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BIOTECHNOLOGY

Your guide to the Biotech Industry

In collaboration with

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BIOTECHNOLOGY INDUSTRY ORGANIZATION

MEDIA PLANET

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Biotechnology: Healing, Fueling, and Feeding the World

Each day, the dedicated men and women of our nation's innovative biotechnology companies are developing new products to heal, fuel, and feed the world.

Biotechnology innovation has made dramatic contributions to reducing disease. There are more than 200 biologic medicines and vaccines available, which have benefitted millions of patients worldwide. More than 600 new biologic medicines are currently in development, including treatments for cancer, HIV/AIDS, Alzheimer's disease, and many other rare conditions.

Agricultural biotechnology has produced crops that can resist pests, disease, and climate change. Today a record 13.3 million farmers in 25 countries are planting biotech crops. With a projected global population of up to 9 billion people by 2050, our capacity to keep generations of children from hunger and starvation relies on continued improvement in crop yields and nutrition.

The industrial and environmental biotechnology sector is helping meet the challenge of climate change and opening doors to new innovations and products that will revolutionize every aspect of our lives. Global energy companies are partnering with industrial biotech companies to build commercial scale advanced biofuels facilities in the U.S. A wave of biotech start-ups are developing chemicals and plastics from renewable feedstocks.

Throughout the history of biotechnology it has been the science and the business that have driven the pace of advancement. But now, more than ever, it will be public policy that will determine our future. Even the best scientists and businesspeople cannot succeed unless we have the right policy environment to support innovation.

The health reform debate now taking place in Washington and across the country is a good illustration of this truth. There is broad agreement on wanting to achieve universal health care coverage. We in the biotech industry believe that every man, every woman, and every child in America should have access to the best health care possible, including our most innovative products.

Jim Greenwood, President & CEO, Biotechnology Industry Organization (BIO)

The biotech industry is working with the Congress and the Obama Administration to achieve this goal while also maintaining incentives for innovation—because continued biomedical innovation is the nation's best hope for reducing the burden of disease and improving our healthcare and quality of life.

Congress currently is developing legislation that will enable the review and approval of biosimilars, medicines which are similar, but not the same as, pioneering biomedical therapies and treatments. A well-constructed pathway to biosimilars can help lower the cost of biologics while ensuring these medicines are as safe and effective as the innovative products they follow. An effective pathway also must establish an extended period of data exclusivity for innovators, a defined period of time during which the U.S. Food and Drug Administration may not rely on an innovator's data to approve another company's product based on limited clinical studies. With such protection in place, we can balance our common desire to expand access with the imperative to promote further biomedical innovation.

The innovative spirit that lies at the heart and soul of every biotech company can and will provide solutions to disease, hunger, pollution, and global warming. These are tasks at which we dare not fail. And I have every confidence that we will not fail – but that we will succeed beyond even our wildest imagination. I take this confidence from the dedication of the bench scientists, the tenacity and commitment of management, and the indomitable vision and passion of our industry's leaders.

To reach these goals, we must help our political leaders better understand, to appreciate--and ultimately to encourage--the astonishing potential of biotechnology.

I hope that you will find this report on biotechnology informative—and that you will be inspired by our shared vision to heal, fuel, and feed the world.

Jim Greenwood

A special thanks to...

Bio® BIOTECHNOLOGY INDUSTRY ORGANIZATION

BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products.

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Where is the world finding answers?

Biotechnology

Biotechnology is **cutting edge science** that helps people and our planet by developing **medical treatments** for debilitating diseases, creating **new renewable fuels** that reduce fossil fuel use, and producing innovative technologies that **protect our global environment**.

Biotechnology also helps drive our nation's innovation economy, creating high-wage, high-value jobs with a high multiplier effect. The more than **1.3 million Americans employed in the biosciences** help **create an additional 6.2 million jobs**, for business services, contractors and other vendors.

And we're just getting started.

If you are looking for answers to some of our biggest challenges visit www.IAmBiotech.org/learnmore

We're working on answers. For all of us.

Let's work together.

