NanoBiotech News

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Stock market responds modestly

Abraxane comes through with proof of superiority, scientific endorsements

By Jane Salodof MacNeil

SAN ANTONIO, TX -- After months of controversy, the researchers behind the nanodrug Abraxane came through with the goods in its scientific debut at the 26th annual San Antonio Breast Cancer Symposium.

The results of the phase III clinical trial comparing Abraxane to Taxol were as good as American Pharmaceutical Partners, Inc. (APP) said they would be. An overall tumor response rate of 33% vs. 19% for Taxol was just one of the endpoints where Abraxane came out ahead.

Several prominent breast cancer researchers were sufficiently impressed with the data that they endorsed Abraxane at a press briefing. Edith A. Perez, MD, head of the breast cancer program at the Mayo Clinic in Jacksonville, FL, as well as a profes-

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Pharmacogenomics initiative launched

FDA moves to implement guidelines for submitting microarray data for INDs

By Marie Powers

In a move indicative of growing regulatory scrutiny over nanobiotech activities, the U.S. Food and Drug Administration (FDA) has issued proposed guidance on the submission of microarray data that would accompany an investigational new drug (IND) application.

The "Draft Guidance for Industry: Pharmacogenomic Data Submissions" encourages drug and biologic developers to conduct pharmacogenomic tests during drug development and clarifies how the FDA will evaluate the resulting data. The agency released the guidance to help researchers "turn the explosion of pharmacogenomic information into real evidence on new drugs," according to FDA commissioner Mark B. McClellan, MD, PhD.

Pharmacogenomics deals with the small genetic

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Nanocrystalline drug moves into phase II trials for dermatitis indication

By Rosemary Clandos

Nucryst Pharmaceuticals Corp. has launched a phase II clinical trial for its nanocrystalline silver drug designed to treat inflammation and infection associated with an itchy form of eczema -- atopic dermatitis.

A subsidiary of Westaim Corp. (NASDAQ:WEDX; TSE:WED) Nucryst is winking at an $800 million market for anti-inflammatory topical products that treat eczema, psoriasis, and acne if the trials prove the drug's safety and efficacy.

Although the study will answer questions related only to atopic dermatitis -- a condition that affects 20% of the general population -- the product

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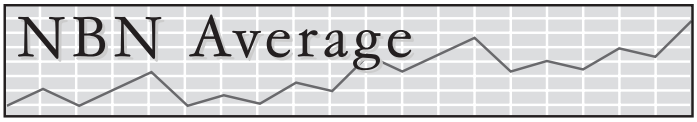

Company	Symbol	Close 12/02	Close 12/09	% Change
Acacia Research Corporation	ACTG	$ 5.50	$ 5.46	-0.73%
Accelr8 Technology	ACLY.OB	$ 2.64	$ 2.50	-5.30%
Aclara Biosciences	ACLA	$ 3.44	$ 3.57	3.78%
Advanced Magnetics	AVM	$ 14.50	$ 14.19	-2.14%
Advectus Life Sciences	AVXSF.PK	$ 0.06	$ 0.06	9.09%
Affymetrix	AFFX	$ 25.44	$ 24.23	-4.76%
Agilent Technologies	A	$ 27.80	$ 26.86	-3.38%
Altair Nanotechnologies	ALTI	$ 2.37	$ 2.16	-8.86%
American Pharmaceutical Partners	APPX	$ 38.58	$ 34.60	-10.32%
Biophan Technologies	BIPH.OB	$ 0.35	$ 0.43	22.86%
Caliper Technologies	CALP	$ 6.42	$ 6.16	-3.99%
Cepheid	CPHD	$ 7.93	$ 8.06	1.64%
Ciphergen Biosystems	CIPH	$ 11.05	$ 10.40	-5.88%
CombiMatrix	CBMX	$ 3.82	$ 3.83	0.26%
Emergency Filtration Products	EMFP.OB	$ 0.52	$ 0.56	7.69%
Flamel Technologies	FLML	$ 31.87	$ 28.16	-11.64%
i-STAT	STAT	$ 12.80	$ 12.58	-1.72%
Nanobac Pharmaceuticals	NNBP.PK	$ 0.80	$ 0.77	-3.75%
Nanogen	NGEN	$ 3.79	$ 6.02	58.84%
Nanophase Technologies	NANX	$ 7.50	$ 7.10	-5.33%
SkyePharma	SKYE	$ 13.57	$ 13.56	-0.07%
TOTAL		220.74	211.26	▼ -4.29%

Nanoscience Technologies launched to commercialize DNA nanomechanics

By Bruce Goldfarb

Innovative research into developing synthetic DNA nanomechanical devices has been spun off by New York University into a publicly traded company. Nanoscience Technologies, Inc. (OTCBB:NANS) will commercialize discoveries from the laboratory of chemist Nadrian C. Seeman, a pioneer in DNA nanotechnology.

