

# NANOBIOTECH NEWS

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## American Pharmaceutical, American BioScience to merge, create Abraxis Bioscience

By Marie Powers

American Pharmaceutical Partners, Inc., (APP) (NASDAQ:APPX) is purchasing privately held American BioScience, Inc., (ABI) -- its parent company and largest shareholder -- to form a biopharmaceutical company valued at \$7.5 billion.

The new entity, Abraxis BioScience, will integrate the U.S. Food and Drug Administration-approved oncology drug Abraxane, which uses the company's nanoparticle-albumin-bound (nab) technology, with the company's deep product pipeline, a hospital-based injectables business with positive operating cash flow, commercial-scale nanoparticle manufacturing capabilities, and a proven R&D and regulatory affairs team.

The all-stock transaction is expected to close during the first half of 2006. ABI, of Santa Monica, CA, currently owns approximately 64.4% of the outstanding fully diluted shares of Schaumburg, IL-  
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## Innovata emerges as first suitor in acquisition play for SkyePharma

By Marie Powers

London-based SkyePharma PLC (NASDAQ:SKYE, LSE:SKP) is reviewing its options after receiving an unsolicited offer from a third party earlier this month. After nearly two weeks of speculation, last week Nottingham-based Innovata PLC (LSE:IOV) confirmed it was the potential suitor in the deal, though more parties may emerge in the coming days or weeks, sources tell *NanoBiotech News*.

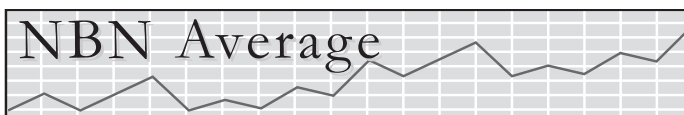
SkyePharma uses a controlled release drug delivery technology to improve the safety and efficacy of existing drugs, with 10 approved products and more than a dozen additional candidates under development in the oncology, neurology, dermatology, pain management, asthma, and cardiovascular therapeutic categories. Its oral, injectable, inhaled, and topical delivery platforms are supported by the company's "enhanced solubilization," or nanopar-  
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## Emory, Georgia Tech developing personalized cancer treatments at new nanotech center

By Steve Lewis

*Editor's Note: This is the sixth in a series of articles featuring seven university-based Centers of Cancer Nanotechnology Excellence (CCNE) recently funded with a \$26.3 million investment from the U.S. National Cancer Institute.*

Emory University's and the Georgia Institute of Technology's new Emory-Georgia Tech Nanotechnology Center for Personalized and Predictive Oncology in Atlanta will function as a discovery accelerator to integrate nanotechnology into personalized cancer treatments through the development of bioconjugated nanoparticles for cancer molecular imaging, molecular profiling and personalized ther-  
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Company	Symbol	Close 11/15	Close 11/29	% Change
Acrogenomics	AGNM	\$ 4.95	\$ 4.85	-2.02%
Advanced Magnetics	AVM	\$ 9.11	\$ 10.66	17.01%
Altair Nanotechnologies	ALTI	\$ 2.31	\$ 2.44	5.63%
American Pharmaceutical Partners	APPX	\$ 45.55	\$ 37.29	-18.13%
Arrowhead Research	ARWR	\$ 4.05	\$ 3.70	-8.64%
Biodelivery Sciences	BDSI	\$ 2.10	\$ 2.45	16.67%
Biophan Technologies	BIPH.OB	\$ 1.85	\$ 1.76	-4.86%
Biosante Pharmaceuticals	BPA	\$ 4.27	\$ 4.37	2.34%
Flamel Technologies	FLML	\$ 17.98	\$ 19.10	6.23%
Introgen Therapeutics	INGN	\$ 5.97	\$ 6.19	3.69%
Nanobac Pharmaceuticals	NNBP.OB	\$ 0.05	\$ 0.04	-6.52%
Nanogen	NGEN	\$ 3.04	\$ 2.85	-6.25%
Novavax	NVAX	\$ 3.49	\$ 3.28	-6.02%
pSivida	PSDV	\$ 5.47	\$ 4.64	-15.17%
SkyePharma	SKYE	\$ 9.23	\$ 8.05	-12.78%
Starpharma Holdings Limited	SPHRY.PK	\$ 3.55	\$ 4.35	22.54%
<b>TOTAL</b>		<b>122.97</b>	<b>116.02</b>	<b>▼ -5.65%</b>

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## Mersana raises \$21 million in oversubscribed funding

By Steve Lewis

Mersana Therapeutics, Inc. (formerly Nanopharma Corporation), a privately-held cancer therapeutics company based in Cambridge, MA, has completed an oversubscribed \$21 million financing.

Fidelity Biosciences and ProQuest Investments led the round, with Rho Ventures, PureTech Ventures, Cape Family Fund LLC, Harris & Harris Group, Inc., and Lansing Brown Investments LLC also participating.

Of note was the fact that Fidelity and Proquest had not participated in funding for the company in the past, says Julie Olson, CEO of Mersana. "All of the previous investors [PureTech, Cape Family, Harris & Harris and Lansing Brown] invested more than they had in the past."

