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Healthy Funding: The Critical Role of Investing in NIH to Boost Health and Lower Costs

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NIH funding is critical to improving health outcomes and reducing the societal costs of illnesses. Congress should increase the NIH budget and then maintain regular, steady increases.

KEY TAKEAWAYS

- Public funding for the National Institutes of Health (NIH) has been critical to discovering new medicines and treatments, improving quality of life, increasing lifespans, and reducing costs to society from illness.
- NIH funding increased 64 percent between 1990 and 2019. But funding as a share of GDP peaked in 2003 and declined through 2015. NIH funding as a share of GDP in 2019 is still 12 percent below 2003 levels.
- Congress should increase the NIH budget by around \$8 billion annually over the next two years, and then maintain regular, steady increases—ideally 2 to 3 percentage points faster than the nominal rate of GDP growth.

OVERVIEW

The federal government, principally through the National Institutes of Health (NIH), funds scientific research related to biology and human health that sets the stage for applied research and development (R&D) activity by industry, ultimately leading to the commercialization of new medicines and treatments. New drugs not only improve the quality and length of lives but reduce the costs to society from illness. In order to accelerate biomedical innovation, Congress doubled NIH founding around the turn of the millennium. The results are paying off with basic and translational research, including discoveries of the genetic basis of disease and development of related diagnostics and therapies. For example, cancer therapies are being tailored not just to a patient's genome but to the genome of that patient's tumors. Other discoveries include sickle cell genomic therapy,^{1.} immunotherapy for breast cancer,^{2.} a universal flu vaccine, the TAILORx genetic screening breast cancer trial,^{3.} and discoveries for the treatment of Alzheimer's.^{4.} NIH funding overall plays an important role, not only in biomedical innovation, but in enabling a competitive U.S. life sciences industry, and the millions of good paying jobs associated with it. In fact, while overall manufacturing jobs have declined in the last two decades, the number of biopharmaceutical industry jobs has grown. As such, increasing NIH funding is important not only to improving the health of Americans, but in reducing health care costs and spurring global life sciences competitiveness.

Boosting NIH funding has long been a nonpartisan issue. For example, at a 2015 forum, former Republican House Speaker Newt Gingrich and Senator Elizabeth Warren (D-MA) both called for significant increases in NIH funding.⁵ And there is currently strong bipartisan support in Congress, with senators Roy Blunt (R-MO) and Patty Murray (D-WA) and representatives Rosa DeLauro (D-CT) and Tom Cole (R-OK) leading the charge for increases in NIH funding. Moreover, Americans are extremely optimistic and interested in biomedical breakthroughs. A recent survey conducted on behalf of the USA Today Network and the Charles C. Koch Institute asked Americans to name three areas of technological change they were most excited about for the future. Medical innovation, including pharmaceutical breakthroughs, ranked number 1, by an equal proportion (61 percent) of Democrats and Republicans, and an even higher share (66 percent) of rural Americans.⁶

However, even with recent increases, NIH funding as a share of GDP in 2019 is still 12 percent below that of 2003. Getting NIH funding to that 2003 level will require Congress to appropriate an additional \$7.4 billion in FY 2020.⁷ As such, Congress should increase the NIH budget by around \$8 billion annually over the next two years, and then maintain regular steady increases—ideally 2 to 3 percentage points faster than the nominal rate of GDP growth.

This report briefly discusses the structure and role of NIH. It then examines NIH funding history over the last two decades, and reviews the scholarly evidence on the role of drug innovation in improving human health and its effect on the U.S. economy. The report then reviews studies examining the role of NIH on biomedical innovation and how it supports U.S. biopharmaceutical

industry competitiveness. Finally, the report discusses how, in an effort to foster a thriving biopharmaceutical industry, many of America's major competitors have increased funding for government biomedical research at a much faster rate than the United States.

THE STRUCTURE AND ROLE OF THE NATIONAL INSTITUTES OF HEALTH

The National Institutes of Health funds scientific research that sets the stage for the industry-led applied research and development (R&D) activity leading to the commercialization of new medicines and treatments.^{8.} NIH comprises 27 institutes and centers, each with a specific research agenda whose focus is on a particular disease or body system.^{9.} Congress provided NIH a \$37.3 billion budget in 2018, and appropriated \$39.1 billion in NIH funding for 2019.^{10.} Around 83 percent of NIH's budget funds extramural research through grants, contracts, and other awards, and is performed by more than 300,000 individuals working at over 2,500 hospitals, medical schools, universities, and other research institutions in all 50 states.^{11.} About 11 percent support intramural research by NIH scientists at NIH's main campus in Bethesda, Maryland.

The majority of NIH funding is for "basic" research that aims to extend the frontiers of biological understanding, with an estimated one-third of funding supporting clinical research (including patient-oriented research, clinical trials, epidemiological and behavioral studies, as well as outcomes and health services research) that is more applied in nature.¹² NIH also supports training grants that help develop the U.S. scientific and medical workforce. In 2016, NIH grants directly supported the training of more than 9,500 predoctoral students and almost 5,900 postdoctoral fellows.¹³

NIH researchers contribute new-to-the-world life sciences research. Over 115,000 scholarly articles published in 2016 acknowledged NIH grant support.¹⁴ Moreover, each R01 grant, the most common type of NIH research project grant, leads to an average of 7.36 published research articles.¹⁵ These grants are subsequently cited by other researchers: It is estimated that each NIH research grant leads to an average of almost 300 citations in academic literature.¹⁶ The groundbreaking life sciences research supported by NIH is attested to by 153 NIH-supported researchers having won Nobel Prizes.¹⁷

NIH-funded basic life sciences research—for instance, into understanding the fundamental processes by which diseases develop and are transmitted, or identifying novel biomarkers signaling the presence of a disease—creates a platform for innovation that has laid the groundwork for not only the discovery of new medicines, but also new tests (e.g., blood tests for biomarkers), new procedures (e.g., improved cardiac stents that substitute for surgery), and new equipment (e.g., gene sequencers).¹⁸ It has supported discoveries that have contributed to a reduction in both deaths from cancer and rates of disability due to stroke, heart disease, hepatitis B, and osteoporotic fractures.¹⁹ NIH-supported research has also led to the development of anti-AIDS drugs; the discovery of neurotransmitters and then antidepression treatments that leverage selective serotonin reuptake inhibitors (SSRIs); and treatments that reduce scar-tissue formation.²⁰

While all 27 NIH institutes, centers, and initiatives play an important role in life sciences innovation, the unique role of several particular units is worth highlighting.

Accelerating Medicines Partnership

The Accelerating Medicines Partnership (AMP) is a public-private partnership between NIH, the Food and Drug Administration, life sciences companies, and nonprofit organizations to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets for therapeutics.^{21.} AMP is focused on four disease areas: Alzheimer's; type 2 diabetes; autoimmune disorders of rheumatoid arthritis and lupus; and Parkinson's. The idea is closer cooperation among scientists at NIH, in academia, and within industry can help better coordinate research, and make it more efficient and effective. For each project, scientists from NIH and industry have developed research plans aimed at characterizing biomarkers and distinguishing biological targets most likely to respond to new therapies. These projects not only leverage non-NIH funding (an average of 25 percent over the four projects), but improve research effectiveness.

The National Center for Advancing Translational Science

Established by Congress in December of 2011, the National Center for Advancing Translational Sciences (NCATS) focuses on ways to reduce, remove, or bypass system-wide bottlenecks in the translational process: the process of turning observations from within laboratories, clinics, and communities into interventions that improve the health of individuals and the public-from diagnostics and therapeutics to medical procedures and behavioral changes.^{22.} The core goal of NCATS is to help get more treatments to more patients more quickly. NCATS focuses not on specific diseases, but rather on what is common among them and in the translational science process. Essentially, NCATS studies translation on a system-wide level as a scientific and operational problem.^{23.} NCATS initiatives focus on topics such as discovering new therapeutic uses for existing molecules; improving the availability of rare disease information, treatment, clinical studies, and general awareness for both patients and the medical community via programs such as the Rare Diseases Clinical Research Network (RDCRN); tissue chips for drug screening; and toxicology in the 21st century.^{24.} NCATS also administers the Cures Acceleration Network to advance the development of high-need cures and reduce significant barriers between research discovery and clinical trials. Under the program, NCATS may make grants of up to \$15 million per year that must be matched by other parties at a rate of 1:3.

