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Industry Study

Final Report
Biotechnology Industry

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Biotechnology 2012

Abstract

What is the next big thing? Business leaders, academics, government officials, and indeed adversaries are all trying to identify the next technological breakthrough that will transform business and society while providing for profits, markets, prestige, and leverage to those who can master it first. Biotechnology, the science of applying biologic solutions to a wide variety of challenges in the agriculture, defense, healthcare, industrial, and environmental markets, has the potential to be the technological breakthrough for the 21st century. Born in the early 1970s and in the growth phase of the economic life cycle, the modern biotechnology industry in the United States (U.S.) is at an inflection point where profits are materializing yet costs remain high, research is advancing yet translational science is waning, and the promises of societal good are equaled by fears of societal harm.

The U.S. has a comparative advantage in the global biotechnology industry. The comparative advantage results from early industry leadership, support for basic research, scale and clusters, entrepreneurial dynamism with venture capitalism, and strong government support. This provides the U.S. biotechnology industry with strong barriers to entry and a favorable competitive environment vis-à-vis international competitors while contributing to U.S. economic prosperity and national security. This strategically significant industry will be critical in the next few decades in developing solutions to society's most vexing problems driven by global megatrends of population growth, resource scarcity, and climate change. The U.S. biotechnology industry advantage is not absolute and the risks associated with the megatrend challenges will not be mitigated without collaboration and cooperation between government, business and academe to support basic research and translate science into safe and effective commercial products.

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Places Visited

Domestic

California
Bay Bio, South San Francisco
Burrill & Company, San Francisco
Gen Probe, Inc., San Diego
J. Craig Venter Institute, San Diego
Joint Bio Energy Institute, Emeryville
Nuvasive, Inc., San Diego
Sanford-Burnham Institute, La Jolla
Scripps Research Institute, La Jolla
Solazyme, South San Francisco
SRI International, Menlo Park
University of California at San Francisco QB3 Garage, San Francisco

ICAF Seminar
BioInformatics, LLC
J. Craig Venter Institute, Synthetic Genomics, Inc
Johns Hopkins University, Enterprise and Regulatory Affairs
Journal of Commercial Biotechnology
Merck & Company, Inc
Monsanto Company
President's Commission on Bioethics and Public Sentiment
Toffler Associates
U.S. Department of State, Trade and Policy Office
U.S. Patent & Trademark Office, Policy and External Affairs

Maryland
Center for Biosecurity of University of Pittsburg, Baltimore
Edgewood Chemical Biological Center, Aberdeen Proving Grounds
MedImmune, Frederick
Montgomery College Biotechnology Research & Innovation Lab, Germantown
University of Maryland Biotechnology Institute, Center of Marine Biotechnology, Baltimore

Massachusetts
AMGEN, Cambridge
Broad Institute of MIT and Harvard, Cambridge
Charles River Laboratories, Wilmington
Harvard Stem Cell Research Institute, Children's Hospital, Boston
Massachusetts Biotechnology Council, Cambridge

Pennsylvania
Janssen Biotech, Inc., a Division of Johnson and Johnson, Malvern

Washington, D.C.
Biotechnology Industry Organization
Food and Drug Administration

National Institutes of Health

International

Malaysia
Malaysian Biotechnology Corporation, Kuala Lumpur
Orchid Life Incorporated, Buloh
Technology Park, Kuala Lumpur
Tissue Culture Laboratory, Forestry Research Institute Malaysia, Kepong
U. S. Embassy, Kuala Lumpur

Thailand
Ecolab Southeast Asia Regional Technical Center, Pathumthani
National Center for Genetic Engineering & Biotechnology, Pathumthani
Shrimp Biotechnology Business Unit, Pathumthani
U.S. Armed Forces Research Institute of Medical Sciences, Bangkok

Taiwan
American Institute in Taiwan, Taipei
Biotechnology & Pharmaceutical Industries Promotion Office, Taipei
Council of Agriculture Taiwan Forestry Research Institute, Taipei
Department of Health, Food and Drug Administration, Taipei
Genomics Research Center, Academia Sinica, Taipei
Industrial Technology Research Institute, Chutung
Institute for Biotechnology and Medicine Industry, Taipei
Nankang Biotechnology Incubation Center, Taipei

Introduction

Twenty-first century global challenges will be driven population growth, resource scarcity, and climate change megatrends. These megatrends will result in increased demand for food, water, fuels, and healthcare. If left unaddressed, increased demand and lack of adequate supply may lead to starvation, privation, economic stagnation, and global instability. Finding a solution to this problem will be a challenge to United States (U.S.) policy makers in the coming decades. The science of biotechnology has the ability to mitigate the risks associated with these megatrends and the negative outcomes they engender, but only if the U.S. biotechnology industry – made up of stakeholders in government, academe, and business – continues to invest in innovations and maintains a comparative advantage.

The U.S. biotechnology industry leads in the larger, global industry as it expands into regenerative medicine, genomics, nanotechnology, bioinformatics, biosimiliars, personalized medicine, and biofuels. This leadership position postures the U.S. to be at the forefront of innovations to solve some of society's most vexing problems across healthcare, agricultural, food, industrial, environmental, and defense. Finding solutions that address these global challenges is crucial to maintaining stability in the world and is important to U.S. security and economic prosperity. To continue its pace of innovation, the biotechnology industry requires public-private-academic partnerships that support basic research, have the ability to convert science into useful products, and can commercialize products to achieve policy, social, and market goals. Biotechnology's central role in developing solutions to achieve these goals illustrates its importance to national security because biotechnology underpins each of the four pillars of the U.S. National Security Strategy (NSS): Security, Prosperity, Values and International Order.

The focus of this report of study is an assessment of the overall health of the biotechnology industry and its strategic importance to national security. It analyzes the U.S.'s relative position in the global marketplace given its current comparative advantage and market leadership. This report first defines the biotechnology industry, its stakeholders, and the sectors in which it competes. Further, it examines the structure of the industry and conduct of firms in the marketplace to assess its overall performance and health. In reviewing current industry trends and challenges, the report identifies the issues potentially affecting the future health of the industry and its near and long term outlook. The report closes with specific policy recommendations to address the issues and challenges and ensure the U.S. maintains its comparative advantage.

Industry Definition

The biotechnology industry in the U.S. applies biological sciences to develop solutions to a wide variety of challenges in the agriculture, defense, healthcare, industrial, and environmental markets. It is a producer-based industry that applies common technology platforms, such as genetically modified (GM) organisms, to manufacture products for a variety of markets. Firms in the biotechnology industry use similar processes to render products and services across a diverse array of markets by commercializing scientific discoveries. This dynamic results in competition between firms and across multiple consumer markets that is a distinguishing characteristic of the biotechnology industry. The industry is made up of a variety of stakeholders working in different industry sectors to meet market demands.

Stakeholders

Biotechnology industry stakeholders are collectively referred to as a networked "Triple Helix." The triple helix consists of stakeholder communities in academe, business, and government. A well functioning triple helix is critical to the biotechnology industry's health and to ensuring scientific discoveries are commercialized in the form of useful products that create value and meet market and policy goals.

Academe: Scientists and researchers are an essential component within the biotechnology industry. These stakeholders are interested in the free and open exchange of ideas to build upon the global base of knowledge regarding natural and manmade processes. This is done primarily through scientific research, experimentation, scholarly works, and the publishing of results in scientific journals. Examples of academe include universities, private research institutes, research foundations, hybrid organizations, and collaborations.

