Leadership in Decline

Assessing U.S. International Competitiveness in Biomedical Research

The Information Technology and Innovation Foundation and United for Medical Research

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Executive Summary

Advances in life sciences—including pharmaceuticals, biotechnology, and medical devices—were a major driver of global economic growth in the second half of the twentieth century. Since World War II, the United States has stood firmly at the forefront of the life sciences revolution, with this leadership built upon a solid commitment to robust and sustained federal investment in biomedical research and development (R&D), channeled primarily through the National Institutes of Health (NIH).

This public investment laid the foundation for the development of scores of breakthrough pharmaceutical drugs and therapies—from personalized gene therapies to synthetic skin to cures for certain types of cancer—and has catalyzed the development of a globally competitive, high-wage life sciences industry in the United States. Today, the U.S. life sciences industry supports more than 7 million jobs and contributes $69 billion annually to U.S. gross domestic product (GDP).[1]

But U.S. leadership in the global life sciences industry is today under threat on two fronts. First, federal investment in biomedical research through NIH has decreased, both in inflation-adjusted dollars and as a share of GDP, nearly every year since 2003. Put simply, the United States is not sustaining the historically strong investment in biomedical research that once propelled it to global life sciences leadership.

At the same time, global competition has intensified, as a growing number of countries, including China, Germany, India, Singapore, Sweden, the United Kingdom, and others have recognized that life sciences represents a high-wage, high-growth industry and have taken measures seeking to wrest life sciences leadership from the United States.

These nations have not only significantly expanded their financial support for biomedical research, they have also implemented a range of policies designed to enhance their biomedical innovation ecosystems, such as tax incentives through "patent boxes," regulatory reforms to speed drug approvals, and immigration and education policies designed to attract and to educate the best life sciences talent. As this report demonstrates, in an increasing number of indicators—from trade balances in pharmaceuticals to shares of global pharmaceutical-industry output—such policies and investments have enabled several countries' life sciences industries to become competitive with that of the United States.

China, for example, has identified biotechnology as one of seven key strategic and emerging (SEI) pillar industries and has pledged to invest $308.5 billion in biotechnology over the next five years. This means that, if current trends in biomedical research investment continue, the U.S. government's investment in life sciences research over the ensuing half-decade is likely to be barely half that of China's in current dollars, and roughly one-quarter of China's level as a share of GDP. And China already has more gene sequencing capacity than the entire United States and about one-third of total global capacity. Other countries are also investing more in biomedical research relative to the sizes of their economies. When it comes to government funding for pharmaceutical industry-performed research, Korea's government provides seven times more funding as a share of GDP than does the United States, while Singapore and Taiwan provide five and three times as much, respectively. France and the United Kingdom also provide more, as shares of their economies.[2]

Yet the challenge to U.S. biomedical research competitiveness is not just that other countries are investing relatively more in biomedical R&D as a share of their economies. Nor is it simply that federal funding for biomedical research peaked in 2003, in both inflation-adjusted dollars and as a share of GDP, and has been slipping since. Another problem is the lack of consistency and predictability in the level of U.S. biomedical research funding. To be sure, the 2009 American Recovery and Reinvestment Act (ARRA)

included a welcome, albeit temporary, increase in NIH funding.[3] But the positive impact of that ephemeral surge has not been maintained, and NIH funding is threatened with a drastic rollback by the looming automatic sequestration scheduled to be triggered January 2, 2013 (unless Congress reaches a budget deal in the interim).

The sequestration would slash NIH funding by at least 7.8 percent, leading to a $2.4 billion reduction in 2013, the largest cut in the agency's history. This whipsaw, boom-bust cycle introduces tremendous uncertainty into the biomedical research enterprise, making it difficult for researchers, research institutions, and businesses to make long-term planning and investment decisions. In such an environment of constrained and uncertain funding levels, private investigators with promising biomedical research proposals who can't secure funding in the United States will increasingly look to pursue opportunities abroad. In other words, part of the challenge to U.S. international competitiveness in biomedical research stems from uncertainty generated by the inability to sustain robust levels of funding for biomedical R&D on a consistent basis.

It is striking that, while many competing countries, such as the United Kingdom, face the same challenges as the United States in terms of budget deficits and high unemployment in a sluggish global economy, these countries are choosing to secure their future well-being, not by just sustaining, but by increasing their investments in biomedical research. They are doing so because they recognize that the most viable solution to such challenges is to help grow key sectors of their economies, such as life sciences. And they recognize that the only way they can do this is by making the necessary investments in research that provide the fundamental foundation for life sciences innovation and a bio-based economy, including new drugs, diagnostics, therapies, and devices.

This report documents the foundational role public investment plays in underpinning a nation's competitiveness in the life sciences. It assesses the intensifying competition for global life sciences leadership through case studies of four countries—the United States, China, the United Kingdom, and Singapore—that illustrate the commitments that competitor nations are making to enhancing their life sciences competitiveness through increased public investments and comprehensive policy reforms. It then assesses countries' performances in the life sciences-industries as measured by a variety of indicators, including countries' share of total patents granted in biotechnology and trends in countries' levels of trade balances, employment, and share of global output in the pharmaceutical industry.

THIS REPORT DOCUMENTS THE FOUNDATIONAL ROLE PUBLIC INVESTMENT PLAYS IN UNDERPINNING A NATION'S COMPETITIVENESS IN THE LIFE SCIENCES.

Finally, the report concludes by demonstrating that the United States' commitment to NIH has been a decisive factor in building U.S. life sciences leadership and driving economic growth. It is therefore paramount, even in times of tight budgets, that Congress, not only preserve, but expand NIH funding and reject automatic, across-the-board spending cuts. Congress should strive to fund NIH consistently at a level representing at least 0.25 percent of GDP. Our nation's baseline policy going forward should be to grow NIH funding at a rate that accounts for inflation, embraces emerging avenues of research that can propel U.S. innovative leadership, and reflects the catalytic effect biomedical research has on our nation's economy.

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"The United Kingdom's Strategy for UK Life Sciences sets a goal that "The UK will become the global hub for life sciences in the future."

"The United States accumulated a $136.7 billion trade deficit in pharmaceutical products over the last decade, at a time when the pharmaceutical trade balances of many competitors steadily increased."

"China has the world's largest next-generation sequencing capacity, with more sequencing capacity than the entire United States and about one-third of total global capacity."


The Role of Public Investment in Life Sciences Industry Competitiveness

Whether in the United States, the United Kingdom, China, or other countries, public investment has played a critical role in catalyzing the development of nations' life sciences industries. As an analysis of the economic impact of the life sciences sector on the British economy found, "publicly funded research has played a central role in the origins of the U.K. biotechnology industry."[4] Likewise, federal funding through the National Institutes of Health has made possible the development of a robust life sciences sector in the United States. Moreover, once developed, the competitiveness of a country's life sciences industry is sustained and improved through public research investment. Public investment in biomedical research is especially effective for two reasons: first, it lays the foundation of knowledge upon which industries can build; and, second, it generates extremely high rates of return, both as private return and return to society at large.

Cockburn and Henderson find that even when productivity is narrowly defined to the life sciences sector (with no broader effects), public-sector biomedical research funding has a private rate of return of 30 percent per year. Other authors have found even higher public rates of return, at least 37 percent, from investment in biomedical research.[5] (When combined, this rate of return is 35 times greater than the current cost of capital to the United States Treasury.) This broad impact can be seen quite clearly in the United States, where between 1965 and 1992, fifteen of the twenty-one top-grossing drugs were developed in part on discoveries enabled by federally funded research, seven of which drugs were directly related to the NIH.[6] These 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. More recently, NIH-funded research into monoclonal antibodies has supported the development of new monoclonal therapy-based drugs that, in 2010, accounted for five of the top twenty best-selling drugs in the United States.[7] 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."[8]

The evidence that public-sector R&D plays a fundamental role in developing basic knowledge for drug discovery is also consistent with findings by other authors. Rake finds that because there is a positive association between technological opportunities and the number of new pharmaceuticals, public support of scientific research directed to certain diseases may enhance the relevant technological opportunities and consequently the number of new pharmaceuticals.[9] Bosi and Laurent developed an econometric model that shows that the optimal level of public funding for medical R&D is higher than the current one. Bosi and Laurent conclude that, in 2011, a $1 billion public investment in medical R&D would increase GDP by 0.048 percent annually, or roughly $6 billion.[10]

Some will assert that public R&D is not needed, because private-sector R&D will expand to compensate for decreases in federal funding. But, in fact, economic research shows clearly that public R&D funding is a complement, not a substitute or alternative, to private sector R&D funding. One reason for this is that industry is able to build on the knowledge and understanding of discoveries from publicly supported life sciences research, making their own research more productive and effective. These "spillovers" provide firms with a common platform of basic knowledge, and thus precipitate even greater levels of innovation.[11] In general, an additional dollar of public contract research added to the stock of government R&D has the effect of inducing an additional twenty-seven cents of private R&D investment.[12] However, for the life sciences industry, a dollar of NIH support for research leads to an even greater increase in private medical research, roughly thirty-two cents.[13] One survey of over sixty academic articles on whether public-sector


PUBLIC SECTOR INVESTMENT IN BIOMEDICAL RESEARCH FUNDING HAS A PRIVATE RATE OF RETURN OF 30 PERCENT AND A PUBLIC RATE OF RETURN OF AT LEAST 37 PERCENT.

