The Long COVID Cure Initiative
at PolyBio Research Foundation

OUR MISSION

To deliver treatments to millions of Long COVID patients by translating key academic findings into real-world diagnostic tests, faster and more targeted clinical trials, and accessible patient-ready therapies.

OUR GOAL

Translate scientific progress into effective treatments, delivered to millions of patients years sooner than would otherwise be possible.

The Long COVID Cure Initiative (LCCI) is built to:

Accelerate the Timeline to Clinical Adoption of Treatments

By building the missing infrastructure across diagnostics, trials, commercialization, and clinical adoption, LCCI starts to deliver validated diagnostics and clinical trial results **in the next 1-5 years**, with knowledge of what works built directly into broadscale medical education - **bringing treatments to patients decades sooner than the current trajectory.**

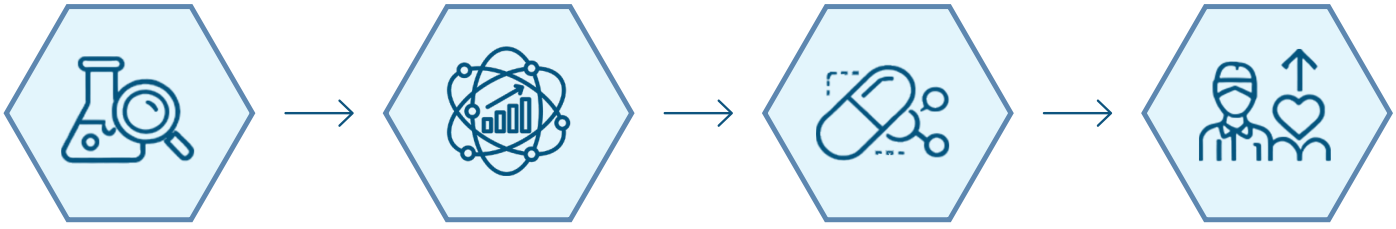
Broaden the Long COVID Treatment Portfolio

Instead of 1–2 narrow therapies that may only manage symptoms (our current trajectory), LCCI enables **multiple treatments** targeting multiple root causes of Long COVID to be trialed and approved over the next decade, greatly increasing the likelihood that patients can be matched to an effective therapy.

Unlock Public and Private Investment

By validating diagnostics and de-risking trials, LCCI makes Long COVID a tractable and investable area for biotech and pharma. This enables our ~$100M (5-year) philanthropic budget to unlock **$300M+ in follow-on investment** (both public and private), accelerating the development of additional treatments beyond what philanthropy alone could fund.

Our PolyBio LCCI strategy:



Validate Diagnostics → **Commercialize Diagnostics** → **Mobilize Smarter Trials** → **Scale Clinical Adoption**

Result: millions of patients receive viable treatments years sooner

WITHOUT POLYBIO	WITH POLYBIO
No validated diagnostics for Long COVID	Diagnostics for multiple Long COVID biological subgroups
Limited pharmaceutical engagement	Millions in pharma engagement and R&D
Few non-targeted treatments	Many targeted Long COVID treatments

The Challenge

Long COVID has left hundreds of millions of people worldwide with crushing fatigue, neurological dysfunction, blood vessel issues, and other life-altering symptoms. Many people additionally sustain heart attacks, strokes, or other serious complications following infection with the SARS-CoV-2 virus. In the United States alone, the economic impact of Long COVID is estimated in the trillions of dollars, with millions pushed out of the workforce.

However the Long COVID disease process is not a mystery. Over the past five years, PolyBio's international research consortium and other scientific teams have published hundreds of papers demonstrating clear biological abnormalities in patients with the condition. For example, some Long COVID patients do not fully clear SARS-COV-2 after initial infection. Instead, a small amount of the virus remains in their tissues where it can drive chronic symptoms. Immune dysfunction, neuroinflammation, microclots, and other measurable - and potentially addressable - problems have also been documented in Long COVID.

Despite this advancement we face a major problem: despite having major leads on the biology of Long COVID, "real-world" uptake of this data is lagging far behind academic discovery; there are **no validated diagnostic tests to guide care and no Long COVID FDA-approved treatments.**

Thus begins the next phase of our mission: To deliver treatments to millions of Long COVID patients by translating key academic findings into real-world diagnostic tests, faster and more targeted clinical trials, and accessible patient-ready therapies.

