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Can TGen live up to all the hype?

Dr. Jeffrey Tegen is TGen's scientist extraordinaire and the man who is helping put Arizona on the bioscience map

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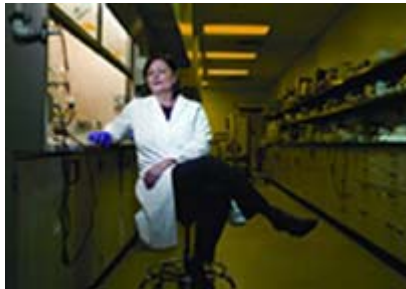
Ten Biotech Companies to Watch

by Dean Meadors

TGen clearly symbolizes Arizona's growing biotech economy, but a surprisingly diverse group of up-and-coming tech firms will ultimately bear the burden of bringing new products and discoveries to market. The state has spawned hundreds of high-tech, high-hope startups thus far, and their origins include everything from TGen itself to Tom's Motesenbocker's garage. From Flagstaff to Tucson, the state's next-generation powerhouses bring to Arizona an intriguing mixture of excitement, ambition, diversity, promise ... and technologies you might never have heard of.

We picked 10 of the best based on their potential, their pedigree and their performance. They offer products ranging from artificial hearts and gene-expression profiling to stent crimping and laboratory software. But they have a lot in common, too—great resumes, traction in the marketplace and the potential to dominate with technology. They're helping lead Arizona to a new economic future.

Meet TechConnect's "Ten Companies to Watch in 2005."



Ribomed Biotechnologies, Phoenix

You've heard it for years: The early detection of disease is critical to successful treatment. Now the genomics experts at Ribomed Biotechnologies in Phoenix are taking the adage to a whole new level.

Founded in 1999 by Dr. Michelle Hanna (under the clever name "Designer Genes"), Ribomed exploits the fact that

many diseases are caused by slight alterations to the gene sequence, which, in turn, changes the behavior of proteins. Hanna's process (she holds two patents, and another 10 are pending) allows scientists to detect small cellular changes early on.

The result: more prompt and accurate diagnoses of problems, giving doctors extra time to begin treatment. These cellular changes occur in both inherited and developed conditions such as cancer, Alzheimer's disease, heart disease, diabetes and aging.

Looking more closely at aging, it turns out cells change as they age too, and some of these changes happen because certain genes are "silenced" (shut off)

as we grow older. Some of these genes appear related to aging, and perhaps some can be switched back "on." This is all in the future, of course, so in the meantime, "We're all aging," says Hanna.

Ribomed's expertise and the chemical compounds it makes (called reagents) appear useful for another critical need—the early detection of pathogenic organisms likely to be used in a terrorist attack. The company has received funding from both the Department of Defense and the Homeland Security Agency to incorporate its technology into portable devices capable of detecting bacterial and viral agents. The finished system would continuously monitor outdoor urban areas for traces of chemical threats.

Ribomed's potential is obvious. The company was selected as a finalist for the "World's Best Technologies 2005 Award" from the National Association of Seed and Venture Funds, and the Federal Laboratory Consortium for Technology Transfer.

Hanna, a Phoenix native and Arizona State University graduate, is consolidating Ribomed's two locations into a single downtown facility across the street from TGen. She renovated a 30,000-square-foot building and will occupy half. The remainder will be leased to fledgling biotech companies. "I waited five years for someone to build an incubator, an accelerator, or build some lab space downtown, but it never happened," she says. "So I did it."



Machine Solutions Inc., Flagstaff

Dan Kasprzyk and Tom Molsenbocker are living proof there's real value to "happy hour." An after-work drink in 1999 (both were then employed by W.L. Gore) led to a business partnership, and the two never looked back. "We shook hands and off we went," says Kasprzyk.

In 2000, the pair incorporated with \$1,000 in the bank, a corner of Tom's garage and a rented mailbox. They made a great team. Molsenbocker is the master engineer, strong in equipment design and automation. Kasprzyk, also an engineer by trade, brought 16 years of experience with stents and catheters—and a flair for marketing.