R&D crowds out private sector investments concludes, "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 science] industry. It is worth noting that there are, so far as we are aware, no systematic quantitative studies that have found a negative impact of public science."[14]

Moreover, the literature suggests that public-sector funding disproportionately affects small firms. Small biotechnology firms allocate much larger portions of their budgets to R&D, and small, venture capital-backed firms deliver a disproportionate share of technological breakthroughs.[15] Similarly, NIH and venture capital funding increase employment and R&D within small life sciences firms to a greater degree than capital from traditional financial institutions.[16]

Taken together, the evidence is clear that public investment in biomedical research generates very high rates of public and private return, proving to be among the most effective ways of stimulating broader economic growth.

Biomedical Research Competitiveness—Country Case Studies

Following are case studies assessing the biomedical research competitiveness of four countries: the United States, China, the United Kingdom, and Singapore.[17] These examine trends in these countries' investments in biomedical research over the past decade and document the broader policies they have implemented to bolster the competitiveness of their life sciences sectors. The countries chosen to compare with the United States each illuminate certain facets of the intensifying global competition for life sciences leadership. China's government is investing hundreds of billions in life sciences research even as the country is attracting significant amounts of venture capital and foreign direct investment and is producing more and more life sciences innovations. The United Kingdom has adopted a life sciences-competitiveness strategy and has renewed its investments in biomedical research. Singapore has made competitiveness in the life sciences a national priority. The picture that clearly emerges from these case studies is that other countries are targeting the life sciences-industry as a key driver of their economies and are implementing concerted, comprehensive, and aggressive policies designed to position their life sciences industries among the world's leaders.

United States

The life sciences industry is one of America's strongest performers in terms of creating many high-wage jobs. Life sciences-industry jobs pay an average wage of $84,992.00—almost double the average U.S. wage.[18] In part because of these high wages, 1.2 million jobs in the life sciences industry support an additional 5.8 million jobs indirectly.[19] Employment in the life sciences grew 5.7 percent from 2001 to 2006, almost twice the rate of the 3.1 percent increase in employment in the overall private sector.[20] In total, the life sciences industry accounts for $69 billion in U.S. economic activity and represents one of the country's most vital industries.[21]

The most important reason the U.S. life sciences industry is so strong is that the United States has a long tradition of public support for biomedical research. U.S. policy toward biomedical research is rooted in a strong bipartisan consensus on the value of basic research that emerged following World War II. During that war, investments in research led to fundamental new knowledge and increased understanding, applications of which were central to the war effort. For example, profound discoveries in biology, such as the value of antibiotics, saved tens of thousands of lives that would otherwise have been lost to infectious disease. This bipartisan consensus led to steady increases in support for basic scientific research, beginning in the late 1940s (a 150-fold increase, from 1945 to 1961, to $460 million, and a further

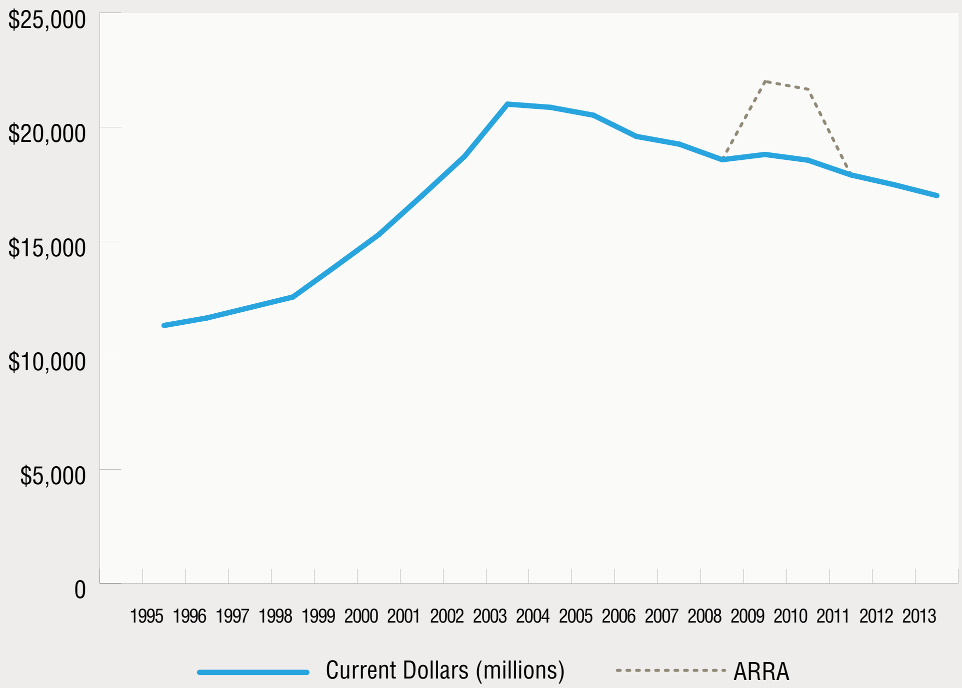
increase to $1 billion by the late 1960s).[22] Biomedical research was singled out for special attention with the passage of the National Cancer Act of 1971.[23] Although the war on cancer was very much aimed at ameliorating the human suffering and economic effects of cancer, it rested on a strong appreciation that critical advances were most likely to follow from undirected basic research, an argument supported by robust empirical data.[24] As Figures 1 and 2 show, the bipartisan, postwar consensus in support of substantial investment in biomedical research culminated in a doubling of funding for the National Institutes of Health, beginning in the late 1990s and continuing throughout the early 2000s. This increase in NIH funding was supported by both the Clinton and George H. W. Bush Administrations and Congressional appropriators from both sides of the aisle.

The doubling of NIH funding that had been enacted by the early 2000s was intended to define a new baseline for sustained investment in biomedical research through NIH. However, NIH funding since then has failed to keep pace with inflation, and the gains made in the prior decade are eroding. This is illustrated in both Figure 1—which shows the federal government's investment in NIH in inflation-adjusted dollars from 1995 to 2013—and Figure 2—which displays NIH funding as a share of GDP over the same time period. Using inflation-adjusted dollars, NIH funding peaked in 2003 and has decreased in every year but one since.[25]

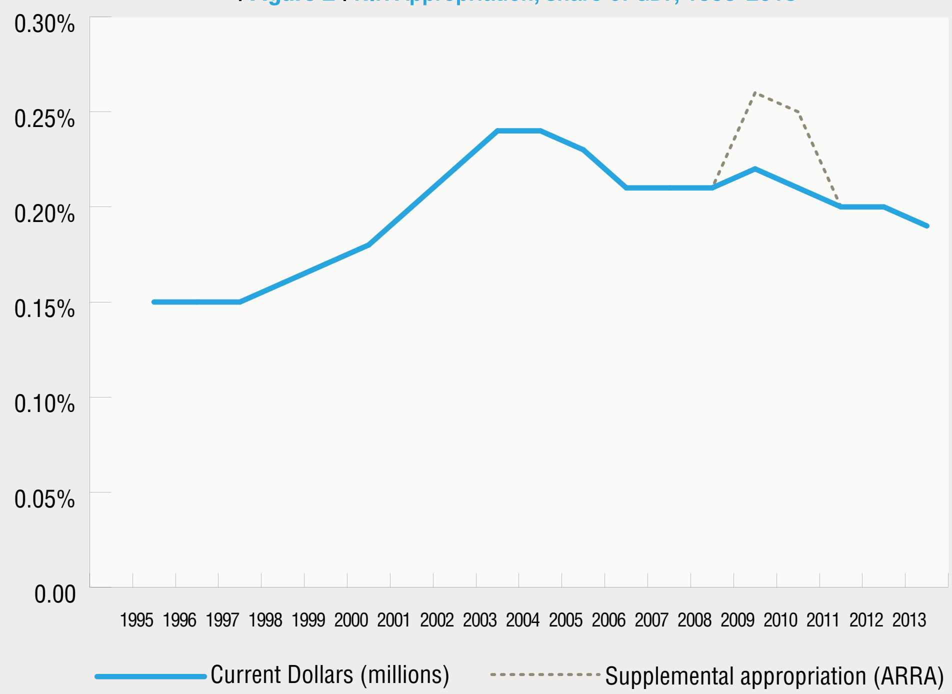
In inflation-adjusted dollars, the NIH funding level requested for 2013 will

NIH funding peaked in 2003 and has fallen nearly every year since[25]

| Figure 1 | NIH Appropriation, constant 1995 dollars (millions), 1995-2013



| Figure 2 | NIH Appropriation, share of GDP, 1995-2013



actually roll funding back to 2001 levels. While the American Recovery and Reinvestment Act did result in an ephemeral bloom of funds, NIH funding in constant dollars has subsequently resumed its downward trend. Likewise, as a share of GDP, baseline U.S. funding for NIH (aside from the one-off supplementary ARRA investment) peaked in 2003 at 0.24 percent of GDP and has been on the decline since, standing now at 0.19 percent of GDP. As a share of GDP, U.S. investment in NIH has reverted back to 2001 levels. These trends contrast starkly with those seen in many other countries.