Our Solution: The Long COVID Cure Initiative

The Long COVID Cure Initiative (LCCI) bridges the gap from academic research to real-world uptake **via a targeted four-step plan** that integrates diagnostic test validation, commercialization, clinical trial acceleration, and targeted medical education into a single coordinated platform. Each step is designed to remove bottlenecks that currently slow progress - cutting red tape, reducing coordination failures, and accelerating the path from research to real-world care. **Our goal is that LCCI will turn scientific progress into effective treatments, delivered to millions of patients years sooner than would otherwise be possible.**

STEP 1

Validate Diagnostics (VIPER)

Overview: Many promising diagnostic tests for Long COVID are being developed in research labs, but remain unvalidated, non-standardized, and unavailable for use in clinical trials or patient care. VIPER addresses this gap by systematically identifying and validating the most promising diagnostics - including tests for SARS-CoV-2 persistence, immune dysfunction, and other core biological drivers of disease. By rigorously testing the most promising diagnostics head-to-head, VIPER identifies which tests truly work - providing the clarity needed to guide clinical trials and treatment decisions.

Program Outcomes

- **Validated, trial-ready Long COVID diagnostic platforms** that reliably identify key biological drivers and patient subgroups
- **Diagnostics capable of guiding targeted clinical trials and treatment decisions**, reducing trial failure risk
- **10+ year acceleration** to validated diagnostics compared to the current path of fragmented, lab-by-lab validation

STEP 2

Commercialize Diagnostics

Overview: Even when diagnostics are scientifically validated, many stall at the point of commercialization - lacking the business, regulatory, and operational support needed to actually be ordered by doctors in a clinic. Our goal is to move VIPER and other validated diagnostics from the lab into clinical practice so that patients can access reliable tests, trials can be biomarker-guided, and health systems can deliver targeted care at scale.

To maximize this process, **our commercialization engine program** will catalyze the transition of diagnostic tests from academic research labs through successful commercialization, ensuring that validated tests are able to achieve outside investment and maximally reach patients. Our commercialization advisory board of top experts will provide VIPER diagnostic and related teams with access to strategic partners, guidance on regulatory and intellectual property strategy, and access to capital, ensuring validated diagnostics become real clinical products, not stalled discoveries.

Program Outcomes

- **Multiple Long COVID diagnostics are commercialized**, via new companies or industry partnerships
- **15+ years acceleration** from scientific validation to real-world adoption
- **Follow-on private investment unlocked**, de-risking pharma and diagnostics industry engagement

STEP 3

Mobilize Smarter Trials

Overview: Current Long COVID trials often fail because they lump heterogeneous patients into one single treatment group. In other words, they do not account for the fact that there are multiple drivers of Long COVID (e.g. SARS-CoV-2 persistence, immune dysfunction, clotting problems), each of which require specialized therapy.

To fix this situation, we will use validated VIPER diagnostics to appropriately select and track Long COVID patients into strategic trials of drugs - or combinations of drugs - targeting different disease drivers. This will greatly increase the chance that patients are paired with therapies that improve their specific symptoms, increasing industry's willingness to bring targeted therapeutics into the space, and upping the chance that trial drugs successfully gain FDA approval.

To accelerate running Long COVID trials as quickly and effectively as possible, we are building **a national, diagnostics-guided, clinical trials network purpose-built for Long COVID.** By standardizing trial endpoints and embedding validated diagnostics into trial design, the network allows trials to enroll faster and generate clearer, decision-ready results - incentivizing greater pharmaceutical investment while accelerating the path to effective treatments. The network will provide funding and/or capital for:

a) *Clinical trials of repurposed generic drugs (including combination therapies):* A number of potentially effective generic drugs for Long COVID are effectively "stuck on the shelf" - the fact that they are affordable and generic is exactly why no pharma companies are paying for them to be trialed. Our support will move these trials forward, allowing any drugs that work to be quickly and affordably delivered to patients.

b) *Industry-led trial of novel medications:* Despite strong scientific rationale, many promising Long COVID therapeutics fail to advance because early industry entry is too risky, slow, or capital-intensive. We will address that gap by de-risking early-stage industry involvement - supporting industry-led trials and novel therapeutics that would otherwise stall.

