How the Biopharmaceutical Industry Contributes to Open Scientific Knowledge

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Price controls reduce valuable knowledge generation and sharing. For example, some of the knowledge pharmaceutical companies produce in the course of drug development spills over to competitors.

The development of new drugs requires years of painstaking, risky, and expensive research that, for a new pharmaceutical compound, takes an average of 11.5 to 14 years of research, development, and clinical trials at a cost of $1.7 to $3.2 billion.[1] Many nations either limit or are considering limiting drug prices as a way to shrink the growth of health care costs, even though drug prices in nations that belong to the Organization for Economic Cooperation and Development (OECD) grew more slowly than total health care costs from 2005 to 2013.[2] This is a mistake, because price controls come at the cost of a slower pace of drug discovery, as expert studies show that the relationship between drug company revenues and research and development is almost one to one.

Price controls also reduce valuable knowledge generation and sharing, which enable a healthy drug innovation ecosystem. Indeed, much of the R&D that biopharmaceutical companies conduct ends up supporting the overall biopharmaceutical knowledge commons. For example, multiple academic studies demonstrate that a portion of the knowledge biopharma companies produce in the course of drug development spills over to competitors and to university and government researchers, in part through patent disclosures and filings, but also through published findings in open scientific journals available to researchers. In 2017, industry researchers were authors or coauthors of more than 12,790 scientific journal articles on subjects ranging from the effect of changes in cerebrospinal fluid on Alzheimer's to the effect of osteoporosis therapies for postmenopausal women, to reducing toxicity effects from new Car-T cancer cell therapies.[3] Moreover, that same year biopharma companies provided over $2.5 billion in research

funding to America's universities—in all 50 states—accounting for more than 60 percent of industry funding of university research. As such, just as limiting the National Institute of Health (NIH) budget has a negative effect on the generation of knowledge to support drug innovation to improve and extend lives, so too does limiting drug prices.

BIOPHARMA COMPANY ROLE IN DRUG INNOVATION

An increasingly common—but incorrect—opinion is that pharmaceutical companies (both small-molecule traditional and large-molecule biotech) have cut back considerably on their R&D, and now largely rely on discoveries made by small start-ups. In reality, the industry invests considerable resources in R&D, with the top 30 companies globally (ranked by revenue) being responsible for 77 percent of global pharmaceutical R&D funding. According to the National Science Foundation, in 2014, biopharma companies invested over $56 billion in R&D in the United States, up from $48 billion in 2008.[4] Moreover, according the U.S. Bureau of Economic Analysis, the industry had the fastest growth in R&D capital stock from 2005 to 2016 (231 percent) than any other industry; 33 percent faster than the business average.[5]

In 2014, biopharma companies invested over $56 billion in R&D in the United States.

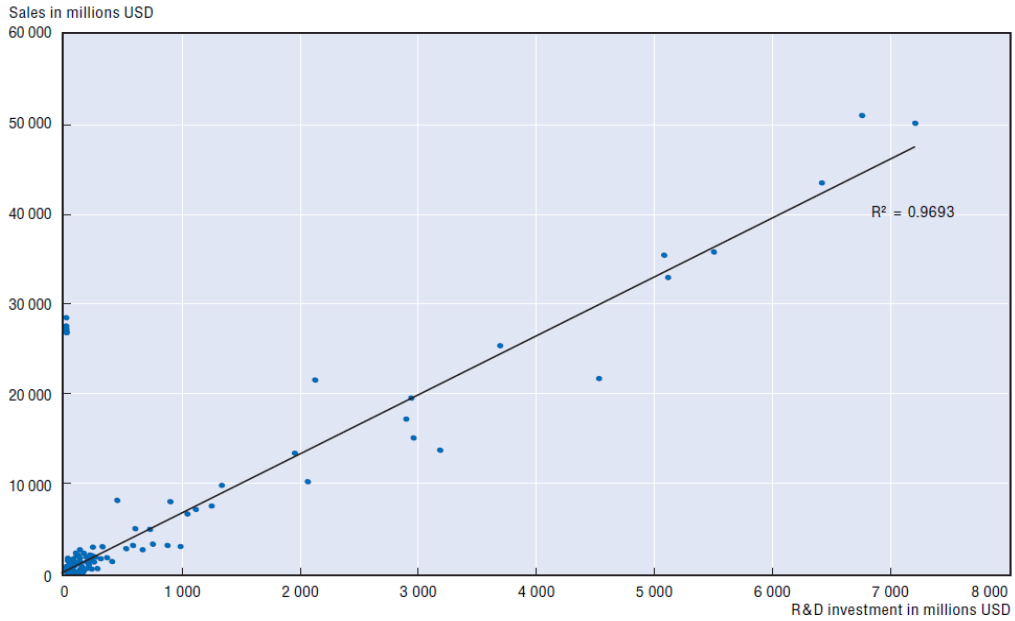
Indeed, the U.S. life-sciences sector is extremely research-intensive, investing over 21 percent of its sales in R&D, while accounting for 23 percent of domestic R&D funded by U.S. businesses—more than any other sector, in the United States or any other nation.[6] And measured by R&D expenditure per employee, the U.S. biopharmaceutical sector leads all other U.S. manufacturing sectors, investing more than 10 times the amount of R&D per employee.[7] Strong private and public sector investment has made the United States the world's largest global funder of biomedical R&D investment over the past two decades—a share some analyses suggest has reached as high as 70 to 80 percent.[8] And besides benefiting from better treatments the industry produces, the U.S. economy benefits from the 4.7 million direct and indirect jobs the industry is responsible for creating.[9]

