SEARCHING FOR THE NEXT WAVE

SPECIAL REPORT
RIPPLES OF INNOVATION FROM UNEXPECTED PLACES

+ THE 4TH ANNUAL WORLDVIEW SCORECARD
NATIONS GO FOR THE BIOTECH GOLD

MARATHON MEN: 3 ENDURING LIFE SCIENCE LEADERS
DROWNING IN DATA? FLOOD CONTROL FOR THE FUTURE
The biological revolution happening now has expanded our vision far beyond what we could have imagined even a decade ago. Never have scientists been better equipped to defy the notion of impossible. Today, every innovation inspires another. Every discovery fuels our shared determination to improve life.

Let’s harness our momentum and keep asking the question that will change the world: “What if?”

lifetechnologies.com
The data-driven side of Scientific American WorldView also keeps expanding into new areas. Once again, Cutting Edge Information in Research Triangle Park, North Carolina, offers one of its unique data sets elucidating social media’s growing impact on subsectors of the biotechnology field. In addition, we unveil preliminary findings from a brand new survey of commercial bio science leaders around the world, conducted by the Pugatch Consultum in the United Kingdom. Finally, the international consulting firm Monitor provides an analysis of valuable strategies for a sustainable life sciences industry within this changing international landscape.

As always, we remain overwhelmingly grateful for the support of our sponsors: Novo Nordisk, our Marquee Sponsor, Amgen; Life Technologies; the São Paulo Research Foundation, FAPESP; the organizations of Queensland, Australia; The Malaysian Biotech Corporation; and Biopain. They make it possible for us to cover global life science innovation. As further examples of the teamwork behind this publication, we want to thank our Board of Advisers and dedicated journalists around the world who help to create this publication. Similarly, our readers and the thoughts that they pass along contribute to the ongoing perspective that provides a global view.

Yourviews: [LETTERS, OPINIONS, CRITIQUES]

THINK LOCAL AND GO GLOBAL
As international competition in biotechnology intensifies, as indicated in the Scientific American Worldview Scorecard, the San Francisco Bay Area is embracing globalization to strengthen our life science cluster. International business is creating jobs locally, allowing our companies to access new markets and funding sources abroad, and providing outsourcing opportunities for our entrepreneurs who are pursuing lean business models. The Bay Area, long a Mecca of life science innovation, is attracting global companies seeking to capitalize on our rich talent base, especially in the area of biologics. Bayer HealthCare and others have established global innovation centers in the Bay Area in recent years, creating hundreds of new jobs for the industry. BayBio also hosts a steady stream of international delegation visits. Delegations come to the Bay Area to establish collaborations with our companies, to experience firsthand the entrepreneurial spirit driving our cluster, and to learn from the deep experience residing here — the birthplace of biotech.

We encourage international participation in our educational programs and partnering events.

Bay Area companies, large and small, are benefitting from increased global connectivity. Capital access is top of mind for entrepreneurs, startups and early-stage companies. Foreign sources of capital are helping fund research and discovery. To grow with a lean business model, outsourcing services are enabling companies to do more research. Clinical-stage companies, in search of patient populations and new markets, are accelerating the drug approval process by going abroad earlier. Companies are conducting clinical trials at lower costs and accelerating access to new treatments. By doing so, they are establishing themselves in new markets, and most importantly, they are bringing new treatments to more patients worldwide.

Globalization is creating a dynamic environment with great opportunities. We are finding that openness and a willingness to collaborate empowers Bay Area companies to explore new frontiers.
Collaboration Brings Brighter Days Ahead

At the Florida-based Tradition Center for Innovation (TCI) research park, my colleagues and I have seen firsthand how working together can help bridge the gap between innovation and care. The anchor institutes at TCI—which include Mann Research Center, Martin Health System, Vaccine & Gene Therapy Institute (VGTI) Florida and Torrey Pines Institute for Molecular Studies—set out to build a new model of life science innovation that was conceived with the purpose of accelerating translational medicine. Torrey Pines makes drug candidates, VGTI develops them into vaccines and Martin Health System runs clinical trials on them. Under the umbrella of Florida Innovation Partners, we work together to discuss individual and collective operations and plans, including developing talent, sharing resources, enhancing technology and collaborating on research. VGTI worked with Martin Health on a flu trial in 2009 with one of their vaccines. Time was critical, and they were able to put the study together in a matter of a few weeks. Having a hospital that conducts clinical trials is a huge benefit to the existing not-for-profit research institutes because it provides access to patients in a collaborative setting. Physicians and researchers work together, literally, in a laboratory or doctor’s setting, depending on what stage the trial is in. The speed at which Martin Health reviews, approves and begins trials greatly enhances the ability for the institutes to accelerate discoveries. Based on what I saw and on my experiences, I would venture to say that collaboration is the force behind “Brighter Days Ahead.”

Andrew Favata
Vice President
Mann Research Center
Port St. Lucie, Florida

We endorse Jo Pisani’s (a partner at PwC in the U.K.) view that developing different biotech business models that embrace efficiency, innovation and collaboration is key to biotech’s future (2011 “Scientific American Worldview,” “Brighter Days Ahead”). The Florida-based Tradition Center for Innovation (TCI) research park, my colleagues and I have seen firsthand how working together can help bridge the gap between innovation and care. The anchor institutes at TCI—which include Mann Research Center, Martin Health System, Vaccine & Gene Therapy Institute (VGTI) Florida and Torrey Pines Institute for Molecular Studies—set out to build a new model of life science innovation that was conceived with the purpose of accelerating translational medicine. Torrey Pines makes drug candidates, VGTI develops them into vaccines and Martin Health System runs clinical trials on them. Under the umbrella of Florida Innovation Partners, we work together to discuss individual and collective operations and plans, including developing talent, sharing resources, enhancing technology and collaborating on research. VGTI worked with Martin Health on a flu trial in 2009 with one of their vaccines. Time was critical, and they were able to put the study together in a matter of a few weeks. Having a hospital that conducts clinical trials is a huge benefit to the existing not-for-profit research institutes because it provides access to patients in a collaborative setting. Physicians and researchers work together, literally, in a laboratory or doctor’s setting, depending on what stage the trial is in. The speed at which Martin Health reviews, approves and begins trials greatly enhances the ability for the institutes to accelerate discoveries. Based on what Pisani envisions and on my experiences, I would venture to say that collaboration is the force behind “Brighter Days Ahead.”

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At Amgen, we believe that the answers to medicine’s most pressing questions are written in the language of our DNA. As pioneers in biotechnology, we use our deep understanding of that language to create vital medicines that address the unmet needs of patients fighting serious illness – to dramatically improve their lives.

For more information about Amgen, our pioneering science and our vital medicines, visit www.amgen.com

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JUDY ABATE
VICE PRESIDENT, OPERATIONS
JAY SHERIDAN
VP OF BUSINESS DEVELOPMENT

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s a pioneer in insulin production in the 1920s, Novo Nordisk was one of the first companies to undertake large protein research and development to improve human health. Now operating in 75 countries and the first multi-national pharmaceutical company to build an R&D site in China, Novo Nordisk stays motivated in its pursuit of the perfect insulin.

With a biotech venture fund that supports innovative upstream therapies and a distinctively collaborative R&D culture, Novo Nordisk now boasts a very diverse pipeline of diabetes products that goes beyond insulin. Mads Krogsgaard Thomsen (pictured right) shares the thinking behind Novo’s innovation strategy in this candid exchange with contributing editor John Rennie. He focuses on sustaining product-driven growth while keeping patients’ needs in mind at all times.

SCIENTIFIC AMERICAN:
Novo Nordisk has a history that stretches back to 1923. What themes have been consistent in its strategies throughout this period?

MADS KROSGAARD THOMSEN:
From the beginning, Novo Nordisk has approached the challenge of diabetes with the entire picture of patient needs in mind. Imagine a patient’s life from a disease that was once a death sentence, but we certainly realized that the first insulins had many drawbacks. Ever since then, we have worked tirelessly to innovate insulin-based treatment, creating versions that were either purer or more closely based on human insulin, with the introduction of the Novo-pen back in 1985. But delivery of insulin therapy is an important area for innovation, patients need to be able to fit these regimens into their busy lives. Because when patients improve their glycemic control, they are really improving their long-term health. That’s part of the advantage of our newest degludec aparat compound, which combines two of the company’s insulins, one known fast-acting and one novel ultra-long-acting, to give a very stable dual-action profile. The patient can get both products with one shot instead of two.

Our insulin degludec product is also with FDA, awaiting approval. If that’s approved, then we think that further innovation could come in developing a once-weekly, long-acting basal insulin. That’s actually going to be difficult to do because we’re getting very close to mimicking normal basal insulin secretion.

SA: Recently, Novo Nordisk retooled its R&D approach by dropping its small-molecule strategy and combining its biology and chemistry programs. What has been the effect on the company’s products, and on its new product pipeline?

MKT: For us it has paid off in a very big way. About five years ago, we came to the realization that we needed to work not only on the protein backbone but we could also add chemical side chains onto specific sites on the protein backbone to further enhance the drug’s therapeutic potential. That choice has led us to our having quite a few new drug candidates for diabetes in and the R&D pipeline.

So you can see we’re kind of a protein-design company. We do protein engineering, but we’d also design proteins by adding side chains to further optimize their clinical characteristics. If you look at degludec, it’s actually the side chain that gives it its ultra-long-action profile.

MT: We were actually the first multinational pharmaceutical company to set up R&D facilities in China; we started in 1997. This past September we cut the ribbon on a newly expanded R&D center in Beijing, which features state-of-the-art research facilities. Because we have been so impressed by the high level of academic science in China, we formed a research foundation five years ago with the Chinese Academy of Sciences. We expect to keep our scouting efforts up in China— to look for innovation efforts in both universities and start-ups. In India, we’re expanding our center in Bengaluru to a staff of 200 who can help us with the biostatistics, the medical writing, and the data management, the information technology, and so on.

Costs from diabetes are already 10 percent of the global health care burden and that’s only going to increase, particularly in developing countries, which is where the greatest growth in diabetes is taking place.

MT: We are using our protein technologies to diversify from blood-sugar control into control of blood pressure and weight management, and into the control of late-stage diabetic complications. Initially the ones associated with the eyes and nerves and kidneys, the so-called microvascular complications. To this end we are also on the lookout for both academic partnerships and biotech startup licensing opportunities that can contribute to this effort.

We can also work on making even more selective insulins—ones that act only in specific organs. For instance, people put on weight when they take insulin for different physiological reasons. But if we create insulins that targets just the liver, we can completely sidestep those reasons and avoid the weight gain. But coming up with these tissue-selective insulins or oral insulins basically means re-writing the standard insulin textbooks because they involve a whole different pharmacology. That’s just the kind of thing that Novo Nordisk likes to take on.

SA: Novo Nordisk is based in Denmark, a small country. How does it attract the size and quality of scientific workforce it needs?

MKT: Actually, Denmark has a strong tradition of diabetes research and also a long history of both basic and applied protein research. So it has not been too difficult to recruit much of the needed talent from within the country.

The Novo Nordisk Foundation has dedicated $150 million to a protein research center at Copenhagen University. That has helped to make Copenhagen University a powerhouse in protein research, which seriously increases the talent mass in Denmark. That strength also helps to attract talent from abroad to come and work at the center. Novo Nordisk

MT: Novo Nordisk works extensively with the World Health Organization (WHO) and its experts to try to make sure that non-communicable chronic diseases are high on their 21st century agendas. Costs from diabetes are already 10 percent of the global health care burden and that’s only going to increase, particularly in developing countries, which is where the greatest growth in diabetes is taking place.

Undiagnosed and untreated or inadequately-treated diabetes will, 10 to 15 years later, lead to blindness, kidney failure, amputations, cardiovascular attacks, reduced productivity and quality of life, and premature death. Governments in these emerging markets know that, and are more receptive to offers of help from Novo Nordisk.

For the past 10 years we have worked closely with the Chinese Ministry of Health to deliver diabetes education to the people, particularly in the rural areas. Ninety million people suffer from diabetes in China, but only half of those are diagnosed, and only half of those get any sort of treatment. We have been able to help out with educating maybe 40,000 physicians, particularly in rural areas where the understanding of diabetes is really limited.

SA: What are the next great frontiers for innovation in diabetes?

MT: We are using our protein technologies to diversify from blood-sugar control into control of blood pressure and weight management, and into the control of late-stage diabetic complications. Initially the ones associated with the eyes and nerves and kidneys, the so-called microvascular complications. To this end we are also on the lookout for both academic partnerships and biotech startup licensing opportunities that can contribute to this effort.

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Emerging nations throughout the world are formulating and executing policies for biotechnology development. What issues will influence their chances of success?

INTEREST DRIVERS
Several drivers account for the surge of interest in biotechnology. For one thing, R&D creates more—and increasingly sophisticated—biotechnological products, particularly for medicine and agriculture. In addition, demand for those products is growing worldwide as the global population increases and expanding middle classes expect more than the basic necessities of survival.

Healthcare, having a prominent position among those expectations. “When a consumer middle class emerges in an area, the first thing it wants is healthcare,” says Burrill. “People think of it as a right, not a privilege.” In Africa and Asia, growing numbers of informed and financially secure citizens drive their countries to improve healthcare access, according to Brian Williams, global clients and markets director for the auditing and consulting company PwC. Wherever the new players are, Williams points out, they must ask a key question: “How do we develop healthcare systems and care models that provide disease management in a way that does not replicate the mistakes of the European and U.S. markets?”

Improving the food supply represents another opportunity for biotechnology. “A renaissance in thinking and action is needed in which a new agriculture, based on modern bio-scientific knowledge and harnessing the best of biotechnology, is translated into food products through entrepreneurship by small to multinational entities,” says Margarita Escaler of the National Institute of Education in Singapore’s Nanyang Technological University. The challenge, she says, is to create a “lab-to-market” path. For countries that rely on biotechnology mainly for agricultural production, regulatory issues loom just that. “The Philippines are in final stages of formulating their low-level policy. That’s important as they’re a large importer of corn and soybeans,” Adams says. “What effect will national policies have on local and international markets for biotechnology? Government policy won’t drive decision-making.” Williams says. “But you might have manufacturers who want to take broad access,” he says. “Some companies have announced transformative investments in healthcare there.” He adds, “Singapore is similar. It has a highly-educated, English-speaking populace, penetration of mobiles, and defined government policy with demonstrable effect in attracting manufacturers.” Just as important, the city-state made its decision to invest in biotechnology only after it had set up its supporting infrastructure. According to the IP-protection metric on the Scientific American Worldview Scorecard (see page 24), however, both South Korea and Singapore earn only fair scores, and improvements in their IP might bolster their biotechnology capabilities.

large. “The single biggest issue in agricultural trade is low-level presence,” Adams says. This involves the tendency of agricultural products to contain foreign matter, including samples of genetically modified crops, as they move from farm to port for export. As Adams says, “You may have something approved in a country of export that’s not yet approved in the country of import.” For example, small amounts of Liberty Link 601, a biotech-derived, herbicide-tolerant rice approved for commercialization in Australia, New Zealand, the Philippines and Europe, destinations that had not approved it. Scientists see no way to ferret out such species. Consequently, governments must develop policies on the amounts to allow. Stimulated by international agencies, some of the emerging biotech nations are doing just that. “The Philippines are in final stages of formulating their low-level policy. That’s important as they’re a large importer of corn and soybean,” Adams says. “What effect will national policies have on local and international markets for biotechnology? Government policy won’t drive decision-making,” Williams says. “But you might have manufacturers who want to take market share in every market where there’s an opportunity—and hence be receptive to government policies that might benefit them in the long term.”

ELEMENTS OF SUCCESS
According to Williams, “To be successful in biotechnology, jurisdictions must have not only a rule of law, protection of intellectual property and support of private enterprise, but also an educated populace that evolves into end-market development of excellence, and R&D clusters around biotechnology that include clinical testing and hospitals.” As exemplars creating the appropriate infrastructure, Williams cites two “Asian tigers”: South Korea and Singapore. “South Korea has high mobile telecommunications penetration and broadband access,” he says. “Some companies have announced transformative investments in healthcare there.” He adds, “Singapore is similar. It has a highly-educated, English-speaking populace, penetration of mobiles, and defined government policy with demonstrable effect in attracting manufacturers.” Just as important, the city-state made its decision to invest in biotechnology only after it had set up its supporting infrastructure. According to the IP-protection metric on the Scientific American Worldview Scorecard (see page 24), however, both South Korea and Singapore earn only fair scores, and improvements in their IP might bolster their biotechnology capabilities.

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AFRICA'S RED BIOTECHNOLOGY

By Elie Dolgin

Only investment and risk will boost medical R&D

In the Acumen Fund—headquartered in New York, with regional offices in India, Pakistan, Kenya and Ghana—typically wait longer than other VCs to recoup their financial investment, "raise further capital." That problem also speaks to the types of investors in Africa, who will put money into information technology or healthcare delivery but don’t usually appreciate what it takes to develop drugs or medical devices.

The solution could be in educating investors about Africa’s potential for a life sciences industry. That industry, however, isn’t likely to take off until investor mindsets change, says Paul O’Riordan, cofounder and chief executive officer of Synexa Life Sciences, a biotech in Cape Town. “There’s no way you’re going to have a thriving biotech sector in South Africa or any other part of Africa,” he says, “unless you have the kind of private, risk-taking, smart venture capital funds that you have in other parts of the world.”

“arke notes that the lack of capital caused him and his other startups to quickly become self-sustaining through sales. Unfortunately, this results in companies being judged based on their revenue, rather than on their underlying intellectual property. “In

Of course, the investment climate in Africa isn’t the same as in Asia. In Africa, “you tend to raise in rand what you need in dollars,” says Greg Starke, chief executive officer of PoVascular, a Bioventures-backed medical device company in Cape Town. “Then, you adjust your business plan to the amount of money that’s available, which is the most terrible habit, and we’ve done it more than once. You fall on your face every time with that approach.”

The financing gap remains one of the Acumen Fund’s invest-ment initiatives. “There is no mechanism to transition them into concrete projects.”

The funding environment is so abysmal here that you’re left with very few options,” says Nino Pires, chief executive officer of business development at Alfa Biolog-ics, a tissue-engineering company in Pretoria, South Africa, that has relied on government technology funds for its limited financial support. Some African executives hoped to over-come the funding hurdle with ven-ture capital (VC).

One of the greatest roadblocks to funding is the lack of good ideas. “Most of the innovation is stagnating in Africa,” says Solomon Nwaka, acting director of the African Network for Drugs and Diagnostics Innovation, an Addis Ababa, Ethiopia-based drug de-velopment initiative. “There is no mechanism to transition them into concrete projects.”

But others paid for themselves with results in companies being judged based on their revenue, rather than on their underlying intellectual property. “In

Some investors believe that VC firm dedicated to life sciences innovation. Established in 2001, the Cape Town-based fund had a total of 80 million rand ($12 million) that it used to support eight homegrown biotechnology startups in South Africa. Most of the invested funds flopped, as might be expected, but others paid for themselves with notable returns after large drugmak-ers bought up the companies. In 2008, for instance, Abraxis BioScience, a Los Angeles company now owned by New Jersey-based Celgene, snapped up two Bioventures-backed companies—Port Elizabeth-based Shimosda Bio-tech and its subsidiary PlatCo Tech-nologies—for $15 million upfront plus potential milestone payments. Still, the fund did not sustain itself or attract more investment, and it per-formed worse than the Johannesburg Stock Exchange, which often grew by up to 20 percent annually over the past decade. One central problem with Bio-ventures came down to the size of the fund. “The big issue was that we just didn’t have an adequate amount of capital,” says Bioventures founder Hassan Masum. Acumen’s invest-ment is to identify and scale innovative business models that are showing a different way to address issues of poverty.”

RISK BEGETS SUCCESS

In the United States, early-stage life science funds typically manage at least $500 million. That might sound like an impossible sum of capital for a developing-world VC, but BioVeda China, based in Shanghai, has raised more than $170 million since its in-ception in 2005.

“Funds that everyone else had.” —HEATHER SHERWIN

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y all accounts, industrial biotech is poised to surge as demand for petroleum-based fuels, chemicals and materials remains high and geopolitical instability surrounds many of the oil-producing nations. The worldwide market for industrial, or “white,” biotech is expected to grow from $170 billion in 2008 to about $660 billion by 2020, according to an estimate from McKinsey & Co., a New York City-based consultancy. Further, some world-class examples of industrial biotechnology production are arising in unexpected places, including bioplastic polymers and ethanol from New Zealand, amino acids for animal feed from Malaysia and industrial enzymes from Denmark.

“As the main alternative to fossil fuels for both the transportation and chemical markets, the [industrial bio-tech] sector could grow exponentially as companies scale up and commercialize their technologies,” says analyst Marie Daghlian, of Burrell & Co., a life sciences investment firm in San Francisco. “The growing global energy market is valued at more than $6 trillion and there’s plenty of room for many different players and technologies.”

The question is, How can an emerging area grab a slice of industrial biotechnology?

TECHNOLOGY FROM TREES

New Zealand’s 108 dedicated biotech companies generated about $289 million in sales last year nearly half from exports of bioscience goods or services. Unlike many other industrial biotech countries, which rely on sugar cane, grain, corn and other crops for their feedstock, New Zealand’s biomass resources consists principally of pine trees, with smaller quantities of Douglas fir and eucalyptus.

