MILKEN INSTITUTE

ACCELERATING INNOVATION IN THE Bioscience Revolution

REPORT FROM THE 2011 LAKE TAHOE RETREAT

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Proceedings and recommendations from
the September 2011 Milken Institute
Lake Tahoe Retreat

April 2012

Acknowledgments

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About the Milken Institute

A nonprofit, nonpartisan economic think tank, the Milken Institute works to improve lives around the world by advancing innovative economic and policy solutions that create jobs, widen access to capital, and enhance health. We produce rigorous, independent economic research—and maximize its impact by convening global leaders from the worlds of business, finance, government, and philanthropy. By fostering collaboration between the public and private sectors, we transform great ideas into action.

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It's been almost a decade since the Human Genome Project was completed, raising hopes that cures for a whole range of deadly and debilitating diseases might be within reach. But today those hopes remain unfulfilled.

Thousands of brilliant scientists around the world continue to toil away in labs, seeking an end to scourges like heart disease, cancer, and Alzheimer's. But despite their tenacious efforts, tens of millions of patients continue to suffer from these diseases, and many die prematurely. Progress has bogged down—not just because of scientific challenges but also because of financing, regulatory, and structural hurdles.

With lives hanging in the balance, how can we accelerate the realization of scientific advances? Is there a better way to conduct medical research in the 21st century? What will it take to finally realize the promise of breakthrough treatments and cures?

1 Creating a culture of innovation: The challenge behind the Lake Tahoe Retreat

In September 2011, a remarkable cross-section of leaders from the medical research community gathered to tackle these questions at an intensive weekend retreat. This high-level event, convened by the Milken Institute with support from Sanofi, had an ambitious goal: to challenge the notion of business as usual and jumpstart innovation in biomedical science.

The attendees included world-renowned scientists and physicians as well as distinguished names from across the medical field: heads of government agencies, medical school deans, biopharmaceutical CEOs, top venture capitalists and analysts, directors of major medical centers, influential philanthropists, representatives from major foundations, and patient advocates. One participant dubbed the assembled group "the board of directors of the bioscience ecosystem." They were joined by disruptive innovators from multiple industries who were on hand to discuss the tools and business models that promote creativity in other disciplines.

Training so much intellectual firepower on a single goal produced a robust exchange of ideas. In order to make the conversation as candid as possible, the proceedings were held off the record. (As a result, this summary does not identify the individual speaker behind each statement or opinion expressed. However, many of the participants sat down for separate interview sessions that *were* on the record. Some of their comments are included as sidebars throughout this report, with attribution.)

The hallmark of the Milken Institute Lake Tahoe Retreat was a shared sense of urgency. Why?

- → Especially in light of unprecedented R&D spending, the number of new drugs introduced in recent years has been disappointing.
- → Though investigators have made heroic efforts, it's taking longer to introduce new drugs.
- → Venture capital is shying away from biotech startups.
- → The pharmaceutical sector's business model is under pressure. Company valuations have been sinking under the weight of investors' risk aversion.

In short, after decades of success, the great biomedical innovation engine is sputtering, and the medical field *itself* is clamoring to fix it.

Addressing these issues is not merely about retooling an industry that's in trouble. At the end of the day, it all boils down to the human toll: For example, more than 35 million people worldwide suffer from Alzheimer's disease, 2.1 million with multiple sclerosis, and 25 million with cancer.

There is a great deal of impatience with the status quo in medicine. And it's not just coming from the general public; investigators themselves are frustrated with their rate of progress. Individual researchers and their families, like everyone else, have been touched by illness and suffering. In many cases, personal experiences and losses shaped their career choices and continue to motivate their efforts in the lab.

The sheer number of lives at stake brought this extraordinary cross-section of leaders to Lake Tahoe. For 44 hours, some of the best minds in medicine, business, policy, and government pledged to rethink everything: from the way research is conducted to the way risks are assessed to the way companies are structured.

They discussed the impediments to innovation, from the siloed nature of research initiatives ("we have more soloists now than jazz bands") to overregulation ("it's now easier to form a company in Shenzhen than in Palo Alto").

And they explored new approaches that could build momentum, from harnessing the power of crowdsourcing to creating multidisciplinary networks.

Participants were asked to check any preconceptions at the door. They put aside personal and organizational agendas, spoke candidly, and challenged each other. This approach led to probing questions and a constructive exchange of ideas that ran late into the evenings. There was never a moment when the participants stopped listening to each other or became defensive, even when their own turf came under scrutiny. The discussion never devolved into a litany of complaints; the focus remained on solutions.

Many of the investigators and industry leaders present have worked in the medical field for decades, and their commitment to fixing what is broken was apparent. They found a great deal of common ground concerning mission, tactics, and tools. Most important, they came away convinced that collaboration is key.

The medical research community is a wide-ranging network of academic and for-profit biopharmaceutical researchers and research centers, funders and investors, established and startup companies, regulators, marketers, medical professionals, and patients. If this complex and multifaceted ecosystem worked more holistically and seamlessly, the results could transform health care and accelerate cures.

A former high-level government regulator in attendance summed it up: Today most medical research is a golf match, in which the players focus on their individual scores. But what we need is a basketball game, with everyone playing their position on the same fast-paced team. The dialogue at the Milken Institute Lake Tahoe Retreat had that dynamic quality—and it left participants inspired to impart that sense of teamwork and energy to the medical community at large.

This report recaps the discussions, starting with an overview of the current state of bioscience and medical research. It explores the regulatory, financial, competitive, political and other barriers that are slowing innovation, and describes the tangible solutions participants generated for overcoming them.

JAY SCHNITZER
Director of Defense Sciences Office, DARPA

"Saying that we got to our current position of leadership by doing things a certain way and that if we continue to do them the same way we will go forward is completely false. That's driving by looking in the rearview mirror, and that just doesn't work. We have to do things differently. We have to disrupt—disrupt in a huge way how we do the business of innovation in this country, particularly in the biomedical sphere. We have to get ideas from their earliest concepts into products that benefit patients in a much different fashion. That will make a huge difference to our country."

2 The state of bioscience

America's place in the world in the 21st century will depend in large part on its ability to remain at the forefront of lifesaving innovation, said Institute Chairman Michael Milken.

The United States sets the standard for biopharmaceutical innovation, a role that is the result of decades of heavy investment in research and education. Since the 1980s, hundreds of billions of dollars of value have been created. Its regulatory regime, a thoughtful intellectual property system, and the ability to attract foreign scientific talent to top-flight research universities were among the factors that propelled the U.S. into a position of global leadership.

The biomedical industry is a vital source of high-wage, high-value jobs for the U.S. economy. According to the U.S. Labor Department, it directly accounted for 1.2 million private-sector jobs in 2009, as well as $96 billion in wages and $213 billion in output.

Even more important than the economic impact are the results that really count: lives saved, life spans lengthened, and suffering averted.

For all these achievements, however, innovation is still moving too slowly—and the industry itself wants to step up the pace. Its leaders are asking themselves tough questions, privately and in groups, and expending energy and resources in pursuit of workable answers. They're asking whether they are structured correctly for complex research efforts; whether they're sufficiently open to collaboration; whether they have the right businesses models; whether they have the right people; and whether the whole ecosystem works together as seamlessly as it could.

There are concrete reasons why researchers think that the United States should and will remain the global leader in the sector, including market forces and the powerful, world-class institutions that have already been built. There is also a perception that the openness of American society makes the U.S. naturally well suited to scientific pursuit.

Part of the imperative to act is the need to shore up American competitiveness. But the issue is not purely a matter of national interest. There is a belief that if the U.S. can reignite its sputtering innovation engine, the whole world will benefit. Other nations can learn from our experience, implement best practices, and drive advances that will propel the entire research enterprise forward on a global basis. The result would be a virtuous cycle that advances scientific understanding and benefits patients everywhere.

For now, that vision is just a goal. The participants who gathered at the Lake Tahoe Retreat spoke with one voice about the need to jumpstart innovation and to do it quickly. Some went so far as to characterize the current situation an "innovation crisis."

Case in point: On average, about 40 new companies used to be formed each year in Cambridge, Mass., to transfer research insights from academic labs to the private sector for development and commercialization. However, over the past couple of years, that number has fallen to just 15.

