Stop Looking for a Silver Bullet. Start Mixing the Long COVID Cocktail.

Like HIV or cancer, long COVID is not a single problem—it's a layered disease involving multiple biological mechanisms.

September 17, 2025 By Jon Douglas and The Sick Times

After spending over $20,000 out of pocket on long COVID treatments that promised relief but delivered mostly disappointment, I turned to what science suggested might actually work: monoclonal antibodies.

My journey to access two COVID-19 monoclonal antibodies — lab-created proteins designed to mimic the body's natural defense against the virus — quickly morphed into Kafka with a stethoscope. The pharmaceutical company blamed the Food and Drug Administration (FDA). The FDA pointed back at the company. It felt like trying to get a straight answer from a Magic 8 Ball with a bureaucratic hangover.

In desperation, I contacted a medical concierge company in Texas that claimed they could provide the monoclonal antibodies I sought for nearly $10,000 cash through a hush-hush agreement, with no guarantee of authenticity. I declined, though in retrospect, it might have been my best shot at remission.

Across the long COVID community, people who've accessed these therapies sometimes report a miraculous remission. But here's what keeps me up at night: If some people are finding relief, why aren't we scaling what might work? And why aren't we trying multiple interventions at the same time?

From watching other medical breakthroughs, I've learned that it often takes multiple approaches working together to tackle complex diseases. Take HIV. In the 1980s, it was a death sentence wrapped in stigma, delivered with breathtaking cruelty. Now, a combination of three therapies, each attacking the virus at different points in its life cycle, transformed HIV from an inevitable ending into a manageable chronic condition.

David Ho, who pioneered this combination approach, told me that combination treatments would be key for long COVID, just as they were for HIV. Recent HIV research has pushed this idea even

further, including one study with an immune system–modulating drug that scientists are also exploring for long COVID.

Other complex diseases, like tuberculosis, with its RIPE protocol, and cancer, with its cocktails of chemotherapy, immunotherapy, and radiation, similarly demand complex solutions. They're symphonies of dysfunction, and it takes a conductor who understands every discordant note to guide them back toward harmony. We even learned this lesson with acute COVID-19, as successful antivirals for the acute disease involve combining two drugs.

The success of these combination strategies raises an obvious question. Why haven't we pursued similar approaches for people with long COVID? Like HIV, cancer, or even acute COVID-19, long COVID is not a single problem — it's a layered disease involving viral persistence, immune dysfunction, inflammation, and neurological disruption. Tackling it with just one treatment is like trying to put out a wildfire with a garden hose.

Combination therapies aren't just helpful; they're necessary. Getting them to patients will require bold action from every corner of the system: patients who advocate for themselves, physicians who stay current with the science, researchers who design smarter trials, drug companies that are willing to collaborate, and government agencies that clear the path for innovation.

Why combination therapy makes sense

The scientific evidence has revealed something both clear and deeply complex. Long COVID involves multiple biological mechanisms that are all tangled up together like headphone cables in your pocket.

According to research from members of PolyBio's Long COVID Consortium, long COVID is a systemic, tissue-based disease, rooted in viral persistence and immune system disarray. It includes SARS-CoV-2 reservoirs hiding out throughout the body, an overactivated and dysfunctional immune system, endothelial damage, inflammation in the brain, autoimmunity, and more. Scientists have found this evidence from tissue biopsies, imaging, proteomics, and functional assays across international research sites.

Some researchers have also found chilling parallels between long COVID and cancer, such as one study showing that SARS-CoV-2 can turn off critical tumor suppressor genes. In biopsies and autopsies, SARS-CoV-2 RNA has been found embedded deep in tissues such as the colon, brain, and other organs throughout the body months and even years after initial infection. In short, people with long COVID show similar immune system cell markers to those with viral-related cancers.

This isn't cause for panic, researchers stress, but for awareness and urgency. It's another compelling reason why single-drug approaches feel almost quaint in the face of such biological complexity.

Given the complexity of disease mechanisms, one drug will simply never be enough. Research supports a combination approach. Within our arsenal, we have antivirals, monoclonal antibodies, intravenous immunoglobulin (IVIG), immunomodulators including JAK inhibitors and IL-15 superagonists, treatments for the gut, extracorporeal therapies, and much more.

On the near horizon are computational approaches to finding these combinations, based on large datasets like those from the massive National Institutes of Health's (NIH) RECOVER program. These approaches are becoming increasingly sophisticated. For example, scientists at Gladstone Institutes and University of California, San Francisco (UCSF) recently demonstrated this power by analyzing gene expression changes in Alzheimer's disease and then systematically searching through 1,300 existing drugs to find ones that could reverse those changes.

They narrowed it down to 10 FDA-approved drugs. From electronic medical records of 1.4 million people, they found that patients taking some of these drugs were already less likely to develop Alzheimer's. And when they tested the top two candidates in combination in mice with Alzheimer's, the researchers found further evidence for this treatment's potential.

The same computational firepower could revolutionize long COVID treatment. Instead of testing single drugs in isolation, we could systematically search for combinations that reverse the specific gene expression patterns, immune dysfunction, and cellular damage we see in people with long COVID.

