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Defining the nanoscale science, inventions, life forms

U.S. patent office initiates nanotechnology classification project

By Marie Powers

The U.S. Patent and Trademark Office (USPTO) in Alexandria, VA, is a step closer to determining when and how to classify a new technology as "nano."

According to Bruce M. Kisliuk, a director in the agency's biotechnology group, and participants in the USPTO's recent second nanotech customer partnership meeting, the agency is forging ahead with a painstaking review of existing and proposed technologies as part of its nanotechnology classification project.

The USPTO has been grappling with several key characteristics when defining patents that fall under the nanotech umbrella. (See *NanoBiotech News*, Oct. 8, 2003, p. 1.) Predictably, size is a major factor, since an existing invention scaled down to nanoscale does not necessarily constitute a new

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Could it be nano based?

SkyePharma, First Horizon ink $50M deal for 'undisclosed' cardiovascular product

By Marie Powers

SkyePharma PLC (NASDAQ:SKYE), based in London, last week reached an agreement granting First Horizon Pharmaceutical Corporation (NASDAQ:FHRX) the exclusive U.S. marketing and distribution rights for an "undisclosed" cardiovascular product that is currently under review by the U.S. Food and Drug Administration (FDA).

In a public statement, Peter Laing, director of corporate communications in SkyePharma's London headquarters, says the company expects approval of the drug by the end of this year. Laing

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Biophan acquires 51% of TE-Bio, seeks development of nanofilm battery for $500M implant

By Steve Lewis

Biophan Technologies, Inc. (OTCBB:BIPH), a Rochester, NY-based developer of biomedical technology, has acquired a majority interest in TE-Bio, LLC, a company developing a long-life power source for use in implanted medical devices such as pacemakers, defibrillators, neurostimulators, and drug pumps. The technology is based on a patented innovation in the utilization of thermoelectric materials,[1] using nanoscale-based, thin-film materials to convert thermal energy produced naturally by the human body into electrical energy.

Biophan purchased 51% of TE-BIO in exchange for a commitment of $300,000 per year in research and development for three years, as well as the commitment of its management infrastructure, it sales and marketing, and technical support.

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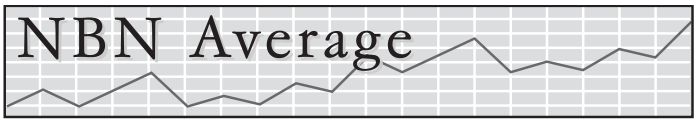

Company	Symbol	Close 5/18	Close 5/25	% Change
Acacia Research Corporation	ACTG	$ 5.11	$ 5.37	5.09%
Accelr8 Technology	AXK	$ 2.15	$ 2.73	26.98%
Aclara Biosciences	ACLA	$ 3.70	$ 3.73	0.81%
Advanced Magnetics	AVM	$ 10.20	$ 9.99	-2.06%
Advectus Life Sciences	AVXSF.PK	$ 0.05	$ 0.05	0.00%
Affymetrix	AFFX	$ 30.33	$ 30.17	-0.53%
Agilent Technologies	A	$ 25.40	$ 24.73	-2.64%
Altair Nanotechnologies	ALTI	$ 2.10	$ 2.42	15.24%
American Pharmaceutical Partners	APPX	$ 34.76	$ 33.70	-3.05%
Biophan Technologies	BIPH.OB	$ 1.04	$ 1.05	0.96%
Caliper Life Sciences	CALP	$ 5.90	$ 5.70	-3.39%
Cepheid	CPHD	$ 8.18	$ 9.03	10.39%
Ciphergen Biosystems	CIPH	$ 6.97	$ 7.73	10.90%
CombiMatrix	CBMX	$ 3.38	$ 3.97	17.46%
Flamel Technologies	FLML	$ 24.82	$ 25.38	2.26%
Nanobac Pharmaceuticals	NNBP.PK	$ 0.45	$ 0.46	1.11%
Nanogen	NGEN	$ 5.52	$ 6.53	18.30%
Nanophase Technologies	NANX	$ 6.24	$ 6.88	10.26%
Novavax	NVAX	$ 4.30	$ 4.43	3.02%
SkyePharma	SKYE	$ 9.75	$ 11.31	16.00%
TOTAL		190.35	195.35	▲ 2.63%

Xintek's carbon nanotube-based X-ray device nears commercial launch

By Steve Lewis

Xintek, Inc., formerly known as Applied Nanotechnologies, Inc., is moving steadily toward its first commercial launch of a carbon nanotube (CNT)-based X-ray machine. The Chapel Hill, NC-based company manufactures carbon nanotube materials and carbon nanotube enabled cold diode and triode cathodes, AFM tips and X-ray tubes.

