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Nanotech Puts Cancer in the Crosshairs

For those of you who have heard me give presentations, you already know that I am excited about the prospects for using nanotechnology to help control and eradicate cancer. In fact, as you will soon read, my partners and I have invested a significant amount in nanotech start ups with promising cancer treatments.

Unfortunately, when it comes to treating cancer, modern medicine is still in its infancy. By and large we still rely on debilitating chemotherapy regimens which take a shotgun approach to curing cancer by essentially poisoning patients in an effort to eradicate tumors.

As I have mentioned before in these pages, nanotech represents a bright spot in the fight against cancer. Researchers are increasingly turning to therapies based on particles measuring less than 200 nm. At that scale, particles passively target weaker-walled cancer cells and help localize treatment while increasing its effectiveness.

The medication Doxil, produced by Ortho Biotech Products LP (a unit of **Johnson & Johnson** [JNJ]), uses this approach to treat certain myeloma and ovarian cancers. It incorporates chemotherapy into 100-nm liposome particles that circulate through the blood over long periods and slip into the pores of tumor blood vessels, helping to concentrate treatment at the disease site.

Cambridge, Massachusetts-based Tempo Pharmaceuticals—in which my firm Lux Capital is an investor—is working on a nanoscale delivery system with better control over the release of its active ingredients (*see Companies to Watch, June 2007*). Its particle, in fact, aims to release two drugs sequentially: The first trapping the particle inside the tumor, the second attacking the tumor from within.

Cancer researchers believe that further engineering the shape or surface properties of nano-particles can enable the particles to actively target tumors, and thereby maximize their diagnostic or therapeutic function at the cancer-site while minimizing collateral damage to healthy tissue. The targeting mechanism can be something like folic acid, which binds selectively to folate receptors common to ovarian, breast, lung and colon cancers.

Five years ago, virtually all research into nano-enabled treatments that actively targeted cancer was driven by government funding, and performed at the academic level. In 2004, the National Cancer Institute (NCI) launched a $144.3 million Alliance for Nanotechnology in Cancer. The aim was to pool the resources of researchers, clinicians, and public and private organizations to develop and translate cancer-related nanotechnology research into clinical practice.

Developments in this field have accelerated since then, according to Piotr Grodzinski, Director of the NCI's Alliance. "If you look at where we were five years ago, there was nothing mature enough that the FDA would even consider. Today there are 20-30 small companies in both diagnostics and therapeutics. A handful of those are in clinical trials, and we expect another three or four will file applications this year."

A New Crop Delivers

While many of these venture-backed start-ups label themselves as pharmaceutical companies, their efforts have largely concentrated on developing versatile nanoscale delivery platforms that can incorporate different therapeutics, targeting technologies and other functions according to need.

"We're not trying to reinvent every aspect of the science," said Seth Feuerstein, president of Carigent Therapeutics in New Haven, Connecticut. "We focus on delivering current drugs better, and we're also working with companies whose drugs haven't yet been approved to help make them more effective."

Nanotech represents a bright spot in the fight against cancer with new therapies based on particles measuring less than 200 nm.

Launched last May, Carigent is among the most recent additions to the sector. Its delivery platform is based on a well-characterized, FDA-approved biodegradable chemical platform called PLGA. The company's nanoparticles incorporate a high density of attachment sites on their surface, enabling them to carry out multiple functions like targeting tumors, enhancing diagnostic images, treating diseased tissue or concealing the whole package from the body's natural defenses.

A handful of companies—including Avidimer Therapeutics, Liquidia Technologies, Insert Therapeutics, Intradigm and BIND Biosciences—are sharing a similar approach.

Avidimer Therapeutics in Ann Arbor, Michigan, is coating its nanoscale delivery vehicle with multi-branched dendrimers to which it can attach other functional molecules such as folic acid for targeting tumors and the cell-killing cytotoxin MTX to help treat them.

Liquidia Technologies in Morrisville, North Carolina is developing a

process to efficiently and precisely engineer nanoparticles to share a specific size, flexibility, structure and other properties. Spun out of the University of North Carolina (UNC), the start-up's approach enables it to incorporate therapeutic agents inside the particle in any concentration, or even use them to mold the actual particle.

"Our process is very gentle, so it can mold proteins without denaturing them," said Luke Roush, Liquidia's vice president of business development.

In addition to a research collaboration with UNC to determine how specific particle properties determine distribution through the body, the company is also developing nano-enabled treatments for lung, breast and prostate cancer.