Venture capital has been abandoning the biopharmaceutical sector, the attendees agreed. As one participant said, "We have a major paradox in front of us. The potential of science is higher than ever, but the outlook for funding has never been bleaker." The fall-off has been driven by the basic business risks of financing startups, compounded by the inherent complexity of the science involved and ever-higher regulatory hurdles. Without venture capital and ready access to other sources of funding, new business formation will continue to decline, and the U.S. could lose its status as the world's intellectual and commercial

leader in this field. Such an outcome would damage the U.S. economy and imperil many high-wage jobs. It is instructive to note that in 2010, more biotech companies were formed in China than in the U.S.

Another problem: We now spend roughly $100 billion a year on research and development from public- and private-sector sources combined. That's the highest level of investment ever, but the number of new approved drugs has steadily fallen. In 2010, for example, only 22 new medicines were approved, one of the industry's poorest showings, especially when measured against the costs.

Just weeks after the Lake Tahoe Retreat, the FDA announced that 35 new medicines were approved in fiscal year 2011, a hopeful sign. Whatever the yearly fluctuations, however, it is clear that productivity is not commensurate with investment in R&D.

"Despite the remarkable insights we now have into health and disease—such as the Human Genome Project, stem cells, the computational revolution, and systems biology—the output has been slow," remarked one participant.

"What we have now," said another attendee, quoting Nobel laureate Sydney Brenner, "is science with 'low input, high throughput, and no output.'"

Given this flagging momentum, even small increases in productivity would make a real difference. As one industry leader said: "Even modest improvements in quality would be meaningful. Just going from a 7 percent to a 9 percent success rate in early research would change the game."

SUSAN DESMOND-HELLMAN
Chancellor, University of California, San Francisco

"What I feel coming through in this meeting is a sense of healthy impatience about getting back to why we all care about this, which is to make healthier lives and to make sure that our collective efforts make an impact faster and more affordably. There are a lot of things that need to change to do that, but the two most important are that we must come out of our collective silos and that we must challenge conventional wisdom."

The financial picture

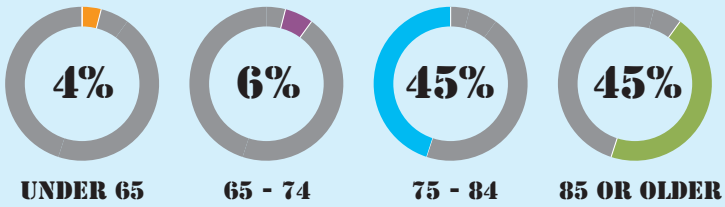
Large pharmaceutical companies face dwindling output and soaring costs. Merck, for example, was the most admired company in the world for much of the 1980s, and one of the most valuable. Other pharmaceutical companies, with huge research budgets, were also considered blue chips, and were highly valued for their scientific acumen and boldness.

Conducting research to build up drug pipelines was seen as a linear process: invest, conduct R&D with your own research talent, wait, harvest the benefits in the form of a blockbuster drug. Indeed, many business school case studies touted the success of pharmaceutical companies—specifically their research operations.

But over time, this business model has come under increasing strain, largely because of the growing complexities of science, the long time horizon required to develop treatments, and uncertainties regarding the drug approval process. As one participant said: "We hear too often from our investors that we should cut R&D spending and instead do share buybacks."

ALZHEIMER'S DISEASE FACTS

Age distribution of Alzheimer's patients in the U.S., 2010



Incidence

454,000 new cases annually in the United States

The incidence of Alzheimer's is highly age dependent.

INCIDENCE IN THE U.S. (2010):
Ages 65 to 74: 5,300 in 100,000
Ages 75 to 84: 17,000 in 100,000
Over age 85: 23,100 in 100,000

Prevalence

5.4 million cases in the U.S.
35 million to 37 million cases globally

Gender: Nearly 2 in 3 of diagnosed are women.
Race: Studies have also indicated a higher prevalence in Hispanic and African-American populations.

Mortality

82,476 annual deaths (2008 figures)
Note: Deaths from dementia can be ambiguous; it may not always be listed as the underlying cause of mortality. Deaths attributed to Alzheimer's disease increased 66% from 2000-2008.

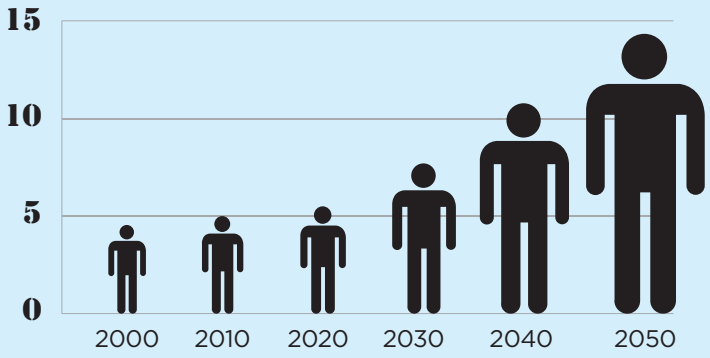
Overall: 6th leading cause of death
Ages 65 and over: 5th leading cause of death

A global crisis

Over the next 20 years, the number of patients with dementia is anticipated to increase by 40 percent in Europe, 63 percent in North America, 77 percent in the southern Latin American cone, and 89 percent in the developed Asia Pacific countries.

By comparison, expected increases are 117 percent in East Asia, 107 percent in South Asia, 134-146 percent in the rest of Latin America, and 125 percent in North Africa and the Middle East.

Projected number of people ages 65 and over with Alzheimer's disease in the U.S. (in millions)



Economic burden

UNITED STATES (2010)

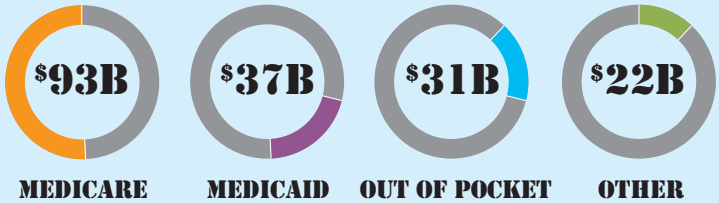
Direct costs in medical expenditures: $183 billion (up $11 billion from 2009)
Indirect costs: NA
Unpaid care: $202 billion
2009 research budget of the leading nonprofit research organization (Alzheimer's Association): $26 million (2009)
Projections: Payments are projected to hit $1.1 trillion by 2050, including a seven-fold increase in Medicare and a five-fold increase in Medicaid.

GLOBAL (2009)

Direct costs (medical and nonmedical): $352 billion
Indirect costs: NA
Unpaid care: $251 billion

Clinical trial enrollment

Patients in active, non-recruiting intervention trials: 23,961
Number of active, non-recruiting intervention trials: 56



Aggregate costs of care by payer in the U.S., 2010

FRANCIS COLLINS
Director, National Institutes of Health

"There's never been a time where we've had a greater outpouring of discoveries about the nature of disease, many of them from basic science uncovering the molecular causes of both rare and common diseases. And yet paradoxically, the ability to turn that information into clinical applications seems to have slowed down. Government support of medical research has been dwindling, venture capital is hard to find for biotechnology, and pharmaceutical companies are reducing their investments in R & D. If there was ever a time when we all need to get together in the same room and figure out how to take this wonderful scientific opportunity and apply the most bold, audacious principles of innovation to make those products happen, it is now. But we cannot afford to be inefficient. We can't afford to waste time. We can't afford to waste resources."

While Big Pharma has seen its price/earnings ratios decline, valuations of the most cutting-edge startups and of smaller biotech companies have held steady—leading to the conclusion that innovation is still highly prized. Even so, the typical deal to acquire a startup or a small company has changed. In the past, large companies licensed the results of promising research and paid for additional R&D to see it through to commercialization. But today small firms want to sell themselves *in their entirety* to larger pharmaceutical companies, not just license their work. According to one former pharma CEO, many venture capital investors have become nervous about the long-term outlook for the sector and want to cash out as soon as possible. Waiting patiently for returns was once a hallmark of venture investing, but it's no longer the norm in this sector.

NIH Director Francis Collins urges the assembled group to think big and set audacious goals for what bioscience can achieve.