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Biosimilars and Fair Patent Protection

Karen, a mother of two school-age children in a Northern Virginia suburb, is finally hitting her stride. After several years of dedicated child-raising, she has established herself as a well-liked teacher at a widely respected private school. By Nicole Gray

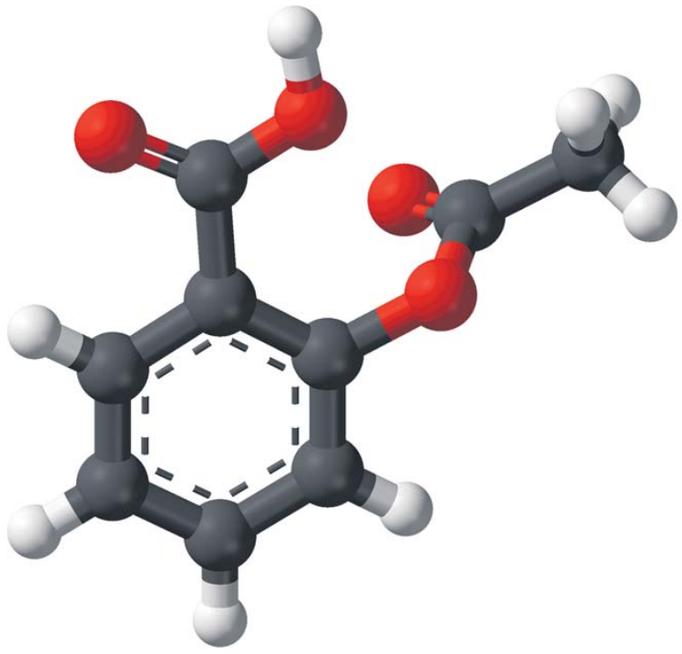
Karen's career horizons are bright, as she is completing her Master's degree in Education. Within the last year, she has joined a book club and taken a long-anticipated trip to Eastern Europe, where she and her family created life-long memories. At the same time, she has been experiencing bouts of joint pain, stiffness and swelling. It's also become harder for her to be active, despite her recent foray into Ashtanga yoga. Her need to spend weekend mornings in bed both saddens and embarrasses her. Several months before her 40th birthday, Karen visits her doctor – and her suspicions are confirmed. Karen has rheumatoid arthritis (RA).

Twenty years ago, Karen would have been sidelined by her "rheumatism." She probably would have settled in for an extended period of disability punctuated by chronic dosing of non-steroidal anti-inflammatory drugs (NSAIDS) at gut-busting levels. However, the availability of biologic, monoclonal antibody-based therapies means that most likely, Karen will be able to keep teaching, studying, parenting – and looking towards the future.

Currently, there are six FDA-approved biologics for treating RA. These drugs modify biological responses by targeting pro-inflammatory cytokines, such as tumor necrosis factor (TNF) or interleukins. In the process, RA symptoms are reduced and in best-case scenarios, disease progress is significantly slowed down. Although many patients cannot tolerant some of the medications, since there are several options, patients are often able to find a suitable treatment regimen. Fortunately, after several months, Karen's rheumatologist has found the right therapeutic strategy for her. He also likes the fact that there are nine years of data available for his target product, assuring him of the drug's safety and therapeutic durability.

According to BIO, there are more than 200 biological therapies and vaccines being used to treat not only RA and other immune disorders, but also cancer, diabetes, and HIV. Overall, 325 million patients worldwide are benefiting from biological-based therapeutics. New therapies in development are targeting Alzheimer's disease, heart disease, diabetes, and multiple sclerosis. Since 2004, when the FDA first explored guidelines for a process that would allow manufacturers to create follow-on biologics based on innovator biologics, advocates for these "biosimilars" have pushed for an expedited approval process and limited patent protection for innovators in order to offer cheaper biosimilar therapeutic options. However, caution is warranted. There is a fundamental difference between chemically synthesized small molecules and biologics. The European Medicines Agency's (EMEA) overarching biosimilar guideline specifically states that biosimilar products "by definition" are not generics, and that the generic approach "is scientifically not appropriate" for these products," says David Beier, Senior Vice President of Global Government & Corporate Affairs, Amgen – the world's largest biotechnology company. "While we have long-supported an approval of a pathway for biosimlars, we need to ensure that it strikes a balance in allowing access to safe and effective biosimilar medicines for patients, and providing fair incentives for the discovery of new medicines. There are no short cuts to patient safety."

Proteins are typically 100- to 1000-fold larger than chemically synthesized, small molecules, with difficult-to-characterize structure-function relationships. They are inherently unstable, and because they are made by living cells and even very minor changes in a biosimilar from the pioneer product can significantly alter the efficacy and side-effect profile of the biologic. Therefore, unlike the generics approval process, which was ushered in under Hatch-Waxman in 1984 and does not require clinical trials, the biosimilars approval process must be stringent, with ample clinical study to ensure quality, safety, and efficacy.1



The goal of the Obama administration is Congressional approval of a health-care reform bill by the August recess, roughly six weeks away. A key area of focus has been identifying cost-savings opportunities, including creating a pathway for biosimilars, in the federal health-care budget in order to achieve a targeted $2 trillion in savings, and to fast-track the legislation that will support those goals.

