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The Power and Promise of a

Collaborative Biopharmaceutical Ecosystem

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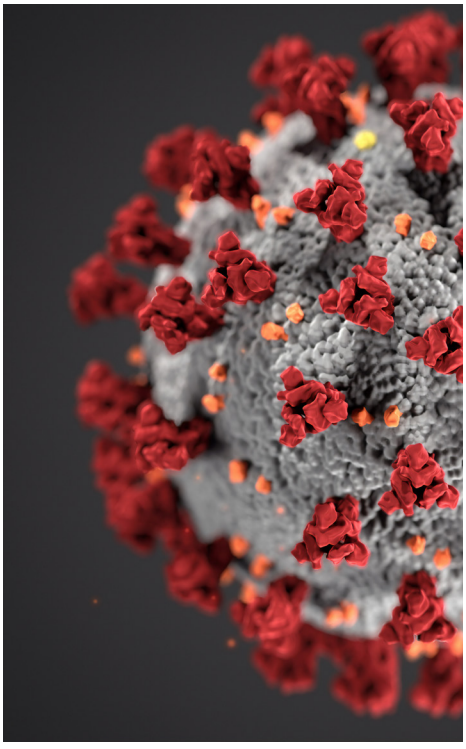
Introduction: The Power of Partnerships in Health Care

Partnerships and a policy and regulatory environment that supports and promotes collaboration play an important role in fostering innovation across the entire health care ecosystem. Collaboration is essential to advancing complex science, promoting improved health outcomes for patients and populations, and supporting a more effective and efficient health care system. The partnerships we see across the health system have become increasingly diverse, multifaceted and often multi-sectorial, spanning across and between major health care industries and the public and private sectors to include biopharmaceutical companies, health insurers, hospitals, government agencies and other public health groups and non-governmental organizations.

COVID-19 COLLABORATION

Biopharmaceutical Partnerships in Context: Joining Forces to Combat COVID-19

Stakeholders around the world are working tirelessly to research, develop and manufacture safe and effective COVID-19 treatments and vaccines. Such an urgent and substantial undertaking requires robust collaboration across the research and development ecosystem and now more than ever it is critical that both public and private assets be brought to bear in addressing COVID-19. Armed with experience garnered from previous outbreaks and decades of knowledge about infectious diseases, America's biopharmaceutical companies have joined forces to fight COVID-19. Companies are leading by collaborating with each other and key health stakeholders on efforts to address the global health crisis through developing diagnostics, treatments and vaccines to help save lives and restore the rhythms of daily life for billions of people. Partnerships that typically take months to plan and formalize are now coming together on an abbreviated timeline, pulling on the process and infrastructure that the industry and ecosystem has been developing over decades. A selection of illustrative examples of collaborations designed to address the COVID-19 pandemic appear throughout the report.



The growing trend toward strategic intra- and cross-sector collaboration to address critical biomedical and public health challenges takes many forms ranging from joint ventures, informal and formal affiliations, to research consortia, and formal public-private partnerships facilitated by federal agency partners.[1] A Deloitte study analyzing the ways in which partnerships have impacted biomedical progress found a significant increase in collaborative models like joint ventures and consortia in recent years, noting that between 2005-2014, 334 new research and development (R&D) consortia formed—approximately nine times the number of consortiums formed during the previous decade.[2]

This movement towards increased strategic partnership is perhaps unsurprising considering the benefits. Partnerships across the health care ecosystem have the capacity to extend and streamline the continuum of care, drive innovation and advance information sharing, facilitate innovative contracting arrangements, improve communication and feedback mechanisms and generate value—all of which ultimately contribute to better health outcomes for patients.

Recently there has been an increased focus on the role and importance of broad public-private partnerships in light of the global coronavirus pandemic, as we have seen an unprecedented level of collaboration around solutions to address and combat COVID-19. That said, it is important to recognize that collaborative initiatives and strategic partnerships are occurring across the health system to address a broad range of today's most pressing health challenges. It is critical that we acknowledge the essential role these collaborations play to all kinds of patients and to society at large and that a supportive policy and regulatory environment is in place to ensure that we can continue to build on the successes to date. This report seeks to provide a snapshot of the diverse array of collaborative efforts currently being pursued across the biopharmaceutical space to advance medical progress, improve patient outcomes and contribute to a stronger, more productive and healthier society.

The Role of Partnerships Across the Biopharmaceutical Research Ecosystem

The benefits and critical role of partnerships and cross-sector collaboration have not been lost on the biopharmaceutical industry. America's biopharmaceutical companies are at the heart of the robust research and development (R&D) ecosystem that develops more innovative medicines than any other country in the world. For decades we've relied on biopharmaceutical companies to lead the way in advancing medical discoveries that improve and even save lives—a role that has never been more critical than it is today in the context of the COVID-19 pandemic. From screening vast global libraries of medicines for potential treatments, to sharing learnings from clinical trials in an effort to advance new therapies, to investing and collaborating with governments, hospitals and insurers to research, discover, develop and manufacturer potential treatments and cures—the biopharmaceutical industry has been at the forefront of the global effort to address the pandemic.[3]

> "We [NIH] always need a pharmaceutical partner.... I can't think of a vaccine, even one in which we've put substantial intellectual and resource input, that was brought to the goal line without a partnership with industry."
>
> ***Anthony Fauci, Director National Institute of Allergy and Infectious Diseases[4]***

As COVID-19 has demonstrated, the complexity of biopharmaceutical R&D, scaling production, manufacturing and distribution, and education around the importance of biopharmaceutical innovation to public health, is often beyond the ability of any one organization or sector to advance alone. Thus, partnerships and collaborations are foundational to advancing and accelerating innovation, overcoming complex scientific challenges and addressing technological, logistical, and manufacturing capacity challenges to meet projected demand for potential COVID-19 treatments and vaccines.