Government-owned Scion, the trading name of the New Zealand Forest Research Institute Ltd., is developing processes to convert waste cellulosic biomass into sugars and lignin. “The sugar solutions are being used to explore manufacturing of modified bioplastic polymers as well as various biofuels and in-microbe production of new product precursors,” said Elspeth MacRae, Scion’s general manager for manufacturing and bioproducts.

Auckland-based LanZaTech has developed two strains of proprietary gas fermentation microbes that produce ethanol and other chemicals from non-food resources, including carbon monoxide-rich industrial flue gases from steel manufacturing, oil refining and chemical production, as well as gases generated by gasification of forestry and agricultural residues, municipal waste and other waste gases. The enzymes are effective throughout a wide range of hydrogen content and are resistant to typical gas contaminants. LanZaTech has signed several demonstration and production agreements, including ones with two of China’s largest steel mills, Baosteel Group and Shougang Group.

“Growing’ Amino Acids

Malaysia’s biotechnology market, fueled by a 16 percent annual growth rate, is on track to reach $283 million this year, while its number of biotech firms is expected to double to 400 by 2013. This growth is driven in part by the government’s BioNexus Program, which provides financial assistance to accredited companies, and by a new $100 million venture capital fund jointly administered by Intrayys Sdn Bhd and Exoreus Sdn Bhd, with the Malaysian Biotechnology Corporation (BiotechCorp) acting as corporate adviser.

Possessing abundant biomass, Malaysia is a natural magnet for international companies. Last August, BiotechCorp signed a $660 million, 10-year agreement with South Korea’s CJ Cheiljedang Corporation and France’s Arkema SA to build a bio-methionine production plant on 70 hectares in Malaysia. Bio-methionine is a sulfur essential amino acid widely used in animal feed that is mainly produced synthetically from propylene. The plant will make a range of other bio-chemicals, or mercaptans, which are also used as intermediates in agrochemicals and pharmaceuticals.

“The investment will further stimulate the growth of the industrial biotechnology sector and provide commercial opportunities for the industry,” said BiotechCorp chief executive officer Datuk Dr Mohd Nazlee Kamal. “More significantly, it’s a leap for Malaysia as a knowledge-intensive and cost-effective industrial biotechnology hub in the region.” The 80,000-ton capacity plant, the world’s first large-scale bio-methionine plant, is expected to come online in 2013.

DENMARK AND DUCONT

Denmark has more than 150 biotech companies developing pharmaceuticals and industrial enzymes. Chief among the latter are Novozymes and Danisco, which together account for more than 70 percent of the worldwide production of enzymes used for detergents and chemicals, food, fuel, textiles, pulp and paper, as well as for processing wastewater.

Headquartered in Copenhagen, Danisco operates in more than 40 countries. Its food product ingredients include antimicrobials, antioxidants, sweeteners and emulsifiers. In addition to enzymes, its industrial biotech division, Genencor, produces hydrocolloids, plastics and betaine, a chemical used for deicing, fermentation and crop protection. Last year, DuPont acquired Danisco for $6.3 billion in cash and assumption of debt.

“Biotechnology and specialty food ingredients have the potential to change the landscape of industries, such as substituting renewable materials for fossil-fuel processes and addressing food needs in developing economies, that will generate more sustainable solutions and future growth for the company,” said DuPont chief executive officer Ellen Kullman at the time.

Danisco and DuPont have been collaborating in a $50 million joint demonstration plant in Tennessee to produce 250,000 gallons of cellulosic ethanol annually from corn cobs and switchgrass. They plan to open a U.S. plant in 2013 capable of producing 25-50 million gallons from corn cobs, and another facility to produce commercial quantities of ethanol from switchgrass.

MORE BIOFUELS AHEAD

The market for biofuels could more than triple by 2020, according to a 2010 World Economic Forum white paper. Worldwide sales of biodiesel and ethanol will surge to around $95 billion in 2020 due to mandates alone. In addition, the market for bio-based chemicals should grow to 9 percent of all chemicals by 2020 while the demand for biomass for heat and power generation by the United States and EU27 countries alone will more than double by 2020, according to the report.

In fact, industrial biotech is expected to drive the growth of biotechnology overall as a portion of the world’s GDP from 0.5 to 1.0 percent in 2009 to 2.7 percent in 2030, according to a recent report by the Organization for Economic Co-operation and Development. As the examples used here show, emerging regions can excel at industrial biotechnology by using available natural resources as drivers or developing entirely novel approaches to biotechnology processes.
A MODERN GREEN REVOLUTION

Emerging areas need genetically modified crops developed by and for them by Emily Waltz

With the ever-expanding list of threats to global food security, it’s all hands on deck to deploy every plant-breeding and genetic-modification technology available. Multi-national corporations gave the world a start with herbicide-tolerant and insect-resistant soybeans, maize and cotton. Those crops, however, largely benefit growers in industrialized nations. To accommodate a burgeoning population, dwindling natural resources, climate change, political instability and changing lifestyles in developing nations, genetically modified (GM) crops must do more.

To that end, scientists in developing countries are taking on a larger role in the research and development of GM crops that benefit their home-bred crops. These crops must withstand drought, tolerate salinity, resist disease, offer additional nutritional value and bring better economic returns to farmers. China, India, Brazil and Argentina are known for leading the developing world in commercializing GM crops, but some of the most interesting crop traits in the pipeline are coming from other nations.

RICE AND BEYOND

In South Korea, for example, researchers at the National Academy of Agricultural Science, part of the country’s Rural Development Administration (RDA) in Suwon, are developing rice varieties that tolerate environmental stress and contain added nutritional benefits. The rice varieties are among the more than 120 traits in 19 crops in the works at RDA, says Soo-Chul Park, director of RDA’s National Center for GM Crops. As part of RDA’s Bio-green 21 Project, the administration will devote 88 million per year over the next 10 years toward the development of 20 new biotech crops.

Another 80 GM crops are under development by private-sector companies or universities in Korea, according to Park. One of the most advanced of these is a virus-resistant chili pepper developed by Nongwoo Bio in Suwon. In field trials the pepper proved resistant to cucumber mosaic virus, which has recently overcome conventionally bred varieties.

Despite Korea’s significant investment in aghotech, no GM crop has been approved for commercial cultivation by the government. Nongwoo’s pepper, along with an herbicide-tolerant lawn grass developed by Jeju National University and a handful of rice varieties from RDA, will likely be among the first, says Park. But that might not happen for another five years, he adds. Public and farmer acceptance of biotech crops is low, and that has curbed the regulatory process.

SEEKING FOOD SECURITY

Pakistan presents another interesting case. Despite social instability, the country’s scientists have a long history of working with GM crops. Six research centers in Pakistan are capable of performing the kind of DNA recombination needed to develop transgenic plant varieties, according to the most recent report on Pakistan from the USDA Foreign Agricultural Service (FAS). One of those centers, the National Institute for Biotechnology and Genetic Engineering in Faisalabad, is transferring six different salt- and drought-tolerance genes into local varieties of wheat and testing them in field trials. The group is also developing salt- and drought-tolerant cotton, potatoes, sugarcane and tomatoes as well as virus-resistant cotton and potatoes.

International Service for the Acquisition of Agri-Biotech Applications (ISAAA). Most of that hectarage consists of insect-resistant cotton varieties, the only GM crop to be approved for commercial production. Large-scale field trials of insect-resistant and herbicide-tolerant maize are complete and are awaiting approval by government authorities.

A GOVERNMENTAL GREEN LIGHT

Some regulatory clarity arrived in Kenya last year after the government signed three sets of biosafety regulations, paving the way for commercialization of biotech crops. The regulations make Kenya the fourth country in Africa to allow cultivation of biotech crops, following South Africa, Egypt and Burkina Faso. It was good news for Kenyan scientists, who have for years been collaborating with international groups to develop GM crops specifically for Kenya and Africa. For example, the African Agricultural Technology Foundation in Nairobi, in a partnership with the International Maize and Wheat Improvement Center in El Batan, Mexico, is developing a drought-tolerant maize, and the Kenya Agricultural Research Institute (KARI) in Nairobi is collaborating with the Donald Danforth Plant Science Center in St. Louis, Missouri, on transgenic, virus-resistant cassava.

Cassava is one of the most important crops in sub-Saharan Africa, but nearly one-third of it is destroyed each year by disease, says Claude Faquett, who leads the virus-resistant cassava project at the Danforth Center. The Danforth Center and its partners built two biotech centers—one in Kenya and one in Uganda—in an effort to transfer technology and expertise to African scientists so that they may produce more biotech crops on their own, says Faquet. Kenya’s KARI and Uganda’s National Agricultural Research Organization have been recruiting and training young scientists to run the biotech centers. The goal is to create a nucleus of researchers who stay long enough to train others and sustain the technology, says Faquet.

In a project conducted entirely by African researchers, scientists at Kenyatta University in Nairobi are transforming maize with drought-tolerance genes from an African endemic resurrection plant called Xerophyta viscosa. Initial cloning work for the project was done by Jennifer Thomson, an emeritus professor in the department of molecular and cell biology at the University of Cape Town, South Africa. Thomson has also developed a maize variety that resists African endemic maize streak virus. “This project has no interest for multinationals as it is a problem only in Africa,” says Thomson. After years of work, she and her colleagues are gearing up to apply for field trials in South Africa. “When we started I was told: ‘Don’t even think of it if you don’t have a computer-controlled glasshouse,’” she says. “We didn’t even have a glasshouse.”

Now Pakistan’s academic leaders—including Muhammad Iqbal Choudhary, director of the International Centre for Chemical and Biological Sciences at the University of Karachi—are urging the government to adopt a national strategy to maximize opportunities to use biotechnology. These leaders see biotech crops as a solution to the country’s food-security issues, which have been exacerbated by natural disasters, says Choudhary. More than 2.6 million hectares of biotech crops are already grown in Pakistan, making it the eighth largest grower in the world, according to the Special Report: Searching for the Next Wave
BUILDING BIGGER BLUE MARKETS

From food to fuel, innovation through aquaculture is making a splash

BY KARYN HEDER

he year 2012 marks a turning point in aquaculture and marine biotech. For the first time, more of the world’s sup- ply of fish will come from aquaculture than from wild catch, a trend that is expected to accelerate in the 21st cen- tury. Developing in lock step, demand for captive-fish feed and biofuel is driving innovation in algae bioreactors.

With the first written account of aquaculture appear- ing in China in 460 b.c., it seems fitting that Asia produces 90 percent of world’s cultured fish, with China alone producing 62 percent in 2010. Much of the innovation in marine biotech is happening in China, while intensive R&D is taking place in nearly every other country in East and Southeast Asia.

“The word on the street is ‘expect to be surprised,’” says Barry Costa-Pierce, professor of fisheries and aquaculture at the University of Rhode Island. “Viet- nam has rocked the world in the last few years with the farmed catfish. Almost overnight the pangasius, or tra, has be- come one of the world’s major seafood commodities.”

Both the European Union and the United States have become major importers of Asian fish, with the United States bringing in 36,300 tons during the first six months of 2011, according to the United Nations Food and Agri- culture Organization (FAO), which tracks the global aqua- culture industry. Vietnamese catfish is becoming the “new tilapia,” according to Costa-Pierce.

In fact, says Randall Brummett, senior aquaculture specialist at the World Bank, “Demand for seafood is go- ing nowhere but up.” And that drives investors to look at aquaculture as a high-growth industry.

“It’s a sector that makes a lot of sense for us to be in,” says Drew Tarlow, an investment professional at Pegas- sus Capital, a private equity firm. His team’s main focus is identifying opportunities for growth and “most of all, making sure that we have a team on the ground that is lo- cal and understands the regulatory environment.”

Interest in marine biotechnology is rapidly increas- ing, as the tools for studying marine organisms make it possible to grow previously uncultivable organisms in the laboratory. The biotech industry owes its very existence to marine organisms, given that the ubiquitous tools of quick and low-cost DNA amplification were originally isolated from deep-sea hydrothermal vents. The applica- tion of genomics in aquaculture is still at the early stages, but many Asian countries are eagerly adopting the tools of marine biotech for economic development. Most proj- ects are aimed at increasing productivity and reducing disease resistance.

FISHING FOR FOREIGN INVESTORS

In 2008, the top aquaculture producers after India and China were Vietnam, Indonesia, Thailand and Bangla- desh, but other countries in the region are rushing to catch up. The post-war government of Sri Lanka, for example, is anxious to expand its aquaculture footprint.

“Sri Lanka is on the cusp of the blue revolution,” says Asanka Wittachy, head of the Sri Lankan government’s new Foreign Investment Promotion & Project Facilitation Unit. “The past year has seen the dividends of the govern- ment’s initiatives in the form of a dramatic increase in investment in aquaculture facilities throughout the coun- try, especially the formerly war-ravaged north and east... nations look to international collaborations to expand their existing blue biotech capabilities.

Sri Lanka is not alone in its strong support of blue bio- technology. Malaysia, for instance, has launched two gov- ernment-industry partnerships in the last year. The first, conducted by the Center for Marker Discovery and Valida- tion (CMDV), aims to speed up breeding for desired traits by using marker-assisted selection to pair DNA markers with growth-enhancing genes. One of the Center’s first us- ers will be Jefi Aquatech Resources, a tech-savvy shrimp producer and breeder that hopes to assist Malaysia in becoming a leading shrimp producer. In the second, the Aerospace Malaysia Innovation Center (AMIC) is working to isolate algae capable of industrial-scale production of jet fuel, supported by funds from Malaysia’s government, the European Aeronautic Defence and Space Company, and Rolls Royce.

Other nations look to international collaborations to expand their existing blue biotech capabilities. For ex- ample, while Chile already has a thriving salmon aqua- culture industry, it is now attracting investments in sea- weed farming. In December 2011, a joint venture between InnovaChile CORFO (the Chilean Economic Develop- ment Agency), the Universidad de Los Lagos and BAL—a Berkeley, California-based biofuels firm—broke ground on a facility to process the brown seaweed Macrocystis pyrifera as a fuel source in Los Lagos. The facility has al- ready harvested 40 dry metric tons of seaweed from its Chilean seaweed farms, and it developed an engineered E. coli bacterium that is capable of fully metabolizing sea- weed sugars into fuel.

“Blue biotechnology is also taking root in Africa, where Chinese investors are planning for full-scale commercial fish farming in countries such as Ghana and Tanzania, says Costa-Pierce. “Everybody and their brother and sister is focused on Africa because Africa has enormous resour- ces for aquaculture,” he says. “It’s the next great frontier.”
Applied Molecular Biology/Adap-
propriate Technology Transfer program,
the SSI’s precursor, in 1988, won a
MacArthur Foundation “genius
grant” in 1997 for her work in Central
and South America, which she used
to found and help fund SSI the next
year; and incorporated the SSI office
in Managua in 2004.

That same year, she says, “North-
ern investigators—people from the
U.S. who were doing a site visit—sug-
gested using barcodes [to track the
data], and I got all upset.” She
explained to her Northern friends that
it would be rude to foist their ways on
their host country. “I thought, ‘This is
Nicaragua. We don’t need that’.” And
of course two months later the Nica-
raguans came to me and said, ‘Hey,
we have to follow 4,000 children and
there are no addresses in the city of
Managua. How about we use barcodes
and GIS [geographical information
systems] and fingerprint scans?’ Coming
from the Nicaraguans, it made
sense.” Working with the Nicara-
guan Ministry of Health, SSI has been
tracking those 4,000 children for eight
years now. Household visits data are
collected and patients and biological
samples are tracked on a range of mo-
bile devices (PDAs, tablets and smart
phones) and integrated into back-end
databases like OpenClinica and Mi-
crosoft Access that help streamline
data management and ensure good
clinical and laboratory practices.

The Nicaraguan health ministry,
Harris relates, was “very interested in
the tools we were using and just the
fact that we were able to get infor-
mation rapidly because we were us-
ing computerized systems.” Within
several weeks, her Nicaraguan col-
leagues put in place a system that, she
says, “in an hour or less could run a
report on an entire week’s vaccination
campaign so you would know exactly
how many children had been vacci-
nated and where and to what as op-
posed to spending weeks compiling
that data.” Soon, that system spread
to several health centers in Managua.

“What was really novel was the way
[the Nicaraguans] put all of it togeth-
er, totally by Nicaraguans,” she says.

CODED IN COUNTRY

The Nicaraguan health ministry
wanted to collect and track ever-in-
creasing amounts of data, Harris ex-
plains. They’d started using Mi-
crosoft Access, “which only has room
for 100,000 records, and each individ-
ual health center has between 60,000
and 80,000 people,” she says. “But if
you look at all of Managua, which has
1.5 million people, you can’t use a sys-
tem like that.”

Rather than buying something
that could cost millions of dollars in
software licenses and would not be
disposable to the local needs in a cost-
effective way, SSI’s IT team looked for
open-source alternatives. “They’d
gotten plugged into the developing-
country informatics world by work-
ing with colleagues in Africa and
Asia through various networks of
open-source informatics groups like
OpenMRS and the mobile technolo-
gies group OpenROSA,” she says.

SSI decided on an existing open-
source platform called OpenClinica,
and Harris says they are poring over
nearly the entire system for our
health center- and hospital-based
studies in Managua.

“Bottom line is we started with
informatics person and our infor-
matics team in Nicaragua [now] in-
cludes a number of junior developers
and data managers,” Harris says. “A
key point was hiring local program-
ners to adapt existing open-source
software to fit our needs. We sup-
port initiatives like Coded in Coun-
try—coined by collaborators Dimagi
and Episerver—because the idea
should be that if you’re creating appli-
cations in developing countries you
shouldn’t be using developed-country
programmers. She adds, “there is a
lot of programmers everywhere.
That’s not what’s hard to find. What’s
hard to find in developing countries
are the resources, not the people.”

REBOOTING THE SYSTEM

Homegrown software yields
public-health breakthroughs
in Nicaragua

BY BILL CANNON

he ability to collect, share and analyze
data is cru-
cial to biotech
research. In
emerging na-
tions, where
informatics tools are often limited,
local programmers are creating their
own tools tailored to the particular
needs of their communities.

That’s just what Eva Harris—pro-
fessor of infectious disease at the Uni-
versity of California, Berkeley, and
president of the San Francisco-based
nonprofit Sustainable Sciences Insti-
tute (SSI)—found while working in
Nicaragua. Her organization, with of-
fices in Managua, develops molecular
laboratory information-management
systems, spins off public-health in-
formation systems and arranges in-
ternational workshops to help share
information technologies (IT) across
regions—including Africa, Asia and
Central and South America. In the
process, SSI’s meticulous biological
information-management methods
have led to scientific and public-health
breakthroughs. (See “The Hidden Flu.”)

Harris herself is no stranger to
improvisation. Recalling work from
more than 25 years ago, she says, “In
Nicaragua, I had brought in a set of
molecular biology tools,” but was told
that setting up a molecular biology lab
“couldn’t be done because there was
intermittent running water and elec-
tricity, and it was the second-poorest
country in the hemisphere. I ignored
all that, and we set up PCR in the mid-
dle of a war, which then became
the national diagnostic system for leish-
maniasis and many other diseases.”

SETTING UP A SYSTEM

That success led to longitudinal
studies of infectious diseases—and
a lot of data collection with the ac-
companying needs for storage and re-
trieval. Meanwhile, Harris started the

THE HIDDEN FLU

Influenza “was not considered to be a major
problem in Nicaragua or in tropical countries,”
says Eva Harris, a professor of infectious dis-
ease at the University of California, Berkley,
and president of the nonprofit Sustainable
Sciences Institute (SSI). That was until Aubree
Gordon—then one of Harris’s graduate stu-
dents and now an SSI and UC Berkeley faculty
colleagues—spent time in Nicaragua.

Gordon had been looking at data from a longitu-
dinal study of children and the mosquito-borne
virus that causes dengue fever, and wondered if
there were any similar data on influenza. She checked
at the Nicaraguan Ministry of Health, and there was
not much data specifically about flu. But once
we started looking at our study’s clinical data, she
was able to see very distinct peaks of what’s called
’influenza’—like illness,” which is a clinical manifesta-
tion that matches the clinical picture of influenza,”
Harris says. “It was very clean data.”

The peaks occurred in June and November of
the study years, Harris says, “so [Gordon] went back
to samples we had saved because we thought they
might be dengue” and with her Nicaraguan collea-
gers they identified antibodies that indicated an acute
influenza infection. Further prospective studies by
the team confirmed yearly seasonal epidemics of
influenza comparable to those in the United States.
It has been a catalyst that has helped reduce poverty, spread democracy, increase life expectancy, drive economic growth, and protect human rights. Innovation has the power to forever alter the human experience breaking down geographic barriers, providing cures for diseases once thought incurable and creating new sources of energy. While the potential of innovation and the value it can provide to people around the world is limitless, innovative industries face many challenges.

In order for companies like Amgen to focus on these markets, it will be vital for governments to demonstrate their commitment to innovation.

innovation continues to fundamentally change the world in which we live. Innovation encompasses the application of knowledge and insight into the creation, production and distribution of new products and services. At its best it has advanced the human condition.

It is the promise of future breakthroughs that drives the scientists at Amgen, who are constantly seeking novel treatments for serious illness through cutting-edge biomedical research that constantly pushes the boundaries of scientific inquiry.

Serious diseases are the most common and costly of all health problems in both developed and developing countries alike. Serious diseases not only place substantial strains on national healthcare systems but also on a country’s overall economic productivity. Decreasing healthcare spend on medicines may achieve status quo budgetary objectives. But at what cost? Such decreases can simultaneously create the potential for substantially greater costs in the future as patients need greater and more expensive treatments that could have been prevented through the use of innovative medicines.

