Unleashing the Promise of Biotechnology

Advancing American Innovation to Cure Disease and Save Lives

Biotechnology companies are working every day to solve the greatest challenges facing our society — whether it's finding a cure for cancer, protecting against bio-terror threats, or creating renewable energy sources. Yet despite the urgent need for scientific breakthroughs in these areas, current government policies are holding back the potential and promise of biotechnology.

What's needed is a policy environment that incentivizes the magnitude of investment necessary to translate the scientific potential that resides in the thousands of American biotech companies into the breakthrough cures, treatments, enhanced agricultural products, vaccines to defend against bioterrorism and revolutionary biofuels that can transform society. Only by transforming the policy environment can we create a robust innovation economy that helps America compete globally by maintaining our position as world leader in biotechnology research and development. And only by investing in biotech today can we discover the new treatments and cures that will not only save lives, but reduce long-term health care costs by keeping people healthier and reducing chronic disease.

To this end, I began a process last summer of interviewing thought leaders within and outside of our industry for the purpose of envisioning game-changing strategies. We contracted with Dr. Elias Zerhouni, former Director of the National Institutes of Health, to conduct an analysis of the challenges we face and a more comprehensive survey of medical experts, academic researchers, and other life science leaders to suggest out-of-the-box, big ideas to significantly advance biotechnology's chances to succeed.

Over the past six months, we worked with BIO Board members and staff to review these ideas, debate their merits, and offer alternative and additional approaches to develop a comprehensive national policy strategy.

The policy agenda summarized in this brochure is the result of this rigorous policy development process. It reflects the input and suggestions gathered throughout this process from biotech CEOs, venture capitalists, current and former government officials, academic and medical researchers, patient advocates and other experts. Our recommendations reflect the big, bold and daring thinking required to create new models to encourage investment in innovation and to speed up the discovery of scientific breakthroughs. In short, this agenda will enable the biotechnology industry to fulfill its promise to help, heal, fuel, and feed the world.

Sincerely,

James C. Greenwood
President & CEO, BIO

Biotechnology is all around us and a big part of our lives, providing breakthrough products to cure disease, protect against bio-terrorism, feed the hungry, and clean our environment. At its simplest, biotechnology harnesses cellular and biomolecular processes and puts them to work to help solve our most intractable problems.

Society has tapped just a small fraction of the many potential uses — and benefits — of biotechnology. Every day, research scientists explore new ways to improve our quality of life using biotechnology. In fact, biotechnology presents some of the most promising opportunities for helping policymakers achieve their goal of supporting innovation in health care, renewable energy, and green technologies. However, biotech research and development is a particularly high-risk undertaking because of the substantial start-up costs, lengthy experimentation period, and possibility that the technology will not prove viable. That puts biotechnology companies at the mercy of investors. Complicating matters, the regulatory review processes are not keeping up with rapidly advancing science and are making it a more difficult environment to develop new treatments and products.

Fully realizing the promise of biotechnology requires a comprehensive national strategy that fine-tunes some policies and overhauls others. In the pages that follow, we outline a policy agenda that we believe will enable U.S. biotech companies to transform the innovative ideas of today into the realities of tomorrow.

I. Promoting Investment in Innovation

Congress has historically provided tax incentives to high-risk endeavors (such as oil and gas exploration, alternative energy, and high-tech start-ups) as a means for encouraging new investment. However, current tax law does not do enough to foster investment in health care, green technology, or energy-focused biotechnology companies. Given the economic and societal benefits of

FEATURES OF THE TYPICAL BIOTECH COMPANY

- Unprofitable — 3 or more years away from having product revenue
- Private company (70% of the biotech industry is private)
- Fewer than 50 employees
- Completed one round of venture capital financing
- 5 products in development, with a lead product in Phase II clinical trials, a secondary product in Phase I clinical trials, and 3 pre-clinical products

ensuring a robust biotech industry in the United States, it is imperative that Congress and the Administration adopt policies that recognize the unique financial structure and capital needs of biotech companies.

The proposals described below are designed to incentivize investors, strengthen small business, and promote innovation in the United States.

Small Business Investor Incentives

Incentivizing Small Biotech Investment: Angel Investor Tax Credit

Modeled after numerous state programs, a federal Angel Investor Tax Credit would provide an incentive for individuals to invest in emerging biotech companies researching innovative technologies. To be eligible, investors would have to invest in a company with fewer than 500 employees performing qualifying research. The credit would be equal to 50% of their investment.

