Adopting an Open-Source Approach to Pharmaceutical Research and Development

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Summary

The U.S. pharmaceutical industry conducts over half the world’s research and development (R&D) in pharmaceuticals and accounts for well over $1 trillion in economic output annually. Yet despite the industry’s massive size, there are still no approved therapies for approximately 95% of human diseases—diseases that affect hundreds of millions in the United States and around the world. The disparity between industry inputs and societally valuable outputs can be attributed to two key market failures. First, many medicines and vaccines have high public value but low commercial potential. Most diseases are either rare (afflicting few), rapidly treated (e.g., by antibiotics), and/or predominantly affect the global poor. Therapies for such diseases therefore generate limited revenue streams for pharmaceutical companies. Second, the knowledge required to make many high-value drugs is either underdeveloped or undershared. Proprietary considerations may prevent holders of key pieces of knowledge from exchanging and integrating information.

To address these market failures and accelerate progress on addressing the overwhelming majority of human diseases, the next administration should launch a new program that takes an open-source approach to pharmaceutical R&D. Just as open-source software has proven a valuable complement to the proprietary systems developed by computer giants, a similar open-source approach to pharmaceutical R&D would complement the efforts and activities of the for-profit pharmaceutical sector. An open-source approach to pharmaceutical R&D will provide access to the totality of human knowledge and scientific expertise, enabling the nation to work quickly and cooperatively to generate low-cost advances in areas of great health need.

Challenge and Opportunity

Approximately 95% of human diseases (~9,500 in number) lack any approved therapies. At the current rate of discovery, it would take 2,000 years to find therapies for all known human diseases. The result is that hundreds of millions of people in the United States and around the world lack medicines and vaccines that are essential to a healthy life.

Simply put, the status quo with respect to drug development has failed. The pharmaceutical industry expends huge amounts of money—often funded with taxpayer dollars—to develop and procure medicines and vaccines, straining national and personal budgets. Moreover, our legacy system of pharmaceutical R&D is unacceptably slow. It now takes 10–20 years for the pharmaceutical industry to develop a single new medicine or vaccine. Pharmaceutical R&D efficiency is declining exponentially: Moore’s Law in reverse. Finally, investment by the existing pharmaceutical industry is driven by profit potential, not societal need. Hence, diseases that afflict many but offer limited revenue streams continue to remain neglected.

It is time for a transformational change in how our nation approaches pharmaceutical R&D. COVID-19 has made it resoundingly clear that we need more medicines, vaccines, and antibody therapies—and we need them to become available fast and made accessible to all. The response to COVID-19 has also demonstrated the value of open R&D in medicine. Thanks largely to unprecedented levels of collaboration, information sharing, and grassroots innovation, our understanding of the disease and the efficacy of potential treatments has advanced at a remarkable pace. Progress on a vaccine for COVID-19 has been record-breaking in comparison with any previous vaccine. Such openness must be further expanded and become the new normal. Right now, most of our nation’s pharmaceutical R&D enterprise is divided among individual labs or companies, with little communication across disciplines or among different research teams. Pharmaceutical R&D is too often conducted secretly, separately, privately, redundantly, and chaotically. And public funds are given to private pharmaceutical companies without guarantees of affordability or openness. We must move instead towards a world in which pharmaceutical R&D is carried out collaboratively, cooperatively, transparently, flexibly, and efficiently. An important step is making key aspects of pharmaceutical R&D—especially publicly funded R&D that is supported or conducted by government—open source.

Plan of Action

The next president should launch a new effort to support an open-source approach to pharmaceutical R&D. Such an approach would differ from conventional approaches and compliment them in four ways:

- First, an open-source approach would enable the entire scientific community to work together on challenges that are difficult for any single entity to solve (in keeping with the open-source mantra in software that “with enough eyes, all bugs are shallow”).
- Second, an open-source approach would draw on the sum total of human knowledge, without being constrained by discipline-specific technical expertise, or being limited to knowledge with high profit potential
- Third, an open-source approach would focus on creating universally accessible medicines and vaccines with substantial public-health benefits, even when those medicines and vaccines do not generate substantial revenue streams.
- Fourth, an open-source approach would create knowledge accessible to all, and accelerate the advance of science.

As explained in an influential 2006 paper, an open-source approach to pharmaceutical R&D would achieve these goals by integrating six foundational capacities: (i) public and open data

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and other informational resources; (ii) affordable and widely available tools, algorithms, and models; (iii) advanced computation; (iv) crowdsourcing and crowd commentary; (v) generics and low-cost drug manufacturing; and (vi) the power of sharing, collaboration, and community.