The Xintek device, which employs a process called field emission, will be much smaller and more efficient than current X-ray machines, explains Otto Zhou, PhD, chairman of Xintek. "If you look at the different electronic devices used today [i.e., those employing CRT tubes], they are based on a thermionic source; this requires a very high temperature," he notes. "The implications are that they waste a lot of energy. Also, the devices are very large, and need thermo insulation."

Through the use of field emission -- exciting electrons by an electrical field -- the electrons can be maintained at room temperature, enabling devices such as computers. "They can be made smaller, more efficient, and you can increase the lifetime of the device," Zhou explains.

Field emission itself is not a new concept, says Zhou; it is actually about 30 years old. "But," he poses, "where do you find the materials to deliver the kind of electrons required [for X-ray machines]? That's where CNT comes in; they have turned out to be very good electron emitters."

The advantages of the device, says Zhou, include more than just smaller size and greater efficiency. "You can make the devices portable," he says. "You can increase the resolution image of smaller structures for greater accuracy, and you can image a moving part -- for a visual effect much like a time-frame film."

Technology takes award

Xintek's CNT work was recently recognized by Frost & Sullivan, San Antonio, TX, which gave the firm its 2004 Technology Innovation Award.

"Having identified the potential that exists for CNT-based field emission applications, Xintek has focused its efforts in this direction, thus culminating in the creation of their first CNT-based X-ray device," notes Deepa Doraiswamy, a research analyst in Frost & Sullivan's Semiconductor Group. "The company has targeted September 2004 for the commercial launch of this device. This would potentially position Xintek as one of the prime movers to have crossed the last mile from lab to market for nanotube based field emission products."

The novelty of this technology, says Doraiswamy, "has aided Xintek to extrapolate this proficiency to the fabrication of CNT field emission cathodes for flat panel displays. The commercial launch of Xintek's inventive technology is expected to drive a new generation of technology revolution in the carbon nanotubes market and the overall nanotech industry as well."

Zhou says Xintek is still on target for the launch, but would only specify that it would occur "some time this year." He added that Xintek has a partner for the launch, but that their name cannot yet be disclosed. As for the commercial potential, he notes, "you only have to look at the number of hospitals and X-ray machines there are."

Seeking to raise cash

Earlier this year, Xintek -- then still called Applied Nanotechnologies -- announced that it was approaching VC firms for the first time, in an effort to raise $10 million. (See *NanoBiotech News*, Jan. 28, 2004, p. 2.) "We have been talking to a few VC's from the U.S. and Taiwan, and private investors from Europe," reports Shan Bai, Xintek's CEO. "It is still the plan to wrap up by June or July." However, he adds, this will have no impact on the timing of the commercialization of their X-ray product.

"The commercialization of the first product is independent from this round of financing," he says.

Xintek was established in October 2000 to develop and commercialize nanotechnology-based applications in various industries. The

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From neural implants to drug delivery systems

Magnetic forces may turn some carbon nanotubes into metals

By Marie Powers

A study published last week in the journal *Science*[1] finds that the basic electrical properties of semiconducting carbon nanotubes change when they are placed inside a magnetic field. The phenomenon, unique among known materials, could cause semiconducting nanotubes to transform into metals in even stronger magnetic fields.

Scientists at Rice University in Houston, TX, found that the "band gap" of semiconducting nanotubes shrank steadily in the presence of a strong magnetic force, according to lead researcher Junichiro Kono, PhD, assistant professor of electrical and computer engineering at Rice. The research, which involved a multidisciplinary team of electrical engineers, chemists, and physicists, sheds new light on the unique electrical properties of single-walled carbon nanotubes (SWNTs).

By their very nature, semiconductors can either conduct electricity in the same way metals do, or they can be non-conducting, like plastics and other insulators. This transformation allows the transistors inside a computer to be either "on" or "off" -- two states that correspond to the binary bits of electronic computation.