Researchers in Seeman's lab make molecular tinker toys out of synthetic DNA, exploiting the molecule's branching and stickiness to create stick figures. By taking advantage of the architectural properties of DNA, the group has created cubes, truncated octahedrons, and other nanomechanical shapes.

The research has far-reaching application in pharmaceutical development, nano-electronics and materials science. Ultimate goals of the approach include the development of a biochip computer, nanorobotics, and the rational synthesis of biological molecules.

Nanoscience Technologies licensed intellectual property from Seeman's lab, including a portfolio of five issued U.S. patents and three pending applications -- and all discoveries coming from the lab in the future. The company has exclusive worldwide rights to develop, manufacture, use, lease or sell any product related to the research project.

Nanoscience Technologies will pay NYU $1.6 million over a four-year period. The initial payment of $300,000 to NYU was funded by the private placement of 1,220,192 shares of common stock for $400,000, which was completed in October 2003.

Formerly an inactive shell corporation with no assets or liabilities, an aggregate of 12.8 million of the 23.7 million shares of outstanding common stock were contributed back to the company for cancellation on Oct. 20. As a result, the company now has a

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NanoBiotech Deals

Acquisitions, Alliances, Collaborations, Licensing Agreements, Mergers

Companies/Organizations	Date	Deal Type	Details
Affymetrix, Inc. Santa Clara, CA (NASDAQ:AFFX) *and* Qiagen N.V. Venlo, The Netherlands (NASDAQ:QGENF)	10/31/03	Collaboration	This alliance is designed to optimize Qiagen's siRNA-mediated gene silencing technology using Affymetrix GeneChip microarray technology. The companies are working to standardize analysis of gene silencing effects on a genome-wide basis. Terms of the deal were not disclosed.
Affymetrix, Inc. Santa Clara, CA (NASDAQ:AFFX) *and* Arcturus Biosciences, Inc. Mountain View, CA	12/4/03	Collaboration	Affymetrix and Arcturus are jointly developing new tools that will enable researchers to conduct gene expression analysis on paraffin-embedded clinical biopsy samples using Arcturus reagents and a new Affymetrix custom human array. The companies say that Arcturus' Laser Capture Microdissection instruments and Affymetrix's Paradise Reagent System for processing formalin-fixed, paraffin-embedded tissue samples will provide researchers with the ability to perform whole genome expression analysis on biopsy samples. Terms of the deal were not disclosed.
Nanoscience Technologies, Inc. New York, NY (OTCBB:NANS) *and* New York University New York, NY	11/20/03	License agreement	NYU granted to Nanoscience a license to certain pre-existing inventions and certain intellectual property to be generated by a designated research project being conducted at NYU relating to DNA nanotechnology. Nanoscience has agreed to provide to NYU minimum funding in the amount of $1.7M in installments commencing on 9/15/03 through 5/1/07, plus additional fees and expenses. The agreement further provides that NYU grants to Nanoscience an exclusive worldwide license to develop, manufacture, use, lease or sell any licensed products and/or processes related to the research project, together with the right to grant sublicenses. Nanoscience will pay a royalty fee of a varying amount from sales of products and for sublicenses. Nanoscience also has issued shares of its common stock to NYU.
Protiveris, Inc. Rockville, MD *and* UT-Battelle LLC Oak Ridge, TN	12/3/03	License agreement	Protiveris finalized an agreement with UT-Battelle to acquire the worldwide commercial rights to proprietary sensor technologies. Developed by scientists at Oak Ridge National Laboratory, the sensor technologies are covered by several issued patents detailing utility across a broad range of applications. Protiveris will be applying these sensor technologies to microcantilever measurements of biomolecular interactions. Terms of the deal were not disclosed.

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total of 10.8 million issued and outstanding shares -- nearly 45% of which is owned by NYU.