Business: Private industry translates advances in scientific discovery and knowledge into products and services and then competes to sell them in the market. Businesses often engage in their own scientific experimentation and research to support technology and product development. Included in this community are firms providing biotechnology related goods and services as well as a host of firms that provide critical financial, advocacy, and publishing support. Profit is the major driver for private industry, determining competition in the market and focusing technology development and innovation. Since private industry is dependent on the health of the market, it strives to ensure its products provide value to customers and to work across the triple helix to create conditions that are likely to result in a reliable and stable product market.

Government: Government is responsible for security of the country and its citizens and promotion of general prosperity. Thus, government supports innovation that provides the technologies, goods, and services to meet the changing demands of the population and environment and enables industry to remain competitive in the global market. Supporting innovation and security may, at times, be at odds. The government must establish effective policies to balance the needs of citizens and the market. Government institutions sharing this responsibility include: the National Institutes of Health (NIH), U.S. Patent and Trademark Office (USPTO), Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and the Presidential Commission for the Study of Bioethical Issues.

Major Sectors

The biotechnology industry is producer-based whereby the same or similar technologies are applied to a range of products and services serving multiple markets. It serves the agricultural, defense, environmental, healthcare, and industrial sectors and competes in each sector's markets. The industry's stakeholders work to develop technologies that have application across these sectors and markets. By addressing unmet consumer needs through the application of revolutionary science, the biotechnology industry radically changes the manner in which products and services are manufactured and delivered. These innovative applications can be disruptive to longstanding, traditional industries, but the diversity and breadth of markets to which they apply create increased value for the consumer. Current biotechnology industry efforts are focused across the agriculture, defense, healthcare, and industrial and environmental sectors.

Agriculture: The agricultural biotechnology (AgBio) markets in this sector include seed genomics and agricultural productivity. GM organisms form the core of the biotechnology industry's input to the agriculture sector. Crops produced through genetic modification already permeate the U.S. and world food supplies. Other research efforts in AgBio include developing plants and animals that improve crop and livestock yields, increasing nutritional and health benefits in food, and reducing the use of herbicides and pesticides. Finally, AgBio animal health products increase animal breeding, disease resistance, and meat quality.

Defense: Defense markets include prevention, detection, remediation and treatment of both manmade and natural biological threats. The bio-defense sector employs many solutions common to the other sectors, but for national security and defense customer bases and purposes. Products and services in the defense sector provide for event or incident protection and prevention; agent and toxin detection and diagnostics; and vaccines, therapy, and remediation.

Healthcare: In the healthcare sector, the industry competes in three markets: pharmaceuticals, diagnostics, and medical devices. Biopharmaceutical drugs compete in the larger pharmaceutical market. Biopharmaceuticals are distinct from chemical drugs in that they consist of large molecule biologics produced in living cells. Biologics offer protein therapeutics, cell therapies, vaccines, and organ and tissue replacement (regenerative medicine). The concept of personalized medicine is heavily dependent on biologics. The diagnostics market includes detection, identification, and evaluation tests for genetic traits, viruses, and drugs. The medical devices market includes physical aids that take on biological functions, such as pacemakers and prosthetics.

Industrial and Environmental Products: Markets in this sector include biologically produced fuels and industrial chemicals. For example, biotechnology companies already produce fuels for use in aircraft and diesel engines using algae and enzyme-based processes. Enzymes are used to produce industrial chemicals and compounds to manufacture plastic and other materials.

Industry Performance

Porter's Five Forces Model and McKinsey's Strategic Game Board are used to assess the structure and conduct of the biotechnology industry. This analysis provides a framework to measure the biotechnology industry's performance and determine overall industry health.

Structure of the Industry

The modern (post 1970) biotechnology industry remains in the growth phase of the economic life cycle. It consists of large, multinational firms; small, entrepreneurial firms; public and private entities; government regulators and funders; and, academic-based researchers and developers. A highly competitive and regulated industry, biotechnology is reliant on the proprietary knowledge of its firms. While complex interactions within and between the elements of the triple helix impact the structure of the industry, Porter's Five Forces Model is the lens used to view how these interactions impact the power of buyers and suppliers, the threat of new entrants and substitute products into the industry, and the degree of rivalry amongst firms. The relationship of these forces directly impact firm conduct and overall health of the industry – should forces move in one direction or the other, firm strategies must change to remain profitable.

Datamonitor, a respected market research firm, provides assessments for each of Porter's Five Forces. Datamonitor assigns a score of one to five for each of the forces, with one indicating

weakness, five indicating strength, and a three indicating moderate.[1] The Datamonitor ratings for the forces and descriptions of each force in the industry provide the structural analysis for the biotechnology industry.

***Buyer Power**:* Buyer power in the biotechnology industry is moderate.[2] Significant buyer power is exerted by major buyers like the concentrated U.S. agribusiness sector and large private sector and government insurers who command lower prices on biotechnology products. Even with the emergence of biologically similar (biosimilar) drugs which are comparable to generic small molecule drugs, many life-saving drugs have few valid substitutes allowing for higher priced biologics and tempering of buyer power.[3]

Supplier Power: Moderate supplier power is exhibited in the industry by the manufacturers of reagents and laboratory equipment, software publishers, and similar firms.[4] Contributing to diminished supplier power is the high degree of choice between suppliers and the limited differentiation among them. Conversely, supplier power is strengthened when key inputs are available from one source, there is low likelihood of backward integration, buyers cannot substitute certain raw materials or equipment, and suppliers have ample choice of customers in other markets.[5]

New Entrants: The threat of new entrants in the biotechnology industry is low since most firms benefit from intellectual property protections that create formidable barriers to entry.[6] Biotechnology start-up firms must gain approval for products from relatively conservative government regulators who require lengthy and costly approval processes. Additionally, these firms typically have long periods with little profit and high fixed costs requiring a high degree of hard to find capital backing and further reduce the threat of new entrants.[7]

Substitutes: Substitutes pose a moderate threat in the biotechnology industry. Although the principal substitutes for biologics are conventional drugs produced by chemical synthesis, many biologics are the sole treatments for specific diseases or are more effectively than existing conventional drugs. AgBio faces risk of substitution of GM seeds with less controversial, selectively bred seeds that benefit from wider acceptability due to less skepticism about potential health risks.[8]

Rivalry: Rivalry in the biotechnology industry is strong because the industry is in the growth phase of the economic life cycle and there are large numbers of start-ups and small to medium-sized firms alongside a small number of large firms. The struggle to discover a 'biotechnology blockbuster' requires lengthy, costly, and high-risk R&D investment and challenging clinical trials. This results in increased strategic partnerships between firms to spread risk and decreases rivalry. Also, strong growth in the U.S. market in recent years eased rivalries as each player could increase revenues without taking market share away from competitors. These counterbalancing forces keep rivalry assessed as moderate across biotechnology.[9]

Firm Conduct within the Industry

Within the industry competitive landscape outlined in Porter's Five Forces analysis, individual firms must decide where, when, and how to compete in order to be profitable. Using the Strategic Game Board model, this section analyzes the strategies used by biotechnology firms

to harness and maintain profits in the industry. The success of the individual firm strategies at the micro-level determines the overall health of the industry at the macro-level.

Where to Compete: As previously stated, biotechnology firms compete in the agricultural, defense, environmental, healthcare, and industrial market segments. Within the industry, healthcare is the predominant market segment as it has received the largest amount of research funding. Additionally, globalization brings expanding markets to biotechnology while scientific development remains predominantly in the U.S. and production is moving to lower cost centers in Asia.