The company produces four categories of products: stent crimping, catheter-balloon pleating and folding, swaging, and catheter/stent testing. All are based on a patented system called MSI Radial Compression Technology. "Crimping" is applying pressure evenly to a surface from all sides. In MSI's case, they do it to surfaces which are extremely small and fragile.

Stents are small devices implanted in an artery to increase blood flow. The best known application is in coronary arteries, and the impact has been huge: Heart disease is no longer the leading killer; cancer is. Some stents are coated with drug-eluting products, which Kasprzyk says "is a big reason why Machine Solutions has been able to sustain the growth it has."

The company has hundreds of clients, including giants like Johnson & Johnson, Boston Scientific, Medtronic and Guidant. Sales in 2004 were \$12 million, up from \$7 million a year earlier, and Kasprzyk expects sales to approach \$20 million in the current year. An additional 20,000 square feet of office and manufacturing space is being added in February, and the employee workforce is now at 47.

MSI's proprietary technology is primarily responsible for the rapid growth, but Kasprzyk acknowledges their timing was good. MSI grabbed market leadership almost immediately, and there's still plenty of growth in the company's four existing categories.

Meanwhile, Kasprzyk is looking for opportunities elsewhere. One possible area is consumer products such as wire, cable and fiber optics—each of which might benefit from MSI's unique technology.

5AM Solutions, Phoenix

5AM Solutions already boasts one distinction: It's the first company to choose Arizona as home solely because TGen was here. It certainly makes sense, especially since co-founders Brent Gentleman and Rob Daly have prior experience with a top TGen investigator, and because 5AM specializes in software to streamline the conduct of scientific research.



When the Human Genome Project was completed two years ago, it created a vast sea of data for researchers to share and access. Enter 5AM's Web-based software, which allows scientists anywhere in the world to more easily stay in touch with research results, clinical updates, status information or administrative tasks. "Most folks now use paper notes," says Gentleman.

He believes the Web helps create good science. "It makes it easy for researchers to document what they're doing, and without the software, an incredible amount of time gets wasted," he says. "Large-scale projects just can't be managed by e-mail anymore."

Gentleman and Daly first looked at Arizona at the suggestion of Dr. Dietrich Stephan, a key TGen scientist and a former client. They came for a visit and met with Dr. Jeffrey Trent, TGen's president, who convinced them Arizona was deeply committed to bioscience leadership. Says Gentleman: "We have great respect for the research being conducted at TGen, and we know we can contribute to its success. The message of 'bench to bedside' captured our imagination."

The curious name came from the founders' desire to be memorable, yet not be associated with any specific technology. Gentleman likes the fact it hints at dawn and a new beginning.

The founders already count TGen and the Arizona Disease Control Research Commission as clients, and are poised to launch a Web-based, monthly subscription service employing their software. The new service would allow researchers to "rent" customized software for the length of their study, then pay for it as they go.

Gentleman insists 5AM is driven solely by a desire to help researchers get their job done. "We ask ourselves, 'Who needs to know what, when?'" And if things work out as he hopes, next year will see 5AM's business triple.



AmpliMed, Tucson

Most technology companies expect to survive by creating something entirely new, a breakthrough product or process. Not AmpliMed Corp. The small Tucson-based pharmaceutical company, a spinoff of the University of Arizona, would rather root through the trash bin and find an abandoned jewel. It thinks it just did.

AmpliMed's promising anticancer drug is Amplimexon, based on the compound Imexon, which was first developed in Europe nearly 30 years ago to stimulate depressed immune systems. Imexon was abandoned by its German discoverer, however, before its potential was fully explored.

According to AmpliMed, the re-discovered compound has some very intriguing properties, including the ability to kill certain cancer cells. But what really makes it interesting is that it seems to cause few of the toxic or troublesome side effects of other chemotherapeutic drugs. Amplimexon looks especially promising for use alongside other treatments that are effective but dangerous. Now in Phase II trials, Amplimexon seems to have most likely applications with pancreatic cancer, lung cancer and malignant melanoma.