Stimulating Private Capital for Biotechnology: R&D Partnership Structures

Due to the lengthy drug development process, small biotechnology companies often have difficulty obtaining early-stage financing for their research and development and, because they are not yet profitable, are unable to immediately use their tax assets (i.e., tax credits and losses) to offset income. The development of new partnership structures that allow a biotech company's investors to offset their income with the company's tax assets would significantly stimulate much needed private investment in biotechnology.

Improving Capital Gains Treatment for Small Businesses: Section 1202 Reform

Section 1202 of the Internal Revenue Code provides for a reduced capital gains rate for qualified investments in certain small business stock. However, due to the

BIOTECH COMPANIES ARE QUINTESSENTIAL SMALL BUSINESSES

- 48% of typical biotech companies are at least 3 years away from having product revenue.
- 71% of typical biotech companies have less than 25 employees. 90% have fewer than 100 employees.
- 43% of typical biotech companies have less than a year's worth of cash on hand.
- 77% of typical biotech companies have less than $50 million in gross assets.

Source: BIO Emerging Companies Section Membership Survey, 2011

VENTURE CAPITAL INVESTING IN BIOTECH HAS DECLINED AND REMAINS LARGELY STAGNANT

- According to Pricewaterhouse Coopers, the first quarter of 2011 marked the fewest biotech venture deals of any quarter since 2003.
- The average deal for the first round of funding in the first quarter of 2011 was $2.2 million, the smallest average size for such deals since 2005.
- At the industry's peak in 2007, U.S. biotech companies raised $5.2 billion in venture capital financing. In 2010, the industry raised just $3.7 billion in venture capital, 30% less than 2007's total.
- The troubled IPO market and financial crisis have contributed to the reduced size of the United States biotech industry. The number of public biotech companies in the U.S. has decreased by 25% since January of 2008.

***In India, the Biotech Industry Partnership program provides grants and soft loans to companies conducting high-risk research, which has fostered a* 20% annual growth rate.**

Source: Beyond Borders: Global Biotechnology Report 2008, Ernst & Young

Worldwide, **35%** *of pharmaceutical companies* **outsourced projects** *to Asia in 2009, with China and India the top two destinations.*

Source: "Annual Outsourcing Survey," Contract Pharma (2009)

valuable intellectual property and successive rounds of financing inherent in biotech innovation, biotech companies do not meet the definition of qualified small businesses under Section 1202. Modifications to the small business definition and other changes in Section 1202 would encourage investment in research performed by capital-intensive, small biotech companies.

Doubling Private Funding: Matching Grants for Investments in Start-Ups
A small business early-stage investment program would provide matching grants to venture capitalists that specialize in funding small, innovative companies. The government grants would match investments in targeted small businesses, including emerging biotech companies, essentially doubling their financing by enabling seed financing to spur further investment.

Small Business Tax Incentives

Removing Financing Restrictions: Section 382 Net Operating Loss Reform
Section 382 of the Internal Revenue Code restricts the usage of net operating losses by companies that have undergone an "ownership change." However, small biotech companies are unintentionally caught in its scope due to their reliance on outside financing and investment deals. Exempting net operating losses generated by qualifying research and development by a small business from Section 382 and redefining "ownership change" to exclude certain qualified investments (like those in rounds of venture financing) would enable small biotech companies to increase their value when preparing for mergers or initial public offerings.

Nearly a third of small U.S. biotech companies have been approached to move their R&D operations **offshore**, *and CEOs named China and India as two prime destinations.*

Source: Therapeutic Discovery Project Post-Award Survey. Penn Schoen Berland, prepared for BIO.

Incentives for Non-Investor Capital

Increasing R&D Investment: Tax Holiday on Repatriated Investments in Small Biotechs
Many small biotechnology companies rely on collaborations with large multi-national corporations to fund their research and development. A repatriation tax holiday on funds brought back to the United States from abroad would incentivize these large companies to repatriate earnings they are holding overseas and give them the ability to invest in and collaborate with small biotechs conducting groundbreaking research here at home.

Rewarding Innovative R&D Businesses: U.S. Innovation Box
Many Western European countries have implemented reduced corporate tax rates on income stemming from certain types of intellectual property. Allowing for a reduced corporate rate on this type of income would make investment in U.S. biotechnology more attractive and competitive, and would provide innovative companies with a greater return on their R&D expenses — allowing them to undertake more research projects here in the United States.

Most big pharmaceutical companies have announced **significant cuts** *to research and development activities.*

Source: Reuters, "Analysis: Big Pharma strips down broken R&D engine," 11 May 2011.