Semiconducting materials like silicon and gallium arsenide have a narrow "band gap" -- a low energy threshold that corresponds to how much electricity it takes to flip a transistor from "off" to "on." Among nanotubes with band gaps comparable to silicon and gallium arsenide, the researchers found that the band gap shrank as they applied high magnetic fields.

In short, while some SWNTs are metals and some are semiconductors, the semiconductors probably become metals in very strong magnetic fields and switch back to their original semiconducting state when the field is turned off. Controlling the metallicity of the nanotubes could lead to novel magneto-optical or magneto-electrical switching devices, Kono tells *NanoBiotech News*.

Ideal candidates for biosensors

While the researchers still are conducting basic research and have not envisioned direct nanobiotech applications for the discovery, carbon nanotubes are known to be ideal candidates for the development of

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Microfluidic device serves as magnetic tweezers to manipulate biomolecules

By Jane Anderson Cassell

Scientists at the National Institute of Standards and Technology (NIST) in Boulder, CO, have developed a micromachined fluid-cell platform that enables them to control and position magnetic microparticles which can be tethered to biological molecules.

Described in a recent issue of *Applied Physics Letters*, the chip-scale, microfluidic device works together with a magnetic force microscope, and is intended to serve as magnetic tweezers that can stretch, twist and uncoil individual biomolecules such as strands of DNA.

Magnetic tweezers trap magnetic microparticles in tailored magnetic field gradients, says author Elizabeth Mirowski, an NIST post-doctoral researcher.

Magnetic particles 2 to 3 micrometers across are suspended in a fluid and injected into the device. The surface of a thin membrane enclosing the fluid is dotted with an array of thin film pads made up of a nickel-iron alloy. When a magnetic field is applied, each particle is attracted to the closest nickel-iron "trap."

Because of the magnetic anisotropy inherent in the particles, rotation of the magnetic poles generating the magnetic field gradients that capture the particles imparts torque to the microparticle and, consequently, to a biological molecule attached to the particle, Mirowski says. The torsional motion can be used to stretch, twist, or uncoil the biological molecule with a smaller force than that resulting from lateral displacement of the particle, she says.

According to Mirowski, the magnetic tweezers platform is a micromachined device consisting of fluid flow channels etched into silicon, a thin 200 nm Si3N4 transparent window, and an array of patterned Permalloy magnetic elements (1 mm x 3 mm x 30 nm dimensions). The number of elements depends on the size of the window and the minimum distance between traps that is necessary for the application.

The elements generate local magnetic field gradients, which are generally insufficient in strength to provide localized confinement of the magnetic particles (3 mm diameter), she says. But with an external applied magnetic field, the domains align and the magnetic particles are trapped in the local field gradients of the elements.

"Since the magnetic particles are commercially available and can be readily attached to biological sample molecules such as DNA, each element in the array can be assigned an individual biological sample, such as a strand of DNA," Mirowski says, adding that the sample can be transported between

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technology, Kisliuk and others agree. Inherency -- the manipulation of a known material at the nanoscale to produce a novel outcome -- remains another issue, since examiners must determine whether newly discovered properties or phenomena are inherent in the material or unique to nanoscale. Finally, Kisliuk and experts in the field continue to discuss the principle of enablement -- whether an inventor can "enable" others to use a discovery whose mechanism remains unclear -- with respect to nanotech applications.

"How to define nanotechnology and nanobiotechnology has been a key issue," admits Ronald A. Bleeker, a partner with the Washington, DC, law firm Finnegan, Henderson, Farabow, Garrett & Dunner, LLP. "Nanotechnology is a very broad, inclusive term. Even when you focus on nanobiotechnology, you have to consider different groupings of technology, such as molecular-scale drug delivery systems and micromachines."

A tedious process

Characterizing nanotechnology -- both from the standpoint of intellectual property (IP) protection and for the development of practical search engines -- is a major goal of the nanotechnology classification project, Kisliuk says. The process is tedious, beginning with a text search of existing patents that uses both related and exclusionary terms. Once the initial search identifies a group of patents, each must be thoroughly reviewed by examiners to determine whether they "fit" into the new classification schedule.