One investor/analyst recounted his experience with more than 200 deals over the decades: "In the last six years, there have been 305 major biotech acquisitions, about 40 a year. That is actually fairly robust. Of these companies, just over half were private when they were bought; the rest were public. Eighty-four percent of the companies focused on products in Phase I, Phase II, and Phase III trials. Sixteen percent of the companies were pure technology platforms—tools that aided or abetted drug discovery. Most of the acquisitions were based on small molecules with 43 percent based on proteins and large molecules." He pointed out that the average valuation of the acquired companies was $1.6 billion, which indicated young, innovative companies were not undervalued. As he put it: "People will pay for innovation. If you hit the innovation curve and a pharmaceutical company wants to buy you, they will pay five times the invested capital. That's a big win. And in fact if you look at the last six years, the pharmaceutical industry has spent $240 billion buying biotech companies, which is a very robust number."

The same investor noted that "if you have a first-in-class, best-in-class, very novel molecule, or a very novel tool, there will be a huge premium paid for that and you can make a very satisfactory return." Despite the returns, however, investors in both the venture and public markets have lost their appetite for risk.

Optimism about prospects for the biopharmaceutical sector has waned for multiple reasons, including reduced government spending, high regulatory hurdles, and longer development times. In a period fraught with uncertainties, investors are loath to take on more risk.

Behind the innovation slowdown

What are the drags on biomedical innovation? Attendees identified the factors below as areas that need to be addressed:

- An increasingly conservative perspective on investment in this sector.
- A failure by the funding and regulatory communities to re-examine risk models that many view as overly rigid. On the regulatory front, for example, a terminally ill person can't choose to opt in to an experiment without huge roadblocks due to the fact that all patients (even those who are dying) are treated with the same risk profile.
- A failure to appreciate what can be learned from failure.
- Inadequate collaboration among organizations, institutions, and even competing companies, despite the introduction of new technologies that should make data-sharing and cooperation more feasible than ever. This stems from the insularity and siloed approach that governs most research communities.
- A failure to quickly adopt — or even test — new research and problem-solving tools such as crowdsourcing.
- Regulatory approval processes and application processes for government grants that can be cumbersome, time-consuming, and opaque. The FDA's approval process has lost some of its former clarity and has added additional steps for some types of drugs.
- Inadequate collaboration between regulatory scientists and industry.
- Inadequate access to certain types of data (failed drug trials, "outmoded" drugs, large patient groups, etc.) because of privacy constraints and the slow adoption of electronic medical records.
- A general unwillingness to embrace new incentives, such as prizes awarded for successes.
- A failure to communicate the sector's positive purpose and story.

Most participants agreed that these issues are frustrating, but no one was so pessimistic as to believe the problems can't be addressed. There was a general consensus regarding what should be done and which solutions offer the greatest promise.

3 Research

The need for multidisciplinary approaches

Medical advances are complex and require a multidisciplinary, multisector approach. We also know that openness fuels innovation; *open innovation* requires platforms linking people around the world and across organizational boundaries.

In some ways, this notion violates one of the traditional operating rules of science, which is to hold onto discovery and ideas rather than sharing them openly. But it *is* possible to conduct research differently, and the headway made against HIV/AIDS proves it. As one government official asked: "How can we recapture the urgency of the AIDS model, which brought researchers together with a shared goal that transcended so many barriers?"

The prevailing culture in the research community must open up to broader influences. As one researcher put it, "Disease and treatment models have typically been the product of research undertaken from a single discipline's perspective. Conceptual models developed around such a narrow focus may no longer stand up to scrutiny when examined from a multidisciplinary point of view."

FasterCures Executive Director Margaret Anderson outlines her vision for a more collaborative, patient-centered research model.

Unfortunately, most research institutions, pharmaceutical firms, and biotech companies have been *talking* about open, multidisciplinary research but not actually putting it into practice. Too few organizations have truly embraced this way of doing business. But some companies and some institutions (like MIT's Media Lab and the Broad Center) have been successful at opening up the innovation process and can serve as models.

Broader, deeper, and more intense collaboration is needed among investigators working across disciplines, and even between firms and institutions. "In 1993, when I went to MD Anderson, they viewed Sloan Kettering as a competitor. That's no longer the case – they're focused on the same goal," said Milken Institute Chairman Mike Milken. "Biotech and Pharma used to consider themselves competitors, but now they're both in a fight for survival."

MARGARET ANDERSON
Executive Director, FasterCures

"We cannot conquer disease without engaging patients. One way to bring patients into the system is by ensuring the data collected through electronic health records can be used for research purposes. EHR systems for clinical research can improve the clinical trial process by finding patients who match specific trial criteria, thereby speeding up accrual. These will also connect the trial to patient records, ensuring that patients and their providers are kept abreast of trial information and treatment protocols in real time."

Creating new structural models and management skills

One academic researcher described how his work requires a team of physicists, computer and laser engineers, M.D.s, geneticists, and a number of other scientists. He pointed out the difficulty of getting these groups to understand each other and communicate effectively. As the director of a lab, he views himself as a curator of knowledge as much as someone who designs and carries out experiments. It's his job to understand a number of highly technical disciplines to make collaboration work. As he put it: "Understanding and translating between different disciplines is required when you bring researchers together to solve a problem."

The "knowledge curator" function can be taught, but it remains relatively rare. Even so, it is needed. The question is how to codify that role and train people to fill it effectively in science, academia, and industry.

Running a lab full of highly educated, creative people with unique traits and multiple viewpoints is no small challenge, but scientists rarely study the subject of management. This gap in their training will only be compounded as research becomes more integrated. Teaching investigators how to manage people, along with how to manage the research process, can decrease tensions and increase productivity and innovation. As one participant said, "We need trust, transparency, and space for collaboration." Another noted: "I spend a lot of time with my academic teams and in the companies I started helping them learn how to interact in a positive way."

Communicating becomes more challenging as you add greater numbers of participants with different backgrounds and expertise to a given project. As innovation processes become more open, managing the flow of ideas will grow more difficult, too. Collaborative software platforms and programs will be a crucial piece of the puzzle.

Individuals face tangible career and funding risks when they venture outside their disciplines, especially in academic institutions. Traditional disciplines and departments continue to hold enormous sway in research institutions for a variety of reasons, including tenure.

Most universities and academic institutions are typically constructed around disciplines, not problems. This mentality is starting to change, albeit slowly. Only a few institutions have moved past their time-honored boundaries. One participant described implementing this sea change: "Typically what happened in an academic institution was that you were in a single department or discipline. So we created cross-disciplinary institutes. For example, we created an institute for cell engineering, and it didn't matter what faculty appointment you had to work there."

Another researcher recounted breaking out of the siloed mentality by setting up an independent institution to pursue an integrated, systems approach to biology that went beyond the conventional university framework.

Shaking up a culture of conservatism

Even at the most conservative medical schools, government research institutions, or major pharmaceutical firms, hidebound traditions must be upended. As one researcher put it, "You can either be a 'why?' organization or a 'why not?' organization."

Conservatism affects private-sector firms as well as research institutions and universities. "Almost all companies risk becoming rigid as they grow," said one investor and business leader. "They start to take themselves too seriously. From a historical point of view, large companies have a hard time with innovation. Blockbuster didn't invent Netflix. Wal-Mart didn't come up with Amazon. Google didn't invent Facebook, and Facebook didn't invent Twitter." Another participant noted that "when Steve Jobs developed the iPod, he did so in secrecy – not because he was concerned that a competitor would steal the idea, but because he feared Apple's corporate white blood cells would kill it."

The impetus for a major corporation to reinvigorate its culture needs to come from the top, said one participant. "You need CEO involvement to create opportunities for companies to work together with each other and with universities. Scientists don't feel they have the license to do that."

That observation was echoed by a Fortune 500 CEO from outside the medical field. "The CEO must be the company's chief innovation officer," he said. "My calendar probably looks a lot different from most CEOs'. I spend at least 50 percent of every day just thinking about the next big idea. If I have eight innovators in a company of 200,000, then I've got more than anybody else. And I don't have eight." In other words, innovation—*even when it is a stated goal coming from the CEO*—remains rare.

Harnessing the potential of young investigators

Research often requires multiple degrees—perhaps an M.D. and a Ph.D.—and that sets up a paradox: Most dual-advanced-degree investigators don't complete their academic studies and training until their mid-30s, but the most productive period for researchers is in their 20s. To alleviate this problem, new programs should be developed to combine disciplines, or to combine full proficiency in one field with good, working-level knowledge of related areas.