Small Business Innovation Research Program and Small Business Technology Transfer Program

The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, collectively known as America's Seed Fund, represent one of the largest sources of early-stage capital for technology commercialization in the United States, allowing U.S. owned and operated small businesses to engage in federal research and development that has a strong

potential for commercialization.^{25.} NIH's SBIR program funds early-stage small businesses that are seeking to commercialize innovative biomedical technologies; STTR is similar but requires small businesses to engage with a research institution. Eleven federal agencies operate SBIR/STTR programs. Of the institutes or centers within NIH, 24 have SBIR and STTR programs. In 2017, NIH's SBIR and STTR programs invested almost \$1 billion (\$861 million for SBIR; \$121 for STTR) into promising, young, innovative life sciences start-ups. In 2017, NIH funded 1,520 start-ups. For FY 2019, NIH will disburse \$1 billion in SBIR funds and \$141 million for STTR, which will be disbursed over a series of two phases: Phase 1 feasibility studies (grants of up to \$150,000) may be extended into Phase II development activities (funded at \$1 million), with a possibility of a Phase IIB competing-renewal award.^{26.} SBIR plays a key role in America's innovation system, particularly in the life sciences sector. A number of groundbreaking life sciences start-ups got a kick start from SBIR, including Genzyme (biotech therapies), Affymetrix (GeneChip), Amgen (biopharmaceuticals), Jarvik Heart (artificial heart), Biogen/Idec (neurological, autoimmune therapies), Millennium Pharma (gene databases), Geron (telomerase inhibitors for cancer treatments), and Neocrine Bioscience (neurological and endocrine pharmaceuticals).^{27.} SBIR plays a major role in making projects that would not happen otherwise possible. For instance, a study of NSF SBIR Phase II recipients found that 75 percent thought their projects probably or definitely would not have proceeded absent program funding: 34 percent were definite and 41 percent thought it unlikely.^{28.} In short, NIH's SBIR/STTR program represents an indispensable asset within America's life sciences innovation system.

NIH Centers for Accelerated Innovations and Research Evaluation and Commercialization Hubs

The NIH Centers for Accelerated Innovations (NCAI) and the NIH Research Evaluation and Commercialization Hubs (REACH) are focused on accelerating the translation of scientific discoveries into commercial products. The programs represent public-private partnerships, with expertise and resources from the federal government, academia, and the private sector, that will change the way discoveries with scientific and commercial potential are identified and developed. The National Heart, Lung, and Blood Institute started NCAI in September 2013, and is the primary federal supporter of the program, merging the strengths of 14 high-impact research institutions.^{29.}

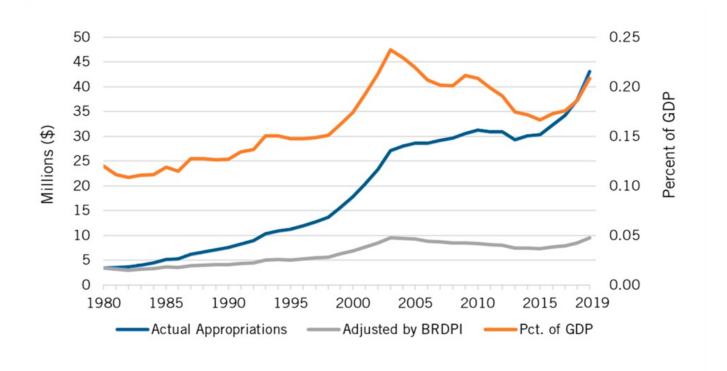
REACH grants qualified institutions both an initial investment and additional resources to nurture innovators to identify and develop high-priority early-stage technologies related to NIH's objectives. It also provides infrastructure for identifying the most promising technologies; funding for product-definition studies (e.g., feasibility studies, prototype development, and proof-of-concept studies); coordinated access to expertise in areas concerning early-stage technology development (including scientific, regulatory, reimbursement, business, legal, and project management); and skills development and hands-on experience in entrepreneurism. There are three NIH Research Evaluation and Commercialization Hubs: the Long Island Bioscience Hub, ExCITE, and MN-REACH. Congress chartered the hubs as part of the 2011 SBIR/STTR reauthorization, with the vision that the hubs would provide Phase 0 proof of concept partnerships to help get more promising start-ups into the SBIR program.

NIH FUNDING TRENDS

NIH appropriations grew significantly from the late 1990s to the early 2000s (the period in which Congress doubled the NIH budget), more slowly through 2015, and then more sharply in the last few years (see figure 1).

Using this measure, NIH funding fell by nearly 25 percent from 2003 to 2015. Recent appropriations have restored some of that loss, but NIH funding is still 9 percent below where it was in 2003, adjusted for inflation

However, nominal changes in funding do not present an accurate picture as they fail to account for inflation—in this case, the rising cost of conducting medical research (known as the biomedical research and development price index or BRDPI). Using this measure, NIH funding fell by nearly 25 percent from 2003 to 2015. Recent appropriations have restored some of that loss, but NIH funding is still 9 percent below where it was in 2003, adjusted for inflation (See figure 1). In order to have kept the BRDPI-adjusted NIH funding at 2003 levels, Congress would have needed to appropriate an additional \$4.1 billion for 2019.





But even with recent increases, NIH funding as a share of GDP in 2019 is still 12 percent below 2003 levels.

In short, it is misleading to view the NIH doubling as a period of unprecedented funding increases that permanently put NIH funding on a new and higher level. In fact, if Congress had simply kept up the average real annual growth of the NIH budget from 1971 to 1998 (3.34 percent per year using the BRDPI index), in 2019, the funding levels would have been \$8.2 billion higher than actual appropriations (in current dollars).³¹ So, essentially, rather than doubling the NIH budget and then building on that new base, Congress prefunded only a portion of what would have been historically normal increases.

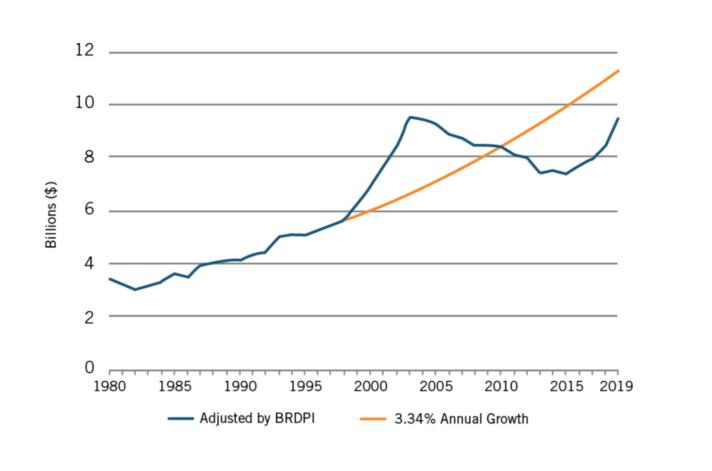


Figure 2: NIH Appropriations: Actual vs. Trend ³²

An important lesson from NIH doubling is it being followed by inflation-adjusted cuts is worse than regular increases achieving the same level at some future point in time. Boom and bust cycles lead to an array of problems, such as misleading signals sent to graduate students and young biomedical researchers leading to an oversupply of graduate students relative to later resources.³³ In 2013, the American Society for Biochemistry and Molecular Biology conducted an online survey

of 3,700 scientists across America.³⁴ Forty-six percent had laid off scientists or expected to do so soon, while 55 percent knew of a colleague who had lost their job. In addition to cutting existing staff, 53 percent had to turn away promising young researchers because of a lack of funds. A more recent survey of researchers holding NIH or National Science Foundation grants found that nearly half had abandoned an area of investigation they considered central to their lab's mission, and more than 75 percent had reduced their recruitment of graduate students and research fellows.³⁵ These cuts have been particularly damaging to the research prospects of both new investors and young scientists who often have the most original and creative ideas, and were not able to see those ideas tested in a laboratory. In essence, Congress needs to apply a goldilocks approach to NIH funding (regular, steady increases), ideally 2 to 3 percentage points faster than the nominal rate of GDP growth—and not perpetuate the boom-and-bust cycle that accompanied the doubling of NIH funding in the late 1990s and early 2000s.

There is little risk of increases not being used productively. Even with the recent increases, there is clear evidence that increased funds would have been used productively. For example, in FY 2018, just 17.8 percent of R01 research grant applications were funded, compared with 24 percent in FY 2003.³⁶ Harold Varmus, former director of NIH, has argued that NIH could approve around one-third of applications and still fund the best science.³⁷

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Another way to look at this is to examine the rejection rates for highly qualified proposals. NIH uses impact scores, which are the sum of 10 reviewers who each score applications from 1 (best) to 9 (worst). Scores 1 to 3 are considered "high impact," with 3 being described as "excellent" and "very strong with only some minor weaknesses."³⁸ Eleven percent of AO (first submission) Type 1 (applying for support of a project that has not yet been funded) applications submitted from FY 2012–2016 received combined scores of 30 or lower, but 37 percent of these were not funded —at least not within that application.³⁹ And ninety-two percent of proposals with a combined score of 31 to 40 (very good, strong but with numerous minor weaknesses) were not funded.

The low rate of approvals is somewhat self-correcting in the following, unfortunate way: Low rates of approvals mean fewer of the world's top scientists and medical talent are moving to the United States, instead often going to other nations that offer more opportunities, such as China, Singapore, and the United Kingdom. In addition, low approval rates mean less research being performed and less support for promising graduate students, many of whom may switch out of biomedical research to other fields. In other words, the U.S. supply of highly talented biomedical researchers is anything but fixed, and increased NIH funding will only help grow that pie—and with it medical discoveries and good biomedical jobs.