Because it can take up to two decades and billions of dollars to develop safe and effective innovator biologics, the issue of data protection, also referred to as "data exclusivity", is at the very center of the debate around biosmilars. There are currently two versions of biosimilars legislation in Congress, the "Promoting Innovation and Access to Life-Saving Medicine Act" (H.R. 1427, introduced by Henry Waxman, D-CA and colleagues in the House and S. 726 introduced by Chuck Shumer (D-NY) in the Senate) and the "Pathway to Biosimilars Act" (H.R. 1548 introduced by Anna Eshoo (D-CA), Jay Inslee (D-WA), and Joe Barton (R-TX) in the House. The "Promoting Innovation" bill provides five years of data exclusivity, while the "Pathway" bill provides 12 years. Beier believes Congress will support patients by providing incentives for the creation of new medicines through protections against unfair copying of clinical data.

Estimated federal cost-savings over a 10-year period, associated with allowing biosimilars to enter the market, range from $6 billion (with 12 years of data exclusivity) by the Congressional Budget Office (CBO), to $14 billion by the Pharmaceutical Case Management Association, to $70 billion by Express Scripts. In addition, the Obama administration's FY 2010 budget proposal estimated total savings of $9.2 billion over 10 years, based on 7 years of exclusivity. All numbers were derived based on various assumptions about market penetration, biosimilar discounting and data exclusivity. It should also be noted that CBO only estimates 10% savings in year one of biosimilars. Whereas traditional generics are discounted up to 80% cheaper than branded products, the expense associated with the biosimilar approval process will cut the discount significantly.2

Clearly, safety matters, but it is also important to consider the impact on the biotechnology industry – which employs 180,000 professionals in the United States – if insufficient patent protection creates a disincentive to continue aggressive biologics research and development. Obama recently spoke of the drive "to seek a cure for cancer in our time." That quest must be supported on all levels. "At a time when the Obama administration is investing so much in cancer research, we must not stifle the development of medical advances and the next generation of breakthrough therapies," says Beier.

1. Kresse G-B. Eur J Biopharm. 2009. doi.10.1016/j.ejpb.2009.02.014
2. MAlik NN. Drug Discovery Today. 2008; 13:909-12.

News in Brief: A Tactical Approach

Tactical Therapeutics Inc. ("Tactical") is a virtual biopharma company located in lower Manhattan, New York. Tactical's platform technology involves development of safer and deliverable small molecules by chemical restructuring of pharmaceutical agents. Currently Tactical has two cancer drugs and it intends to File an IND for its first oncology product – Carboxyamidotriazole Orotate (CTO) in 2009.

CTO is a cytostatic agent with anti-VEGF-1 activity (angiogenesis) and PI3 inhibitory activity (anti-proliferative and antimetastatic) through its effect on signal transduction inhibition. It shows promise in the treatment of solid cancers, especially in combination with current cytotoxic therapies both in early and late stages. CTO was shown to have synergistic effects with cytotoxic drugs in preclinical colon cancer (5-Fluorouracil) and glioblastoma (Temozolomide) models. Preclinical drug development has been supported by the founder, angel and private investors.

Phase I testing of CTO is expected to start later in 2009. Tactical plans to develop CTO on the Fast Track as a Cancer drug for glioblastoma and other solid tumors. To advance further, Tactical needs to raise Round B of funding and/or partner with a large Pharmaceutical company.

Generally, it is large pharmaceutical companies that dominate this business since the resources required are extremely large. However, it is not unusual for a small virtual company to discover a breakthrough technology that has a strong potential for advancing state-of the art science. Tactical's technology involves chemical modification of small molecules to make safer, more effective and affordable cancer drugs. Tactical has built a strong intellectual property portfolio for CTO ensuring world-wide proprietary rights.

The founder, Rashida A. Karmali, Ph.D, JD, MBA, was a Cancer Scientist at Memorial Sloan-Kettering Cancer Center, New York, before becoming a Patent Lawyer. A Scientific Advisory Board, and preclinical and clinical CROs have assisted her. Private investment is used mainly for drug development programs.