Sanofi's Elias Zerhouni, a former NIH director, argues for a cross-disciplinary approach to research that erases traditional boundaries.

Luckily, there is some experimentation going on in this area. However, as a medical school dean said, "The best place to influence innovation is in medical schools, but the hardest thing in the world is to change a medical school's curriculum."

Young investigators may be the source for brilliant new ideas going forward. But constrained research budgets could have a serious impact on their ability to stay in science. We need to ensure that they have a stable funding pipeline, whether that support comes from government or philanthropic sources.

The United States also needs to reform immigration policies so that outstanding researchers receive green cards when they finish their training. As a nation, we can't afford to educate the best and the brightest —and then deny them the chance to stay and work here.

ELIAS ZERHOUNI
President of Global R&D, Sanofi; former Director, National Institutes of Health

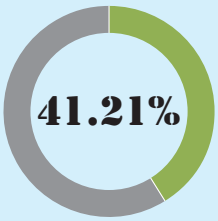
"I have a very deep sense that we need to fund young investigators early and find ways of supporting that. So to me, it's very important to be open about talent—anywhere that talent is—and not lose the ability we've had in this country for them to come here. I'm an example of that. It doesn't matter who you are. It doesn't matter where you come from. You can, in fact, make a difference and contribute here. And if you do, we recognize you. And that ability, I think, is something only America has had for the past 50 years. I hope it will have it for the next 200 years."

CANCER FACTS

United States

Incidence (2011)

1.3 MILLION
new cases annually
Age-adjusted incidence rate:
464 in 100,000



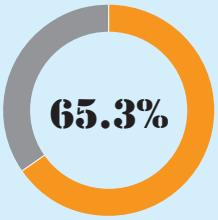
LIFETIME RISK:
1 IN 2 diagnosed

Prevalence

11.9 MILLION cases

Mortality

571,950 deaths annually
2nd overall leading cause of death
Age-adjusted mortality rate:
181.3 in 100,000



5-YEAR RELATIVE SURVIVAL RATE

U.S. economic burden (2011)

Direct costs (medical):
$102.8 BILLION

Indirect costs (morbidity and mortality):
$161 BILLION

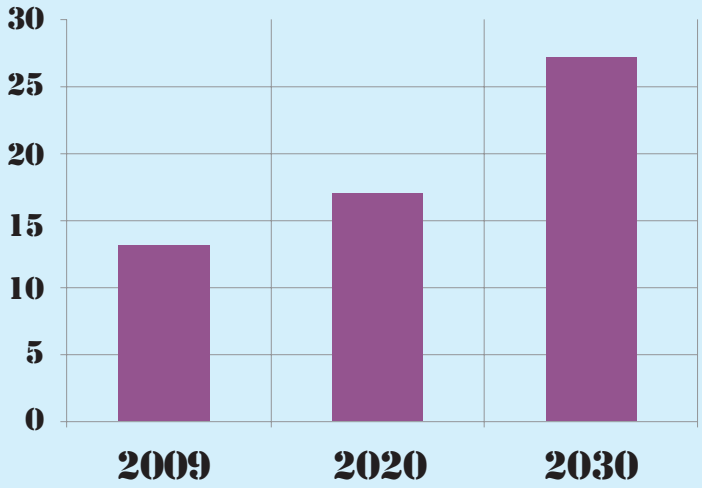
A global crisis

Incidence
12 MILLION
new cases annually

Prevalence
25 MILLION
total cases

Mortality
7 MILLION
deaths annually

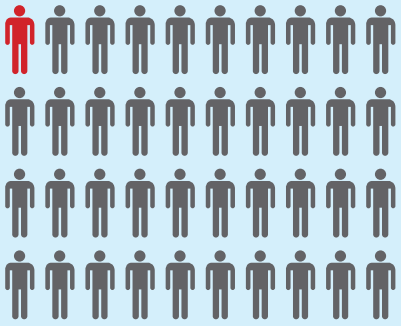
Global projections - New annual cancer cases (in millions)



Prostate cancer in the U.S.

Each year, prostate cancer alone accounts for 240,890 new cancer diagnoses.
There are 2,355,500 total cases in the U.S.

Ages **40-59: 1** in **40**



Ages **60-69: 1** in **15**

Ages **70** and older: **1** in **8**

Focusing on translation

Researchers and industry executives alike recounted promising scientific breakthroughs that died on the vine because of a lack of resources and the lack of a clear path forward to take the ideas from an academic lab into the marketplace.

To increase our odds of bringing more promising ideas to fruition, participants believe we need to strengthen our infrastructure for translational research, which is the critical bridge between basic and clinical research. More effective translational efforts such as biomarkers, target and pathway validation, animal models, and small pilot clinical trials will speed up the process and increase our odds of getting to a viable therapy quicker.

The newly created NIH National Center for Advancing Translational Science (NCATS) is one path forward. NCATS was put in place to work with all sectors to develop innovative ways to bypass time-consuming bottlenecks in the R&D process.

Embracing failure

Organizations have to change the way they view failure, recognizing it as an inevitable—and potentially enlightening—part of the innovation process. That notion has been around since at least the time of Thomas Edison, but acceptance of failure as a routine cost of doing business comes hard to corporations—and also to the sort of high-achieving individuals who are drawn to prestigious research projects. Fear of failure inhibits risk-taking and can calcify an organization.

Ideally, said one participant, you fail fast in order to conserve resources. But no researcher wants to end a project early and give back the money. As a result, they continue working, clinging to hopes of better results, or they use their remaining resources to pursue related efforts.

This model has to give way. Open attitudes and frank acknowledgments of failure need to become the norm. One research director went so far as to suggest that certain types of failures should be rewarded since they provide such valuable teaching opportunities. "I want to fail even more," he said.

We have vast new computational power at our disposal, said Peter Diamandis of the X Prize Foundation. But bioscience has barely begun to harness its potential to process vast quantities of data and deploy tools like crowdsourcing to solve complex problems.

Deploying new tools

With the advent of potentially game-changing technologies that support investigation, research practices cannot remain static. One attendee, who leads a major research institution, said: "There's an explosion of technology that's giving us information about medicine. Genomic sequencing is the most extraordinary [example]. Over the past 11 years, the power of sequencing has increased by one million-fold. No previous technology in history has increased in power that fast. But how do we translate this research and technology into new treatments?" Our newfound knowledge of the human genome will transform the way research is conducted—perhaps right down to whether the use of mice models will continue to make sense.

Sequencing involves many terabytes of data, however, and translating that information into useful research is probably beyond the scope of any single entity. It will require ambitious coordinated efforts between different types of organizations. Successful collaboration on this scale will require platforms, processes, and tools. Which institution or entity will plan and build the infrastructure needed to make this a reality?

Advances in computing are expanding our knowledge base exponentially. This increase in computational power and speed has enabled researchers to process massive amounts of data, develop synthetic approaches to biology, and "test" molecules using simulations. This can be a boon to the previously mentioned "fail fast" dictum, since some compounds can be rapidly weeded out through simulations. But the biosciences have yet to take full advantage of the computational power now at their disposal.

Opening up innovation

It's no secret that "the more information you make available to researchers, the faster you can innovate." Open innovation can link the efforts of multiple researchers—and beyond that, it can even bring *patients* into the process. While the group expressed some skepticism about patients accurately reporting their own findings, 23andMe was highlighted as an example of successful patient participation.

Social media offers new avenues for creating these information-sharing networks. Disease groups have already begun using Facebook and other social media tools to communicate, form groups, and keep each other abreast of developments. "We don't need to attack scientific problems in any one physical location with any one academic discipline," said one leading researcher. "Innovation will emerge from multi-disciplinary virtual networks." Another observed that over the next decade, social media could turn out to be a valuable approach to managing clinical trials.

Crowdsourcing

Crowdsourcing—a process that trains the power of a large group on a specific problem—is another approach with huge potential. The "hit rate" for solutions from crowdsourcing is quite high, in some cases up to 40 percent. That's a remarkable finding, especially when you consider that problems are generally put out on the web for this sort of open brainstorming because they are, by definition, beyond the problem-solving ability of the organization posting them.