Within the biomedical research ecosystem there are a wide range of formalized partnerships focused on advancing new medicines through development.[5] This report will highlight partnerships focused on advancing science, technologies, or the process more generally. These types of partnerships may vary based on the number and types of partners involved and the goal of the partnership *(see "Types of Biopharmaceutical Partnerships" for examples)*.

One form of collaboration that has become more widespread over the past decade is engagement by traditional and non-traditional partners who jointly establish the structure, governance, risk sharing, and approach to intellectual property (IP) that may be generated as a result of the partnership, as well as jointly determine the objectives and measures of success.[6] This shift has enabled more efforts focused on broader scientific challenges aimed at improving care for ever more complex diseases and allows partners to come together to solve problems throughout the development lifecycle.

Taken together, the partnerships fostered and enabled by an innovation-friendly, collaborative biopharmaceutical ecosystem help catalyze R&D and innovation, support efforts to scale up manufacturing or production quickly, and to facilitate patient access to new treatments and potential cures and ultimately promote better public health and patient health outcomes. Through case studies and analysis of existing partnerships and collaborative efforts, this report provides a closer look at the real-world impacts of partnerships and illustrates the power and importance of a collaborative biopharmaceutical ecosystem.

Types of Biopharmaceutical Partnerships

Joint venture: two or more entities enter a collaboration to jointly contribute to R&D-related activities to achieve a specific objective

Consortium: three or more parties pool resources and work together to achieve a common goal, such as accelerating scientific discovery in a particular disease area or technology.

Cooperative Research and Development Agreement (CRADA): an agreement between one or more government entities and one or more private entity (a company, university, non-profit, etc.) to collaborate on research and development.

Licensing agreement: a non-government entity, usual a company, pays the government for rights to develop a patented government invention.

Catalyzing and Fostering R&D and Innovation

Partnerships across the biopharmaceutical ecosystem have helped propel our society into a new era of innovation. The R&D process is, by nature, an incredibly risky, time consuming and resource-intensive undertaking and this process has only grown in complexity over the last decade. Today, it takes an average of 10-15 years for a new medicine to advance from discovery through pre-clinical stages and only 12 percent of molecules entering clinical development ever end up receiving approval.[7] Despite the high rate of failure, there are about 8,000 medicines in clinical development globally and 74% have the potential to be first-in-class treatments for diseases such as rare cancers, neurological disorders (e.g. ALS) and genetic disorders (e.g. hemophilia).[8] As science and the needs of patients become more complex—or more urgent as in the case of COVID-19—collaborations have not only become increasingly multifaceted but also increasingly critical to furthering R&D and innovation.

"Today, most important developments in medical science typically begin in laboratories, such as the discovery of specific new biological molecules, processes, or pathways, or innovative applications of existing knowledge. In most cases, these discoveries in and of themselves have limited effect beyond meeting a fairly narrow research goal. Their real impact for public health generally comes after several more significant steps - including further R&D, testing, approval by appropriate regulatory bodies (such as the FDA), manufacturing, and distribution."

NIH Office of Technology Transfer[9]

In order to address some of the most challenging health conditions patients face today, cross-sector and multi-stakeholder collaborations have become essential. Increasingly we are seeing partnerships being leveraged across the health system to develop innovative, lifechanging and lifesaving treatments and cures. For example, between 2005 and 2014 the number of new biopharmaceutical R&D partnerships formed more than doubled, shooting up from around 4,000 in 2005 to approximately 9,000 in 2014.[10] These collaborative efforts help support and foster important biomedical innovation and R&D in myriad of ways including expanding available information and resources through knowledge sharing, spreading financial risk and new pathways for funding, and enabling diverse insights and expertise from multiple stakeholders to coalesce around innovative solutions. As scientists learn more about complex mechanisms of disease, these benefits to biopharmaceutical partnerships have never been more important to advancing innovation that helps improve and save lives of patients in need.

COVID-19 COLLABORATION: RESEARCH AND DEVELOPMENT

PhRMA members have established partnerships with each other and government agencies for the research and development of COVID-19 vaccines and treatments.

- **PUBLIC-PRIVATE PARTNERSHIPS –** There are multiple ongoing public private partnerships established in 2020, with government agencies including HHS, CDC and NIH, industry, academic institutions, non-profit organizations, biopharmaceutical companies and a range of patient advocacy and community organizations. One initiative aims to coordinate a research strategy for prioritizing and accelerating the development, evaluation and approval of the most promising treatments and vaccines for COVID-19. Stakeholders are establishing master protocols, clinical trial networks, sharing learnings in real time and utilizing additional innovative approaches to create efficiencies across the ecosystem. The other initiative aims to deliver millions of doses of safe and effective vaccines for COVID-19. This is part of a broader collaboration strategy to accelerate the development, manufacturing and distribution of COVID-19 countermeasures.
- **INDUSTRY-INDUSTRY PARTNERSHIPS –** One specific example shows how two PhRMA member companies joined together in an unprecedented manner to share resources, research and technology to develop a COVID-19 vaccine. One company provided the recombinant DNA technology and the other provided the adjuvant technology allowing more vaccine doses to be produced.
- **INDUSTRY-BARDA (HHS)/DARPA (DOD) PARTNERSHIPS –** Many pharmaceutical companies are partnering with the Biomedical Advanced Research and Development Authority (BARDA) and some are partnering with the Defense Advanced Research Projects Agency (DARPA). Some companies are leveraging long standing contracts with the authority, while some companies with no existing marketed medicines are establishing new contracts with the authority. Company contracts with BARDA are helping support the development of vaccines and treatments for COVID-19, by supporting research, development and clinical development. Collaborations with DARPA expand capabilities for rapid development, manufacturing and distribution of therapies.
- **INDUSTRY-ACADEMIA PARTNERSHIPS –** Another biopharmaceutical company partnered with a research university and was granted a global exclusive license to develop, manufacture, and commercialize a novel monoclonal antibody duo treatment to treat or prevent COVID-19, and help expand access globally.
- **INDUSTRY-INSURER PARTNERSHIPS –** One company is partnering with a large health insurer to bring together symptom tracking, in-home testing and in-home infusions to detect, intercept and treat COVID-19 early with a COIVD-19 neutralizing antibody that received Emergency Use Authorization from the FDA.
- **INDUSTRY-GLOBAL FOUNDATION PARTNERSHIPS –** Multiple life science companies, including PhRMA members are sharing their expertise and assets with global foundations in the fight against the global pandemic.