Personalized Medicine Redefines Patient Care

The "one-size fits all" concept of medicine is going by the wayside, thanks to the growth spurt of "personalized medicine." By Marilyn Kochman

With this concept, genetic screening and other tests are used to determine an individual's molecular or genetic profile; the information is then used to customize treatment for disease, as well as develop preventative regimens for conditions the individual is susceptible to. Traditionally, treatment for a patient is based on his or her specific characteristics, including age, gender, height and weight, family medical history, and so on. But today's cutting-edge technologies provide greater understanding of both the patient, the disease, and the treatment that would be most effective.

Some experts claim that most medications, no matter what the disease, are effective for only about half the people who take them. This means countless individuals waste money on drugs that don't work, suffer unpleasant side effects and_ worst of all_ in life-threatening situations, lose precious time. But with today's sophisticated diagnostic and screening tools, it is often easier to more closely identify which treatment will work best for patients suffering from conditions as serious as cancer, cardiovascular disease, or infectious diseases.

WHY OLD-FASHIONED APPROACHES TO MEDICINE FALL SHORT

"We in the medical community have approached diagnoses in a very simplistic fashion: 'this person has Crohn's disease, that person has multiple sclerosis,'" said Dr. Eric Topol, director of Scripps Genomic Medicine and director of Scripps Translational Science Institute, La Jolla, CA. "Each disease we see as physicians is actually a lot of different diseases at the molecular level. If we can zoom in on the root cause of the disease for that individual, we can tailor a treatment or preventative strategy so the person gets a cure, a true preemption, or much better optimal management."

PERSONALIZED MEDICINE-TOOLS OF THE TRADE

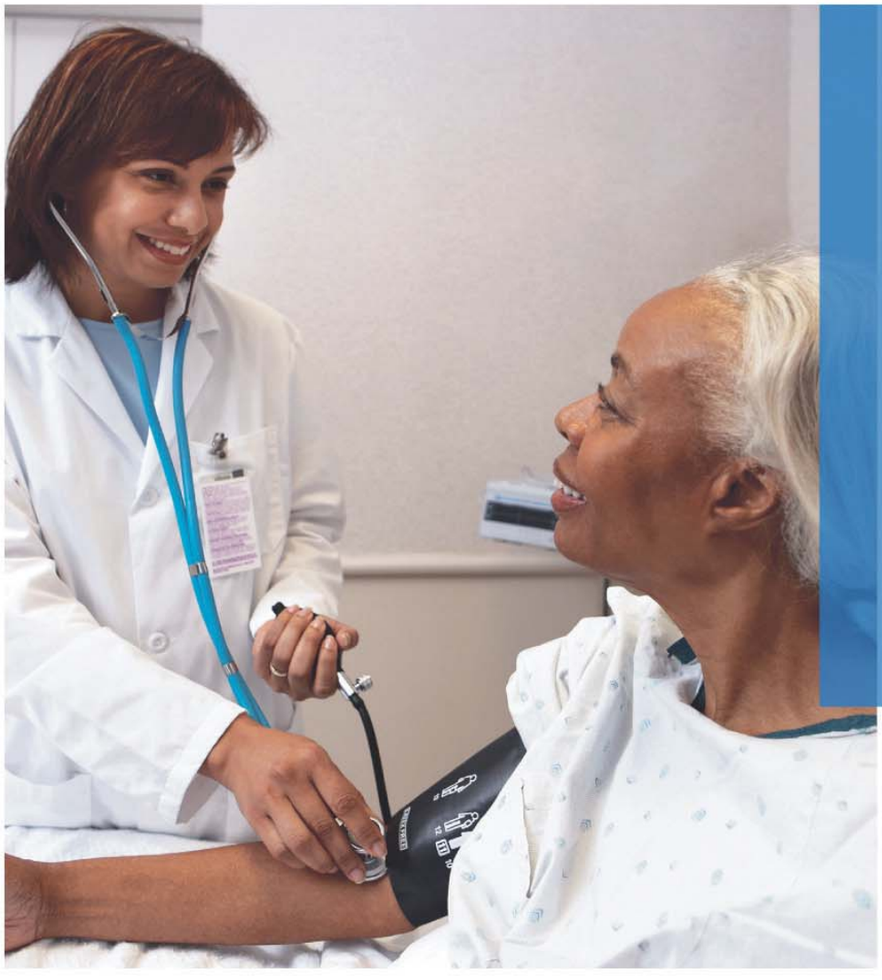
Zooming in on root causes of disease, of course, requires cutting-edge technologies. "At the beginning of this century, it took many years and cost billions of dollars to completely map the human genome for the first time," said Greg Lucier, Chairman and CEO of Life Technologies. "DNA sequencing instruments, particularly ones from Applied Biosystems (now Life Technologies), were critical to this accomplishment, and succeeding generations of technologies have allowed us to sequence the genome at ever lower cost and with greater efficiency."