In addition, crowdsourcing—given its open, informal structure—is cross-disciplinary by design. In some cases, even gifted amateurs and people without direct experience with the problem provide valuable insights and solutions. "Lots of failed compounds and public-domain compounds exist and can be researched," observed one innovator. "Can we ask the crowd if there is a valid use for these compounds?"

One way to use crowdsourcing is simply to crunch large amounts of data. This strategy has worked in a number of instances, dating from NASA's decision to open up its Mars landing data files and ask others to help process the data.

DENNIS GILLINGS
Chairman and CEO, Quintiles

"It's important to share successes, because of course that begets other successes, and human beings learn from that. But sharing failures in the drug development process is also important . . . Understanding what went wrong in fairly similar drugs can help with the design of programs and the design of new drugs that overcome those difficulties. The trial-and-error process gets accelerated when both successes and failures are shared."

A large group brings a massive amount of insight and experience to bear on a particular problem. One example: A Canadian mining company once asked a crowd of experts to help it find gold, offering a prize of $500,000 to anyone who correctly identified areas where it could mine. That $500,000 incentive led to gold findings worth $10 billion to $15 billion.

In the biosciences, crowdsourcing has already been used to determine protein folding as a means to understand molecular structures. One participant suggested crowdsourcing could be used to determine why the prescription drug Vioxx worked so well in some people but had catastrophic side effects in others. Using this approach to determine the genetic makeup of people who responded so differently could be useful in finding how the drug might be employed in the future.

Crowdsourcing does raise concerns about how for-profit and non-profit private-sector firms can protect their intellectual property. A company that has invested time and money in R&D might feel reluctance to use these techniques to search for solutions. Though transparency is ideal, companies feel a natural inclination to maintain secrecy around IP, especially when they've sunk billions into research.

However, one participant urged an end to that mindset. "Many institutions, including MIT, put their courses online. They don't worry that they're giving away their IP," he said. "And if you want to learn accounting, you can just buy a book and teach yourself. Those books don't destroy formal accounting courses. The risk of putting information in the public domain is not that great. We overestimate it."

MICHAEL IDELCHIK
Vice President, Advanced Technologies, GE Global Research

"The precompetitive space is important, and data could be shared. There are certain standards of privacy that need to be accommodated within that data sharing. There is understanding of IP and understanding what actually is precompetitive, which could get some people concerned, especially in small biotech firms.

"But in my view, the knowledge base of the industry, which is accumulated in the FDA and in a lot of pharmaceutical companies, is really not used properly today. We have to deal with the data that we have and make them accessible to a larger community through either the FDA, or under the FDA's guidance, or under industry cooperation and guidance. That will really accelerate a lot of invention, a lot of new ideas, a lot of new technology. It will get them to market faster."

Solutions for research

- **THINK BIG.** "Big, hairy, audacious goals are where it's at," said the head of one government agency. A Fortune 500 CEO put it this way: "Bold goals stir souls. It's all about developing impossible goals and unrealistic timelines and challenging people to accomplish the impossible." One such ambition might be the creation of a therapeutic roadmap for cancer through a concerted effort involving academia, industry, and government. Another might be making major progress against a specific disease like Alzheimer's. We need only look to the patient-driven, highly collaborative fight against HIV/AIDS to see what kind of swift progress is possible when the bar is set high.

- **INNOVATE HOW WE INNOVATE.** Research is typically a linear process, in which ideas often get far down the line before someone asks a simple question that invalidates the direction. More open innovation and even cooperation among competitors might bring validation to an earlier stage in the process.

- **PUT GREATER FOCUS ON TRANSLATING BASIC DISCOVERIES INTO PRACTICAL APPLICATIONS.** Invest in initiatives that increase our odds for bringing a breakthrough to market faster. One tangible way to do this is to support critical translational research efforts such as the NIH's new NCATS, which aims to streamline processes that could advance progress for all diseases.

- **DON'T BE AFRAID OF NEW TOOLS.** Crowdsourcing, social media, and other new tools can accelerate innovation by harnessing more brainpower than has ever been deployed.

- **FOCUS ON THE DISEASES WITH THE GREATEST NATIONAL IMPACT FOR PILOT OR DEMONSTRATION PROJECTS.** Good candidates include obesity, diabetes, and neurological disorders.

- **DEFINE THE METRICS OF SUCCESS.** We should learn from success stories, working backwards to understand what mechanisms actually worked and employing best practices more widely.

- **SUPPORT YOUNG INVESTIGATORS.** Ensure the availability of funding for innovative young scientists, since most breakthrough work occurs early in an investigator's career.

- **CREATE A TASK FORCE.** We need a broader, more diverse group of advocates and supporters charged with bringing the public and private sectors together to keep information flowing and build support for multidisciplinary initiatives.

- **DEFINE THE PRECOMPETITIVE SPACE.** The early stages of research represent a crucial period when investigators can collaborate before someone captures ownership of intellectual property as well as market share. However, getting industry players to collaborate with each other and with academia remains a significant challenge because of their natural inclination to protect IP. The legal complexities at this stage, including anti-trust and IP issues, need to be redefined.

- **RE-EXAMINE THE WAY WE VIEW RISK.** The current way we address risk is a one-size-fits-all approach with all patients bound by the same rules. We have to ask why our view of risk does not allow for individual choice—for example, allowing gravely ill patients to opt in to trials.

4 Regulation

Regulation plays a pivotal role in the biomedical field. Patient safety is the overriding goal—but it's vital to balance that mandate with the need to efficiently evaluate urgently needed treatments. "The purpose of regulation is to promote public health. We need to refocus the conversation accordingly," said one former regulator.

Attendees at the Lake Tahoe Retreat expressed concern about the effect of the regulatory process on innovation. A less-than-transparent, often-cumbersome approval process was viewed as adding to the uncertainty around drug development—and time and uncertainty are factors that discourage investment.

We need to recapture the collaboration and urgency we brought to the fight against AIDS and apply that model to the search for other disease cures, said FDA Commissioner Margaret Hamburg.

Concern was expressed about how well investors actually *understand* the drug approval process; more communication is needed. As one participant said, "From a market and investment perspective, the best regulations are the ones that are the most transparent."

Participants discussed the issues facing the FDA, noting that the agency has been constrained by a shortage of trained and experienced regulatory scientists. Programs are needed to educate scientists to work as regulators, and some participants discussed proposals to use external experts to fill the gap. They argued that the FDA needs additional funding to increase the depth of its expertise and keep the review process moving efficiently and effectively.

MARGARET HAMBURG
Commissioner, U.S. Food and Drug Administration

"We need new tools, new understanding, new strategies and approaches to help us as efficiently and effectively as possible to review the medical products that come before the FDA. And we need to be working closely with industry and academia to build out the science that's critically needed for medical product development and review. We also need to look at important issues of regulatory reform within the walls of the FDA so that we can better serve the people, ultimately, in terms of being a gateway for innovative products to move from the laboratory into peoples' homes and into our health-care system to make a difference."

Regulatory solutions

→ **EARLIER ENGAGEMENT WITH COMPANIES BRINGING PRODUCTS FORWARD.** As one participant said: "When I look back at the most important factor in getting a drug through the approval process, it was early discussion with the FDA." A more integrative approach between investigators and regulators can make the process more efficient.

→ **MAKE SURE THE FDA HAS THE HUMAN CAPITAL IT NEEDS.** The regulatory process itself requires innovation, and we need to offer more training programs in regulatory science. The private sector can recruit quickly, but the FDA has difficulty acquiring and retaining talent. Addressing the current staffing gap may require participation by experts outside of the agency.

→ **LOOK TO THE FAA.** The Federal Aviation Administration's model of outsourcing some quality-control work to industry-expert advisory boards is a possible model. Other regulatory agencies — both within and without the U.S. — should be studied as well.

→ **REMOVE REGULATORY REDUNDANCIES.** Companies should have to do each step only once.

→ **REMEMBER THAT CHANGE IS CONSTANT.** Even if we devised an ideal regulatory system, it would become obsolete at some point. It's not about fixes, per se; it's about setting up a continuous innovation model.

→ **ESTABLISH SAFE-HARBOR PROVISIONS.** The National Institutes of Health created a fund to support high-risk research. Three to five percent of budgeting should go toward a safe-harbor space where innovation can happen and companies can work together without the cloud of antitrust issues.