The results of a text search depend largely on the terms that are used and the structure of the query, Kisliuk points out. A patent analysis conducted last year by researchers from the University of Arizona and the National Science Foundation that sought to define the scope of nanoscience and engineering (NSE) claims between 1976 and 2002 by country, institution, and type of technology produced more than 76,000 patents using "nano" as the key word, and more than 89,000 when including terms such as self-assembly, quantum dot, and molecular modeling.[1]

Chemicals, pharmaceuticals lead the way

The researchers found that the fastest nanotech-related growth over the most recent five years had occurred in the chemical and pharmaceutical fields, followed by semiconductor devices. In 2001 and 2002, the most important nano-related topics were nucleic acids, pharmaceutical composition, laser beams, semiconductor devices, and optical systems.

In November 2001, the USPTO conducted its own text search on nanotechnology using 102 related terms and excluding unrelated terms such as "nanometer" and "nanosecond." The initial search resulted in 5,000 issued patents. When the process was repeated in February 2003, the list contained 7,000 patents.

"All this tells us is that these terms appear in the patent -- not necessarily in the claims," Kisliuk cautions. "So, yes, there has been growth in the use of nanotechnology terms and, we can assume, growth in nanotech patents as well."

A more refined definition

This spring, the USPTO conducted a new search based on a stricter definition used by the National Nanotechnology Initiative (NNI) at the National Nanotechnology Coordination Office (NNCO) in Arlington, VA. NNCO characterizes a discovery or invention as "nanotechnology" only if it meets all four of the following criteria:

1. research and technology development at the atomic, molecular, or macromolecular scale in a length scale of approximately 1 nm to 100 nm;
2. the understanding, creation, and use of structures, devices, and systems that have fundamentally new properties and functions because of their nanoscale structure;
3. the ability to control -- to see, measure, and manipulate -- matter on the atomic scale to exploit these properties and functions; and
4. the ability to integrate these properties and functions into systems spanning from nano- to macroscopic scales.

Using the NNI definition, in combination with the USPTO's own terms and exclusions, the new search contained 185 terms and produced a list of 6,000 patents, Kisliuk says. When examiners narrowed the list only to those patents where the relevant terms were included in the IP claims, however, the list shrank to just 1,100 issued patents.

Bryan W. Bockhop, a partner in the Atlanta law firm Arnall Golden Gregory LLP, recently conducted his own U.S. nanotech patent search, uncovering 6,000 patents and 5,000 published patent applications containing "nano" in the text. The conclusion of all these disparate results?

"The important issue is not so much the number of patents but how you define the technology," maintains Bockhop, who also serves as co-chair of the American Intellectual Property Law Association's nanotechnology subcommittee.

"Because most of nanotech crosses boundaries with other technologies, the definition is not something that the USPTO has clearly pinned down yet,"

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Bockhop says. "Until that's pinned down, it's hard to say how the patent office will handle these claims."

Interdisciplinary nature of nanotech

Due to the interdisciplinary nature of nanotechnology, perhaps the most likely outcome from the nanotechnology classification project is the creation of what Kisliuk calls a "cross-reference art collection," or subclass, rather than a separate nanotech classification. Thus, an invention that is principally a semiconductor would be classified as such but cross-classified into the nanotech subclass, he explains.

"The examination area usually has a sense of when a new classification is needed," Kisliuk says. "But nanotech is unusual because it's so interdisciplinary. When we did our queries, we actually identified the patents and looked to see where they were classified. The three main areas were biologics, materials, and electrical -- especially devices and semiconductors. Examiners now are alert to new discoveries in these areas that relate to nanotechnology.

"In the classification project, we are placing patents that we identify into a draft nanotechnology schedule," he continues. "We'll see where the principal technology lies and modify the schedule as necessary. Once we get a classification scheme, we'll have a lot better handle on the actual number of patents that fall into the nanotechnology bucket."

With a database of more than six million U.S. patents, growing at a rate of 3,500 to 4,000 new patents per week, an updated classification system can't come too quickly, according to industry experts. While no significant nanotech case law exists yet, Bockhop expects lawsuits eventually to focus on claims regarding size and form factor -- changes in the outward dimension of a device or invention.

Case law is coming, expert says

"My reading of case law is that, if a change in form factor gives rise to a new technology, it's likely to be patentable," he says. As an analogy, reducing a gold brick into particles that, when sprinkled into bottles of colored water, change the color of the water might be a patentable change in form factor, Bockhop says, but simply reducing the size of a gold brick by cutting it in half would not.