How to Compete: As in other industries, firms within the biotechnology industry can compete using a niche strategy, low cost strategy, or hybrid strategy. The predominant strategy in the biotechnology industry is the niche strategy, whereby a firm seeks to differentiate its product from its competitor's to gain a comparative advantage. For example, a large biotechnology firm may focus solely on agricultural innovations such as modifying a plant to gain larger and healthier yields. In order to remain competitive, firms with constrained capital resources must choose to collaborate, partner, or form alliances in an effort to spread risk, gain expertise, and develop a marketable product. Bringing a biopharmaceutical product to market could take up to 10 years and cost in excess of $1 billion. As such, few firms within the biotechnology industry can afford to fund product development from discovery through production and commercialization. Therefore, the firms must make a strategic decision on the maturity of a potential technology and whether to continue to invest or refocus their resources. Even firms who can afford to fund the entire process often choose to outsource specialized areas of development and production processes to smaller firms with superior expertise to gain greater flexibility and to reduce their overall risk.

When to Compete*:* The decision as to when biotechnology firms enter, expand, or leave a market is based on the size of the market, strength of intellectual property assets, feasibility of innovative processes, degree of venture capital (VC) backing, and favorability of the regulatory environment. Due to the extended period of time it takes to develop a marketable biotechnology product, a firm must forecast the consumer need and profitability of the product and the possibility of similar products entering the market prior to making a decision to invest in the development. To mitigate this problem, firms choose to acquire, be acquired, or invest in products in late stage development where the risk is substantially less.

Industry Performance

Both current and projected performance in the biotechnology industry is positive in both financial and growth terms. Currently, the industry consists of over 1,800 enterprises and employs over 197,000 people with an average annual salary of $111,000.[10] The U.S. biotechnology industry has been profitable since 2009, earning a $4.2 billion profit in 2011 and an expected $4.7 billion in 2012.[11] [12] The estimated 2012 revenue of the global biotechnology industry is expected to increase 9.9% from 2011.[13] It is expected to sustain a steady rise in market capitalization and compound annual growth rate (CAGR) through the next five years. The U.S. biotechnology industry earns nearly 38% of the global biotechnology revenue with revenues expected to increase 3.9% to $87 billion in 2012.[14] The U.S. biotechnology industry has a trade surplus of approximately $900 million and the industry's market value is expected to grow by an annual

average of 5.8% through 2015.[15] These increases are nearly triple the forecasted growth of U.S. Gross Domestic Product of 1.9%.[16]

Based on the current and projected financial and growth metrics, it is clear the biotechnology industry in the U.S. is healthy and strong. Although there are numerous hurdles frustrating stakeholders and decreasing profits, these hurdles are not insurmountable and firms continue to find successful strategies to achieve profitability and health. U.S. leadership in the industry continues to benefit national security as firms seek solutions to the toughest challenges to global security issues like energy, food, healthcare, and climate change. While the current health of the industry is strong, trends pose opportunities for and challenges to continued U.S. leadership and the wellbeing of the industry.

Industry Trends

Current biotechnology trends provide insight into emerging opportunities and future challenges to maintaining the continued health of the industry. These trends include the emergence of innovative business models; pressures for improved capital management; and increased public and regulatory scrutiny.

Continued Evolution of the Biotechnology Business Model

Previously successful firm strategies to enter the biotechnology industry and become profitable where products are brought to market through a combination of basic and applied research, angel investing, VC, and eventual initial public offering (IPO) or merger no longer serve as models for new entrants. Market wide reductions in investment capital availability appear to be pressuring biotechnology firms to seek strategic partnerships and joint ventures up and down the value chain. In this model, specialized firms collaboratively work with technical experts and capital rich firms in what has been termed "open innovation." This allows firms to reach the value inflection points necessary to continue product development, but as the trend continues, firms experience increased pressure to achieve these milestones in order to maintain partnerships. This trend could increase industry profitability as risk is spread to more manageable levels and strategic partnerships increase biotechnology knowledge. The trend also poses risks as it becomes more difficult to maintain control of sensitive intellectual property across partnerships that span across borders and regulations. Also, increased uncertainty about successful firm strategies may act as another barrier to entry potentially blocking new innovations.

Pressures to Improve Capital Efficiency

There is a trend for biotechnology firms to be efficient and creative in financial support of technology development. Since the economic downturn in 2007, startup biotechnology firms have seen increasing challenges in accessing the capital necessary to take an innovation from concept to market. Beyond the high cost of development, firms also required funding for IP protection and regulatory approval processes which increase the period of time required for investors to acquire real returns on investment. Additionally, many start-up firms do not succeed in introducing a product to the marketplace. While family assets and wealthy speculators, angel investors, can be tapped to begin the development process, firms quickly discover greater need for investment, but VC investors are increasingly unwilling to back early stage biotechnology and government R&D funds are stagnant and potentially falling. Innovative firms have successfully acquired investors by increasing capital efficiency through strategic partnerships,

licensing of intellectual property, use of low-cost publicly provided offices and lab space (incubators), and better business management. Increased capital efficiency means that biotechnology firms are more business savvy and better managed, but too stringent of capital controls could keep important innovations off the market and on the bench.

Increased Public and Regulatory Scrutiny

Public sentiment and perception has been an influencing factor in biotechnology since the beginning and this trend is increasing as the industry matures. The term biotechnology typically elicits a range of emotions, from wonder and amazement to fear and rejection. Firms had mixed success in early debates on genetically modified crops and the use of embryonic stem cells that limited industry growth and profitability. As the pace of scientific advancement in the biotechnology field increases, there is a danger that the industry will manufacture products faster than the public can resolve concerns over the potential health, ethical, property, and other issues associated with those products. Without successfully addressing the trend in public skepticism, the biotechnology industry cannot attain its total profit potential due to inability to access the global marketplace.

The emergence of a new business model, increasing pressure on financial stewardship, and public and regulatory scrutiny are key industry trends. These trends have varying impact across the biotechnology industry, in some cases raising additional challenges and changing firm conduct in others. Maturity of the biotechnology industry will result in continued evolution and innovation, but downward manifestations of current trends could negatively impact the health of the industry and decrease the U.S. comparative advantage.

Industry Challenges

Access to Capital

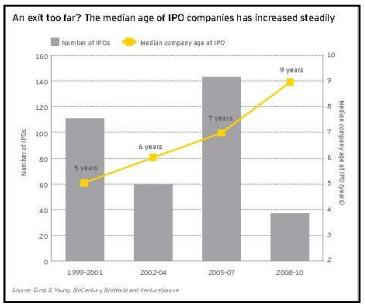
The U.S. biotechnology industry relies on capital from the government (e.g. federal grants, contract, and tax incentives) and private sector (e.g. angel investment and venture capital) to support research, development, and growth. As government budgets are reduced and VC grows more limited innovation is stifled increasing pressure on the health and U.S. leadership of the industry.

Even though U.S. federal funding commitments for life science research, which includes biotechnology, only accounts for 25 percent of total U.S. R&D expenditures, those dollars fund over 50 percent of all basic research and are critical to sustaining U.S. scientific leadership.[17] Through the NIH, the vast majority of these funds are dispersed to diverse aspects of life sciences, including human health and medical care. This federally funded research leads to commercially viable diagnostics, therapies, and treatments for patients and to the development of innovative new lines of scientific inquiry. The high costs associated with this level of research stretch timelines to gain returns on investment beyond periods acceptable to private entities.[18] Lack of impetus for private ventures to fund diverse and fundamental life sciences research is a main reason why government funding to biotechnology research is so critical.

NIH funding doubled from 1996 to 2003, but has remained somewhat stagnant since then falling behind inflation ostensibly decreasing in value.[19] For 2012, over 50 percent of NIH's $32 billion budget funds research with an estimated $5.6 billion going

Figure 1 - Firms Seeking IPOs are

directly to biotechnology-related research. Current concerns over the U.S. federal debt and annual deficits, including a looming sequestration in fiscal year 2013 budget, may lead to potentially severe, reductions in basic research funding. It is not likely that any government funding reductions for research would be made up by the private sector, which supports work directly focused on bringing its biotechnology products to market. Therefore, reduced government funding poses a challenge to innovation and growth in the biotechnology industry.