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WHY BIOMEDICAL RESEARCH MATTERS

Even in a \$20 trillion economy, the \$39.1 billion NIH budget is still a considerable amount of money. What do Americans get from that investment, and why should they support this use of their tax dollars? There are three principal reasons. The first is improvement to their overall health. New drugs help enhance the quality—and length—of Americans' lives. And even though they can be expensive, on net, drugs reduce the societal costs from disease. But the development of new drugs requires an enormous amount of research and development; a not insignificant share of which is early-stage basic and foundational—and funded by the federal government. The second reason is the development of better drugs and treatments leads to reductions in the cost to society from illness. And the third is NIH funding plays an important role supporting the competitive strength of the U.S. biopharma industry—an industry that, unlike many others, has not gone offshore or suffered hollowing out at the hands of foreign competitors—with the result being millions of good jobs in all 50 states.^{40.}

NIH Funding Increases Biomedical Innovation

Before discussing the health and economic benefits of new medical discoveries, including new drugs, it is important to examine the role of publicly funded research, especially by NIH, in spurring biomedical innovation. Studies show NIH funding plays an important role in biomedical innovation for example, by supporting the graduate research education of most life scientists in medical research laboratories today. Another way is by directly funding research.

Between 1965 and 1992, federally funded research laid the groundwork for the discovery of 15 of the 21 top-grossing drugs, 7 of which were directly related to research discoveries made by NIH.⁴¹ They included breakthrough antidepressant drugs that leveraged discoveries about neurotransmitters to develop selective serotonin reuptake inhibitors (SSRIs), anti-AIDS drugs, and drugs used in heart surgery. NIH-funded research into monoclonal antibodies has supported the development of new monoclonal therapy-based drugs that, in 2010, accounted for 5 of the top 20 best-selling drugs in the United States.⁴²

A study of 32 innovative drugs introduced before 1990 found that without the contributions of government laboratories and NIH-supported universities, approximately 60 percent of those drugs would not have been discovered or would have had their discoveries markedly delayed.⁴³ A 2011 study by Stevens et al. revealed that over the past 40 years, 153 new FDA-approved drugs, vaccines, and new indications for existing drugs were discovered from fundamental research carried out in public-sector research institutions (PSRIs).⁴⁴ They found that, "PSRIs have contributed to the discovery of 9.3 to 21.2 percent of all drugs involved in new-drug applications

approved during the period from 1990 through 2007." In a study of 478 drugs approved by FDA from 1998 to 2005, Sampat and Lichtenberg determined that 12.7 percent of drugs had an underlying academic patent, including 5.8 percent of standard-review drugs and 22.6 percent of priority-review drugs. It also found even larger indirect effects on the innovation process, with 23.7 percent of standard-review drugs, 45.8 percent of priority-review drugs, and 32.7 percent of all new drugs citing an academic patent.⁴⁵ Likewise, Lowe found that about 15 percent of new drug discoveries come from knowledge generated by academic labs.⁴⁶ Most of this research was funded by the federal government broadly, and NIH specifically.

The Battelle Memorial Institute discovered that, "NIH funded research produced an average of 5.9 patents per \$100 million in R&D expenditures from 2000–2013—or at a rate of one patent per every \$16.9 million in NIH funding."⁴⁷ The report went on to find that, "NIH patents also averaged 5.14 forward citations, meaning the NIH is an integral part of the knowledge chain for \$105.9 million in downstream R&D leveraged for every \$100 million in taxpayer funded research." A 2018 study found that every additional \$10 million in NIH funding generates 2.7 patents.⁴⁸ Toole concluded that a one-time \$1 investment in public-sector basic research yielded \$0.43 in annual benefits in the development of new molecular entities in perpetuity—a remarkable return on investment.⁴⁹ Cleary et al., discovered that NIH funding contributed to published research associated with all 210 new drugs approved from 2010-2016.⁵⁰ Another study found that 10 percent of NIH grants are cited by patents, 30 percent are cited in articles that are then cited in patents, and 5 percent result in papers citing successfully approved drugs.⁵¹

Moreover, Kneller determined that NIH-funded labs and universities generally produce new discoveries that are more advanced, more likely to be considered "novel," (as opposed to advances that are based on a preexisting substance that is modified and resubmitted for approval), and more likely to support "orphan drugs" (substances that address rare diseases or conditions).⁵²

As one survey concluded, "While it is very difficult to be precise about the pay-offs of publicly funded research [in biomedical science], we conclude from a survey of a wide variety of quantitative and qualitative academic studies that the returns from this investment have been large, and may be growing even larger."⁵³ And as the National Academy of Sciences noted, "Fewer investments in basic research (by NIH) can result in fewer new drug therapy candidates, which in turn can result in fewer investments by private industry to advance promising candidates."⁵⁴ And after reviewing over 60 academic articles on the impact of federal funding on biomedical innovation, Cockburn and Henderson concluded, "There are a number of econometric studies that, while imperfect and undoubtedly subject to improvement and revision, between them make a quite convincing case for a high rate of return to public science in this [life-sciences] industry."⁵⁵

And we are seeing continued progress. For example, over the last two decades, cancer mortality rates have declined by 25 percent, in part because of NIH-supported breakthroughs such as genomic analysis of tumors, precision medicine (e.g., treatment of a tumor by targeting a specific mutant gene that drives it), and use of immunotherapy with checkpoint inhibitors. Indeed, RO1

applications to NIH's National Cancer Institute increased by almost 50 percent between 2013 and 2018.⁵⁶ And new drugs are being approved at significant rates, with 19 new cancer drugs approved by the FDA in 2018.⁵⁷

It is important to keep in mind that, while this generation of knowledge from NIH funding plays a role in drug development, it is usually foundational in nature and contributes to a process whereby drug companies must invest billions more to actually identify, develop, test, and bring to market compounds.

Improvements in Health and Reductions in Costs From New Drugs

While it is clear that NIH funding helps spur discoveries that enable the development of drugs and treatments, what is the effect of these discoveries, particularly the development of new drugs, on health? The evidence is clear that better drugs improve health. A study by Lichtenberg and Peterson estimated what the health results in Sweden would look like if doctors and hospitals were constrained to only using medicines and technology created before 1997. The authors concluded that pharmaceutical innovation was responsible for 5.6 months of the 1.88-year increase in average life expectancy in Sweden between 1997 and 2010.^{58.} In another study, Lichtenberg found that, from 1996 to 2003 in the United States, improvements in drugs led to an increased life expectancy of 0.41 to 0.47 years.^{59.} Moreover, as Lichtenberg explained, "During the period 2000–2011, the premature (before age 75) cancer mortality rate... declined by about 9%.... In the absence of pharmaceutical innovation during the period 1985–1996, the premature cancer mortality rate would have *increased* about 12% during the period 2000–2011."^{60.}

But illness also imposes tremendous costs on society, not just in direct medical costs, but also indirectly through factors such as early mortality and lost work. Leaving aside the value of new drugs on quality and length of life, it is important to examine their impact on the economy through reduced medical and other costs. Illness and early mortality impose a large cost on the productivity of individual workers—to say nothing of their quality of life—and, therefore, reduce the nation's potential wealth.

If that the only thing federally funded biomedical research resulted in was better health, it would be appropriate to classify it, for budget terms, as an expenditure. In fact, biomedical research leads to new drugs that reduce total costs in society, and as such deserves to be classified as an investment—in the sense that money spent today yields societal returns tomorrow. Lichtenberg estimated a social return from pharmaceutical innovation of 67.5 percent.⁶¹ In other words, every dollar spent generates \$1.67 in benefits. Another study estimated the total social return from biomedical research (public and private) is 150 percent, implying that society would benefit from a significant increase in research spending.⁶²

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Overall, the evidence that biopharmaceutical innovation has led to significant net economic benefits—and the potential for even further economic gains—is strong. For example, progress against various diseases since 1970 have increased national wealth by \$3.2 trillion per year.⁶³ In fact, there is some evidence that these and other related studies undervalue the economic returns, and that conventional methods underestimate the economic value of health gains by 30 to 80 percent.⁶⁴

Because diseases impose significant costs on the U.S. economy, continued and even faster rates of life sciences innovation must be integral to a longer-term national growth strategy. The Milken Institute concluded that the most common chronic diseases cost the U.S. economy an estimated \$1 trillion each year, and could cost upwards of \$6 trillion by 2050.⁶⁵ A study conducted by the Harvard School of Public Health and the World Economic Forum found that cancer cost the global economy about \$250 billion in 2010, and anticipated that cost will rise to at least \$458 billion by 2030.⁶⁶ Cardiovascular disease cost an estimated \$863 billion in 2010, rising to \$1 trillion by 2030; diabetes cost \$500 billion in 2010, rising to \$745 billion by 2030; and mental illness cost \$2.5 trillion in 2010, rising to \$ 6.0 trillion by 2030.⁶⁷ Another study that estimated the population's willingness to pay to reduce the risk of disability or death associated with noncommunicable diseases. It estimated that individuals would be willing to pay \$22.8 trillion in 2010 to reduce this risk significantly, and that number would grow to \$43 trillion in 2030. Another study found that seven chronic health conditions led to lost economic output of \$1 trillion per year, including lower output and lost work days.⁶⁸

NIH funding should be seen as an investment that generates economic returns for U.S. taxpayers.