Formed in 1991 by four faculty members from the Arizona Cancer Center—Dr. Evan Hersh, Dr. David Alberts, Dr. Robert Dorr and Dr. William Remers—AmpliMed is a private company based at UA but funded with venture capital. A year ago, it brought in as CEO Robert Ashley, an experienced pharmaceutical executive, to help guide products through the lengthy and expensive FDA approval process.

Despite its excitement over Amplimexon, AmpliMed doesn't appear to be a one-trick pony. The compound has yielded an additional 30 chemicals that have been patented and might have commercial application. Further down the road, a product called Amplizone might be the next big thing. Currently in animal studies, Amplizone might prove to be effective against ovarian cancer, breast cancer and certain types of prostate cancer.

"There's plenty we can mine from the AmpliMed pipeline," says Ashley, but he doesn't see the company building an ivory tower. Most needed services can be contracted out more efficiently, but he does see an infrastructure for clinical and regulatory development that would allow AmpliMed to take on additional drugs.

"We have numerous opportunities to grow," he says, "but it's hard to plan until we know exactly what we've got."



SynCardia Systems, Tucson

All companies dream about owning a market segment that's big ... and growing bigger. Tucson's SynCardia Systems—a privately held medical-equipment company literally formed around a single product—has found exactly that. SynCardia builds a temporary artificial heart capable of completely replacing the functions performed by the real thing. Called the CardioWest Total Artificial Heart (TAH), the device offers hope to severely ill patients with end-stage congestive heart failure facing imminent death.

SynCardia was founded in 2001 by Dr. Marvin Slepian, an entrepreneurial physician with a history of inventing medical devices. Slepian, who holds 25 patents, received his medical degree from the University of Cincinnati College of Medicine. He has a number of other startups to his credit, including Focal, Endotex, Angiotrax, NVR Labs and ISRx. He is currently professor of cardiology at University of Arizona.

SynCardia began by assuming an existing heart-substitute product, improving it and bringing it successfully to market. In October, it became the first temporary total artificial heart to gain FDA approval for temporary use. The purpose of the TAH is to keep seriously ill patients alive long enough to receive transplants. Currently, about 270 of the devices are in use.

Slepian sees enormous potential. After an initial funding of \$2.5 million in venture capital, another \$3.7 million in private financing was raised last year "to further advance the product development and commercialization" of the product. The funds also will be spent to improve the portability of the \$100,000 product, and to further expand its use in Europe. U.S. sales doubled last year over the previous year.

The stakes are huge. More than 5 million Americans suffer from congestive

heart failure, and an estimated 250,000 die each year. While 100,000 sufferers are candidates for transplants, only about 2,500 are performed each year, partly because nearly a third die before a donor heart is found.

The CardioWest Heart, once used by a patient for more than three years, offers full circulatory support and maximum cardiac output. Even the sickest patients become healthier, making them better candidates for transplant. If the \$100,000 device can be adapted and approved for long-term use, which Slepian believes can happen, the size of SynCardia's market increases dramatically.

Integrated Biomolecule, Tucson

Even the hottest, fastest-growing biotech companies can be small. Consider Tucson's Integrated Biomolecule Corp. (IBC), an organic chemical company with lots on its plate but only 10 employees. Strongly rooted in applied chemistry, IBC was started in 1992 to synthesize organic compounds such as peptides, carbohydrates and other materials of high complexity and purity.



Partly to fulfill its own needs, the company soon expanded into sophisticated laboratory testing for a wide variety of clients including pharmaceutical, food and biotech firms.

It found a particularly strong niche in the nutritional-supplement industry, and today IBC is the leading supplier of chemical analysis to this segment. IBC can perform a wide variety of chemical tests, including delicate projects like shelf-life analysis, product-failure analysis and the assay of minerals and metals so sensitive that results are measured in parts per trillion. IBC created a proprietary computer network to assist in designing special protocols for synthesizing organic compounds of particularly high purity and yield.

The company now performs gene-expression analysis for genomics researchers, fuel-additive studies for government, and testing of biological fluids and clinical trial support for the pharmaceutical industry. It hasn't done business yet with TGen, but is hoping to soon.