While government funding is critical to the advancement of basic biotechnological research, private capital provides the necessary funds for firms to support manufacture and delivery of products and services. As the aforementioned capital efficiency trend explained, Biotechnology startup firms are considered high risk investments, VC investors have moved out of early stage financing,[20] and new biotechnology firms are required to seek investment from angel investors, family members, and charitable foundations which only fund early stage R&D.[21]

To acquire VC from investors looking for huge returns and move beyond basic research, startup companies must undergo increasingly stringent due diligence reviews and demonstrate high potential for success.[22] Previously, if a firm could secure $20 million in VC funding, it received all of the funding up front. Today, if funding can be secured, a small portion of the funding is made available immediately and the rest is given out over time after the firm meets a series of milestones.[23] VC investors only provided the biotechnology industry $3.92 billion in 2011, well below the $6.17 billion 2007 peak.[24]

Additional pressures on a firms access to capital and availability of VC is the lower confidence that the public is showing in biotechnology startup stocks. Since 2008, the public market for funding has been especially challenging for new biotechnology firms. IPO investors are demanding proof of concept data prior to purchasing young companies' stock.[25] By 2011, the median age of the typical biotechnology IPO had increased nine years (Figure 1).[26] Since VC is tied up in startups for longer periods of times, there is a reverse ripple effect further delaying the investment of VC funding into other emerging firms. If left unaddressed, the issues surrounding acquisition of private sector capital could derail the biotechnology product pipeline, stall growth, and destroy U.S. leadership in the industry in the long term.

The access to capital challenge has not been totally destructive to the industry. Potential rivals in the marketplace have found themselves bedfellows as firms across the industry partner to survive. These partnerships gave the startups access to billions of dollars to pursue the R&D needed to commercialize their innovative technologies and increased credibility about the potential of their products with investors.[27] Large firms found the partnership gave them access to more efficient R&D capabilities than their own departments and an ability to begin developing the new products and earnings opportunities necessary to meet shareholder expectations.

Although it has found some new ways to address challenges relating to capital access, the biotechnology industry needs continued access to more traditional methods of financing.

Currently, the U.S. is reaping the benefits of a strong and healthy biotechnology industry, but long-term prospects are grim if basic research stagnates and stops yielding promising new biotechnological innovations or new entrants find they are unable to bring innovations to market.

Risk of Biotechnology Misuse

The biotechnology industry holds great significance to U.S. security; indeed, the current NSS explicitly and implicitly assigns the industry several responsibilities in advancing major U.S. interests in the areas of security, prosperity, and international order. These assignments demonstrate the government's positive view of the industry, but should biotechnological breakthroughs be misused to cause harm, the industry faces significant risks to its continued health. While the science of biotechnology holds revolutionary potential in the healthcare, agriculture, defense, and industrial production and environmental sectors, its misuse raises significant national security concerns.

The NSS seeks to prevent attacks on the homeland, deny terrorists weapons of mass destruction, and counter biological threats.[28] It recognizes that the effective employment of a biological weapon could risk the lives of hundreds of thousands and carry grave economic, social, and political consequences.[29] The 2004 National Research Council report entitled Biotechnology Research in an Age of Terrorism provides insight into biotechnology's possibilities, but also illustrates the magnitude of its associated security challenges. The report outlines seven classes of biotechnology activities that have dual use and pose a significant risk of misuse (Figure 2). The now-widespread knowledge and ability to engage in these activities holds significant risk of misuse by terrorists or other international actors as avenues of attack against the U.S., its allies, or vital interests.

Seven Classes of Experiments of Dual Use Concern

1. Rendering a vaccine (human or animal) ineffective

Figure 2 –Classes of Experiments

Although there are significant risks to all facets of national security posed by the misuse of biotechnology, there is no comprehensive federal policy. The NIH published a policy to address risks to public health and the environment posed by research involving recombinant deoxyribonucleic acid, but a significant amount of dual use biotechnology falls outside the purview of these guidelines. Although the National Security Staff formed an Interagency Policy Committee to assess potential oversight mechanisms in November 2011, the committee has yet to publish specific guidance.[30] Biotechnology firms have acknowledged the risks of dual use applications, implemented varying security precautions to maintain control and accountability of products and research, and some would prefer to use industry standards rather than sometimes difficult to interpret government policies. Should biotechnology's misuse lead to significant loss of life and economic losses, the industry could find itself in a situation similar to the nuclear industry following Japan's Tsunami.

Acceptance of Biotechnology Innovations

The first few pages of the 2011 U.S. National Military Strategy cite population growth and its impact on water and food scarcity, global climate change and the risk to populations near coastal areas, and geo-political energy security risks as some of the major security threats to the

United States and its allies.[31] Armed with the latest scientific breakthroughs, biotechnology firms discover new methods to address these maladies and many others facing the world. As these solutions are developed there are growing concerns about consumer acceptance of biotechnology products. If controversy over the research methods, ethics, and health impacts of biotechnology-derived products and services continue the industry's profitability will diminish.

Although the science of biotechnology provides the basis to develop incredible products and services that could be applied in innumerable manners across the entire economy, none of the science matters if consumers are unwilling to purchase those products. European and Asian concerns over the risks of consuming GM food, the ethical debate over embryonic stem cell research, and negative perception of patent-related litigation on GM seeds demonstrate the challenges the industry faces in garnering public support across the scope of industry activities and products. These and other concerns will continue will continue to manifest themselves as science advances and may impact the profitability of some segments of the industry. The biotechnology industry's handling of previous debates was suboptimal and further isolated the industry from lucrative markets and customers.

Firms must find a way to keep the science behind their products digestible for consumers. Biotechnology firms must not disregard the tremendous opportunities and advances available to them should worldwide populations change their perceptions of various biotechnology products and services. With comprehensive strategic communication planning the industry can begin to turn the tide on public sentiment and move behind this debilitating challenge.

Regulatory Environment

The biotechnology industry requires an effective and coordinated regulatory framework in order to stay healthy, maintain public confidence and advance the rate of growth. From the production of new drugs and medical research, to increasing food production, the biotechnology industry has made some amazing discoveries that have benefited many while simultaneously bringing economic advantages to the nation. However, these innovations bring threats and uncertainties along with the opportunities. Therefore the federal government has the responsibility for the safety of new products that are developed and commercialized. The challenge is to ensure public safety while keeping the U.S. biotechnology industry profitable and at the forefront.

The present approval system was established in 1938 by the Food, Drug, and Cosmetic Act of 1938 (FFDCA) which requires all food and drugs be approved for safety and efficacy by the FDA, (this was extended to include medical devices in 1976). The FDA requires the biotechnology industry to comply with a stringent approval process which necessitates significant capital investment. This process is not only expensive, but requires years of testing many potential products in the R&D phase of food and drug manufacturing.

There appears to be a broad agreement that the biotechnology industry as whole needs to be regulated. The questions remain: how much is necessary and where should efforts be focused in order to balance risk and benefits between government, industry, and society? The FDA is responsible for keeping public safety and product efficacy foremost as it deals with an industry whose success hinges on its ability to be extremely innovative. One of the current challenges is the perception that regulations focus on drugs and agriculture as a whole, with little distinction between chemical and biologic products. This gives the impression that the FDA has taken a one-

size fits all approach. An approach that is incongruent with the distinctions between the different categories.