From a budgetary point of view, the company had determined that \$21 million was the amount it needed to raise in this round, says Olson. It was "oversubscribed," she explains, because other companies that wanted to participate could not.

With completion of the financing, Jay Moorin and Joyce Tsang, partners at ProQuest Investments, Jason Rhodes, principal at Fidelity Biosciences, and Martin Vogelbaum, partner at Rho Ventures will join existing members Julie Olson and Charles Harris of Harris & Harris Group, Inc. on the board of directors.

The money was raised, Olson says, because "We have compounds in preclinical development and need to move our pipeline forward. This funding will enable us to take our lead product, which has established pre-clinic proof of concept, into the clinic, and to advance other programs so have we have a pipeline behind this product."

The company's technology is based on the discoveries of Mikhail Papisov, MD, of Massachusetts General Hospital, who devised a stealth material called Fleximer that enhances the pharmacokinetics and safety of drugs. "He developed a biodegradable and bio-inert macromolecule," Olson explains. "Other polymers currently being used are either bioreactive, like carbohydrate polymers, or are not biodegradable. The material we work with is quite unique."

Many compounds, she notes, have gone into the clinic in cancer and showed activity in humans, but

could not be developed further due to toxicity. "We took those compounds, some of which are generic, have linked them to Fleximer and shown in many cases we can reduce toxicity," Olson asserts.

For example, Papisov and his colleagues have shown that a water soluble macromolecular conjugate of the cancer drug camptothecin (CPT) demonstrated greater effectiveness than unmodified CPT, with lower toxicity.<sup>1</sup> The company's intellectual property portfolio includes an exclusive license from the Mass General for the core patents<sup>2</sup> and for a complementary technology that links Fleximer to therapeutics.<sup>3</sup>

### Finances solid

Mersana, or Nanopharma as it was then known, was launched early in 2002 by PureTech Ventures, a Boston-based life science venture creation company. Its \$1.1 million in seed financing was led by a \$700,000 stake from Harris & Harris Group, Inc.

The current round of financing is sufficient to carry the company forward for several years, says Olson. "We expect this will take us through the end of 2007, and into 2008," she asserts.

As for the company name change, which became official on Nov. 10, 2005, she says it does not signify any change in the company's management or goals and objectives. "Nanopharma was a good name conceptually for the company because we attach cancer compounds to a nanoparticle, but there tended to be some confusion," she concedes. "There are several companies in biotech that start with 'nano.' Plus, when you hear 'nano' you tend to think of traditional nanotechnology company, and that does not communicate that we are a biotech company."

*Editor's Note: Contact Julie Olson at (617) 498-0020.*

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2. U.S. Patents 5,811,510, 5,863,990, and 5,958,398: Biodegradable polyacetal polymers and methods for their formation and use.

3. U.S. Patent 5,582,172: System of drug delivery to the lymphatic tissues. ©

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## New drug candidates treat atherosclerosis with anti-angiogenic compounds delivered via nanoparticles

By Steve Lewis

Kereos, Inc., of St. Louis, MO, presented pre-clinical data on two therapeutic candidates for cardiovascular disease (CVD) at the American Heart Association Scientific Sessions held earlier this month.

The first presentation, "Magnetic resonance molecular imaging predicts the effectiveness of targeted drug delivery in atherosclerosis," was made by Samuel A. Wickline, MD, co-director of the Cardiovascular Division and professor of medicine, biomedical engineering, and physics, and Gregory Lanza, MD, PhD, assistant professor of medicine and bioengineering, both at Washington University School of Medicine in St. Louis, who developed the technologies from which Kereos was launched in 1999.

It reports on a ligand-targeted emulsion to inhibit angiogenesis, one of the fundamental processes underlying atherosclerosis. They also reported that magnetic resonance imaging (MRI) can be used to assess the delivery of the targeted therapeutic and predict response to it.

A second presentation, "Intramural delivery of Rapamycin with alpha-v-beta-3-integrin-targeted paramagnetic nanoparticles inhibits stenosis following angioplasty," reported on a targeted agent to reduce stenosis, or narrowing of the blood vessels to the heart, after angioplasty to open arteries clogged by atherosclerosis.

The Washington University researchers also demonstrated in a poster the use of a ligand-targeted MRI emulsion in evaluating the effectiveness of L-arginine therapy in peripheral vascular disease (PVD).

"These presentations are all variations on a theme," explains Wickline. "We've invented this nanoparticle that can carry drugs; those that we use to carry the drugs to the sites of pathology can be quite varied, and we can target them to any sites we choose and can deposit the load in a precisely targeted area. We can also have many drugs on a particle."

The process of angiogenesis in CVD is identical to that in tumor growth -- which, Wickline explains, is why the dual thrust of the company's research makes so much sense. "That's one of the keys in targeting angiogenesis -- that we can target both tumors and atherosclerosis, which actually becomes kind of like a tumor," he says. Treating atherosclerosis with anti-angiogenic compounds is fairly new, he says.

Wickline says the studies constituted proof of principle for both the therapeutic and targeting capabilities of the nanoparticles. "We demonstrated that if you take the nanoparticles, inject them and use MRI to image them, you can determine if there is a lot of angiogenesis at the site, and that it will respond to anti-angiogenic drugs," he says.