Alzheimer's disease, for example, imposes significant costs on the economy of around \$226 billion per year, or 1.5 percent of GDP. By 2050, without improved understanding or the ability to slow the onset of the disease, direct costs could reach \$1 trillion dollars.⁶⁹ Similarly, Parkinson's disease costs \$14.4 billion per year in direct medical costs, increased costs of care, and lost productivity.34 Huntington's disease and amyotrophic lateral sclerosis (ALS) together cost approximately \$2.5 billion.⁷⁰ In total, neurodegenerative diseases impact 5.8 million Americans and cost \$262 billion.⁷¹ Continued drug innovation would yield significant economic benefits moving forward. One study found a 1 percent reduction in mortality from cancer would deliver

roughly \$500 billion in net present benefits, while a cure would deliver \$50 trillion in present and future benefits.⁷² In this sense, NIH funding should be seen as an investment that generates economic returns for U.S. taxpayers.

NIH and BioPharma Companies Play Complementary Roles

NIH funding is often subject to two major misconceptions. The first, usually by advocates on the left, is NIH funding can substitute, wholly or in part, for biopharmaceutical-industry fundingand in so doing lead to the development of drugs in the public domain. The second, usually by advocates on the right, is the private sector can take the place of NIH funding for basic and foundational research. Both views represents a lack of understanding of the complementarity between NIH funding and industry funding.

Notwithstanding its importance for early-stage biomedical research, NIH funding does not result in the development of drugs. Instead, publicly funded researchers perform the upstream, earlier-stage research elucidating the underlying mechanisms of disease and identifying promising points of intervention. In turn, private-sector researchers perform the downstream, applied research that results in the discovery of drugs that treat diseases, and have carried out the development activities necessary to getting them to market.⁷³ Federally funded basic life sciences research tends to be concentrated within the basic science of disease biology, biochemistry, and disease processes, with a major goal of the research being the identification of biomarkers and biologic targets new drugs could treat.⁷⁴ While the private sector does invest in basic scientific research, including at U.S. universities, the preponderance of its activity is applied R&D focused on the discovery, synthesis, testing, and manufacturing of candidate compounds intended to exploit biologic targets for the purpose of curing medical conditions.⁷⁵ Therefore, considerable investment is required to bring a drug to market, even after basic research has already been conducted. In fact, one study found that biotechnology companies invest \$100 in development for every \$1 the government invests in research.⁷⁶

In contrast, some on the right make the opposite case: Why spend taxpayer dollars to support NIH research when industry can do the work? The scholarly evidence is clear that federal support for basic and early-stage applied research is a complement to private research in that industry is able to build on the knowledge discoveries made from publicly supported life sciences research, thereby making their own research more productive and effective. In this sense, publicly funded basic research generates more than just papers, knowledge, and postgraduates; public-sector funds increase the productivity of the industry as a whole by facilitating an environment of readily valuable basic science. Public research within the life sciences industry leads to the development of "infrastructure knowledge," or skills acquisition, techniques, and research tools that increase the expected rate of return for private-sector R&D projects.⁷⁷ Indeed, a 2000 study by the U.S. Joint Economic Committee found, "Federal research and private research in medicine are complementary. As medical knowledge grows, federal research and private research are becoming more intertwined, building the networks of knowledge that are important for generating new

discoveries and applications."⁷⁸ Likewise, the findings of a 2017 NBER report "suggest that NIH funding spurs private patenting by either increasing total firm R&D expenditure or increasing the efficiency of these expenditures."⁷⁹

Specifically, Ehrlich found that a dollar of NIH support for research leads to an increase of private medical research of roughly 32 cents.⁸⁰ Other studies have concluded that an additional 10 to 30 cents of private-sector R&D occurs for every dollar of government funding for university or government laboratory research.⁸¹ A 2013 report by Battelle found that, looking solely at federal support for the Human Genome Project between 1988 and 2012, every dollar of federal funding helped generate an additional \$65 in genetics-related private activity.⁸² (This activity in turn produced nearly \$3.9 billion in federal taxes and \$2.1 billion in U.S. state and local taxes in 2012 alone.)

Moreover, research has shown a strong positive correlation between private R&D investment in a given year, and public R&D spending in the year prior.⁸³ To sum up, as an OECD study argued, "It is particularly important for government-funded research to continue to provide the early seeds of innovation. The shortening of private-sector product and R&D cycles carries the risk of under-investment in scientific research and long-term technologies with broad applications."⁸⁴

NIH Funding Supports U.S. Biomedical Competitiveness

While the principal rationale for increased support for NIH funding is improvements in health and concomitant reductions in health care costs, an ancillary but important benefit is U.S. biomedical industry competitiveness.

The sector provides valuable benefits to the U.S. economy, including through over 1.2 million direct jobs, and an additional 3.5 million indirect and induced jobs.⁸⁵ Moreover, employment in life sciences sectors has been growing since 2001.⁸⁶ Employment in biopharmaceuticals (both production and research) increased by 22 percent between 2001 and 2016. During this same period, total U.S. nonfarm employment increased only 9.5 percent, and employment in manufacturing actually declined 27.6 percent. Biopharmaceutical employment hardly decreased during the recent recession, and resumed growing in 2013.

And these are good jobs: Workers in the industry earned an average wage of \$124,400 in 2016, compared with the median personal income in the United States for full-time wage and salary workers of just under \$43,000. As such, biopharmaceutical industry wages exceeded average private wages by 50 percent or more in 43 states. In 24 states, the premium topped 75 percent.⁸⁷

Moreover, America continues to produce a robust number of biopharmaceutical start-ups, many of which can trace their origins to NIH funding at universities—or at NIH itself. These start-ups employ 35,000 workers across 1,600 firms.⁸⁸ And over the last decade, biopharmaceutical start-

ups have grown, accounting for 66 percent of all firms in the industry in 2016—a 10-year high. Since 2007, the number of start-ups has increased by 56 percent, from 1,000 firms in 2007 to 1,600 firms in 2016.

These start-ups help drive regional prosperity and growth. A Massachusetts Biotechnology Council white paper estimated that each new biotech job created in and around Boston's strong biotech start-up ecosystem generated five indirect jobs within the same region.⁸⁹ For comparison, each job in manufacturing (a traded sector) supports only three indirect jobs, while each job in the food and beverage industry (a non-traded sector) supports up to just one indirect job.⁹⁰

Many of start-ups were born in universities that received NIH funding to support the research. For instance, AUTM's Better World Project highlights the case studies of a number of start-up life sciences companies that sprang from research funded by NIH or NSF and conducted at U.S. universities. The report "The Economic Contribution of University/Nonprofit Inventions in the United States: 1996–2015" cataloged the impact academic patents and their subsequent licensing to industry, including in the life sciences, had on the U.S. economy from 1996 to 2015. It found that over 11,000 start-ups had formed on this basis since 1995, and academic technology transfer has contributed to \$1.3 trillion in gross U.S. industrial output, bolstered U.S. GDP by up to \$591 billion, and supported 4,272,000 person years of employment.⁹¹ It also noted that over 200 drugs and vaccines have been developed through public-private partnerships involving university technology licensing since 1980.⁹²

NIH's support for research, particularly at research universities, makes the United States a more attractive location globally for companies developing biomedical innovations. As Michael Lawlor wrote, "Despite the fact that much valuable research is conducted in Europe and Japan, all major international pharmaceutical companies feel the need to establish research relationships or laboratory locations to keep abreast of the new developments in the United States."⁹³ This is why virtually all of the top internationally headquartered biopharmaceutical firms have significant presence and employment in the United States.⁹⁴

Another reason for America's relatively strong competitive position in the industry is the United States has done well in developing new drugs. A 1999 review of the pharmaceutical industry's global competitiveness concluded the United States had a competitive advantage due in large part to its strong research capabilities, the availability of revenues from drug sales, an environment that is conducive to science entrepreneurs, and the relatively efficient FDA review process.⁹⁵ Between 1975 and 1979, Europe brought to market 149 new drugs, while the United States contributed only 66.⁹⁶ The United States reversed this trend in each of the five-year periods since then, with a significant decline in the share from Japan, and a rise from other nations, such as India and China. Over the last 15 years, the three-year average of new drug approvals issued per year in the United States has risen steadily from a low of 72 in 2003 to as many as 106 in 2014.⁹⁷ This is also reflected in the United States, Europe, and Japan) in biotechnology, medical technology (generally medical or veterinary science), and pharmaceuticals between 1999 and 2013.