Industry observers also are watching to see how the USPTO deals with claims involving life forms at the nanoscale.

"The current attitude seems to be that, where life forms interact with inorganic structures, these are seen as patentable inventions," Bockhop says.

During the customer partnership meetings and informal visits, IP attorneys and nanoscience researchers and executives also have questioned whether examiners fully understand and give appropriate attention to claims and are current on their training, Kisliuk says. While the nanotech classification project is underway, the USPTO is providing additional training for examiners who handle claims in key areas and is advising them to consult with each other when reviewing claims that are interdisciplinary in nature, he points out.

Of course, the industry also wants to know when the USPTO will have a handle on the true number of U.S. nanotech patents.

"We're working on that," Kisliuk says. "It's not a quick resolution, but we hope to complete the classification project by the end of this year."

Editor's Note: Contact Bruce Kisliuk at (571) 272-0700, Ron Bleeker at (202) 408-4019, and Bryan Bockhop at (404) 873-8696.

Reference

1. Huang Z, Chen H, Yip A, et al. Longitudinal patent analysis for nanoscale science and engineering: Country, institution, and technology field. *J Nanoparticle Res* 2003; 5(3-4):333-63. ⊙

Xintek from Page 2

company obtained an exclusive license of proprietary technologies developed by Zhou, the company's co-founder, and his collaborators from the University of North Carolina at Chapel Hill (UNC-CH). Zhou is founding director of one of the largest federally funded research centers on carbon nanotubes, the North Carolina Center for Nanoscale Materials, and his research at UNC-CH has been supported by the federal agencies including the Department of Defense, NASA and the National Science Foundation. Among his patents is the one awarded for the X-ray machine.[1]

Other potential CNT applications being researched by Xintek include nanoprobes for probing molecular structures. "We are looking to commercialize the probe," says Zhou, adding that he has several patents pending on the processes involved.

Editor's Note: Contact Otto Zhou at (919) 291-1838 or Shan Bai at (919) 524 4702.

Reference

1. US Patent 6,553,096. Zhou, et al. X-ray generating mechanism using electron field emission cathode. ⊙

Biophan *from Page 1*

"TE-Bio holds a worldwide exclusive license to the patent from Biomed Solutions, LLC, for making biothermal batteries out of thermo-electric materials; they generate heat through these materials and generate electricity by exciting semiconductor nodes," explains Michael Weiner, CEO of Biophan. "The technology has been used to power certain spacecraft, like the Voyager."

Unrecognized potential

The nanotechnology originated with Biomed Solutions, LLC, of which TE-Bio is an affiliate (Biomed owns the other 49% of the company) and from which Biophan was spun off. However, it was at first thought that the nanofilm-powered batteries had limited application.

"One of our scientists predicted that you would eventually be able to put enough of these semiconductor nodes on a nanoscale basis onto thin film, but that you couldn't get much more power than 50 microwatts," Weiner recalls.

The initial plan was to use the technology to make a trickle charger (A trickle charge is a continuous constant-current charge at a low [about C/100] rate that is used to maintain the battery in a fully charged condition), and TE-Bio was set up for the purpose of commercializing the battery.

"I went to the board and said we'd get involved, to try to sell to larger biomedical device companies," says Weiner. "But in the course of our due diligence, independent consultants determined it was not only feasible for thin-film nanoscale technology to produce 50 microwatts, but that it could eventually do over 100."

A significant difference

The difference was significant, and it was what led to the TE-Bio investment. "Instead of [having only enough power for] recharging a pacemaker, we had enough to power one," says Weiner. "It's enough for a defibrillator in pacemaker mode; you need 300 volts to restart a heart, but you could trickle charge that device and make a difference in the life of a patient. It could also be applicable to implantable drug pumps and to the entire class of microfluidic labs on a chip; it's very hard to power them."

Several device manufacturers are interested in the technology, says Weiner. Applications, he notes, include smaller biosensors. "There's a lot of interest in various forms of having them communicate outside the body to a local receiver or even a GPS system," he notes. "The problem is, all of these additional diagnostics take power, and batteries take up space. To be able to put a thin film coating on the outside of the device generating power is a big deal."

Weiner says it will take one to two years to build a working prototype. "Once we prove it works, we will be selling OEM to manufacturers of devices; they would then take it to the FDA," he says. "It could potentially be on the market within a year of having enough proof of concept to have a customer bet on it."