Such capabilities might some day enable tailored therapy, says Wickline. "You can see if a particular drug should be used on a particular patient, instead of looking at population statistics and determining that the drug is likely to work," he says. "Once you have the diagnosis and give the specific drug, it then has the intended effect, which you can also come back and show by imaging." In this 'show, treat, re-image' process, he notes, "We use each individual as their own control."

In the second study, the researchers found that drug delivery using the ligand-targeted emulsion reduced the amount of stenosis by nearly 50% following balloon overstretch injury in animal models. "This really inhibits plaque development," Wickline says. "The drug is released at the site, targeted with an anti-proliferative. You don't have to put a stent in -- you just put the nanoparticles with the drug (in this case Rapamycin) in, which seems to inhibit primary plaque growth as well."

This could ultimately become useful as a tool for delivering a drug locally without a stent -- and in the right place, Wickline explains. "Sometimes the endothelium does not cover up the stent, and this causes thrombosis. The nanoparticles actually get inside the vessel wall." No needle was necessary; the nanoparticles just "seeped through the cracks" in the vessels.

### Potential stent adjunct

In the future, he hypothesizes, the nanoparticles could be used as an adjunct to a resorbable stent. "The stent would prop the vessel open, but the drug would have its effect over some period of time, inhibiting the inflammation that causes restenotic response," he notes.

The subject of the poster presentation, PVD, involves reduced blood flow that can cause pain in remote areas of the body such as the legs. "Normally, when you try to look for vessels that are not well supplied with blood, you use X-ray angiography," Wickline says. "It is not very sensitive, because you cannot see the really small vessels. This molecular imaging tool can find those small vessels, because you can put in the nanoparticles targeted to them and detect their signal -- sniff them out, as it were." This ability can also lead to more personalized medicine, he adds.

While the traditional imaging method, X-ray

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**Abraxis BioScience** from Page 1

based APP. Based on APP's closing stock price of \$47.61 on Nov. 25, the combined company would have a market capitalization value of approximately \$7.5 billion on a fully diluted basis.

"We believe this merger is a unique opportunity to combine the strengths of a development-stage biotechnology company with those of a growing and profitable injectable pharmaceutical business to create a fully integrated, global biopharmaceutical leader," says founder Patrick Soon-Shiong, MD, who serves as executive chair of APP and chair and CEO of ABI and is slated to become chair and CEO of Abraxis BioScience once the merger is consummated.

"By integrating breakthrough science, validated by the successful commercial launch of the first in-class albumin bound particle chemotherapeutic, applying proprietary nab technologies to compounds of known activity -- thus enabling rapid clinical development -- and leveraging the manufacturing and distribution expertise as well as sales and marketing infrastructure of APP, we are creating a differentiated biopharmaceutical enterprise with the potential for high, sustainable growth and a lower development risk profile," according to Soon-Shiong.

In a conference call to investors and analysts on Monday, Soon-Shiong described the merger of APP and ABI as a "transforming event" that will maximize the opportunity for sustained high growth and enhance long-term profitability and shareholder value.

ABI brings to the table 50% of the profits from North American sales of Abraxane and the marketing rights for the rest of the world. A regulatory filing for Abraxane has been submitted in Canada, and regulatory filings in Europe and Mexico are expected to occur during the first half of 2006, according to company documents. Regulatory filings in other countries, including China, Russia, Korea, Australia, New Zealand, Hong Kong, and Taiwan, will follow later in 2006 and early in 2007.

Abraxane for injectable suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) was approved by the U.S. Food and Drug Administration (FDA) in January 2005 (see *NanoBiotech News*, Jan. 12, 2005, p.1) and launched commercially on Feb. 8, 2005, producing record first quarter net sales and net income for the company. (See *NanoBiotech News*, May 4, 2005, p. 1.) The drug currently is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy, but Soon-Shiong is eager to expand the indications to early stage breast cancer as well as lung, ovarian,

head and neck, and melanoma cancers. A series of clinical studies have positioned the company to move in that direction. (See *NanoBiotech News*, April 13, 2005, p. 1 and Nov. 9, 2005, p. 1.)

Prior to the merger announcement, ABI licensed the marketing rights to Abraxane for Japan to Taiho Pharmaceutical Company, a Tokyo-based oncology company, for upfront and milestone payments in excess of \$50 million in addition to undisclosed royalties. The companies have established a joint steering committee to oversee the development of Abraxane in Japan for the treatment of breast, lung, gastric, and other solid tumors.

Annual taxane sales in Japan are growing, with the Japanese market for chemotherapy agents being approximately \$3 billion. Tokyo-based Taiho is part of Otsuka Pharmaceutical Ltd., one of Japan's largest pharmaceutical companies.

"Taiho is the preeminent Japanese pharmaceutical company in the oncology chemotherapy field, and we believe they are the right partner for us to build a market for and introduce Abraxane in Japan," Soon-Shiong explains. "They have excellent relationships with key Japanese opinion leaders, an experienced product development group with a strong track record, a powerful sales and marketing infrastructure, and a significant portfolio of oncology products."