Insert Therapeutics and Intradigm are also working on targeted treatments, but both companies are also exploring the use of a Nobel-prize winning therapy based on RNA interference (RNAi).

In order to operate, our cells constantly switch protein production on and off through specific gene functions. An active gene produces a specific protein, but when the body has enough of that protein, the gene releases an inhibitor to stop production. Cancer, by nature, confuses or even reverses this process. So the idea behind RNAi therapies is to deliver the chemical signals that throw the switch on production of selective proteins.

"Most treatments based on antibodies are analogous to stacking sandbags for flood control," said Mohammad Azab, CEO of Intradigm. "Our technology aims to stop the rain, instead of stopping the flood."

In Intradigm's case, the target isn't the cancerous cells, but rather the creation of new blood vessels that feed them. The company hopes to begin its Phase I trials by the end of 2008.

Insert, a subsidiary of **Arrowhead Research** [ARWR], is developing the delivery vehicle to carry the RNAi technology of Calandro Pharmaceuticals, another Arrowhead company. The company hopes to enter clinical trials sometime early this year.

The ties at BIND

Lastly, there's BIND Biosciences which is less forthcoming about the details of its targeting mechanism, the therapeutic it will deliver, or even whether its first clinical candidate will address cancer or cardiovascular disease. CEO Glenn Batchelder said, however, that the company's nanoparticles are created by manipulating the physicochemical properties of clinically validated biomaterials.

BIND's ability to precisely control these parameters enables it to use a combinatorial approach to determine what precise number of ligands and other functional molecules will do the job best. On its surface, that sounds like an obvious approach. But BIND is perhaps the only company pursuing it, and the result could be an important competitive edge in the long term.

"The conventional wisdom was that if you wanted to make a targeted particle, you added ligands; and more ligands meant stronger targeting," said Omid Farokhzad, an assistant professor at Harvard Medical School who cofounded BIND with Robert Langer, an Institute professor at the Massachusetts Institute of Technology.

It turns out the opposite may be true, Farokhzad added. Namely a low concentration of ligands can actually make for better targeting.

This could pose unforeseen problems for companies developing such particles, because it suggests mathematical models won't predict the most effective number of targeting ligands to attach.

It gets even more complicated: Every characteristic you add to a nano-delivery system comes at the expense of another one, says Farokhzad. Particles that excel at targeting cancer, for example, are more likely to trigger the body's natural defenses against interlopers. Attaching certain molecules will help cloak targeting agents from the body's defenses, but only at a cost to their ability to zero in on cancer cells.

As you figure in all the different functions that nanoparticles are intended to perform, the complexities grow; and even if you happened to attach the optimal number of functions on your first attempt, the challenge remains to consistently reproduce that balance in other particles.

BIND's combinatorial approach will help it build libraries of possible combinations by testing hundreds of candidate profiles in rapid fashion.

The Insider

Here's a controversial question: What if you didn't have to die? When asked this, first my eyes rolled; then my eyebrows raised. This month be sure to read the special three-way interview with Aubrey de Grey, who will eventually either prove to be off his rocker or prove to have helped you avoid a rocker in the first place. Weighing in with a more conventionally credible scientific point of view is David Sinclair, Harvard rising-star, founder of recently public company **Sirtris** [SIRT] and venture partner at my firm Lux Capital.

While a "cure" for aging might seem far-fetched, and a "cure" for cancer, less so—a lot of smart people (and the smart money backing them) are trying to turn cancer into a treatable condition like diabetes. Nanotech is front and center attacking cancer like a molecular military, replete with covert and timed attacks, Trojan horses that would make Ulysses proud.

Also, you read it here first: One of the great frontiers of technology (both hardware and software) is the haptic interfaces and displays that we react to and interact with. The molecules and materials from Apple's iPhone to Cambrios' touch-screen materials to flexible displays are putting the "active" in interactive. This is an area ripe for innovation and change—meaning it's also ripe for in-the-know investors to position themselves ahead of others. The future, like information, is here—it's just unevenly distributed. As always, here's to thinking big about thinking small...and to the emerging inventors and investors who seek to profit from the unexpected and the unseen....

Nano in the News

Sunny Days for SunPower

Solar cell manufacturer **SunPower** [SPWR] announced partnerships with **Hewlett-Packard** [HPQ] and **GE**'s [GE] Energy Financial Services unit—HP will work with SunPower to install the company's solar power systems and some of its facilities, while GE will provide project finance to SunPower's solar plant projects, picking up majority stakes in many projects.