Company president Edward F. Cowle declined to describe specific projects or applications intended for development. "The license was just signed, and we're just getting started," he says. "We're still putting together collateral material that will explain all these things."

Over-the-counter trading of Nanoscience Technologies is expected to commence during the first quarter of 2004. "We're not in a hurry, because we funded what we had to," says Cowle.

Editor's Note: Contact Edward F. Cowle at (212) 557-4005. ⊙

Nanocapsules may offer safe, efficient delivery for tumor-targeting biopharmaceuticals

By Marie Powers

As it nears completion of a one-year, $250,000 grant from the National Cancer Institute (NCI), privately held GeneSegues, Inc., of Minneapolis, MN, is scaling up to launch the next preclinical phase in its development of antisense therapeutics for advanced head neck and prostate cancers based on a nanoencapsulated delivery system. Human trials of the tumor-targeted nanocapsules in conjunction with an investigational new drug (IND) application are expected to begin in 2006, says Gretchen M. Unger, PhD, the company's president.

Antisense oligonucleotides have generated keen interest as therapeutic molecules since their initial demonstration in the 1970s, but their full realization as effective human therapies has been limited by inadequate drug delivery to the specific cellular compartment of targeted tissue, Unger points out. The delivery system developed by GeneSegues "delivers macromolecules intact to the nucleus of cancer cells without generating an inflammatory response," she tells *NanoBiotech News*.

Nano-sizing the particles is the key, says Unger, who comes to nanobiotech drug development from a background as an industrial coatings chemist and process engineer. Below the threshold of 50 nm, biologics behave more like small molecules, with optimal penetration of tumors and cells, she explains. The patented nanocapsule developed by GeneSegues also protects the fragile biologics while misleading the immune system in a formulation Unger likens to a therapeutic "Trojan horse."

By taking advantage of caveolar endocytosis for efficient transit, "the nanocapsules are distributed throughout the body within 40 seconds but are taken up only by the cancer cells," she says, adding that the active compound accounts for more than 60% of the nanocapsule's total weight. Initial studies of the nanocapsules were successful using a topical formulation, demonstrating the compound's ability to penetrate even the body's most resistant cellular structure. Additional studies show tumor-targeted nanocapsules home in on solid tumors following systemic administration, which is the principal route of administration the company is pursuing.

GeneSegues' preclinical work has focused on treatment of recurrent squamous cell carcinoma of the head and neck -- a disease with a five-year survival rate of less than 50% that has not improved in more than two decades -- with advanced prostate cancer as a follow-on. More than 140,000 of these cases are diagnosed annually in the U.S., Europe, and Japan, Unger says. During in vivo experiments, a systemic nanocapsule formulation has demonstrated the ability to eradicate 9mm to 11mm cisplatin-resistant tumors in mice, with no metastasis in distant organs, such as the kidneys or liver.

To leverage its resources, GeneSegues also is adapting the delivery technology for other potentially significant commercial applications.

Commercial production to begin in 2004

"By modifying the nanocapsule formulation, we have demonstrated proof of principle capabilities in areas of cardiovascular drug delivery, siRNA cellular delivery, tumor imaging, and drug discovery work pertaining to functional genomics research in laboratory animals," Unger says. GeneSegues is studying plans to begin commercial production next year of mouse reagents for third-party genomics research, using the nanoencapsulation process.

Unger has presented the nanoencapsulation methodology to the American Association of Pharmacy Scientists (AAPS) and the American Association for Cancer Research (AACR). A manuscript describing the nanoencapsulation process is under review for publication in a peer-reviewed journal.

Founded in 1999, GeneSegues funded all of its early research through a family round of financing, according to Unger. This spring, the company received the NCI grant through a special initiative within the Small Business Innovative Research (SBIR) program. The initiative, Flexible System to Advance Innovative Research for Cancer Drug Discovery by Small Business (FLAIR), is designed to support drug discovery and development.

With one patent received this fall[1] and four Patent Cooperation Treaty (PCT) applications in

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sor of medicine at the Mayo medical school in Rochester, MN, called for the U.S. Food and Drug Administration (FDA) to hurry up and approve Abraxane so oncologists could get the new, improved form of paclitaxel to their patients.