In addition to Abraxane, ABI brings a deep pipeline of oncology and critical care products based on the company's novel nab technology platform; natural product, therapeutic, and reverse peptide libraries; a research, clinical development, and regulatory team; and intellectual property (IP) built around the nab tumor-targeting technology platform and a tumor-secreted protein known as SPARC (Secreted Protein, Acidic and Rich in Cysteine). ABI has 130 issued and 126 pending patents around the nab platform, Abraxane, and its product pipeline.

**Six NDAs to be filed in 2006-07**

"We expect to be able to use ABI's patented nab technology in other applications to facilitate the efficient, rapid creation of new drug products," Soon-Shiong predicts. "The efficacy risk should be mitigated by developing new drugs using active agents already approved by the FDA. We anticipate that at least six investigational new drug applications [NDA] will be filed through 2006 and 2007, including nab-docetaxel, a solvent-free nab form of the leading taxane Taxotere, which has a current market size of in excess of \$1 billion."

ABI's oncology pipeline candidates target multiple molecular tumor targets including tubulin  
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**Abraxis BioScience** from Page 4

(nab-docetaxel), m-tor (nab rapamycin), HSP-90 (nab-17AAG), topoisomerase 1 plus tubulin (nab-thiocolchicine dimer), and the vascular endothelial cell (oral seco-taxane).

In addition to providing the technological platform for a wide range of oncology drugs, ABI's nab technology also provides a foundation for development of drugs to treat peripheral arterial disease and coronary artery disease. Coroxane, nab paclitaxel, is in mid-stage clinical trials for both coronary and peripheral artery restenosis. Applications relating to coronary artery disease using Coroxane with bare metal stents are in phase II, peripheral arterial disease is in phase II/III, and shunt patency in hemodialysis patients in phase I.

APP brings to the combined company an injectables franchise focused on oncology, critical care, and anti-infective markets; leading market shares across 186 products; a strong history of product approvals; and a product pipeline that includes more than 20 abbreviated NDAs pending at the FDA and more than 40 additional products in development, according to Soon-Shiong. The company also has developed a strategy to compete in the large low molecular weight heparin market.

APP also brings commercial scale protein-engineered nanoparticle manufacturing capacity in the U.S., an established relationship with group purchasing organizations, and a track record of high growth and profitability. Based on estimated revenues of more than \$500 million for 2005, APP's compounded annual growth rate from 1998 through this year is more than 33%, Soon-Shiong maintains.

**Positive cash flow predicted**

The combined company is expected to have positive operating cash flow. ABI's operating expenses are estimated to be approximately \$50 million in 2005 and are projected to be \$75 million to \$100 million next year, including the company's costs for clinical trials.

In July, APP's board of directors formed a special committee of independent members to evaluate and recommend options with respect to APP's potential merger with ABI, Soon-Shiong revealed. Under the terms of the agreement, ABI will merge into APP in a tax-free transaction, with APP issuing approximately 86 million additional shares of APP stock to the ABI shareholders, raising the ABI shareholders' fully diluted ownership of the combined entity after the merger to approximately 83.5% from 64.4% owned through ABI. The boards of directors of both companies have unanimously approved the merger agreement.

APP plans to file detailed merger documents

with the SEC and mail these to shareholders of APP early next year, Soon-Shiong told investors and analysts. The merger is expected to close during the first half of 2006.

**Analysts are cautious**

Despite Soon-Shiong's obvious enthusiasm for the deal, analysts appear more cautious and investors didn't warm immediately to the news. At CIBC World Markets Corp. in New York, analyst Elliot Wilbur didn't even wait until the end of the day to downgrade APP's stock from "buy" to "hold," citing concerns that shareholders will incur significant up-front dilution, with other products in the company's pipeline not expected to produce a revenue stream until 2009 or 2010. A day later, analyst Vinny Jindal at Wedbush Morgan Securities in Los Angeles also downgraded the stock from "sector outperform" to "sector perform."

In defending the merger agreement, Soon-Shiong cited analysts' own valuation of Abraxane in the U.S. alone as worth approximately \$35 per share, or about half the market cap of the merged company. Adding the company's milestone payments, product pipeline, and IP payments more than justifies the transaction price, Soon-Shiong says.

"We have an opportunity to grow a new model of biotech/biopharmaceutical company," he says, noting that the company has been "organically grown" with margins exceeding 50%. Market uptake of Abraxane in the U.S. has been strong, Soon-Shiong adds, despite the challenges of a new sales force and no published data at the time of product launch. Since that time, three editorials and three trial results have been published, and a survey of 75 oncologists conducted by the company in August indicated 91% of the doctors intended to increase their use of Abraxane over the next three months.

The current U.S. taxane market numbers 325,000 patients and generates \$1.2 billion in revenues, but Abraxane provides opportunities to generate increased dosage per cycle, an increased number of cycles, new indications for combination therapy, and new tumor types. "We believe we can redefine the market significantly as we move forward," Soon-Shiong says.

But investors also appear skittish, at least for now. The stock fell more than 16% on Monday, closing at \$39.78 on volume of 7.9 million shares. That slide continued on Tuesday, with the stock off another 5% to close at \$37.29, with 2.8 million shares changing hands. Over the past 52 weeks, APP has traded in a range between \$27.37 and \$58.73, with the high reached in early April.