A government-funded effort to support open-source pharmaceutical R&D could take several forms. This effort could be housed at an independent nonprofit center, or could comprise a new program within the National Institutes of Health (NIH)’s National Center for Advancing Translational Sciences (NCATS). This effort could even exist as a part of a new global hub co-founded by the United States in collaboration with other countries and funders. Indeed, entities from Europe, Africa, Latin America, and South Asia are already working on the concept of open-source pharmaceutical R&D. The United States should not be left behind.

However, it is important for the heart of this effort to exist outside of the academic and private sectors and their respective incentive structures. Universities are publication-oriented instead of product-oriented. Private entities are generally profit-seeking, and the consulting firms that often win government contracts typically do not conduct scientific research or create new products, let alone new paradigms. The effort should also be nimble and nonbureaucratic, focused on developing societally beneficial therapies, and characterized by an ethos of creativity, a deep feel for the subject, an open source and community spirit, and working for the public good. Possible implementation options could be recommended by a committee of accomplished innovators who have previously taken ideas from concepts to large-scale results in scientific and social realms.

There are five Initial areas of highest impact for open-source pharmaceutical R&D: (i) off-patent repurposing of existing medicines and vaccines,5 (ii) discovery of entirely new medicines and vaccines, (iii) creation of one or more scientific-information commons built on public data6 and resources, (iv) creation of open platforms (e.g., a Github for pharmaceuticals) to grow and connect relevant scientific communities, and (v) expanded artificial intelligence and computational capabilities to advance research.7 Clinical trial funding would be key, in order to translate research into interventions that have direct health impact. Partial precedents for open-source pharmaceutical R&D are numerous and include the NIH NCATS COVID-19 OpenData Portal, the Government of India’s Open Source Drug Discovery Initiative, and a new U.S./Europe/South Asia/Africa/Latin America global hub led by NIH NCATS, the European infrastructure for translational medicine (EATRIS), and the Government of Brazil’s Fiocruz.

The next administration should fund this effort with a minimum budget of $100 million in year one and $200 million in year two. We believe that this funding level, a fraction of the billions per

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new drug required in traditional industry approaches,\(^8\) would be sufficient to first deliver multiple therapeutics that are affordable and serve areas of great health need, and secondly establish a firm paradigm of open-source pharmaceutical R&D. To be truly transformational, the federal government should eventually increase funding to a few billion dollars per year. This effort would directly improve health. But in addition, expect that it could generate four types of economic returns: (i) direct cash savings, in the form of reduced expenditures on health care and hospitalizations by government, with an ROI of potentially more than 100% annually;\(^9\) (ii) some direct revenues, while maintaining openness and affordability; (iii) indirect returns created by improved health; (iv) and other indirect returns.

Federal funding for open-source pharmaceutical R&D should be viewed as an investment with indirect but major returns. By efficiently integrating the capabilities and knowledge of individuals, academics, and industry players in the pharmaceutical sector, open-sourcing R&D will—as already demonstrated in the IT sector—boost markets while delivering materially useful products for all Americans. Initial public investment to create open-source infrastructure for pharmaceutical R&D and unlock new data troves could increase the commercial viability of certain medicine or vaccine opportunities. In turn, this could spur private-capital investment and trigger waves of innovation, similar to ARPANET’s evolution into the Internet. We envision bipartisan support for this powerful approach.

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\(^9\) See, e.g., Giamarellos-Bourboulis EJ, Tsilika M, Moorlag S, Renieris G, Papadopoulos A, Netea, M, Activate: Randomized Clinical Trial of BCG Vaccination against Infection in the Elderly, Cell, https://doi.org/10.1016/j.cell.2020.08.051 (vaccination of the elderly with the off-patent tuberculosis vaccine BCG reduces the risk of all respiratory infections by 45%). The US spends $14.5 billion yearly on treating such infections (specifically, acute bronchitis, upper respiratory infections, influenza and pneumonia) in the elderly. Agency for Healthcare Research and Quality, Medical Expenditure Panel Survey, 2017. https://meps.ahrq.gov/mepstrends/hc_cond_icd10/. Approximately 65% of those payments, or $9.4 billion, are made by the US government. Reduction of that $9.4 billion by only 10% (as opposed to by 45%) would amount to nearly $1 billion in cash saved annually by the US government, from this single repurposing project alone. For a $100M investment, that amounts to an ROI of over 1,000%.
Frequently Asked Questions

What is the “market failure” in the pharmaceutical research enterprise?