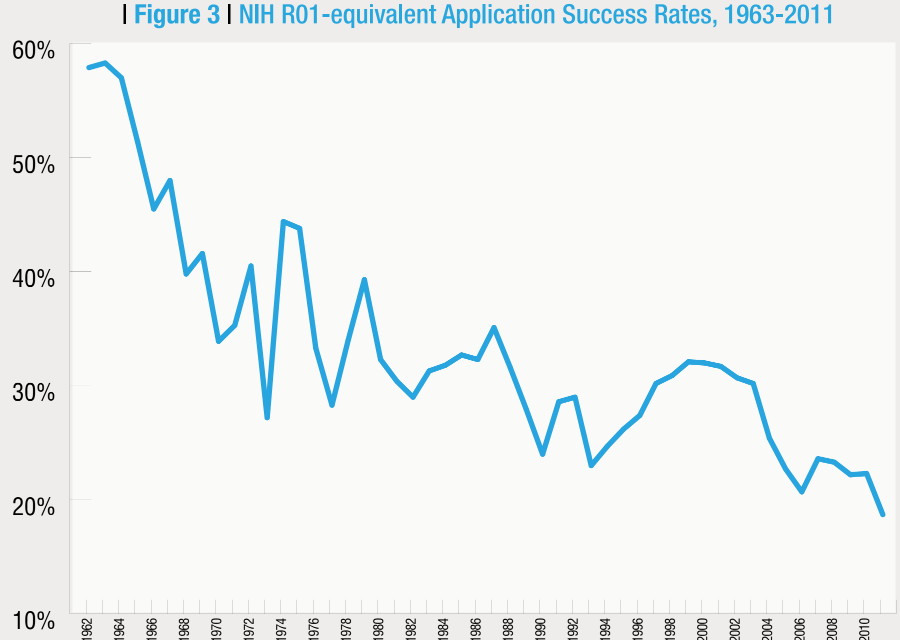
One consequence of the relative decline in NIH funding in constant dollars is reflected in Figure 3, which presents the success rate of applications for investigator-initiated basic research grants at NIH—the "R01" grants—from 1962 to 2011.[26] While this rate declined steadily from the 1960s to the early 1990s, it improved or held steady from 1993 to 2003, in large part through the increases in NIH funding during that window. But after peaking in 2003, success rates resumed their downward slide, with no indicators today providing any hope for a reversal of this trend.[27]

This means that fewer than one in five basic research grant applications to NIH is successful today. Although there are several reasons for this, the most important is simply insufficient funds. The consequences of a rejected grant application are most severe for first-time applicants, often delaying careers—or derailing them at their outset. NIH data show that the average age of Ph.D. applicants at the time they win their first grant approval increased from thirty-four in 1970 to forty-two in 2005.[28] The negative implications of such low success rates are profound. The opportunity costs of so many unfunded opportunities for exploration are difficult to calculate, though certainly large. But perhaps the most pernicious and stifling consequence is that, in such a competitive climate, applicants are discouraged from pursuing the most innovative ideas because those are usually seen as the most risky, the most uncertain of returns. They are therefore discriminated against by grant reviewers, understandably reluctant to take a chance and risk scarce funding. In a world facing so many challenges for which the solutions can only be found in innovations in the life sciences, this situation is highly counterproductive. Moreover, promising young researchers who are unable to get their research grants funded may be increasingly attracted to opportunities abroad, especially as a number of foreign countries ramp up their governments' investments in biomedical research. This is particularly troubling given that, of all the STEM (science, technology, engineering, and math) fields, the United States has the highest share of native-born U.S. scientists in the biomedical fields.[29]

Indeed, the slackening pace of federal investment in R&D—not only in biomedical research, but across the broader fields of U.S. science and technology—is quite real and significant. From 1987 to 2008, federal R&D investment grew at just 0.3 percent per year in inflation-adjusted dollars—much lower than its average annual growth rate from 1953 to 1987, of 4.9 percent—and ten times lower than the rate of GDP growth over that period. In fact,

Low grant application success rates discourage researchers from pursuing higher-risk ideas[29]

| **Figure 3** | NIH R01-equivalent Application Success Rates, 1963-2011




to restore federal support for research as a share of GDP to 1987 levels, the United States would have to increase its total federal support for R&D by almost $150 billion per year.[30] Recognizing the extent of this underinvestment, the Obama Administration's *A Strategy for American Innovation: Securing Our Economic Growth and Prosperity*, released in February 2011, called for "the largest increase in federally-funded research in history," which would make "continuous investments to double funding for three key basic research agencies: the National Science Foundation, the Department of Energy's Office of Science, and the National Institute of Standards and Technology laboratories."[31] While increased funding for these agencies is important, the administration should not have neglected to include NIH for increased funding to at least restore, if not exceed, the commitment the country made in 2003 to investing in biomedical research as a share of the economy. While the administration did introduce a *National Bioeconomy Blueprint* in April 2012,[32] which contains numerous welcome and needed recommendations to strengthen the U.S. biomedical innovation system, the *Blueprint* cannot be implemented without increased federal funding.

Several commentators have raised concern about the eroding levels of U.S. public investment in biomedical research. As noted previously, economists have argued that the optimal level of public funding for medical R&D is higher than current expenditures.[33] The Federation of American Societies for Experimental Biology concurs, recently concluding that, "The current level of United States investment in research is insufficient. There are clear indicators of unmet need, and other countries are substantially increasing their contributions. . . . Other nations are seeking to capitalize on the abundant scientific opportunities. Between 1999 and 2009, the Asian region's share of worldwide research and development expenditures grew from 24 percent to 32 percent, while U.S. R&D expenditures declined from 38 percent to 31 percent. The European Community has recently urged its member nations substantially to increase their investment in research, recommending budgets of €80 billion ($108 billion) in 2014–2020, a 40 percent increase over the previous seven year period."[34]

Likewise, a recent paper in the *Journal of the American Medical Association* argues, "The United States' position as the dominant investor in a range of research and development programs is declining. Biomedical research requires a new strategic, comprehensive, long-term policy-making framework, with focused decision-making mechanisms that permit efficient and effective governmental planning. Leadership on research policy to conceptualize this new framework is required. A new funding model within this framework is also needed to ensure US preeminence in biomedical research. Without these steps the consequences could be devastating."[35]

China

China has committed itself to developing a globally competitive life sciences industry by the end of this decade—if not sooner—and has aligned its policies regarding investment, technology, and talent toward becoming a world leader. In fact, biotechnology—including biopharmacy, bio-engineering, bio-agriculture, and bio-manufacturing—is one of the seven priority strategic and emerging industries (SEIs) identified in China's Twelfth Five-Year Plan (2011-2015).[36] Beijing has announced it will invest $1.5 trillion over the next five years in these seven SEIs, aiming to increase their contribution to GDP from 2 percent in 2008 to 8 percent by 2015 and 15 percent by 2020.[37] To put this in context, for the United States to match China's commitment to these SEIs as a share of its GDP, it would have to pass an American Recovery and Reinvestment Act every year for the next five years and dedicate close to 100 percent of the funds to industry.[38] China's government has pledged to invest 2 trillion yuan ($308.5 billion) on biotechnology, a "strategic pillar" industry, over the next five years.[39] By comparison, the United States will fund the National Institutes of Health at approximately $30.7 billion in 2012. Projecting that level with modest increases (if nothing changes) over the next five years, the United States government will invest approximately $160 billion in life sciences research. In other words, as a share of GDP, the U.S. government's investment in life sciences research over the ensuing half-decade is likely to be roughly one quarter China's.

The consequences of China's out-investing the United States are already becoming visible, and could ultimately be profound. Ample government funding has put China on the cusp of becoming the world leader in genome sequencing.