Investors responded modestly to the news, which was presented on Friday. APP's stock (NASDAQ:APPX) increased from $33.92 on Thursday to $35.92 per share by Monday. It closed at $34.60 on Tuesday, down a total of 10.3% from the week before any news was released. APP's 52-week range is $10.55-$44.15. Movement in the stock may have also been affected by additional positive news that the company's generic equivalent of Wyeth's Pipracil, Piperacillin for injection, received FDA approval. The drug, which is not derived using nanotechnology, is a third-generation antibiotic indicated for the treatment of serious infections caused by pseudomonas. Piperacillin is active against a variety of Gram-positive and Gram-negative aerobic and anaerobic bacteria.

APP's parent company, American Bioscience, Inc., in Santa Monica, CA, added to the hoopla with a poster presentation on new research that may explain why the nanotechnology works. A new acronym emerged -- NAB, or nanoparticle albumin-bound -- that can go before paclitaxel or any other drug modified by the same process.

"The $64 million dollar question is, will the FDA approve this drug? And, I think, why won't they?" said Amir L. Ecker, a principal in ACT Capital Management, a Wayne, PA-based venture capital firm that has been a major APP investor.

Patrick Soon-Shiong, MD, founder, chairman and CEO of American Bioscience and APP, set off the latest controversy in September when he announced that Abraxane had proved itself superior to Taxol in the clinical trial crucial to winning FDA approval. Soon-Shiong declined to give the data, however, insisting that the information be presented at a scientific meeting. This, in turn, brought announcements of a class-action lawsuit by investors charging he had mishandled and misrepresented the trial. (See *NanoBiotech News*, Nov. 5, 2003, p. 1.)

From the outset, Soon-Shiong had his sights on the San Antonio symposium, which this year drew more than 6,000 oncologists from 81 countries. The symposium had never allowed late additions to its program, however. But it broke precedent, adding a "late-breaker" session Friday night so that fresh research from four major studies could be presented.

Let the data speak

Investigator Joyce O'Shaughnessy, MD, delivered the Abraxane data. She is co-director of breast cancer research and director of breast cancer prevention at Baylor-Charles A. Sammons Cancer Center, US Oncology in Dallas, TX.

The study randomized 229 women to Abraxane, and 225 to Bristol-Myers Squibb Co.'s Taxol. A large number were in Russia, which recently participated in several major trials, according to O'Shaughnessy.

All the patients had metastatic breast cancer, so high response rates were not expected for either drug. Among the high points for Abraxane were tumor response rates of:

- 42% vs. 27% among patients receiving their first chemotherapy for metastatic breast cancer;
- 26% vs. 13% in patients with liver metastases; and
- 43% vs. 25% in patients with lung metastases.

Median time to progression, another key measure, was longer with Abraxane: 21.9 weeks vs. 16.1 with Taxol. While both treatments were well tolerated and completed by 98% of patients, women on Abraxane received a higher dose of paclitaxel, the active drug in both formulations.

Lower toxicity is a major bonus

APP has built a large part of its case on the claim that Abraxane has lower toxicity than Taxol. Despite no pretreatment with steroids, as is required so that patients can tolerate Taxol, none of the women on Abraxane had hypersensitivity reactions. Moreover, only 9% of the women on Abraxane had grade 4 neutropenia compared to 22% on Taxol.

Abraxane did have a higher incidence of grade 3 sensory neuropathy: 10% vs. 2%. Patients recovered significantly faster, however: a median of 22 days vs. 79 days. O'Shaughnessy suggested this was a sign that patients were receiving more paclitaxel in their tumors, since neuropathy is a side effect of paclitaxel and not the solvent that adds to Taxol's toxicity.

APP has been saying all along that its drug is less toxic because it does not use Cremophor, a castor oil derivative, to package the insoluble taxane. Instead, Abraxane delivers paclitaxel in a nanoparticle between 100 nm and 200 nm in size that slips through gaps between cancer cells to penetrate tumors.

Albondin is the carrier

What was not clear up to now was how the nanoparticle gets inside the tumor cell. Neil Desai, PhD, vice president, research and development at American Bioscience, presented new research that attributes the process called transcytosis to albondin, also known as the gp60 receptor for albumin, a protein that transports fatty acids within the body. Albondin takes the albumin-bound nanoparticle

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through the cell wall, according to Desai.

Once inside, albumin releases the drug. In contrast, Desai said Cremophor has an affinity for paclitaxel and resists letting go. He presented data documenting higher tumor penetration with Abraxane.