A market failure occurs when individual market participants, acting in rational self-interest, produce a suboptimal or economically inefficient outcome in aggregate. There are persistent market failures in pharmaceutical discovery. Most diseases offer limited revenue streams that cannot justify the cost of developing treatments in the private sector. Other valuable interventions, such as widely available off-patent medicines or vaccines, go undeveloped or underdeveloped because of limited pathways towards market exclusivity. The public interest would be better served with more therapies and vaccines for more ailments. But since private pharmaceutical companies cannot develop these pharmaceuticals profitably, preventable death and suffering results. A pharmaceutical R&D enterprise built almost exclusively on a for-profit business models is incompatible with many of our society’s healthcare needs.

Will an open-source approach to pharmaceutical R&D approach replace the traditional pharmaceutical industry?

No! These models of drug development are complementary. Because open-source pharmaceutical R&D focuses on areas of market failure (where private industry is not active), it does not directly compete with for-profit pharmaceutical companies. Some of the techniques and approaches developed through open-source R&D could ultimately be adopted by for-profit companies, spurring innovation and growth in the private sector that supports discovery of yet more drugs and vaccines. An open-source approach will also establish a universally accessible body of scientific knowledge and data that all industry can draw on. By reducing R&D costs for industry, this resource will expand the collection of diseases and drugs that offer viable investment opportunities for the private sector. The information technology (IT) sector provides a successful precedent for an open-source approach. In IT, private companies frequently leverage open-source code to develop new product offerings. Open-source approaches have been widely embraced by the major IT industry players, who now pursue such approaches side-by-side with, and in support of, classic proprietary approaches.

Why is an open-source approach to pharmaceutical R&D important now?

The need for an open-source approach to pharmaceutical discovery has come sharply into focus during the COVID-19 pandemic. The United States must be able to use the entirety of its scientific arsenal to combat existential threats like COVID-19. By funding a new effort to support an open-source approach to pharmaceutical R&D, the next administration can create the infrastructure that will allow our nation to deploy its collective capacity to quickly develop new medicines and vaccines and/or adapt existing treatments against pressing health threats.

How much does the federal government spend on pharmaceutical R&D now?
The NIH is the nexus of federal funding for pharmaceutical research in the United States. The NIH received $41.7 billion for the 2020 fiscal year. NIH funding is essential for furthering our understanding of basic science and fueling the breakthroughs of the future. However, the NIH does not focus on developing end-product health solutions, nor does it focus on the health-policy considerations and collective health benefits associated with delivering and prioritizing end-product medicines and vaccines. Additional funding is needed for a new entity or program focused on open-source pharmaceutical R&D that leverages the knowledge and infrastructure created by the NIH and academic biomedical institutions—while uniquely supplementing and extending the capabilities and expertise of those institutions.

Why must the federal government act to support open-source pharmaceutical R&D? Why not incentivize the private sector to address this issue directly?

The persistence of massive market failures in the pharmaceutical industry—despite efforts to create incentives that encourage the private sector to address these failures—shows that it is time for government involvement. A government-funded entity focused on open-source pharmaceutical R&D will not only directly produce medicines and vaccines for diseases that are neglected by the existing pharmaceutical industry, but will also reduce some of the barriers and costs that limit private-sector investment in such diseases. In essence, government support for open-source pharmaceutical R&D will make it easier for the private sector to address market failures directly. We expect that the new open-source entity, will catalyze innovation and entrepreneurial activity that fuels the future growth of the U.S. pharmaceutical industry.

Aren’t there already efforts to make medical data and research open? What would this new effort add?

A truly open-source approach to pharmaceutical R&D is characterized by three key features. First, an open-source approach enables the entire scientific community to work together simultaneously on difficult challenges. Second, an open-source approach draws on the sum total of human knowledge instead of being constrained by discipline-specific technical expertise, or being limited to knowledge that can create patents or high revenues. And third, an open-source approach focuses on creating universally accessible products and scientific findings, without regard to profit and publication incentives.

Other forms of openness in the pharmaceutical sector are also valuable, but may not meet all three of these criteria. “Open innovation” often means having more people contribute to a discovery process. Yet open innovation can be as limited as two large companies collaborating in a novel way. Open innovation can also reference a crowdsourced contribution to a wholly proprietary product, even when the fruits of that effort are not publicly accessible. “Open access” typically refers to publications in journals. Open-access journal articles may be widely or universally available at no cost, but are often produced as the outcome of a scientific inquiry conducted by a single lab or research group. “Open data” similarly refers to data that are widely or universally available at no cost, regardless of whether or not those data were collected via a
collaborative process, and often only after a significant time lag. An “open source” approach to pharmaceutical R&D integrates and enhances all of these forms of openness.