The country's recent $60 million purchase of 128 cutting-edge genome sequencers through the Beijing Genomics Institute (BGI) has given it the world's largest next-generation sequencing capacity—with more sequencing capacity than the entire United States or about one-third of total global capacity.[40] With China now able to rapidly and inexpensively produce individual human genome sequences, one expert argues that, "China's sequencing power has the potential to tip the balance in innovation: the inventions and ideas that currently underlie the success of U.S. biotechnology."[41]

A key insight into China's life science competitiveness strategy is that it seeks to create a public investment lead relative to other nations, which will allow it to attract a significant share of private-sector investment.[42] Evidence that aggressive public investment leads to expanded private investment is already emerging from China's biotechnology venture-capital market. On February 4, 2011, the website *ChinaBioToday.com* reported that venture capitalists invested more than $1 billion in China's life science market in 2010—an increase of 319 percent over 2009.[43] By contrast, although, at $4.4 billion in 2010, U.S. venture-capital biotechnology investment is over four times China's level, it has fallen 20 percent since 2007. China has already become the world's second largest source of venture capital for inventions involving medical technology, after the United States. As *Scientific American* notes, "This disparity of VC dollars reflects a transition in which emerging markets are ushering in a new era of biotechnology enterprise."[44]

The increase in biotechnology venture capital flowing into China is mirrored by the dramatically increased foreign direct investment by Western biotechnology and pharmaceutical firms in China. Such examples include:

- In 2009, Novartis announced it would invest $1 billion in R&D in China over the next five years, including a significant expansion of the Novartis Institute of BioMedical Research in Shanghai, China. Novartis also invested $250 million to build a new global technical center in Changshu, China to develop and manufacture active pharmaceutical ingredients.[45]
- AstraZeneca committed over $300 million to the development of an innovation center in the Zhangjiang Hi-Tech Park in the Pudong area of Shanghai, which will be an equal with the company's R&D centers in Wilmington, Delaware, and Manchester, U.K.[46]
- Merck recently announced a statement of intent with BGI to develop a relationship in R&D to create value from the massive output of genomic information made available through DNA sequencing and analysis.[47]
- In April 2011, Ascletis Inc., a US-China specialty life sciences venture focused on cancer and infectious-disease therapeutics, launched operations in Hangzhou, China, having raised $100 million in private equity funding in China and the United States.[48]

These companies are attracted to China's large market, its large pool of skilled talent, and its science infrastructure, the last two supported directly by government life sciences funding. With regard to the first of these, China's prescription drug market is the world's second-largest, next to that of the United States, and is growing at more than 20 percent annually.[49] But it's not just large domestic markets and massive government investments funding science parks, academic researchers, and the development of a national health infrastructure that is fueling China's rapid increase in life sciences-competitiveness. Talent is a key part of the equation as well, and the number of Chinese undergraduates studying in the life sciences surpassed U.S. levels five years ago. China's universities produce more graduates and post-graduates in life science than any other country in the world. Among all foreign nations, China boasts the highest number of recipients of U.S. doctoral degrees awarded in the biological sciences. Some 4,500 Chinese students received Ph.D.s in life sciences from Western universities in 2007 alone.[50] Nor has China been content with educating future talent; it has aggressively courted world-class life sciences talent, with the result that at least 80,000 Western-trained Ph.D.s in life sciences have returned to China to work in industry or academic institutes.[51]

The message is clear: China is emerging as a formidable competitor to the United States in the field of life sciences. The country has already achieved several notable biotechnology successes, including being the first to sequence the genome of the virus that causes severe

acute respiratory syndrome (SARS) and to create a diagnostic tool for SARS detection, as well as developing foodstuffs genetically modified to confer immunity against hepatitis B and other viruses. More innovations will come. A PricewaterhouseCoopers report, *Medical Technology Innovation Scorecard: The Race for Global Leadership*, predicts that China will have the strongest gains (amongst nine leading biotech countries) in developing next-generation lifesaving products in the coming decade.[52] As George Baeder and Michael Zielenziger of the consulting firm Monitor conclude, "China's life sciences industry is today gathering a critical mass of highly skilled talent, savvy and focused venture investors, and growing government support as its market for drugs and medical devices takes off," thus positioning it with "the potential to create a more vigorous pipeline for new drugs," than the Western model.[53]

While China's emergence as a life sciences power holds the promise to unlock new discoveries that will benefit all the world's citizens, it also threatens U.S. life sciences leadership. It's clear that China's government views biotechnology as a key strategic industry, positioned to employ millions of Chinese, which is why China is investing aggressively to capture the greatest possible share of scientific, employment, and economic growth benefits from life sciences advances.[54] Make no mistake: China's commitment to making consistent and sustained investments in biotechnology is ultimately capable of dislodging the United States from its position as the world's life science leader—unless the United States matches China's commitment to investing in its life sciences industry and providing an institutional and regulatory framework supporting it.

China's sequencing power has the potential to tip the balance in innovation: the inventions and ideas that currently underlie the success of U.S. biotechnology.

United Kingdom

When David Cameron's coalition government took office in May 2010, amidst the continuing global economic recession and a deep U.K. budget deficit, the new government announced an austerity package that cut funding for many government agencies by 25 percent. Although the new British government understood that not every expenditure should be equally targeted—evidenced by the fact that it held national investment in scientific research at existing levels through a "flat-cash" agreement—even that arrangement still corresponded to an effective 10 percent cut in scientific investment, after allowing for inflation.[55] In other words, the British response was to flat-fund scientific research, much as the United States is now flat-funding NIH.

While U.K. investment in scientific research had been spared deep budget cuts, markets nevertheless gained the impression that the new coalition government was not strongly committed to the scientific research enterprise. Though many factors were at play, the government's decision to freeze science funding and slash capital spending was followed by massive layoffs in the country's pharmaceutical industry.[56] This included Pfizer's closure of its R&D operation in Sandwich, Kent (where Viagra was discovered), which had employed about 2,400 people.[57] At the same time, the number of U.K. biotech firms decreased by 3 percent between 2009 and 2011,[58] in part because more than a third of the country's listed biotech sector companies failed between 2008 and 2010.[59]

But as John Bell, President of the British Academy of Medical Sciences, explains, it was really "Pfizer's departure from Sandwich [that] caught people unaware. It sent shockwaves up and down Whitehall. It was a wake-up call for action."[60] As a result, in December 2011, the British government reversed course, reaffirming its commitment to the British life sciences industry by launching a comprehensive new *Strategy for UK Life Sciences* designed to bolster the competitiveness of the United Kingdom's life sciences sector.[61] The *Strategy* features substantial new investment in

THE *STRATEGY* FEATURES SUBSTANTIAL NEW INVESTMENT IN LIFE SCIENCES RESEARCH, AS WELL AS REFORMS TO U.K. TAX, REGULATORY, AND TALENT POLICY AND SETS A GOAL THAT, "THE UK WILL BECOME THE GLOBAL HUB FOR LIFE SCIENCES IN THE FUTURE."

life sciences research, as well as reforms to U.K. tax, regulatory, and talent policy and sets a goal that, "The UK will become the global hub for life sciences in the future."[62]

Out of the United Kingdom's £4.6 billion ($7.5 billion) annual science budget, £1 billion ($1.6 billion) will be invested in 2012 by two life sciences focused sectoral research councils, the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC).[63] The United Kingdom will also invest £800 million ($1.3 billion) to boost research fostering the development of ground-breaking medicines, treatments, and care for patients.[64] Moreover, the *Strategy* will allocate £310 million ($500 million) in new funding to support the discovery, development, and commercialization of research.[65] This includes £130 million ($211 million) for Stratified Medicines (that is, to support treatments targeted at specific populations) and £180 million ($292 million) for a novel Biomedical Catalyst Fund, which will assist small to medium-sized enterprises (SMEs) and academic entrepreneurs in avoiding the "Valley of Death" to turn promising ideas into innovative technologies and profitable businesses.[66] Other funding in the *Strategy* includes investing £75 million ($122 million) in the European Bioinformatics Institute at Cambridge, £15 million ($24 million) in a Cell Therapy Technology and Innovation Center (TIC), and £60 million ($98 million) to improve health-data-links between the National Health System and clinical researchers.