Another of the challenges with industry regulation is that there is no one agency that serves as the single approval authority. There are four agencies that share oversight of the biotechnology industry in the U.S.: the FDA, USDA, EPA, and the USPTO. These agencies must evaluate and balance the risks and potential benefits when making decisions with regards to biotechnology.

Similar to chemical and biologic product regulation, GM foods are regulated by various government agencies as well. In the United States, USDA regulates GM plants. However, GM animals are regulated by the FDA.[32] This has generated great controversy and misunderstanding among the public. FDA regulates GM animals under new animal drug application provisions of the FFDCA. Therefore, new animal drugs fall under the jurisdiction of FDA's Veterinary Medicine Advisory Committee for approval. Unfortunately, consumers were perplexed on why the FDA's regulatory procedures had veterinarians regulating food meant for human consumption. Consumers naturally wonder why the USDA does not have jurisdiction over the food applications. This only exacerbates negative public sentiment naturally resident in an already confused consumer.[33]

These misunderstandings feed negative public sentiment and slow public acceptance and commercialization efforts. Nowhere is this more evident than in Congress, where 40 members recently cited serious concerns with FDA's review and approval process. Over 50 consumer and environmental groups endorsed these concerns.[34] Several congressional bills are currently under debate to shape various aspects of the biotechnology industry. Collectively, misunderstandings lead to lengthy approval processes as the FDA attempts to answer all Congressional and advocacy group concerns. This further threatens market commercialization, as potential producers shy away from an increasingly uncertain and complex approval process.

Sustaining Innovation

Biotechnology clusters, human capital, and intellectual property protection are key elements to sustaining biotechnology innovation in America, necessary to keep the industry healthy and the U.S. in a leadership role. Initiated in 1973 with the development of gene splicing techniques, a unique amalgamation of biotechnology clusters emerged across the U.S. These clusters are characterized by strong intellectual property rules, the world's best universities, sustained government support, and diverse private investors form the foundation of a biotechnology industry built on an innovative workforce.[35] The foundation of U.S. biotechnology innovation is the nation's Science, Technology, Engineering, and Mathematics (STEM)-capable workforce. "To succeed in the complex field of biotechnology firms and nations need skilled scientists and other workers for [research and development] and supportive activities."[36] Sustained excellence in innovation will require increased U.S. commitment to STEM education.

***Global Biotechnology Clusters*:** Biotechnology clusters are centers of innovation that leverage the collective efforts of academe, firms, and capital sources (public research grants and private venture capital) in a geographic region. These innovation centers include service-support firms that provide scientific products, good academic institutions to train scientists, research hospitals, and large patient population to conduct clinical trials. The report of study team visited U.S. biotechnology clusters the team visited in Boston, San Francisco, and San Diego. Each utilized

prestigious academic institutions in those clusters to produce intellectual property that drive innovation. The array and fit of these clusters provide near to midterm assurances that the U.S. will remain the leader in the global industry comparative advantage in biotechnology clusters.

Many countries are replicating the biotechnology cluster model with mixed results. The U.S. still dominates the global market in terms of innovation, Europe is second with six of the top 10 countries on the Scientific America Worldview rankings. Overall, the U.S. is ranked number one with a sizable point margin ahead of Denmark, Sweden, Canada, and Australia. The U.S. also took the number one ranking in the IP and Education/Workforce categories.[37] A strong U.S. biotechnology cluster model of innovation is positioned to take advantage of revolutionary new biotechnology ideas in biofuels, genetically replicated organs, nanotechnology, bioinformatics, or new fields not yet conceived.

The study team observed, during international field studies, that biotechnology clustering is globally recognized as an important and synergistic industry relationship. Canada, Asia, and Europe have all implemented the biotech cluster model with mixed results. Even though Canada shares a border with the U.S., the largest biotechnology market in the world, and has been partnering with developing countries, it still lacks intensity and talent retention. Asia, on the other hand, has a comparative advantage in labor costs, potential market size, and scientific degrees. However, Asia (except Japan) has poor IP protection which stifles capital investment. In addition, the study team witnessed a very unbalanced clustering in the Asian countries visited, with the government more heavily involved in attempting to drive innovation. This seemed to lead to a lack of initiative on the part of the industry and academe legs of the triple helix there. Europe has an advantage in industrial biotechnology such as enzymes, but still lags behind the US in innovation. To date, planned international biotechnology cluster development has fallen short of expected innovation results. However, in the long term, the U.S. comparative biotechnology advantage could decline due to overseas scientific human capital improvements, mergers/acquisitions, cheaper clinical trials/manufacturing, and a decrease in NIH biotechnology spending.

***Human Capital*:** The human capital challenges impacting the industry and its capacity to innovate are the same facing much of the high-technology economy: the U.S. education system must produce the needed scientists, technicians, engineers, mathematicians, and related professionals to support the industry and sustain growth. "At current rates, [Associate or Higher Degrees] conferred would have to increase by about 10 percent a year to eliminate the [~3 million] shortfall – or the economy would need to slow its demand for higher education workers."[38] Many foreign STEM students remain in the U.S. on work visa, but many of these workers are being lured back to their home countries with incentives. The study team observed this point during international field study visits. Many of our Asian hosts noted that they received both their education and experience in major U.S. institutions, but were now back in their home countries.

The challenges facing the U.S. labor force in meeting the needs of the rapidly growing biotechnology sector are a function of its interdependence with the U.S. education system. Some trends across the education system give pause and point to the need to take action to reverse course and shore-up the U.S. STEM advantage. Without increased throughput and retention in these important fields, our biotechnology advantage is at risk. Finally, the overall population must be better technically versed to benefit from and understand emerging biotechnology.

***Intellectual Property Protection*:** A scientifically literate workforce is not the only factor for continued innovation; the industry's intellectual property must also be protected. Patents are the means to that end; they sustain innovation and safeguard the interests of both the public and private investors. Viewed from the angle of innovation policy, patents aim to foster innovation in the private sector by allowing inventors to benefit financially from their inventions.[39] The incentive mechanism of patents has been traditionally contrasted with their negative effect on competition and technology diffusion. Patents have long been considered to represent a trade-off between incentives to innovate on one hand, and competition in the market and diffusion of technology on the other.[40] However, recent evolutions in science & technology, patent policy, and progress in economic analysis of patents, have nuanced this view: patents can hamper innovation under certain conditions and encourage diffusion under others. The impact of patents on innovation and economic performance is complex, and fine tuning of patent design is crucial if they are to become an effective policy instrument. Recent federal court cases such as Mayo v. Prometheus (diagnostic test to set dosing) and Myriad (isolated DNA sequence related to breast cancer) have brought to light that there is still disagreement, uncertainty, and friction on which biotechnology innovations are patentable under U.S. law.[41]

Emerging Technologies

The biotechnology industry has the potential to continue to revolutionize and redefine the way healthcare, energy, agriculture and industrial applications are provided through new and emerging technologies. As the cost of food, fuel, healthcare and industrial products continues to rise due to increasing demands and limited resources, biotechnology's emerging applications provide increasingly valuable opportunities to reduce costs and increase yields. This section discusses some of the most noteworthy emerging areas within biotechnology.