Theranostics

Kereos Inc., in St. Louis, isn't limiting its focus on treating cancer *[Full disclosure: my venture firm Lux Capital is an equity investor in Kereos]*. The company is developing its targeted nanoparticles to deliver imaging agents to the cancer site.

Notably, CEO Robert Beardsley said the design of his company's nanoparticles avoids the task of balancing stealth and targeting functions.

"We don't try to evade the body's immune response," he said. "Those of our droplets that don't adhere at the disease site are cleared from the body. If we did do things like stealth it would change the way we target cells."

Kereos's technology helps highlight the vasculature around tumors, where it can help detect much smaller tumors—about 1 to 2 mm—in an MRI image. The technology can also highlight the tumor's perimeter and margins, aiding plans for surgery and therapy.

The company hopes to begin clinical testing of its nano-delivery system this year. If successful, it will be adding therapeutics to its nanoparticles, which could eventually allow physicians to image tumors and treat them, all in one stroke.

This combination of diagnostics and therapeutics into a single treatment is the focus of an emerging field of study called theranostics.

While potentially revolutionary, theranostic technologies face an uphill battle when it comes to FDA approval.

"It will not happen without changes to the way drugs are approved," said Beardsley. "It can be done, but it's both cost and time prohibitive unless we protect the safety of the public and show improved efficacy of treatments."

Howard Soule, an Executive VP at Michael Milken's Prostate Cancer Foundation, agrees. But he puts the responsibility of improving the efficiency of clinical testing on companies Kereos and its nanotech brethren, not on the Food and Drug Administration (FDA).

Currently, the regulatory approval of an experimental medication in oncology is based on whether it improves patients' survival. Determining that particular end point, however, extends the clinical testing process, increases its overall cost and prolongs time to market.

The approval process could be significantly accelerated if companies demonstrate to regulators that there are intermediate endpoints that correlate to meaningful clinical outcomes.

"The FDA is not the enemy; the enemy is us," said Soule. "The FDA will not discover a new endpoint or biomarker that will help develop drugs better. But they would welcome such technology. Discovery of progression biomarkers will require rigorous scientific research."

Displays: Ubiquitous and User Friendly

The display business is red hot these days. In early January, **Sony** [SNE] introduced the first commercially available organic light emitting diode (OLED) television, signaling what could be a brighter, higher contrast future for flat panel TV screens. Meanwhile, in November, **Amazon.com** [AMZN] introduced its Kindle, an electronic book reader that, like Sony's PRS-505 reader, uses a low-power electrophoretic display technology that mimics paper.

But the biggest splash came last June, when **Apple** [AAPL] introduced the iPhone. Admittedly, it wasn't the first time a touch-screen appeared in a hand-held device. But Apple took an extra step by enabling its display to detect and respond to two or more simultaneous contacts on the display surface.

Of course, before Apple ever made multi-touch screen displays portable, conventional touch screens were already gaining traction in handheld video games, PDAs and GPS devices. Jennifer Colegrove, a senior analyst at market research firm iSuppli believes that these single-touch screens will expand to planes, automobiles, machine-control systems and home appliances. She estimates that global revenues for the leading technologies are on track to almost double from $2.4 billion to $4.4 billion between 2006 and 2012.

The market for conventional touch screens is divided among over a dozen different technologies—all of which comprise three components: the film and sense mechanism, the integrated chip (IC) that makes sense of where and what kind of touch the screen registers, and software to interpret the data.

Expect conventional touch screen applications to expand aboard planes, automobiles, machine-control systems and home appliances.

Of course different touch screens rely on different mechanisms to register touch. The dominant architecture uses resistive technology, and represents over two thirds of the 100+ manufacturers selling touch screen components. Resistive screens offer adequate image quality at a relatively low price.

The number of competitors in this sector—among them, **Tyco Electronics** [TEL] and Touch International—will keep the price down and slow revenue growth to about 3% a year, Colgrove reports.

Notably, **3M** [MMM] sold its resistive touch screen business to Texas-based Touch International last June, citing plans to focus on alternative technologies.

Among those alternatives are surface capacitive touch screens, which rely on sensing a finger's electrons rather than waiting for the pressure of its touch. The higher image quality, greater durability and lighter touch of these displays come with a higher cost and price, which helps them weigh in at 20% of the touch screen market's overall value.