Supporting Industry Collaborations: Section 197 Amortization Reform
Small biotechs typically have intangible assets that are amortizable under Section 197 of the Internal Revenue Code. Reforming that law to provide for faster cost recovery for intangible assets acquired by investors would encourage large company investors to invest at an earlier stage in small biotech companies' research.

Policies to Stimulate a Bio-based Economy

The "Bio-based Economy" refers to economic activity and jobs generated by:

- the use and conversion of agricultural feedstocks to higher value products;
- the use of microbes and industrial enzymes as transformation agents or for process changes; and
- the production of bio-based products and biofuels.

The proposals below seek to elevate the concept and awareness of the bio-based economy and highlight the outstanding job creation and rural/rust belt economic development potential of industrial biotechnology and biorefinery commercialization.

Agriculture

Reauthorization and Enhancement of the Biomass Crop Assistance Program (BCAP)
BCAP is the key program encouraging and facilitating farmers and landowners to produce new purpose grown

energy crops (PGECs) for advanced biofuels and bio-based products. Beyond reauthorizing the program through December 2017, we can further enhance it by:

1. Ensuring funds are directed primarily to production of next generation crops for biofuels and bioenergy;
2. Establishing a dedicated funding mechanism for awarded contracts;
3. Providing for eligibility of non-food Title I crops; and
4. Clarifying eligibility of certain other PGECs.

Federal Crop Insurance for Purpose Grown Energy Crops

Currently, there is no formal federal crop insurance program available to producers of new PGECs. Requiring the U.S. Department of Agriculture's Risk Management Agency to finalize its ongoing feasibility study of developing a crop insurance program for certain biofuels and bio-product feedstocks — and appropriately funding the Commodity Credit Corporation — would enable the formal establishment of such a program.

Feedstock Sustainability Enhancement Grants

The continued development of domestic sources of energy, including for biofuels and renewable chemicals, depends upon the sustainable availability of consistent, high yield, good quality feedstocks. Establishing a grant program through the U.S. Departments of Agriculture and Energy would enable the funding of demonstration projects that utilize practices to enhance biofuel and bioenergy feedstock sustainability.

Codifying and Expanding the Definition of Renewable Chemicals

Many of the programs in the 2008 Farm Bill's Title IX renewable energy programs are not available to renewable chemicals and bio-based products, despite their profound potential benefits to rural America. Codifying a more expansive definition of eligible renewable chemicals and bio-based products would enable enhanced participation of renewable energy projects in programs such as the Biorefinery Assistance Program and Rural Energy for America Program.

Tax

Tax Credit for Production of Qualifying Renewable Chemicals

Renewable chemicals and bio-based plastics represent an important technology platform for reducing reliance on foreign oil, creating green U.S. jobs, increasing energy security, and reducing greenhouse gas emissions. By providing a renewable chemicals tax credit in the form of a federal income tax credit for domestically produced renewable chemicals, Congress can create jobs and other economic activity and can help secure America's leadership in the important arena of green chemistry. The credits would be general business credits available for a limited period per facility, and taxpayers would be subject to a competitive application and review process to ensure conformance with legislative intent.

Tax Code Reforms to Increase Availability of Advanced Biofuels and Facilitate Energy Security

Current tax law on advanced biofuels does not provide an ordered pathway toward U.S. energy security. Policymakers can help incentivize bringing commercial volumes of affordable advanced biofuels to market in the near term by amending the current tax code to:

1. Extend the Cellulosic Biofuel Production Tax Credit through 2016 and add eligibility for algal biofuels;
2. Allow advanced biofuel facility developers the option of electing to receive an investment tax credit;
3. Provide for eligibility of biorefinery retrofit projects;
4. Provide eligibility to federal Section 1603 Grants in Lieu of Tax Credits program; and
5. Extend and expand eligibility for cellulosic biofuel property accelerated depreciation.

Defense

Strategic Biorefinery Initiative and Offtake Authority

Development of domestic sources of renewable biofuels and bio-based products would yield substantial energy security benefits. The Department of Defense is uniquely positioned to help accelerate production

and deployment of these vital products through establishment of a Strategic Biorefinery Deployment Program to finance construction of the first five commercial military advanced biofuel biorefineries. Under such a program, a biorefinery "fly-off" would identify and fund construction of the most promising projects. The authority to enter into long-term (up to 15 years) offtake agreements for procurement of advanced biofuels for military use would further enhance the Department of Defense's ability to facilitate development of domestic sources of renewable biofuels.