The anticipated growth of Arizona's bioscience industry bodes well for IBC and its president and founder, Robert Green. "Initially, most of our business came from out-of-state," Green says. "Over the last three years, Arizona has become much more important as a market."

Integrated Biomolecule recently moved into its new headquarters and science center in Tucson's Rancho Vistoso Tech Center 20 minutes northwest of Tucson. The state-of-the-art, 18,000-square-foot facility is architecturally sweeping and futuristic with a computer-controlled environment, clean-room space, fire-suppression system, robotics and lots of advanced testing equipment. IBC's secret is its automation and instrumentation. "There are no other labs in the country that run like ours," Green says. "Our labs are fully automated and computer-controlled. They run 24/7."

In the past four years, Integrated Biomolecule's business has grown fivefold. Says Green: "This is the right time, and Arizona is the right place."



W.L. Gore, Flagstaff

The dominant employer at the north end of the bio-corridor is W.L. Gore's Medical Products Division. Best known for its GORE-TEX® fabrics, W.L. Gore is headquartered in Newark, Del. According to legend, founder Bill Gore selected Arizona for its Medical Products

Division in 1967 after a hiking trip to the pine hills of Flagstaff. The company makes implantable medical devices such as artificial arteries, sutures, patches and interventional prosthetics in a total of nine individual facilities.

The privately held company has been named one of the best companies in America to work for, but it maintains a stubborn, stony silence about its operations. There is no communications function in Arizona. All requests for information are referred to the legal department, or to corporate headquarters in Delaware. The facility employs "more than 1,000" workers and it manufactures "more than 50" major products. Revenues, growth or projections are not released, but an indication of strong growth is hinted.

Gore shuns titles, preferring instead to organize itself into teams structured around market opportunities. It operates internally on a "lattice" system, which allows employees to communicate directly up or down the organization without having to go through formal management layers.

The latest emphasis at Gore is developing products to permit more noninvasive surgery, even to repair arteries buried deep in the chest. In the past, procedures to implant synthetic grafts required large incisions, increasing patient risk. Gore's innovative new TAG Thoracic Endoprosthesis is inserted via catheter through a small incision in the patient's leg. The hope is faster surgery, better results and faster recovery times. Low-key or not, Gore will remain a key part of the burgeoning biotech industry here—especially in northern Arizona—because of its size, its momentum, its technical expertise and its economic impact.

Medicis, Scottsdale

Medicis differs from TechConnect's other selections in two important ways: It's the only publicly held company on our 2005 list (MRX, NYSE), and its success depends not just on technology, but also on vanity. The Scottsdale pharmaceutical firm focuses solely on products that enhance personal appearance. And when you look at the numbers, the company is sitting pretty.



For the past five years, the firm's average annual growth rate is a muscular 21%. More impressive, The Wall Street Journal reports that for the previous 10-year period, Medicis ranks ninth among all publicly traded companies in performance, and first among pharmaceuticals.

"It shows how consistent we've been," says CFO Mark Prygocki. When Medicis relocated to the Valley in 1995, it had 12 employees. It now has 150 in the Scottsdale headquarters and a total of 300 worldwide.

Medicis has a four-part growth strategy including boosting its existing brands, R&D development of new products, strategic marketing alliances, and making new acquisitions. "We have more than a half-billion in cash we can use," Prygocki says.

Medicis offers six major groups of skin-care products, including treatments for fungal infections, acne, rosacea and other skin maladies and conditions. In 2002, Medicis struck gold by importing a dermal filler called Restylane. Injected under the skin by a dermatologist, Restylane adds volume and fullness to skin, correcting wrinkles and folds.

"It's like a nonsurgical facelift," Prygocki says, "and you can have it done on your lunch hour."

After Medicis acquired an exclusive license to Restylane from its Swedish

developer, it created a publicity tornado. "It's been on every major television show (including Oprah and The Today Show) and in every major magazine," says Prygocki. "It's really been a hot product."