American Bioscience has indicated it is trying to apply its technology to docetaxel (Taxotere), another taxane in competition with paclitaxel, and to other compounds. Desai estimated about half the compounds identified in drug discovery are insoluble, and that, he said, is a major obstacle to developing some of the most potent compounds.

A diverse future for NAB

I. Craig Henderson, MD, of the University of California San Francisco, suggested that NAB could be the answer to a problem that long perplexed cancer researchers. Why does increasing the dose of many drugs not make them more effective? Getting more drug to the patient does not necessarily get more drug to the tumor, he said.

Henderson and Perez were so enthusiastic about Abraxane that they were questioned at a press briefing on whether they had stock in APP. Both said they had nothing to do with the companies behind Abraxane or the clinical trial -- that they had, in fact, only recently seen the data.

Survival data is yet to come. O'Shaughnessy said it is not mature, but the trial should have data on about a third of the patients in six months or so. Meanwhile, another phase III trial has started with a different dosing schedule, she said.

APP has formed a new subsidiary, Abraxis Oncology, to market Abraxane, assuming the FDA gives approval. For Ecker, getting the drug to market will be the best answer to a lawsuit he describes as frivolous

"If it has a reasonably safe side effect profile, get it out there where it's treating tens of thousands," he said. "The doctors will know. The market will tell you right away whether it's successful." ⊙

Microarray data from Page 1

differences that help to explain why some people respond positively to a drug while others don't respond at all or experience a negative side effect. Genetic differences also can predict variations in drug metabolism. Pharmacogenomic testing can be smoothly integrated into the drug development process, the FDA maintains.

The guidance, which is open to public comment for 90 days from its release on Nov. 3, provides recommendations to sponsors holding INDs, new drug applications (NDAs), and biologics license applications (BLAs) on the timing for submission of pharmacogenomic data, the formats that should be used, and the methodology the FDA will use in regulatory decision making. This guidance covers only tests developed in conjunction with drug therapy, but the FDA eventually plans to provide guidance on the use of genetic or genomic techniques for biological product characterization, such as cell bank characterization and bioassays.

Iconix helps guide FDA

Mountain View, CA-based Iconix Pharmaceuticals, Inc. has worked with the FDA's Center for Drug Evaluation and Research (CDER) since late 2002 on the pharmacogenomics initiative. The company's DrugMatrix platform, a large-scale chemogenomics reference database and informatics system, contains the results of thousands of gene expression and molecular pharmacology experiments. Its Drug Signature library is the largest collection of predictive biomarkers in the pharmaceutical industry, according to the company.

"The FDA came to us with two questions," recalls Jim Neal, CEO of privately held Iconix. "If the agency asks for and receives microarray data, how does it know if the drug developer used a good standard and produced good data? Second, how should the agency interpret the gene expression profile?

"Gene expression data for new drug candidates must be viewed in the context of well-characterized drugs and reference compounds, if it is to have any meaning," Neal says.

Iconix completed more than 15,000 expression array experiments in the construction of DrugMatrix, which has demonstrated the ability to profile experimental compounds independent of the specific microarray platform used to generate the gene expression data. The company installed DrugMatrix at the FDA last January and has partnerships with other life sciences companies, including MDS Pharma Services (NYSE:MDZ), Incyte Corporation (NASDAQ:INCY), and Amersham Biosciences (NYSE:AHM). Iconix also has collaborations with Schering-Plough Research Institute (NYSE:SGP), Millennium Pharmaceuticals, Inc., and Eisai Co., Ltd.

Iconix is now developing a model "mock" submission of microarray data for the FDA to test the actual submission of an IND under the proposed guidance. The research is designed to provide the agency with hands-on experience using chemogenomic data and tools, including the application of molecular toxicology markers to predict drug actions. Streamlining the approval of new

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Microarray data *from Page 5*

molecules could reduce the overall cost of new drug development, Neal points out, but the FDA still needs to ensure the safety of new drugs.

The mock submission from Iconix presents a toxicology evaluation of an approved drug that combines traditional toxicology methods with the novel use of gene expression data and genomic-based biomarkers of drug toxicity. The mock submission depends heavily on the use of DrugMatrix and Drug Signature.