But the United Kingdom hasn't stopped there. It is expanding incentives for private-sector life sciences investment, including the introduction of a "patent box," a measure that will reduce corporate taxes on profits from patents to 10 percent starting on April 1, 2013.[67] (The United Kingdom is one of eight nations that taxes corporate income from the sale of patented products at a lower rate than other income.)[68] The United Kingdom's introduction of the patent box was clearly an effort to make the country a more attractive location for life sciences research, and it is already having the intended effect. For example, Sir Andrew Witty, GlaxoSmithKline's CEO, noted that the introduction of the patent box "has transformed the way in which we view the United Kingdom as a location for new investments, ensuring that the medicines of the future will not only be discovered, but can also continue to be made here in Britain."[69]

The United Kingdom will also introduce an "above the line" R&D tax credit to improve the visibility and certainty of the credit. It will expand use of National Health System NHS Innovation Challenge Prizes in both life sciences research and health care delivery. Through an "Early Access Scheme," the United Kingdom will revamp its regulatory drug approval system to increase the speed and efficiency of bringing innovative therapies to market. Finally, the United Kingdom has also focused on reforming its institutions to improve its life sciences competitiveness. The United Kingdom is the only nation to have a dedicated cross-government Office for Life Sciences, led jointly by Health and Business Ministers. And it recently launched a model Industry Collaborative Research Agreement and a Translational Research Partnerships program, both designed to boost collaboration among academics, clinicians, and industry to help deliver the medicines of the future faster.[70]

To be sure, life sciences have long been one of the United Kingdom's most important industries. In fact, the UK's life science industry is the third largest contributor to the British economy, with more than 4,000 companies contributing £50 billion to GDP (about 5 percent of total UK output), investing over £50 billion in research, and employing over

165,000 people.[71] The sector generated a trade surplus of approximately $80 billion over the past decade. Eight percent of global biopharmaceuticals are being developed in the United Kingdom.[72] However, the British government understood that it could not rest on its laurels and take its life sciences sector for granted. That's why it penned what amounts to a life sciences competitiveness strategy for the country and substantially increased its investment in the sector. The British case exemplifies the intensifying global competition in the life sciences industry and demonstrates that, even a nation with an illustrious life sciences history—from discovering the structure of DNA to developing medical resonance imaging (MRI) technology—must demonstrate continued commitment to invest for the future.

Singapore

Singapore has aggressively pursued global prominence in innovative life sciences research over the past decade, seeking to establish twenty-first-century pharmaceutical and biotechnology industries as pillars of its economy. Substantial material resources have been dedicated to the task, and some success has been achieved, although the country still has some distance to go.[73] Established in 2003, Singapore's Biopolis provides dedicated research and residential facilities, and co-locates public research institutes with corporate laboratories in order to foster collaboration.[74] On top of this infrastructure, Singapore's government has provided direct funding for pharmaceutical industry R&D, investing nearly five times as much in the industry as did the United States in 2009, on a share

> **Eight of the top ten global pharmaceutical firms now have their regional headquarters in Singapore, including Johnson & Johnson, Pfizer, GlaxoSmithKline, Merck, Sharpe & Dohme, Bayer, Roche, Sanofi, and AstraZeneca.[76]**

of GDP basis.[75] This material support, along with Singapore's business-friendly regulatory environment—for example, it takes fifteen minutes to register a business online, three weeks to receive approval for clinical trials, and only twenty-four to thirty-six months for a manufacturing facility to be operational—has attracted several large players in the pharmaceutical industry. Eight of the top ten global pharmaceutical firms now have their regional headquarters in Singapore, including Johnson & Johnson, Pfizer, GlaxoSmithKline, Merck, Sharpe & Dohme, Bayer, Roche, Sanofi, and AstraZeneca.[76] Singapore has also put in place a number of policies aimed at supporting and attracting international talent to complement local expertise.[77] The Novartis Institute for Tropical Diseases, for example, houses more than a hundred researchers representing eighteen nationalities.[78]

Despite these successes, there are several areas in which Singapore's strategy could be refined. The quality of intellectual property protection available for innovations in Singapore is rated as markedly lower than that of most other major players.[79] A number of commentaries have noted a failure to focus on specific fields of expertise, and argued that even the generous support provided is inadequate without the kind of focus and specialization most often associated with world-class excellence. Moreover, Singapore's efforts to apply such focus have not enjoyed a uniformly congenial reception among some of the expatriates attracted to Biopolis, leading to some turmoil and turnover.[80]

Nevertheless, Singapore's commitment and focus have borne fruit. The country's share of global pharmaceutical output has more than tripled since 1995 (although it is down somewhat since its 2006 peak).[81] And the country's surplus in pharmaceutical-goods trade has boomed, rising from a deficit of 0.01 percent of GDP in 2003 to an impressive surplus of 2.07 percent of GDP in 2010.[82] If Singapore is able to successfully address the challenges it is now facing and then maintain a sound strategy over the long term, its status as a formidable competitor in biopharmaceuticals will only strengthen further.

A CLEAR PICTURE EMERGES FROM THESE INDICATORS: THE COMPETITIVE POSITION OF THE U.S. LIFE SCIENCES INDUSTRY HAS BEEN ERODING OVER THE PAST DECADE.

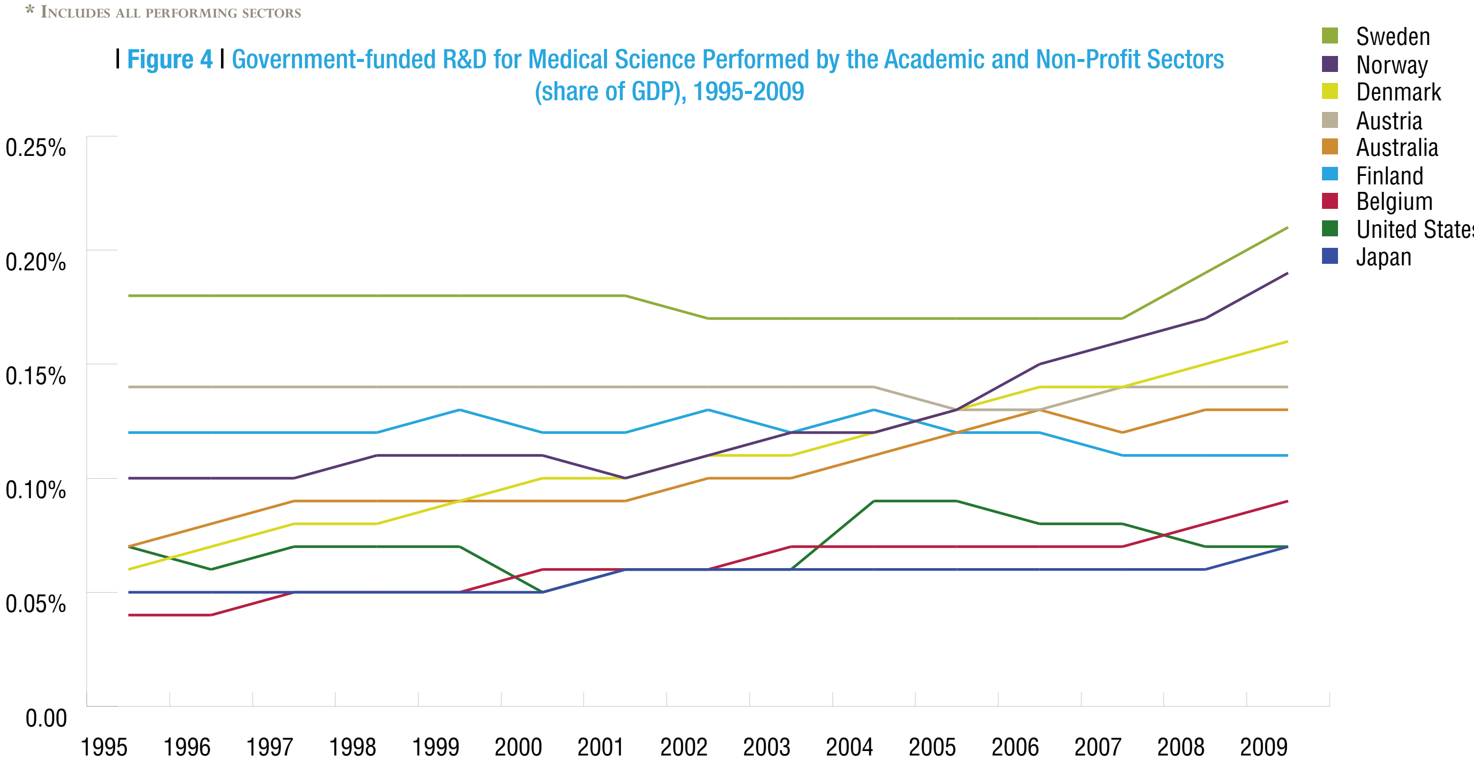
Quantitative Assessment of Countries' Life Sciences Competitiveness

A set of countries is analyzed with five indicators: government support for medical-science R&D, biopharmaceutical patents, pharmaceutical-industry output, trade balance in pharmaceuticals, and pharmaceutical-industry employment. Although a consistent set of countries is preferable, a flexible set was necessary due to a lack of comparable data for the first and fifth indicators. A clear picture emerges from these indicators: the competitive position of the U.S. life sciences industry has been eroding over the past decade.