Innovation in an Age of Austerity

Medicines that treat serious illness and allow patients to remain contributing members of their countries provide significant economic benefit. Healthier people have higher earnings, are more likely to be employed and work more hours. According to the British Medical Journal, increases in health improved economic growth by 30 percent. Without access to innovative medicines, these economic benefits may not be realized.

As the population ages and more people become hindered by serious diseases, patients will look to governments—especially those that control access to medicines—to have policies in place that will provide medicines to help their population live stronger, healthier, more productive lives.

The process of bringing a biotech medicine to market is a lengthy one, infused with risk and cost at each step along the way. Out of every 10,000 new compounds ever reviewed by regulatory approval. New medicine development takes an average of 10-15 years and costs approximately $1.3 billion per new medicine. As biotech companies expand, they look for investment climates that support innovation and that will enable patient access to medicines.

Unfortunately, in response to pressures to decrease healthcare costs and expenditures on medicines, many governments around the world are only considering the direct and indirect healthcare costs. Attracting inward investment and supporting the ecosystem of innovation requires a policy framework that includes: 1) robust intellectual property protection; 2) government pricing policies that reward high quality and innovation; 3) consistent, transparent, and inclusive government reimbursement policies; 4) harmonized regulatory systems; and 5) holistic approaches to healthcare reform. It is possible to support the ecosystem of innovation and meet budgetary constraints.

Budgetary constraints need not impact innovation; rather, it is possible to support innovation, provide access to patients and decrease overall costs. Proposed budgetary costs should be evaluated not only in terms of decreased spending, but also on their overall impact on and value to an economy. Cost-containment measures that do not do so, in the long-term, undermine growth and job creation, and slow access to critical medicines and ultimately, progress. Everybody can win if Ministries of Health, Finance, Economy, and Science and Technology as well as academia and the private sector work collaboratively to develop policies that recognize the value of innovation while acknowledging the need to reduce spending and other constraints faced by governments.

Emerging countries are beginning to recognize the interconnectedness between health and wealth and are starting to prioritize innovation. In countries including Brazil, Turkey, Russia and China, governments have identified biotechnology as a priority sector for growth. The value is apparent—investing in biotechnology not only provides for economic growth, but it also helps achieve domestic priorities such as improving access to medicine, raising the quality of life and growing science and education in the community. Governments seeking to grow biotechnology in their countries should create predictable and transparent policy environments that recognize and reward innovation critical to ensuring that innovative medicines reach patients who need them most.

Policies that support innovation are built around four key principles. First, governments should take a comprehensive approach and assess all elements of value that a new medicine will provide to patients. Second, new policies should contain mechanisms that allow for flexibility over time. It is critical to assess the total benefits and costs of a medicine over time, by segment and population in a real-life context. Third, it is crucial that policies ensure that patients get timely access to innovative medicines. Lastly, governments, health providers and manufacturers should work together to explore new pragmatic ways of managing spending on medicines. If implemented, these principles will help governments attract investment and spur economic growth.

At Amgen, for example, we are seeing increasing demand for our biotech products beyond our traditional markets, including emerging markets. In order for companies like Amgen to target these markets, it will be vital for governments to demonstrate their commitment to innovation.
like the 2012 Olympic games in London honor athletes, we unveil the world’s premier performers in biotechnology. Both the Olympics and biotechnology rise from a competitive spirit, while displaying the power of teamwork and camaraderie.

As more than 200 countries parade their best of the best in the opening ceremonies in London, spectators watch the soon-to-be competitors enjoying a well-deserved celebration. Likewise, we celebrate the leaders in biotechnology, while simultaneously encouraging those lagging behind the most productive countries. The parallels between the Olympics and biotechnology run even more deeply, including variations in rules around the world impacting performances. At the 1972 games in Munich, for example, a last-minute rule change banned gold medal-favorite Bob Seagren’s vaulting pole, forcing him to compete with unfamiliar equipment, although he still fought his way to a silver medal. Similarly, champions in biotechnology must find ways to perform under the pressure of shifting rules in different lands. For instance, some biotechnology crops can be planted in certain countries but not in others, and pharmaceutical regulators often talk about harmonization more than they achieve it. In the end, all players in the biotechnology industry could benefit from Seagren’s never-give-up attitude.

As the world of biotechnology evolves, so does the Scientific American Worldview Scorecard. This year, we expand the list to 50 countries. We also increase the depth of the Scorecard categories by adding a metric that measures a country’s policy climate and stability. In addition, we delve more deeply than ever into the protection of intellectual property (IP) and its impact on innovation in biotechnology. This year’s Scorecard also examines data in some new areas, including collaboration and medical tourism, which shows the interactive nature of a range of elements related to a country’s capabilities for generating innovation in biotechnology.

The developing legacy of Scorecards also allows us to start looking across time at trends in country scores and rankings. Some of the data in this section also provide insight on the behavior of biotechnology as an industry since the economic crisis that started in 2007. In particular, a few data points suggest that some recovery could be underway around the world.

Beyond the countries that climb our Scorecard podium, this year’s version places more emphasis than ever on the value of smaller companies and countries with less mature biotechnology industries. The breadth of this industry and its ongoing expansion makes it possible for a wide range of players to compete, especially ones who make the best of their inherent capabilities, such as natural resources, or team up with other players around the world. —THE EDITORS
The protection of property rights extends beyond country borders, but it must be balanced with other factors. Typically, intellectual property (IP) protection is in the form of patents, and it directs much of the development of innovation in biotechnology. In short, biotechnology—especially when arising from innovative R&D—depends on strong IP protection. The connection between IP protection and innovation arises from many features of this field: the great time requirements from the start of research until a product reaches the market, the financial costs at all stages, the high risks of failure at many stages of innovative R&D and the relative ease for outside parties to steal a company’s hard work and deny them a return on their R&D investment by reverse-engineering products and selling them at reduced prices. As shown later (page 50), the strength of a country’s IP protection can have far-reaching consequences, extending to areas such as clinical trial activity. In that case, IP protection not only affects the interest of foreign firms to sell pharmaceuticals in a country, but it also influences if the country’s scientists and physicians get to participate in the global drug-development industry, which often results in faster domestic approvals and solutions tailored to domestic needs. Moreover, a country might better afford enhancements to its healthcare infrastructure due to its participation in clinical trials.

**BUILDING A BROADLY BASED METRIC**

A WIDE RANGE OF ELEMENTS MUST BE CONSIDERED—BOTH LARGE AND RELATIVE— TO ASSESS A COUNTRY’S CAPABILITIES IN BIOTECHNOLOGY, AND SUCH A METRIC MUST ADAPT OVER TIME.

As the cover section in this issue reveals, a wide range of parameters impacts a country’s overall success in biotechnology, as well as capabilities in particular areas of the field in general. Moreover, excelling in some industry-supporting topics—such as education, IP, overall government support and so on—can lift even unexpected countries into prominence in some forms of biotechnology. Likewise, capabilities in the same categories impact larger players in the international world of biotechnology. Consequently, the Scientific American Worldview Scorecard consists of a collection of metrics. To help readers locate and assess the techniques used to calculate the numbers behind the Scorecard, a tan background color denotes the methods behind each measurement.

For the past three years, the Scorecard consisted of five fundamental categories: IP, Enterprise Support, Intensity, Education/Workforce and Foundations. This year’s Scorecard adds a sixth category, Policy and Stability. Each of the six categories—except IP—consists of several sub-categories. For example, Foundations arises from five sub-categories, which measure the overall money spent on biotechnology R&D, the biotechnology industry’s spending on R&D, the government’s financial contribution to supporting R&D, the quality of a country’s infrastructure, and a country’s environment for entrepreneurship. By using such a wide range of key categories and subcategories, the Scorecard—especially when presenting the results for each category—provides an opportunity for readers to explore any ranked country’s attributes. Moreover, government leaders and biotechnology experts in any ranked country can review their performance in comparison to other countries.

**METHODOLOGY:** This year’s Scorecard includes 50 countries. In large part, the constraining factor for inclusion arises from the availability of data. With the available data, the Scorecard arises from a straightforward quantification. For each sub-category, the lowest- and highest-ranking countries receive a 0 and 10, respectively, and we normalize the data for the other countries to that range. Calculating a country’s mean across the sub-categories provides its overall category score. For the IP category, which includes no sub-categories, the single score—based on the normalization from 0 to 10 for the lowest-to-high-ranking countries—serves as the category score. Finally, the sum of the means from a country’s six category scores, normalized to a scale from 0 to 50, provides its overall score.

To give every country as equal an opportunity as possible for the Scorecard to detect specific strong points, we use a variety of gross and relative measurements. For example, the Foundations sub-category includes gross and relative measurements, such as the total amount of money spent in a country on biotechnology R&D and that number relative to the country’s GDP. A full appreciation of the depth of information provided in the Scorecard section requires an assessment of a country’s performance in sub-categories and categories, as well as its overall score.

**IP**

The protection of property rights extends beyond country borders, but it must be balanced with other factors.


Despite the age of this index, it is still regarded as the leading global index of IP protection.

**SCIENTIFIC AMERICAN | WORLDVIEW**

WEBVIEW SCORECARD
INTENSITY

Seven sub-categories in combination indicate a country’s level of energy devoted to biotechnology

The intensity category consists entirely of relative measurements that impact a country’s biotechnology capabilities. Like the label suggests, this category quantifies how much effort a country applies to creating innovative biotechnology. Because this metric assesses relative, rather than absolute, performance, these measurements level the field for smaller countries, because any country that makes an effort could score strongly in this category.

METHODOLOGY: Of the seven categories, three of them—“public biotechnology companies per million population,” “public company employees per capita” and “public biotechnology company revenues per GDP”—come from company disclosures and information published in a journal article (Huggett, B., Hodgson, J. & Lähteenmäki, R. Public biotech 2010—the numbers. Nature Biotechnology 29, 585–589 (2011)). For the first two of these sub-categories, we divided the company and employee counts, respectively, by the 2011 mid-year population, according to the U.S. Census Bureau International Data Base. In “public biotechnology company revenues per GDP,” we used the 2010 GDP as sourced from the IMF World Economic Outlook Database. For “biotechnology patents per total patents filed for PCT” (the Patent Cooperation Treaty), “biotechnology venture capital as a percentage of GDP” and “biotechnology R&D as percentage of total business expenditures on R&D,” the data came from the Organisation for Economic Co-Operation and Development (OECD). The last sub-category of Intensity, the “proportion of public biotechnology companies,” came from the number of public companies listed in Huggett et al, divided by the sum of public and private companies in the OECD Biotechnology Statistics Database.

Denmark and Estonia lead this category. Denmark grabs the top spot through a combination of high scores in public biotechnology companies, employees and revenue in those companies, plus high ranking in its percentage of patents directed at biotechnology and the proportion of R&D spending on biotechnology. Estonia slips into second with a high ranking in “biotechnology R&D as percentage of total business expenditures on R&D,” gaining its number-two ranking largely due to a lack of scores in the other sub-categories. Switzerland, in the third spot, scores reasonably high in most of the sub-categories, especially in “biotechnology R&D as percentage of total business expenditures on R&D.” This example indicates one of the reasons to explore a country’s performance on a variety of metrics. Here, for example, Estonia

+ Countries with the best balance of this mix of relative measurements could offer the best biotech environments.
ENTERPRISE SUPPORT

A biotech-friendly environment is what distinguishes countries most likely to attract investment.

Anyone in business prefers to establish a company in a supportive location, and biotechnology companies also seek such environments. In short, the most alluring countries provide measures that encourage business and resources for the needed capital. In our Scorecard, Enterprise Support measures a country’s performance in these characteristics. In countries that score high on Enterprise Support, starting and growing a biotechnology business is easier than in countries that score low in this category.

METHODOLOGY: The overall Enterprise Support category includes four sub-categories. The “business friendly environment” sub-category comes from “ Doing Business 2012,” which was produced by the World Bank and the International Finance Corporation after surveying local experts on a synthetic business case. This approach includes some limitations because it relies on a hypothetical specific business of a specified size and refers to conducting a business in a country’s largest city, with the exception of certain countries such as China. The “biotechnology venture capital” sub-category comes from measurements performed by the OECD. The “venture capital availability” score comes from an index based on an international survey (Schroeh, K. The Global Competitiveness Report, 2011–2012 (World Economic Forum, 2011)). The last component, “capital availability,” was derived from the Milken Institute Capital Access Index.

For the second year, Hong Kong and Singapore top the list for Enterprise Support. This reflects their dedicated programs to promote inward investments. Both Singapore and Hong Kong possess relatively tiny domestic markets, which detract from inward investment, but they both serve as excellent staging points to reach the large and growing pan-Asian market. Nonetheless, Hong Kong, Singapore and the biotechnology promoting–regional initiatives in Europe and the United States face a crucial question: Do investments in promoting biotechnology—either through tax incentives or more direct measures—deliver a return, or are individual taxpayers and industry simply subsidizing biotechnology R&D projects that will deliver little commercial value?

Like the Intensity category, some countries that garner high expectations for biotechnology growth score at the low end of our Enterprise Support category. For example, the BRIC nations—Brazil, Russia, India and China—were highlighted in last year’s Scientific American Worldview, and the actions of many experts and companies in the biotechnology industry seem motivated by the assumption that these regions will continue to grow, but each of these countries finishes in the bottom half of the countries ranked here for Enterprise Support.
The educational background of a country’s citizens serves as a crucial element of the foundation of a biotechnology workforce.

To develop a successful biotechnology industry, a country depends on a wide range of elements, including its people. Working scientists, engineers, technicians and others form the very basis of biotechnology. Furthermore, the fast-paced changes in biotechnology demand an educated workforce, composed of people who can adapt as needed when new technology becomes available or when new research platforms must be developed. Beyond the scientific skills, the biotechnology industry also requires a variety of other skill sets from its workforce, including the ability to interact with researchers and experts from other fields. Many people in biotechnology must also understand and work efficiently at the intersection of science, business and government. These constraints place a high demand on countries to educate a strong and diverse biotechnology workforce.

Overall, the leaders in this category—Thailand, Saudi Arabia and Ireland—might not make everyone’s immediate impression-based shortlist for top countries. To some extent, a lack of data gave these countries some advantage, and they scored high where data were available. For example, both Thailand and Saudi Arabia performed effectively in “talent retention.” Some of the most interesting results involve the movement of talent. For example, a lower score in talent retention means that more Ph.D. graduates did express a desire to stay in the United States, which creates “brain drain” for the home country of those graduates. As described in the methodology, the objective of this metric is not to measure the attractiveness of the United States, but rather it is a reflection of the sentiment among individuals well-acquainted with their native countries that there are better opportunities elsewhere. The ranks for brain drain changed this year; India—passing China—took over the largely undesirable position of having the most U.S.-trained scientists who want to stay in the United States after graduating. Behind these countries, Russia comes in third for brain drain. In contrast, the United States, United Kingdom and Australia—in descending order, with Germany and France close behind Australia—lead the “brain gain” sub-category. Notably, no country comes close to the brain gain of the United States.

**Key:**
- Post-secondary science graduates / capita
- R&D personnel / thousand employment
- Ph.D. graduates in life sciences / capita
- Talent retention
- Brain gain

**Methodology:** To generate a metric that evaluates a country’s biotechnology education and workforce capabilities, we use five sub-categories. The first, “post-secondary science graduates per capita,” comes from UNESCO figures for graduates, divided by the 2011 mid-year population based on figures from the U.S. Census Bureau International Database. For “Ph.D. graduates in the life sciences per million population” and “R&D personnel per thousand employment,” we turn to OECD figures. To create a metric for “talent retention”—the reciprocal of brain drain—we calculated the percentage of a country’s doctoral recipients who did not express definite intentions to stay in the United States following graduation there, as reported by the U.S. National Science Foundation’s “2010 Survey of Earned Doctorates.” (The United States is the leading destination for out-of-country doctoral students; the measures of desire to stay in the United States are used as a general metric of desire to not remain in one’s native country, rather than a measure of the attractiveness of the United States.) Conversely, “brain gain” represents a country’s share of the global corpus of students studying outside their countries, which we assessed based on OECD’s “Education at a Glance 2011.”
A strong base provides enough strength to foster, support and maintain a biotechnology industry over time

significant consideration for doing business in a particular country is the quality of its infrastructure. For example, biotechnology R&D requires stable electricity supplies, and frequent brownouts or blackouts force companies to invest in and maintain backup measures, such as diesel generators. In addition, virtually any industry dealing with physical goods requires an effective transportation infrastructure, including adequate and affordable fuel supplies. Other elements, such as port efficiency, impact a biotechnology company’s ability to send or receive time-sensitive materials, such as perishable biological drugs or other compounds. Although large foreign enterprises might simply use capital to overcome a country’s weak enterprise support, weaknesses in infrastructure can loom so large that foreign companies and investors think twice before trying to resolve such issues. So, a country interested in generating a biotechnology industry should build strong Foundations.

As an indicator of future-growth potential, this subcategory includes metrics on spending in R&D, both by industry and governments. Nonetheless, Finland leads this category without investing a large actual amount of money in R&D. Instead, this country’s high relative investments in biotechnology push it upward on this list. It also scores high in infrastructure and creating opportunities for innovation and entrepreneurship. A high rating in the latter category indicates that researchers receive encouragement to spin off ideas into new ventures, which further stimulates organic domestic growth.

Other comparisons in this category also show that spending alone does not push a country to the top of our Foundations score. For example, the United States spends the most on biotechnology R&D, but Sweden presents a more appealing Foundations package with a high proportion of business expenditures on and government support of biotechnology R&D, plus a very high score in “innovation and entrepreneurship opportunity.”

More information often lies in the details behind numbers. As an example, consider that Israel and Finland place first and second, respectively, in “business expenditures on R&D,” but Israel’s business expenditures come largely from foreign countries (as shown on page 47), which means that other countries see Israel as an excellent global location for R&D. By comparison, local businesses account for most of Sweden’s spending on biotechnology R&D, suggesting that Finnish companies possess the monetary might and confidence to invest in R&D at home.

+ ...the United States spends the most on biotechnology R&D, but Sweden presents a more appealing Foundations package....
POLICY & STABILITY

A government’s overall stability—as compared to generally accepted global norms—contributes to a biotech-friendly image.

This Scorecard’s traditional categories—IP, Intensity, Enterprise Support, Education/Workforce and Foundations—provide an extremely useful overall assessment of a country’s innovation environment. However, a country’s policies and general stability also affect its impact on the innovation-driven nature of biotechnology. In general, this category assesses a government’s ability to perform, such as maintaining a stable environment. Moreover, this category explores a government’s power to develop and put in place effective rules and laws, and to enforce them, both of which play key roles in how biotechnology succeeds or fails in that country. Indeed, the addition of this category reflects the ongoing impact of government on a country’s capabilities in biotechnology.

As expected, many of the established markets in North America and Europe receive high scores in this category, as do Hong Kong and Singapore, which have implemented broad political and economic measures to become commercially attractive. Perhaps surprisingly, the United States places a nearly middle-of-the-pack 20th, pulled down by scores in every sub-category, with an especially low score in “political stability and absence of violence/terrorism.” In addition, some countries regarded as having strong potential in biotechnology—such as the BRIC nations—score poorly in Policy and Stability, which indicates an additional impediment to investment. Although foreign companies might self-finance improvements in infrastructure, companies are challenged to impact a country’s issues related to Policy and Stability. Accordingly, domestic policy-makers and other stakeholders must resolve policy and stability issues to create an investment-conducive environment.

METHODOLOGY: The Worldview Scorecard’s Policy and Stability metric consists of four sub-categories derived from measurements developed by the World Bank’s 2011 World Governance Indicators. “Political stability and absence of violence/terrorism” measures perceptions of the likelihood that a country’s government will be destabilized or overthrown by unconstitutional or violent means, including politically motivated violence and terrorism. “Government effectiveness” measures perceptions of the quality of public services, the quality of the civil service, the degree of a country’s independence from political pressures, the quality of policy formulation and implementation, and the credibility of a government’s commitment to such policies. “Regulatory quality” measures perceptions of the ability of the government to formulate and implement sound policies and regulations that permit and promote private-sector development. Last, “rule of law” measures perceptions of the quality of contract enforcement, property rights, the police and the courts, as well as the likelihood of crime and violence.
**THE 2012 SCIENTIFIC AMERICAN WORLDVIEW OVERALL SCORES**

**THE BROAD COLLECTION OF SCORECARD CATEGORIES AND SUB-CATEGORIES PROVIDE AN OVERALL SCORE, BUT DO NOT FORGET THE DETAILS**

Any multi-factorial assessment demands a summation—a single score that condenses the analysis. In that spirit, we present the countries in an order based on the sum of the Scorecard metrics. In reviewing this list keep in mind that there is a complex set of measurements behind the final number. By analogy, the winning team of baseball’s World Series includes batters with higher and lower batting averages, pitchers with more strikes out and ones with fewer. Likewise, just the number of wickets lost in a cricket match does not determine the outcome. Instead, both winning and losing teams in any sport tend to include players who excel in some areas and lag behind in others. Similarly, some countries that finish high on the overall scores listed here falter in some aspects related to driving innovation in biotechnology. Consequently, this list provides the most value when assessed in concert with the elements that comprise it.