→ **MAKE MORE INFORMATION AVAILABLE.** Build a program across the industry to make the FDA's database of failed drugs available to researchers interested in applying new insights to old or dead-end research avenues. That's how AIDS got tackled effectively. IP is the big barrier to this.

→ **CREATE "OPT-IN" PROVISIONS FOR TRIALS.** Allowing patients to join research trials on their own initiative would shift the focus. Today we are heavily focused on the risks, but if we allow patients to make their own decisions about furthering cures, researchers can balance risks and potential benefits more realistically.

→ **MAKE IT EASIER FOR PATIENTS TO WAIVE THEIR HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) RIGHTS.** If patients are willing to share their information, it would open up more data for research and review. If HIPAA can't be modified, use other means (such as Facebook and other types of social media) so that individuals are empowered to share their personal information in an open-source fashion for the benefit of science if they choose.

→ **EXAMINE THE FDA'S RISK MODEL.** Society has become more risk averse. One participant remarked that clinical trials of the Salk polio vaccine probably would not have been allowed in the current climate. But zero tolerance for risk results in zero reward. The FDA's risk model and mindset must be re-examined to make certain it does not stifle innovation, even as it keeps patient safety paramount.

5 Financing

The current model for conducting research tends to be focused around a single company doing all the work on its own, or perhaps as the result of an acquisition. This model concentrates rewards, but it also concentrates costs and risks. In addition, it entails costs that are harder to quantify, such as when a talented team dedicates years to working on a drug that fails to make it through trials. This model has led companies to favor projects that could produce blockbuster drugs rather than drugs targeting smaller groups or treatments that involve riskier approaches to research.

The industry needs new models for allocating resources and managing risk. "Research is being directed to the lowest-risk areas, not to where the greatest impact would be," said one industry leader. "Scientists are innately conservative. In a field whose mantra begins 'first, do no harm,' there will be conservatism. That's not a criticism; it's a reality. We need to be aware of this dynamic."

Conservatism is not only a characteristic of research institutions and large firms. The broader investment community has become overly cautious as well. The capital markets are not viewing research favorably. Another industry leader recalled that investors' unease with his ambitious drug development research agenda "caused me to have to take my company private. We were publically traded and the market didn't believe in the risks I was taking. The analyst community did not understand the premise."

"We've become risk-averse as a society," said one of the innovative scientists in attendance. "We're reluctant to try crazy ideas. Unless we learn to value big, potentially disruptive ideas, we won't see transformational breakthroughs."

Risk management

Participants agreed that the portfolio approach offers a good way to manage risks and pick winners. One company measured risks to determine its research bets by gathering an enormous amount of internal information that it uses to build a model encompassing regulatory risks, marketing risks, and almost every other type of risk imaginable. It then uses this model to construct *another* model that attempts to forecast return on investment. The company is now moving toward designing diversified research portfolios that reduce the risk of losing all of its investment to less than 10 percent. Finally, this firm makes its investments and manages its risks by assembling research portfolios that share development costs to the extent possible with outside partners so that "if the portfolio is six drugs, the development costs are not six-times-one, they are three-times-one."

BETH SEIDENBERG
Partner, Kleiner Perkins Caulfield & Byers

"Venture capital investing is tremendously risky. But, on the other hand, if the venture capitalists do not embrace risk, then quite frankly, we're not doing our job. The problem that we're having now is that there's tremendous uncertainty in the regulatory environment, in the reimbursement environment, in the broader health-care system with health-care reform on the horizon, and in the financial markets. There's more and more risk aversion, and the financial markets now only look quarter to quarter. But it often takes 10 years to have a drug candidate get to market. And then your probability of success is less than 10 percent. Talk about risky."

DIABETES FACTS

Incidence (2011)

1.9 MILLION

new cases annually among Americans over age 20

Prevalence

25.8 MILLION

total cases in the U.S. That's **8.3 percent** of the nation's population.

18.8 MILLION

Diagnosed

7 MILLION

Undiagnosed (40 percent of patients are unaware they have diabetes)

Projections

Total prevalence estimated to rise to

44.1 MILLION

by 2034

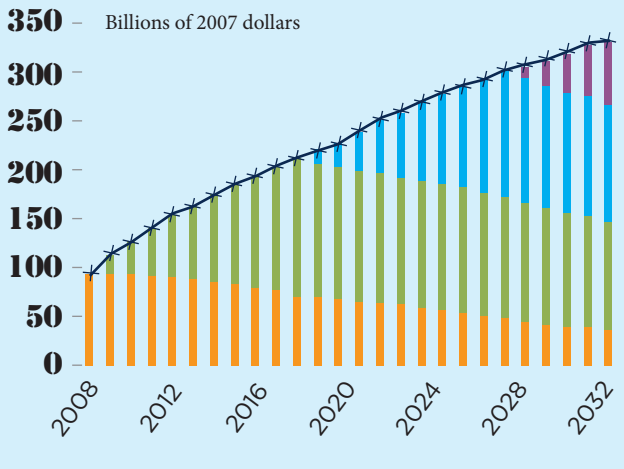
Mortality and Morbidity

71,832 DEATHS

in 2007 (and listed as a contributing factor in an additional 160,000 deaths)

Diabetes is the leading cause of kidney failure, non-traumatic lower limbs amputations, and new cases of blindness among adults.

Diabetes is a major cause of heart disease and stroke, and the seventh leading cause of death in the United States.



Projected direct spending on diabetes and its complications for different cohorts, 2008–2033

Economic burden

United States (2007)

It is estimated that one-third of Medicare dollars are spent on people with diabetes.

$116 BILLION
Direct costs of medical expenditures

$58 BILLION
Indirect costs (including disability, work loss and premature mortality)

$336 BILLION
Projected direct costs by 2034

2010 research budgets for the leading nonprofit research organizations:

$33.5 MILLION
ADA RESEARCH FOUNDATION

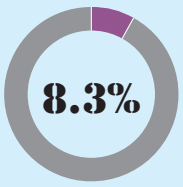
$107 MILLION
JUVENILE DIABETES RESEARCH FOUNDATION

A global crisis

Prevalence:

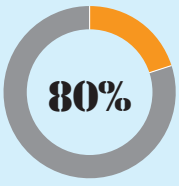
346-366 MILLION

total cases in 2010 (8.3% of the world's adult population)



Regional variation:

80% OF PEOPLE with diabetes live in low- and middle-income countries. The highest regional rates are for North America and the Middle East/North Africa.



Projections:

Prevalence estimated to rise to

552 MILLION

cases by 2030

Direct cost of medical expenditures 2010:

$465 BILLION

FRANK L. DOUGLAS
CEO, Austen BioInnovation Institute

"Unfortunately right now, at the FDA, because of societal demands, there is the view that there should be no side effects. The venture capital community especially has become very risk averse, and I think we need to bring it back into balance. When we have a very deadly disease, or a disease that is chronic and that takes a tremendous toll on the patient or the society, then we need to try to innovate new solutions. Some of those innovations may carry with them risks, so we need to understand the risk, we need to monitor, but we need to push ahead nonetheless."

Sharing costs—and by implication, sharing risk—can take a variety of forms. A company could, for example, invite an outside private-equity investor to participate in the development of a new drug. The goal would be to have the investor put money into R&D, share in the winnings, and partly compensate the pharmaceutical company if the drug fails and there are losses.

That type of risk-sharing arrangement is similar to the use of contingent value rights (CVRs). In these deals, an investor makes a small cash payment up front to participate in the development of a drug—or to buy or invest in a firm—with the final price determined by the value created by the success of the drug, based on an agreed-upon formula. A variation on this model involves forward-selling the royalty streams from a drug under development.

Another approach involves forming a consortium of large pharmaceutical companies that identify areas of interest. If more than half of the companies agree on a direction, the consortium seeks out early-stage research. The advantage of this model is speed, entrepreneurial acumen, and the ability to work well with academic institutions.

Although small venture capital–backed companies are now more eager to sell themselves to big pharmaceutical firms than to license their products, Big Pharma is not as enthusiastic about this type of arrangement because it involves so many other costs, from real estate to labor (especially in Europe, where there are greater labor protections).