Spotlight on Collaborative R&D Efforts

Today's biopharmaceutical landscape has entered a new era of innovation ushering in treatments and cures previously unimaginable. Thanks to medical advances we're able to tackle some of the most challenging diseases patients face using novel therapies and groundbreaking approaches. However, as scientists learn more and more about the underlying mechanisms of disease and available treatments become more targeted, tailored and effective, the R&D process has become increasingly complex and risky. Partnerships across the health system—like the two highlighted below—ensure that stakeholders are working together providing access to a broader information pools, distributing the risk of development across multiple participants, and improving the research and development process itself. "

Alzheimer's Disease Neuroimaging Initiative (ADNI)[11]

Launched: 2004

Partners: Government Agencies: The National Institutes of Health (NIH) and the Foundation for the NIH, **Academic Institutions:** The Northern California Institute for Research and Education (NCIRE), The Alzheimer's Therapeutic Research Institute (ATRI) at the University of Southern California and the Laboratory of Neuro Imaging at the University of Southern California, **Nonprofits:** Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD), Alzheimer's Drug Discovery Foundation, Abbvie, Alector, Alzheimer's Association, **Industry:** Araclon Biotech, Bioclinica, Biogen, Cogstate, Denali Therapeutics, Diamir, Eisai Co., Ltd., Eli Lilly and Company, Euroimmun AG, Fujifilm Toyama Chemical Co., Ltd., General Electric Company, Genentech, Janssen: Pharmaceutical Companies of Johnson & Johnson, H. Lundbeck A/S, MagQu, Merck & Co., PeopleBio, Pfizer Inc., Piramal Enterprises, F. Hoffmann-La Roche AG, Saladax Biomedical Inc, Servier, Takeda Pharmaceutical Company Limited

ADNI is a global research effort that assess clinical, imaging, genetic, and biospecimen biomarkers for the early detection and tracking of Alzheimer's disease (AD). ADNI's multi-site, longitudinal prospective study uses biomarkers and clinical measures to assess the brain structure and function over the course of AD. ADNI has developed a set of standardized protocols that compare results from multiple study centers, improved clinical trial efficacy, established methods for early detection of AD and helped discover some of the mechanisms of normal aging. The collaborative effort makes all of their data available without embargo to be used by qualified researchers worldwide. Currently, over 1000 scientific publications have used ADNI data.

ADNI's model of collaboration highlights the important role of academic/industry partnerships and serves as an example for additional initiatives related to AD and other diseases. For instance, the University of Pittsburgh and Pfizer announced a partnership study to develop a computational model that would help identify the drivers of schizophrenia, AD and other related neurological disorders. The study will leverage ADNI's publicly available datasets to improve researchers understanding of these diseases.

"The clinical trials that are being initiated now are starting to use the biomarkers identified [by ADNI]... so it's absolutely a success."

Dr. Laurie Ryan, National Institute on Aging[12]

California Institute for Biomedical Research (Calibr)[13,14]

Launched: 2012

Partners: Nonprofits: Scripps Research, Bill and Melinda Gates Foundation, Welcome Trust, Juvenile Diabetes Research Foundation, Cure SMA and California Institute for Regenerative Medicine (CIRM), Industry: Bristol Myers Squibb (BMS), Intarcia Therapeutics, Sirenas, Merck & Co., Pfizer Inc. and ShangPharma Innovation Inc.

Calibr is a novel, nonprofit translational research institute dedicated to creating innovative medications that address patients' unmet needs. Calibr's research interests span cancer, autoimmunity and inflammatory diseases, metabolic and cardiovascular diseases, infectious and neglected diseases, age-related and degenerative diseases. The partnership's unique operating model leverages the sales generated from discoveries and reinvests in further innovative research. Calibr's strategic research partnerships enable the development of therapeutic candidates by translating lab-based discoveries into tangible patient outcomes. Calibr in collaboration with industry and non-profit partners works to further accelerate research and development of novel therapeutic strategies for diverse unmet medical needs. For example, California Institute for Regenerative Medicine (CIRM) has partnered with Calibr and provided $8.4 million to begin a Phase 1 clinical trial testing an investigational drug for osteoarthritis patients.

"We wanted to build a new model that more effectively bridges the world of basic research and the world of drug discovery that's historically been the purview of big pharma and biotech."

Peter Schultz, President and CEO of Scripps Research[15]

Cure Huntington's Disease Initiative (CHDI) Foundation[16,17]

Launched: 2012

Partners: Nonprofits: Huntington's Disease Society of America (HDSA), Healthcare Distribution Alliance (HDA), the HSC Health Care System and Critical Path Institute (C-PATH), Huntington's disease (HD) Legacy **Industry:** Charles River Labs, Ionis Pharmaceuticals, Pfizer Inc.

The CHDI Foundation, a science management organization, seeks to develop drugs that slow the progression of Huntington's disease and help lower barriers to entry for other non-profit groups seeking to collaborate on HD therapies. CHDI's novel virtual model encourages scientific collaboration on numerous research projects by directly connecting academic and industrial researchers in their pursuits of drug discovery and clinical development. The non-profit aims to de-risk therapeutic approaches to make them appealing to companies and investors so they'll be seen as good investments and will take them on to full clinical development.

