific, it avoids the broad immune suppression that causes side effects.

If costs come down, this could even be an outpatient, first-line treatment. And the implications go beyond myasthenia gravis, because this mRNA CAR T cell approach could eventually extend to other autoimmune diseases, such as lupus or rheumatoid arthritis. It is a real next step in long-lasting, precise immunotherapy.

James Howard is the director of the myasthenia gravis clinical trials and translational research program at the University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

Commercial challenges of treating an extremely rare disease

Allan Reine: Chronic granulomatous disease (CGD) is a rare inherited immune disorder in which certain white blood cells — specifically

phagocytes — cannot effectively kill specific bacteria and fungi. Individuals experience recurrent, often severe infections and inflammatory complications, such as bowel-like disease that can be profoundly debilitating. Average life expectancy extends into the fourth decade. Although allogeneic bone marrow transplantation can be curative, it carries substantial risks. For those not eligible, lifelong prophylactic antibiotics and antifungal therapies are required.

Prime Medicine selected CGD as one of its first programs to demonstrate the potential of its prime-editing technology — believed to be the most versatile and precise genome-editing approach. The team sought diseases that existing gene-editing technologies could not address effectively, and CGD was a clear fit.

Prime's ex vivo approach corrects the defective gene in a patient's own hematopoietic stem cells before reinfusion. Unlike allogeneic transplantation, this autologous approach eliminates graft rejection and graft-versus-host disease.

Results from an ongoing phase 1/2 clinical study have been remarkably promising. In the first two treated patients, Prime observed what can be described as a functional cure — with neutrophil activity normalized above the level needed to prevent infections. Early results suggest a beneficial effect in both patients' inflammatory bowel disease.

Because CGD is rare — affecting about 1,000 US individuals, and only 250 with the targeted subtype — the commercial opportunity is limited. Nonetheless, given the strength of the early data, Prime is actively engaging with the US Food and Drug Administration (FDA) to bring this potentially transformative therapy to patients in need.

Allan Reine is the chief executive officer at Prime Medicine, Cambridge, MA, USA.

Patients with metastatic breast cancer urgently need novel treatments. Credit: ANP / Alamy.

Immunotherapy for metastatic breast cancer

Sara Hurvitz: The BRIA-ABC trial is an exciting study focused on people living with metastatic breast cancer. Even though cancer care has come a long way, metastatic breast cancer is still rarely curable, and only a small fraction of patients benefit long-term from current immunotherapy or targeted treatments. That is why this trial was designed — to see if a new cell-based immunotherapy, called Bria-IMT, can actually improve outcomes for people who have already gone through many prior treatments.

The trial is currently open and enrolling at around 40 centers. The main goal is to find out whether combining Bria-IMT with an immune checkpoint inhibitor can extend overall survival compared to the standard chemotherapy that a doctor would typically choose. Researchers are also tracking other key outcomes such as progression-free survival, response rates, safety, quality of life and even how long patients stay free of metastases to the brain or spine. On top of that, they are exploring biomarkers and other signals that could help predict who benefits most.

What really sets BRIA-ABC apart is how inclusive it is. It welcomes individuals with all breast cancer subtypes, including patients who cannot work but are able to take care of themselves — and those with brain metastases and people who have already had extensive prior treatments, even antibody–drug conjugates or checkpoint inhibitors. Plus, it uses a real-world comparator arm, making the results much more meaningful for everyday clinical practice.

Sara Hurvitz holds the Smith Family Endowed Chair in Women's Health at the Fred Hutchinson Cancer Center, Seattle, WA, USA.

Inhaling better brain function

Jeffrey Weiss: The NEST trial — short for Neurologic Stem Cell Treatment Study — is a human clinical study exploring whether stem cells taken from a patient's own bone marrow can help improve neurological function. The cells are isolated, then reintroduced into the body through the bloodstream and the nasal passages, allowing them to potentially reach the brain and promote repair.

The idea actually grew out of earlier work treating eye diseases with stem cells. In 2010, I performed the first retinal-stem cell surgery, and as we treated more eye patients, we also noticed unexpected improvements in neurological symptoms, too — people regaining movement or speech, even getting out of wheelchairs. That is what led to the creation of NEST about nine years ago, and I am the principal investigator working with Steven Levy, CEO at MD Stem Cells.

Since then, we have treated roughly 200 patients from all over the world. The procedure itself takes less than an hour and uses conscious sedation. Bone marrow is drawn from the hip, processed, and then reintroduced intravenously and through the nose, where cells may migrate into the brain.

Many patients report improvements within weeks, sometimes even the next day. Although it is not a cure, the results have been remarkable for conditions such as amyotrophic lateral sclerosis, Alzheimer's disease, stroke, Parkinson's disease, traumatic brain injury and chronic multiple sclerosis, offering hope and quality-of-life gains where no treatments existed before. The team's work continues both in the USA and Dubai.

Jeffrey Weiss is founder and CEO of Micron Ophthalmic, Parkland, FL, USA.

New cholesterol target offers hope for heart patients

Stephen Nicholls: The Lp(a)HORIZON trial is a major global study focused on something called lipoprotein (*a*) (Lp(*a*)), which is a type of cholesterol particle that carries a protein called apolipoprotein (*a*). High levels of Lp(*a*) have been linked genetically and epidemiologically to atherosclerosis, heart attacks and strokes. But until now, we have never had a treatment that truly targets and lowers Lp(*a*) in a meaningful way.

That is where this study comes in. It is the first large cardiovascular outcomes trial testing a new therapy called pelacarsen, designed specifically to reduce Lp(*a*). The goal is to see if lowering these levels can actually translate into fewer heart attacks, strokes and deaths. The trial is fully enrolled — about 7,000 participants worldwide — and it is being led by an international team. Results are expected around 2026.

The primary endpoint looks at major cardiovascular events such as death from heart disease, myocardial infarction, stroke and coronary revascularization. Researchers are also measuring all-cause mortality and doing detailed biochemical analyses to see how changes in Lp(*a*) levels relate to outcomes — for example, whether people with the highest baseline levels get the biggest benefit.

Safety and tolerability are key too. Pelacarsen typically lowers Lp(*a*) by about 80%, and most healthy people naturally have low levels, so it is expected to be well tolerated. If successful, this study could open a brand-new frontier in heart-disease prevention.

Stephen Nicholls is director of the Victorian Heart Institute at Monash University, Melbourne, Victoria, Australia.

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