Plus, they can be adapted for multi-touch applications. Colgrove expects this sub-sector to grow at 30.8% from $112.9 million in 2007 to reach $433.1 million by 2012.

Multi-touch Mania

The multi-touch capability of surface capacitive screens makes them a likely alternative route for companies hoping to get a leg up on Apple, whose proprietary projective capacitive technology grabbed the

early lead in multi-touch phones.

This lead isn't in any danger near term. Samsung reportedly released a multi-touch cell phone in Korea, but details about the device are limited. LG Electronics, **Research in Motion** [RIMM] and **Nokia** [NOK], meanwhile, hope to release similar products over the next two years. Another firm in this space is Germany-based **Balda AG** [BAD.DE], which owns a 50% share in Taiwan's TPK Solutions Inc. My sources tell me that Balda is one of the main suppliers of the iPhone's touch screen modules.

Other companies like Sharp Electronics and Sony are pursuing optically-driven approaches to develop multi-touch displays. Then there are the companies that provide ICs for interpreting multi-touch interactions. Leaders include **Cypress Semiconductor** [CY], **Synaptics** [SYNA] and Quantum Research Group.

All three of the top touch screen display technologies—as well as LCDs, plasma displays and others—rely on the use of indium tin oxide (ITO), a transparent, conductive coating material. Because of growing demand there is a shortage of ITO.

One of my venture firm's portfolio companies, Cambrios Technologies is developing a cost-effective alternative to ITO films, which are generally deposited with vacuum processes. Cambrios's alternative is an ink-like liquid infused with metallic nanostructures. By changing the concentration of nanoparticles or the parameters of the ink's deposition, the company can produce transparent films with electrical resistances that are comparable to ITO. But they leverage less expensive manufacturing methods, such as spin coating and slot die processes. Plus, Cambrios's material doesn't share ITO's brittleness, which is important to flexible displays. Cambrios hopes to launch a product for the resistive touch panel industry sometime this year.

Flat Screens 2.0

Large-screen organic light emitting diode (OLED) displays have been "just over the horizon" for almost 10 years. But, earlier this month, Sony changed that by unveiling the first commercial OLED television at CES, the Consumer Electronics Show in Las Vegas.

Unlike LCDs, which require a backlight to illuminate their content, OLED displays emit light directly, allowing them to power fewer components and deliver brighter images.

Sony's XEL-1 TV features groundbreaking contrast, brightness and color in a screen measuring 11 inches from corner to corner, and 3-mm front to back.

"What matters now is how quickly the technology can get a foothold," said Barry Young, senior VP at market research firm DisplaySearch. "And Sony's TV isn't priced for rapid adoption."

Sources priced the XEL-1 between $1,700 and $1,900, while Sony's website lists it at $2,500. Its cost—and its value— stem from its use of active-matrix OLED (AM OLED) technology, which incorporates transistors within the display itself to deliver brighter, sharper images with quick response times that capture movement onscreen.

Other companies may not be far behind with comparable products. Samsung SDI, Chi Mei EL (aka CMEL), **LG Philips** [LPL] and **Matsushita** [MC] are all developing larger AM OLED devices.

All of them confront serious technical and manufacturing challenges. In theory, AM OLEDs should be cheaper to make than LCDs because they don't require an LCD's backlight, color filter, or polarizer. But the manufacturing challenges associated with the AM circuitry and display structures grow progressively difficult as screen size is increased.

Despite these issues, Young expects to see 30-inch AM OLED TVs on the market by 2010. Since cost is a function of production volumes, their price should drop as manufacturing scales up.

Meanwhile, 2- to 3-inch passive OLED displays are already being integrated into cell phones and portable media players. As of last year, Samsung SDI began shipping the devices in volume, while CMEL started production in Taiwan. Both companies have announced plans to double OLED capacity.

E-Paper is a Page Turner

Anyone doing their shopping on Amazon over the holiday season is probably familiar with the company's new book-sized electronic reader, the Kindle. Like Sony's PRS-505 reader, the $399 Kindle can download books for viewing on a 6-inch diagonal, bi-stable display that mimics paper. Amazon's Kindle has gotten rave reviews and sold out in less that five and a half hours.