Solutions for attracting capital

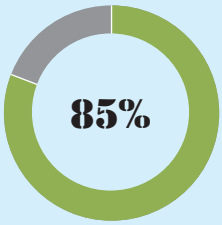
→ **CHANGE THE TAX CODE.** Pre-1986, companies in other industries could write off risk the same way oil companies wrote off dry wells. If you drilled ten holes, and nine came in dry but the last one was a gusher, you could write off the cost of the nine dry wells against the proceeds from the gusher. Research-driven companies should have the same benefits as oil companies.

→ **SHARE DEVELOPMENT RISKS WITH A DRUG'S BENEFICIARIES.** Type 2 diabetes and certain other diseases represent huge costs to insurance companies and businesses, many of which self-insure. Why not form consortiums of the groups that would benefit if a particular type of research were successful? If, for example, research were undertaken to eliminate Type 2 diabetes (or obesity), thousands of self-insured companies, as well as insurers, would benefit. Why not go to those groups for investment?

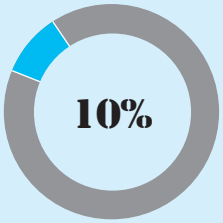
→ **FORM RESEARCH CONSORTIUMS AROUND SPECIFIC DISEASES.** Large pharmaceutical companies can fund small companies or even academic institutions by setting up research consortiums to focus on particular projects. A small group within the consortium could manage the relationship and the investment.

MULTIPLE SCLEROSIS FACTS

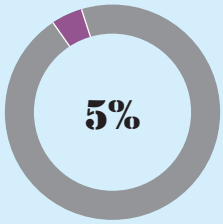
Prevalence by MS sub-type



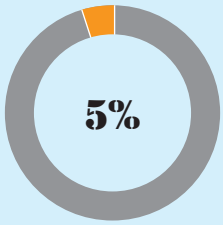
RELAPSING-REMITTING



PRIMARY-PROGRESSIVE



SECONDARY-PROGRESSIVE



PROGRESSIVE-RELAPSING

Countries with the highest estimated incidence out of 100,000 population

176 Hungary

150 Slovenia

149 Germany

135 United States

133 Canada

130 Czech Republic

125 Norway

122 Denmark

120 Poland

110 Cyprus

Incidence

Global:
Age-adjusted incidence rate is
30 in **100,000**

Prevalence

United States:
400,000
cases

Global:
2.1 MILLION
cases

Annual research budget of the leading nonprofit research organization

National MS Society:
$36.9 MILLION
(2010)

Clinical trial enrollment

23,065 PATIENTS IN ACTIVE, NON-RECRUITING INTERVENTION TRIALS

73 ACTIVE, NON-RECRUITING INTERVENTION TRIALS

6 Competitiveness

Retaining its position as the world's top innovator in the biosciences should be a national priority for the United States, given the prominence of the sector and its ability to generate high-wage, high-value-added jobs. And America continues to hold many advantages that should allow it to stay in the vanguard.

Yet capital that would otherwise have been invested in the United States has been going to countries with fewer barriers and more opportunity. It is now easier, participants said, to form a company in Shenzhen, China, than in Palo Alto. China has been able to develop a growing number of creative, well-trained investigators. Once Chinese regulators decide on a goal, they are more willing to remove obstacles toward the achievement of that goal than their counterparts in the United States and Europe. This is why more biotech companies were started in China in 2010 than in the U.S.

"This was an experiment," Sanofi CEO Chris Viehbacher told the attendees. "Where we go from here depends on you."

The aim, however, is not to *defeat* China—or anyone else—in the biomedical arena. Global competition in this sector should not be viewed as war. Instead, the rise of China should serve as a wake-up call for the United States, spurring the nation out of complacency so that it will perform at an even higher level. "In 1957, when the Soviet Union successfully launched Sputnik, the response of the United States was not to attack the Soviet Union, but to surpass it in science," recalled one participant. "If the United States rises to the biomedical challenge, the entire world will be better off."

It is important to remember that competitiveness is not just determined by investment, laboratory initiatives, or sophisticated new tools. At its core, it is about human capital. The competition for top scientific talent is now global, and we need to recognize it as such. The U.S. needs to make it easier for talented graduate students to not only study here, but stay and conduct research here. A prominent policymaker in attendance said: "Issuing EB-5 visas is a good step forward for encouraging international investment in U.S. entrepreneurial activity."

Solutions for competitiveness

→ **MAKE IT EASIER TO OBTAIN VISAS.** The United States has always welcomed the best and brightest from around the world, but conditions are much tighter now. People now come here for a world-class education, but then they're forced to leave, taking the benefits of that training with them. Said one executive and researcher, himself an immigrant: "I don't know if I could get a visa to stay in the United States if I had to pursue it now."

→ **INCREASE USE OF ELECTRONIC MEDICAL RECORDS.** Given the increased capacity of computers to handle "big data," electronic health records will greatly expand the ability of researchers to look at larger patient groups. But hospitals and doctors' offices across the United States have been slow to make the transition to digitizing records. We need a concerted national effort to see this through.

7 Prevention

Many chronic diseases are preventable, and previous research by the Milken Institute shows that lifestyle-related diseases exact a terrible toll—not only in human suffering, but in economic terms.

Despite the scale of the problem, very little innovation has been brought to bear on the concept of prevention. As one researcher indicated, there is a strong correlation between certain types of foods—fast food, in particular—and diabetes. Yet there is very little pressure to change what he called "diabetes factories."

Solutions for prevention

- → **WORK TO CHANGE LIFESTYLE.** Seventy percent of all U.S. health-care costs are related to lifestyle. We need to educate people so they understand that losing weight is good for them—and for America.
- → **INNOVATE TO ENCOURAGE WELLNESS.** If we don't take innovative approaches to encourage Americans to adopt healthier habits, we are missing an opportunity. At the same time, we need to develop medications that address obesity, which is primarily lifestyle-driven but very difficult to curb.
- → **MAKE BUSINESS MORE ACCOUNTABLE.** Accountability for prevention has to begin in the private sector. Companies can do more to change their employees' lifestyles and save money doing it. As one participant explained: "My company serves as a good model. [It] went from 28 percent to 21 percent obesity through information, motivation, accountability, and incentives. Our 2005 health-care costs were $1 billion. Given the national corporate rate of increase, it should now be $1.5 billion, but instead it's $750 million. The company's wellness program reduced blood sugar on average 45 percent. If every company adopted this plan, we could take $800 billion out of national health-care costs … more than enough to pay for all medical research."

8 Politics

Basic science, regulatory infrastructure, and other public health priorities largely depend on government funding—and the elephant in the room is the federal deficit. As one participant said: "There are a number of programs that can be cut, but bioscience isn't one of them."

Participants pointed to the positive economic impact of investing in science and innovation, noting a Battelle report that shows how a $3.8 billion investment in the Human Genome Project drove $796 billion in economic impact, created 310,000 jobs, and launched the genomic revolution. Adjusted for inflation, that's a return on investment of 141:1.

There are other ways to measure — and communicate — the broader economic and strategic benefits of robust funding for science. "Advances in biomedicine and pharmaceuticals could represent one of the greatest economic stimuli ever," said one business leader. "It would transform the costs associated with sickness into the productivity of health." It's staggering to imagine the tremendous boost to the economy that would come from eliminating cancer.

JAMES GREENWOOD
President and CEO, Biotechnology Industry Organization; former member of Congress

"We're in a position right now where society and members of Congress say, 'We really want to cure diseases. We really want to save money in the health-care system. We want to promote innovation. We want to create jobs.' And yet many of the policies that Congress adopts are completely inimical to those goals. So we need to try to figure out, what are the messages that we have to give to Congress? If policymakers start to hear it from patient organizations, from employers, and from people from different walks of life, it may ring a little bit more true."

The problem is a cultural divide: A large segment of the population is either uninterested or even downright hostile to science, despite the positive impact it has had on society. One participant said: "I worry about the culture wars. People don't understand that bioscience is an investment, not spending. Innovation in health care reflects core American values. If we're for nothing else, we should be for innovation."

The current political climate is, in some ways, more conducive to negative results. "There is a large potential for harm that can come from misunderstanding. The wrong legislation can have a very real and negative impact," one attendee warned.

Political solutions

- → **MAKE IT EASIER TO OBTAIN VISAS.** The United States has always welcomed the best and brightest from around the world, but conditions are much tighter now. People now come here for a world-class education, but then they're forced to leave, taking the benefits of that training with them. Said one executive and researcher, himself an immigrant: "I don't know if I could get a visa to stay in the United States if I had to pursue it now."