That investment is enabled by revenues. Indeed, research into pharmaceutical economics continually shows that robust revenue streams and innovative pharmaceutical output are strongly tied to one another. As the OECD report "Pharmaceuticals Pricing Policies in a Global Market" explains, "There is a high degree of correlation between sales revenues and R&D expenditures."[10] As figure 1 shows, that correlation is almost 1 to 1 (0.97). Recent data from the United Kingdom's Department of Innovation, Universities, and Skills R&D Scoreboard also exhibits a very strong relationship between R&D expenditures and sales for the largest 151 pharmaceutical firms worldwide in terms of expenditures on R&D.[11] Henderson and Cockburn found that R&D expenditures are directly proportional to the amount of sales revenues available to undertake R&D investment.[12] Likewise, Gambardella determined sales revenue from previous periods have a significant, positive impact on current-period biopharma R&D.[13] In other words, when biopharma company revenues decline through price controls or other policy measures, biopharma R&D also declines—and that means the pace of drug innovation falters.

This relationship is tight because pharmaceutical sales are the main source of revenue pharmaceutical companies use to generate the funding needed to finance research into, and development of, future generations of innovative medicines. Overly restrictive price controls levied against pharmaceuticals, by definition, mean less revenue for biopharma companies to invest in R&D. For example, Golec and Vernon found that because of European Union (EU) drug-price regulations, "European Union pharmaceutical firms are less profitable, spend less on R&D, and earn smaller stock returns than U.S. firms."[14] By using data from 1986 through 2004, they showed that the economic trade-off for the EU, by maintaining real pharmaceutical prices constant over 19 years, was forgoing about 46 new medicine compounds. They took this one step further by presenting a counterfactual scenario where, if the United States had adopted EU-type price controls over the same time period, then the result would have been 117 fewer new medicine compounds.[15] Price controls also delay the launch of drugs in markets with controls.[16] In other words, the debate about price controls is not really one about whether society wants lower prices in exchange for lower drug company profits; it is about whether society wants lower drug prices in exchange for less and slower drug innovation—that is, cheaper prices today, and less effective drugs when our children become adults.

If the United States adopted EU-type price controls over the same time period, the result would have been 117 fewer new medicine compounds.

Figure 1: R&D Expenditures and Sales in the Pharmaceutical Industry, 2006[17]



Note: The data were prepared on the basis of annual reports and consolidated accounts received up to and including 31 July 2006. Annual reports with a year-end older than 30 months from the cut-off date or a publication date older than 24 months from cut-off date are excluded.

Source: DIUS (2007).