Many recent trials testing single drugs have delivered disappointing results, not necessarily because the treatments didn't work, but because they were mismatched to the underlying biology. Yet their secondary analyses tell a far more intriguing story. These trial results make a strong case for testing combination therapies tailored to people with long COVID based on their specific symptoms and biological measurements. Leading long COVID researchers, like Michael Peluso at UCSF, have committed to iterating on these trials rather than abandoning promising hypotheses.

We need focused, intensive studies that pair antivirals with monoclonal antibodies and immune modulators, add gut-targeted therapies, and track every measurable biomarker.

What's the holdup?

So if the science is this compelling and the need is this urgent, what's the holdup?

Pharmaceutical companies are hesitant to act. They worry that a failed trial could hurt their brand, and many don't see a profit in treating a condition still clouded by stigma. Long COVID is often dismissed as "just COVID-19" even though research shows it's a distinct, multisystem disease.

Yet we have a proven blueprint for rapid drug development. Pfizer's development of Paxlovid took less than two years from concept to treating patients by running different stages of development in parallel rather than in sequence, leveraging machine learning tools, and enabling rapid decision-making through streamlined regulatory interactions. The same urgency and innovation that created Paxlovid could accelerate combination therapies for long COVID.

Regulatory uncertainty makes things worse. The FDA hasn't issued clear guidance for long COVID therapies, especially for combinations. Without that direction, drug makers and researchers are left guessing, which slows everything down.

Government efforts also haven't filled the gap. The NIH's $1.6 billion RECOVER initiative promised adaptive trials and cutting-edge science. Instead, it launched conventional studies, testing things like brain games and exercise routines. RECOVER may now be shifting course with its new Treating Long COVID initiative, which announced new trials earlier this week.

Meanwhile, researchers developing biomarkers and mechanistic studies were sidelined by government funding. Without validated biomarkers to identify which patients have viral persistence versus immune dysfunction versus neuroinflammation, combination therapy trials risk lumping together vastly different patients, which is a bit like trying to treat every driver with car problems the same way, whether they have a flat tire or need a new engine. It's a recipe for failure.

And then there's cost. Many promising therapies, like monoclonal antibodies and antivirals, run for thousands of dollars per patient. Insurance rarely covers them, which means access gets determined not by medical need but by whether you happen to have the equivalent of a used car sitting around to spend on healthcare.

The science is advancing, but the systems meant to deliver it are stuck in neutral. And patients are paying the price.

What we can do now

Despite all these obstacles, there's something genuinely remarkable happening in long COVID research. We have an army of clinicians, scientists, researchers, advocates, and people with lived experience who are all willing to grapple with these complex diseases together.

Instead of the usual academic silos where everyone stays in their specialty, long COVID researchers are in the trenches together. And here's the thing that gives me hope: this unprecedented collaboration is actually working.

At the Keystone Symposia last month, researchers zeroed in on viral persistence and immune dysregulation, finding traces of viral proteins lingering in tissues and blood, and mapping how people's immune systems are stuck in chronic overdrive.

The result was a shared, evolving picture of how the virus hides, how immunity misfires, and where intervention might finally break the cycle.

This is what happens when everyone pulls in the same direction, toward advancing combination therapies, and toward a real, tangible hope. We each have a role to play:

- Patients: Show your doctors recent studies from leading researchers around the globe. Be their

teacher. Join trials if you can. Document your experience as it builds the case for treatment access.

- Doctors: Read papers from the leading researchers. Connect with these researchers. Advocate for your patients with insurance boards. Read the CoRE at Mount Sinai guide for providers or the Bateman Horne Center's guide.

- Researchers: Push for trials that reflect the multisystem nature of this illness. Develop biomarker pipelines that can identify which patients have which biological drivers. Follow LIINC's model of small, intensive pathogenesis trials that combine treatments while tracking broad physiological impacts. Treat patients like collaborators, not just subjects.

- Policymakers: Fast-track combination protocols. Expand funding beyond outdated RECOVER frameworks. Recognize that time is of the essence. Sustainable progress requires sustained investment. We truly can't do this without the NIH.

- Pharma: The market is not small. Millions are suffering. Partner with patient-led research groups. Repurpose what already exists. And know this: history remembers who showed up when it mattered.

I've been lucky to have a doctor who pushes for combination therapy at my local clinic, even if it means challenging the system. But getting these therapeutics is still next to impossible, and when you can get them, the prices are staggering. I'll likely be paying out of pocket, which is possible only because of privileges most patients don't have.

Long COVID stole my early thirties and shattered my sense of certainty. But it also gave me a purpose: to crack open the science, challenge broken systems, and fight for a future where millions aren't forced to push the same boulder uphill every single day.

Writer William Gibson famously said, "The future is already here — it's just not evenly distributed." For long COVID, this future holds effective combination therapies. At the edge of that future is a truth. Science alone won't save us. Solidarity might.

Jon Douglas is a technology professional at Microsoft and Long COVID advocate who serves on RECOVER's biospecimen access committee and a RECOVER-TLC working group. He is also the author of In It for the Long Haul, a memoir about his journey with Long COVID. Follow him on X or Bluesky.

This article was published by The Sick Times, a website chronicling the long COVID crisis, on September 12, 2025. It is republished with permission.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.realhealthmag.com/article/stop-looking-silver-bullet-start-mixing-long-covid-cocktail