In recent years, CHDI along with Ionis Pharmaceuticals have made notable progress by developing an anti-sense oligonucleotide therapeutic approach, a promising new therapeutic strategy that was subject to substantial investment from Roche. In 2017, Roche licensed the therapy (IONIS-HTTRx) following the successful completion of the Phase 1/2a study. Roche assumed the responsibility of all development and commercial activities for this drug designed to target the underlying cause of HD.[18] In addition, CHDI is a sponsor of a worldwide Huntington's disease observational study and registry called Enroll-HD which aims to recruit 20,000 HD family members to build a research platform to enhance clinical trial recruitment efforts. Numerous studies and analyses have been completed using the data generated from Enroll-HD that help elucidate the underlying mechanisms of HD.

"Our long standing partnership with CHDI is built on our mutual commitment to developing novel therapies for Huntington's disease. As an organization, our work with CHDI has led to a much larger commitment to support the HD research community, through investments in methodologies, tools and personnel dedicated to this rare disease."

Birgit Girshick, Corporate Executive Vice President, Discovery & Safety Assessment, Biologics Testing Solutions, and Avian Vaccine Services at Charles River

Lung Cancer Master Protocol Lung-MAP

Launched: 2014

Partners: Government Agency: National Cancer Institute (NCI), National Cancer Trials Network, SWOG Cancer Research Network, Friends of Cancer Research and Foundation for National Institutes of Health, **Nonprofit:** Addario Lung Cancer Foundation, Lung Cancer Alliance, LUNGevity Foundation, Lung Cancer Foundation of America, American Lung Association, Lung Cancer Research Foundation and American Cancer Society, **Industry:** Amgen Inc., AstraZeneca PLC, Genentech, Merck & Co. and Pfizer Inc.Lung-MAP is a unique multi-drug clinical trial that is designed to match patients with studies looking at numerous investigational treatments simultaneously. Through novel scientific advancements, researchers can improve lung cancer treatment by focusing on the specific genetic mutations of a given patient. The goal of Lung-MAP is to create a new approach to clinical trials that better fits this personalized approach to treatment. The trial design uses a targeted method to screen patients who are then assigned to a trial arm based on the genomic profile of their tumor. Every year during the course of the study, researchers screen about 500 to 1,000 patients for changes in over 200 cancer-related genes. This novel clinical trial design increases R&D efficiency by allowing multiple drugs to be tested simultaneously and pooling patient recruitment across all the drugs included in the study. It also benefits patients by ensuring they are matched to the candidate treatment most likely to work for them. Lung-MAP is now available at over 700 medical centers and community hospitals and registered more than 1,800 patients across the U.S.[19]

"The Lung-MAP cooperative model will transform the lung cancer research landscape, speed up the development of effective and safe treatment options, and significantly improve outcomes for patients"

Kim Norris, President/Co-Founder, Lung Cancer Foundation of America[20]

Supporting Public Health and Improving Patient Outcomes

Prescription medicines have proven to be one of the most promising means to addressing public health concerns such as HIV and hepatitis C, and today's public health crises, including antimicrobial resistance and COVID-19, are no different. We've seen firsthand how medicines can be one of our best defenses against major public health crises, saving countless lives and limiting the spread of disease by treating people before they infect others. That said, while researching and developing new treatments and vaccines is critical to tackling a wide range of public health challenges, they are only effective if they reach patients, which often requires robust partnerships to scale up manufacturing and distribution and educate health care providers, patients, caregivers and payers regarding their potential value.

To truly ensure meaningful public health progress, it's critical that broader programs and coordinated measures are put into action. These measures might include patient and provider education or comprehensive prevention strategies. By enabling stakeholders with different core capabilities and expertise to come together, partnerships between biopharmaceutical companies and other key health system players can help tackle major public health challenges and improve population health. Often this is seen through major public-private partnerships which call upon the resources and expertise of private biopharmaceutical companies while utilizing the reach, insight, and authority of government or NGOs.

COVID-19 COLLABORATION: GLOBAL ACCESS

PhRMA members are part of COVAX, a coalition of governments, global health organizations, manufacturers, scientists, private sector, civil society and philanthropy.

- **INDUSTRY-GLOBAL ALLIANCE PARTNERSHIPS –** Some PhRMA member companies plan to donate their vaccine, if successful, to COVAX. COVAX is a pillar of the Access to COVID-19 Tools (ACT) Accelerator, which was launched in April 2020 by the World Health Organizations (WHO), the European Commission and France in response to the pandemic and will provide access to vaccines in lower-income countries around the world. The United States has committed several billion dollars to the effort to expand COVAX's reach.

Spotlight on Partnerships Promoting Public Health

A holistic approach to advancing public health must go beyond any single aspect of health care and health system delivery. It requires multi-faceted and collaborative frameworks and interventions. Put simply, a treatment or cure is only as good as patients' ability to access and effectively utilize it. There are many factors that must be taken into account. The snapshot below illustrates a broad range of collaborative efforts aiming to address these factors and improve public health and patient outcomes.

Antimicrobial Resistance (AMR) Action Fund[21]

Launched: 2020

The AMR Action Fund, launched in late 2020, is the largest public-private partnership supporting the development of new antibiotics. With funding from over 20 leading biopharmaceutical companies, global foundations and development banks, the AMR Action fund is an initiative that seeks to invest over US $1 billion to bring 2-4 new antibiotics to patients by 2030 by investing in companies developing innovative antibacterial treatments. It will also work with governments to help advance policies that will encourage a sustainable pipeline of new antibiotics to fight the highest priority bacterial threats.