Regenerative Medicine: Regenerative medicine techniques and approaches include, but are not limited to, the use of stem cell transplantation and the reprogramming of adult stem cells to generate various human tissues. Regenerative medicine products and therapies have the potential to revolutionize healthcare by either augmenting the body's own regenerative potential or regenerating new tissue to replace defective or diseased tissue.[42] What differentiates regenerative procedures and techniques from current conventional medical therapy is regenerative medicine offers the cure or replacement for the failing, impaired, or damaged tissues, rather than normal symptomatic treatments or drug therapies for the same conditions.[43]

With national healthcare expenditures, totaling 2.2 trillion dollars annually (17.9% of GDP), including Medicare costing $431 billion and Medicaid costing $345 billion annually[44] are indicators that our healthcare costs are unsustainable. The cost benefits of regenerative medicine curing previously untreatable diseases are a potential benefit for both the government and the health insurance industry. Much of healthcare costs occur from symptomatic treatments of chronic diseases, their subsequent complications, cost of prescription drugs, and then follow-on treatments. Regenerative medicine has the potential to reduce these costs by focusing on functional restoration of damaged tissues rather than abatement or symptomatic treatment; the effect can potentially reduce the reoccurring costs of common debilitating diseases such as, diabetes, arthritis and cardiovascular disease and cancer.[45]

Bioinformatics: Bioinformatics, a nascent discipline within the field of biotechnology, enables rapid advances in biotechnology that can help to generate innovative solutions to enhance national security. Bioinformatics is the application of computer science and information technology to the fields of biology to manage and analyze data from biologic research.[46] Bioinformatics bridges the gap between basic research and industry, enabling the development of innovative biotech products. As an enabler discipline to the biotechnology industry, bioinformatics merges many scientific and technical disciplines for generating new knowledge of biological systems to enable the development of end-use applications.

Disease, war, and biological terrorist have killed hundreds of thousands of Americans. The 1918 Spanish flu, now understood as the H1N1 influenza virus, killed 675,000 Americans.[47] In 2001, five Americans died and 17 others were sickened in a spate of anthrax-laced letter mail attacks.[48] Over 3,000 U.S. troops have been killed and over 31,000 others grievously wounded by improvised explosive devices (IED) attacks in Iraq and Afghanistan.[49] Rapid advances in biometrics, bio-inspired design and bio-defense, all enabled through bioinformatics, are offering science-based, end-use applications that can enhance national security and provide the U.S. with the ability to operate preemptively to deny adversaries the ability to create an asymmetric event.

Biofuels: The U.S. is the world's number one consumer of oil – a fossil fuel that the world consumes at the rate of 82.8 million barrels per day[50]. The global demand for oil is forecasted to increase 31% by 2035.[51] As a fossil fuel there is theoretically a limited quantity of oil available, and some experts predict oil will be depleted within the century. The U.S. demand for oil, driven by the transportation sector's demand for fuels, requires a dependency on other countries for almost 60% of its oil supply, including several countries deemed unstable.[52] The competing global demand for this fossil fuel and its inevitable depletion, CO_2 emissions contributing to the green house gas effect and global warming, and the dependency on foreign oil supplies and volatile pricing compels the U.S. to develop an alternative liquid fuel option. Biofuel is an emerging technology that can provide the transportation sector a liquid fuel alternative to petroleum-based fuel.

The attractiveness of a biofuel as an alternative liquid fuel is that it is not derived from fossil fuel, has fewer emissions when burned, it is renewable, and can be domestically produced. While biofuels have existed for over a century, they have not been able to bridge the technology "valley of death" -- the gap separating technology development and technology deployment.[53] Consequently, biofuel has not been available as a mass-consumed fuel option for transportation. However, the biotechnology industry can provide solutions to many of these barriers. Some of the barriers biotechnology can address include adequate feedstock supplies, manufacturing scalability, sufficient energy content, and competitive pricing with government-subsidized gasoline. Ultimately, government, industry, academe and consumers all have a role in the success of bridging the "valley of death" that will eventually lead to the development and manufacturing of a liquid biofuel alternative to petroleum-based fuel.

Nanotechnology/Biotechnology Convergence: Nanotechnology, similar to biotechnology, comes with high expectations, promising exciting new pathways to medical diagnosis, early treatment, and disease prevention. A nanometer (nm) is one billionth of a meter. As a matter for comparison, the size of a human blood cell measures 2,000-5,000 nm in length and a strand of DNA has a diameter of 2.5nm.[54] The U.S. National Nanotechnology Initiative defined

nanotechnology as: "the science, engineering, and technology related to the understanding and control of matter at the length scale of approximately 1 to 100 nanometers, but also R&D of materials, devices, and systems that have novel properties and functions due to their nanoscale dimensions or components."[55]

Advances in both biotechnology and nanotechnology but more importantly, the union of these two fields create a "bio-convergence" where biology joins electronics, making possible breakthrough advances across the spectrum of healthcare. [56] Nanomedicine applies this technology for the betterment of human life. This technological leap facilitates and accelerates the equally astounding advancements made within the biotechnology industry. Nanotechnology creates a significant synergistic impact in healthcare, and has nearly unlimited potential benefits for society. Nanotechnology, in medicine, is the future of healthier living, and the medical community is actively using nanotechnologies to create better drug delivery systems that make the absorption of medication more effective and safer.[57] New nanotechnologies will permit the acquisition of an immense amount of biological information and then quickly analyze it for disease biomarkers allowing pre-symptomatic treatment of diseases. Early diagnosis, targeted treatment, and personalized devices all act to augment the medical advances promised from biotechnology. Currently, nanoscale drug delivery systems account for 75% of sales while the most widely used nanotechnology in medicine is nano-enhanced in vitro diagnostic techniques.[58] In short, nanotechnology represents new areas for innovation in medicine allowing the U.S. to maintain the leadership role in biotechnology.

Genetically Modified Animal Agriculture: GM feed crops have been widely accepted throughout the United States. Although a majority of U.S. consumers have accepted GM food from feed crops, it is unknown whether or not they will similarly accept GM foods from animals.[59] This is an even more sensitive concern internationally where GM food from feed crops is still being resisted. The study team observed this, as every organization questioned on the Asian international field study stated concern about potential national and international reaction to GM food in their country. Concern that some seemed to believe could be mitigated through education and awareness on the safety of GM foods. Regulatory bodies play a crucial role in influencing public awareness and acceptance. Advancing both public awareness and acceptance for biotechnology's role in animal agriculture is absolutely critical to successful commercialization of GM animals and the ability to feed the world's growing population.

If the world is to feed 9 billion people by 2050, it will need to more than double the current level of food production.[60] Growing urbanization leads to an increased demand for livestock food products, as city-dwellers' diets are richer in animal proteins and fats.[61] Favorable public sentiment for GM food products would enable biotechnology to help close the ever-widening global food gap. At present, there are no GM animal food products approved for human or animal consumption in the United States.[62] However, one application under research for commercialization is the AquAdvantage Salmon. This product has the potential to increase aquaculture productivity and human health.[63] The fish's bio-engineered genetic makeup enable it to grow at twice the rate of Atlantic salmon and they reach the market in half the time (approximately 18 months versus 3 years.)[64]

In the final analysis, successful commercialization of GM animal agriculture is all about awareness and acceptance. If successfully commercialized, this technology can help us achieve

our national interests and improve our national security. Where there is death from starvation and malnutrition, there is instability and insecurity in the world. Defeating world hunger can result in improving our national security posture by reducing our military commitments to "hot spots" throughout the world and preempting an important factor (hunger) that often has led to extremism and expansionism.

OUTLOOK

Financing challenges, a conservative regulatory environment, an emerging business model, and mixed public sentiment are industry trends that will continue to shape the industry environment. Globally, unmet demands for food, water and energy will stimulate industry growth given world population growth, shifting demographics and competition for limited natural resources. Overall, the biotechnology industry is healthy and has a favorable outlook, but in the next five years, reduced public funding, greater social awareness, and increased foreign investment will influence industry growth.