*Editor's Note: Contact Patrick Soon-Shiong at (310) 826-8505. ☺*

## SkyePharma from Page 1

ticulate, technology, which includes nanosuspensions and solid lipid nanoparticles ranging in size from 40 nm to 1,000 nm.

The company has licenses or partnerships with a variety of big pharma firms, including GlaxoSmithKline PLC (NYSE:GSK), Merck & Co., Inc. (NYSE:MRK), Novartis AG (NYSE:AZN), and Baxter International Inc. (NYSE:BAX). In May 2004, SkyePharma inked a deal with Alpharetta, GA-based First Horizon Pharmaceutical Corporation (NASDAQ:FHRX) for the exclusive U.S. marketing and distribution rights for Triglide, a formulation of fenofibrate that can be taken without food, reducing elevated plasma concentrations of triglycerides and LDL cholesterol under either food or fasting conditions. (See *NanoBiotech News*, May 26, 2004, p. 1.) The drug was approved by the U.S. Food & Drug Administration in May 2005 and launched in the U.S. in July 2005.

### Mechanisms still unpublished

SkyePharma touts its solubilization technology, noting that particles are generated through cavitation forces and can be sprayed or freeze-dried to improve dose uniformity, bioavailability, stability, and formulation of poorly soluble drugs. Nevertheless, the company has not fully described the mechanisms of action in published papers or industry symposia, says Robin Campbell, PhD, senior biotechnology analyst in the London office of Jefferies International Limited (NYSE:JEF). SkyePharma may have shared information with partners under confidentiality agreements, Campbell adds, but its nanoparticulate technology isn't a factor in analysts' valuation of the company.

Instead, SkyePharma's Flutiform is likely driving the acquisition bid, especially since Innovata

has a particular focus on the delivery of drugs to the lungs, Campbell says. Flutiform (fluticasone/formoterol) is a fixed-dose combination of an anti-inflammatory and a fast-acting beta agonist designed to compete with blockbuster products such as GlaxoSmithKline's best-selling Advair (salmeterol/fluticasone) and AstraZeneca's Symbicort (formoterol/budesonide). The product has completed phase II trials, and SkyePharma had been negotiating with commercial partners to underwrite phase III trials. The company's stock fell to a 2.5 year low in September when SkyePharma failed to secure a partner and reported it would raise GBP 35 million to pay for phase III trials.

With the stock price still depressed, "the company is not very expensive, [so] a suitor can buy the company to get the drug," Campbell points out.

Innovata was formed in July 2005 from ML Laboratories PLC's acquisition of Britain's Quadrant Technologies Limited and a minority interest in Innovata Biomed Limited. The company develops inhalation products for respiratory disease and for pulmonary delivery of a wide range of other therapies. While not a known entity in nanotechnology, Innovata develops inhalation dry powder formulations, either by using spray drying techniques or conventional particle size reduction methodologies. Its Clickhaler dry powder inhaler has been demonstrated as a potential delivery vehicle for spray-dried nanocrystal colloidal budesonide.<sup>1</sup>

Like SkyePharma, Innovata conducts in-house product development as well as funded collaborative programs with big pharma companies, though its market value is less than half that of SkyePharma's.

SkyePharma's board of directors has appointed Lehman Brothers Europe Limited as its

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## NanoBiotech News releases 2005 Nanomedicine, Device & Diagnostic Report

A new executive briefing has for the first time compiled a comprehensive status report of all nano-based drugs and medical devices, providing a remarkable look at the market's quickening pulse. According to data compiled in the just-released *NanoBiotech News 2005 Nanomedicine, Device & Diagnostic Report*, 61 nanotech-based drugs and delivery systems and 91 devices or diagnostic tests have entered preclinical, clinical, or commercial development.

Each of the 152 listings in the *2005 Nanomedicine, Device & Diagnostic Report* includes the associated company or academic research center name, product name, type, indication and status. Additionally, senior *NanoBiotech News* reporters have interviewed key experts for an in-depth analysis of the state of the industry and the products currently under development.

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**SkyePharma** *from Page 1*

financial adviser on the potential acquisition. Company spokesman Peter Laing declined to provide additional details about the bid, citing government regulations governing the outstanding offer.

Campbell maintains his "buy" rating for the stock, with a target price of 75 pence and a potential sale price of 20% premium to current levels. But the pricing issue is complicated, he admits.

"I don't believe that just one suitor will end up in the frame," he tells *NanoBiotech News*. A number of parties have expressed interest, with Vectura Group PLC (LSE:VEC) one that has been named but publicly denied formal talks.

"I would imagine big pharma to be running its slide rule over SkyePharma, too," Campbell adds, noting that a company interested in Flutiform could decide "we're interested in the lunch -- let's buy the restaurant." Novartis AG has declined comment on public speculation of its interest in SkyePharma.

Over the past 12 months, shares of SkyePharma have traded between \$6.24 and \$13.64 on the Nasdaq and are down 30% year-to-date. On Nov. 29, the stock closed down to \$8.05.