	1997–2001	2002–2006	2007–2011	2012–2016
Europe	79	46	52	75
United States	84	67	65	88
Japan	29	21	20	32
Other	4	14	12	38

Table 2: Number of New Chemical or Biological Entities ⁹⁸

GLOBAL COMPETITION IN LIFE SCIENCES INDUSTRY

While the United States leads in life sciences, it would be a mistake for policymakers to believe that the United States can rest on its laurels. While NIH spending as a share of GDP has fallen since 2003, a number of other countries, including China, have made long-term commitments to grow biomedical sciences industry. Competitor countries have improved their institutional framework surrounding biomedical research through innovations such as generous tax incentives for biomedical innovation and regulatory reforms. But a significant factor has been increased public funding for basic research. One recent review of the efforts by several countries found that, "Although the United States continues to rank first in nearly all measures of innovation, the countries profiled continue to make significant efforts to try to close the gap with the United States."^{99.} It continued, "The trends over the past five years continue to suggest that, in all but a few areas, the United States is not keeping pace and is actually losing ground."^{100.}

China's Life Sciences Strategy

As with other advanced industries China has sought to be global competitive in, the Chinese government views biotechnology as a strategic industry. In fact, through the central government's "Made in China 2025" plan, biomedicine as a key target. The plan set out the following goal to be achieved by 2025:

Promote a large number of enterprises to achieve drug quality standards and systems that are in line with international standards, among which at least 100 pharmaceutical enterprises obtain U.S., EU, Japanese, World Health Organization authentication and achieve product export; according to international drug standards, develop and promote 10-20 chemical drugs and high-end drugs, 3-5 new traditional Chinese medicines, 3-5 new biotech drugs complete drug registration in Europe, U.S. and other developed nations, speed up the development of internationalization of domestically produced drugs.

Before 2020 when international patents for blockbuster drugs expire, achieve over 90% generic production. Achieve breakthroughs for 10-15 important core and critical technologies; begin to establish national drug innovation system and innovation team.¹⁰¹

In addition to the national plan, at least 19 of China's 23 provinces have their own Made in China 2025 plans focused on biomedicine. 102

China's central, provincial, and local governments provide an array of incentives to biopharmaceutical companies, including subsidized laboratory and small-scale production space and free manufacturing space for up to five years. China also provides generous tax incentives to biopharma companies, including a 15 percentage point reduction in corporate income taxes, and a very generous R&D tax incentive.¹⁰³

Chinese governments have also established over 110 bioscience research parks. For example, Shanghai's "Pharma Valley"—a 10-square-kilometer life sciences hub—is home to more than 500 biotech companies.¹⁰⁴ The Ministry of Science and Technology has committed to building as many as 20 new bioscience research parks by 2020, with a total output value of the firms therein surpassing 10 billion yuan (\$1.45 billion).¹⁰⁵

The government also funds biomedicine start-ups directly. More than 1,000 government-funded venture capital firms seeking to provide as much as \$798 billion in capital have been established.¹⁰⁶ This led to an increase in Chinese biotech venture funding from \$0.5 billion in 2015 to \$2.5 billion in 2018.¹⁰⁷ Moreover, in the first half of 2018 alone, China-based venture capital funds invested \$5.1 billion into U.S. biotech firms, ahead of the \$4 billion for all of 2017.¹⁰⁸

Likewise, the Chinese government is investing significant amounts of money in key research areas. In 2010, the China Development Bank provided a \$1.58 billion line of credit to the Beijing Genomics Institute (BGI), a private genome-sequencing center, to buy 128 advanced DNAsequencing machines. With this purchase, BGI became the world's largest genetic sequencer, accounting for roughly a quarter of all DNA data sequenced in the world in 2014.¹⁰⁹ Since 2016, it has allocated around \$398.8 million (2.7 billion yuan) for stem cell research projects, 10 percent of which will be allocated to gene editing.¹¹⁰ And China has devoted \$9.2 billion to its 15year Precision Medicine Initiative launched last year that seeks to map 100 million human genomes—far in excess of the Obama administration's \$215 million investment targeting 1 million patients.¹¹¹ The Chinese government provided \$295 million for fundamental stem cell research under the twelfth Five-Year Plan.¹¹² China also produces 150,000 life science graduates annually. Annually, more than 10,000 Chinese citizens studying or working in the life sciences in the United States return to China after being aggressively recruited via the private sector or induced by government initiatives such as the "Thousand Talents" program.¹¹³ Chinese researchers have increased the number of published genome-related papers from 4.5 percent of the world's papers in 2010 to 17.3 percent by 2014.

Biopharmaceutical Competition From Other Nations

According to OECD, of 25 nations, the United States ranked second from last in inflation-adjusted growth in health research expenditures from 2006 to 2015. Only Italy (-27 percent) was below the United States (-1 percent). In contrast, Denmark increased funding by 185 percent, South Korea by 177 percent, Germany 65 percent, and the United Kingdom 55 percent (see table 2). Moreover, at least 10 other nations have doubled their life sciences research budgets (when controlling for inflation). And unlike the United States, few of them are likely to cut investment levels going forward. In short, the notion that the U.S. lead in the biopharmaceutical industry is unassailable, only because Congress supported the doubling of the NIH budget at the turn of the millennium, is wishful thinking at best.

At least 10 other nations have doubled their life sciences research budgets (when controlling for inflation). And unlike the United States, few of them are likely to cut investment levels going forward.

Country	Percent Change Since 2006
Denmark	185
Korea	177
Sweden	154
Austria	79
Germany	65
United Kingdom	55
Ireland	42
Netherlands	37
Belgium	32
Australia	27
Japan	11
Israel	9
United States	-1
Italy	-27

Table 2: Government Budget Outlays for R&D ¹¹⁴

We see this commitment across a number of nations. In the United Kingdom in 2012, the Cameron government expanded its commitment to the life sciences.¹¹⁵ The government's "Strategy for UK Life Sciences" identified a number of institutional initiatives to enhance the competitiveness of the biomedical industry, including the creation of a "patent box" to lower the tax rate on income from new patents, faster regulatory approval for new drugs, and institutional reforms.

Over the past 15 years, Singapore has moved aggressively to increase its share of global life sciences research. In 2003, the government created Biopolis, which provides dedicated research and residential facilities, and places public research institutes next to corporate laboratories in an effort to foster collaboration. Singapore has also provided direct funding to support research and development by the pharmaceutical industry, devoting five times the percentage of its economy to this effort as the United States.¹¹⁶ Firms in Singapore are further aided by its business-friendly environment. On average, it takes only three weeks to receive approval for clinical trials, and a manufacturing facility can become operational within two to three years. As a result, the country is now the regional headquarters for eight of the top ten global pharmaceutical firms. Altogether, these efforts have had positive results. Singapore's trade in pharmaceutical goods shifted from a deficit of 0.01 percent of GDP in 2003 to a surplus of 3.86 percent in 2012.¹¹⁷ A report by Singapore's Agency for Science, Technology, and Research, within which there is a separate Biomedical Research Council, is explicit about the government's goal of using a collaborative and integrated research and development system to become an attractive investment location for highvalue-added manufacturing by global companies.¹¹⁸ The government has also worked to incorporate university research into its efforts, attracting outposts from leading research institutions—including MIT, Duke, Johns Hopkins, Chicago, and Carnegie Mellon—and recruiting leading scientists.¹¹⁹

In 2014, the Australian government announced the creation of a new Medical Research Future Fund, which began operations in January 2015 with \$780 million, accrued an account balance of \$6.4 billion by 2018, and has a target size of \$14 billion by 2020.¹²⁰ If the Fund reaches its goals, it will roughly double government funding for medical research. The creation of a large endowment fund to underwrite medical research should provide stability in funding. Its intended operation seems similar to that of the Wellcome Trust in the United Kingdom, which had an endowment of \$22 billion in 2013, and the Howard Hughes Medical Institute in the United States, with an endowment of \$17 billion.

CONCLUSION

There are at least four major justifications for a strong and growing U.S. government investment in life sciences research. First, funding leads to better medicines and health outcomes for Americans, and this reduces societal health care costs. Second, funding supports the ecosystem conditions that enable a vibrant U.S. life sciences industry, with life science start-ups employing 35,000 workers across 1,600 firms—around 13 percent of which are growing rapidly in employment and output.^{121.}

Third, NIH funding helps support U.S. biopharmaceutical industry competitiveness. The United States has tough—and growing—competition for life sciences industry leadership, with a number of nations investing more as a share of their GDP, including Denmark, Norway, Sweden, the United Kingdom, and Spain. Moreover, many other governments, including China, are expanding investments in life sciences research because they want to grow a competitive industry. While these investments will increase biomedical innovation, it would be folly for the United States to depend on these nations for future biomedical innovation, given then enormity of the challenge and opportunity for biopharma innovation. There are thousands of diseases, including such major ones as heart disease, cancer, mental illness, and Alzheimer's, that cause human suffering and impose massive economic costs. Other nations cannot and will not pick up the slack if U.S. investments in biomedical research do not keep pace with economic growth.

Finally, the United States cannot afford to depend on foreign nations such as China for drugs. As the Government Accountability Office has noted, there are problems with the safety and efficacy of drugs from China. In addition, the Defense Department has a keen interest in ensuring a domestic supply of, and not being reliant on a potential adversary for, certain drugs. Robust NIH funding helps ensure America is not overly dependent on potential adversaries.