As in the prior Scientific American Worldview Scorecards, the United States landed at the top of the list in overall innovation. Nonetheless, the United States does not lead in all categories. In fact, it only places first in one category, IP. Top scores for intensity go to Denmark and Estonia. Thailand and Saudi Arabia score highly in Education/Workforce due to the strong desire of their students to return home following external doctoral studies. In Foundations, Finland and Sweden take the top spots. For our Policy and Stability category, Finland and Denmark takes the lead amongst a close finish by the top-5. For most of the countries in our Scorecard, some aspect of their contribution to an innovation-spawning environment for biotechnology deserves praise, while another area might require some fine-tuning, or perhaps an overhaul.

In this year’s Scorecard, some aspect of the sub-category “political stability and absence of violence-terrorism” Likewise, in the category of Education/Workforce, the United States takes the sixth spot overall, but receives a relatively low score in “post-secondary science graduates per capita.” Although this metric includes a relative aspect, it does not seem like a place that the United States might fall behind so many other countries.

So the overall value of the Scientific American Worldview Scorecard does not simply acknowledge performance and the behaviors related parties can formulate a government officials and other related parties can formulate a plan to enhance their homegrown and imported capabilities in this innovation-driven field.

**METHODOLOGY:** As a methodology reminder, the ranked list of the Scorecard arises from a collection of averages and totals. Each country received a score in six categories—IP, Enterprise Support, Intensity, Education/Workforce, Foundations and Policy and Stability—in which all but one were composed of sets of sub-categories. Based on 0–100 scores, for lowest to highest, we averaged the sub-category scores to determine the category score. The overall innovation score represents a simple sum of the category averages, normalized to a scale of 0–50. Given that the normalization involved in calculating the category scores considers each sub-category on equal weighting, this scorecard gives equal importance to a business friendly environment, public biotechnology companies per capita, Ph.D. graduates in life sciences per capita and every other sub-category. In addition, the calculations for averages in each category ignore any gaps in the individual sub-categories.

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<th>Rank</th>
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**TAKING A LOOK AT THE TOP-5**

IN MANY RESPECTS, ONLY A FEW POINTS SEPARATE THIS YEARS SCORECARD LEADERS, AND THE DISTINGUISHING FEATURES ARISE IN SPECIFIC CAPABILITIES

At the top of our Scientific American Worldview Scorecard, just a five-point spread separates the top-five finishers: the United States, Denmark, Singapore, Finland and Sweden. With overall scores, respectively, of 38.0, 37.2, 35.6, 34.6 and 33.3, not much numerical space lies between these countries on this combined metric. Such a close grouping at the top fuels the question: What specific features distinguish these countries in terms of their innovation capabilities in biotechnology?

A graphical representation of the category scores for the top-five countries provides an immediate impression that even the leading countries perform diversely within this group. For example, the top finisher, the United States, only obtains the top score within this group for a single category, IP. Otherwise, the United States places a distant second in Intensity, a close second in Enterprise Support, an even closer second in Education/Workforce, fourth in Foundations and last—among the top-five countries—for Policy and Stability. This analysis reveals that even the leading countries must work to improve their overall support of innovation in biotechnology. Likewise, these comparisons indicate that the top countries have to continue to work hard if they hope to maintain their spots as leaders in this field.

Within the top five, Finland’s finishes in the categories demonstrate its potential to move up on this list. In this group, Finland earns the most top finishes in the Scorecard categories: Education/Workforce, Foundations, and Policy and Stability. The data show that Finland wins most of these categories by small margins. For example, four of the top five—all but the United States—finish the Policy and Stability category with a spread of less than 6 percent, with Finland just nudging out the competition. Finland grabs even closer victories in Foundations and Education/Workforce, leading Sweden by less than 2 percent in the former and passing the United States by about 2.5 percent in the latter.

Nevertheless, even the best of the best do not always perform at the top. In the Intensity category, for instance, Finland lags behind in the top-five countries, where category-leading Denmark earns a score that outstrips Finland by more than six times. Among the top five, though, the graph shows the scatterplot of results, with Denmark at the top and the remaining three leaders finishing about halfway back to Finland. So even among the top nations, maintaining the Intensity behind innovation in biotechnology turns out to be a battle.

The comparison of results among the top-five countries also reiterates the importance of looking more deeply into our Scorecard data. The value of our findings dive much deeper than a simple ranking of countries based on the overall score.

In reviewing this year’s results, countries at the bottom five of the overall results will quickly see opportunities to improve their scores in the future. First, the bottom-five countries—Argentina, India, Philippines, Ukraine and Indonesia—receive overall scores that vary by just 2.5 points. Perhaps as expected, each of these countries finishes with consistently low scores across the Scorecard categories. By comparison, the top-five countries achieve relatively high scores across the categories. Consequently, getting to the top requires more consistent efforts and achievements across the range of metrics explored in the Scientific American Worldview Scorecard. Overall, the bottom-five countries seem to perform the best in IP, receiving an average score of about 4.6. By dropping the lowest IP-scoring country from this group, Indonesia, the average IP score climbs to nearly 5.6. Nonetheless, even the bottom five’s IP leader, the Philippines, only earns an IP score of 6.84, which looks reasonable on the graph of the bottom-five countries across the Scorecard categories. But even this IP score languishes in the bottom half of scores from all of the countries in this year’s Scorecard.

Across all of the categories for the bottom-five countries, Fidelities reveal the most room for improvement. Recall that this Scorecard category assesses a country’s investment in biotechnology R&D, the components of biotechnology spending on R&D from businesses and the government, plus the quality of the country’s infrastructure and support of innovation and entrepreneurship.

For the complete list of countries on this year’s Scorecard, Argentina, India, Indonesia and the Philippines land at the very bottom of the Fidelities scores, and Ukraine sits only ninth from last. Among the sub-categories that make up our Foundations score, these countries show a need to improve in all of them.

In our new category, Policy and Stability, these countries also exhibit an inclusive opportunity to improve. The bottom-five overall scoring countries also lie among the last six finishers in this category. In particular, these countries score extremely low in the sub-category of “regulatory quality,” where they rate an average score of 0.90—compared to an average score of 9.44 for the five countries that lead the scoring in the Policy and Stability category.

So in short, the bottom-five countries overall earn about 10 times lower scores in “regulatory equality” when compared with the top countries in Policy and Stability. Like the countries at the top of this Scorecard, the data for those at the bottom also depend on more than one cumulative number. Only by exploring the category and sub-categoray results across the Scorecard—comparing overall standings and relative results—can a country plot its path toward a more innovation-friendly place for biotechnology.

**OPPORTUNITIES FOR IMPROVEMENT FOR THE BOTTOM-5**

For countries on the low end of our Scorecard results, the numbers across the categories reveal how they can climb the chart.
The results indicate some consistency as well as some volatility.

First, let’s consider the scores over the years (above). To compare the overall Scorecard results, we normalized the innovations scores. In addition, we normalized the overall scores for each country and listed them in descending order. The results show the United States at the top each year, with a relatively consistent overall score. The volatility of the overall score appears in many of the other countries’ scores. In fact, only France and Spain show consistently improving scores across the Scorecard’s history. No country, however, received consistently decreasing scores.

Adding the rankings over the years reveals the dynamic nature of the Scorecard (left). First, simply comparing the overall scores for the top-five countries shows more consistency over time than their rankings. Likewise, variability appears in closer examinations of the data over time. For example, Canada’s overall scores are in a fairly narrow range—28.6 to 32.9, just a 13 percent difference between the country’s best and worst score—but its overall ranking lands at three in one year and 11 in another. Moreover, Canada earned its highest overall score in 2012 but only ranked seventh that year, and it ranked the highest overall in the year that it earned the lowest overall score.

The rankings also display downward trends for some countries. For example, Iceland, Israel, Italy, Russia, South Africa and Turkey consistently drop on the list. Perhaps most surprising, Germany earned the same overall ranking, 16th, every year.

In exploring the developing scores over time, the charts here show that both the overall score and the ranking must be considered to assess a country’s biotechnology-innovation capability, particularly as it relates to other countries. In addition, ongoing trends can only be explored by comparing the results over a period of years.
PODIUM POSITIONS IN BIOTECHNOLOGY

IN AN OLYMPICS OF BIOTECHNOLOGY EVENTS, THE MEDALS WOULD GO TO THESE COUNTRIES

The Scientific American Worldview Scorecard provides an overall score for the ability to innovate in biotechnology. This industry, however, includes an immense range of elements that come into play when competing with participants around the world. This map shows the countries that climb onto the podium to receive medals for their excellence in specific measurements of success in biotechnology.
A BALEANCE OF EXPANSION & CONTRACTION

EXAMINING THE NUMBER OF PUBLIC BIOTECHNOLOGY COMPANIES AND THE MARKET CAPITALIZATION REVEALS SOME OF THE DYNAMICS IN THE INDUSTRY, AND A HINT OF RECOVERY


In general, the data show that far more public biotechnology companies exist in the United States than in any other country. However, the U.S. total has been decreasing, which indicates that companies are either liquidating, delisting or consolidating. On the other hand, the number of public biotechnology companies consistently increased over the past four years in Australia, France and Israel.

Similarly, and using the same sources, the Scientific American Worldview Scorecard reports on the market capitalization for a series of countries. The market capitalizations of the United States and the combined figure for Australia, Austria, Belgium, Canada, China, Denmark, Finland, France, Germany, Hong Kong, Iceland, India, Ireland, Israel, Italy, Japan, the Netherlands, Norway, Poland, Russia, Sweden, Switzerland and the U.K.—even shows signs of improvement in their 2009 data. Consequently, these countries might make good homes for growing biotechnology companies.

SMALL COMPANIES & SPECIALIZATIONS

LOOKING MORE CLOSELY—BEYOND JUST THE LARGE PLAYERS—REVEALS BIOTECH OPPORTUNITIES

In many metrics related to biotechnology, large companies obscure the contributions from smaller ones. Here, we define “smaller” biotechnology companies as ones with fewer than 50 employees. To assess the impact of such firms in several countries, we plot the percentage of small biotechs—relative to the overall number of biotechnology companies in a country—and the percentage of the country’s overall biotechnology R&D performed by the smaller companies, all based on the latest data from the OECD Biotechnology Statistics Database as of December 2011.

The observed trends suggest multiple possibilities. Some countries, like Estonia or Spain, could have a high percentage of small biotechnology firms for two reasons: Either few or no large companies exist in the country, or the number of smaller firms simply eclipses the larger ones. When the data show a small percentage of smaller biotechnology companies, there is only one explanation: The nation lacks smaller companies. That could indicate a good environment for larger biotechs, and perhaps a challenging one for smaller companies.

This plot also shows how much of a country’s R&D comes from its smaller biotechnology companies. This reveals, on average, whether a country’s small biotechnology companies perform R&D or focus on non-R&D areas, like services. Reviewing this graph shows that biotechnology as an industry consists of a wide range of opportunities, and a country can build an industry that specializes in one area or across a variety of fields.

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<th>% OF DEDICATED BIOTECHNOLOGY FIRMS BY APPLICATION</th>
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TALLIES OF TEAMWORK

BIOTECHNOLOGY COMPANIES AROUND THE WORLD MUST RELY INCREASINGLY ON COLLABORATION

Today’s global, domestic and industry-specific market forces make it impractical—if not impossible—to survive as a large, fully integrated biotechnology company. Consequently, companies must collaborate. As the data here show, different perspectives reveal distinct aspects of how a country’s biotechnology companies collaborate. For one thing, universities and industry can collaborate. Without such collaboration, university research—an increasingly vital source of advances in basic and even applied science—can languish, rather than being transferred to industrial partners for further development, implementation or commercialization. We explore that aspect through data collected in the World Economic Forum Executive Opinion Survey, 2010. This survey scored countries on a scale of 1–7, moving from none to extensive collaboration. To make the variations more evident, we normalized the data to a scale of 0–100. The results include relatively high university-industry collaboration on R&D in the leading biotechnology countries, including the United States, Switzerland, Finland, the United Kingdom and Sweden. Low scores on this metric send a clear message: Foster better collaboration to leverage existing R&D activities.

A second indicator of collaboration arises from the R&D expenditures generated by foreign-controlled companies. A high percentage of foreign investment in R&D can be considered a compliment, because it means that foreign firms regard a country as a better place to invest in R&D than their own countries. On the negative side, too much foreign investment can stymie one of the benefits of a strong domestic R&D program, which is its ability to solve domestic problems—such as managing local parasites or curing locally prevalent health conditions—or to provide agricultural and environmental applications suited for a country’s geography and climate. When the majority of R&D funding comes from foreign sources, however, these benefits are less likely to emerge, because the so-called off-shoreers typically lack adequate interest in domestic issues. Furthermore, R&D is just one component—and often not the most lucrative one—of commercialization, so the foreign R&D investors could reap the greater share of the ultimate benefit from the R&D effort. Accordingly, countries with a large share of foreign control of R&D should build on their established R&D infrastructure and encourage greater investments by domestic firms.

Based on OECD data, we plot the percentage of a country’s biotechnology R&D that comes from foreign companies, plus these foreign expenditures as a percentage of GDP. The results reveal particularly high percentages of foreign investments in biotechnology in some countries, including Ireland, Israel, Hungary and Belgium. Japan relies on the lowest percentage of foreign investment, just 4.7 percent. In all of the countries plotted, the foreign investment in biotechnology R&D equals only a few percent—at most—of the country’s GDP.

To explore where companies find teammates, we plot data on domestic and foreign collaboration. Using data published by OECD, based on Eurostat’s Community Innovation Statistics 2008 and national data sources, we present the national and international collaborations as a percentage of innovative firms. Although these numbers are not specific to biotechnology, the results indicate more international than national collaboration by many of the countries, including Austria, Belgium, Estonia, Finland, Luxembourg and the Slovak Republic.
To examine the ongoing use of and research in agricultural biotechnology, we combined a collection of data sets. For the land planted in genetically modified (GM) crops, we rely on 2011 data from the International Service for the Acquisition of Agricultural Biotech Applications (ISAAA). These numbers show that most plantings are in the Americas, where the United States plants 69 million hectares, more than twice as much as Brazil, which is number two on the list, planting just over 30 million hectares. Given the geographic sizes of India and China, the GM plantings in those countries—10.6 and 3.9 million hectares, respectively—represent a very small portion of their arable land.

Although not shown here, the ISAAA data also reveal some new entrants to the list of GM planting nations. For example, Pakistan planted 2.6 million hectares in GM crops in 2011, Myanmar planted 0.3 million hectares, and Sweden and Germany both planted less than 0.05 million hectares. Although those figures on planting seem fairly small, keep in mind that every country on the list below the top five—the United States, Brazil, Argentina, India and Canada, in descending order—planted fewer than 4 million hectares.

Much of the interest in GM plants relates to commodity crops, including corn, soybean and cotton, which make up the majority of planted crops. Even so, countries might also apply biotechnology to specialty crops, such as local plants like cassava. Consequently, the GM-crop plantings fail to expose some important details in the world of agricultural biotechnology. To look for some of the key countries interested in applying biotechnology to specialty crops, we turned to data from Jamie Miller and Kent Bradford, both of the Seed Biotechnology Center at the University of California, Davis (The regulatory bottle-neck for biotech specialty crops. Nature Biotechnology 28:1012–1014 (2010)). These authors reported publications by country for a range of GM specialty crops, including “fruits, vegetables, nuts, turf and ornamental crops.”

Here, we plot the overlapping data between ISAAA’s hectares planted in GM crops and the GM-specialty crop publications noted by Miller and Bradford. Like the number of GM hectares planted, the United States also published far more articles, 75, on specialty GM crops than its closest competitor, India, which published 28 articles. Although no apparent correlation exists between the two data sets, the graph shows that some countries that lag in planting GM crops are nonetheless invested in research on GM specialty crops. For example, China ranked fifth on the ISAAA list of GM plant growing with only 3.9 million hectares—nearly 18 times less land than that planted in the United States—but it ranked third on the list of GM specialty publications with 24—nearly one-third as many as the United States. Likewise, India’s GM specialty publications indicate growing interest in that country. In addition, Germany planted less than 0.05 million hectares of GM crops but it published 16 articles on GM specialty crops, putting it in the top five.

Many sources—including stories in this issue’s cover section and Country Spotlights—cite Africa as a target application for agricultural biotechnology, but where will the innovations occur? Published data (Beintema, N. & Stads, G.-J. African Agricultural R&D in the New Millennium (International Food Policy Research Institute, Washington, DC, 2011)) on the spending toward agricultural biotechnology in countries across the African continent suggest that Nigeria, South Africa and Kenya might be among the future leaders.
**DRILLING DOWN ON IP**

**MANY FACTORS CONTRIBUTE TO A COUNTRY’S REPUTATION FOR PROTECTING INNOVATION IN BIOTECHNOLOGY**

Intellectual Property lies at the heart of biotechnology, and many experts consider strong IP protection as a requirement if companies hope to recoup their R&D investments. Nonetheless, IP strength surpasses simply recovering R&D costs. Novartis, for example, diverted hundreds of millions of dollars in research from India following an unfavorable patent ruling, and this example indicates that weak IP can also impact how much R&D investment—and, by extension, how many spillover innovations—a country receives.

One index of pharmaceutical-related IP shows that strong IP scores are associated with greater levels of clinical trials (Pugatch, M.P., & Chu, R. The strength of pharmaceutical IPRs vis-à-vis foreign direct investment in clinical research: Preliminary findings. *Journal of Commercial Biotechnology* 17:306–318 (2011)). Nonetheless, the relationship might not be directly causal: Strong IP might encourage more clinical trials; more clinical trials can encourage stronger IP laws; or the relationship might be indirect and complex. Still, this correlation demonstrates the importance of strong IP protection beyond simply selling innovative products.

Examining relative specialization of patents—including patent applications—shows that Israel, Switzerland, and the United States file a large proportion of patent applications in medical technology, and India, Belgium, and Switzerland file a large proportion of patents in pharmaceuticals (World Intellectual Property Organization, 2011 World Intellectual Property Indicators). Interestingly, South Korea and Japan—two developed nations with strong innovation outside the life sciences—demonstrate low activity in both areas.

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**TOURISM FOR TREATMENT**

**THE SEARCH FOR LOWER-COST MEDICAL TREATMENTS DRIVES A GROWING INDUSTRY**

Patients Beyond Borders estimates that medical tourism—traveling to another country to save money on a procedure or treatment—makes up a $15 billion market, which is growing at 25–35 percent each year. Two trends drive medical tourism. First, rising healthcare costs in developed nations enhance the likelihood that citizens will seek less expensive treatments in other countries. Second, as citizens in emerging economies attain greater wealth, they might travel for treatment by a world-renowned expert in a selected procedure. According to data from Patients Beyond Borders, traveling for a treatment generates average savings of 30–90 percent relative to U.S. prices.

**AVERAGE SAVINGS RELATIVE TO U.S. COSTS**

![Graph showing average savings relative to U.S. costs for various medical procedures in different countries.](https://example.com/graph)

Data from Patients Beyond Borders also show that the average cost of a range of medical procedures varies widely from one country to another. We should add that the costs of medical procedures in the United States also vary by location, as well as by the materials and equipment used in the procedure, and individual needs even impact the cost. In addition, the numbers reproduced here for procedures in other countries do not include any costs related to travel or accommodations. Nonetheless, the data show the potentially large savings that can arise from medical tourism. This industry can also drive a country to upgrade its medical capabilities and facilities, which can enhance the region’s biotechnology industry in other respects, such as the ability to host clinical trials or even to fund basic research.
A unifying rallying point for any diverse nation has always been the commitment to science, discovery, and innovation. In 1962, at the height of Cold War polarization, president John F. Kennedy threw down a technological gauntlet, calling on the United States to send a man to the moon within the decade. The mission to enter the Space Age, an era that would undoubtedly push the limits of knowledge and scientific understanding even further. This effort set a clear national agenda, motivating policymakers, scientists, and citizens alike that the frontiers of innovation were indeed the purview of democracy and freedom, cast in stark relief to the threats of tyranny and injustice.

In our own era, the threats we know are global (pan-demics, bioterrorism, chronic disease, water and food insecurity, economic unsustainability) and their scientific solutions will require the effort, knowledge, and motivation of many nations, great and small. There has never been a better time to reignite the call for scientific ingenuity and discovery on an international scale as we collectively endeavor to face 21st century challenges.

But what is the true structure of a scientific revolution? What is the true structure of a scientific revolution? In his famous treatise on the topic, Thomas Kuhn posits that major conceptual revisions in thinking regarding the nature of our world (which he calls a “paradigm”) are the key life drivers of science and innovation. More recently, however, the physicist Freeman Dyson, in his book Imagined Worlds, takes on this concept-driven model of science in favor of a tool-driven version. He argues that while big conceptual changes in thinking (Darwin’s theory of evolution, Einstein’s relativity) attract the most attention in science, discovery, and innovation, it is biology that is most tethered to our digitized age, and the co-revolutions in chip processing speed, bioinformatics, genomic sequencing, and related areas are pushing science forward in ways that we are only beginning to understand and creating the potential for an entire new set of scientific tools. If any one company could lay claim to being the ultimate “tool-enabler” for the new biology, it would have to be Life Technologies. Aptly founded in a humble San Diego garage in 1987 and now based in Carlsbad, California, the company has become, through both organic growth and strategic acquisitions, one of the most diversified and robust sources of scientific research products in the world. Now operating in 160 countries and establishing unique and powerful partnerships with research centers, clinical laboratories, governments, philanthropic organizations and patient advocacy groups, its commitment to empowering science and those who practice it has never been stronger. Consider a few timely examples in which Life Technologies’ products have had a profound impact on the critical work of scientists around the globe to improve lives.