Bi-stable displays—so called because their earliest forms defaulted to either a black or white screen—generally reflect light like ordinary paper (hence e-paper) rather than relying on a backlight. More notably, however, is their ability to retain an image without a constant supply of electrical power. As a result, e-paper can significantly prolong battery life. Amazon reports its Kindle can be read for a week or more without charging up.

One downside may be cost. Estimates differ, but a 6-inch bi-stable technology could run anywhere from $50—comparable to an LCD—to about $90 to $100 if you include the backplane and the specialized electronics that drive the device.

The lack of competition doesn't help either. Currently, E-Ink in Cambridge, Massachusetts, is the only commercial supplier, and its two product lines reflect the prospective end-markets. E-Ink's segmented displays exhibit very basic information in applications such as USB memory sticks, smart cards and battery indicators. But E-Ink also offers larger, active matrix displays with reconfigurable formats. For these products, the company has partnered up with thin-film transistor specialists like Prime View and LG Philips.

E-Ink—whose displays are limited to black and white images—may not be the only supplier for long. Several other companies are working on their own versions of the technology, including SiPix, **Qualcomm** [QCOM], French start-up Nemoptic and even Japanese tire maker **Bridgestone** [BRDCY.PK]. Virtually all of them, including E-Ink, are developing color displays. Stay tuned.

Nano in the News

NanoDynamics Looks to the Middle East for Investment

Following the lead of big Wall Street banks, fledgling nanotech company NanoDynamics also turned to the cash-rich investors in the Middle East. NanoDynamics is planning to list on the newly established Dubai International Financial Exchange (DIFX). Interestingly, Altair Nanotechnologies [ALTI] raised $40 million from a Dubai-based group. NASDAQ owns a 20% stake in the DIFX.

Thinking Small: Aubrey de Grey vs. David Sinclair

Here's a three-way interview with controversial Aubrey de Grey on his theory to end aging—something he calls a disease. He holds a controversial PhD and dubs his ideas Strategies for Engineered Negligible Senescence (SENS). David Sinclair weighs in on de Grey's ideas. Sinclair is Associate Professor of Pathology at Harvard Medical School and Director of the Glenn Laboratories for the Biological Mechanisms of Aging. In 1997, he found the cause of aging in yeast, a first for any species; in 2003 discovered a gene controlling this process. Dr. Sinclair is a co-founder of both Sirtris Pharmaceuticals (NASDAQ: SIRT) and Genocea Biosciences and a Venture Partner at Lux Capital.

How do you define aging and why view it as a disease?

de Grey: Aging is the lifelong accumulation of changes to the structure of our bodies—changes that are side effects of the processes which keep us living for as long as we do, but that eventually compromise those processes, leading to disease, debilitation and finally death. Aging is a biological phenomenon that's bad for you, and thus that it is a valid and feasible target for postponement and eventual defeat by medicine.

Sinclair: *I have stronger views. Aging is nothing special. It is a set of diseases that arise due to the deterioration of our bodies. If you read the definition of "aging" vs. "disease" in Stedman's Medical Dictionary, if a condition occurs to the majority of the population as they get older it is called "aging", otherwise it is a "disease". If some condition occurs to most of us, then that is even greater reason to slow or prevent it.*

For a theory to be scientific, it should be testable and refutable. What are you doing to test your theory?

de Grey: I have a technological proposal for maintaining the body in full working order indefinitely. You could call that a theory as it would be falsified if my proposed treatments were developed and applied and the animals (or humans) that received them died on schedule. We're funding research at five universities, focused on two of the most challenging (and most neglected by other funding sources) of the seven SENS strands: the removal of indigestible material that accumulates in non-dividing cells, and the obviation of mutations in the mitochondria.

Sinclair: *The SENS proposals are testable. Work in my lab is based on the hypothesis that we will be able to extend lifespan by tapping into the body's natural defenses against disease and deterioration. Many people now think that we have the technology to extend lifespan by slowing and treating age-associated diseases, and that we will be able to test the hypothesis over the coming decades.*

Have you seen commercial or investor interest?

de Grey: The funding received has been philanthropic. But we're taking care to obtain the best IP positions we can in respect of university research that we're funding, so as commercial incentives to invest rises the risks fall. The pioneers who take the leap into the unknown first will be the biggest winners. Our biggest donor so far, Peter Thiel, runs a very successful hedge fund, Clarium Capital, and investment group, the Founders Fund [and founded PayPal]

