Congress of the United States

U.S. House of Representatives
Committee on Science, Space, and Technology

Subcommittee on Research and Technology

"Policies to Spur Innovative Medical Breakthroughs from Laboratories to Patients"

Written Testimony
of
Dr. Marc Tessier-Lavigne

Rayburn House Office Building
Room 2318
Thursday, July 17, 2014
9:00 – 11:00 a.m.

Thank you, Chairman Bucshon, and members of the subcommittee, for the invitation to speak to you today about a critical issue facing the nation: how best to stimulate public and private sector biomedical research and development activities to drive medical breakthroughs for poorly treated diseases.

As president of The Rockefeller University, I bring the perspective of the academic research sector. Rockefeller is a research institution in New York City home to 75 laboratories and about 1,200 scientists working on advancing knowledge of biological processes in most fields of biomedicine, from brain science to cancer biology to metabolic disease.

Rockefeller has been extraordinarily successful at making discoveries that have advanced the fight against diseases such as cancer, HIV/AIDS, Alzheimer's disease and stroke. One measure of our success is that our faculty have been honored with 24 Nobel Prizes in medicine and chemistry over our 113-year history, more than any other institution in the world.

As former chief scientific officer at Genentech, a leading biotechnology company, I also bring a perspective from industry on how best to enable tomorrow's scientific and medical breakthroughs.

Overview

In my presentation today, I will address the following points. First, despite great health gains over past decades, the burden of disease continues to grow. However, if we invest adequately in basic biomedical research, we can create the knowledge that will in turn trigger private-sector investment to develop therapies to conquer such diseases. But industry will concentrate its investment in the United States only if we remain research leaders and maintain adequate incentives for R&D investment. I will take these points in turn.

The need and opportunity for new therapies

Let's start by celebrating the great advances in health we've enjoyed in past decades. Mortality from heart disease and stroke has been cut in half in 40 years. HIV/AIDS has been transformed into a disease that's manageable without hospitalization. Life expectancy in the United States has increased by 10 years since 1950. [1]

But we must also recognize the urgent need for new therapies. Death rates from cancer remain stubbornly high. Infectious diseases are becoming resistant to our arsenal of antibiotics. Chronic diseases like Alzheimer's and diabetes are on the rise.

The suffering is immense, and the costs of care could bankrupt us. Just one example is that without effective therapy, the cost for Alzheimer's is estimated to grow to $1.2 trillion a year by 2050 in the U.S. because of the aging of the population. [2]

The good news is that we're in a golden age of disease research, thanks to sequencing of the human genome and development of other powerful technologies. If we make the necessary investments, we can understand why tumors spread, we can learn why nerve cells die in Alzheimer's disease, and we can unlock the secrets of our immune system.

And that knowledge is needed for us to conquer cancer, defeat dementia, and develop vaccines for HIV. Our lack of understanding of what goes wrong in the brain in psychiatric diseases

explains why drug discovery efforts for these devastating conditions have ground to a halt. The equation is simple: no knowledge…no treatments…no cures.

A vibrant public-private partnership drives development of therapies

So how can we best enable the generation and application of scientific knowledge to bring new medicines to patients and the marketplace? The answer to this question requires an understanding of the drug discovery process and stakeholders.

There are two facts about the process that I need to highlight at the outset.

The first is the inherently complex nature of the drug discovery pyramid. For every drug approved by the FDA at the top of the pyramid, the foundation consists of dozens of insights into diseases generated over a period of decades, largely through federal funding of basic, knowledge-driven research. In between, for every 24 drug discovery projects initiated based on those fundamental discoveries, only nine candidate drugs eventually enter human clinical trials, only one of which will make it all the way to approval.

The second fact is that progressing from 24 drug-discovery projects to one FDA approved drug that can help patients takes on average 10-15 years and more than $1.2 billion – a huge and lengthy investment. [3]

Despite these challenges, the ecosystem works thanks to four major groups of stakeholders that coordinate their work in the stepwise process of biomedical discovery and drug development. Their combined efforts have resulted in approximately half of all new drugs today being discovered in the United States.

At the foundation are academic and governmental institutions engaged in fundamental research. Scientists at Rockefeller and thousands of others embedded in academic research institutions across the country conduct the bulk of the critically important work that underlies the drug development process. This knowledge-driven research is funded by the federal government, through competitive grants, and to a lesser extent by philanthropic interests.

Biologists at this stage investigate how the body works in both health and in disease. They strive to understand what makes normal cells turn cancerous, how brain circuits normally function but sometimes malfunction in neurological or psychiatric diseases, and what causes the immune system to mistakenly attack the body's own tissues.

These discoveries also rely in essential ways on advances in instrumentation, tools, and methodologies generated by the harder sciences: physics, chemistry, math and computer science. In recent years, such technological progress has driven an extraordinary acceleration in biomedical discovery. As one example, the cost of sequencing an organism's genome has dropped to a fraction of what it was during the Human Genome Project, both in terms of cost and the time needed to perform the task. Today, many of our laboratories have the ability to sequence an entire human genome in days or weeks instead of the decade and more it once took, and for only a few thousand dollars instead of the roughly $2.7 billion that was needed initially. [4]

While academic research labs generate most of the biological insights into disease, the 10- to 15-year odyssey of making and testing candidate drugs is mostly the work of pharmaceutical

companies. They determine whether potentially disease-causing processes identified by basic scientists can be blocked or corrected. Can a compound be created that prevents, say, a cancerous cell from multiplying? If such a compound is found, then it must be thoroughly tested in the laboratory, in animals, and eventually in humans. This work is typically done on a scale not possible in academic labs.