During initial talks, Innovata suggested combining the companies -- a strategy that could allow the second-tier company to eliminate a potential

competitor, Campbell points out. But a bid or merger on this basis likely would be based more on a stock swap than a cash buyout, which may not sit well with SkyePharma's major shareholders, who already are unhappy with company management and the entire strategic review process, he says.

At its current stock price, Innovata has a market value of approximately GBP 130 million (U.S. \$224 million) compared to SkyePharma's market value of approximately GBP 350 million (U.S. \$602 million).

No matter what scenario emerges, the potential value of SkyePharma's therapeutic agents rather than its nanoparticulate drug delivery system likely will set the target price for the deal.

"I don't think the SkyePharma board would approve a deal on the drug delivery basis," Campbell says. "I'm looking at someone who's interested in Flutiform and maybe could realize some value from other assets by selling those rights to other parties."

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**Reference**

1. Ostrander KD, Hovey DC, Knapp DA, et al. Potential delivery advantages of spray-dried nanocrystal colloidal budesonide with the Clickhaler. *Resp Drug Delivery* 2000;7:447-9. ©

**CCNE** *from Page 1*

apy. While the awarded amount is \$3.66 million for the first year, officials at the CCNE expect the total funding to reach up to \$20 million over a five-year period.

"Our key goals are to do translational science in cancer with nanotechnology, and reduce the morbidity and improve survivability of cancer patients with new applications," says Jonathan Simons, MD, director of the Cancer Center at Emory Winship Cancer Institute, professor of materials science and engineering at Georgia Tech and co-principal investigator.

Shuming Nie, PhD, principal investigator of the project, a Georgia Cancer Coalition Distinguished Scholar, and associate professor of biomedical engineering, chemistry, hematology, and oncology at Emory and Georgia Tech, adds, "We want to push a couple of technologies into clinical trials at the end of this five-year project."

**The 'dream team'**

The Emory/Georgia Tech CCNE will comprise 75 researchers and administrators working at six different institutions across the country. At

Emory, the cross-disciplinary teams will include basic researchers in biomedical engineering, pathology, radiology, urology, pharmacology, biochemistry, molecular biology and medical and surgical oncology. Leading Georgia Tech scientists will come from departments of biomedical engineering, electrical and computer engineering, materials science and engineering, chemistry and biochemistry.

"The joint Department of Biomedical Engineering at Georgia Tech and Emory University provides a truly collaborative environment for multidisciplinary research in 'Bio+Nano+Info,' and for translating bioengineering technologies and basic discoveries into clinical medicine," says Nie.

"This is kind of a 'dream team' concept of how a great engineering school with a real intense interest in nanotechnology R&D and a cancer center would work together for one goal," adds Simons.

This partnership between Emory and Georgia Tech, he continues, "Was really consolidated and enhanced by the competition for the [NCI] grant." He notes that in 2002, the two schools started a program called 'nano engineers as

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oncologists.' "We take [the engineers] into the clinic, and the clinicians learn how quantum dots work in the lab," he explains. "Instead of making microprocessors, we are trying to improve the survival of cancer."

The team has already been hard at work under previous funding. In 2004, the U.S. National Institutes of Health (NIH) in Bethesda, MD, awarded \$10 million to develop a multidisciplinary research program in cancer nanotechnology, and to develop a new class of nanoparticles for molecular and cellular imaging. Earlier this year, the National Heart, Lung, and Blood Institute of the NIH awarded \$11.5 million to researchers from the institutions for a program designed to characterize plaque formation at the molecular level and to develop techniques to diagnose plaque in the earliest stages of formation.

**Four platform technologies**

As for the research that will be the focus of the new CCNE, Nie says it will include four platform technologies that are already in various stages of development.

"There is the therapeutic component -- nanoparticle cancer drugs," he says. "We have finished several runs of in vivo animal studies, and as early as next year we hope to be in phase I/II clinical trials." Although nothing has yet been published about this research, Nie says, "We've gotten outstanding results." The actual technology has not been disclosed yet, either, but he told *NanoBiotech News* it involves nanoparticles targeted to tumors. "We hope to go into the clinic even before the end of the [five-year] project," says Nie.

The second platform is a cancer tissue diagnostic technology that uses semi-conductor quantum dots to analyze cancer biomarkers. "We've done quite a lot of work since early this year, and have several articles in process," says Nie. "I believe we will be in clinical trials within two years."

The third technology involves the screening and detection of circulating tumor cells in blood samples. "That is still in progress, but we hope within five years to be in the clinic," says Ne.

The team is also working on the development of a targeted imaging agent (a subject of the NIH grant work). "This might also go into clinical trials by the end of the five years," predicts Nie, who notes that some of the work to date has already been published.<sup>1,2</sup>

"These four platform technologies for cancer are the focus of our program," says Nie. "While these are specifically for breast cancer and prostate

cancer, we also want to be involved with colon cancer and lung cancer. We want to nanotype, or fingerprint, precisely each patient's cancer so that we can prescribe the right therapy for each of our patients."