In short, increasing NIH funding such that it reaches the same R&D-to-GDP ratio as after its doubling in 2003—and continuing to increase it at a slightly faster rate than nominal GDP growth —will yield dividends for the U.S. economy for generations to come in the form of better health and more cures, reduced health care costs, and a vibrant and globally competitive U.S. life sciences industry.

ENDNOTES

- 1. Gina Kolata, "These Patients Had Sickle-Cell Disease. Experimental Therapies Might Have Cured Them," *The New York Times,* January 27, 2019, https://www.nytimes.com/2019/01/27/health/sickle-cell-gene-therapy.html
- 2. Sharon Begley, "Roche Scores First U.S. Approval Immunotherapy for Breast Cancer," *STAT*, March 8, 2019, https://www.statnews.com/2019/03/08/roche-tecentriq-first-breast-cancer-immunotherapy/
- 3. This showed that 70 percent of women with early stage breast cancer would not respond to chemotherapy, and will produce significant savings in health care costs.
- 4. Pam Belluck, "New Drug Trial Seeks to Stop Alzheimer's Before It Starts," *The New York Times,* May 15, 2012, https://www.nytimes.com/2012/05/16/health/research/prevention-is-goal-of-alzheimers-drug-trial.html.
- 5. David Nather, "Elizabeth Warren, Newt Gingrich Team Up for NIH," *The Boston Globe,* July 27, 2015, https://www.bostonglobe.com/news/politics/2015/07/27/elizabeth-warren-and-newt-gingrich-agree-call-for-more-nihfunding/CPpaRgBL2w2hZej2n1rgPL/story.html
- 6. Ipsos, "Americans Report Positive Attitudes and Optimism Toward Technology," news release, March 1, 2019, https://www.ipsos.com/en-us/news-polls/americans-report-positive-attitudes-and-optimism-toward-technology.
- 7. This assumes a 3 percent increase in GDP in 2019 and 2020.
- 8. Everett Ehrlich, "An Economic Engine: NIH Research, Employment, and the Future of the Medical Innovation Sector" (United for Medical Research, 2011), 3, http://www.eyeresearch.org/pdf/UMR_Economic Engine_042711a.pdf.
- 9. National Institutes of Health, "Institutes, Centers, and Offices," https://www.nih.gov/institutes-nih.
- Judith A. Johnson and Kavya Sekar, "NIH Funding: FY1994–FY2019" (Congressional Research Service, October 2018), 1, https://fas.org/sgp/crs/misc/R43341.pdf; Jocelyn Kaiser, "NIH Gets \$2 Billion Boost in Final 2019 Spending Bill," *Science*, September 14, 2018, https://www.sciencemag.org/news/2018/09/nih-gets-2-billion-boost-final-2019spending-bill.
- 11. Johnson and Sekar, "NIH Funding: FY1994–FY2019," 1.
- 12. Pierre Azoulay et al., "Public R&D Investments and Private-Sector Patenting: Evidence From NIH Funding Rules," *The Review of Economic Studies*, vol. 86 (January 1, 2019):117–152, https://doi.org/10.1093/restud/rdy034
- 13. U.S. National Institutes of Health, "Turning Discovery Into Health: Impact On Our Nation," https://www.nih.gov/sites/default/files/about-nih/impact/impact-our-nation.pdf.
- 14. Stephen Ezell, "The Bayh-Dole Act's Vital Importance to the U.S. Life-Sciences Innovation System" (Information Technology and Innovation Foundation, March 2019), https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system#_ednref20.
- 15. Ibid.
- 16. Ibid.

- 17. National Institutes of Health, "Turning Discovery Into Health" (NIH, December 2017), https://www.nih.gov/sites/default/files/about-nih/discovery-into-health/nih-turning-discovery-into-health.pdf.
- 18. Ehrlich, "An Economic Engine," 3.
- Federation of American Societies for Experimental Biology (FASEB), "Federal Funding for Biomedical and Related Lifesciences Research" (FASEB, 2017), https://www.faseb.org/Portals/2/PDFs/opa/2016/Federal_Funding_Report_FY2017_FullReport.pdf.
- Ruchika Nijhara et al., "Bypassing Bypass Surgery and Other Success Stories from the National Institutes of Health," Journal of the Association of University Technology Managers, vol. 17, no. 2 (2005), https://pdfs.semanticscholar.org/c52e/b097d30f3308d7996c38f129c718c031b6d7.pdf.
- 21. National Institutes of Health, Accelerating Medicines Partnership, "Overview," https://www.nih.gov/researchtraining/accelerating-medicines-partnership-amp.
- 22. National Institutes of Health, National Center for Advancing Translational Sciences, "Center Overview," https://ncats.nih.gov/about/overview.
- 23. National Institutes of Health, National Center for Advancing Translational Sciences, "About the Center," https://ncats.nih.gov/about/center.
- 24. National Institutes of Health, National Center for Advancing Translational Sciences, "Transforming Translational Science," https://ncats.nih.gov/files/NCATS-factsheet.pdf.
- 25. National Institutes of Health, "What Are SBIR and STTR Programs?" https://sbir.nih.gov/.
- Matthew Portnoy, "HHS SBIR/STTR PHS 2017-2 Grant Omnibus Webinar" (PowerPoint presentation, June 29, 2017), https://sbir.nih.gov/sites/default/files/FY17 HHS SBIR-STTR Grant Omnibus Webinar - Slide Presentation -6.29.17.pdf.
- Jere Glover, "Testimony Before the Committee on Small Business and Entrepreneurship, United States Senate, Reauthorization of the SBIR/STTR Programs—The Importance of Small Business Innovation to National and Economic Security," January 28, 2016.
- National Academies Press, "SBIR/STTR at the National Institutes of Health," https://www.ncbi.nlm.nih.gov/books/NBK338147/.
- 29. National Institutes of Health, National Heart Lung, and Blood Institute, "About NCAI and REACH," https://ncai.nhlbi.nih.gov/ncai/aboutncai/mission.
- 30. NIH, Office of the Budget, https://officeofbudget.od.nih.gov/approp_hist.html; NIH Bureau of Economic Analysis, https://officeofbudget.od.nih.gov/gbipriceindexes.html.
- 31. This is building on an earlier study from 2007; Stephen J. Heinig, et al., "Sustaining the Engie of U.S. Biomedical Discovery," *The New England Journal of Medicine*, (2007): 142-1047, https://www.nejm.org/doi/full/10.1056/NEJMsb071774.
- 32. .National Institutes of Health, Office of the Budget, Appropriations History by Institute/Center (1938 to Present), accessed February 25, 2019, https://officeofbudget.od.nih.gov/approp_hist.html; National Institutes of Health, Office

of the Budget, GDP Index, accessed February 25, 2019, https://officeofbudget.od.nih.gov/gbipriceindexes.html; Bureau of Economic Analysis.

- 33. John Van Reenen and Richard B. Freeman, "Be Careful What You Wish For: A Cautionary Tale About Budget Doubling," *Issues in Science and Technology*, vol. 25 no. 1 (2018), https://issues.org/p_freeman/.
- 34. American Society for Biochemistry and Molecular Biology, "Nondefense Discretionary Science Survey—2013: Unlimited Potential, Vanishing Opportunity" (ASBMB, 2013), http://www.asbmb.org/uploadedFiles/Advocacy/Events/UPVO Report V2.pdf. The poll has been criticized for the fact that its voluntary, online nature does not make it a statistically valid sample of scientists. See: Jeffrey Mervis, "Dog Bites Man? Researchers Say U.S. Government Should Fund More Science," *ScienceInsider*, August 30, 2013, http://news.sciencemag.org/funding/2013/08/dog-bites-man-researchers-say-u.s.-government-should-fund-morescience; See also: United for Medical Research, "Sequester Profiles: How Vast Budget Cuts to NIH Are Plaguing U.S. Research Labs" (UMR, December 2013), http://www.unitedformedicalresearch.com/advocacy_reports/sequestrationprofiles/.
- 35. Paul Basken and Paul Voosen, "Strapped Scientists Abandon Research and Students," *The Chronicle of Higher Education*, February 24, 2014, http://chronicle.com/article/Strapped-Scientists-Abandon/144921/; See also: Richard Harris, "When Scientists Give Up," National Public Radio, September 9, 2014, http://www.npr.org/blogs/health/2014/09/09/345289127/when-scientists-give-up.
- 36. NIH, "Research Project Success Rates by Type and Activity for 2018," https://report.nih.gov/success_rates/Success_ByActivity.cfm; See also: Oh et al., "The Good R01."
- 37. Harold Varmus, *The Art and Politics of Science* (New York: W. W. Norton & Company, 2010), 150.
- 38. NIH, "Scoring Table for Research Grant Applications," https://www.niaid.nih.gov/grants-contracts/scoring-summarystatements
- 39. NIH Office of Extramural Research, "Resubmission and Award Rates for Unfunded AO Applications," 2017, report.nih.gov/UploadDocs/OpenMike-Resubmission-rates-by-overall-impact-score-Feb-17-2017_4.xlsx.
- 40. Joe Kennedy "How to Ensure That America's Life-Sciences Sector Remains Globally Competitive" (Information Technology and Innovation Foundation, March 2018), https://itif.org/publications/2018/03/26/how-ensure-americas-life-sciences-sector-remains-globally-competitive.
- 41. Ibid, 11.
- 42. Ibid, 12.
- 43. Robert A. Maxwell and Shohreh B. Eckhardt, *Drug Discovery: A Case Book and Analysis* (New Jersey: Humana Press, 2011).
- 44. Stevens et al, "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines."
- 45. Bhaven N. Sampat and Frank R. Lichtenberg, "What Are the Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation?" *Health Affairs*, 30, no. 2 (2011): 332–339, https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2009.0917.
- 46. Derek Lowe, "Drugs Purely From Academia," Science, February 2, 2016,

https://blogs.sciencemag.org/pipeline/archives/2016/02/02/drugs-purely-from-academia.