Weiner says the market for implantable batteries is estimated at $500 million a year.

Editor's Note: Contact Mike Weiner at (585) 214-2441.

Reference

1. US patent 6,640,137. "Biothermal Power Source for Implantable Devices." ⊙

Magnetic forces *from Page 3*

biological sensors and other "smart" components that capitalize on their exceptional strength and lightness together with novel electrical properties. Some researchers have been studying the use of carbon nanotubes in neural implants, orthopedic applications, and drug delivery systems. (See *NanoBiotech News*, Jan. 14, 2004, p. 7.)

In tests at the National High Magnetic Field Laboratory (NHMFL) at Florida State University in Tallahassee, the researchers put SWNTs in fields up to 45 Tesla. According to their findings, the SWNTs will likely become metals at over 100 Tesla. Kono is arranging additional experiments with research groups in Toulouse, France, Tokyo, and at New Mexico's Los Alamos National Laboratory. All of these use pulsed magnets to create even stronger magnetic fields, he says.

Initial research was supported by the Welch Foundation, the Texas Advanced Technology Program, the National Science Foundation, the NHMFL, and the State of Florida. Kono plans to seek additional funding for the next experimental phase. He also will present initial findings about the SWNT research at several conferences this year, including next month's Cooperative Phenomena in Optics and Transport in Nanostructures in Dresden, Germany.

Editor's Note: Contact Junichiro Kono at (713) 348-2209 or visit www.ece.rice.edu/~kono/.

Reference

1. Zaric S, Ostojic GN, Kono J, et al. Optical signatures of the Aharonov-Bohm phase in single-walled carbon nanotubes. *Science* 21 May 2004; 304:1129-31. ⊙

SkyePharma *from Page 1*

also indicated the drug addresses a side effect of cardiovascular drug treatment and is expected to generate millions of dollars in sales annually.

When pressed by *NanoBiotech News* about whether the drug uses SkyePharma's nanoparticulate technology, which the company has been developing since 2000, Laing declined to provide additional information "at the request of our partner," until the product is approved. A listing of the company's technology platforms, however, cites a "solubilization," or nanoparticulate, cardiovascular product in phase I clinical trials.

Sources at Alpharetta, GA-based First Horizon, attending this week's UBS Warburg Global Specialty Pharmaceuticals Conference in New York, also declined to comment further on details of the drug compound.

Significant implications for both firms

Despite the unknown mechanism for this particular product, the deal has potentially significant implications for both companies. Ten approved products now incorporate SkyePharma's technologies in the areas of oral, injectable, inhaled, and topical delivery. Many of these are supported by the company's patented "enhanced solubilization" capabilities, both through nanosuspensions and solid lipid nanoparticles.

In addition to in-house development, the company has licenses or partnerships with a variety of big pharmaceutical firms including GlaxoSmithKline PLC (NYSE:GSK), Merck & Co., Inc. (NYSE:MRK), Novartis AG (NYSE:NVS), AstraZeneca Pharmaceuticals PLC (NYSE:AZN), and Baxter International Inc. (NYSE:BAX).

First Horizon Pharmaceutical Corporation is a specialty pharmaceutical company that markets and sells prescription products with a primary focus on cardiology, women's health, pediatrics, and gastroenterology. The company has a portfolio that includes 14 branded prescription products. Of these, six are actively promoted to high-prescribing physicians through a nationwide marketing and sales force of more than 300 representatives.

The terms

According to terms of the agreement, SkyePharma will receive a total of up to $50 million in milestone payments and 25% of First Horizon's net sales of the product. First Horizon will pay $5 million to SkyePharma when the agreement is signed and up to an additional $15 million thereafter, contingent upon milestones related to the FDA approval. In addition to the initial $20 million in payments, SkyePharma will receive up to $30 million in sales-based milestone payments.

SkyePharma will manufacture and supply the product from its Lyon, France, manufacturing facility. The London firm also will make a contribution of up to $5 million to First Horizon's initial marketing expenses to establish the product.

First Horizon intends to begin marketing and distribution shortly after FDA approval, according to the companies. The Alpharetta firm also obtained the right of first refusal to negotiate a license to develop and commercialize a future cardiovascular product using SkyePharma delivery technology.