Program Outcomes

- **Multiple effective Long COVID treatments for different disease drivers identified**, spanning both repurposed generics and industry-led therapies
- **Faster, higher-quality clinical trial results**, reducing uncertainty and trial failure risk
- **Increased pharma engagement**, driven by validated diagnostics, clearer endpoints, and de-risked trial infrastructure

STEP 4

Scale Clinical Adoption

Overview: Even when diagnostics and treatments are validated, adoption into routine care is often slow, uneven, and limited to specialist centers. The CoRE Clinic at Mount Sinai will serve as the national distribution engine for VIPER diagnostics and LCCI treatments. By embedding VIPER/LCCI findings into a Continuing Medical Education (CME)-accredited program, CoRE will convert research breakthroughs into routine clinical practice - rapidly and at scale. As validated diagnostics and therapies emerge, they will be immediately integrated into medical education training modules and standard clinical guidelines, ensuring physicians nationwide know what to test, how to interpret results, and how to treat patients effectively.

Program Outcomes:

- **7,000+ clinicians** trained per year
- Broad clinical adoption **accelerated by 5+ years**
- Rapid national penetration of new standards of care, ensuring that once treatments are validated, patients gain timely access across academic centers, community clinics, and primary care settings

Why PolyBio?

PolyBio's LCCI addresses coordination failures that no single lab, clinic, or company can solve alone. PolyBio is uniquely positioned to execute this plan because it already operates at the center of the Long COVID ecosystem - linking science, clinical care, trials, commercialization, and patient communities.

SCIENTIFIC LEADERSHIP

PolyBio directs the $42M Long COVID Research Consortium (LCRC), the leading global collaboration of Long COVID scientists, shaping research priorities and identifying the strongest diagnostic and therapeutic signals.

CLINICAL TRIAL CAPACITY

PolyBio leadership works directly with the Mount Sinai CoRE Clinic and UCSF LIINC program, the two most advanced Long COVID trial sites worldwide, with deep experience running decentralized, biomarker-guided trials in complex chronic disease.

CLINICAL ADOPTION ENGINE

Through CoRE, PolyBio already reaches thousands of clinicians annually via medical education. This provides a built-in pathway to rapidly embed validated diagnostics and treatments into routine care.

INDUSTRY, REGULATOR, AND PATIENT ACCESS

PolyBio maintains active relationships with biotech and pharmaceutical partners, FDA-linked trial design efforts, and every major Long COVID patient organization - allowing LCCI to de-risk industry participation and align research with regulatory and patient realities.

Bottom line: LCCI scales infrastructure that PolyBio already leads, converting scientific progress into treatments faster and at national scale.

Platform Expansion: Applying the LCCI Model Beyond Long COVID

LCCI is designed as an execution platform, not a one-off disease program. If successful in Long COVID, the same infrastructure - validated diagnostics, diagnostics-guided trials, commercialization pathways, and clinician adoption - can be applied to other infection-associated chronic illnesses that share similar biological and systemic bottlenecks.

Potential future areas include chronic Lyme and other vector-borne diseases, Epstein-Barr virus–associated chronic conditions like multiple sclerosis, aging and longevity, and related infection-driven chronic illnesses where PolyBio already has scientific and clinical relationships.