Sinclair: *For aging research to be profitable, it needs to have a clearly defined product. An anti-aging pill is not the answer. Hence, the amount of investment in aging research is still relatively small. In the case of Sirtris Pharmaceutucals (Nasaq: SIRT), the company I co-founded in 2004 with Christoph Westphal, we have seen it is possible to raise over $100M for technology based on aging research, but primarily because there are clearly defined product(s) in reach. In the case of Sirtris, they are developing drugs to treat Type II diabetes, MELAS, an inherited mitochondrial disorder, and other diseases of aging. Their products could reach the market by 2010. Hopefully, the success of Sirtris will lead to greater interest from academics and investors in making practical use of the discoveries in the aging field to help society and provide investor returns.*

Isn't reversing aging going against nature?

de Grey: Reversing aging is going against nature to exactly the same extent that the wheel, vaccines and airplanes are. They're all natural—what's unnatural is not using the abilities we're born with to improve our world.

Sinclair: *Antibiotics, anesthesia, and vaccines "go against nature" but how many would volunteer to go back 200 years.*

What social and economic consequences result from a 400 year lifespan?

de Grey: There won't be frail, decrepit people living their last years in pain and suffering, soaking up society's wealth. There will be fewer


Aubrey de Grey


David Sinclair

children—a trend that's already begun on a massive scale throughout the developed world (and without compulsion). Changes will happen to the economy as we reorganize the pension system and adult education/retraining to accommodate serial careers. These changes will hit us when they become widely anticipated as a result of work on animals—which could be as little as ten years from now.

Sinclair: *I agree there will be massive changes if people live 400 years but I also think there will be time to get ready. If we succeed in making people live an extra 10 years, that will be a major accomplishment, and one that we will have to deal with in terms of the economy and social structure. Having people live into their 90's, being able to play tennis, watch their grandkids graduate from college, and live more productive lives would be welcome and would save on healthcare costs because long-lived people tend to die quicker.*

Are your approaches to anti-aging research competitive or complementary?

de Grey: David focuses on "tuning" the body's anti-aging machinery: getting the most out of our inbuilt genetics to combat aging. I focus on augmenting that machinery in ways that medicine can do but evolution couldn't. So David's approach is much easier than mine and will probably succeed much sooner. David's work promises to be a "bridge" to mine: it may allow people to live maybe a few years longer, (and the extra years will be healthy), but the bigger benefit will keep people going just long enough for SENS to arrive, when otherwise they wouldn't quite have made the cut. That's why he and I strongly support a portfolio approach to funding for the war on aging, hastening both types of technology.

Sinclair: *Essentially Aubrey and I agree. We think aging is abhorrent but treatable. He is also correct that our approach is one part of the challenge but an important one because it would the first step in that journey, and is often the hardest.*

Follow the Money

A monthly look at who is getting funded and who's giving it.

Venture Capital Funding

NanoGram

Location: Milpitas, CA
CEO: Kieran F. Drain
Funding Announced: 1/15/2008
Investors: Global Cleantech Capital, Mitsui Ventures, Nanostart AG, TEL Venture Capital, Rockport Capital Partners, **Harris & Harris Group** [TINY], Institutional Venture Partners and Technology Partners
Funding Amount: $32 million (Series C)
Notes: Milpitas, CA-based NanoGram Corp. (NGC) raised $32 million to fund the development of NGC's silicon solar technology and nanomaterials-based products for flat panel displays, solid-state lighting, batteries and printed electronics. Existing investors were joined by a slew of new investors, including Global Cleantech Capital and the venture capital arms of Japanese conglomerate Mitsui & Co. and semiconductor equipment manufacturer Tokyo Electron.
Outlook: NGC was founded in 1996 with funding from Institutional Venture Partners, with an initial focus on communications equipment. It was segregated into three separate companies in 2002—NeoPhotonics focused on the communications sector, NanoGram Devices (NGD) was formed to focus on batteries for medical devices and NGC was established to develop new applications from the residue intellectual property. Early investors have already seen an exit—NGD was acquired for $45 million in 2004. Now, it is cashing in on the exploding demand for solar manufacturing equipment. NGC is a company worth watching.