In the summer of 2011, during the deadly E. coli outbreak in Europe, the Life Technologies Personal Genome Machine™ (PGM™), a sequencing instrument that uses semiconductor technology to read millions of letters of genetic code in about two hours, allowed researchers to analyze and identify the strain of the pathogen. Knowing the bacterium’s origin enabled Life Technologies scientists to quickly develop a custom test (assay), which enabled health officials to detect the strain in food samples. What used to take weeks now took a matter of days, potentially saving numerous lives.

In 2010, Life Technologies donated thousands of DNA kits used to confirm identities and reunite children displaced by the Haitian earthquake with their families. The breadth of kits within the Applied Biosystems® human identification product line have been essential in courtrooms and crime labs across the United States and internationally, helping to exonerate the innocent and enabling law enforcement to identify the perpetrators.

In November 2011, the company launched its GeneArt® Algae Engineering Kits for the photosynthetic microbe Synechococcus elongatus. These GeneArt® Engineering Kits help create the first standardized system for algal research and metabolic engineering. The algal strains in the kits are model organisms for the study of photosynthesis and its circadian rhythms and nutrient-regulated gene activity. Used for the production of biofuels, nutraceuticals and specialty chemicals, they are the first strains that can be stored frozen at −80 degrees Celsius, which simplifies their standardization and accessibility. As biofuels become an ever more important aspect of the future energy portfolio, this technology will no doubt take center stage in research labs everywhere.

In early 2012, the company made headlines with the introduction of another revolutionary genetic analyzer, the Ion Proton™ Sequence, a machine designed to decode an entire human genome in a single day for $1,000. The scalability, speed and cost points that this innovation offers the field of genomics are truly game-changing, in the most genuine sense. Cancer and rare disease research will be significantly impacted in both developed and developing markets. The accessibility of this desktop-size, $1,000 analyzer will no doubt aid in what is a fundamental mission of the company: to put cutting-edge science into the hands of many.

These are just some recent examples of the impact of this unique manufacturing tool. The technology tools of Life Technologies’ scientific arsenal are no less impressive, including the GeneArt® Precision TALs (TAL effector proteins) that allow researchers unprecedented specificity in genome editing and gene activation and repression. This proprietary TAL technology, according to the co-inventors, will enable genetic experiments unachievable with existing methods.

From DNA sequence to cell and tissue function, the broad and deep spectrum of life sciences is covered by all of these product lines. According to Life Technologies CEO Greg Lucier, the research infrastructure in life sciences is still too expensive. To address this global concern, the company strives to make products that are “more economical, faster and easier to use.” That is democratizing science while empowering it. And these are truly the tools of the next revolution.

And while the toolmakers—the real providers of innovation’s right stuff—are often the unsung heroes in the pursuit of knowledge, let us not forget Archimedes’ view of science and those who practice it has never been stronger. Pursuit of knowledge, let us not forget Archimedes’ view of science and those who practice it has never been stronger.

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This past spring, testing equipment from Life Technologies aided The Shizuoka Institute of Science and Technology in central Japan in its effort to identify non-locally produced eel (a major food source critical to the region’s economy). The DNA tests, cheaper by a factor of one thousand than the methods used in the past to detect eel fraud, employed the same CMOS chip technology that powers Life Technologies’ most recent sequencing product line.

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Three biotech trailblazers—a scientist, a CEO and a venture capitalist—share secrets of their success & their visions for the future

By Richard Gallagher

OF THE MANY KINDS OF EXPERTS NEEDED TO GROW THE biotech industry, three stand out: the scientific innovator, on whose vision the whole sector depends; the multi-tasking CEO, who can transform those fragile ideas into robust products and healthy companies; and the daring venture capitalist, who offers insight and support while making the required investment over many years.

This article profiles an A-list luminary from each category. Lee Hood, Richard Pops and Terry McGuire lay claim to stunning success in their chosen fields, and their individual stories instruct and inspire others in biotechnology. Although they followed different paths to make their contributions, they shared an adventure in the growth of an industry through tenacity, courage, candor, patience, goodwill and a positive attitude. Most of all, they share a passion to change the world.

TRIPLE-A RATED

LEE HOOD: MAKING THE FUTURE HAPPEN

From the day in 1970 that he became an independent researcher, Lee Hood has divided his attention equally between problems at the leading edge of biology and the invention of tools to explore new dimensions of data space. “Most hard problems in biology require new instruments and new analytic approaches,” he says. “The biology has driven the technologies that I’ve developed, they are utterly, intimately related one to another.”

The instruments that Hood developed include automated sequencers for DNA and proteins, automated synthesizers for DNA and peptides, and the ink-jet array for synthesizing large numbers of oligonucleotides. He developed all of these between the early 1970s and early 1990s. “These are the machines that revolutionized modern biology,” says Jim Heath, a California Institute of Technology (Caltech) professor, pioneer in fluidics and nanotechnology, and a long-time collaborator of Hood’s. “Not only did Lee devise these instruments and do the science that demonstrated their power, he also moved them from the lab to the marketplace.”

Considering that Hood faced “establishment skepticism” throughout his career, his achievements are even more remarkable. “My big science view, my cross-disciplinary view, my ideas about technology and computational tools driving biology haven’t always fit well with my peers,” he admits. For example, in 1987–1988, Hood proposed a new cross-disciplinary department at Caltech, his home of 15 years. “The president liked the idea, but said that I’d have to persuade my colleagues. I got enormous support from the chemists and engineers but the biologists were implacably opposed.” They preferred that the instrument-maker join the engineering department. It
was not until he founded the Institute of Systems Biology (ISB) in Seattle, Washington, in 2000 that Hood finally got free in a cross-disciplinary environment to perfect his approach of “biology driving technology that in turn spurs computational and mathematical tools.”

Given the formidable barriers, what fueled Hood’s success? “At dinner one evening, many years ago,” Ed Lazowska, professor of computer science and engineering at the University of Washington, told me. “I asked Lee’s wife, Valerie, ‘Why do you think Lee’s doing this?’ I asked her if he’s that smart, even when it’s staring him straight in the eye.’”

Hood’s approach of “biology driving technology that in turn spurs computational and mathematical tools.”

Companies are starting to recognize defeat, even when it’s staring them straight in the eye.”

Hood’s approach to most companies is to be closely involved in the development of 14 companies, including Amgen, Synetex, Darwin [now Cellecta], Rosetta, MacroGenics and Integrated Diagnostics.

“My approach for most companies is to be closely involved in the development of 14 companies.”

NORTHWEST BLOWS COLD AND HOT

In 1992, the University of Washington (UW) recruited Hood to create the department of molecular biotechnology, in part supported by Bill Gates. The department was spectacularly successful from a scientific perspective: two faculty members created key techniques for proteomics, a third invented crucial software for the Human Genome Project; and the ink-jet DNA synthesizer was developed, “Lee develops a field, the rest of biology eventually follows, and by that time he has moved on to his next big thing.” —Jim Heath

Hood’s current big thing is P4 medicine, defined as the intersection of systems biology and the digital revolution. P4 stands for predictive, preventive, personalized and participatory. “Systems biology is a holistic approach to understanding biology and disease. Combining it with business and social networks and digital consumer devices that measure personal information will transform the practice of healthcare,” he says.

P4 medicine utilizes large populations, treating individuals on the basis of average behavior. “That’s exactly the wrong way to do medicine because we are genetically diverse and we see very different environments,” Hood says. Instead, he suggests, the focus should be on actionable gene variance, one component of P4 medicine. “These are functional variations in genes which, if the doctor knows you have them, empowers him or her to do something to improve your health.”

Another component of P4 medicine is the stratification of disease. For example, Hood is using induced pluripotent stem cells (iPSCs) to begin categorizing Alzheimer’s disease into its different subtypes. Once subtypes are identified, he will approach drug companies to test the 100 or so drug candidates that have proved ineffective at the population level on these distinct patient subpopulations. While his friend Bill Gates points out that “Lee’s contributions to the world of medicine and biology are already visible every day and everywhere,” Hood is far from finishing contributing. “In the next five years I expect to have three or four pilot projects that have been really allocentrically transformative and show that this new P4 medicine is much more than a sale of my name,” Hood says. “I’d also like to see a better world. And two, it was really fortunate that none of the seven years, we’ve looked at 600 business plans and chosen 12,” Hood says. “Eight of those are still doing very well. We pushed the envelope, we wanted to try things that were very experimental, so it was expected that some of them would fail. Overall, it has been quite a remarkable success.”

A Medical Revolution

According to Jim Heath, “Lee develops a field, the rest of biology eventually follows, and by that time he has moved on to his next big thing.”

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High expectations, but don’t be surprised if Hood pulls it off. As Jim Heath says, “There’s a famous quote from Alan Kay: ‘The best way to predict the future is to invent it.’” Heath adds, “Lee predicts the future, and then he makes it happen. He is an amazing guy.”

POINTS OF VIEW

ON THE TRAITS OF SUCCESSFUL ENTREPRENEURS

McGuire: It’s not good enough to be intellectually smart, you need to be clever, clever enough to figure out new ways to make things happen. Plus, you need ambition that is beyond monetary, a desire to see a better world. That doesn’t necessarily come in the most humble package, but you can’t take on this size of challenge and not be strong willed.

McGuire: “Having a clear picture of the future that is very different to what other people have, and an ability to drive towards that future, are the key points in changing the world. You also have to have a talent for getting things done, for recruiting the necessary people and for leading them.”

Paps: There’s no central-casting type that’s successful in biotech but high achievers do share an enormous capacity for work and the ability to embrace complexity. They have an instinctive understanding of science that’s quantitative and qualitative. Decision-making is based on data, and the best in the business have an understanding of where the data are taken from.

ADVISE FOR THE NEXT GENERATION

Hood: Young biologists must be cross-disciplinary. You need a good background in math, physics and chemistry and an ability to
Richard Pops: The Ceaseless Pursuit of the Perfect Portfolio

The career of Richard Pops could not be easily replicated. By the age of 28 he was CEO of Alkermes, a private venture-backed company housed in a building adjacent to the Massachusetts Institute of Technology (MIT). Focused on understanding the blood-brain barrier, Alkermes was a modest-size science company of 20-odd people, but its scientific credentials were stellar: The founders were all members of the National Academy of Sciences. That was in 1991. Twenty-one years on, Pops remains the CEO (there was an interregnum between 2007 and 2009), but his company is unrecognizable. Alkermes is now a 1,200-employee, international biotech company headquartered in Dublin, Ireland, with a portfolio of 20 commercial products.

From being one of the youngest CEOs in biotech, 49-year-old Pops is now one of the longest tenured. This is a source of satisfaction but it also points out to Pops one of the great weaknesses of the biotech model. “Many people don’t get that CEO position until their late 40s,” he explains. “It then takes a decade to grow one of these companies to any reasonable level, say to get to drug approval. It’s a grueling endurance game and most people don’t do it again. A lot of expertise in biotech simply exits after it. For his part, Pops, who was working on financing biotech companies to any reasonable level, says to get to drug approval. It’s a grueling endurance game and most people don’t do it again. A lot of expertise in biotech simply exits after it.”

Bucking the Trend

Pops bucks that trend. He was appointed CEO by Michael Wall, a veteran biotech investor and a shrewd judge of character. “I was looking for a CEO for Alkermes, and Richard and I had dinner together,” Wall explains. “Yes, he was young, but he was smart and he was humble. I didn’t just talk about himself. Plus, he didn’t have the baggage of being associated with the industry for a long time.”

For his part, Pops, who was working on financing biotech companies from Wall Street at the time, was undaunted about being dropped into a sink-or-swim environment. “Your own bias is that you will figure out a way to succeed,” he says. “You can’t build a company, attract great people or plan for the future if you harbor any doubts that you are going to fail.”

This was not merely naïve enthusiasm. Planning thoroughly and working incessantly, Pops followed two cardinal rules, rules that he follows to this day. One is diversification. “You must be sufficiently detached emotionally from your own projects to build a suite of opportunities that are different,” he explains. “Each program must live or die on its own merits rather than be unified by a single hypothesis.” The importance of the strategy is borne out by looking back to what he and analysts thought were its most valuable assets in the early 90s. “They didn’t turn out to be so,” says Pops, “while some of the projects we didn’t rate so highly surprised us.”

The second rule is a relentless pursuit of improvements to the programs. “You have to be as clever as you possibly can, in terms of learning, understanding and reducing risk,” Pops says. “As boring as that sounds, there are all kinds of ways to accelerate decision points, learn more earlier, enrich data sets sooner and take a less conventional approach to development.”

This extremely active management of the business is a Pops hallmark. “I met Rich when I was developing a small company that used microspheres for drug delivery,” says Bob Langer, professor at MIT and founder of a multitude of biotechnology companies. “Our downstairs neighbor was Alkermes, and they were trying to deliver drugs across the blood-brain barrier. We talked about a merger, which actually did happen. When we looked at the technology we thought that it wasn’t that good, but we thought Rich Pops was fantastic.”

In contrast to the many biotechnology companies founded on a certain scientific principle or single drug candidate, Pops never gave his charges the luxury of believing that any one thing they were working on in the early days would take off. “In a lot of companies, most of the work is focused on getting a single product that works. If it does, things are wonderful; if it doesn’t, they aren’t,” he says. “Instead, we partnered extensively, we financed and made acquisitions, and we developed internally; we gave ourselves multiple ways to be successful and relied on the power of the portfolio to get us to the next level of development.”

The recent acquisition of Elan Drug Technologies (EDT), a $1 billion deal that included redomiciling the company in Ireland, has been textbook: Pops active, engaged leadership to build the business. Alkermes has made a series of acquisitions over the years, including Erytech—Bob Langer’s company—in 1992, Medisorb in 1996, and AIR [Advanced Inhalation Research] in 1999, but EDT was special. “What’s fascinating about the EDT transaction,” Pops enthuses, “is that, despite its scale relative to our company, it was a low-risk undertaking. We understood it so well, we had both a qualitative and quantitative sense of how the deal would transform our business.”

The merger had its origins in a one-off meeting between Pops and Elan CEO Kelly Martin in 2011, set up by a mutual friend who knew both businesses well. With a clear logic for the seller—who felt that he would not get the

On Living Life

Pops: I think of myself as having a pretty balanced life. When you do what I do, though, you never stop working. That doesn’t mean sitting front of a computer in the office, but when I am on a run with my 18-year-old son, or playing tennis or on vacation I am letting things run in the background. Sometimes the solution to some problem will arise after days and days. My philosophy of life is determined optimism. I am always able to turn adversity into opportunity.

McGuire: I take great pleasure in working with remarkable individuals. It's a joy to be able to have a business that is growing and in the life science business. It's a joy to be able to work with interesting people.
full value for EDT when it was sitting inside a business that had one major biologic on the market and a second drug, for Alzheimer's disease, in trials—and a clear logic for the buyer—in the complementarity between the science and commercial products of the two companies—negotiation of the appropriate terms was all that was required.

**BIOTECHNOLOGY’S REPRESENTATIVE**

Pops is as active outside Alkermes as he is inside. He sits on the boards of several biotechnology companies, of the Pharmaceutical Research and Manufacturers of America (PhRMA) and of BIO, whose president-elect he was in 2003–2004. According to BIO president and CEO Jim Greenwood, Pops often puts in the long hours to develop BIO’s policy positions. And he is a terrific communicator, as impressive under quietly intimidating cross-examination in a Congressional hearing as he is calm in the in-your-face interrogations of television’s Mad Money.

"I don’t spend a lot of time looking backwards. I look ahead, through a prism of optimism."

—Richard Pops

Why does PDUFA [Prescription Drug User Fee Act] V matter to them? Can you think of anything more arcane than the concept of user fees for new drug applications?

A TYPICAL DAY

**McGuire:** Almost every day includes some level of activity with companies we invest in, whether it is going to a board meeting, or interviewing a VP-level candidate. I may also meet with the partners in my company, talking about their investments, sharing where my companies stand and looking at all new investment opportunities. Then there’s time spent representing Polaris and talking about the industry generally.

**Hood:** I talked once with a fellow who ran a global problem-solving company. His experts came from two places: big city environments where everyone competes, and small places where an experience fusion of independent intellectuals; and very small places where there is a strong sense of self-reliance. I grew up in Montana. By the time I was six and seven, I used to go hiking alone in the surrounding mountains. My mother was all for us being independent and doing things on your own. When I left Montana I had the strong feeling that I could do anything I wanted to do, and that is an important attitude to have if you want to change the world.

**DO YOU USE TWITTER?**

Pops: I do (@popsalks). It’s an important means of communication although I am mindful of the legal constraints. For example, I never tweet about a product of ours. If there’s an exciting publication that’s germane to topics that we are interested in, I’ll tweet the links to that.

**McGuire:** Helping develop the now-standard model for academic–entrepreneur relationships is something I’m proud of. It’s an active partnership that builds over many years, even decades, sometimes that wasn’t common when I started. It’s something that we have honed and gotten really good at, and it’s spawned a number of really wonderful companies.

Pops: I am not ready to say that yet, I think of it as a work in progress. What I have enjoyed most is the creative process of assembling the disparate assets and scientific talents to create a whole that is substantially more interesting than any of its parts. It’s inherently a creative process.

**AHEAD, WITH OPTIMISM**

Richard Pops is as enthusiastic about his job today as he was in 1991. “There is something incredibly motivating about going to work every day with a group of people attracted there because they know that they are doing good things.”

His approach has changed little over the years. “I don’t spend a lot of time looking backwards,” he says. “I look ahead, through a prism of optimism.” He also remains “incredibly hands-on” and trusting of his own instincts. “The most important thing is that the person at the top is decisive,” he explains, “and you have to be comfortable making decisions on limited information.” Accumulated experience helps with this. “With experience, pattern recognition comes into play and you can begin to see things.”

For Pops, even after 21 years, Alkermes is a work in progress. “The job is still seductive because it is really hard to do well,” he says. “If you are successful you are making an enormous contribution and also have the satisfaction of achieving something that’s difficult to do.”

**What’s the most exciting aspects of your career were, on the biology side, solving the fundamental mysteries of antibody diversity—for which I received the Lasker Prize—and, on the technical side, the development of the automated DNA sequencer. Being able to read and write the source code of life with sequencing and synthesis was intellectually and emotionally really exciting.**

McGuire: As Pops says, “There’s an old adage: ‘The world is run by a few people’ and that work according to Pops. “Disease really resonates,” he says. “Everybody has people in their families—or they themselves—who are suffering from something. It’s an enormous influence on policy. Who shapes the views of policy makers?”

**Hood:** Yes, with help. I am a recent convert to Twitter (@csilbeleehood). It seems like a great way to get the message out but I am skeptical of the signal-to-noise in social media. Some people put an enormous amount of time into it and get not very much out.

McGuire: I should but I don’t. My tech partners look on me as a Lud-dite. Someday I’ll get there.
Terry McGuire: The Adventure Capitalist

On returning to the United States, he gained a master’s degree from the Thayer School of Engineering at Dartmouth College, where he now chairs the board of overseers, and an MBA at Harvard Business School. His first taste of the venture-capital business came at Golder Thoma Cressy in Chicago. “I was one of the fortunate few. Only six or seven out of a class of 800 MBA graduates got positions in the venture-capital industry,” he recalls. Incredibly, his Gaeltacht experience played a part. “Out of the blue, the interviewer asked in Irish if it was cold outside. I said, ‘No, it wasn’t cold, but it was wet.’ From there, we hit it off and I ended up getting an offer. Given all my education, the key part of it was learning a little bit of Irish!”

To utilize his engineering background, McGuire found himself looking at late-stage investments, which was not his predilection. So, when a position offering the opportunity to get involved in early-stage companies arose at Boston firm Burr, Egan, Deleage & Co. in 1988, he jumped at it. “Burr, Egan had a diversified approach, including biotech,” McGuire says. “At that point we were all generalists, we did a bit of everything.” But in the early 1990s, specialization became more pronounced and, while the company’s San Francisco office had expertise in biotechnology and medical technology, there was no one in Boston concentrating on it. McGuire raised his hand. “They gave me a shot, and my very first biotech investment was in Cubist Pharmaceuticals, which is now public and trading at a $2.6 billion market cap,” he grins. “I got into the biotechnology business without any formal schooling in medicine or biology, or even in chemistry, but I was trained as an engineer and generalist, and we pick things up.”

As McGuire immersed himself in biotechnology, he also developed his characteristic approach that has made him the most loved of venture capitalists, which is to build long-term partnerships with leading entrepreneurs. “A lot of entrepreneurs and venture capitalists look upon the relationship as a transaction: A wants to buy money from B; B wants to buy stock from A. My inclination was to look deeper than that.”

The first and most fruitful of a series of partnerships was with Massachusetts Institute of Technology professor Bob Langer. Together, Langer’s lab and McGuire and partners have launched 18 companies over two decades. “By the time we met, Bob was already a legend, an incredibly prolific inventor, researcher and entrepreneur,” McGuire explains. “A friend was starting a company with Bob and invited me to take a look at it. We met and got on well. I’m from Buffalo, Bob’s from Albany, and there was Upstate New York easiness about us. I was excited about what he was doing with the company, and it went from there.”