- 47. Battelle Technology Partnership Practice, "Patents as Proxies Revisited: NIH Innovation 2000 to 2013" (Battelle Technology Partnership Practice, 2015), https://www.acadrad.org/wp-content/uploads/2017/04/Patents-as-Proxies-Revisited.March_.Final_.pdf
- 48. Pierre Azoulay et al., "Public R&D Investments and Private-Sector Patenting: Evidence From NIH Funding Rules," *The Review of Economic Studies*, vol. 86, (January 1, 2019):117–152, https://doi.org/10.1093/restud/rdy034
- 49. Andrew A. Toole, "The Impact of Public Basic Research on Industrial Innovation: Evidence from the Pharmaceutical Industry" *Research Policy* vol. 41, (February 2012): 1–12, https://www.sciencedirect.com/science/article/abs/pii/S004873331100117X.
- 50. Ekaterina Galkina et al., "Contribution of NIH Funding to New Drug Approvals 2010–2016," Proceedings of the National Academy of Sciences, March 2018, https://www.pnas.org/content/115/10/2329.short
- 51. Danielle Li, Pierre Azoulay, and Bhaven N. Sampat, "The Applied Value of Public Investments in Biomedical Research," *Science*, April 7, 2017, http://science.sciencemag.org/content/356/6333/78.abstract
- 52. Robert Kneller, "The Importance of New Companies for Drug Discovery: Origins of a Decade of New Drugs," Nature Reviews Drug Discovery 9 (November 2010): 867–882, https://www.ncbi.nlm.nih.gov/pubmed/21031002.
- 53. Iain M. Cockburn and Rebecca M. Henderson, "Publicly Funded Science and the Productivity of the Pharmaceutical Industry" (working paper, National Bureau of Economic Research, January 2001), http://www.nber.org/chapters/c10775.pdf.
- 54. Theresa Wizemann et al., *Breakthrough Business Models* (Washington, D.C.: The National Academies Press, 2009).
- 55. Ian M. Cockburn and Rebecca Henderson, "Publicly Funded Science and the Productivity of the Pharmaceutical Industry," (working paper no. 10775, National Bureau of Economic Research (NBER), 2001), accessed February 17, 2016, http://www.nber.org/chapters/c10775.pdf.
- 56. National Institutes of Health, "Research Portfolio Online Reporting Tools (RePORT)," https://report.nih.gov/.
- 57. Claire Dietz and Matthew Bin Han Ong, "FDA Approves 19 New Cancer Drugs and Biologics in 2018—and Don't Forget Two New Endpoints and 'Real-time' Review," *The Cancer Letter,* January 25, 2019, https://cancerletter.com/articles/20190125_2/.
- 58. Frank R. Lichtenberg and Bille Pettersson, "The Impact of Pharmaceutical Innovation on Longevity and Medical Expenditure in Sweden, 1997–2010: Evidence from Longitudinal, Disease-Level Data" (working paper, CESifo, July 2012).
- 59. Frank R. Lichtenberg, "The Effect of Pharmaceutical Innovation on Longevity: Patient-Level Evidence From the 1996– 2002 Medical Expenditure Panel Survey and Linked Mortality Public-Use Files," (working paper no. 10775, National Bureau of Economic Research (NBER), 2001), http://www.nber.org/chapters/c10775.pdf.https://www.nber.org/papers/w18552.

- Frank R. Lichtenberg, "The Impact of Pharmaceutical Innovation on Premature Cancer Mortality in Canada, 2000-2011" (working paper no. 212139, National Bureau of Economic Research, June 2015), http://www.nber.org/papers/w21239.
- 61. Frank R. Lichtenberg, "Pharmaceutical Innovation, Mortality Reduction, and Economic Growth" (working paper, NBER, May 1998): 100–103, https://www.nber.org/papers/w6569.
- 62. Selma J. Mushkin and J. Steven Landefeld, *Biomedical Research: Costs and Benefits* (Cambridge, MA: Ballinger Publishing Co., 1979).
- 63. Kevin M. Murphy and Robert H. Topel, "The Value of Health and Longevity," *Journal of Political Economy*, vol. 114, no. 5, (October 2006): 871-904.
- 64. Darius Lakdawalla, Anup Malani, and Julian Reif, "The Insurance Value of Medical Innovation," (working paper no. 10775, NBER, 2015), https://www.nber.org/papers/w21015.
- 65. Ross DeVol et al., *An Unhealthy America: The Economic Burden of Chronic Disease—Charting a New Course to Save Lives and Increase Productivity and Economic Growth* (The Milken Institute, October 2007), https://www.milkeninstitute.org/publications/view/321.
- 66. D.E. Bloom et al., "The Global Economic Burden of Non-Communicable Diseases" (Geneva: World Economic Forum, 2011), https://www.world-heart-federation.org/wp-content/uploads/2017/05/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf.
- 67. Ibid.
- 68. Partnership to Fight Chronic Disease, U.S. Workplace Wellness Alliance, "The Burden of Chronic Disease on Business and U.S. Competitiveness," *Almanac of Chronic Disease: Excerpt From the 2009 Almanac of Chronic Disease* (2009), https://www.prevent.org/data/files/News/pfcdalmanac_excerpt.pdf, accessed March 8, 2016.
- 69. "Alzheimer's Disease," Centers for Disease Control and Prevention, last modified March 5, 2015, http://www.cdc.gov/aging/aginginfo/alzheimers.htm; "Changing the Trajectory of Alzheimer's Disease: How a Treatment by 2025 Saves Lives and Dollars" (Alzheimer's Association, 2015), http://www.alz.org/documents_custom/trajectory.pdf.
- V. Divino et al., "The Direct Medical Costs of Huntington's Disease by Stage. A Retrospective Commercial and Medicaid Claims Data Analysis," *Journal of Medical Economics*, 16, no. 8 (August 2013): 1043–50, http://www.ncbi.nlm.nih.gov/pubmed/23789925; Jane Larkindale et al., "Cost of Illness for Neuromuscular Diseases in the United States," *Muscle & Nerve* 49, no. 3 (March 2014): 431-438, http://onlinelibrary.wiley.com/doi/10.1002/mus.23942/abstract; Lyanne Alfaro, "Your \$220 Million to the ALS Ice Bucket Challenge Made a Difference, Study Results Show," *Business Insider*, August 20, 2015, http://www.businessinsider.com/your-220-million-to-the-als-bucket-challenge-made-a-difference-2015-8.
- 71] Adams Nager and Robert Atkinson, "A Trillion-Dollar Opportunity: How Brain Research Can Drive Health and Prosperity" (Information Technology and Innovation Foundation, July 2016), http://www2.itif.org/2016-trillion-dollaropportunity.pdf.
- 72] Joseph V. Kennedy and Robert D. Atkinson, "Healthy Funding: Ensuring a Predictable and Growing Budget for the National Institutes of Health" (Information Technology and Innovation Foundation and United for Medical Research, February 2015), 2, http://www2.itif.org/2015-healthy-funding.pdf.