Near-Term: 2013-18

The near-term strategic outlook for the biotechnology industry remains positive, though growth will be slower than previously forecast. The industry continues to recover from the 2007 economic downturn that stymied industry growth, but some downward pressures persist. Industry development in response to global, unmet demands, the regulatory environment and access to capital has historically been drivers in industry growth and will continue in the short-term.[65] Megatrend pressures will lead to applied R&D that will provide a means to satisfy domestic and global demand to unmet needs. The negative effects of unmet global needs should create prioritized funding opportunities for the industry. For example, the industry has the capacity to make further advances in GM products (agriculture and livestock) and water purification to meet the demand for food and potable water for the world population of 2050. The industry also has the growing capacity to control or eradicate diseases, improve the general health of an aging population, and provide clean, renewable energy sources that have no adverse effects to the climate. The five major factors driving the five-year outlook are reduced government funding, social awareness and acceptance, industry consolidation, and foreign investment.

Reduced Government Funding: U.S. government funding for life science R&D, including R&D applicable to the biotechnology industry, has remained relatively flat over the last several years but, has kept pace with inflation. Although there is general popular and political agreement that federal funding of life science research is a priority, current concerns over the federal debt and deficits, including a looming sequestration in fiscal year 2013 budget, may lead to future reductions in R&D funding. With reduced future budgets, government funding in support of biotechnology will face fierce competition from other national priorities such as defense, education, and social welfare programs. Reduced government funding is a threat to innovation and development in the biotechnology industry.

Social Factors: To date, public acceptance of biotechnology has been mixed and promises to remain so for the near-term. Ethical debates over stem cell research and GM food have affected major categories of biotechnology R&D and continue to have the potential to affect industry

growth. For example, the debate over the public health implications of GM plants and animals in the food supply limits GM food entry into major markets. As the scientific community improves its communication and provides a moderating view of the science, benefits and risks of GM foods, the image of "Frankenfish" on the dinner plate will evaporate, and GM foods will become more socially acceptable to a better educated, more rational and aware public. Finally, the fuel-versus-food debate highlights the need to understand fully how biotechnology development in the energy sector can affect prices in the food sector.

Industry Consolidation: Mergers and acquisitions (M&A) are common during the maturation of an industry and biotechnology is no exception. Recent consolidation in the biotechnology industry is the result of several factors including pharmaceutical patent expirations, a business model that no longer seeks full vertical integration, decreasing public funding of R&D, and venture capitalist being less willing to risk early investment. In the near-term, M&A will likely increase as investor confidence continues to return.

Increased Foreign Investment: Reduced capital inflows in the U.S. and Europe stemming from the economic downturn creates opportunity for countries like China and Brazil, whose emerging economies are expanding rapidly, that have capital to invest. As the U.S. biotechnology industry struggles for funding from traditionally reliable sources, it will be forced to rely on offshore global funding. This capital could come with conditions that require U.S. firms to establish a presence in countries where capital originates or that require teaming with firms located in countries where capital originates. Overtime, this will erode the U.S. leadership in the industry. Additionally, intellectual property (IP) generated from research by U.S. firms under foreign influence will be at greater risk since many foreign countries lack strong IP protection. With increased exposure of foreign investment, the U.S. risks proliferating its IP advantage to foreign competition, which will reduce the U.S. comparative advantage in the biotechnology industry.

Long-Term: Beyond 2018

Several environmental factors will influence industry growth in the long-term, including declining use of non-renewable fossil fuels, geopolitical insecurity, U.S. national security, and environmental sustainment, all influenced by rapid population growth. As genomics-based, personalized medicine and synthetic biology evolve, the role of biotechnology in U.S. national security will increase. The pressures created by global unmet needs caused by megatrends will require prioritization of fiscal resources to ensure sustainable and renewable food and energy supplies. If sufficient intellectual rigor is given to prioritization of R&D dollars in the near-term, the biotechnology industry will be poised to innovate broad, long-term solutions to global market demands. The biotechnology industry is projected to grow moderately in the long-term, with an accommodating regulatory environment, advances in personalized medicine, a better-educated STEM workforce, and advances in synthetic biology acting as catalysts.

Regulatory Environment: Over the long-term, the regulatory environment should adapt to advances in biotechnology R&D. As the public becomes more familiar with the advantages in public health and environmental biotechnology innovations, agencies involved in regulation and oversight will adapt to new demand for biotechnology products and services and will refine their processes. This will allow the industry and the regulatory community to move forward with greater confidence and efficiency, positively influencing growth. For example, greater understanding of

the public health benefits of GM foods will enable regulatory agencies to take definitive positions on the issue, enabling the industry to advance with confidence in choosing where, when, and how to compete. Secondly, as the pharmaceutical regulatory community adapts to the science of biotechnology, regulatory oversight of biopharmaceuticals R&D will become more efficient (as it did with biosimilars), allowing drugs to be brought to market sooner and at lower cost.

Personalized Medicine: Remarkable advances in biotechnology and related medical sciences should make personalized medicine a reality. Breakthroughs in genomics will allow a person's DNA to be sequenced and stored affordably, permitting the industry to tailor medicines unique to an individual's biomarkers. These medications will be appropriate for that patient only and may be detrimental to a patient with different biomarker physiology. As understanding of DNA grows over the next decade, personalized medicine will improve health and increase life expectancy, with an anticipated decrease in overall healthcare costs.

Human Capital: The U.S. workforce innovation advantage is likely to continue beyond 2018, but without a significant shift in current trends, the gap between industry requirements and college output will widen. While U.S. STEM graduates are declining, foreign countries continue to incentivize STEM programs and produce increasing numbers of advanced degree holders. Although questions exist about the comparative quality of these degrees from many parts of the world, in the long-term, international students' STEM proficiency will directly compete with the U.S. workforce. The U.S. biotechnology industry recognizes this concerning trend and has embarked on various efforts to increase interest in STEM education in order to sustain innovation. This effort will have limited near-term impact, but it may start to reverse the trend beyond 2018.

Synthetic Biology: Of the advances in biotechnology, synthetic biology may offer some of the greatest potential. Through advances in bioinformatics and, genomic sequencing, manipulation, and synthesis, synthetic biology offers the potential to drive rapid growth across a wide range of existing market sectors such as healthcare (personalized medicine), agriculture (higher crop yields), energy (biofuels), and the environment (degrading hazardous compounds). Additionally, advances in synthetic biology have tremendous potential to open new market segments to the biotechnology industry.

Outlook Summary

For the near-term, the U.S. biotechnology industry will remain the leader in the global marketplace. However, the industry must increase its efforts to secure sufficient public funding for R&D as well as promote STEM education to secure a sustainable, competent, and innovative workforce for the future. The biggest impediment to the industry meeting broad national security requirements involves U.S. government policy and prioritization of resources that will enable the industry to achieve its full production and mobilization potential. Declining public funding of R&D and political hesitance to resource biosecurity/biodefense commensurate with known bio-threats will leave the nation vulnerable to biological attack. According to a congressional blue-ribbon panel report, terrorism is the most significant threat to U.S. national security, and terrorists are likely to use a weapon of mass destruction (WMD) somewhere in the world in the next five years, more than likely that WMD will be a biological weapon.[66]

The biotechnology industry's responses to the near and long-term challenges must be commensurate with technical innovations and national urgency. It must remain vigilant in its strategy to address these challenges, as foreign competitors are making advances that could result

in the erosion of U.S. firms' market share. Where government funding has or will be reduced, private industry must find the means or domestic partnerships to fund R&D and to innovate.

Policy Recommendations

The issues facing the biotechnology industry cannot be solved by one entity working in isolation. The following recommendations address the challenges facing the industry with the recognition that while the U.S. government may need to take the lead in their development and implementation, it will need to partner with the other members of the triple helix to ensure they are thoughtfully implemented.