Deeya Energy

Location: Fremont, CA
CEO: Vic Mahadevan
Funding Announced: 1/7/2008
Investors: New Enterprise Associates (lead), Draper Fisher Jurvetson, BlueRun Ventures and DFJ Element
Funding Amount: $15 million (Series B)
Notes: Energy storage company Deeya Energy raised $15 million to finance a manufacturing facility it plans to set up in Gurgaon, India. CEO Vic Mahadevan was formerly a senior executive at Compaq Computer and seasoned operator of three start-ups prior to Deeya. He is developing recyclable "L-cell" batteries as an alternative to conventional lead acid batteries. The company claims its batteries will be 3x as cheap with comparable performance. Deeya intends to ship product by the second quarter of 2008.
Outlook: Deeya Energy has initially chosen to target telecom infrastructure in India—it wants to supply back-up power solutions to telecom towers, and the market is ripe for picking. India is seeing the dual problem—there is runaway growth in telecoms, with 6-8 million new cellular phone subscribers being added every month, while power supply is spotty and unreliable. Telecom companies are forced to install back-up power systems. Its product strategy could prove very effective and later Deeya can move to more mainstream markets such as energy storage for renewables such as solar and wind.

Nanochip

Location: Fremont, CA
CEO: Gordon R. Knight
Funding Announced: 1/22/2007
Investors: Intel Capital and JK&B Capital
Funding Amount: $14 million (Series C2)
Notes: Nanochip, a fabless chip company developing storage products for consumer electronics, is applying micro-electro-mechanical systems (MEMS) together with atomic force probe tips as read-write heads to create flash memory chips capable of holding several tens of gigabytes of data per chip, with the goal of eventually attaining terabyte-level storage. Nanochip's technology is based on the method of data registration and the tip/media interface, rather than pushing the physical limits of lithography. The company intends to use the money for prototyping, expecting to have usable samples ready for testing and limited customer deployment by 2009.
Outlook: An investment from semiconductor leader Intel suggests that Nanochip's technology has merit. Given the profusion of multimedia devices such as **Apple**'s [AAPL] iPhone and the possibility of fast media distribution over wireless internet, there is a burgeoning need for high-capacity storage. Nanochip's products could fill the gap, but cost competitiveness with non-solid state media is a significant issue.

Nano in the News

New Electrode for OLED Products
French high-performance materials manufacturer Saint-Gobain and organic light-emitting diode (OLED) start-up Novaled developed a new transparent conducting electrode that is significantly better than indium tin oxide (ITO) and will enable the manufacturing of large OLED lighting products.

Companies to Watch

Amyris Biotechnologies Inc.

Private

www.amyrisbiotech.net **510-450-0761**

Emeryville, CA

Chief Executive: John G. Melo

What it does: Applies synthetic biology to develop anti-malarial drugs and pioneer cost-effective, environmentally safe alternatives to petroleum-based fuels.

Amyris Biotechnologies has received its share of press lately for a prospective biofuel technology that appears on track to deliver more energy than ethanol, enable lower cost, lower-polluting biofuel blends, and plug easily into the existing petroleum infrastructure.

But the company had a very different agenda four years ago, when it was primarily focused on developing a cost-effective treatment for malaria —a disease afflicting 300-500 million people worldwide

The project, in which Amyris still plays a role, is part of a non-profit collaboration with the University of California and the Institute of OneWorld Health. Amyris's approach was to use synthetic biology to produce artemisinin, a key ingredient for anti-malarial drugs.

"The drug exists today, but it is expensive and not widely available in developing countries," said CEO John Melo. "Our goal is to make it more affordable to those who need the drug most."

Researchers at Amyris addressed the challenge by inserting genes into select microbes to alter their metabolic pathways, and enable them to produce specific compounds. The strategy was then to scale up the production of these cellular factories through a fermentation process resembling the one used by LS9 Inc. (*see Companies to Watch, August 2007*).

Amyris expects to transfer its manufacturing technology for artemisinin to a leading pharmaceutical company sometime this year, Melo said.

Along the way, the company discovered its synthetic biology could also engineer microbial systems that produced hydrocarbons. These hydrocarbons are the platform on which the company plans to develop its biofuels.

The biofuels are derived from renewable feedstocks, such as sugar cane, corn or cellulosic biomass. Plus, preliminary analysis indicates that they could result in an 80% reduction in life-cycle greenhouse gas emissions compared to petroleum-based fuels, said Melo.

In late 2006, Amyris launched a new research program focused on developing a diesel fuel compound. The company hopes to enter pilot production this year, and launch a commercial product as early as 2010. Further out, the company plans to develop renewable substitutes for gasoline and jet fuel.