Energy

Repurpose and Retrofit Grant Program for Expanding Production of Advanced Biofuels

Repurposing or retrofitting existing idled or underutilized U.S. manufacturing facilities is one of the most time and cost effective ways to build out the advanced biofuels and renewable chemicals sector. Establishing a federal matching grant program through the U.S. Department of Energy to fund up to 30% of costs would facilitate investments in such repurposing and retrofitting projects while helping to rapidly expand U.S. production capacity for advanced biofuels and renewable chemicals.

Synthetic Biology for Enhanced Sustainability of Biofuels and Renewable Chemicals

The advancing field of synthetic biology has the potential to enhance greatly both the economic and environmental sustainability of fuels and chemicals manufacturing. Establishing a Synthetic Biology Research and Development Grants Program through the U.S. Department of Energy would support research that could help enable the cost effective sustainable production of advanced biofuels, renewable chemicals and other technologies that reduce or minimize greenhouse gas emissions, including biological processes for removing carbon dioxide from the atmosphere.

Industrial Bioprocess R&D Program

The use of industrial biotechnology for the production of renewable chemicals and bio-based products is enabling dramatic improvements in industrial energy efficiency as well as a host of renewable alternatives to traditional petrochemical-based products. Establishing an Industrial Bioprocess Research and Development program through the Department of Energy would fund projects in industrial biotechnology for renewable chemicals, bio-based products, and renewable specialty chemicals.

II. Creating an FDA that Turns Hope into Cures

The American population is growing older — life expectancy is up by a decade since 1965 and 72 million Baby Boomers are about to enter Medicare. It has never been more critical to support an industry that is working to cure diseases and will impact all Americans by saving lives and dollars. It is imperative that the U.S. Food and Drug Administration (FDA) recognizes its national role in advancing innovation by reviewing innovative products in a timely manner and promoting a consistent and science-based decision-making process that is reflective of patient needs. By facilitating the creation of a 21st century FDA and more effective clinical research and development processes, the proposals below help establish a clear and effective pathway for turning hope into cures.

Elevating FDA and Empowering Operational Excellence

Include Innovation in FDA's Mission Statement

FDA must have both the capacity and commitment to incorporate the latest scientific advances into its decision-making so that regulatory processes can keep pace with the tremendous potential of companies' cutting-edge science. Congress can help encourage medical breakthroughs by updating FDA's mission to incorporate modern scientific tools, standards, and approaches.

Establish a Fixed Term of Office for the Commissioner of Food and Drugs

Encouraging consistent and stable leadership at FDA — with protection from the political influence that typically occurs during a Presidential Administration transition — would better equip the agency to fulfill its mission as a science-based regulator to promote and protect the public health. The law should be amended to provide that the President appoint the Commissioner to a six-year term of office. Once confirmed, the Commissioner would be removable by the President only for pre-specified reasons — neglect of duty, malfeasance in office, or an inability to execute the FDA's mission.

Grant FDA Status as an Independent Agency
The FDA regulates nearly a quarter of the consumer goods supplied to the American public. As such, the agency should have the same authorities to make budget, management, and operational decisions as afforded other independent agencies such as the Environmental Protection Agency. This would empower the agency to work more effectively with the President and Congress to carry out its mission to promote and protect the public health, and would also enhance the agency's ability to obtain quality and consistent leadership.

Establish an External Management Review Board for FDA
The FDA is a large, complex organization. Amending the law to establish a Management Review Board (consisting of experienced external advisors) that conducts periodic reviews of FDA's management and organizational structure and provides fresh, visionary, and independent thinking and recommendations on how to improve FDA's ability to fulfill its mission could help the agency address its chronic operational challenges.

Advancing Regulatory Science & Innovation

Release FDA Funding to Support Regulatory Science Public-Private Partnerships
Congress established an independent, nonprofit foundation to support public-private partnerships for the purpose of advancing FDA's mission through, for example, the formation of collaborations to advance

> ***Discoveries in biomedical research are slow to find their way into patient care because the agency (FDA) relies on* 20th-century methods *to evaluate* 21st-century science.**
>
> Dr. Margaret Hamburg, FDA Commissioner

the use of biomarkers, surrogate markers, and new trial designs to improve and speed clinical development. However, Congressional appropriations bills have subsequently restricted FDA's ability to transfer federal funding to the foundation. These funding restrictions should be lifted so that the foundation can fulfill its intended purpose and promise.