Langer states simply that the two see eye to eye. “He treated me like a generalist,” McGuire says. “I set out to excel at what I see as my one strength, which is very different from other forms of investment, and succeeded. “Though just a tiny fraction of the capital markets, venture capital has a true impact on the economy,” he points out. “For example, 20 percent of U.S. GDP is generated by companies that received venture capital to get started and they employ one in 10 people in the private sector.”

He also conceived of, and convened, the first global venture-capital congress. “We shared ideas on how to support innovation and how to support one another in different regulatory and legislative environments,” McGuire explains. “Ten years ago, venture capital was a few pockets. Now, every major economy has recognized the importance of innovation, and the importance of venture capital to that. If you go to one of these meetings and talk to the Chinese, Indians and Brazilians, it’s red-hot growth.” Not surprisingly, the congress has become an annual event. “In all respects, we are on a frontier,” McGuire says, “and you have to be prepared for a constant evolution. The approach that worked five years ago probably won’t work today. And I don’t want to it. I want to be enveloped in innovation.”

“Terry is one of the fairest people I’ve ever met. He’s direct, honest and doesn’t play games....” —Bob Langer

VENTURING BEYOND

McGuire is an important figure in U.S. and international venture capital circles. He served as chairman of the National Venture Capital Association in 2009–2010, during which time, he says, “There was a huge push for regulation of the venture-capital business, as fallout from the financial crisis.” But he notes that “the key players have been very accommodating, and strategic.”

McGuire and his partners have launched over 80 companies. What’s more, his presence is most noticed in the Irish diaspora. “Terry has been a major source of support for me,” says Irish entrepreneur and biotech innovator Steve Arlow. “He’s always been in touch. We talk at least once a month.”

The cognition of McGuire’s work is that he’s the type of guy who always takes a personal interest in his portfolio companies and their founders. McGuire’s approach is irrefutably humanitarian in nature and as such, it’s the exact opposite of the cold, clinical, commercial investment philosophy that has come to define so much of the venture-capital industry. McGuire’s approach of patience is now being chosen by more and more investors who understand the value of investing in longer terms, as opposed to just trying to achieve a quick profit. This is a significant shift in the industry, one that McGuire is proud to be a part of.
Brazil is a home of 13 percent to 18 percent of the species on the planet according to recent studies.

The Research Partnership for Technological Innovation Program, PITE, supports joint university-industry research, with companies from Brazil and from overseas. The Innovative Research in Small Businesses Program, PIPER, supports research in small businesses, focused on science and technology problems, which have a high potential for commercial or social return.

The Research Innovation and Dissemination Centers (RIDCs) also include research geared to innovation among their activities. These multidisciplinary centers produce scientific knowledge in areas such as cell therapy, human genome, molecular biotechnology, cancer research and treatment, applied toxicology, sleep disturbance, optics and photonics, atomic and molecular physics, ceramic materials, violence and studies of metropolitan areas. Each RIDC promotes the application of its research results via partnerships with industry and/or with public institutions.

The protection of intellectual property is supported by the National Institute for Patenting and Licensing Technology (Nuplante). This is also a way to create a strategic base for university-industry partnerships and encourage technology transfer.

RENEWABLE ENERGY

The FAPESP Program for Research on Bioenergy, BIOEN (http://bioenfapesp.org) integrates comprehensive studies on sugarcane and other plants that can be used as biofuel sources. Research includes biofuels production from biomass and its impacts, ethanol industrial and bio-refineries technologies and ethanol applications for motor vehicles.
Beyond confidentiality, intellectual property (IP) also raises questions in open-innovation environments. Even though members of the Idea-Connection team develop the solutions, the clients keep the IP. To make that possible, Wurtele explains, “We can screen out applicants who may not be able to transfer the IP. For instance, people working at certain universities may be restricted from IP transfer.”

In many ways, IdeaConnection creates a triple-win situation—for the client, for IdeaConnection and for the members of the solution team. One team member, Harry Jacob, a biotechnologist from India, was awarded $11,000 for his contribution to a solution costing $11,000 for his contribution to a solution, and he also has to be paid for success—and only pays if the results from the solution team meet those criteria.

Best of all, everything remains confidential. IdeaConnection’s solution team doesn’t even know whom it is helping. “Because our hand-picked problem solvers are carefully screened beforehand and then form small teams of experts, we can give them much more information about our client’s problem than companies using crowd sourcing,” says Scott Wurtele, chief executive officer at IdeaConnection.

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THE FUTURE STRENGTH OF CUBA’S BIOPHARMACEUTICAL INDUSTRY DEPENDS ON EXPANDING INTERNATIONAL COOPERATION.

founded, including the Center for Genetic Engineering and Biotechnology (CIGB), the Immunoassay Center, the Center of Molecular Immunology (CIM) and the Government Center for Quality Control of Medicines (CECMED). These institutions became the foundation of Cuba’s “Scientific Pole,” which is the biopharmaceutical cluster west of Havana that comprises 24 research institutions, 58 manufacturing facilities and employs over 7,000 scientists. Together these entities produce 385 of the 888 essential medications registered for domestic use, according to CIM director Agustín Lage. This includes a dozen vaccines, genetic antiretrovirals for people with AIDS and over 40 biopharmaceuticals. Cuba’s Scientific Pole also developed many innovative products, including a vaccine against type-B bacterial meningococcal disease, a synthetic antigen vaccine against Haemophilus influenzae type b (the first in the world) and Nimotuzumab, an anti-tumor epidermal growth factor receptor.

Several factors drive Cuba’s success in the pharmaceutical industry. Most important, the government keeps investing in the development of science and technology, including $567 million in 2010, up from $338 million in 2005. Structurally, Cuban biotech functions according to a “closed loop” model that groups research, development, manufacturing, marketing and distribution interests under one roof, thereby encouraging collaboration.

Locally produced biopharmaceuticals supply 80 percent of domestic needs and the sector is now the country’s second largest export earner after nickel. Moreover, Cuba’s exports of biopharmaceutical products increased fivefold between 1995 and 2010. The future strength of Cuba’s biopharmaceutical industry depends on expanding international cooperation. Strategic alliances with Brazil, and importantly, China and India—the source of 44 percent of Cuba’s raw materials for biopharmaceutical products—enhance the health of Cuba’s biotech sector, along with its diversification of market share through the development of biomedical information and software, diagnostic screening systems and nano- and neurotechnologies. Indeed, island biotechnology economies must evolve and adapt to survive.

CuBa’s burgeoning biopharmaceutical sector helps keep the island economy afloat

IN THE 1950S, U.S. PHARMACEUTICAL GIANTS, including Abbott Laboratories and Bristol-Myers Squibb, manufactured basic analgesics and various vaccines in Cuba. When the revolutionary government came to power in 1959, these labs, along with nearly all other private holdings, were nationalized, sending U.S.-Cuba relations into a downward spiral marked by a comprehensive economic embargo. Still in place today, these sanctions effectively prevent the island from acquiring U.S.-sourced medications, vaccines and the raw materials to domestically produce them.

The severing of ties between the two countries throt-tled Cuba’s universal health system, which guarantees care and treatment for its 11 million citizens. In response, Cuba turned to Eastern Bloc allies, Finland and others for scientific training with the goal of establishing a biopharma-ceutical industry.

In 1981, the island’s first biotechnology research and manufacturing center was founded and began producing alpha interferon, followed by recombinant proteins. Building on this success, several scientific institutions were

BIOTEC: THE MAGIC PILL?

FRENCH BRED

Biotech thrives in a science park outside Paris

BY PAUL McNALLY

BIOTEC, A SANOFI-OWNED biotechnology park in a modest Parisian suburb, is known as the go-to destination for life science firms in France. Home to nearly 30 companies, it is a vibrant community that nurtures the ambitious growth plans of its tenants whether small or large, new or established.

Launched in 2003, the 20-acre park provides a flexible R&D facility that can be scaled according to tenants’ changing circumstances. Biosci-tech president Jean-François Boussard likens it to an ecosystem. “I use the symbol of a pond,” he says. “We’re in a closed space. You need to keep a good temperature, level of sunlight, areas of shade for some. There are smaller organisms that are eaten by the big ones. Each organism in the pond is autonomous, but works alongside the others.”

Bioscitech seeks to attract businesses as early as possible in their development. One of the newest arrivals, bioinformatics specialist Helios Biosciences, employs just four people. Boussard believes the park acts as a “safe harbor,” where investors and suppliers can trust its tenants and know that they must be serious about doing business because they are based there. “This type of place allows firms to develop more rapidly,” he says. “Businesses are here because they have ambition, they have turned towards the market and investors should take note.”

However, encouraging companies to stay on the campus once they reach maturity, or after a bigger firm acquires them, is one of Bioscitech’s biggest challenges. In 2010, for example, when AstraZeneca bought NovoLog for $500 million, it Red Boussard says, “We need to manage a paradox: The success of the resident companies is sometimes a failure for Bioscitech.”

Despite these challenges, Bioscitech has plans for its own expansion. Support from the French state investment fund Caisse des Dépôts will allow work to get underway to extend the park—potentially doubling its rentable space in 10 years. But Boussard is cautious about growing too fast. “We need to monitor what happens,” he says. “The park has the ability to grow, but we’re not seeing a phase of significant growth [in the wider industry].”

Indeed, in Bioscitech’s 2011 survey, residents reported a 15 percent year-on-year decline in revenue. Most companies shared a pessimistic view of 2012, which they believe will be no better than 2011 in terms of raising funds either through winning contracts or equity. “Biotech as a sector is hard-going,” says Bous-sard. “It’s always been hard, so it can be either a bit less difficult, or a bit more. It’s not like Internet phenomena with very fast life cycles and big peaks and troughs.” Nevertheless, many companies want to move to Bioscitech. As Bous-sard says, “The principle is that the more companies we have in the same place, the better their visibility!”
GERMAN BREW
A convergence of research, industry and digital know-how makes the Berlin-Brandenburg region a center for biotech innovation
BY ULRICH HOTTELET

Usuallu, you first get a product and afterwards you look for a problem that it solves,” says Christian Regenbretg, head of the tumor cell stem cells working group at the pathology institute of the Charité university hospital in Berlin. “Fortunately, with the HANA Oncolyzer it is the other way round,” says Felix M’mboyi, executive director of the African Biotechnology Foundation, adds that 800 million Africans are determined to harness the power of GM technology to fight hunger.

However, much of Kenya’s success is the result of a group effort with other African countries determined to harness its climate and provide an ample harvest for its people.

“AFrica as a continent is facing one singular challenge that [others] ... are not facing, and that is food security,” says Felix M’mboyi, executive director of the African Biotechnology Stakeholders Forum. He adds that 800 million Africans aren’t always sure of where they’ll get their next meal. So African countries are uniting. As M’mboyi asks: “Is it not better to consume biotech food, than to starve to death?”

Kenya’s 40 million people, crowded into 224,000 square miles, face recurring drought, rainy season flooding, soil erosion and poor water quality due to water pollution. It’s a little wonder then that 90 percent of GM research in Africa focuses on agriculture, including maize, sorghum, cassava and bananas. For example, M’mboyi says that confined field trials to test drought-tolerant maize are happening in five countries, including Kenya. Three groups are running these trials, including the Kenya Agricultural Research Institute (KARI), which is also researching how to bio-fortify sorghum, a mainstay crop in East Africa, with vitamin E. M’mboyi points out the severe deficiency of this vitamin among Kenya children, and he adds that sorghum “is cheap and easy to grow.”

Other crops will also provide more food for Kenyans. Francis Nang’ayo, of the African Agriculture Technology Foundation, says that Striga-resistant maize is ready for the fields. Forty tons of the weed-resistant seed will be given to farmers this planting season. If things go as planned, the seed will produce an extra 375,000 tons of maize, so 34 million people can be fed. Likewise, drought-tolerant maize trials are ongoing. Nang’ayo says. Two are completed and show promising results. Two more should be completed soon. These trials are happening in numerous countries, including Kenya, supported by a grant from the Bill & Melinda Gates Foundation.

SEEDS OF HOPE
Like her neighbors, Kenya looks to GM crops for food security
BY CHRISTINE BAWL

LAST YEAR, KENYA ADOPTED the necessary legislative and regulatory framework to produce and import genetically modified (GM) crops. Since then, the country has made steady progress toward developing and refining robust varieties that will withstand the harsh conditions of its climate and provide an ample harvest for its people. However, much of Kenya’s success is the result of a group effort with other African countries determined to harness the power of GM technology to fight hunger.

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HOME TO FIVE UNIVERSITIES, 20 RESEARCH INSTITUTES AND 30 PHARMACEUTICAL COMPANIES, THE BERLIN-BRANDENBURG REGION IS A BREEDING GROUND NOT ONLY FOR NEW THERAPIES, BUT ALSO FOR HEALTHCARE-RELATED IT SOLUTIONS.

GM crops will not be an “instant solution” for Kenyan farmers, M’mbiyo says, but “scientists are telling us it will improve productivity to a certain level.” In Kenya, he says, GM technology can help with insect pests, like the maize stalk borer, which destroys 35 percent of that crop. Miriam Kenya, chair of the National Biosafety Authority board, echoes his measured optimism. “The promise of biotech is yet to be established in Kenya, and Africa as a whole,” she says. “What is expected is that the cost of production should go down due to pest resistance.”
**DESSERT BLOOM**

Qatar harnesses biotechnology to bring life to its harsh landscape  
**BY VICTORIA SCOTT**

The Qatari desert is a truly desolate place. Aside from the urban sprawl of the country’s capital, Doha, most of this tiny peninsula’s land is barren desert, with plant life making only a fleeting appearance after rare winter rainfall. Nonetheless, Masood Al-Marri, director of Qatar’s Biotechnol-

ogy Center, recently announced that Qatar is aiming to be the region’s greenest country within five years. Given the searing heat of the emirate’s summers, where temperatures often reach 120 degrees Fahrenheit, that plan sounds extremely ambitious.

Although Qatar generates the world’s highest per capita GDP, driven by its enormous oil and gas reserves, its farmers only produce around 10 percent of the food that the country needs. Consequently, food security represents a crucial issue, and Qatar’s Biotechnology Center thinks that it might have an answer. In a three-year project run in conjunction with ABBA, a Qatar-based biotechnology company, the Biotechnology Center provided a 50-square-meter area of sabkhas, or salt flats, on Qatar’s west coast. “The land there has a salinity that is twice sea water,” says Al-Marri. “We gave them the worst land, to test the efficiency of their technique.” ABBA’s method uses mycorrhizal fungi that colonize a plant’s roots to give it more access to nutrients in the soil. “It acts as an extension for the roots, which means the plants need less water,” says Al-Marri. “And no fertilizer is used, so the whole project is organic.” The site is irrigated with treated sewage from the nearby town of Dukhan. The project returned startling results: before and after pictures show a desert transformed into an oasis of green. Fruit and vegetable plants are heavily laden. Al-Marri holds up a juicy corn on the cob that’s sitting on his desk. “This comes from the project,” he tells me with a smile. “We have only one concern, and that’s about the plants possibly absorbing heavy metals from the soil,” says AI. “So, we just sent samples away for testing. But if there is con-


tamination, we can see if changing the source of treated water helps, as the Dukhan area is very industrial. And even if the plants are absorbing heavy metals, this means they’re cleaning the underground water sup-

ply, which is also a good thing.”

In addition, the Qatari government hopes that greening the desert will create a carbon sink. “Qatar is an oil producer, so it would be great if we could capture some of the CO2 we produce,” Al-Marri explains. “There’s also evidence that greening could change the local micro-climate. And of course, it will make the country more beautiful,” he says, adding, “We all feel better when we see green.”

**PARTNERS IN PROGRESS**

India and Russia build a network to cultivate new biotech connections  
**BY SHAILAJA MEELAKANTAN**

**RECOGNIZING THAT COLLABORATION rather than competition offers a cost-effective way forward in biotechnology, India and Russia will soon unveil the Russia-India Biotech Network (RIBN). This Internet-based portal is being jointly developed by the Russia Biotechnology Society and the Federation of Asian Biotech Associations (FABA). Upon comple-

tion, the portal will have cost about $650,000—but the two nations are hoping that it will generate millions of dollars in cooperative ventures. RIBN aims to nurture a range of collaborations, including joint aca-

demic programs and collaborative re-

search projects. Currently, only about 15 Indian biogenetics manufacturers operate in Russia, but the network is designed to spur increases in that number. Furthermore, Russia hopes its companies will grow with the help of technology transferred from India. “India is a couple of decades ahead of Russia [in biotech research and man-

ufacturing] because Russia was mostly importing drugs instead of in-house manufacturing,” says Shakti Nagap-

pan, executive secretary of FABA. Now,

Indian technology in bioinformatics, vaccines and nanobiotechnologies. Both governments see huge potential in innovations in biotechnology, a fact that should ease technology transfer. The online portal will be sup-

ported by two physical offices that will enroll partners into the RIBN subsystem. Once in the system, In-

dian and Russian companies can surf through the portal and short-list po-

tential collaborators or partners. “That is the first level of search, which nor-

mally would take months, but using the portal, it will not just be quick, it will also be reli-

able,” says Nagapan. He adds that once companies have zeroed in on potential collaborators, they can ini-

tiate contact through the portal, and will also be able to conduct online presentations through two-party or multi-party conferences. The preliminary online portal sys-

tem is being developed using Indian expertise, and FABA is in final negotia-

tions with pharmAB, a German com-

pany, for their proprietary technology. In the first year Nagapan and Vasilov expect 100 companies from each na-

tion to join the network, with a 20–30 percent growth in those numbers each year. From India, a chunk of the first 100 companies will be large biopharma companies looking for outlets in Russia to increase sales, says Nagapan, but the network is expected to benefit small and medium enterprises the most.

“Biotech cannot be developed just by governments or scientists or business people,” says Vasilov. “Bringing together enterprises, tech-


tologies and countries is necessary. That is the exact reason why such a network will help.”

**THAILAND**

Thailand’s National Center for Genetic Engineering and Biotechnology (BIOTEC). The initiative includes full internship scholarships for Thai sci-

entists at Novartis laboratories in Eu-

rope, the sharing of Novartis expertise to accelerate a wide range of projects at BIOTEC laboratories in Bangkok and throughout Thailand, and bio-

prospecting for potentially medically useful microorganisms across Thai-

land’s vast array of forest, rural, urban and fresh- salt water ecosystems. “The partnership with Novartis shows us that our work is up to the international level,” says Kantawim Kirtikara, BIOTEC’s U.S.-educated executive director. “Novartis realizes that we have the knowledge and expe-

rience in finding and identifying po-

tentially useful microorganisms and

natural compounds.” Kirtikara notes that BIOTEC has maintained an ex-

tensive collection of microorganisms for more than 20 years—cultures gathered, in her words, “from the forest, the soil, the beach, the mangroves and the sea.” She adds, “We have to be creative. We look at lichens on the...
A SIGNIFICANT ADVANCE in gene-based therapies—gene therapy 2.0, if you will—could be just over the horizon at Tocagen, in San Diego, testing a novel strategy for treating brain cancer that relies on a sophisticated process of inserting genes and using their products—proteins—to orchestrate a precise, life-saving attack on disease.

Tocagen’s current trial involves patients with glioblastoma multiforme (GBM), a highly aggressive, incurable form of brain cancer that carries a grim prognosis. Even with surgery, radiation and chemotherapy, the average person diagnosed with GBM survives only about 14.6 months, with less than five percent of patients living beyond five years. The company hopes to dramatically improve that prognosis by delivering a retrovirus—called Toca 511—directly into the tumor. Toca 511 selectively infects cells that are dividing and those with defective immunity, which allows it to target cancer cells. After this infiltration, it hijacks the cellular machinery to replicate and spread, all while using the tumor to evade the body’s immune clearance. Toca 511

"...A DELIVERY SYSTEM, OR A GUIDED MISSILE TO DELIVER THE GENE OF INTEREST TO KILL THE CANCER CELLS FROM WITHIN.”

—HARRY GRUBER

transfects the cancer cells with a gene that sparks production of a protein called cytosine deaminase (CD). Several weeks after introducing Toca 511, repeated oral doses of Toca FC, an extended release form of the antifungal drug, FC (flucytosine), begin. Within cancer cells carrying the retrovirus, FC reacts with the CD protein to create a well-known, powerful and short-lived anti-cancer drug, 5-FU (5-fluorouracil). Since 5-FU only kills cancer cells when they are dividing, patients continue cyclical FC treatment for six months or more to attack newly active regions within the tumor. Harry Gruber, Tocagen’s chief executive officer, describes Toca 511 as “a delivery system, or a guided missile to deliver the gene of interest to kill the cancer cells from within.”

In the early 1980s, Tocagen co-founders Gruber at Jilly’s chief, now executive vice president, research and pharmaceutical development—were researching new treatments for genetic diseases at the University of California, San Diego. Gruber and Jilly later brought back the technol-

gy, launching Tocagen in 2007. Early testing in mice with brain tumors showed that Toca 511 spread throughout the tumor without affecting surrounding healthy tissue, and tumors were eradicated with high FC doses. Eighty percent of the mice sur-
vived to the end of the six-month study, while all untreated animals died in about a month. The phase I clinical trial of Toca 511 in humans is ongoing. If this attempt at gene therapy 2.0 proves successful, Tocagen hopes to aim its ground-breaking treatment at advanced breast, colorectal and prostate cancers.