"First Horizon is a perfect partner to promote this product to cardiovascular physicians as well as general and family practitioners," says Michael Ashton, SkyePharma's CEO. "They have a significant sales force, a proven ability to move market share in this therapeutic area, and a commitment to evaluate future product opportunities utilizing our drug delivery technologies.

"This product also moves the company closer to our objective of fully commercializing our investment in the Lyon, France, manufacturing operation," Ashton adds.

Investors like the news, despite secrecy

Robin Campbell, PhD, senior biotechnology analyst in the London office of Jefferies & Co. (NYSE:JEF), gave his seal of approval to the deal, reiterating his "buy" recommendation on SkyePharma shares following the announcement on May 17. The stock closed that day at $9.43 on volume of 194,700 -- up from $9.09 on volume of 81,900 the previous week.

This activity was dwarfed, however, by the activity following SkyePharma's announcement on May 19 that the FDA had approved its new drug application (NDA) for DepoDur -- a novel single-dose sustained-release injectable formulation of morphine -- for the treatment of pain following major surgery. That product is being licensed in the U.S. by Endo Pharmaceuticals (NASDAQ:ENDP) of Chadds Ford, PA. SkyePharma's stock climbed $2.07, or 21%, to close at $11.82 on the DepoDur news.

SkyePharma, which has traded in a range between $8.75 and $14.50 during the past 52 weeks, closed May 25, at $11.31.

First Horizon stock fell slightly on May 17, closing at $16 on volume of 434,100, down from $16.28 the previous week. The stock has been climbing steadily since then, however, closing May 25, at $17.47, up from $17.29 the previous day. Earlier this month, the company also reported first quarter net income of $5.0 million on total revenues of $32.0 million.

Editor's Note: Contact Peter Laing at +44 207 491 5124. ⊙

NIST *from Page 3*

researchers and research facilities and then referenced when needed by releasing the sample from the trap and sorting it.

So far, the research team has demonstrated that the traps attract individual particles and that the microscope tip can gently drag particles with pico newton forces.

Additional applications

"We are currently exploring the possibility of the magnetic tweezers for manipulation and measurement in addition to sorting," Mirowski adds. "Lateral forces can be applied to the biological sample by trapping each end of a molecule in a magnetic field gradient and then displacing one field gradient with respect to the other. Torsional manipulation can be accomplished with a rotating magnetic field."

Using this technique, the researchers can obtain information about the cohesion forces due to hydrogen bonding, molecular motors and protein interactions with DNA, she says.

"We are currently working on aspects of the device to implement it in manipulation and measurement for high throughput analysis of individual molecules with particular attention to sequencing via nanopores or DNA unzipping, torsional manipulation for structural control and studying the effect of DNA conformation or protein recognition," Mirowski says.

Because the magnetic tweezers platform is a MEMS-based device, it should be relatively amenable to commercialization, Mirowski says. She estimates that the device could be commercialized in one to three years.

"Our mission is to provide metrology standards to industry and to hasten the technical development now underway within various companies. Therefore, commercialization of the device would be most likely undertaken in cooperation with industry," she says.

Mirowski notes that the device consumes very little power when compared with other magnetic tweezers techniques. "Other techniques require constant current to immobilize magnetic particles and hence local heating and damage to the samples can occur," she says. "We are continuing to make amendments to the device so that power consumption and sample damage remains at a minimum. We are also looking at making the elements sub-micrometer in size."

Editor's Note: Contact Elizabeth Mirowski at (303) 497-4458.

Reference

Mirowski E., Moreland J., Russek S. Integrated microfluidic isolation platform for magnetic particle manipulation in biological systems. *Applied Physics Letters*, 84:10 1786-1788. March 8, 2004. ⊙

NanoBiotech Patent Watch

System and method for manipulating nanotubes

Assignee: Zyvex Corporation (Richardson, TX)
Patent: 6,723,299
Date: April 20, 2004
Summary: A system and method are disclosed which allow for manipulation of nanotubes. More specifically, embodiments of the present invention enable various types of manipulation of nanotubes using an organic material that is presented to the nanotubes. For example, a preferred embodiment of the present invention enables cutting of nanotubes into shortened nanotubes. Other types of nanotube manipulation that are enabled by embodiments of the present invention include dispersing nanotubes, enabling dissolution of nanotubes, and noncovalently functionalizing nanotubes.