Create an FDA "Experimental Space" to Pilot Promising New Scientific and Regulatory Approaches
The FDA has developed several initiatives to advance regulatory science. However, FDA's ability to incorporate modern science into its regulatory processes has been limited because there is no entity within the agency with unified responsibility for systematically analyzing the findings and recommendations from these initiatives, and with clear authority to pilot promising scientific and regulatory approaches. An FDA "Experimental Space," led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new approaches are integrated into agency operations at all levels.

Enhance FDA's Access to External Scientific and Medical Expertise
Scientific and medical knowledge, techniques, and technology are advancing at a more rapid pace today than at any other time; however, FDA's capacity to access information about these advances has not kept pace despite the widespread perceptions of the agency as the global standard bearer for science-based regulatory review. It is essential that FDA's access to scientific and medical advice be enhanced by improving the operations of FDA Advisory Committees, establishing Chief Medical Policy Officers in the immediate offices of the Center Directors, and providing FDA staff with additional avenues for accessing external scientific and medical expertise.

Enabling Modernized Patient-Centric Clinical Development

Increase Access to Innovative Therapies through Progressive Approval
Patients, particularly those with illnesses for which no adequate therapy exists, want access to promising new therapies earlier in the drug development process. Expanding and improving the accelerated approval

pathway into a progressive approval mechanism would provide patients timely access to needed therapies, while helping ensure smaller biotech companies are able to maintain operations through extensive phase III clinical testing. Only innovative products for unmet medical needs, significant advances to standard of care, targeted therapies, or those that have been approved by the European Medicines Agency or other mature regulatory agencies would qualify for progressive approval.

Of the 54 orphan drugs approved between 1998 and 2007,* 58% *were discovered and developed by biotech companies.

Nature Reviews/Drug Discovery, November 2010

Empower FDA to Utilize a Weight-of-Evidence Approach to Establish Effectiveness

FDA is statutorily required to approve applications for new drugs when they have been demonstrated to be safe and there is "substantial evidence" that the new drug is effective. FDA typically requires two "adequate and well controlled" studies under this standard. A weight-of-evidence approach to data analysis, however, allows the decision-maker to look at all data and information, whatever its value, and give each appropriate consideration.

***Between 1999 and 2005, the average length of clinical trials* grew by 70%. *Currently, the average time from discovery of a drug to getting it to patients is* 10 to 15 years.**

Source: Tufts Center for the Study of Drug Development

Leverage Electronic Health Records to Facilitate Clinical Research

Using health information technology (IT) such as electronic health records in clinical research will improve and speed up the drug development process while decreasing costs. However, there are significant barriers preventing widespread use of health IT in clinical research, including slow adoption by providers and lack of standards. To help remove those barriers, Congress should create a Clinical Informatics Coordinator in the Office of the Commissioner of Food and Drugs charged with developing processes to validate and encourage the use of health IT in clinical research and establishing pilot projects to use health IT in clinical research.

Require FDA to Disclose to Companies Reasons for Non-Approval

Current law implies that new drug and biologic applications must either be approved or denied. In practice, however, there is a third response in which FDA neither approves nor officially denies the application (which would require FDA to give the company specific procedural rights such as a hearing); rather, FDA finds the application to be incomplete in some way and therefore ineligible for approval. When FDA makes such a finding, it should communicate to the company in clear terms why risk was determined to outweigh benefits and why tools such as Risk Evaluation and Mitigation Strategies are insufficient (in addition to indicating what must be done to address any deficiencies). This will help ensure a consistent and transparent risk-benefit evaluation and provide the company with better information on what, if any, additional studies are required to achieve approval.

III. The Road to a Brighter Future for Agricultural Biotechnology

For the past two decades, the United States has played a leadership role in agricultural biotechnology innovation, contributing billions of dollars to the U.S. GDP. Unfortunately, the U.S. regulatory system for plant and animal biotechnology, which was designed in the mid-1980s to facilitate product development, is fast becoming an impediment to the development

and commercialization of safe, beneficial products. Today, developers of agricultural biotechnology are less certain about the length and scope of federal regulatory approvals and the susceptibility of approvals to legal challenge. Greater certainty is needed to drive scientific innovation and reassure international trading partners, which is essential to U.S. producers of genetically-engineered products. While the underlying statutory authorities and regulatory framework for agricultural biotechnology are sound, to improve the process it will be important for Congress to give necessary direction to the federal agencies responsible for implementing the governing statutes that most directly impact genetically-engineered plants and animals. BIO therefore will propose a series of appropriate directives for the Congress to enact.

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