Resources in Thailand also en-
hance this collaboration. “Expertise in taxonomy and isolation of Acti-
nomycetes, a class of bacteria known to produce relevant compounds for drug development, acquired during the partnership also have enabled BIOTEC to accumulate 6,000 more strains over the past six years,” Abela reports. “These strains are assets of Thailand and are now maintained at the BIOTEC Culture Collection, making them available for other re-

search programs in Thailand, outside the BIOTEC-Novartis scope.” The next stage of the joint venture will screen strains of microbes for anti-

parasitic activity.

No new medicines have yet been produced as a result of the first phase of the BIOTEC-Novartis collaboration, but as Abela says: “New medicines do not appear overnight. The interface of the chemical, biological and pharma-
cological universes is highly complex.” Nonetheless, says Kirtikara, “We are quite realistic that the major ben-
et that BIOTEC will get out of this partnership is not financial. It is the training of our people.”

GENE THERAPY 2.0

San Diego-based Tocagen aims a protein at brain cancer

BY SHARON GUYNUP

Southern Europe’s biggest biotechnology event will showcase the sector’s solutions to society’s greatest challenges: healthcare, food, sustainable development and energy supply

BioSpain 2012, one of Europe’s leading biotechnology events, to be held in Bilbao

www.biospain2012.org

BIOSPAIN 2012, ONE OF EUROPE’S LEADING BIOTECHNOLOGY EVENTS, TO BE HELD IN BILBAO

Northern Europe’s biggest biotechnology event will showcase the sector’s solutions to society’s greatest challenges: healthcare, food, sustainable development and energy supply

“a delivery system, or a guided missile to deliver the gene of interest to kill the cancer cells from within.”

The main countries represented at BioSpain 2010 in terms of the number of companies, were Spain (77 percent), France (5 percent), the United Kingdom (3.5 percent), the United States (3 percent) and Germany (2 percent). A total of 25 countries were represented at the event.

According to data from BioSpain 2010, the program of break-out sessions, which is currently under development, will again cover a wide range of topics, focusing on EU challenges for 2020: healthcare and ageing, food, climate change and energy supply. BioSpain has become the foremost event for the sector in southern Europe and its partnering process is ranked 7th in the world in terms of the number of meetings (2,247) and participating companies (441). The main countries represented at BioSpain 2010 in terms of the number of companies, were Spain (77 percent), France (5 percent), the United Kingdom (3.5 percent), the United States (3 percent) and Germany (2 percent). A total of 25 countries were represented at the event.

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BioSpain 2012 will be held at the Bilbao Exhibition Centre, in Barakaldo, is a forum for biotechnology professionals to share expertise, ideas and experiences and has become a major platform for presenting Spain’s biotech sector to the rest of the world.

BioSpain includes a trade exhibition, a partnering event, an investment forum, keynote speeches and break-out sessions on a range of topics with speakers from Spain and other countries, the BIOTEC 2012 scientific congress (organised by the Spanish Society of Biotechnology, SE-Biot), and a career fair.

Since BioSpain’s first edition in 2003, it has become the leading event for Spain’s biotechnology sector and one of the industry’s largest events in Europe, with over 1,300 delegates (15 percent from other countries) from 750 com-

panies (20 percent foreign) and more than 180 exhibitors

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www.biospain2012.org
Queensland’s successful Smart State Strategy has seen the establishment of some of the southern hemisphere’s most substantial research facilities and institutes (66 institutes) and the creation of some 18,000 research-related roles. This has been succeeded by The Queensland R&D Investment Strategy 2020–2020 with the aim to ensure that the investment in R&D will provide a strong, green and innovative economy that is attractive to international investors and collaborators.

Having received strong political bipartisan support, this ongoing strategic positioning has seen the establishment and support of a number of exciting and important initiatives including some as diverse as:

- Therapeutic Innovation Australia (TIA)
  - Queensland Node,
  - Translational Research Institute (TRI)
  - The Eskitis Institute at Griffith University
  - Institute for Health and Biomedical Innovation at Queensland University of Technology (QUT)
  - Wound healing innovation – VitroGro® (QUT and Tissue Therapies)
  - A biofuels pilot facility in Mackay – in Regional Queensland’s sugarcane industry (QUT)
  - Groundbreaking malaria research
  - Pain killers being developed from shellfish found on The Great Barrier Reef
  - Gates Foundation’s interest in the biofortification of bananas for sub-Saharan Africa (QUT)
  - A new medical device for vaccine delivery using a nanopatch/microneedle technology that will revolutionize the way that vaccines are distributed and provided across the world.

Queensland: TURNING SUNSHINE INTO SMART!

Blessed with abundant sunshine and the natural beauty and resources that come with that, it was hardly surprising that—with the blue waters of the Pacific Ocean, the vibrant colored corals of The Great Barrier Reef, the lush green Tropical Rainforests, the red earth of The Outback and the fine golden sands of our beaches—we earned a name as the Sunshine State of Australia. It was where one would go to relax and enjoy all that was good about Australia.

More surprising was the plan in the late 1990’s to take these natural blessings and do more with them. It was a plan to turn Queensland into the Smart State of Australia. Many thought that the members of the then government may have stayed in the sun for too long, and that a knowledge-based economy was an unachievable goal for Queensland.

The sunshine plus our geographic location in South East Asia meant that the economic powerhouses China and India—as well as other regional leaders, including Japan, South Korea and Taiwan—were our biggest trading partners. Their appetites for our resources seemed insatiable, and our economy just continued to grow.

Why would the government think we needed to diversify our economy? They realized that unless innovation was encouraged and became a core part of our activities and a knowledge-based industry developed, we would fail to adapt and meet the demands of a changing world.

None have been more successful than the State of Queensland at realizing that challenge and seizing the opportunity to do something about it. For well over a decade, the State Government has invested heavily to develop the physical infrastructure needed to attract world-class individuals to practice their craft and explore and develop their ideas.

As well as the substantial innovative work they have undertaken, these world-class researchers who now call Queensland home have helped establish links and develop collaborations across the world in a way that has transformed Queensland into a leading and influential life sciences center in the region and recognized by the World Bank as a global innovation hot spot.

We find ourselves in the right place, at the right time. With the infrastructure, expertise, innovative output, systems, people and global networks that we have, we are well-placed to leverage the opportunity that will be generated by the continued growth of the Asian economies and the accelerating development of the Tropics (South East Asia, Latin America and Africa).

Research and business activities already underway in Queensland addressing tropical health, agriculture and environmental sciences will form the basis of significant opportunity in the tropics.

VITROGRO®

- Developed by Zee Upton from Queensland University of Technology’s (QUT) Institute of Health and Biomedical Innovation
- Being commercialized through Tissue Therapies Ltd—working with Cardiff University Wound Healing Clinic in multicentre trials that have shown 82 percent of patients’ wounds partially or completely healing in 12 weeks (These patients had previously suffered for an average of 36 months prior to the Vitro-Gro® trial.).
- Sufferers of chronic wounds (e.g., diabetics) may now be able to avoid amputations due to non-healing wounds.
- The formulation is cost effective and easy to apply directly to the wound.
- VitroGro® provides a ‘scaffold’ for cells to adhere to and migrate upon.
- Earlier Australian and Canadian trials showed that VitroGro® accelerated healing and reduced ulcer size and pain.
- Currently for many patients living with chronic non-healing ulcers, amputation has been the only option.
- The trial results position VitroGro® for approval and planned first sales in Europe in Q2 2012.
- www.tissuetherapies.com
- www.qut.edu.au
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THERAPEUTIC INNOVATION AUSTRALIA (TIA)
QUEENSLAND NODE:
• Consortium of five world class QLD centres in preclinical and clinical translational research.
• Awarded funds from Federal Government to create an entity to translate life science discoveries into products for commercialization.
• The entity facilitates and coordinates the accelerated movement of a discovery across the ‘valley of death’ to proof of concept—producing a ‘reduced risk product’ that is attractive for subsequent investors/commercialization.
• The five members that have the complementary specialist expertise and experience are:
  • UQ Centre for Integrated Preclinical Drug Development (CIPDD) – Tetrad, Australia’s premier provider of preclinical drug development capabilities and bioanalytical support for clinical trials—with data generated accepted by the FDA, EMA, and the Australian Regulator, TGA.
  • Griffith Health Institute (GHI) - Griffith University
    The Genomics Research Centre within GHI is an Australian centre of excellence for genetic diagnosis and gene analysis of common complex disorders. It has a significant population genomic repository with over 8,000 DNA samples to date including resources from the unique genetic isolate population of Norfolk Island. Studies using this isolate and others are directed towards identifying the genes involved in cardiovascular disease, migraine, multiple sclerosis and various types of cancer. Internationally recognized as a global leader in the genomics of migraines and the use of this genetic information for therapeutic and diagnostic outcomes.
  • University of Queensland Centre for Clinical Research – Centre for Clinical Diagnostics
    An academic clinical research organization that develops and clinically validates in Vitro Diagnostics within a GLP environment, providing regulator-ready data.
  • Queensland Clinical Trials & Biostatistics Centre – UQ School of Population Health
    Experts in clinical study design, protocol development, coordination, clinical database development and management, and biostatistics, as well as development, validation and rollout of software applications for clinical studies. Leading several active international collaborations including with: University of Oxford, Imperial College London, University of North Carolina, Amylin Pharmaceuticals Inc. USA, Peking University and Chinese Academy of Sciences. www.therapeuticinnovation.com.au/Research_and_Development/QLD.aspx
  • University of Queensland (UQ) Diamantina Institute
    Specializes in the translational aspects of cancer, arthritis, bone disorders and immune dysfunction research. Took the world’s first cervical cancer vaccine through commercialization to the clinic, and is currently developing a rheumatoid arthritis vaccine.
• Well positioned to take advantage of the stable legal and regulatory environment that Australia offers, and with an active and visible representative industry organization (Life Sciences Queensland Ltd - LSQ), Queensland’s fast-growing, highly skilled workforce makes it an ideal environment for a broad range of research-driven endeavors. The number of scientists and researchers working in Queensland per 1000 people is now greater than the OECD average, and has increased at a rate 1.6 times that of the United Kingdom and 1.8 times the rest of Australia. And while Australia’s economic growth has outpaced the OECD during the last generation, Queensland has outpaced Australia. Queensland’s long-term average growth rate over the past 20 years has been the highest in Australia. As we go to press, there has been a general election in Queensland, and there is a new government. This new government was elected with an overwhelming majority, and it had as a campaign platform the acknowledgement and support of an innovation and knowledge-based agenda, and the important role it plays in shaping Queensland’s future. So while Queensland is still the Sunshine State of Australia—and where all Australians love to come and enjoy their holidays—more than ever it is now also the Smart State of Australia, and increasingly where more and more individuals from across Australia and abroad, who work in the knowledge-intensive industries, now call home. Not only did we turn Sunshine into Smart, we’ve retained the sunshine. Now that is smart!
For further information on your next smart move, and on the life sciences opportunities in Queensland—and who may be best placed to assist your endeavors—please contact Mario Pennisi, CEO of Life Sciences Queensland Ltd on mpennisi@lsq.com.au or visit our website on www.lsq.com.au

ESKITS INSTITUTE
GRIFFITH UNIVERSITY:
• Established in 2003 investigates novel drug and cell-based therapies for human diseases including cancer, infectious diseases and neurological disease.
• Nature Bank – collection of over 200,000 optimized natural product fractions—derived from a diverse collection of over 45,000 samples of plants and marine invertebrates.
• NeuroBank – collection of well characterized human olfactory nerve sheath-derived (hONS) cells from nearly 200 neurology patients. NeuroBank represents excellent disease models of Parkinson’s Disease and Schizophrenia.
• Old Compound Library – Australia’s first and only robotic compound management facility. The pure compounds and natural product fractions comprise propriety and unique libraries available for high throughput screening.
• High Throughput Screening – includes four screening platforms and high throughput cellular imaging capability.
• Numerous industry and not-for-profit collaborations, including the Bill & Melinda Gates Foundation, AstraZeneca, Pfizer, Actelion, Creative Antibiotics, Medicines for Malaria Venture, Drugs for Neglected Diseases Initiative and the TB Alliance.
• Successful drug discovery based on structures using X-ray crystallography and NMR—underpinned by advances in cloning, expression and purification of proteins including those that have defied crystallization or solution structural studies.
• Use BioAffinity Mass Spectrometry to observe ligand-protein complex morphologies, which expands structural genomics efforts.
• www.nature-bank.com.au
• www.griffith.edu.au/eskits

These examples heralded, serve to highlight the opportunities that the Australian Regulatory environment provides and—coupled with the world class infrastructure and people—it is one where many international organizations have already come to undertake many aspects of their clinical and pre-clinical programs. Of particular note is the ability to commence trials in a matter of weeks—rather than months, due to an efficient—yet robust regulatory approval process. It is also noteworthy that it is not necessary to have an IND open in the USA in order to undertake this work in Australia. There have now been a number of instances where human data—derived from early phase trials undertaken in Australia—have been included in IND applications.
be economic rollercoaster ride of the past three years produced profound and complex impacts on the life science industry. Scarcity of venture capital, a dearth of initial public offerings, the 60 percent collapse of price-to-earnings ratios since 2008 and massive cash balances at most large biopharma firms reflect unprecedented uncertainty, and for good reasons. Underlying forces reshaping the global economy and the structural crisis within life sciences clearly indicate that we have entered uncharted territory.

Many hope that incremental gains in U.S. employment and Europe’s apparent ability to inch back from the brink of collapse offer signs that the world is returning to “normal.” However, structural evidence powerfully indicates that we are no more than half way through a period and a type of slow growth unprecedented in recent history. The prolonged balance-sheet downturn characterized by underutilized capacity, unemployment, slack demand and financial repression all contribute to low growth and imply a transition to something new. (For Monitor’s strategic analysis of the global macro transition and the challenges it presents to businesses, go to http://www.monitor.com/growth-in-a-low-growth-economy.)

Big biopharma has cut headcount in the United States and Europe while expanding in emerging markets, shuttered R&D facilities and sought to convert the resulting balance-sheet strength into future earnings growth via acquisitions. It remains unclear whether these decisions will provide the sought after boost to earnings growth—or the consequences of decision. Danger lies in the more common tendency to “choose” between small, inadequate incremental adjustments and radical departures from core competencies—precisely the alternatives most likely to lead to failure.

The prolonged balance-sheet downturn indicates that we are no more than half-way through a period and a type of slow growth unprecedented in recent history. Financial repression all contribute to low growth and im-

Consider the paradox of complexity and convergence emerging globally: entrepreneurial battling liver cancer in Chengdu has more in common with his counterpart in Chicago than his mid-

dle-class neighbor in China. Doing this profitably will re-

quire new channels of communication, difficult portfolio choices and fresh business models. Companies already struggling in their efforts to straddle diverse national markets, therapeutic areas and price points. As senior management is forced to make difficult “where to play” and “how to win” choices, it is essential these choices are framed as innovative and courageous al-

ternatives designed to de-risk these decisions. Danger lies in the more common tendency to “choose” between small, inadequate incremental adjustments and radical departures from core competencies—precisely the alternatives most likely to lead to failure.

In this new environment, five key questions can help frame better strategic choices:

- How to create real value? Demonstrating, communica-

ting and delivering value to patients, providers and payers will get tougher. In a resource-constrained environment, payers—whether government, private insurers or indi-

vidual patients—and those involved in treatment decisions (families and physicians) will set a high bar, demanding proof of superior health outcomes. Creating measurable value means greater focus on disease management and new metrics to replace narrowly defined clinical superiority. Adding complexity, these demands will be as diverse as the customer base. A European health economics story won’t carry much weight in China’s new single-payer system or India’s self-pay market with their vastly different treatment alternatives, hospital costs and economic context.

- How to build intensive competitive advantage? As “big data analytics” reshapes strategy across all busi-

ness sectors, the ability to ask the right questions, analyze and act on massive data streams becomes a key source of competitive advantage. No industry has greater potential to harness data to generate better outcomes and higher value than healthcare. Whether the goal is to improve clinical outcomes at point-of-care, merging clinical and genomic data to identify new pathways or segmenting the customer base, competitive healthcare solutions will de-

pend on rapidly digesting and acting on data-driven in-
sights with maximum impact.

- How to leverage emerging markets’ capital? Sover-

eign wealth funds, state-owned enterprises and a growing pool of emerging market-private capital are reshaping in-

vestment flows. Disillusioned with Organization for Eco-

nomic Co-operation and Development (OECD) bonds and portfolio managers, decision-makers in emerging markets will make nuanced choices driven by policy goals and cor-

porate objectives. They seek partnerships that bring tech-

nologies they can deploy to meet the needs of patients at home and in other emerging markets. Western firms that want emerging-market capital will need to adopt compat-

ible strategies and business models.

- How to protect and manage innovation? Governments around the world are now more open to

regulatory experimentation because of technological change as well as disillusionment with the United States and European Union as the de facto “lead regulator” for critical sectors. Despite agreement among the U.S. Food and Drug Administration (FDA), the National Institutes of Health and industry leaders that the U.S. system is too slow, too bureaucratic and unnecessarily inflates drug costs, Washington seems an improbable site for radical change. Other countries have the flexibility and the neces-

sity to pioneer new approaches. These will build on core principles embodied in the FDA and European Medicines Agency (EMA) systems, but downplay or discard elements that add unnecessarily to development costs or distract at-
tention from the priority of safety and efficacy.

- How to manage diffuse innovation? Ideas and in-

novation capacities are more equally distributed across humanity than ever before. Technology combined with moves toward “open” innovation systems has begun to un-

leash those capacities. Proliferation of early-stage research partnerships, growing emphasis on translational medi-
cine, programs such as the Broad Institute’s efforts to build multi-company research and data sharing all indicate the shift to a more collaborative model. Pressure to deliver measurable better health outcomes means the one-size-fits-all demarcation between healthcare “suppliers” and “provid-
ers” is rapidly blurring.

Overall, the growing importance of clinical data to de-

velopment, regulatory and economic decisions is changing the balance of power—much the same way that grocery store point-of-sale data led retailers to play a crucial role in consumer product-innovation partnerships.

The authors are senior members of Monitor, an international con-
sulting firm that works with the world’s leading corporations, gov-

ernments and social sector organizations to drive growth. For 25 years, Monitor has worked with clients in the healthcare and life sciences industries, employing rigorous strategic thinking to address critical issues and opportunities. The firm helps clients with pipeline productivity and commercial development, organizational capabili-
ties and effectiveness, customer experiences, commercial model and corporate strategy, market access, leadership development, opera-
tional effectiveness and innovation strategy.
The way we communicate today is vastly different from just a few decades ago. From simply getting across an idea to developing a symphony of thoughts and concepts, the available tools largely determine the extent that a message can cover. Like the forward lurches of evolution’s punctuated equilibrium, social media—a completely new and untested toolbox—has emerged in recent years to further jolt the world of communication.

As smartphones and online networking tools fire up social media, and the wildfire keeps spreading farther, the question is: How do biotechnology and pharmaceutical companies use these new tools? First, though, some still wonder if these companies use social media at all. An April 7, 2011, poll conducted online by Genetic Engineering & Biotechnology News asked: “How much do you use social media for your biotech research or business activities?” Among the respondents, 17.3 percent said significantly. Another roughly 60 percent claimed moderate or dabbling use of social media. Most surprisingly, nearly one-quarter of the people who responded claimed ‘no interest’ in social media. For those indifferent respondents, seemingly unaware of the communication revolution underway, it could be time to remember a fundamental principle of Darwinism: adapt or die.

**SOCIAL MEDIA FOR MARKETING MEDICINES**

Early this year, North Carolina–based research firm Cutting Edge Information (CEI) published *Pharmaceutical Digital Marketing and Social Media: Mastering Strategy, Managing Growth, and Mitigating Risk*, which states: “Digital channels are by all accounts the future of marketing.” In this publication, CEI defined social media as “interactive, digital online portals or applications in which users can create, share or otherwise curate content.” So this would include blogs, social-networking sites like LinkedIn, Facebook and Twitter, plus Flickr for images and YouTube for videos.

The data in this report strongly suggest that the “future” in which digital channels take over marketing is already here. As this report points out: “In 2011, for the first time, digital channels exceeded traditional channels as a percentage of the overall marketing mix in terms of channel use—digital channels combined for 54.7% and traditional media combined for 42.1%.” Nonetheless, this report also notes that the pharmaceutical industry lags behind other industries in terms of putting social media to work.

After surveying 31 pharmaceutical companies to develop this report, CEI found that only 56 percent of the pharmaceutical companies use social media for competitive intelligence and market research. On the other hand, CEI found that 82 percent of the pharmaceutical companies use one or more social-media tools in some way. Moreover, the replies from top-10 pharmaceutical companies—the ranking based on annual revenue—indicated using digital approaches for 27.6 percent of their marketing in 2009, and that figure climbed to 49.8 percent in 2011.

The selection of social-media channels will also impact how the pharmaceutical industry uses this technology. When CEI asked its respondents to rate the marketing potential of social-media channels, YouTube ranked at the top, followed in order by Facebook, blogs, Twitter and Google+. Biotechnology companies also appreciate the potential of video. On YouTube, you can find channels from many leaders in this field including Thousand Oaks, California–based Amgen; South San Francisco, California–based Genentech; Carlsbad, California–based Life Technologies; as well as U.K.-based GE Healthcare and Quagen in The Netherlands, just to name a few.