What are some initial steps the federal government could take to support open-source pharmaceutical R&D?

We encourage the next administration to move quickly to launch, and robustly fund, an entity or program dedicated to advancing open-source pharmaceutical R&D via multiple simultaneous efforts. If a more staggered approach is desired, then we recommend two initial, high-impact actions. First, the next administration should establish a fund to support clinical repurposing trials: e.g., trials that test new applications of existing medicines and vaccines. Such trials are crucial to our nation’s ability to combat current and future pandemics. Second, the next administration should establish one or more scientific-information commons (akin to the National Center for Advancing Translational Sciences (NCATS) Biomedical Translator) to support open-source biomedical translational business models. These two initiatives will quickly demonstrate the benefits of an open-source approach, likely attracting greater support for a more expansive effort.
About the Authors

Michael Stebbins is a geneticist and public-policy expert who served as the Assistant Director for Biotechnology in the Obama White House Office of Science and Technology Policy. He is currently the President of Science Advisors, a science and health consulting firm he founded in 2018 to provide science, technology, and public-policy guidance to private companies, philanthropies, and non-profit organizations. While at the White House, Dr. Stebbins’ work led to large initiatives across the federal government to address antibiotic resistance, protect pollinators, improve veterans’ mental health, increase access to federally funded scientific publications and data, promote the preferential purchasing of antibiotic-free meats, reform the regulatory system for biotechnology products, drive federal purchasing of bio-based products, and improve the management of scientific collections. Dr. Stebbins previously served as the Vice President of Science and Technology for the Laura and John Arnold Foundation, science advisor to the Obama Presidential Campaign, and on the Obama White House Transition Team. He is the former director of biology policy for the Federation of American Scientists and worked for U.S. Senator Harry Reid and at the National Human Genome Research Institute. Before coming to Washington, he was a senior editor at Nature Genetics. Dr. Stebbins is on the Board of the Value in Cancer Care Consortium and chair of the Board for Vivli. He serves on the scientific advisory boards for Datavant KOKOMI, and Amida Technology Solutions. He can be reached on Twitter @stebbins.

Miranda Bain is a gender, migration, and health-policy researcher. She has conducted policy and advocacy work and published articles on the intersection of these subjects. She graduated with Phi Beta Kappa honors from the Johns Hopkins School of Advanced International Studies.
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**Nicholaos Krenteras** has almost 20 years of experience in venture capital and private equity and has worked with more than 50 start-up companies in his career. Mr. Krenteras holds an A.B. in International Relations from Brown University and an M.B.A. from the Columbia Business School, where he was a member of the Beta Gamma Sigma Honor Society.

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and represented the student leaders of Tiananmen Square and victims of the Bosnian genocide. He has co-founded an effort to address the world’s most widespread form of malnutrition by adding iron to iodized salt; the effort has reached millions of people. He is a winner of the Brown University alumni association’s highest honor, given to one alum per year, and a life member of the Council on Foreign Relations.

Bernard Munos is a Senior Fellow at FasterCures, a center of the Milken Institute, a co-founder of the Open Source Pharma Foundation, and the founder of the InnoThink Center for Research in Biomedical Innovation, a consultancy that helps biomedical research organizations become better innovators. Before that, he served as an advisor for corporate strategy at Eli Lilly, where he focused on disruptive innovation and the radical redesign of R&D. Several of Munos’ research papers — published in Nature and Science — have helped stimulate a broad rethinking of the pharmaceutical business model by industry, investors, policymakers, regulators, and patient advocates. His work has been profiled by Forbes magazine, and the popular industry publication FiercePharma has named him one of the 25 most influential people in biopharma. He is a member of the Advisory Board of Science Translational Medicine; a non-executive Director of Glenmark Pharmaceuticals; a Board member or Advisor to a dozen other companies or publicly-financed research organizations; a former member of the National Academy of Medicine’s Drug Forum and of the Advisory Council of the National Institutes of Health’s National Center for Translational Sciences (NCATS). He received his MBA from Stanford University, and holds other graduate degrees in animal science and agricultural economics from the Paris Institute of Technology for Life, Food and Environmental Sciences and the University of California, Davis.

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