- → **CALCULATE THE VALUE OF BIOSCIENCE TO THE BROADER ECONOMY.** Quantify the impact of bioscience on the economy and jobs, calculate the job losses that will be caused by the implementation of bad policies, and publicize the results. The Milken Institute once broke new ground by calculating the economic impact of preventable chronic diseases, so this kind of analysis is doable.

- → **SUPPORT THE FDA.** People must understand that for the FDA to perform its core function, it needs to be funded.

9 Recommendations: An action plan for innovation

Accelerating innovation in the biosciences won't happen overnight. But it is important not to lose sight of where we are. The foundation already exists in the United States—with its exceptional research institutions and many of the world's leading pharmaceutical and biotech companies—to increase the level of innovation many times over. The world is filled with talented, smart people, and there is plenty of capital available if investors understand the opportunities before them and are more tolerant of the risks and how to mitigate them.

But the public and policy leaders alike must understand the challenges, the opportunities, and what's at stake. They must also understand that the pace *can* be accelerated if we take the right steps.

The report has laid out multiple ideas for spurring biomedical innovation in the long term. The following proposals were singled out during the final session of the retreat as items that can be implemented immediately:

Policy recommendations for elected officials

- Strongly support public policy initiatives that retain and bolster U.S. leadership in biomedical research and innovation.
- It's time to invest more resources in America's human capital. Begin early by improving the quality of STEM (science, technology, engineering, and math) education in the lower grades and increasing funding for STEM programs in U.S. universities.
- Fix the nation's broken visa system so the world's best students can stay in the U.S. throughout their careers. Clear the roadblocks that prevent them from contributing to the nation's economic growth and its scientific prowess.
- Take the appropriate legislative and regulatory steps to streamline the drug approval process so it is more predictable, with better benefit-risk assessments and more emphasis on patient outcomes. This would encourage long-term investment.
- Support PDUFA (the Prescription Drug User Fee Act) so there is sufficient funding for the FDA to relieve its staffing shortages and make the regulatory and approval processes as efficient as possible.

Revamping the way research is conducted

- Identify the scientists with the greatest potential and fund them early in their careers, when they are most productive.
- Strongly support convergence to bring different disciplines together to solve complex problems. The world is not structured the way university departments developed over time. Barriers between disciplines must come down to accelerate discovery and innovation.
- Go digital, and do it quickly. The digital toolbox is growing, and it can connect and focus many more minds on solving critical problems.

Creating an environment where innovation can thrive

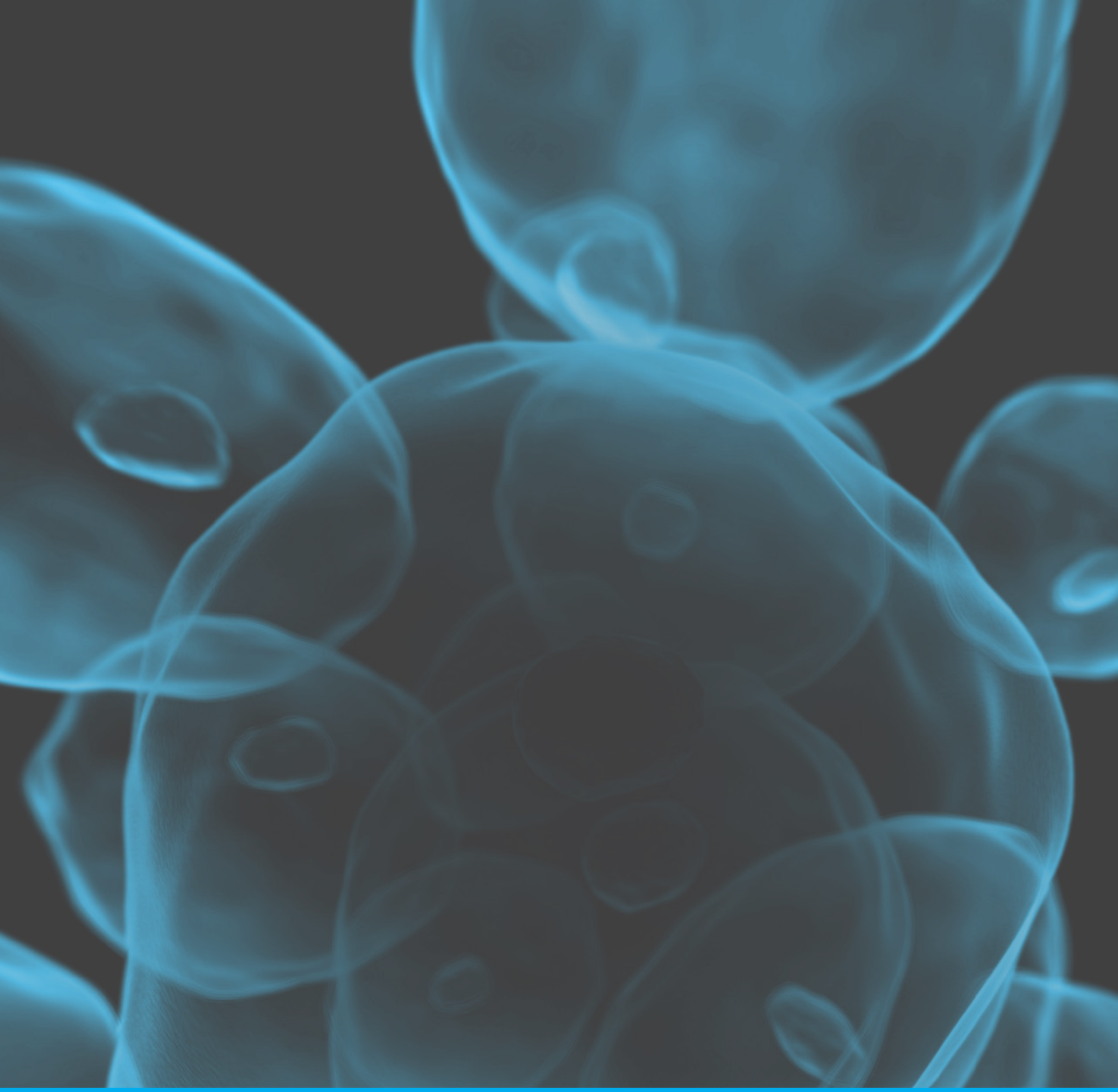
- Designate the National Institutes of Health a national treasure so the public understands its tremendous contributions—not just to science but to the broader economy. Encourage support for the biosciences by driving home the message that medical innovation saves lives, creates jobs, and sparks economic growth.
- Explore new funding models for drug research that combine all types of capital—private, public, and philanthropic—to distribute risks and share returns more widely and efficiently. It's time to create prizes that will motivate people to burst through their limitations.
- Develop a safe-harbor approach to research in the biosciences, especially in the pre-competitive stages, to eliminate disputes over patents or antitrust issues. This would change the health ecosystem by promoting collaboration, data- and information-sharing, partnerships, and faster cures.

Multiple, complex factors are behind the current innovation drought in the biosciences, but the prevailing sentiment around the tables at the Lake Tahoe Retreat was that the obstacles now facing the sector *can* be addressed. If solving problems begins with careful articulation, continues with thoughtful listening, and ends with strategies and proposals arrived at jointly, then this ambitious event was a successful first step toward a long-term renaissance of innovation.

The Lake Tahoe Retreat was meant to do much more than outline the problem—it was focused on identifying concrete solutions. Now the challenge is to turn those ideas into action. Building on the momentum generated by the retreat, many of the participants resolved to reconvene and continue this crucial dialogue at the Global Conference (April 29-May 2, 2012 in Los Angeles). The group has also formed a committee comprised of high-level representatives with influence across the medical research enterprise who can mobilize broader action. They will continue to work through the problems, focusing on implementation and dissemination of the ideas contained here.

For decades, the United States has been an innovator and a leader in the biopharmaceutical industries. It has built up powerful academic, commercial, regulatory, and philanthropic communities that are second to none. It is a tribute to these communities that they have moved forward in concert, and without external prodding, to begin the arduous task of removing any barriers that stand in the way of continued leadership and growth.

It is rare for any industry to address its problems while they are still small. However, when the stakes are life and death, there is no alternative to full-speed ahead.



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