Less than a decade later, genomics has entered a whole new era. For example, Life Technologies just introduced the SOLiD 3.0 system, an instrument that will soon sequence a genome in a matter of days, for roughly $10,000.

"We'll soon reach the $1,000 genome milestone," continued Lucier. "We'll be able to quickly, easily and cheaply sequence the genomes of millions of people _ which will lead to a revolution in medicine. Our genome will tell us what diseases we're particularly susceptible to, or whether a particular pharmaceutical may work for us. As a society, for the first time, our focus will shift from treating disease to preventing it. This will usher in a new era of healthcare."

PERSONALIZED MEDICINE RESOURCES

On May 12, the Personalized Medicine Coalition (PMC) released the second edition of The Case for Personalized Medicine, a landmark report first published in 2006. The work discusses the advances and challenges of personalized medicine , and describes how it is shifting the focus in healthcare from reaction to prevention. Among other data, the report reviews the technological advances enabling personalize medicine, such as tools to decode the human genome, health information technology to integrate research and clinical data, and major studies linking genetic variation and disease. The work is available, for no charge, at www.personalizedmedicinecoalition.org.



Addressing health disparities through **science and education**

At Amgen, we recognize the critical need to address health disparities. This is why we support programs that seek to educate at-risk populations about the diagnosis, treatment and prevention of serious illness. As pioneers in biotechnology, we are committed to increasing the scientific understanding of health disparities and creating vital medicines that dramatically improve patients' lives.

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Beyond Biotech

Population growth and changing diets are putting serious strains on how we produce the food we eat and power the machines we use. As a population, we face a fundamental choice – either put more acres into farming, thereby potentially adding further stress to biodiversity – or increasing the productivity of the acres we currently utilize. The dedicated employees of Syngenta have a clear-cut and passionate point of view: our successful future as a population and a planet is to grow more from less.

By Jeffrey M. Perkel

"There aren't that many more additional acres that can be dedicated to farming," noted Valdemar Fischer, who leads Syngenta's North American crop protection business, "The question is, how can farmers be more productive? Anything we can do to increase yield or improve stability under different environmental conditions is going to help maximize how much a farmer can produce on a given amount of land."

Meeting this challenge requires a delicate balancing act—protecting the environment and responding to the uncertainties of global climate change. "It's a tall order, but modern agricultural technology, along with improved farming practices, will be a major part of the solution," said Morgan.

According to David Morgan, president of the corn and soybean seed business at global ag-biotech giant Syngenta, "The challenge in agriculture today, and for the foreseeable future, is to feed a dramatically increasing world population, protect our increasingly scarce resources, notably water, and provide alternative fuels that can help alleviate dependency on a finite supply and unstable sources of fossil fuel."

Based in Basel, Switzerland, Syngenta employs some 24,000 people in 90 countries, including at least 650 at production and research and development facilities in Texas, Louisiana, Nebraska, and North Carolina. The company spent about $2.6 million per day on R&D in 2008 ($969 million), on sales of $11.6 billion.

In addition to its market-leading lineup of crop protection products, Syngenta's product line reflects two different flavors of ag-biotech. The first is selective breeding, a computer-aided reinvention of the crop domestication farmers have been practicing for millennia; the second is genetic modification. Using a plant pathogen called Agrobacterium, Syngenta scientists endow plants with traits not normally found in agricultural crops. The company's Agrisure® line of corn traits confers corn seeds with built-in resistance to corn borer and rootworm, as well as built-in tolerance to the herbicides glyphosate and glufosinate.

The source of many of these traits is a soil bacterium called Bacillus thuringiensis (Bt) – in particular, a set of genes called cry genes, which wards off insect predation. Recently, the company developed (and submitted for federal approval) a new Agrisure trait called Agrisure Viptera™, which confers insect resistance via a different set of Bt proteins called "vegetative insecticidal proteins," or VIPs.

Just as physicians can better fight infections with multiple antibiotics, VIP-based insecticidal crops should better enable farmers to keep their crops healthy. "We think it's a pretty monumental move in the sense that everything else has been a Cry protein, and these VIPs are a different mode of action," says Agrisure marketing manager Tracy Mader.