Unlocking the Cure to Long COVID

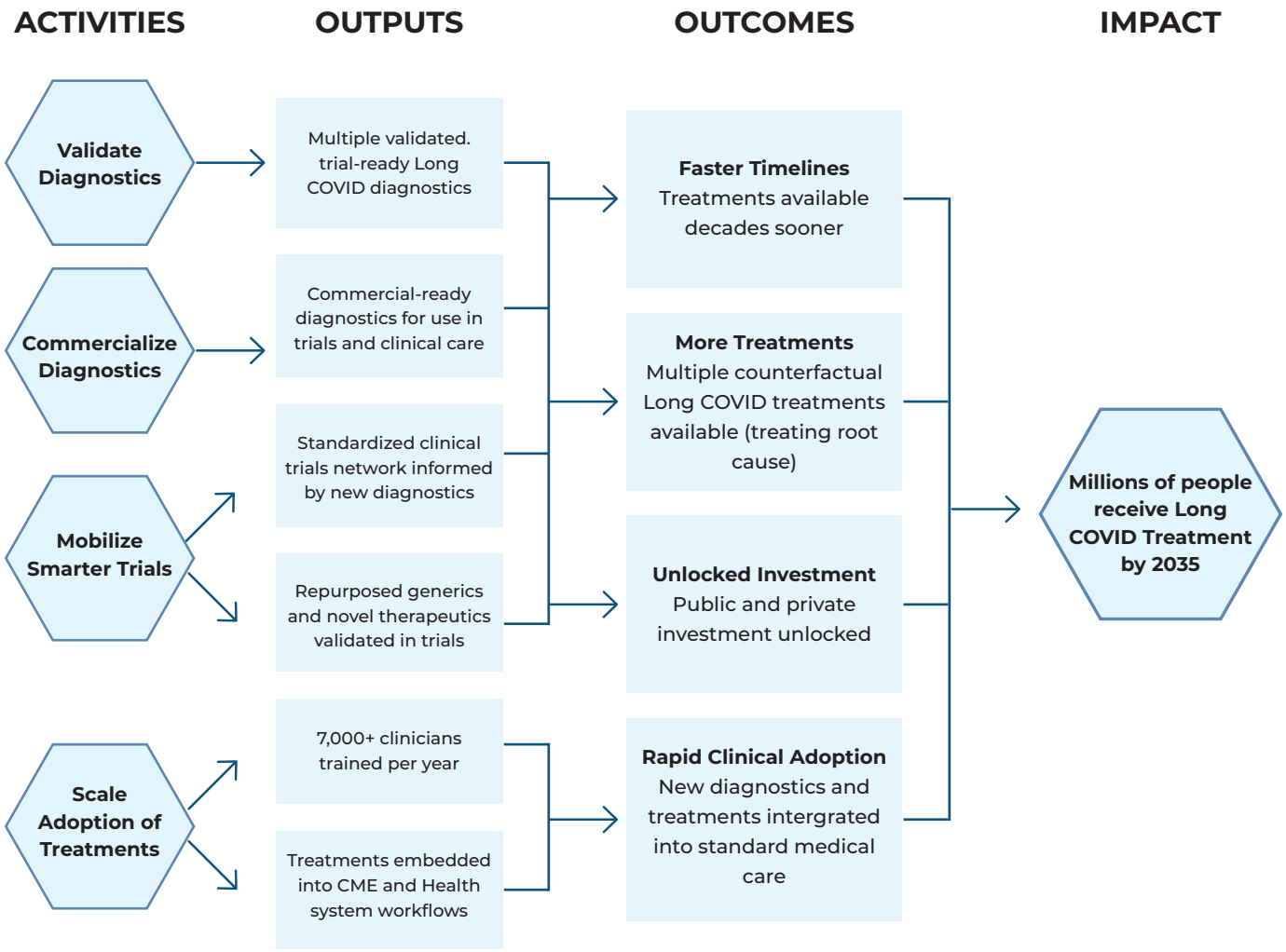
Long COVID represents one of the largest unmet medical needs of our time - not because solutions are unknowable, but because the infrastructure to translate science into treatments has been missing. LCCI is built to close that gap.

By uniting validated diagnostics, smarter clinical trials, rapid commercialization, and large-scale clinical adoption into a single execution platform, LCCI changes the trajectory of Long COVID from indefinite management to tractable cure development. This is the same systems-level approach that transformed HIV from a fatal disease into a treatable condition - and it is now achievable for Long COVID.

PolyBio is uniquely positioned to lead this effort. With deep scientific leadership, proven clinical trial capacity, established commercialization pathways, and a built-in engine for clinician adoption, LCCI is designed not as a research initiative, but as a delivery mechanism for real-world treatments.

With the right investment at this inflection point, we can shorten the path to effective therapies by years, unlock substantial private-sector follow-on investment, and deliver the first real answers to millions of patients. The science is ready. The infrastructure is clear. LCCI is prepared to execute.

Theory of Change



The Team

The LCCI team includes dozens of experts across many institutions, including UCSF, Harvard, and Mt Sinai.

Amy Proal, PhD., Co-Founder and President, PolyBio Research Foundation, and Scientific Director Cohen Center for Recovery from Complex Chronic Illness at the Icahn School of Medicine at Mount Sinai. Dr. Proal coordinates and leads LCCI, including mobilizing trials.

VIPER: Dr. Steven Deeks, MD, Professor of Medicine in Residence at the University of California, San Francisco (UCSF), and a faculty member in the Division of HIV, Infectious Diseases and Global Medicine at Zuckerberg San Francisco General Hospital. Dr. Steven Deeks and team at UCSF lead the core VIPER site.

Commercialization: Sarah Kalloch, MBA, PolyBio Chief Operating and Innovation Officer, directs commercialization and investment teams.