Despite the negative effects on drug innovation, many would seek to impose price controls to limit drug costs. And some advocates go even further, supporting price controls not just because they want lower drug prices, but because they seek a reduced role for biopharma companies within the economy.[18] For them, large biopharma corporations motivated by profits cannot be trusted to discover, produce, and distribute drugs in a way that advances

the public interest. Therefore, they argue government's role should be vastly expanded, both to shrink revenues going to industry with price controls and to expand direct funding of biomedical research so that government takes over a much-expanded role in drug discovery and development. To do that, they advocate an interventionist agenda grounded in two key pillars: imposing drug-price controls and significantly weakening intellectual property laws to empower the generic drug industry. Many complement that with proposals to significantly expand NIH funding and create a network of nonprofit drug-development labs to largely take over drug development and testing. To be sure, Congress should expand NIH funding—not to crowd out biopharma research, but to complement it and to speed up overall drug innovation. But it defies both logic and all available evidence to suggest that government funding of drug development will be as effective as private companies' efforts. Among other reasons for this, Congress is not likely to allocate the necessary funding, and NIH and academic researchers lack the experience and expertise to take scientific discovery all the way to putting a drug on the market, just as academic researchers studying the science of computer chips would be unable to design and manufacture semiconductors at commercial scale.

Even with trade secrets and patents, a considerable share of biopharma research "spills over" and contributes to knowledge discovery and drug development overall, not just in individual firms' labs.

Nonetheless, a key argument drug populists make to support this agenda is that public funding of life-sciences research is open and widely shared, whereas funding by biopharma companies is proprietary and does little more than advance these companies' own bottom lines. In other words, they argue, society should have a system of publicly funded knowledge creation with high levels of knowledge sharing. In describing the drug populists' case, Jennifer Plitsch, a lawyer at Covington and Burling, wrote, "Why should American taxpayers both contribute to drug development and then pay the highest prices in the world as patients?"[19]

In fact, the evidence shows that even with trade secrets and patents—which are critical for enabling drug companies to assume the considerable risks of developing new drugs—a considerable share of biopharma research "spills over" and contributes to knowledge discovery and drug development overall, not just in individual firms' labs. In fact, these knowledge spillovers are very much like public knowledge generated by government agencies such as NIH. This knowledge dissemination occurs in three main ways: 1) spillovers from company research other researchers are able to learn from; 2) funding by biopharma companies of university research, with most of the results open to researchers around the world; and 3) publication of company discoveries in widely available, open science journals. As such, efforts to impose drug-price controls (or to weaken intellectual-property protections) will not only hurt drug innovation in the affected biopharma companies, it will reduce the generation of widely shared knowledge, thus limiting overall life-sciences innovation.

THE DISCOVERIES FROM BIOPHARMA COMPANY R&D SPILL OVER

When companies invest in R&D to develop a product or a production process, they are almost never able to retain all the benefits of that research, even when they patent the discovery. Competitors and others that learn about the research and discoveries are able to capitalize on them. Economists refer to these external benefits as "spillovers."

Economists have long worked to measure the extent of spillovers from business R&D. As one of the original economists doing this research, Zvi Griliches, wrote, "There has been a significant number of reasonably well done studies all pointing in the same direction: R&D spillovers are present, their magnitude may be quite large, and social rates of return remain significantly above private rates.… The estimated social rates of return look, actually, surprisingly uniform in their indication of the importance of such spillovers."[20] A 1998 study by Jones and Williams computed the social rate of return from business R&D conducted in the United States, and concluded that the optimal level was at least two to four times actual investment.[21] The fact that some economists estimate a 7 percent private return and 30 percent social rate of return on R&D suggests the optimal level of R&D investment in the U.S. economy is between three to four times larger than the total current level of private investment.[22] When companies do basic research, the spillovers are even greater—as high as 150 percent.[23] Okubo and colleagues examined many different studies and determined the private return to be 26 percent and the social return to be 66 percent.[24] Most recently, Bloom and Van Reenen examined the change in the rate of R&D spillovers over time, and found spillovers actually increased over the last 40 years, with the ratio of social to private returns increasing from a factor of three to four. They wrote, "There is certainly no evidence that the need to subsidize R&D has diminished."[25] Thus, absent policies that would bring the after-tax rate of private return from R&D closer to the public rate of return—such as through R&D tax incentives—innovations that will improve our lives will come about more slowly.