"The FDA wanted to know what gene expression data submitted as part of an IND package would look like," Neal says. "The mock submission is designed to help the agency determine whether it has the systems and processes in place to handle the volume of data from these submissions."

The mock submission responds to many of the questions raised in the draft guidance, which includes several illustrative examples of required and voluntary submission of pharmacogenomic data. The Nonclinical Pharmacogenomics Subcommittee of CDER's Pharmaceutical/Toxicology Coordinating Committee expects to receive the mock genomic data submission from Iconix early next month.

FDA officials declined to explain the timing of the new guidance beyond information conveyed in the document itself, which notes "pharmaceutical sponsors have been reluctant to embark on programs of pharmacogenomic testing during the FDA-regulated phases of drug development because of uncertainties in how the data will be used by the FDA in the drug application review process."

Any submission of pharmacogenomic data to the FDA "needs to be dealt with on a scientific basis," Neal agrees. As for timing, the FDA's move recognizes the level of consistency of microarray data, which now reflects "reproducible results from batch to batch and lab to lab," Neal says. "Microarrays have been around for a long time, but only in the last few years has this become a robust, stable platform."

Rapid evolution of pharmacogenomics

According to the guidance, the FDA anticipates a rapid evolution of pharmacogenomics, from its current use primarily in studying drug metabolism to its eventual role in predicting the probability that a certain cancer will respond to a particular compound or in identifying the cause of rare, serious drug side effects.

The implicit message of the FDA to the pharmaceutical and biologics community is that "microarray gene expression will become part of the standard new drug development process," Neal predicts. "It's not clear whether these data will be required in five years or 10 years, but the earlier developers get into this technology, the better they will be.

"Each molecule has an impact on many parts of the body -- not just the target cells," he adds. "The FDA wants to understand both the assets and the toxicology impact earlier in the drug discovery process, and chemogenomics improves that predictability. This is all part of the continuing impact of nanotechnology. There are many positive effects on the discovery side, but developers can expect more oversight from the FDA."

Editor's Note: Contact Jim Neal at (650) 567-5500. The draft guidance is available at www.fda.gov/cder/guidance/5900dft.pdf. ⊙

Nucryst Pharmaceuticals *from Page 1*

formulation may also be helpful in the treatment of psoriasis. Additionally, the anti-microbial and anti-inflammatory properties of nanocrystalline silver could potentially be used to treat acne.

"Those are three big market areas for dermatology," Scott H. Gillis, president of the Wakefield, MA-based firm, tells *NanoBiotech News*. "The efficacy and safety profile of our drug will have a big impact on the portion of the market that we can capture."

The trial, which began in late November at 20 clinical sites in the U.S., involves 180 adults with mild to moderate forms of atopic dermatitis. "It's not limited to that population," says Gillis. "It is very possible that it could be used for more severe forms of eczema."

Silver has been used to treat infections for centuries. Some old medical literature states that a thin film of silver foil placed on wounds can reduce redness. For decades, silver nitrate solution and silver sulfadiazine cream has been used to treat burns and chronic wounds. But now, Nucryst has taken silver on a quantum leap into the nano realm.

Nucryst disassembles large crystals of pure silver and reassembles them in a novel nanocrystalline structure that quickly reacts when exposed to body fluids.

"It seems as if this novel form of nanosized silver supercharges its properties," says Gillis. "So it seems to kill bacteria more rapidly and reduce inflammation in a significant way, more than other forms of silver."

Nucryst's in vivo studies have shown that nanocrystalline silver kills microbes within one hour, compared to 24 hours when other forms of silver are used. And it significantly reduces inflammation.

Gillis says researchers don't fully understand all of the healing mechanisms of silver, but in their

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animal studies, they have seen a dramatic reduction in inflammation in contact dermatitis in one or two days. Skin is nearly normal in five days.

Nucryst's nanocrystalline silver could offer patients an alternative to steroids, which may cause side effects such as skin atrophy or thinning, spider veins, and reduced effectiveness with long-term usage.

Since 1998, Nucryst has used its nanocrystalline silver technology in Acticoat, a microbial dressing for burns. In 2001, Nucryst entered a partnership agreement with London-based Smith & Nephew, which moved Nucryst's product from burn units and wound healing clinics in two countries to 27 countries. And product sales are increasing by 50% each year.

"For a small company, we think that partnering is very important," says Gillis.

"However, it's too early for us to have finalized any partnering decisions about our dermatology product."