- 73] Ashley J. Stevens et al., "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines," *The New England Journal of Medicine*, vol. 364, (February 2011): 1, https://www.nejm.org/doi/full/10.1056/NEJMsa1008268.
- 74] Benjamin Zycher, Joseph A. DiMasi, and Christopher-Paul Milne, "The Truth About Drug Innovation: Thirty-Five Summary Case Histories on Private Sector Contributions to Pharmaceutical Science" (Center for Medical Progress at the Manhattan Institute, June 2008), 3–4, https://www.manhattan-institute.org/html/truth-about-drug-innovationthirty-five-summary-case-histories-private-sector-contributions.
- 75] Ibid
- 76] Sabarni K. Chatterjee and Mark L. Rohrbaugh, "NIH Inventions Translate Into Drugs and Biologics With High Public Health Impact," Nature Biotechnology 32, (2014): 56, https://www.nature.com/articles/nbt.2785?messageglobal=remove.
- Dennis Levy and Nestor Terleckyj, "Why Are Government and Private R&D Complements?" Applied Economics, 1991, 23.
- 78] U.S. Senate Joint Economic Committee, "The Benefits of Medical Research and the Role of the NIH," May 17, 2000, https://www.faseb.org/portals/2/pdfs/opa/2008/nih_research_benefits.pdf.
- 79] Pierre Azoulay et al., "Public R&D Investments and Private-Sector Patenting."
- 80] Ehrlich, "An Economic Engine."
- 81] Paul A. David, Bronwyn H. Hall, and Andrew A. Toole, "Is Public R&D a Complement or Substitute for Private R&D? A Review of the Econometric Evidence" (working paper no. 7373, National Bureau of Economic Research (NBER), 1999), http://www.nber.org/papers/w7373.
- 82] "The Impact of Genomics on the U.S. Economy" (Battelle Technology Partnership Practice and United for Medical Research (UMR), June 2013), http://www.unitedformedicalresearch.com/advocacy_reports/the-impact-of-genomics-on-the-u-seconomy/.
- 83] Martin Bailey, "Trends in Productivity Growth" *Technology and Growth: Conference Proceedings, Federal Reserve Bank of Boston* (June 1996), https://www.bostonfed.org/economic/conf/conf40/conf40.pdf.
- 84] Organization for Economic Cooperation and Development (OECD), *Science, Technology and Innovation in the New Economy* (OECD: 2000), http://www.oecd.org/science/sci-tech/1918259.pdf.
- 85] TEConomy Partners, LLC, "The Economic Impact of the U.S. Biopharmaceutical Industry: National and State Estimates" (PhRMA, LLC, May 2016), 1, http://phrmadocs.phrma.org/sites/default/files/pdf/biopharmaceuticaulindustry-economic-impact.pdf.
- 86] Ibid.
- 87] TEConomy Partners, LLC, "Driving Innovation and Economic Growth for the 21st Century: State Efforts to Attract and Grow the Biopharmaceutical Industry" (TEConomy Partners, LLC, June 2017), http://phrmadocs.phrma.org/files/dmfile/PhRMA-Driving-Innovation_06_01.2017.pdf.

- 88] John Wu and Robert D. Atkinson, *How Technology-Based Start-Ups Support U.S. Economic Growth* (Information Technology and Innovation Foundation, November 2017), http://www2.itif.org/2017-technology-based-start-ups.pdf.
- 89] Massachusetts Biotechnology Council, "President Obama, the 111th Congress, and Biotechnology: Working Together Today to Ensure a Healthy Tomorrow" (white paper, MBC, 2009), http://www.bioin.or.kr/fileDown.do? seq=8804&bid=industry.
- 90] Josh Bivens, "Updated Employment Multipliers for the U.S. Economy" (Economic Policy Institute, August 2003), https://www.nrc.gov/docs/ML1224/ML12243A398.pdf.
- 91] AUTM, "Driving the Innovation Economy: Academic Technology Transfer in Numbers," June 2017, https://autm.net/AUTM/media/SurveyReportsPDF/Survey Reports Images/AUTM_2017_Infographic_1.pdf.
- 92] Ibid.
- 93] Michael Lawlor, "Biotechnology and Government Funding," Challenge, vol. 46, no. 1, (2003): 15–37, 21, https://www.jstor.org/stable/40722180.
- 94] Joe Kennedy, "How to Ensure That America's Life-Sciences Sector Remains Globally Competitive" (Information Technology and Innovation Foundation, March 2018), 16, http://www2.itif.org/2018-life-sciences-globally-competitive.pdf.
- 95] David Michels and Aimison Jonnard, "Review of Global Competitiveness in the Pharmaceutical Industry" (U.S. International Trade Commission, 1999), 2–3, https://www.usitc.gov/publications/332/pub3172.pdf. The report found that, "Overall, the U.S. pharmaceutical industry seems to enjoy a domestic environment conducive to researching and developing drugs, protecting its intellectual property, and obtaining regulatory approval to market its products. There is also a strong trend in the United States to invest those profits in new R&D." viii.
- 96] David Michels and Aimison Jonnard, "Review of Global Competitiveness in the Pharmaceutical Industry," 2–3.
- 97] OECD, "Health at a Glance 2017" (table 10.14: annual new drug approvals), http://dx.doi.org/10.1787/888933605635.
- 98] European Federation of Pharmaceutical Industries and Associations, "The Pharmaceutical Industry in Figures, Key Data 2017," 8, https://www.efpia.eu/media/219735/efpia-pharmafigures2017_statisticbroch_v04-final.pdf.
- 99] TEConomy Partners, LLC, "Closing the Gap: Increasing Global Competition to Attract and Grow the Biopharmaceutical Sector," 4.
- 100] Ibid, 14.
- 101] U.S. Chamber of Commerce, *Made in China 2025: Global Ambitions Built on Local Protections* (Washington, D.C.: U.S. Chamber of Commerce, 2017), 79–80, https://www.uschamber.com/report/made-china-2025-global-ambitions-built-local-protections-0.
- 102] "Local Made in China 2025 Plans," The US-China Business Council (September 2016), https://www.uschina.org/localmade-china-2025-plans.

- 103] Worldwide R&D Incentives Reference Guide: 2014–15 (EY, March 215), 42, https://www.ey.com/Publication/vwLUAssets/EY-worldwide-randd-incentives-reference-guide/\$FILE/EY-worldwide-randd-incentives-reference-guide.pdf.
- 104] "China's Biotech Sector to Exceed 4% of GDP by 2020: Authority," *Chinadaily.com*, May 3, 2017, http://www.chinadaily.com.cn/business/2017-05/03/content_29181073.htm.
- 105] Ibid.
- 106] Pan Yue, "China's \$798B Government Funds Redraw Investment Landscape, Here Are the Largest Funds You Must Know," China Money Network, October 31, 2017, https://www.chinamoneynetwork.com/2017/10/31/chinas-798bgovernment-funds-redraw-investment-landscape-largest-funds-must-know
- 107] Sophy Yang, "China's 2,041 Government Guidance Funds Size Reaches \$530B: Report," China Money Network, November 12, 2018, https://www.chinamoneynetwork.com/2018/11/12/chinas-2041-government-guidance-funds-sizereaches-530b-report.
- 108] Peter H. Diamandis, "The Astounding Growth of Chinese VC—and the Tech It's Flowing Into," SingularityHub, August 9, 2018, https://singularityhub.com/2018/08/09/the-astounding-growth-of-chinese-vc-flowing-into-emergingtech/#sm.00001j36ms8t59fgcz1terrecqn7u.
- 109] *2017 Report to Congress of the U.S.-China Economic and Security Review Commission*, 115th Cong. (November 2017), 529.
- 110] Megan Molteni, "A Chinese Genome Giant Sets Its Sights on the Ultimate Sequencer," *Wired*, May 18, 2017, https://www.wired.com/2017/05/chinese-genome-giant-sets-sights-uitimate-sequencer/.
- 111] David Beier and George Baeder, "China Set To Accelerate Life Science Innovation," *Forbes,* July 6, 2017, https://www.forbes.com/sites/realspin/2017/07/06/china-set-to-accelerate-life-science-innovation/#59322ee5e73b.
- 112] *2017 Report to Congress of the U.S.-China Economic and Security Review Commission*, 115th Cong. (November 2017), 529.
- 113] Beier and Baeder, "China Set To Accelerate Life Science Innovation."
- 114] OECD, "Government Budget Appropriations or Outlays for RD," https://stats.oecd.org/Index.aspx? DataSetCode=GBAORD_NABS2007#.
- 115] Christine Bloor et al., "Strategy for UK Life Sciences" (Department for Business, Innovation and Skills/Office for Life Sciences, 2011), http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences.
- 116] Robert D. Atkinson et al., "Leadership in Decline: Assessing U.S. International Competitiveness in Biomedical Research" (UMR/ITIF, May 2012), 14, http://www.unitedformedicalresearch.com/wpcontent/uploads/2012/07/Leadership-in-Decline-Assessing-USInternational-Competitiveness-in-Biomedical-Research.pdf.
- 117] National Science Foundation, Science and Engineering Indicators 2012 (appendix tables 6–3 and 6–29); accessed November 10, 2014, http://www.nsf.gov/statistics/seind14/index.cfm/appendix/tables.htm#c6.

- Agency for Science, Technology and Research, "Annual Report for the Year Ended 31 March 2013" (A*STAR, July, 2013), http://www.a-star.edu.sg/Portals/0/media/yearbooks/ASTAR_Annual_Report_2012_13.pdf.
- 119] Catherine Waldby, "Singapore Biopolis: Bare Life in the City-State," *East Asian Science, Technology and Society: an International Journal,* (September, 2009): 377.
- 120] "Will Australia's New Medical Research Fund be the Biggest in the World?" ABC News, May 21, 2014, https://www.abc.net.au/news/2014-05-21/will-australia-have-the-biggest-medical-research-fund/5454810; "Medical Research Future Fund," Research Australia, https://researchaustralia.org/reports/mrff-research-australia-perspective.
- 121] John Wu and Robert D. Atkinson, *How Technology -Based Start-Ups Support U.S. Economic Growth* (Information Technology and Innovation Foundation, November 2017), 35, http://www2.itif.org/2017-technology-based-start-ups.pdf.

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