Education: David Putrino, PhD, Director of the Cohen Center for Recovery from Complex Chronic Illness at the Icahn School of Medicine at Mount Sinai, leads research and education at Mt Sinai's CoRE Clinic.

POLYBIO

PolyBio advances research on how viral, bacterial, and parasite infections drive chronic disease and aging. We build collaborative projects that identify, diagnose, and treat root causes of infection-associated chronic illness. Focus areas include Long COVID,chronic tick-borne illness, ME/ CFS, Alzheimer's, neuropsychiatric illnesses, and endometriosis – conditions that impact the health and lives of hundreds of millions of people around the world.

SINCE 2021, POLYBIO HAS:

RAISED $42 MILLION+
from private donors and foundations

Founded Long Covid Research Consortium, bringing together top researchers from more than

25+ INSTITUTIONS
to disrupt bureaucracy and speed discovery

COORDINATED 5 POLYBIO GROUP POSITION PAPERS
published in Nature Immunology, Immuno metabolism, Lancet Infectious Diseases, Frontiers in Microbiology, Ageing Research Reviews

HOW WE **WORK**

In a field where siloed science has stalled progress, PolyBio connects the right people and data across disciplines to fast-track diagnostics, treatments, and ultimately cures. We're not just advancing research, we're transforming it by:

DEFINING THE RESEARCH AGENDA
Our team publishes strategic papers in top journals to chart treatment and diagnostic pathways for chronic disease.

SOURCING BREAKTHROUGH SCIENTIFIC OPPORTUNITIES
We identify and support high-potential researchers advancing infection-associated chronic disease science.

ACCELERATING COLLABORATIVE RESEARCH
We conceptualize and manage cross-disciplinary partnerships with leading institutions to drive Long COVID and related research.

SHARING INSIGHTS TO SPEED DISCOVERY
We promote open data, sample sharing, freely-available and public forums to make research accessible and accelerate progress.

PIONEERING SCALABLE SCIENCE-TO-IMPACT MODELS
We develop funding models that move discoveries from the lab to the clinic for patient benefit.

54+ RESEARCH PROJECTS FUNDED

31 AND COUNTING SCIENTIFIC PAPERS

>2730 CITATIONS

350 COLLABORATIVE CO-AUTHORS

Formed strategic partnership with industry:

- Funded 7 clinical trials and/or their analysis infrastructure
- Amy joined the Invyvd SPEAR Study Group to help guide upcoming clinical trials of monoclonal antibody therapy for Long COVID.
- Held 4 Public PolyBio Symposiums
- Number of media mentions: PolyBios's work covered in 48 articles in outlets including the *NYT*, *USA Today*, *Wall Street Journal*, etc.

PROJECTS BY CATEGORY

- TISSUE ANALYSIS: 17
- ADVANCED IMAGING: 5
- FLUID DIAGNOSTIC: 16
- ANIMAL/MODEL: 6
- LONG-TERM CONSEQUENCES: 4
- THERAPEUTIC: 6

13 UNIQUE TISSUE TYPES BEING COLLECTED FOR RESEARCH

- Gut wall (UCSF, Sinai, Karolinska)
- Lung and bronchial lavage fluid (JCVI, Karolinska, Cardiff)
- Lymph node (Penn, UCSF)
- Bone marrow (UCSF)
- Peripheral nerve (Harvard, JCVI)
- Female endometrium (Gladstone Institutes)
- Blood/vessels arteries (NYU)
- Heart/blood vessels (UCSF)
- Brain/nervous system (Georgetown)
- Vagus nerve (University of Washington)
- Craniocervical ligament (Sinai, JCVI)
- Endometriosis (Pittsburgh, JCVI)
- Spinal cord (Brown)

25+ UNIVERSITIES FUNDED WORLDWIDE

Cardiff University, Georgetown University, Harvard Medical School, Icahn School of Medicine at Mount Sinai, J. Craig Venter Institute, Johns Hopkins, Karolinska Institutet, New York University, Paris Cité University, Stellenbosch University, UMass Chan Medical School, University of California San Francisco, University of Colorado Boulder, University of Pennsylvania, Yale School of Medicine, Emory University, University of Pittsburgh, University of Washington, University of Arizona Banner Research Institute, Stanford University, Institut Pasteur France, Gladstone Institutes, Rega Institute Belgium, Joint Genome Institute, INSERM (France), ESPOIRS (France), Brown University