Increasing antimicrobial resistance is a treat to all of us, especially those with chronic conditions. Each year more than 35,000 Americans die due to infections that are caused by superbugs that are resistant to treatment by antibiotics. Without a stable pipeline of new antibiotics, patients face significantly increased risks from many medical services that rely upon the effective prevention and treatment of infections.[22]

"Unlike COVID-19, AMR is a predictable and preventable crisis. We must act together to rebuild the pipeline and ensure that the most promising and innovative antibiotics make it from the lab to patients. The AMR Action Fund is one of the largest and most ambitious collaborative initiatives ever undertaken by the pharmaceutical industry to respond to a global public health threat".

Thomas Cueni, Director General of the IFPMA, one of the organizers of the new fund

NIH Helping to End Addiction Long-Term (HEAL) Initiative[23]

Launched: 2018

Partners: Government Agencies: National Institutes of Health (NIH), Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration (FDA), **Academic Institutions:** University of California – San Francisco, UPenn Medical School, Harvard Medical School, University of Washington, University of Utah, Washington University, University of Vermont, University of California- San Diego, University of North Carolina, Northwestern University, Virginia Commonwealth University, **Nonprofits:** Advanced Medical Technology Association (AdvaMed), American Medical Association (AMA), Biotechnology Innovation Organization (BIO), Chronic Pain Research Alliance, Pharmaceutical Research and Manufacturers of America (PhRMA), **Insurer:** Kaiser Permanente, **Industry:** Amgen Inc., Avid Radiopharmaceuticals, Janssen: Pharmaceutical Companies of Johnson & Johnson, Pfizer Inc., Indivior PLC, Medtronic plc,

The HEAL Initiative seeks to provide scientific solutions to the opioid crisis. NIH HEAL focuses on several study areas to improve preventive and therapeutic interventions, implement effective evidence-based approaches, provide better treatments for long-term recovery and infants born with neonatal abstinence syndrome (NAS)/ neonatal opioid withdrawal syndrome (NOWS). The partnership effort also established standing oversight structures to promote effective collaboration including the NIH HEAL Initiative Multi-Disciplinary Working Group and NIH HEAL Initiative Partnership Committee. These committees seek to ensure strong communication between the public- and private-sector organizations. The Working Group provides a transparent forum to discuss research findings and facilitate exchange of scientific information. The Committee assists NIH in the development of novel treatments through the generation of defined products such as preliminary recommendations for a template application and evaluation dossier for biopharmaceutical and device-based treatments. NIH HEAL has contributed $500 million annually to over 400 research projects. Within the various scientific research priority areas, NIH HEAL Initiative has managed to make some significant strides in advancing their goal to address the opioid crisis. For instance, the biotech company Delpor is using funding from NIH HEAL to develop technology that would provide a longer-lasting delivery system for opioid overdose reversal drugs.[24] This partnership effort is just one example of the accomplishments achieved through the NIH HEAL collaboration.

"With our partners, the NIH will take an 'all hands-on deck' approach to developing and delivering the scientific tools that will help end this crisis and prevent it from reemerging in the future."

Nora Volkow, M.D. and Francis Collins, M.D., Ph.D., New England Journal of Medicine, 2017[25]

Enabling Manufacturing Scalability and Supporting Distribution

Due to advancements in manufacturing processes, today biopharmaceutical companies are able to develop cutting-edge treatments and cures that harness the body's own immune system to fight disease. These treatments, known as biologics, are medicines made from living organisms through highly complex manufacturing processes that must be rigorously monitored and maintained. They include gene and cell therapies, therapeutic proteins, monoclonal antibodies, and vaccines and are used to prevent, treat or cure a variety of diseases like cancer, chronic kidney disease, and autoimmune disorders. These new treatments are not only transforming care for patients, they are changing what's required during the manufacturing and distribution processes. To ensure proper manufacturing conditions are met FDA issues comprehensive regulations surrounding the manufacturing and distribution of these therapies.

Advances in science is leading to emerging new approaches that are much more targeted, tailored and effective at treating individuals. Understandably, the development of completely new medicines requires novel facilities, expertise, standards, protocols and resources. Partnerships have been critical to advancing knowledge within the field, solving problems to overcome barriers, pooling or sharing supplies and equipment and ensuring that new lifechanging medicines are scalable so that distribution is adequately and effectively supported. Moreover, most recently—as the world has raced to find a vaccine to address COVID-19—we've seen just how critical it is to be able to quickly scale, manufacture and distribute medicines as a means for stopping the further spread of disease. This type of capacity is far beyond the reach of any one group or company, and partnerships are already playing a critical role to ensure the biopharmaceutical industry and their partners are able to scale and manufacture a potential COVID-19 vaccine or treatment as quickly as possible upon FDA authorization or approval.[26]

COVID-19 COLLABORATION: MANUFACTURING & DELIVERY

Across the industry, companies are working around the clock to meet the demands of manufacturing enough COVID-19 vaccines to get as many shots in arms as possible. Biopharmaceutical companies are continuously increasing their manufacturing capacity, such that as the U.S. capacity to administer the vaccines increases, the supply will also increase to keep ahead.

- **INDUSTRY-ACADEMIA PARTNERSHIPS –** For example, one company pivoted from their own vaccine development program to support the efforts of another company's candidate, to help address public health needs. Other companies working on treatments, are teaming up with each other and additional manufacturing organizations to ramp up manufacturing of treatment doses as quickly as possible. Others are partnering so that large scale manufacturing can be more efficient, with additional partners providing vial filling and packaging, for example.
- **INDUSTRY-ACADEMIA PARTNERSHIPS –** One biopharmaceutical company is working with the government, a smaller biotechnology firm and an academic institution's for innovation in advanced development and manufacturing to help manufacture bulk drug substance for a COIVD-19 vaccine candidate.