Other indications in the works

In the meantime, Nucryst has considered ways to deliver nanocrystalline silver through inhalation to treat lung diseases and inflammation.

"Conceptually, we can go many places with this technology," says Gillis. "As a small company we need to focus our energy and we've chosen dermatology. It's a natural step from wound dressing."

"In the longer term, we'd like to look at gold and platinum and see if our nanocrystalline structures can enhance the properties of those metals. But I'm a big believer that you need success commercially and scientifically. Once we have success in the other areas, then there is clearly more research that we'd like to do," says Gillis.

Although Nucryst is ahead of its schedule for clinical trials, Gillis says that it will still take about four to seven years before the FDA could approve the eczema product on a traditional track.

Editor's Note: Contact Scott H. Gillis at (781) 224-1444. ⊙

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the works, Unger is scaling up the company's internal production processes and committed to seeing the nanocapsule formulation through to development. Her experience in both engineering and life sciences has heightened her attention to developing a platform that is fully scalable, from the lab to the production line.

"We're always looking for ways to raise money, especially through contract formulation," Unger says, "but we're also looking to develop additional applications of our own formulations -- primarily in oncology therapeutics but also in other applications that make business sense."

Editor's Note: Contact Gretchen M. Unger at (952) 443-3798.

Reference

1. U.S. Patent 6632671: Nanoparticle encapsulation system and method. ⊙

Food-borne pathogens stimulating microarray-based biosensor development

By Bruce Goldfarb

The recent deadly U.S. outbreak of hepatitis traced to imported green onions, which killed three people and sickened 600 in Pennsylvania, is the latest public health scare caused by food-borne pathogens.

Since the emergence of O157:H7, a lethal strain of *E. coli* bacteria, a decade ago, the development of compact microarray-based biosensors to detect food-borne pathogens has become a national priority. The need has become even more urgent in the last two years, as the same technology can be applied to detect bioterror agents.

Major biochip companies such as Affymetrix, Inc. (NASDAQ:AFFX) and Nanogen, Inc. (NASDAQ:NGEN) have expressed interest in the food safety biosensor market, but at present academic research groups appear to have the lead.

At least three university-based research teams are working on the biosensor problem, integrating the efforts of engineering, microbiology and biochemistry to develop a portable device that can detect pathogens rapidly, accurately and affordably.

Technology developed under U.S. Department of Agriculture funding at Purdue University is being spun off into a start-up, BioVitesse (West Lafayette, IN), to commercialize a food safety biosensor.

"We are working towards developing a prototype that we can beta test at a customer site," says Purdue researcher Rashid Bashir, who co-founded BioVitesse in 2002.

An estimated 76 million Americans suffer food-borne illness annually, according to the Centers for Disease Control and Prevention (CDC). The true scope of the problem is unknown, since many cases are mild or undiagnosed.

E. coli O157:H7 hit the national radar in 1993,

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when an outbreak of the deadly strain in ground beef patties sold by a West Coast fast food chain sickened more than 700 customers and resulted in the deaths of four children. *E. coli* O157:H7 is responsible for about 73,000 cases of food-borne illness and 21 deaths annually in the U.S., according to the CDC.

Reducing testing period from days to hours

At present, testing for microbial contamination within the food processing system relies on traditional laboratory methods that take two to seven days to complete. Typically, samples of meat or poultry are obtained during processing and tested in a clinical laboratory.

"Our technology is focused on reducing the total time to result down to a few hours, compared to today's two to seven days," says Bashir.

One of the driving forces behind the development of food biosensors is the U.S. military, which is concerned about the effect an outbreak of food poisoning could have on readiness. In 2001 the U.S. Army Soldier Systems Center in Natick, MA, field-tested a biosensor system developed by researchers at the University of Rhode Island.

At the heart of the suitcase-sized biosensor system are magnetic spheres, 2-3 micrometers in diameter, that are coated with antibodies for pathogens of interest. A sample of food is liquified and mixed with the microspheres, then focused with a magnet in front of a fiberoptic element and energized with laser light. If the sample fluoresces, it's contaminated.

Researchers at Georgia Institute of Technology, in Atlanta, have developed a smaller biosensor based on a laptop computer that can simultaneously detect 12 different pathogens using enzyme-linked immunosorbent assay (ELISA). The Georgia Tech device was tested in 1999 at the Gold Kist poultry processing plant in Carrollton, GA.