**Additional funding from state**

The CCNE application received additional financial support from the state of Georgia. Georgia has devoted a significant portion of its tobacco settlement dollars to statewide cancer initiatives through the Georgia Cancer Coalition. Through its program called "Extraordinary Opportunities in Cancer Research," the GCC committed \$1.1 million in matching funds for the CCNE grant. These funds will be in the form of two additional faculty positions for the project and seed grants available to Emory and Georgia Tech faculty working on the CCNE. The Georgia Research Alliance committed \$2.5 million in support of the CCNE application for nanotechnology equipment, commercialization and economic development and two GRA Eminent Scholars in cancer nanotechnology.

Emory University president James Wagner will provide institutional support of \$1 million to develop a cancer nanotechnology fellowship program. Georgia Tech president Wayne Clough also will provide \$1 million for purchase of nanotechnology equipment and facilities. Significant in-kind support will also be provided by the Centers for Disease Control and Prevention and the American Cancer Society.

*Editor's Note: Contact Jonathan Simons at (404)778-5177 and Shuming Nie at (404) 712-8595.*

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angiography, is unable to evaluate the therapy for at least 40 days after treatment, MRI with the ligand-targeted emulsion provided an assessment within 10 days. "At that point we can monitor the process and see the response to the drugs," Wickline says.

**More specific knowledge**

The technology will offer much more specific knowledge about the impact of drug delivery, says Wickline. "We can image and deliver drugs simultaneously, and be able to predict how much of the material is there based on MRI signals; we know how much drug is in each particle, so if we can figure out how many particles there are, we can know just what is at the site," he explains.

The bottom line, he continues, is that by using standard pharmacokinetics modeling the researchers have determined you might be able to use up to

100 times less drug in the serum than you normally would give in an IV, "Yet get up to 100 times more at the site than you would ever get, even if you used the highest dose."

"Since you are targeting the drug you do not have to use as much in the serum because it is going where it is supposed to go. And, because it is targeted, it will accumulate in even higher doses," he says.

The next milestone for the company, he shares, will not be in CVD, however, but in cancer. "While we are working on ways of treating cancer, atherosclerosis and restenosis with anti-angiogenic compounds, we are going to first move into clinical trials for treating cancer with anti-angiogenic nanoparticles that can be imaged -- within a year," he predicts. "Kereos is in advanced pre-clinical trial status, and moving towards investigational new drug application."

*Editor's Note: Contact Samuel A. Wickline, MD, at (314) 454-8811. ☺*

**Starpharma raises another AUD \$15M to support VivaGel**

By Russell A. Jackson

On the heels of a U.S.\$20 million in development funds from the U.S. National Institutes of Health, Melbourne-based Starpharma Holdings, Ltd., (ASX:SPL, USOTC:SPHRY) now reports receiving another capital infusion of AUD \$15 million.

The plan now is to get the company's lead product, VivaGel, to market and to boost its efforts in developing targeting molecules based on its proprietary nanotechnology for precision placement of receptors on cells.

The latest round of financing, the company reports, "included an AUD \$12 million institutional placement at and AUD \$0.51 and an underwritten share purchase plan (SPP) to raise an additional AUD \$3 million. The institutional placement was oversubscribed. The SPP, also priced at AUD \$0.51, is expected to be well-supported by Starpharma's more than 2000 shareholders."

Patersons Securities, lead manager of the placement and underwriter of the SPP, confirms that more than 70% of the placement was raised through new and existing institutional investors. One of them, reports John Raff, PhD, CEO at Starpharma, is Melbourne's Acorn Capital, which now owns about 8% of the company. "It has been a real supporter," he tells *NanoBiotech News*, "and was the first investor in this latest round."

There are five new institutional investors in

total involved in the latest financing. "Institutions in Australia are getting more interested in nanobiotech," he says. Last month, Starpharma received AUD \$26 million of non-dilutive funding from the U.S. National Institutes of Health to develop VivaGel, a topical vaginal microbicide to protect women from HIV.

"It's a relief to be in the position of having well over two years' cash in the bank and our lead project funded," he says, adding, "the support of some of Australia's leading financial institutions is validation of the commercial opportunities for VivaGel and recognition of the future value of our dendrimer nanotechnology pipeline and of our 33% equity stake in DNT."

The new capital will be used to fund the development of line extensions of VivaGel, including the prevention of genital herpes and to increase collaborative activities with that investee company, U.S.-based Dendritic Nanotechnologies, Inc.

Another collaboration the new money will help Starpharma pursue is its existing relationship with Dimerix Bioscience Pty, Ltd., a company commercializing technology developed at the Western Australian Institute for Medical Research in the field of receptor coupling, specifically G-protein coupled receptors, Raff reports.

That science, he notes, involves the fact that different groupings of receptors on the surfaces of cells result in different signals being sent out. Starpharma has recently completed work -- about four years' worth, in fact -- on the nanostructure needed to group those receptors precisely.

*Editor's Note: Contact John Raff at +61 3 8532 2701. ☺*

## Cancer nanobombs may be added to oncology's armamentarium of therapies

By Julian Zegelman, NanoBioNexus contributor

A new addition to the ever-expanding arsenal of anti-cancer therapeutics was made recently when the University of Delaware researchers introduced a nanobomb potentially capable of literally blowing up and destroying breast cancer tumors.