Spotlight: How Partnerships Support Scalability and Distribution

Some of today's most cutting-edge medicines harness living organisms to produce treatments that target diseases in new, innovative ways. Unlike traditional medicines that are made from chemically synthesized compounds in a lab-settings, these therapies have characteristics and properties that are heavily influenced by the manufacturing process, which means the manufacturing process is often more complex and involved. In other instances, scalability and manufacturing becomes a challenge when there is significant demand for a treatment or cure that a single company or organization is unable to meet alone. The collaborative efforts highlighted below demonstrate the promise and power of partnerships as a means for addressing and overcoming these barriers.

Advanced Regenerative Manufacturing Institute (AMRI); Manufacturing[27]

Launched: 2017

Partners: Industry: Advanced Silicon Group, Advanced Solutions Life Sciences, Boston Scientific, Cell X Technologies, CollPlant Biotechnologies Ltd., Curable, DEKA Research and Development, Embody, Inc., Fibercell Systems Inc, GE Healthcare, Johnson & Johnson, Mayo Clinic, Medtronic, Microsoft Corporation, Miromatrix Medical, Inc., O2M Technologies, OrganaBio, STEL Technologies, LLC, Rockwell Automation, Rooster Bio Inc., United Therapeutics Corporation, Pluristyx, Inc., Trailhead Bio **Academics:** Arizona State University, University of California Los Angeles, Carnegie Mellon University, University of Connecticut, University of Massachusetts Lowell, University of New Hampshire, Texas Heart Institute, University of Virginia, Worcester Polytechnic Institute

ARMI is a member driven non-profit that seeks to make practical the large-scale manufacturing of engineered tissues and tissue-related technologies, to benefit existing industries and grow new ones. This institute is part of Manufacturing USA, a larger organization comprised of 14 institutes. AMRI and the Department of Defense (DoD) jointly fund the BioFabUSA program which seeks to integrate cell and tissue cultures with advances in biofabrication, automation, robotics, and analytical technologies to create innovative research and development tools and FDA-compliant volume manufacturing processes.

BioFabUSA brings together expertise across a range of stakeholders to form a multidisciplinary consortium. Regulatory and preclinical consulting are some of several member support services ARMI provides to its members as part of the BioFabUSA program. These regulatory and preclinical consulting services seek to support this diverse group as part of the larger mission of seeking to support existing industries and grow new ones.

"This is a very exciting time in the regenerative medicine industry. ARMI BioFabUSA brings together diverse groups of stakeholders to facilitate large-scale manufacturing in this field, which requires innovative approaches that ARMI supports through its project calls and is necessary for the continued advancement of regenerative medicine."

Dr. Amy Peterson, Associate Professor of Plastics Engineering at the University Massachusetts, Lowell[28]

National Cell Manufacturing Consortium (NCMC)[29,30,31]

Launched: 2016

Partners: Government Agencies: National Institute of Standards and Technologies (NIST), National Institute of Standards and Technologies (NIST), **Industry:** ACEA Biosciences, Inc., Axion BioSystems, Applied Materials, Inc., Aruna Bio, Bristol Myers Squibb (BMS), CDI Laboratories, Century Therapeutics, Cytiva, Etaluma Inc., Evolved Analytics Inc., Janssen: Pharmaceutical Companies of Johnson & Johnson, Lonza, Lucid Scientific, MilliporeSigma, Nucleus Biologics, RoosterBio, Inc., Sangamo Therapeutics, Inc., Terumo BCT, Inc., and ViCapsys

The National Cell Manufacturing Consortium (NCMC) seeks to advance the U.S. cell manufacturing industry. Cell-based medical technologies are a relatively new approach that is continuing to grow significantly. These novel cell-based health care products include cell therapies, engineered tissues, medical devices and drug testing platforms. Cell-based medical technologies have helped treat patients across various diseases such as cancer, heart failure and autoimmune disorders. However, to bring these life-changing products to market requires the large-scale, cost-effective, reproducible manufacturing of various cell types.Through a collaborative process, the initiative produced a national roadmap for cell therapy manufacturing to help advance efforts across the several workstreams by 2030. According the report, NCMC has had some success in transforming the manufacturing process for cell-based therapeutics into a large-scale, lower-cost, reproducible, and high-quality engineered process.

"The aim is to make these therapies available not just to a few patients, but thousands of patients. We really need new, scalable manufacturing tools and platform technologies to make that happen, and this support from the FDA will help us figure some of that out."

Krishnendu Roy, director of the Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M) at Georgia Tech[32]

AstraZeneca, CEPI, Gavi and Oxford University COVID-19 Agreement; Manufacturing, Public Health[33,34,35,36]

Launched: 2020

Partners: Academic Institutions: Oxford University and Serum Institute of India (SII), **Nonprofit:** Coalition for Epidemic Preparedness Innovations (CEPI), **Industry:** AstraZeneca PLC

The cross-stakeholder collaboration seeks to support the manufacturing, procurement and distribution of 300 million doses of the vaccine by the end of 2020. The agreement between CEPI and Gavi also represents the first advanced market commitment through the Access to COVID-19 Tools (ACT) Accelerator, a global collaboration of philanthropic, multilateral, private sector and civil society partners. The novel financing mechanism will work to

accelerate the development, production and global equitable access to the new COVID-19 tools including in low and middle-income nations.

This partnership effort is among the latest commitment from AstraZeneca to enable global access to the potential vaccine. Additionally, AstraZeneca is also collaborating with global research manufacturing institutes to ensure one billion doses of the vaccine are provided to low- and middle-income countries, with the goal of 400 million produced by the end of 2020. These collaborations are on top of AstraZeneca's individual arrangements with government purchasers, where they agreed to supply 400 million doses to the US and UK after reaching an agreement with Oxford University for its vaccine candidate.