Although there is a dearth of internationally comparable data on biomedical research, some data show the United States underperforming. While international data on government support for biological-science R&D are unavailable, data are available on government support for medical-science R&D. In other words, it is possible to analyze one of the two components of biomedical R&D—the medical component—to infer the trends in biomedical R&D as a whole. Figure 4 shows that the United States trails the developed world in government investment in medical-science R&D as a share of GDP.[83]

Growth in U.S. government funding for medical science has been flat while other countries are increasing their support[83*]

* Includes all performing sectors



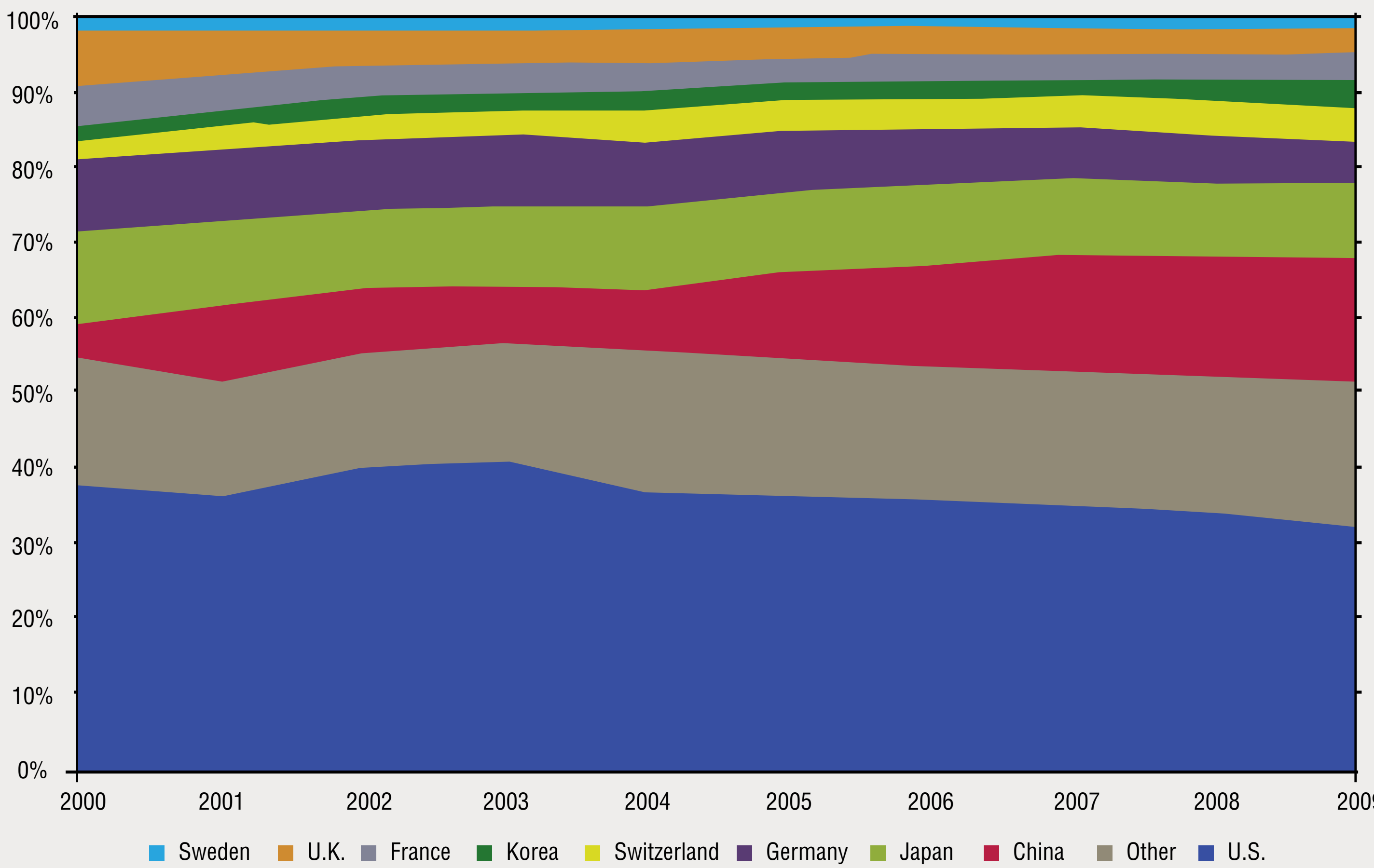
| Figure 4 | Government-funded R&D for Medical Science Performed by the Academic and Non-Profit Sectors (share of GDP), 1995-2009

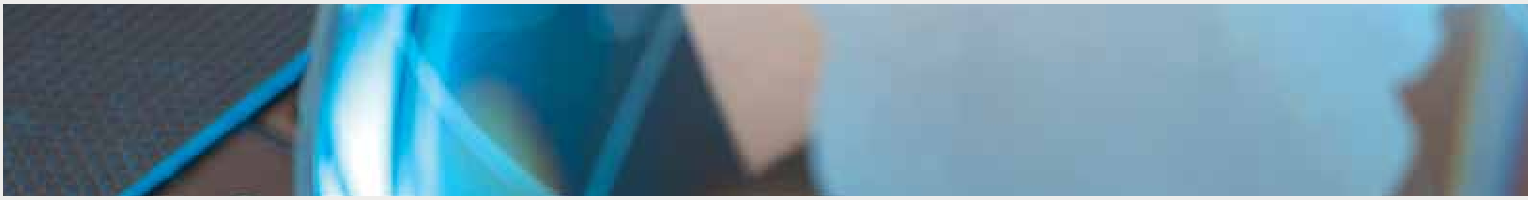
Of those for which data are available, only one country (Japan) invests a smaller share of its GDP in medical science than does the United States. Despite some fluctuations (likely due to differences in classification over the 2000 to 2003 period), in 2009 the U.S. government's investment in medical-science R&D (as a share of GDP) was unchanged from 1995. Meanwhile, Australia, Belgium, Denmark, Japan, Norway, and Sweden all show significant increases in their government support for medical-science R&D. Assuming that support for medical-science R&D and support for biological science R&D are roughly correlated over time, these trends do not bode well for U.S. competitiveness in life sciences.

Figure 5 displays trends in biopharmaceutical patents granted by nine countries from 2000 to 2009. Clearly, the United States remains the world's leading grantor of biopharmaceutical patents, but during the past decade its share of all biopharmaceutical patents awarded fell by 5 percent, from 38 percent to 33 percent. In contrast, China's share of world biopharmaceutical patents experienced a dramatic rise, increasing 12 percentage points from 4 percent in 2000 to 16 percent by 2009.[84] Japan's share held mostly constant, slipping by just 2 percent, while Switzerland's grew by 2 percent. Figure 5 confirms that China is becoming an increasingly serious life sciences competitor, and that its investments in biomedical research are beginning to produce results. To be sure, U.S. inventors were awarded 31,541 biopharmaceutical patents to China's 15,468 in 2009, but Figure 5 graphically illustrates the intensifying competition for global life sciences leadership.

The U.S. share of global biopharmaceutical patents is falling; China's is expanding[84]

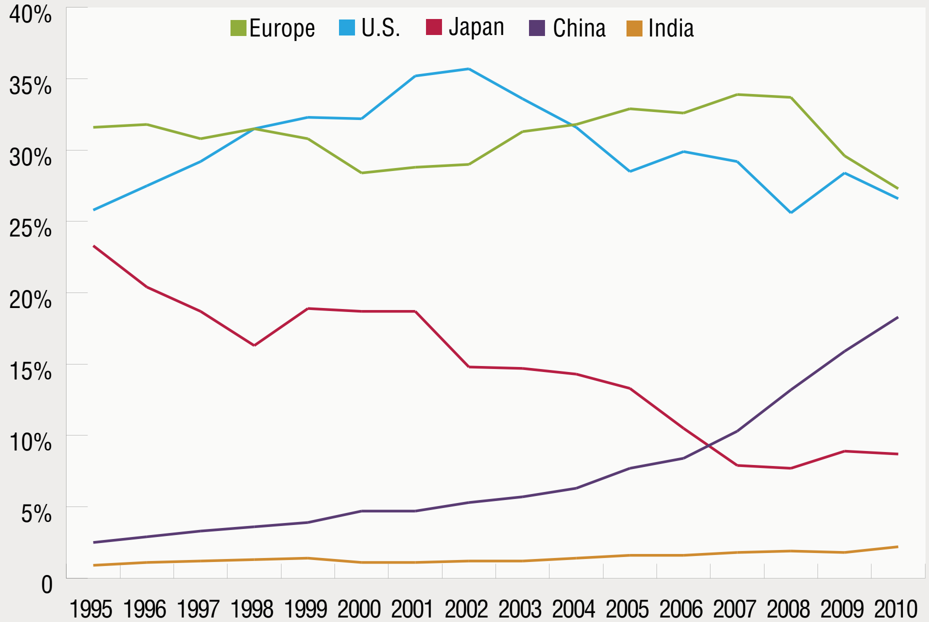
| Figure 5 | Global Share of Biopharmaceutical Patents Granted by All Patent Offices, 2000-2009