Such efforts are paying big dividends, according to National Corn Growers Association statistics. Though 10 million fewer acres are devoted to corn than in 1938, American farmers produced 10 billion more bushels in 2008. Further, since 1988 US corn yield has increased from 85 bushels per acre to 154. Mader says new corn varieties can improve production by an additional 17 bushels per acre. "It's more food per unit of land and per unit of energy," he says.

But biotech is about more than insect resistance products; in-development strains will address such global agricultural pressures as improved water optimization, nitrogen utilization (thereby reducing fertilizer usage), and biofuel production. All of which should help farmers squeeze ever more bushels out of their land, at lower costs per bushel. Says Mader, "With increasing populations and a desire to have sustainable land, technology is the driver."

Biotech dreams

While we have largely come to terms with the fact that we are not immortal, biotech visionaries offer us a dream of a longer, more quality-filled life – and provide a sense of humanity in the face of struggle against disease. Since 1982, when the first recombinant insulin product, developed by Amgen, was approved for the treatment of diabetes, it became clear that there was an untapped reservoir of scientific talent and drive that would change the medical treatment landscape. Since then, the availability of new, biologics-based treatments for cancer, arthritis, blood disorders, genetic diseases, infectious diseases, autoimmune diseases, and diabetes, has changed anticipated outcomes for patients. Statistical misfortune – being the person who develops a rare cancer or early-onset rheumatoid arthritis – is no longer treated as a "let's do the best we can with current treatment options" situation. Instead, disease is recognized as a series of molecular interactions underscored by millions of proteins that can be targeted and modulated. Since 2003, when researchers announced the completion of the draft version of the Human Genome Project, progress has accelerated dramatically.

The ability to uncover pathologic processes and target them for destruction is a source of hope. A patient who perhaps does not understand the specific mechanism of action associated with a complex protein-based therapy still understands what it means to feel better and look forward to being able to go to dinner with his family, pick her child up from preschool, or read that stack of magazines that have been sitting on the coffee table waiting for the perfect lazy afternoon.

We yearn for well-being and a sense of daily rejuvenation. Biotechnology companies like Life Technology, which is "dedicated to improving the human condition" focuses not only on the concept of life as a valuable endpoint in and of itself, but on quality of life. Even it's description of its research and development goals, which include personalized medicine and regenerative science, reflect that ambition. Life is worth the fight.

There is a pugilistic quality to drug development among pioneering biotech companies, as well as their forward-thinking biopharmaceutical counterparts that continue to focus on small-molecule development. Tactical Therapeutics, for example, is dedicated to providing next-wave, cost-effective therapies. Their focus on developing a novel angiogenesis-based drug essentially seeks to fight cancer by cutting off its blood supply, stopping metastatic processes in their tracks, and routing it out of the human body. There is also recognition of the issue of money. The need to deal with supply and demand – both for life and for capital – is part of the human condition. Biopharmaceutical and biotechnology companies recognize this.

BIO, which is comprised of 1,200 members, advocates for biotechnology companies – so that those companies can advocate for us – and for life itself.

By Nicole Gray

syngenta

The world needs more food. By 2050, there will be another 2 billion people on our planet. How do we provide enough high-quality food and preserve our environment? At Syngenta, we believe the answer lies in the boundless potential of plants. We develop new, higher yielding seeds and better ways to protect crops from insects, weeds and disease. So farmers can get more from existing farmland and take less new land into cultivation. It's just one way in which we're helping growers around the world to meet the challenge of the future: to grow more from less. To find out more, please visit us at www.growmorefromless.com

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Bringing plant potential to life

The **beauty** in the beast

Consider the Gila monster.

Scientists did, and used its saliva to isolate a protein that brings new relief for the management of type 2 diabetes. Who could have imagined that a creature so forbidding could bear such a gift? That's the kind of leap scientists make every day.

And they amaze us.

At Life Technologies, our job is to help researchers make these remarkable discoveries. Our products pave the way for breakthroughs in areas from personalized medicine to food safety to biofuels. Whether helping unlock the mysteries of our DNA, or creating the latest tools to advance stem cell research, we believe in doing our part to make life better for all of us.

You can help.

Recognize the power of science to meet the health, energy, and environmental challenges of the 21st century. Promote science education in your children's schools, support scientific literacy in your communities, and urge lawmakers to devote increased funding to biomedical research.

After all, who knows how many more discoveries like the Gila monster protein await?

life technologies™