Studies of the biopharmaceutical industry specifically have also found large spillovers. In one study, Henderson and Cockburn found that "a [research] program whose competitors' programs are in the same and in related fields are roughly 10 percent more productive will be approximately 2 percent more productive itself."[26] In other words, one company's discoveries cannot be captured completely, even in the presence of trade secrets and patents. Bloom, Schankerman, and Van Reenen also found that there are significant technology spillovers in the pharmaceutical industry. Moreover, they found that spillovers are significantly greater in large biopharma firms compared with smaller ones because the latter "tend to operate in technological 'niches'" wherein fewer other firms are operating.[27] One reason spillovers are large in the biopharma industry is that in the United States their share of R&D classified as basic (14.3 percent) instead of later-stage applied and development is higher than any other U.S. industry—and more than twice as high as the U.S. industry average (6.4 percent).[28]

Some drug populists, such as economist Joseph Stiglitz, rail against patents for drugs, claiming they limit spillovers and knowledge sharing, and thereby slow the pace of

discovery.[29] In fact, as we have just seen, studies of the biopharma industry show significant spillovers do exist. Moreover, leaving aside the obvious point that, absent patent protection, there would be much less revenue for biopharmaceutical firms to invest in new drug development (as evidenced by manufacturers of generic drugs investing little in R&D[30]), patent protection actually enables valuable information sharing. Patents and publicly disclosed patent applications are a very important and valid source of insight for companies seeking to follow the therapeutic leaders. Moreover, the fact that companies can "invent around" a patent invention not only spurs innovation, but also competition.

Magazzini, Pammolli, and Riccaboni found that even failed research projects for which patents are filed provide valuable information for companies—including paths not to follow. They found that "patents covering successfully completed projects (i.e., leading to drug launch on the market) receive more citations than those associated to [sic] failed (terminated) projects, which in turn are cited more often than patents lacking clinical or preclinical information."[31] In other words, far from limiting knowledge sharing and innovation, patents actually provide information that is valuable to the research of competitors.

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FUNDING OF UNIVERSITY RESEARCH

There is another way the biopharma industry supports broader knowledge generation. While the industry accounts for 16.8 percent of all U.S. business R&D, it accounts for 61 percent of all business R&D funding of universities.[32] For example, many of the U.S. universities that receive the largest share of their R&D support from industry—including Duke, the University of Alabama at Birmingham, University of Texas MD Anderson, and the University of Pennsylvania—have world-leading biomedical research programs.[33]

There are a number of examples of companies funding university research—as drug innovation relies so heavily on scientific breakthroughs. Companies such as Amgen, GlaxoSmithKline, Novartis, and Vertex have funded research or clinical trials at Duke.[34] AbbVie has entered into a partnership with the University of Chicago for cancer research.[35] Astellas has provided $26 million to M.D. Anderson Cancer Center in Houston to support treatment for acute myeloid leukemia.[36] Novartis has supported more than 300 academic collaborations, such as with Harvard University on the zika virus.[37] Pfizer has established its Global Centers for Therapeutic Innovation as an $85 million partnership with the University of California at San Francisco.[38]

To be sure, NIH provides the lion's share of academic funding for biomedical research. But in 2016, biopharma companies provided over $2.5 billion in research funding to America's universities, in all 50 states. As table 1 shows, life-sciences university R&D funding ranges from a low of $366,000 in Maine to a high of $329 million in California.

PUBLICATIONS IN OPEN SCIENCE JOURNALS

Another indicator of broader spillover and scientific impact comes from bibliometric research of peer-reviewed scholarly articles authored or coauthored by scientists from biopharma firms. Publishing helps spread valuable scientific knowledge. As Tijssen wrote,

"This 'open science' mechanism produces a pool of knowledge that can be used freely by the international scientific community from which corporate researchers draw very heavily."[39] He could have also accurately added, "and from which corporate researchers contribute to."

For decades, biopharma firms have been contributing to the world's knowledge stock by giving paper presentations at scientific conferences and publishing in peer-reviewed scholarly publications.

Table 1: Higher Education R&D Expenditures Funded by Life-Sciences Businesses: FY 2016 (in Millions)[40]