Restylane will certainly contribute future growth, but the firm also has 12 additional products in its pipeline that it believes will hit the market by 2010. And if TV shows like The Swan and Extreme Makeover are any indication, the market for appearance-enhancing products is only going to grow.

"When you look in the mirror," says Prygocki, "what do you want to see? That's where we focus our attention."



Molecular Profiling Institute, Phoenix

It was always the plan—TGen and IGC would create discoveries based on the Human Genome Project, then either spin off separate companies, license the technology or partner with others to speed new medical treatments to market.

After only two years, the first for-profit enterprise was spawned. The Molecular Profiling Institute will analyze the cancer tumors of individual patients, peering inside to learn which genes are working and which ones aren't, then give doctors critical information about what they face and what they should do.

Now the nation's top killer, cancer is essentially an uncontrolled spread of cells. But accepted treatments work with some patients and prove useless with others. Why? At a molecular level, each person is unique. Understanding precisely how will allow the use of therapies tailored to each individual. Oncologists and pathologists can now have a whole new look at what's happening inside their patient's cancers.

For example, tests on a tumor from a recent pancreatic cancer patients' revealed Her-2, a cell surface marker more commonly associated with breast cancer. Knowing this, her treatment was modified to include Herceptin which is typically used in treating breast cancer. The patient experienced dramatic, short-term improvement.

MPI hit the ground running. It entered into a licensing agreement for the U.S. rights to sophisticated MammaPrint® technology developed in Holland by Agendia. MammaPrint® uses gene-expression profiling to predict how a breast-cancer tumor is likely to behave. This is critical because it allows oncologists to formulate tailor-made treatment plans or determine if the patient needs treatment at all.

Currently, everyone receives aggressive treatment because doctors aren't sure how each tumor will react. "Overtreatment is common," says CEO Robert Penny, "because you don't want to miss anyone. Now, we're treating 93 patients to get to the 30 who really require treatment."

MPI also partnered with AmeriPath, a network of pathology labs, to provide its advanced molecular testing to AmeriPath's 3.5 million patients.

Even with its for-profit status, Penny intends for MPI "to help define the standards of care in the future. We have to be able to make money," he says, "but this is really about the patient."

SenesTech, Flagstaff

Because pharmaceutical companies are required to screen new compounds and treatments in animals prior to use in



humans, menopausal women present a unique challenge. In order to create a "menopausal" animal, the ovaries of the research animals are surgically removed.

But to Dr. Loretta Mayer and Dr. Patricia Hoyer, that didn't make sense. Post-menopausal women continue to produce hormones even after the eggs are deleted. Removing the animal's entire ovary creates a whole different testing scenario.

So the pair developed an innovative process which greatly accelerates the natural process. In mice, menopause is complete in 40 days. "What this technology allows are animal models which more closely mimic an aging female," says Mayer.

In 2002, Mayer, Hoyer and Dr. Cheryl Dyer kicked off SenesTech in Flagstaff. Although the founders' roots were in bio-rich San Diego, the trio chose Arizona because Mayer believed the universities here were developing a technology-based approach to translating science to real life. "That's exactly what had happened in San Diego," she says.

SenesTech's discovery might first appear to be rather limited in scope. The truth is exactly the opposite. The obvious market: pet owners who want their pets spayed without the necessity of surgically removing their ovaries and uterus.

"With our technology," says Mayer, "while FiFi is at the vet getting her puppy shots, she gets one more and she'll be sterile without having to undergo an invasive operation." The market for this application alone could be \$300 million.

There are other uses as well, including in agriculture. A female heifer with her reproductive ability intact gains 1 to 2 pounds a day. If she's sterile, she'll gain 4 to 5 pounds a day. The implications for beef production are huge. Also, wildlife populations might be better controlled. Rodent infestations might be averted. And far, far down the road, there might be human potential as well for women undergoing difficult menopausal transitions.

SenesTech maintains only five people because the production has been licensed to Jackson Laboratories for implementation. SenesTech derives licensing and consulting fees, and Mayer sees the company's potential as "pretty much unbounded."