**TWEETING FOR TECHNOLOGY**

Biotechnology and pharmaceutical companies use social media for advertising and more

BY MIKE MAY

**DATA DRILL DOWN**

ILLUSTRATIONS BY JOELLE BOLT
local biopharmaceutical executives enjoy an intimate view of a country’s prospects for market access, the regulatory environment and manufacturing and supply chains. Do these experts consider their country’s current conditions worthy of expanding employment or new investment in research, development or manufacturing? This question forms the basis of our Biopharmaceutical Competitiveness and Investment Survey (BCI), which is a new tool for evaluating the biomedical sector in a given country or region. In essence, the BCI polls key decision-makers—local biopharmaceutical executives—and asks if they would encourage investment in their country when talking with senior company executives, who must allocate capital, technology and resources across dozens of countries. In an industry investing more than $100 billion globally per year, the concerns of these executives represent valuable insights for governments competing for a larger share of this massive investment flow.

The BCI Survey asks executives and experts operating “on the ground” a wide range of in-depth questions about the performance of the country in which they operate. Their answers are then statistically analyzed to produce a quantitative index of that country’s competitiveness in various areas of the biomedical-innovation pipeline. By drawing on firsthand insight from locally stationed biopharmaceutical executives, the BCI’s survey-based approach represents a unique and innovative method for evaluating the biomedical-investment attractiveness of countries.
Although this survey arises from the subjective views of individuals, an expert’s perspective and experiences often influence investment decisions. The BCI captures this element by gathering a large sample of respondents for each country and using statistical analysis to translate responses into concrete measurements. Ultimately, a country’s BCI score might provide an intelligence tool to help policymakers better understand larger trends in their country’s biomedical sector. The BCI score also complements other indices and measurements of national performance, including the Scientific American Worldview Scorecard, allowing a more comprehensive understanding of where improvements are needed.

A BOTTOM-UP APPROACH

Most global indices create a numerical based on the combined sum of other variables that are assumed to reflect an underlying construct. These so-called composite indices often rely on a “top-down” approach, in which the creator determines the best practice or standard, and then evaluates performance against this standard and assigns an overall score. In contrast, the BCI survey—a “bottom-up” approach—measures a country’s performance and compares it to that of other regions. In general, a survey asks experts and professionals about their specific views on and experiences with the subject matter or situation under analysis. Surveys of business executives are often used to gauge economic and commercial activities. One of the first notable studies is a type surveyed 100 companies in six manufacturing industries on decisions concerning foreign direct investment (Lee, J.Y., & Manfield, E. Intellectual property protection and U.S. foreign direct investment. Review of Economics and Statistics 78(2):181–186 (1996)). More recent examples include the 2010 survey of executives by the European Patent Office and several partners, which measured the licensing of environmentally sensitive technologies in developing and developing countries (Patients and Clean Energy: Bridging the Gap Between Evidence and Policy, 2010. http://ictsd.org/downloads/2010/09/study-patents-and-clean-energy_1950.pdf).

The BCI score is based on a large sample of respondents, existing survey-based studies, however, often fail to apply a quantitative measurement to the views of responders. The BCI fills this gap by asking respondents how a given nation measures up with respect to different factors that combine to form an optimal environment for biopharmaceutical commercial development. Statistical analysis of the survey data allows each country to be scored and ranked using numerical variables. The survey examines the entire “ecosystem” in which biomedical innovation takes place by asking seven questions in each of seven major categories:

- scientific capabilities and infrastructure
- clinical environment (from test tube to patient)
- manufacturing and logistics
- regulatory framework
- healthcare financing
- effective market-access activities
- overall market conditions.

For each question, respondents rate a country’s performance in relation to a certain benchmark. Figure 1 gives a brief overview of the combined profiles for the seven major categories. In question 9, a high level of commitment to clinical research by hospitals across the country provides the benchmark. For Question 30, a structured and balanced process for negotiating import duties, prices of your products and obtaining market access.

The four answer options correspond to scores of 0.5, 1.0, 1.5 and 2.0—ranging, in order, from the options representing little interest to a few clinicians, of little importance (mostly in certain departments and hospitals), important (significant emphasis is placed on the ability to conduct clinical trials) and one of the top priorities (identified as a strategic objective).

The overall scores give an idea of the performance and relative competitiveness of the preliminary sample of countries. Generally speaking, countries with a score above 10 generally rank quite competitive position relative to other countries, countries with scores of 70–80 possess reasonable competitiveness, scores of 60–70 indicate a limited ability to compete and those scoring 50–60 struggle. The results by category provide a more “drilled-down” impression of executives’ views of the performance of their country in the seven categories. As the detailed scores show, countries perform well in some areas but lag in others. For example, almost all countries—even countries with exceptional performance in most areas—performed the lowest in healthcare financing. Countries with the lowest overall scores also experience problems with additional areas, including scientific capabilities, manufacturing and logistics, and effective market-access activities. This table includes color-coded indicators of a country’s performance compared to others.

In order to capture specific nuances of country performance, respondents receive a scale of four answers for each question. This scale ranges from the lowest possible performance to the highest possible performance (i.e., the benchmark), but the exact scale varies for each question. This design gives respondents a framework for gauging their views, but in a way that minimizes constraining their answers. Moreover, the BCI covers a wide sample of countries—over 60 developed and emerging economies—and arises from the collective responses of 15–20 biopharmaceutical executives operating in each country.

To score the responses, each question accounts for a total of two points, which means that a maximum score of 14 exists for each category. We give the final category, a single question that captures a respondent’s overall impression of country performance, a maximum score of 2.

The four answer options correspond to scores of 0.5, 1.0, 1.5 and 2.0—ranging, in order, from the options reflecting the poorest to the highest performance. Based on the analysis of all 30 responses, each country receives a score for each category as well as a total score, out of a maximum of 100.

**REVIEWING PRELIMINARY RESULTS**

In March and April 2012, we conducted a pilot study of the BCI, in which more than 250 executives from over 50 countries responded. The preliminary results of 11 countries, which reflect a wide range of developed and emerging economies, offer a glimpse into executives’ views about how these countries can compete in the biopharmaceutical sector. Even these preliminary results reveal that certain countries seem to perform better than others.

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As we collect an even wider data set, the BCI index will provide an increasingly precise understanding of each country’s performance. The full analysis of the 50 countries will be presented later this year. In addition, it would also be valuable to include an open-ended questionnaire in future iterations of the BCI in order to gauge respondents’ views more specifically.

*If you wish to participate in the BCI Survey, please contact Rachel Chu, rachael@pgus-consult.com.*

![FIGURE 1. PERFORMANCE BENCHMARKS.](image)

<table>
<thead>
<tr>
<th>QUESTION 9</th>
<th>How important are clinical trials to hospitals in your country in terms of their commitment to encouraging and participating in cutting-edge research?</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUESTION 30</td>
<td>To what extent is your organization able to effectively negotiate the prices of your products vis-a-vis public healthcare providers?</td>
</tr>
</tbody>
</table>

**PRELIMINARY RESULTS BY CATEGORY**

<table>
<thead>
<tr>
<th>Category</th>
<th>Denmark</th>
<th>Switzerland</th>
<th>Sweden</th>
<th>United States</th>
<th>Israel</th>
<th>India</th>
<th>Greece</th>
<th>Russia</th>
<th>Turkey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>11.58</td>
<td>11.92</td>
<td>13.75</td>
<td>12.83</td>
<td>9.42</td>
<td>11.42</td>
<td>10.58</td>
<td>1.67</td>
<td>62.75</td>
</tr>
<tr>
<td>STRONGLY COMPETITIVE</td>
<td>11.58</td>
<td>11.92</td>
<td>13.75</td>
<td>12.83</td>
<td>9.42</td>
<td>11.42</td>
<td>10.58</td>
<td>1.67</td>
<td>62.75</td>
</tr>
<tr>
<td>REASONABLY COMPETITIVE</td>
<td>11.58</td>
<td>11.92</td>
<td>13.75</td>
<td>12.83</td>
<td>9.42</td>
<td>11.42</td>
<td>10.58</td>
<td>1.67</td>
<td>62.75</td>
</tr>
<tr>
<td>LIMITED ABILITY TO COMPETE</td>
<td>11.58</td>
<td>11.92</td>
<td>13.75</td>
<td>12.83</td>
<td>9.42</td>
<td>11.42</td>
<td>10.58</td>
<td>1.67</td>
<td>62.75</td>
</tr>
<tr>
<td>STRUGGLING TO COMPETE</td>
<td>11.58</td>
<td>11.92</td>
<td>13.75</td>
<td>12.83</td>
<td>9.42</td>
<td>11.42</td>
<td>10.58</td>
<td>1.67</td>
<td>62.75</td>
</tr>
</tbody>
</table>
MOORE’S LAW IS REMAKING MEDICINE

BY ROBERT GOLDBERG

Over the past two years, geneticist Michael Snyder and his colleagues at Stanford University have followed one patient’s health with keen interest. For one thing, Snyder himself was the patient. But more important, the team was able to generate Snyder’s integrative personal ‘omics profile (iPOP)—a highly granular and dynamic view of his genome—and use it to monitor, predict, and treat an surgery at a molecular level and in real time.

Although the iPOP determined that Snyder faced no genetic risk for diabetes, the team’s report in the March 16, 2012, issue of Cell showed that a respiratory virus changed his gene expression and RNA transcription in ways that triggered elevated glucose levels and a higher risk for the disease. Through exercise, a modified diet and diabetes medicines prescribed based on Snyder’s iPOP, his glucose levels returned to normal.

The study demonstrates that sequencing an individual’s genome—a process that less than a decade ago took years and cost $3 billion—could be used routinely to treat disease and improve health.

EXPLOITING INNOVATION

Snyder’s example portrays a rapid convergence between Moore’s law—the doubling of transistors on a computer chip about every two years—and biomedical knowledge. This intersection is the merging of Moore’s law and medical progress could turn today’s costly and cumbersome healthcare tools into smaller, faster and less expensive products that benefit everyone. The combination of these innovations makes the commercialization of personalized and predictive medicine possible.

“When I first did the genome sequencing project,” Snyder recalls, “I was thinking that we could be seconds ahead of the market, but it didn’t take us very long to realize that it was not quite yet to the patient. But more important, their clinical utility is the product of meeting needs that are more patient-centric, less complex and less costly for consumers, providers and others. Second, such innovations create more value for more people than existing approaches. Edison’s light bulb, for instance, obliterated other forms of lighting because it delivered light more cheaply, conveniently and more directly—not because it was less expensive. And just as Edison’s electric power companies and wires allowed the casually deliver light to millions, the rapid spread of the Internet, cloud-based computing and low-cost smart phones and tablets allows for the mass distribution of personalized medicine.

Such innovations creatively destroy mainframe medicine. This revolution, however, spreads faster in emerging markets, because of their strained health budgets and the fact that their technology is lagging for their own healthcare. As a result, many developing countries favor on-the-spot diagnostics, treatment and monitoring, rather than building the traditional healthcare infrastructure. For example, a new tuberculosis test—developed by David Alland of the University of Medicine and Dentistry of New Jersey—uses a DNA lab-on-a-chip to diagnose patients in as little as two hours. The current test, analyzing saliva under a microscope, is less accurate, more expensive and takes months to produce results. Although this kit was produced for the U.S. market, it will be widely used in Africa. Similarly, OneBreath, sponsored by the American College of Chest Physicians, produced a low-cost ventilator for respiratory distress by replacing expensive hardware with proprietary software and inexpensive sensors. Most of these devices are sold in India and Western China, although the technology was originally designed to fight a pneumonia outbreak.

Of course, Singapore, Brazil, China, India and Africa create products in addition to consuming them. India, for example, develops and sells in America and Europe. Life Technologies—which machine can sequence an entire genome in a day—is doing development in India and China. And IBM researchers in Israel helped create the company’s Watson supercomputer.

WESTERN RESISTANCE

Meanwhile, Western healthcare systems discourage this transformation. It is already difficult for the U.S. Food and Drug Administration to keep up with technological advances. Now, government and insurers are demanding comparative effectiveness research (CER) before deciding whether to pay for newly approved medical innovations. CER slows the already sluggish adoption of smaller, more powerful replace-ments for existing technologies. As Topol observes, “Cardiologists get nicely reimbursed for angiograms but not for genetic tests that would avoid angiograms.” While American entrepreneurs must raise additional capital to carry out CER research and lobby for reimbursement, startups in China receive cash from initial public offerings in new products. Also, some entrepreneurs get so enamored with their research that they don’t ask if it’s needed. Ralph Snyder, chancellor emeritus of Duke University, points out that life science companies often ignore “the clinical marketplace and whether their technology will be used by providers and actually improve outcomes.” Consequently, Douglas encourages inventors in China and India an enterprise in new products. In the digital revolution, what would products be determined by how they increase clinical value, reduce clinical complexity and reduce cost to institutions and consumers over time. The key to this process is gathering consumer preferences and clinical response digitally and turning them into design attributes.

The digital revolution not only makes low-cost predictive medicine possible, but it also allows individuals to directly share information about their needs and values. If the medical industry embraces this transformation, and markets (and not bureaucrats decide what products are valuable), it will remain an innovative and renewable source of global health and prosperity.

Robert Goldberg is a cofounder and vice president of the Center for Medicine in the Public Interest.
CALCULATING E. COLI CONTAMINATION

Multiplexing and bioinformatics deliver a rapid test that meets the USDA’s new standards  

BY MIKE MAY

The 2011 Escherichia coli outbreak in Germany, caused by the Shiga-toxin producing E. coli (STEC) with the O104:H4 serotype, claimed 50 lives. The outbreak was a sobering reminder of the dangers of STEC infection, which in humans generates symptoms ranging from mild intestinal complications to more serious kidney problems that, as in this tragic case, can even be fatal. Although the German infections derived from seeds, undercooked ground beef is another source of the bacteria. The U.S. government is now requiring more thorough screening of beef for E. coli, and in order to conduct such testing, food suppliers must turn to new analytical technology.

The U.S. Centers for Disease Control and Prevention (CDC) states that as many as 10 percent of STEC infections lead to hemolytic uremic syndrome, which may result in the deaths of those—known as “The Big Six”—as well as for O157.

Ground beef appeared to cause several cases of the O26-STEC infections in Maine and New York in August 2010, and other examples have linked beef with non- STEC infections—contaminations that were not being tested for. “We were learning that the states that were looking for it, the states that were doing special research projects, were finding non-O157 STECs in really significant numbers,” Elisabeth Hagen, the USDA’s Under Secretary for Food Safety, told Food Safety News. “And in some cases much higher numbers than O157.”

Nonetheless, existing methods did not screen for non-O157 STECs in beef. In fact, the “DRAFT Risk Profile for Pathogenic Non-O157 Shiga Toxin-Producing Escherichia coli (non-O157 STEC),” which was published in August 2011 by the USDA’s Food Safety and Inspection Service (FSIS), states: “[The commercially available diagnostic methods for the isolation of non-O157 STEC are currently quite crude, with around a 10% (or less) recovery rate from PCR-positive samples].” So to test for the non-O157 STECs, the USDA first needed a test.

ACCELERATING THE ANALYSIS

In November 2011, the FSIS published “Detection and Isolation of non-O157 Shiga-toxin Producing Escherichia coli.” This process includes an incubation step alone that can take 22 hours. It scans for the Big Six serotypes—O26, O45, O103, O111, O121 and O145—which cause about 70 percent of the non-O157 STEC infections. According to statistics from the CDC, those non-O157 STECs could cause more than 180,000 infections a year in the United States alone.

Notably, the equipment and reagents listed in the protocol from FSIS include many items produced by Life Technologies in Carlsbad, California. For example, this protocol—and others for food testing—uses Dynabeads, magnetic beads from Life Technologies that isolate pathogens from a solution to make an enriched sample. However, the FSIS protocol takes two days for sample screening and six days to complete the entire infection-confirmation workflow.

“We’re speeding up that process,” says Peyman Fatemi, senior food safety consultant at Life Technologies. The company’s test runs in just 8–9 hours, and it combines advances in sample preparation, a sensitive polymerase chain reaction (PCR) step and sophisticated data analysis.

Starting with 375 grams of ground beef, the Life Technologies assay gains speed and accuracy from optimizing the sample before testing it. Keep in mind that just one gram of beef could include 100,000—maybe even a million—bacterial cells that are just background. “So you need to grow up your bacteria while trying to control for background flora so they don’t overwhelm the sample,” Fa- temi says. “Then, you separate out the bacteria you want, extract its DNA and move to the assay.”

Using Dynabeads, the Life Technologies procedure enriches the sample for O157:H7 and Big Six. The Dyna- beads bind to these specific strains of E. coli, which can be separated from other cells just by using a magnetic particle processor that pulls out the O157 and Big Six cells. Much of the speed behind the Life Technologies approach comes from using a two-stage test. As long as a sample turns out negative for O157 and the Big Six, the process takes roughly 8 hours. A PCR confirmation step—in the event of a positive result from the first stage—requires another hour. The company can then make a decision based on that result. If they want to culture confirm and isolate the specific bacteria, then the process goes essentially to the FSIS protocol to identify the specific contaminant.

SOFTWARE & SIMULTANEOUS SOLUTIONS

The efficiency of the first stage in the Life Technologies platform arises from its simultaneous scan for all seven bacterial strains. Although this approach speeds up the analysis, it complicates the process of developing the test. “The targets get diluted when you start mixing them,” says Eric Liu, product manager of food and environmental safety testing at Life Technologies.

Even then, it takes time to build the best assay. “You design a number of candidate assays based on the target genes, which identify the strains,” says Fatemi. “Then, you test them and pick the one that works the best.”

But users of the assay will also need ways to explore the data it generates. Life Technologies’s RapidFinder Express software provides different options for this analysis. The data can be viewed in a simple positive or negative format, which clearly indicates if samples turned out infected by one or more of the seven strains of bacteria. Further, users can analyze the raw data if they wish. Most important to food suppliers and consumers is ensuring the safety of beef. The more forms of E. coli that producers can quickly and accurately analyze, the more likely that beef can be safely served. In all food safety, however, the producers and the consumers should both do their parts. For the latter, cooking meat fully and washing hands after touching raw beef goes a long way toward avoiding any infections. In short, as long as beef is properly tested and thoroughly cooked, everyone will stay safe.
The continued commercial application of biotechnology worldwide over the past two decades has led to the development of a bioeconomy, whereby substantial economic outputs are derived from the development and use of biological materials. Bioeconomy encompasses all industries and economic sectors based on the values implicit in biological materials that can be translated into new sources of income, environmental sustainability and social well-being.

The potential economic and environmental benefits of biotechnology have created a growing strategic interest in the bioeconomy across the globe. The Organisation for Economic Cooperation and Development (OECD) estimates that bioeconomy will contribute a global average of 2.7 percent to GDP by 2030. However, in order for bioeconomy to succeed, considerable uncertainties and global challenges will need to be addressed.

Malaysia, as one of the most competitive biotechnology hubs in the region, has taken the early critical steps in coordinating and intensifying national efforts to harness bioeconomy’s potential through the implementation of the Bioeconomy Initiative Malaysia (BIM).

Endorsed by Malaysia’s Biotechnology Implementation Council and launched by the Honorable Prime Minister of Malaysia during BioMalaysia 2011 in November 2011, BIM is the framework for the nation to develop a high-income bioeconomy through a sustainable ecosystem of R&D and commercialization in the areas of agriculture, healthcare and industrial biotechnology by 2020.

Strengthened by an environment that is conducive for the development of the local biotechnology ecosystem, BIM attempts to coordinate and intensify the nation’s efforts to capitalize on the potential economic benefits of the entire biotechnology ecosystem and related value chains, in parallel with the Economic Transformation Program (ETP).

This is accomplished by leveraging the participation of private industry in the high-impact opportunities throughout all industries and economic sectors that produce manage and utilize biological resources, including agriculture, forestry, fisheries, food, wellness, chemicals and renewable energy.

BIM will serve as a platform for the government and leading industry players to work in tandem in setting national goals for the application of biotechnology to agriculture production, industry and health, put in place the structural conditions required and develop necessary mechanisms to ensure that policy can flexibly adapt to new opportunities. Innovative policy frameworks, strategic and proactive thinking by both government and private sectors, and public support is required.

Through the BIM, Malaysia is unlocking even greater opportunities in the local and regional biotechnology industry, and enhancing the participation of the private sector. At the same time, the public sector is renewing its commitment to continue to provide and facilitate the necessary support for the development of the approved projects.

By optimizing the nation’s competitive edge through private and public participation, Malaysia continues to further strengthen its local biotechnology ecosystem for the growth and development of a sustainable bioeconomy that will drive the country’s socioeconomic position to greater heights.

Innovative policy frameworks, strategic and proactive thinking by both government and private sectors, and public support is required.

**Malaysia’s Efforts in Harnessing Bioeconomy**

Malaysia established during NBP Phase 1: Capacity Building (2005–2010), the BIM is positioned to further enhance the role of biotechnology as a key cross-cutting technology driver in transforming Malaysia into a high-income, knowledge-based economy.
Nearly 100 years ago, Nobel Prize-winning scientist August Krogh and his wife Marie embarked on a journey to revolutionize diabetes care, driven by her needs as a diabetes patient. Today, Novo Nordisk still takes a deeply human approach to everything we do. As a world leader in diabetes care, we are in a position of great responsibility. We must continue to combine drug discovery and technology to turn science into treatments. We must prioritize research, education, and partnerships around the world to make diabetes a global priority. We must conduct our business responsibly in every way. And most importantly, we can never lose sight of the patient-centric approach that has driven our vision of innovation since our inception.

**Together, we can defeat diabetes in our lifetime.**

For more about us, visit novonordisk-us.com