State	Funding	State	Funding
Alabama	$48.6	Montana	$1.8
Alaska	$0.7	Nebraska	$25.0
Arizona	$10.4	Nevada	$1.2
Arkansas	$9.1	New Hampshire	$7.2
California	$350.9	New Jersey	$22.7
Colorado	$42.7	New Mexico	$2.2
Connecticut	$65.4	New York	$232.4
Delaware	$1.4	North Carolina	$315.5
District of Columbia	$12.2	North Dakota	$0.8
Florida	$76.8	Ohio	$103.5
Georgia	$54.1	Oklahoma	$19.0
Hawaii	$0.7	Oregon	$27.2
Idaho	$1.2	Pennsylvania	$165.3
Illinois	$96.6	Rhode Island	$2.3
Indiana	$37.1	South Carolina	$25.3
Iowa	$29.8	South Dakota	$0.8
Kansas	$17.0	Tennessee	$41.4
Kentucky	$17.1	Texas	$186.1
Louisiana	$24.3	Utah	$27.6
Maine	$0.6	Vermont	$3.2
Maryland	$88.9	Virginia	$36.4
Massachusetts	$75.0	Washington	$43.5
Michigan	$52.4	West Virginia	$10.0
Minnesota	$26.1	Wisconsin	$27.5
Mississippi	$11.1	Wyoming	$0.5
Missouri	$87.4		

At first glance, it may seem odd that biopharma firms publish in peer-reviewed science journals when intellectual property protection is the key to their ability to continue to innovate—and writing for these publications takes valuable time away from industry researchers. Scholars have suggested several reasons why. Hicks has averred that firms publish in order to "participate in the barter-governed exchange of scientific and technical

knowledge." In other words, when all or most firms participate, they benefit from each other's work. And by publishing, firms send signals that they are "contributing to the pool of knowledge," and therefore should be able to access that knowledge.[41] As Rafols, et. al., wrote, "Adopting an Open Science strategy is in this case considered necessary in order to connect to the scientific community and to access its resources in the form of knowledge, qualified labour and informal advice."[42] Similarly, Haeussler found that biopharmaceutical industry researchers share data with university colleagues, basing "their decision to exchange information on factors related to social capital and choose to share data with colleagues when the danger of it being appropriated is low and the prospect of reciprocity is high."[43]

The industry also appears to publish more than other industries. The largest number of partnerships between corporations and academic institutions in the *Nature Index* in 2016 was in the life sciences, with 13,114 collaborations.[44] One reason is intellectual property protection. By obtaining patents for their drugs, companies are more assured their valuable discoveries will be protected, thus rendering the risk of direct copying from information being shared in scholarly journals less than would otherwise be the case.

For decades, biopharma firms have been contributing to the world's knowledge stock by giving paper presentations at scientific conferences and publishing in peer-reviewed scholarly publications. As Henderson and Cockburn wrote in 1996, "The [biopharma] industry is characterized by high rates of publication in the open scientific literature, and many of the scientists with whom we spoke stressed the importance of keeping in touch with the science conducted both within the public sector and by their competitors."[45] A comprehensive review of scholarly publications involving the 16 largest pharmaceutical companies in Europe and the United States showed how widely their scientists are involved in knowledge dissemination.[46] European firms, many of which have substantial R&D and production facilities in the United States, were involved in more than 84,800 scholarly journal publications from 1995 to 2009; American firms more than 78,000. The authors estimated that this accounted for about 4 percent of all scientific journal articles in the field. They found articles to be particularly focused on Pharmacology and Pharmacy, Biochemistry, and Molecular Biology; but also on Chemistry, including Organic Chemistry and Medicinal Chemistry; and Immunology and Infectious Diseases, areas of Clinical Medicine (for example, surgery, hematology, and dermatology). Most of these papers address core scientific issues. For example, according to a paper published in the *Journal of Biological Chemistry*, "A group of Genentech scientists described a type of engineered antibody that is both easier to manufacture and, potentially, reduces certain types of toxicities in animals and humans."[47]

These papers are also mostly collaborative, involving coauthorship with researchers from other organizations, often universities. For example, Novartis and Harvard published 83 joint research articles from 2012 to 2016 in leading scholarly journals, including the *Proceedings of the National Academy of Sciences*, *Nature*, *Cancer Cell*, and *Nature Medicine*.[48] This reflects the basic research-driven nature of the industry and the extensive partnerships

between academic research institutions and biopharma firms, as previously noted. And in many cases, the company contributes to more than 90 percent of the authorship of the articles. [49]

In order to measure the number of scholarly journal articles biopharma companies were involved in as authors or coauthors, the Information Technology and Innovation Foundation (ITIF) used a tool from Microsoft to search for scholarly academic articles with industry authorship.[50] We examined the top 93 companies that, in 2016, accounted for 76 percent of global life science R&D. In 2017, researchers from these companies were authors or coauthors of 12,792 papers, up from 8,322 in 2007—an increase of 54 percent. This worked out to 116 articles for every $1 billion of R&D invested, and 8.8 articles per 1,000 employees. The top five companies in terms of articles were Novartis with 1,249, AstraZeneca (1,072), Pfizer (1,007), Merck (U.S.) (995), and Roche (942).