Balaji Panchapakesan, PhD, assistant professor of electrical and computer engineering at University of Delaware, was the lead investigator on the research team that included Eric Wickstrom, professor of biochemistry and molecular biology at Thomas Jefferson University in Philadelphia, his student Greg Cesarone, and University of Delaware graduate students Shaoxin Lu and Kousik Sivakumar, as well as a UD postdoctoral researcher Kasif Teker.

The nanobomb discovery is the result of ongoing research concentrated on carbon nanotubes. Originally, he says, the research team was evaluating the prospects of using the carbon nanotubes as a drug delivery vehicle. Because they are smaller than the size of any single cell, the nanotubes can provide convenient means for highly selective delivery of drugs into individual cells.

However, as the research progressed, the team made a startling discovery: "When you put the atoms in different shapes and forms, they take on different properties at the nanoscale," Panchapakesan says. "We were experimenting with the

molecules and considering optical and thermal properties, and found we could trigger microscopic explosions of nanotubes in wide variety of conditions."

While explosions in an atmosphere of loosely packed nanotubes in an oxygen environment are a known phenomenon, the work reported by Panchapakesan and his colleagues<sup>1</sup> drastically expands the practical implications of this occurrence by using localized thermal energy imbalance to set off explosions that are intrinsic in nature.

### Like cluster bombs

Panchapakesan says nanobombs are just what they are called -- tiny bombs on the nanoscale. "They work almost like cluster bombs," he said. "Once they are exposed to light and the resulting heat, they start exploding one after another."

The nanobombs are created by bundling the carbon nanotubes together. With a single nanotube, the heat generated by the light is dissipated by surrounding air. In bundles of nanotubes, however, the heat cannot dissipate as quickly and the result is a build-up of thermal energy within the bundle ultimately resulting in an explosion on the nanoscale.

When researchers saw the explosions, they realized it might be possible to use the microscopic bombs to kill cancer cells. They recreated the explosions in solutions including water, phosphate and salt, which meant the nanobombs could be used in the human body. In fact, the explosions were more dramatic in saline solu-

*continued on page 11*

## DNA/RNA Therapies: Opportunities for Future Success

DNA/RNA products represent some of the most innovative and direct technologies aimed at commercializing the human genome. The market is in its infancy with no significant products launched across the seven major markets. Despite the unproven nature of the sector in terms of market potential, it is commanding considerable interest across the biotechnology industry. Datamonitor has identified 99 companies developing DNA/RNA therapies, with 229 products in development. Of these programs, 19 are set to be on the market by 2010.

Published by Datamonitor, *DNA/RNA Therapies: Translating the Genome into a \$1.2bn Market by 2010* analysis provides a comprehensive evaluation of the global DNA/RNA market, encompassing market dynamics, company strategy and comparative benchmarking of the development programs of 99 players by technology and therapy area. Through this special e-mail offer, you can purchase this business solution for just \$7,600 by clicking on this link: <http://www.nhionline.net/products/datamonitormr104.htm>. A full table of contents is also

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**Nanobombs** from Page 10

tions, according to Panchapakesan.

An advantage of this therapy is the fact that a nanobomb explosion is highly selective, localized and minimally invasive, making it a prime candidate for fighting cancer tumors.

Nanobombs are superior to a variety of current treatments because they are powerful, selective, non-invasive, non-toxic and can be used in conjunction with novel medical technology such as microsurgery, he says.

The researchers say there is particular emphasis on breast cancer cells because the nanobomb shockwave kills the cancerous cells as well as the biological pathways that carry instructions to generate additional cancerous cells and the small veins that nourish the diseased cells. Also, it can be spread over a wide area to create structural damage to the cancer cells that are close by.

An advantage this therapy may have over other carbon nanotube treatments is the nanotubes are destroyed along with the cancer cells. Once the nanobombs explode and kill cancer cells, the body's macrophages can effectively sweep out the cell debris and the exploded nanotube along with it.

Other treatments retain the carbon nanotubes and nanoparticles intact. If the debris material finds its way to the kidney or accumulates in the blood vessels, the nanoparticles might cause blockage and create problems. Furthermore, the nanobomb route is probably the only way to use

nanotubes without any cytotoxicity as the nanotubes are destroyed completely.

**Applications in any part of the body**

Current surgical techniques are not precise and cancerous cells are often left behind. In addition, it is common for certain types of cancer in particular parts of the body, such as arteries and veins, to be considered inoperable. Nanobombs can be used to target any remaining cancerous cells and can be used in any part of the body, allowing the creation of nanobomb therapy for a wide variety of cancers.

Panchapakesan points out the nanobomb is a "very simple technique" and as such will likely prove to be "more robust and with the best chance to succeed."

Although optimistic about the future of nanobombs, Panchapakesan cautioned against expecting immediate therapeutic advantages: "We are just getting started in this area. There is plenty of work ahead to successfully translate this into clinical medicine."

*Editor's Note: NanoBioNexus (www.nanobionexus.org) is a contributing content provider for NanoBiotech News. Contact Balaji Panchapakesan at (302) 831-4062.*

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