Bashir's group at Purdue developed a disposable antibody-loaded microfluidic biochip that identifies pathogens by their unique electrical impedance. "We're developing a technology platform that could be applied to any specific microorganism so long as you have the antibodies for it," he says.

In January 2003, BioVitesse signed a license agreement with Purdue allowing the company to develop and commercialize the biosensor system. The company received a Phase I Small Business Innovation research (SBIR) grant from the National Science Foundation, and is presently raising capital.

Although considerably smaller and faster than its clinical laboratory counterparts, the biosensors developed to date are table-top devices and not inexpensive hand-helds, which would be more suitable for widespread use in restaurants, supermarkets and other places where food-borne disease can spread.

"Eventually, in the long term, we would like to have a hand-held device that gives instantaneous detection of specific bacteria from any sample, but there are a lot of practical and interesting challenges to overcome," says Bashir.

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Quantum dots being developed for cancer detection, heart disease

By Rosemary Clandos

After developing a new type of nanocrystal quantum dots for biomedical research, Shuming Nie is already making improvements to them.

Quantum dots are a new class of biological labels that conjugate biological molecules to semiconductor material for targeting proteins and DNA. They replace fluorescent dyes used in medical and biological applications.

Nie, director of cancer nanotechnology at Winship Cancer Institute and associate professor of bioengineering at Emory University, Atlanta, GA, and his team developed the fluorescent dots and now they're finding ways to make them more functional for diagnostics and drug discovery.

"If you make changes in the early stages, that's the best time," says Daniel Farkas, director of molecular diagnostics at Methodist Hospital in Houston, TX, and associate professor of pathology at Baylor College of Medicine. "Once you get a little further down the marketing road, it becomes more difficult to make changes. You reach certain milestones in the development process where you have to put a stake in the ground and move forward, not backward."

Nie's efforts are expected to produce quantum dot technology that can be used for detecting cancer cells and plaque build-up in blood vessels, which causes cardiovascular disease. The dots would be used also for fundamental cell biology, such as labeling the receptors on a cell's surface in order to observe the cell's behavior.

"That is very cool stuff and very futuristic," says Farkas. "It has the potential to create many diagnostics."

Toxicity is still an issue

Nie's long-range goal is to use quantum dots to observe biological processes in humans -- an

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application that's out of the question now because of toxicity issues.

However, in the meantime, he's moving ahead with other tasks that will help him reach that goal, such as changing the surface coating of the dots so they can move across cell membranes. Nie says the results from that research will be published in about six months.

Made from cadmium selenide and having a zinc sulphide cap, the biocompatible dots are water-soluble and they link covalently to large molecules. To energize the dots, researchers use a laser light or mercury lamp.

But having the dots link only to large molecules won't solve many problems in drug discovery. Most pharmaceutical drugs are small molecules and many targets are already known for them. Drug companies would have more use for quantum dots that conjugate with small molecules. So Nie has been researching ways to enable the nanocrystals to link with small molecules and target diseased cells.

Quantum dots were originally developed by a process that associates the color of the dots to their size, which makes it easy to color-code the dots to biologic activity. But sometimes the size of the dots can inhibit optimal usage. Nie's team found that altering the ratios of the materials used to construct the dots changes their emission color, but not their size. Having a uniform size and surface area, the dots will be able to travel at a consistent speed, uniformly bind to their targets, and penetrate deeper into biological tissue.

The group also is making adjustments to the alloy so that the dots will emit color in the near infrared. With that advancement, the dots will have better capabilities to penetrate tissue, skin, and bone.

Working to overcome hurdles

The Nie group still faces some research hurdles though.

"To develop biological sensors, you need to turn the luminescence on and off," says Nie. "If the signal is always on, you can't see any changes in the biological material. You don't know if other molecules have bound to the particles. It's very difficult; we're still thinking about how to overcome that."

And they're a long way off from setting up the dots to target viruses.

The patented technology has been licensed to Quantum Dot Corp., in Hayward, CA., and Crystalplex Corp., based in Pittsburgh, PA. Funding for the project came from the National Institutes of Health -- about $500,000 a year for the last five years, says Nie.

Nie says, "I think we're going to make some significant improvements to this technology and then move on to something else. We'll leave this technology to others and take on a different challenge."

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