To be sure, this is less than the number and rate of articles coming from NIH funding. In 2017, there were approximately 95,000 peer-reviewed journal articles by researchers who had received NIH funding for their work. But given that the vast majority of NIH recipients are academic scholars whose bread and butter are peer-reviewed journal articles, it is not surprising this number is as high as it is. What is perhaps more surprising is that the industry numbers are 13.4 percent of NIH's numbers.

In addition to funding university research, many biopharma firms are also participating in open consortia designed to develop and disseminate discoveries, including open data.

Finally, in addition to funding university research, many biopharma firms are also participating in open consortia designed to develop and disseminate discoveries, including open data. For example, the Open Pharmacological Concepts Triple Store (Open PHACTS) involves a number of companies—including Merck, Novartis, and Pfizer—and universities working to develop and link diverse and complementary drug discovery databases to support drug research.[51] Similarly, companies such as AstraZeneca, Novartis, GSK, Pfizer, Sanofi, and Takeda have funded the Neglected Diseases Initiative to provide a platform for collaborative, nonprofit drug discoveries.[52]

POLICY IMPLICATIONS

Notwithstanding the spillovers and other knowledge dissemination biopharmaceutical company R&D supports, more can be done to increase biopharma innovation and knowledge generation. Clearly, **working to protect robust intellectual property protections, including data exclusivity for biologics, and fighting against drug-price controls—especially in foreign nations—is important, as it ensures companies can earn the revenues they need to invest in the next generation of drug discovery**.[53] But other steps are also needed.

One important step is to expand the R&D credit. As previously noted, the difference between public and private rates of return is significant; and the core policy reason the United States adopted the world's first R&D credit in 1983 was to reduce the difference between these rates. Given the still-significant difference, **Congress should at least double the rate of the Alternative Simplified Credit from 14 percent to 28 percent.** Many would protest that, given its sizeable budget deficit, the United States cannot afford this.

But ITIF research shows that such an expansion would more than pay for itself in net present value terms thanks to faster economic growth.[54] In other words, on a dynamic scoring basis, the expanded credit would generate a net present value rate of return to government tax revenues in excess of the direct tax credit cost.

In addition, both the regular credit and the ASC versions of the R&D tax credit treat funding companies provide to universities less generously than research funding they do in-house. Under both credits, firms can claim a credit against only 65 percent of payments made to institutions for basic research (such as universities). This is the exact opposite of what is economically rational. Therefore, **Congress should eliminate language in the tax code that restricts the definition of basic research to projects "not having a specific commercial objective."**

Congress should also expand the collaborative research credit. Industry funding of university research tends to focus on more basic and exploratory research—which have bigger spillovers—with many of the benefits going to other firms, and society at large. However, firms do less of this kind of research than is economically optimal, which is why a number of other countries, including Canada, Denmark, Hungary, Japan, France, Norway, Spain, and the United Kingdom have, in the last decade, established more generous incentives for this form of research.[55] **Congress should modify the existing collaborative R&D credit, which provides a 20 percent flat credit for collaborative R&D for energy research only, by eliminating the energy restriction.**

CONCLUSION

Biomedical innovation is critical to addressing human health challenges. And a healthy life-sciences innovation system depends on robust public and private funding of biomedical R&D.[56] Public support for biomedical innovation is defended in part on the grounds that much of the information is in the public domain and can be used by a wide range of innovators. At the same time, a number of drug populists and budget hawks argue that governments should impose or increase price controls on drugs, and that doing so will have little negative effect on new drug development. However, as this paper has shown, not only are drug companies' revenues highly correlated with the amount of R&D they invest in, but much of the R&D they fund spills over both to other firms and to the public domain, thereby helping to spur even more life-sciences innovation. Price controls and other steps to reduce revenues, such as weaker intellectual property protections, will mean less knowledge generation and sharing, which will leave with the next generation with drugs that will be less effective than would otherwise be the case.

ENDNOTES

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ERRATA

This report has been updated to correct the data in table 1 on page 7—higher education R&D expenditures funded by life-sciences businesses in FY 2016.

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