Two additional stakeholders, disease foundations and small biotechnology companies, help grease the wheels of this translational process. They function at the interface of the first two, helping sift through mechanisms discovered in academic laboratories to identify the most promising ones. They even sometimes initiate generation and testing of drugs, but typically partner at that stage with larger firms, which have the infrastructure and financial resources needed to drive candidate drugs through human clinical trials.

This division of labor has evolved in response to two main factors, one financial and the other cultural.

Financially, the huge costs and timelines of drug development mean that pharmaceutical firms already manage substantial risks to remain financially viable while making and testing drugs. They do not have any additional resources to fund the fundamental inquiries into disease biology that are needed as the foundation for drug discovery. Small biotech firms have even fewer resources. While disease foundations and other philanthropies provide an important assist, ultimately only the federal government has the resources and the time horizon to invest in basic research that may not see any return, at least in terms of yielding viable drug targets, for a decade or more.

Culturally, academia provides the right kind of unfettered environment where the most innovative scientists have the best chance of exploring new scientific leads to break open new fields. Companies, on the other hand, are better suited to conducting the directed studies needed for drug discovery and drug development because of the massive infrastructure and hierarchical teams that are needed.

Although there are exceptions – some biotech companies do engage in basic research, for example, and academic institutions do occasionally test drugs – the centers of gravity I have just described have been in place for decades because they play to the strengths of each stakeholder.

To give an example of the differences in emphasis, at Genentech, one of the largest biotech companies in the world and one that invests more heavily in basic research than most or all of its competitors, we could only afford about 100 postdoctoral fellows working in basic science when I was there. Postdocs are the workhorses of basic research. By contrast, at Rockefeller, a tiny academic institution by most measures, we have roughly 400 in our laboratories at any given time.

Historically, this drug discovery and development ecosystem works. Thanks in large part to the nation's long-term investment in basic biomedical science, as well as in physics, chemistry, engineering, computer science and other disciplines that have created the advanced instrumentation and data-processing tools biologists rely on, the United States has become the undisputed leader in pharmaceutical breakthroughs.

Benefits to patients and the nation of the bioscience enterprise

Most important, this investment has benefited patients, who have more treatment options than ever before and are enjoying longer and healthier lives.

It has benefited the nation, with new and more effective drug therapies responsible for saving trillions of dollars in overall health care costs. The return on the investment is evident when you consider that the annual spend per citizen per year on the NIH is only $100, a minuscule amount compared to the $8,000 per citizen per year spent on health care.

The biomedical investment also boosts the economy enormously, generating high-paying jobs and increased economic activity.

And it has stimulated private investment in this vital economic sector, luring biotech and pharmaceutical investments in the United States. By one assessment, every dollar of public investment in this area leads to an additional $8.38 of private R&D investment.

How can we stimulate private investment and a focus on breakthrough therapies?

The industrial logic of the biopharmaceutical sector is simple. Companies locate their R&D operations near the sites of scientific innovation in academia, both to tap into the best scientists and their discoveries, and to access the highly skilled workforce trained in their laboratories. And all that is needed to drive them to make significant – even multibillion dollar - investments in breakthrough therapies are two conditions: that there is enough knowledge about disease processes to justify the bets, and that they see a path to getting an adequate return on their investment.

The government's role in supporting a vibrant academic research sector through sufficient NIH and NSF funding is therefore essential. This funding generates the necessary knowledge and attracts industry and private-sector investment. In this ecosystem, there is no substitute for the role of federal funding of basic science.

Basic research funding enables the best minds to tackle the most important problems. It can also help direct them to important areas of need. The NIH-sponsored BRAIN initiative is an example of a strategic initiative that builds on recent scientific breakthroughs to break open our understanding of brain diseases. If the academic sector generates the knowledge, the private sector will rush in to apply it.

Conversely, we have seen that reductions in federal support for science over the past decade have triggered a crisis in the biomedical research enterprise, with many scientists spending more time applying for grants than doing research, and with highly trained young investigators turning away from the field to pursue more stable careers.

If this trend continues, not only will we undermine our research enterprise, we will also see industry relocate to the emerging sites of innovation abroad. While U.S. public investment in science erodes, countries in Asia like China, India, South Korea, Taiwan and Singapore, as well as a number of countries in Europe, are multiplying their investments and striving to become new epicenters of biomedicine. And they are succeeding. Already, they are attracting top talent as, increasingly, individual scientists choose to move to countries where securing funding for their work is less difficult.

Beyond supporting the research sector, government must also address also important structural impediments that make our country less attractive to private sector investment.

The key requirements have been well documented by the major trade organizations. They include sufficient protections of intellectual property, tax policies that are competitive with other countries – including a permanent tax credit for research and development – free trade agreements, fair pricing policies, and investments in STEM education and immigration policies that enable companies to draw on both local talent and the best scientists from abroad. [5]

In conclusion, we now find ourselves at a time of huge medical need—but also enormous scientific opportunity. And yet, we're pulling back. Our basic science investment as a percentage of GDP is at its lowest in 40 years. [6]

The bottom line is one that bears repeating. Adequate federal support of basic science is the single most important factor in ensuring the productivity of the U.S. biomedical sector. It provides the foundation of an entire industry and directly spawns the new knowledge from which medical breakthroughs follow. No knowledge…no therapies…no cures.

Thank you for your attention and your continued efforts to support the biomedical enterprise for the benefit of our citizens and the nation.

References:

[1] http://www.cdc.gov/nchs/data/hus/hus11.pdf#022

[2] http://www.alz.org/alzheimers_disease_facts_and_figures.asp

[3] http://www.phrma.org/news-media/related-resources/key-industry-factsabout-phrma

[4] http://www.nature.com/news/technology-the-1-000-genome-1.14901

[5] http://www.phrma.org/sites/default/files/pdf/2014-economic-futures-report.pdf

[6] http://www.aaas.org/page/historical-trends-federal-rd