Recommendation #1: Regulatory reform to flexibly address differences between chemical drugs and biologics and streamline the approval process

Currently U.S. FDA approval is the "gold-standard" in the global marketplace. However, that does not mean that there is not room for improvement in the regulatory process. The U.S. government has a role and a societal interest in regulating the biotechnology industry. However the questions remain: how much is necessary and where should efforts be focused in order to balance risk and benefits between government, industry and society? Currently, the regulations focus on drugs as a whole with little distinction between chemical compounds and biologic drugs, giving the impression of a one size fits all approach that increases the time and cost of bringing new drugs to market. The government should address these challenges by developing testing structures that address differences between drug types. It should work to create efficiencies while still proving safety and efficacy. This would benefit all parties by speeding the overall time to market for new products and lowering the cost of new and beneficial therapeutics.

The government should also streamline the number agencies that share oversight of the biotechnology industry in the U.S. by giving drug approval to the FDA and food approval to the USDA. This change would make the total process and players much clearer and more straightforward to industry. It would also clear consumer confusion about who is responsible for food safety and perhaps give them more confidence with a single well-defined entity in charge.

Recommendation #2: Develop national biodefense framework to coordinate and synchronize all levels of government

The misuse of biotechnology exposes vulnerabilities in technological capabilities to prevent, detect, and respond to potential biological incidents that complicate timely diagnosis, treatment, and remediation. To fills these gaps the bio-surveillance enterprise should integrate all pathogen diagnostic and detection technologies under a guided national program. Stakeholders across all levels of government protecting health and human safety, and emergency response should operate on a national framework designed to coordinate and synchronize all federal, state, and local capabilities to respond and remediate incidents based on nationally accepted protocols. This will provide a level of defense against bioterrorism needed when the question is not if, but when a bio-attack will happen.

Recommendation #3: Establish framework for oversight of dual-use research and technology development

In order protect the biotechnology industry from the potentially devastating consequences resulting from misuse, government, business, and academe must work together to establish a framework for oversight of all dual use research and technology development, regardless of funding source. While government regulation will surely be involved, this framework should rely, to the maximum extent possible, on prescribed, formal internal review and oversight mechanisms established within the institutions conducting such research or development. Additionally, government, business, and academe within the U.S. must engage their international counterparts at every opportunity in order to build an international consensus around a consistent set of guidelines for oversight of dual use research and technology development. This framework will allow robust biotechnology research and technology to continue, while providing a proactive shield against government and societal backlash, and the potential debilitation of the industry, that technological misuse could cause.

Recommendation #4: Adopt a national innovation strategy

The U.S. should adopt a national innovation strategy. It is essential for the U.S. government to lead in this important area. It must fund R&D and incentivize industry's investment in it. This is critical because R&D is the foundation for innovation, and industry will continue to shy away from unprofitable basic research.

This strategy should assign a lead agency for innovation and task them to coordinate efforts of four pillars: to streamline government rules and regulations, index government R&D investment, incentivize R&D investment through tax incentives, and increase STEM education. The strategy provides a foundation to build government-wide programs and policies increasing innovation. Lastly, the strategy sends a clear signal to all industries, but especially the biotechnology community, that the government understands the multidimensional, interdisciplinary challenges facing this critical domestic industry and desires to partner with the industry to address them.

Pillar 1: Incentivize R&D investment by changing U.S. accounting rules. R&D costs are significant in the biotechnology industry based on the growth stage and structure of the market. It is in the U.S.'s national interest to incentivize R&D in biotechnology to maintain the health of the industry and the U.S. current comparative advantage. U.S. policy makers should pursue an accounting rules change to allow for the capitalization and amortization of R&D costs in the biotechnology industry. Capitalization of R&D costs would provide positive behavioral and economic benefits to the biotechnology industry while increasing U.S. competitiveness with foreign firms. Moreover, capitalization of R&D costs has historical precedence in other industries where there are distinct strategic advantages to be maintained and recognition that technology and innovation are eclipsing the manufacturing based economy.

Pillar 2: Index U.S. federal government R&D investment to inflation. The U.S. government should exempt all biotechnology R&D funding from any future federal budget reductions and increase it's funding at a rate equal or above the annual inflation rate. In addition, or alternatively, it should investigate if future funding should be tied to some other measure of U.S. earning power, such as percent of GDP. The U.S. government should conduct a federal study to determine if there is any advantage to realigning or re-appropriating certain healthcare funding,

such as Medicare, to increase biotechnology R&D budget. This indexing of U.S. government biotechnology R&D investment will ensure that the engine of the biotechnology industry is continually fed at a level to keep it healthy and in a global leadership role.

Pillar 3: Align U.S. biotechnology tax rates with rest of world and allow repatriation of profits at a reduced rate. Federal and local governments should encourage the biotechnology industry to remain in the U.S. by maintaining tax rates on par with the rest of the world. Many large biopharmaceutical firms have sizeable cash reserves in offshore biotechnology business units. The U.S. government should incentivize those firms to bring that money back to the U.S. by allowing repatriation at a reduced tax rate, with the provision that the money be re-invested into R&D here in the U.S. This would have the dual benefit of increasing U.S. government tax revenues and increase funding of U.S. biotechnology R&D, perhaps keeping more R&D on-shore.

Pillar 4: Incentivize STEM education. To increase STEM education, the government needs to intensify efforts to incentivize this area of education. While biotechnology firms have the responsibility for sending clear demand signals to academe, the government must ensure: it is enforcing the right standards to ensure high quality STEM graduates from all levels of the educational system; intensely communicating the significant opportunities available to STEM graduates; prioritizing financial aid for students who choose STEM careers; allowing STEM mentors to deduct time spent with students; and, requiring long term unemployment beneficiaries to enroll in STEM training programs. This will put the U.S. on a path to addressing the concern that the STEM pipeline is currently insufficient to sustain STEM industries, including biotechnology, in the future.

Conclusion

The global biotechnology industry is in the growth stage of the economic life cycle and is expanding into new areas and markets as innovation and discovery proceed at a rapid pace. This dynamic creates hope for discovering solutions to the complex problems presented by the megatrends of population growth, resource scarcity, and climate change. The U.S. has a comparative advantage in the biotechnology industry while generating 38% of global revenues. By leading in a growing, healthy, and transformative industry, the U.S. is uniquely positioned to achieve national policy goals of economic prosperity and national security while contributing to global stability.

While the U.S. biotechnology industry's comparative advantage is secure in the near term, its ability to provide global stability and U.S. economic prosperity faces several challenges that could erode that global position over the long-term. The challenges in access to capital, misuse of biotechnology, social acceptance of some biotechnology processes and products, complexity of the regulatory environment, and sustaining innovation are not insurmountable but must be addressed to ensure continued U.S. leadership. These risks associated with these challenges can be mitigated by policy actions that will ensure the positive industry growth outlook is sustained.

Specific recommended policy actions include regulatory reform to find a streamlined, multiple-pathway approach to overcome the lengthy, one-size-fits all approach to oversight by multiple government agencies. Additionally, local, state, and federal governments should increase the robustness of the bio-surveillance enterprise to better protect against the potential misuse of

biotechnology. Further, government, business, and academe must team to establish an oversight framework for all dual use research and technology development. Finally, the U.S. should also adopt a national innovation strategy that streamlines government rules and regulations, indexes government R&D investment, incentivizes R&D investment through tax and accounting regulations, and increases STEM education.

The long-term health and continued U.S. comparative advantage in the biotechnology industry rely on the ability of academe, business and government to work together to collectively address the challenges before them. This triple helix has shown its collective capabilities to innovate and expand as the industry has grown over the last three decades. The threats facing the U.S. in the coming decades as a result of population growth, resource scarcity, and climate change will demand this same level of cooperation and innovation in order to ensure the economic prosperity and national security of our nation.

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