China is gaining on the United States and Europe as Japan declines

| **Figure 6** | Country Share of Global Pharmaceutical Industry Output, 1995-2010



The U.S. trade balance in pharmaceutical products has been worsening while that of most other countries has been improving

| **Figure 7** | Percentage Point Change in Trade Balance in Pharmaceutical Products (share of GDP), 2000-2010

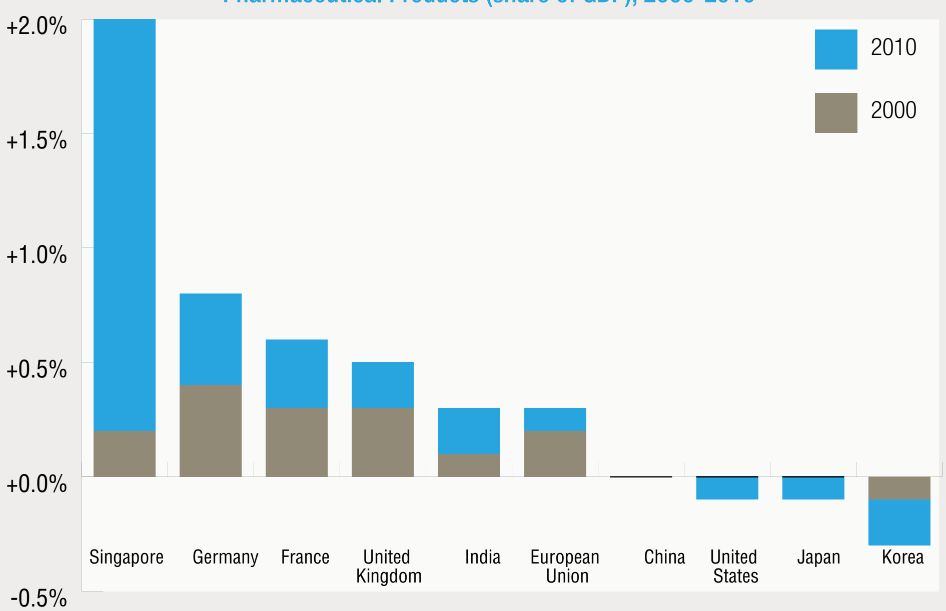


Figure 6 amplifies a key trend evident in figure 5: China's increasing competitiveness in the life sciences. This figure shows countries' shares of global pharmaceutical industry output from 1995 to 2010.[85] China's share of pharmaceutical industry output increased nearly seven-fold, from 2.5 percent in 1995 to 18.3 percent in 2010. Much of China's rise on this indicator came at Japan's expense, as Japan's share fell from 23.3 percent to 8.7 percent.[86] The U.S. share held steady over this period, starting at 25.8 percent in 1995 and ending at 26.6 percent in 2010. However, the U.S. share had risen as high as 36 percent in the early 2000s, before declining in the latter half of the decade. Europe as a whole ended the decade with approximately the same share of pharmaceutical industry output as the United States. Like Figure 5, Figure 6 vividly illustrates China's rapidly increasing life sciences-industry competitiveness over the past decade.

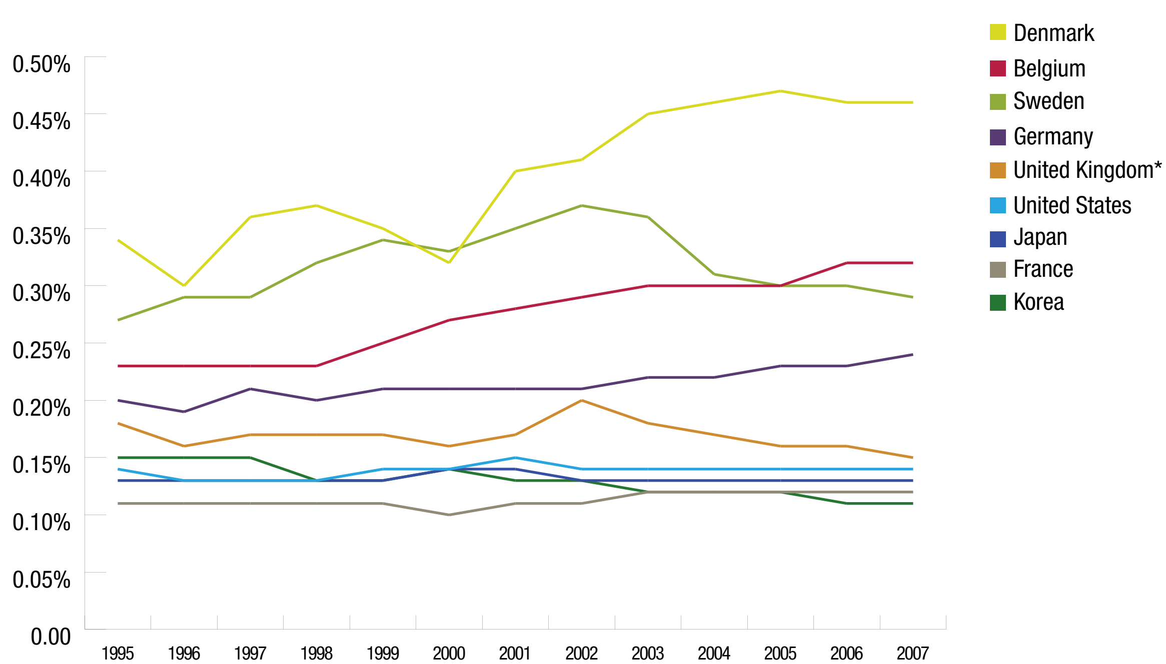
Figure 7 shows ten countries' trade balances in pharmaceutical products (as a share of GDP) from 2000 to 2010. As it has with many products, the United States has run a negative trade balance in pharmaceutical products every year since 1997, and it has accumulated a $136.7 billion trade deficit in pharmaceutical products over the last decade.[87] This stands in stark contrast to countries such as Singapore, Germany, France, and the United Kingdom (not to mention the broader European Union), which accrued healthy pharmaceutical trade surpluses in the 2000s. It is noteworthy that these countries' pharmaceutical trade balances have shown steadily increasing trends,

whereas the U.S. trade balance has been steadily declining. For example, from 2003 to 2010, Germany's pharmaceuticals trade surplus increased in every year but one, while the pharmaceuticals trade balance of the United States decreased in every year but two. From 2000 to 2010, Singapore increased its pharmaceuticals trade balance as a share of GDP by a factor of ten, from 0.25 to 2.63 percent, while the rate doubled in both Germany (0.36 to 0.75 percent) and France (0.26 to 0.53 percent), and increased in the United Kingdom from 0.29 to 0.46 percent. Singapore's sharply rising pharmaceuticals trade balance can be traced in part to the nation's concerted policy focus on improving its biotechnology-industry's competitiveness, which has included increased R&D investments and building an institutional research framework through its Biopolis. Germany, France, and the United Kingdom's rising competitiveness according to this indicator, in the face of U.S. decline, implies that the competitiveness of the U.S. pharmaceutical industry is not increasing at the same rate as that of its peers. It also shows that the concerted policies that several countries have put in place to bolster the competitiveness of their life sciences industries, such as Germany's *The High Tech Strategy of Germany*[88] and the United Kingdom's *Strategy for UK Life Sciences* are having positive effects.[89]

Figure 8 shows trends in pharmaceutical industry employment from 1995 to 2007. As a share of the working age population, U.S. pharmaceutical industry employment has been flat over this period: the share was 0.13 percent in 1996 and the same in 2007, with only slight fluctuations in the interval. Similarly flat trends over this period are also seen in France, Japan, Korea, and Sweden. By contrast, pharmaceutical industry employment as a share of working-age population has increased substantially in several countries, including in Denmark, Belgium, and Germany, demonstrating the growing competitive strength of the pharmaceutical industries in these countries. While these figures confirm that the U.S. pharmaceutical industry is a key component of the U.S. economy and an important source of high-skill, high-paying jobs, employment trends in other countries point to erosion in the United States' relative position. [90]

The pharmaceutical industry is a key component of the U.S. economy, although employment is flat while other countries gain[90] *Employees (not total engaged)

| **Figure 8** | Pharmaceutical Industry Employment (total engaged, share of working-age population), 1995-2007



Conclusion

This report makes the case that federal investment in biomedical research catalyzed the initial development of and sustains the ongoing competitiveness of the U.S. life sciences industry, while generating tremendous rates of both public and private return in the process. Indeed, biomedical research funding has a private rate of return of 30 percent per year and an even higher social return of at least 37 percent. While U.S. life sciences-companies have already produced scores of breakthrough, life-improving drugs and biologicals, innovation in the life sciences is only getting started, as new tools, such as genome sequencing, proteomics, and recombinant DNA techniques, create vast new possibilities for future innovations in the life sciences.