"We are working tirelessly to honour our commitment to ensure broad and equitable access to Oxford's vaccine across the globe and at no profit. Today marks an important step in helping us supply hundreds of millions of people around the world, including to those in countries with the lowest means. I am deeply grateful for everyone's commitment to this cause and for their work in bringing this together in such a short time"

Pascal Soriot, Chief Executive Officer, AstraZeneca[37]

Improving Access to Cutting-Edge Innovation and Cures

Increased innovation and R&D, fortified public health efforts, and strong manufacturing and distribution capabilities—all supported by partnerships—when taken together, ultimately help to speed patient access to groundbreaking treatments and cures. When innovation is incentivized and fostered, patients and providers are educated and empowered, and the right infrastructure and resources are in place to scale up production and delivery of medicines, patients are able to most efficiently and effectively access the treatments they need. Moreover, many biopharmaceutical partnerships are also in place with a specific aim of improving access to medicines and cutting-edge therapies.

No matter how promising a treatment might be, the benefits only go as far as a patient's ability to access that medicine. Collaboration between biopharmaceutical companies and other health system stakeholders help address this challenge and can improve access in many innovative ways. From working with payers to create novel payment models that increase the availability and accessibility to new and/or high-cost medicines, to leveraging the reach of government agencies ensuring specific medicines are widely available for at-risk or vulnerable populations, as well as working with patient groups and non-traditional stakeholders on innovative ways to tackle barriers related to social determinants of health—biopharmaceutical partnerships play a critical role in helping ensure patients can access the treatments and cures they need, when they need them.

COVID-19 COLLABORATION: HEALTH EQUITY AND ACCESS

Biopharmaceutical companies are working with cross functional stakeholders to ensure that when new treatments and vaccines are authorized or approved, they will be available and affordable for all patients.

- **INDUSTRY-ACADEMIA PARTNERSHIPS –** One biopharmaceutical company is working with a HBCU's School of Medicine to study the racial health inequities associated with COVID-19.

Spotlight on Collaborative Initiatives to Improve Access

Thanks to rapid biomedical progress, there are more treatments and cures available to patients today than ever before. That said, for many patients, accessing these medicines can be a challenge. Through strategic partnerships with stakeholders positioned to address the most pressing barriers standing between patients and the medicines they need; the biopharmaceutical sector can help ensure patients are able to access the treatments and cures they need. The case studies below illustrate how collaborative efforts are working to expand patient access to medicines.

Gilead and Satcher Health Leadership Institute at Morehouse School of Medicine Partnership[38]

Launched: 2020

Partners: Academic Institutions: Satcher Health Leadership Institute at Morehouse School of Medicine, **Industry:** Gilead Sciences, Inc.

To better understand the racial disparities that are occurring during the COD-19 pandemic, Gilead partnered with the Satcher Health Leadership Institute at Morehouse School of Medicine to develop a real time, public-facing and comprehensive health equity data platform to help track and address the impact of COVID-19 and other diseases on communities of color in the United States. The tool will provide the ability to collect and study the demographic disparities associated with COVID-19 with the goal of creating actionable, evidence-based policy changes to attain health equity and ensure that disproportionately impacted communities receive resources and support. The database will also examine comorbidities associated with COVID-19, including asthma, diabetes, heart disease, cancer, obesity, sickle cell anemia and depression.

Learnings from the data collected will inform the work that Morehouse School of Medicine conducts in partnership with the Department of Health and Human Services to link patients to culturally competent health, behavioral health and social services. Gilead initially provided $1 million to support resources for tracking health inequities. This also supported the creation of a Black Health Equity Alliance composed of national thought leaders, community representatives, scholars, researchers and policymakers, which will help coordinate COVID-19 education, training, information exchange and dissemination, and policy analysis.

"There are many hurdles in the American healthcare system for people of color – particularly Black people – to access care. The data we are compiling with Satcher Health Leadership Institute will provide the insight we need to help build a better healthcare system for communities of color. We are proud to partner with Morehouse School of Medicine's Satcher Health Leadership Institute to help address these issues."

Douglas M. Brooks, Executive Director of Community Engagement at Gilead Sciences

MIT's NEW Drug Development ParadIGmS (NEWDIGS)[39]

Launched: 2009

Partners: Government Agency: The National Institutes for Health (NIH), **Nonprofits:** Alliance for Regenerative Medicine (ARM), American College of Rheumatology, FasterCures, Innovative Medicines Initiative (IMI), IQVIA, Milken Institute, NORD, **Insurers:** Anthem, Inc., Humana Inc., Kaiser Permanente, **Industry:** AveXis/ Novartis International AG, Bluebird bio, Inc., Biogen Inc., BioMarin Pharmaceutical Inc., Bristol Myers Squibb (BMS), Cardinal Health ,Inc., Janssen: Pharmaceutical Companies of Johnson & Johnson, Merck & Co., Inc., Orchard Therapeutics, **Academic Institutions:** Johns Hopkins University, Massachusetts General Hospital, Dana-Farber Cancer Institute

Biomedical innovation is advancing at unprecedented speed but significant policy, technology and processes change is required to continue developing and delivering new, effective and affordable drugs. MIT NEWDIGS helps catalyze important advancements to enhance the capacity of the global biomedical innovation system. This collaborative uses case-based simulation exercises to develop systemwide solutions for access to biomedical innovation and patient care. Partners for this "think and do" tank include global leaders from patient advocacy, payer organizations, biopharmaceutical companies, regulatory agencies, clinical care, academic research, and investment firms. MIT NEWDIGs has several ongoing projects and initiatives such as the Financing and Reimbursement of Cures in the US (FoCUS) Project which seeks to address the need for innovative financing and reimbursement models for curative therapies. FoCUS aims to create precision financing solutions to ensure access and affordability. In addition, the Adaptive Biomedical Innovation project seeks to align cross-sectional stakeholders in an effort to advance sustainable patient-centered innovation across the product life span.