The organic material used in manipulating nanotubes preferably comprises a soft organic material, soluble organic material, and/or an organic material that acts as a dispersing reagent for dispersing nanotubes.

In a preferred embodiment, the organic material utilized for manipulating nanotubes comprises cyclodextrin.

Inventors: Chen; Jian (Richardson, TX); Dyer; Mark J. (San Jose, CA)

Nano-engineered phosphors and related nanotechnology

Assignee: NanoProducts Corporation (Longmont, CO)
Patent: 6,726,992
Date: April 27, 2004
Summary: Dispersed phosphor powders are disclosed that comprise nanoscale powders dispersed on coarser carrier powders. The composition of the dispersed fine powders may be oxides, carbides, nitrides, borides, chalcogenides, metals, and alloys. Such powders are useful in various applications such as lamps, cathode ray tubes, field emission displays, plasma display panels, scintillators, X-ray detectors, IR detectors, UV detectors and laser detectors.

Nano-dispersed phosphor powders can also be used in printing inks, or dispersed in plastics to prevent forgery and counterfeiting of currency, original works of art, passports, credit cards, bank

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checks, and other documents or products.

Inventors: Yadav; Tapesh (Longmont, CO); Pfaffenbach; Karl (Boulder, CO)

Nanoparticles having oligonucleotides attached thereto and uses therefor

Assignee: Nanosphere, Inc. (Northbrook, IL)
Patent: 6,730,269
Date: May 4, 2004

Summary: The invention provides methods of detecting a nucleic acid. The methods comprise contacting the nucleic acid with one or more types of particles having oligonucleotides attached thereto.

In one embodiment of the method, the oligonucleotides are attached to nanoparticles and have sequences complementary to portions of the sequence of the nucleic acid. A detectable change (preferably a color change) is brought about as a result of the hybridization of the oligonucleotides on the nanoparticles to the nucleic acid.

The invention also provides compositions and kits comprising particles. The invention further provides methods of synthesizing unique nanoparticle-oligonucleotide conjugates, the conjugates produced by the methods, and methods of using the conjugates. In addition, the invention provides nanomaterials and nanostructures comprising nanoparticles and methods of nanofabrication utilizing nanoparticles.

Finally, the invention provides a method of separating a selected nucleic acid from other nucleic acids.

Inventors: Mirkin; Chad A. (Wilmette, IL); Letsinger; Robert L. (Wilmette, IL); Mucic; Robert C. (Glendale, CA); Storhoff; James J. (Evanston, IL); Elghanian; Robert (Skokie, IL); Taton; Thomas A. (Little Canada, MN)

Surface-mineralized spinal implants

Assignee: DePuy Products, Inc. (Warsaw, IN)
Patent: 6,736,849
Date: May 18, 2004

Summary: A spinal implant is provided to integrate with and support vertebrae in a vertebral column. The spinal implant includes a body and a mineralized, bioactive surface coating chemically bonded to a portion of the body.

The coating includes a non-hydroxyl containing carbonated calcium phosphate bone mineral nanocrystalline apatite with chemically absorbed water having a crystal size less than about 1 mu.m. The body of the spinal implant is ring-shaped and defines a central passageway.

Inventors: Li; Panjian (Fort Wayne, IN); Smith; Todd (Fort Wayne, IN)

Apparatus and method for fabricating arrays of atomic-scale contacts and gaps between electrodes and applications thereof

Assignee: Arizona Board of Regents (Tempe, AZ)
Patent: 6,737,286
Date: May 18, 2004

Summary: A method for forming atomic-scale contacts and atomic-scale gaps between two electrodes is disclosed. The method provides for applying a voltage between two electrodes in a circuit with a resistor. The applied voltage etches metal ions off one electrode and deposits the metal ions onto the second electrode. The metal ions are deposited on the sharpest point of the second electrode, causing the second electrode to grow towards the first electrode until an atomic-scale contact is formed. By increasing the magnitude of the resistor, the etching and deposition process will terminate prior to contact, forming an atomic-scale gap.

The atomic-scale contacts and gaps formed according to this method are useful as a variety of nanosensors including chemical sensors, biosensors, hydrogen ion sensors, heavy metal ion sensors, magnetoresistive sensors, and molecular switches.

Inventors: Tao; Nongjian (Phoenix, AZ); Boussaad; Salah (Tempe, AZ) ⊙