For at least the past half century, the United States has stood at the forefront of the global life sciences revolution. But amidst intensifying global competition, continued U.S. life sciences leadership is not assured, and is under clear threat from several directions. The United States is not sustaining the historically strong investments in biomedical research that once propelled it to global life sciences leadership. Baseline federal investment in biomedical research through the NIH has decreased in both inflation-adjusted dollars and as a share of GDP nearly every year since 2003.

At the same time, competing nations are significantly increasing their investments in biomedical research, in many cases investing a larger share of their economies than the United States.

For example, as a share of GDP, Singapore's funding of pharmaceutical industry R&D was nearly five times greater than that of the United States in 2009. And if current investment trends in the United States and China continue, the U.S. government's investment in life sciences research over the next half-decade will be barely half of China's in actual dollars and roughly one-quarter China's level on a per-GDP basis. The impact of other countries' increased life sciences competitiveness is beginning to show up in a number of indicators, including the United States' negative trade balances in pharmaceuticals and its lack of growth in pharmaceutical-industry employment compared with that in competing companies, such as Germany. The dangers of the United States losing life sciences competitiveness include diminished employment, lost economic growth, and loss to U.S. citizens of the benefits of innovative new drugs and therapies.

Some will say that, in times of deepening budget deficits, the United States cannot afford to maintain—let alone increase—its federal investment in biomedical research. But the reality is that, if the United States wishes to reduce its budget deficit (while also reducing its investment and trade deficits) the only way to do so is by increasing targeted investments that spur innovation, productivity, and competitiveness, while cutting budget deficits elsewhere. In doing so, policymakers should distinguish between productive investments—those that expand the productive capacity of the country, drive economic growth, and increase future incomes—and consumptive spending—expenditures that finance present consumption of goods and services, but do not position the country to create future wealth.

Increasing productive public investments will reduce the investment deficit, boost U.S. competitiveness and exports, and generate higher economic growth, which is the single best way to close the budget deficit. In fact, the Congressional Budget Office (CBO) estimates that an increase of just 0.1 percent in the GDP growth rate could reduce the budget deficit by as much as $310 billion cumulatively over the next decade. This approach—investing in boosting the rates of innovation produced by key sectors such as the life sciences—is the most effective way to reduce the budget deficit.

Other countries, like the United Kingdom, recognize these realities; that's why they are making the difficult choices to expand their investments in biomedical research, even in the face of daunting deficits. Put simply, the notion

For at least the past half century, the United States has stood at the forefront of the global life sciences revolution. But amidst intensifying global competition, continued U.S. life sciences leadership is not assured, and is under clear threat from several forces.

that America cannot afford to increase its investment in biomedical research is false; the reality is that America cannot afford not to increase its investment in life sciences research. We have seen this play before. The United States has lost leadership in numerous technologies and industries it created and in which it felt it once had unassailable leads—televisions and advanced displays, consumer electronics, and clean-energy technologies such as solar panels and rechargeable batteries for example—which it then let slip away for lack of strategic investment. If we repeat those short-sighted mistakes in the life sciences, the United States can expect similar results.

The United States must therefore re-establish as a national priority and strategic urgency the strong and continuing support for the National Institutes of Health and similar agencies. Specifically: Congress should maintain the stability of funding levels with minimal fluctuations from year to year; and Congress should maintain NIH funding at a level commensurate with at least one quarter of one percent (0.25%) of national GDP or higher. Our nation's baseline policy going forward should be to grow NIH funding at a rate that accounts for inflation, embraces emerging avenues of research that can propel U.S. innovative leadership, and reflects the catalytic effect biomedical research has on our nation's economy.

Implementing these recommendations—committing to this level of sustained investment—will continue the long tradition of policies that have delivered such a robust record of economic growth and made the United States the preeminent global leader in life sciences for the past three-quarters of a century.

About United for Medical Research

United for Medical Research represents leading research institutions, patient and health advocates and private industry, joined together to seek steady increases in federal funding for the National Institutes of Health. The coalition groups consist of the American Cancer Society Cancer Action Network, American Diabetes Association, American Heart Association, Association of American Universities, Association of Public and Land Grant Universities, BD, Biotechnology Industry Organization, Harvard University, Johns Hopkins University, Life Technologies, Massachusetts Institute of Technology, Melanoma Research Alliance, PhRMA, Research!America, Roche Diagnostics, Stanford University, The Endocrine Society, Thermo Fisher Scientific, University of Pennsylvania, University of Southern California, Vanderbilt University, and Washington University in St. Louis.

About The Information Technology and Innovation Foundation

The Information Technology and Innovation Foundation (ITIF) is a Washington, D.C.-based think tank at the cutting edge of designing innovation strategies and technology policies to create economic opportunities and improve quality of life in the United States and around the world. Founded in 2006, ITIF is a 501(c)(3) nonprofit, non-partisan organization that documents the beneficial role technology plays in our lives and provides fact-based analysis and pragmatic ideas for improving technology-driven productivity, boosting competitiveness, and meeting today's global challenges through innovation.

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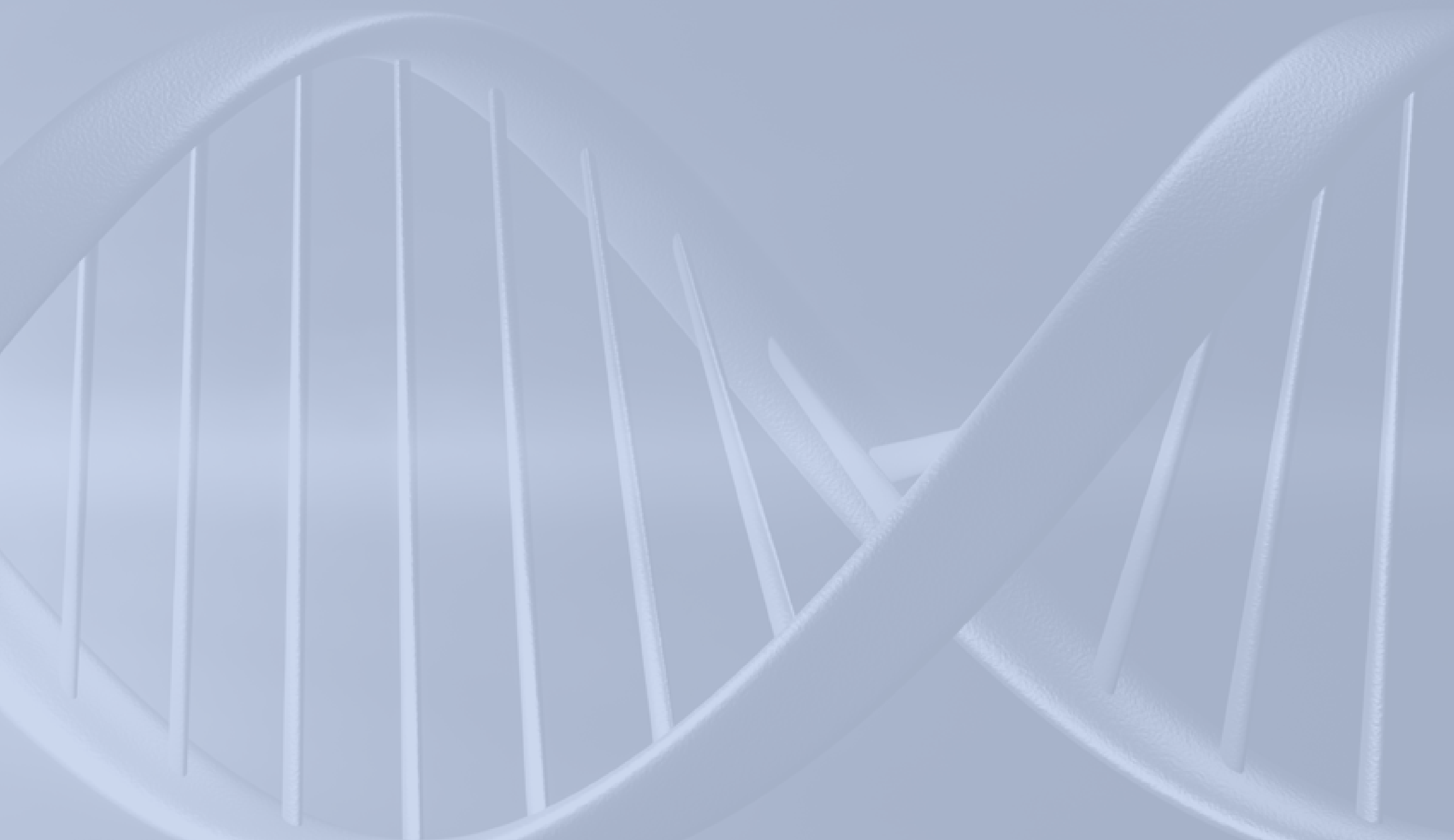

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