"After two years of careful, candid collaboration to survey the challenges and plot a course through them, we feel confident we have designed financial engineering solutions ready to pilot with the healthcare community. We look forward to engaging policymakers and all other system stakeholders to appropriately advance these transformative therapies to patients."

Mark Trusheim, NEWDIGS Strategic Advisor and longtime FoCUS project leader[40]

Going Forward: Fostering the Partnerships and Policies that Support the U.S. Biopharmaceutical Innovation Ecosystem

The broad-reaching and vital benefits of the partnerships that have been formed across the biopharmaceutical and broader health care landscape would not be possible without the robust innovation-friendly ecosystem that exists in the United States. The collaboration that spans across U.S. government, academia, biopharmaceutical companies and other stakeholders is among our country's greatest strengths in moving medical advances forward and has been a cornerstone in of the United States global leadership in biopharmaceutical innovation.

> "We are the place that supports the scientific innovations that lead to these breakthroughs, and, ultimately, to new therapies. But we need to be part of an ecosystem that includes the private sector and philanthropy and advocates in order for that to come true."
>
> ***Dr. Francis Collins, Director of the National Institutes of Health (NIH)[41]***

Furthermore, the impacts of the robust biopharmaceutical industry in the United States are far-reaching and significant. Today the United States represents roughly half of all biopharmaceutical R&D investments globally, the greatest share in the world.[42] As a result, U.S. patients have better access to cutting-edge medicines than those living in peer nations—96 percent of U.S. patients have access to new cancer medicines, for example, while only 56 and 65 percent of patients and France and Canada respectively have the same access.[43] The investments made by the U.S. biopharmaceutical industry also support high-value jobs directly and indirectly, with R&D investments serving as the foundation for over 4.7 million U.S. jobs. Furthermore, for every direct job there are five additional indirect jobs supported.[44] And annually, the biopharmaceutical industry, closely integrated supply chain, wages and benefits results in $1.3 trillion in economic output.[45]

This dynamic innovation ecosystem has not occurred by happenstance; it is the result of carefully balanced policy, regulation and frameworks that have formed an environment that fosters, incentivizes and enables innovative and collaborative efforts that give way to large-scale groundbreaking progress and biomedical advances. For example, much of the success of the U.S. research ecosystem is due to the positive impact of the Bayh-Dole Act on public-private research collaboration. The Bayh-Dole Act was passed by Congress with bipartisan support in 1980 has been instrumental in incentivizing the private sector investment needed to translate discoveries made through government-funded research into useful commercial products.[46] By allowing institutions and grant recipients like universities to license the rights to government-funded inventions to private sector partners, Bayh-Dole promotes important partnerships that help ensure promising technologies and research funded by the federal government don't just sit on the shelf, but are actually developed into useful, potentially lifesaving, products for Americans. The authorization of Cooperative Research Development Agreements (CRADAs) under The Federal Technology Transfer Act in 1986 is another prime example of policy that has helped foster collaboration that supports world-class biopharmaceutical innovation in the United States.[47] By providing a vehicle for federal researchers to partner with the biopharmaceutical industry, CRADAs have incentivized important collaborative efforts further innovation and ultimately help speed patient access to innovative scientific advances.

"The evidence to date shows that there is an unprecedented level of cooperation [in addressing the pandemic] in industry, and that IP has facilitated this worldwide cooperation."

Andrei Iancu, Director of the U.S. Patent and Trademark Office

Policies—like Bayh-Dole and the authorization of CRADAs—that encourage collaboration to advance biomedical progress, have been the bedrock of biopharmaceutical innovation in the United States and have bolstered the U.S. as a global leader in biomedical progress. That said, this position is dependent on a carefully balanced innovation ecosystem that can easily be jeopardized by misguided or short-sighted policy changes. The United States has seen this happen before. In 1989 when the NIH adopted a policy that required a "reasonable pricing" clause in CRADAs between NIH laboratories and private-sector partners, mandating there be a "reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public," the number of CRADAs executed dropped sharply. In 1995 when the NIH removed the clause, there was a significant rebound—in 2018 alone, the NIH entered into 82 CRADAS, executed 298 licenses to NIH inventions and obtained 94 newly issued U.S. patents.[48]

"Collaborating with companies [through CRADAS] helps our basic research move to the next step. Thanks to commercial partnerships, antibodies to target two cell-surface proteins, glypican-3 (GPC3) on liver cancer cells and GPC2 on neuroblastoma cells, will likely begin in clinical trials this year."

Mitchell Ho, Director, National Cancer Institute (NCI) Antibody Engineering Program

This instance should serve as a clear demonstration of how critical the right policies are to collaboration and an innovation-friendly environment is to biopharmaceutical progress, and how sensitive the innovation ecosystem is to changes in regulation. Without the investment of the biopharmaceutical industry the knowledge resulting from basic science research supported by NIH would generate many ideas for potential drugs and drug targets – but very few new medicines. Reducing incentives for the private sector to invest and take risks has the potential to be incredibly detrimental to the robust research and development ecosystem as we know it and would have serious unintended consequences for scientific advancement, patients' health, and the overall progress of society. In fact, as we face a global pandemic and are working tirelessly to address COVID-19, policies that strengthen the biomedical innovation ecosystem by encouraging partnerships across the health system are more important than ever. Policymakers need not look further than our recent history to understand the power of innovation-friendly policy in encouraging collaborations and advancing important scientific breakthroughs, and the delicate balance required to sustain and support the robust American biopharmaceutical ecosystem that has been foundational to health, productivity and economic growth for decades.

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