"In terms of cost, we are targeting our renewable fuels to be cost-competitive with petroleum-based fuels at crude prices above $55 per barrel, thereby providing end-users a 'no compromise' environmentally-friendly transportation fuel alternative," Melo said.

The company completed its first round of financing in 2006, raising $20 million from investors including Kleiner Perkins, Caufield & Byers, Khosla Ventures and TPG Ventures. Last September, it raised $70 million in the first tranche of a Series B round. Duff Ackerman & Goodrich Ventures led the round, with help from existing investors. As the drum bangs louder for cost-competitive renewable fuels, this company will undoubtedly be one to watch.

Heliovolt Corp.

Private

www.heliovolt.net **512-767-6000**

Austin, TX

Chief Executive: B.J. Stanbery

What it does: Manufactures thin-film solar modules using a fast, cost-effective proprietary technology.

Photovoltaic modules based on copper indium gallium selenide (CIGS) technology represent about 10% of the thin film solar market, which is itself a fraction of the overall solar sector. But while CIGS technology is the least developed, it's also the most potentially disruptive. In addition to offering conversion-efficiencies that approach conventional crystalline silicon materials, CIGS is among the few solar technologies that could one day enable building-integrated solar modules.

HelioVolt aims to get an early lead on the market this summer, when it puts the finishing touches on a factory in Austin, Texas, and begins initial production. The plant is expected to reach a capacity of 20 megawatts (MW) this year. But it has the ability to expand to 40 MW as the company needs.

Central to HelioVolt's growth is a proprietary manufacturing process called field assisted simultaneous synthesis and transfer (FASST). As the acronym implies, FASST technology can create high quality CIGS photovoltaic films an order of magnitude more quickly than conventional thin film deposition processes such as co-evaporation. Plus, because the process is faster, it requires a much lower thermal budget.

In terms of their ability to convert light into electricity, HelioVolt's modules don't quite stack up to CIGS modules made by co-evaporation in the lab. But John Langdon, VP of marketing, believes that might change.

"We've made cells with over 12% conversion efficiency, but we believe in the long run we can reach the kind of efficiencies that co-evaporation gets—or about 15% in production," he said, adding that the company's initial products will offer efficiencies closer to 10% to 12%.

Longer term, the company will also seek partnerships with construction suppliers to explore the application of CIGS films directly onto conventional construction materials, such as steel, architectural glass, and roofing. The end goal would be finished roofs and walls that integrate solar-powered electricity-generating systems.

The market for building-integrated materials is virtually non-existent today but, given its potential to reduce the installation cost for solar technology, Langdon believes that it could represent the biggest market opportunity 10 to 15 years out.

The analogy, he says, is air conditioning. "Solar today is like AC was in 1949. Back then everything was window units. When we went to central air, the market grew 1,000-fold," he said.

Founded in 2001, HelioVolt has attracted a total of $110 million in two rounds of financing. The most recent closed last summer after drawing $101 million. Investors included Paladin Capital Group, the Masdar Clean Tech Fund, Sequel Venture Partners, Noventi Ventures, and Passport Capital.

The Emerging Tech Portfolio

Company [symbol]	Coverage Initiated	Current Price	52-week range	Mkt Cap ($mil)	Buy/Sell/Hold
Intellectual Property Incumbents *Leading researchers in the physical sciences, with big potential for spin-offs and revolutionary breakthroughs*					
GE [GE]	8/07	$34.65	$33.90-$42.15	$350,180.00	Buy
Hewlett-Packard [HPQ]	3/02	44.89	38.15-53.48	115,540.00	Buy
IBM [IBM]	3/02	104.53	88.77-121.46	147,320.00	Buy
Materials *Companies producing materials with novel properties that have applications for a wide range of industries*					
Symyx [SMMX]	3/02	6.30	6.95-21.90	210.80	Buy
Life Sciences *Companies that are working at the cutting edge of medical technology*					
Invitrogen [IVGN]	11/05	85.26	55.73-99.15	3,970.00	Buy
Nanosphere [NSPH]	11/07	12.06	11.50-22.04	267.10	Buy
Electronics *Companies that have corralled the key intellectual property that will be the foundation for next generation electronics*					
Nanosys [private]	3/02	n/a	n/a	n/a	n/a
NVE Corporation [NVEC]	7/03	27.45	20.75-41.95	127.33	Hold
Energy *Companies that are developing high-efficiency, low-cost alternative energy technologies*					
First Solar [FSLR]	8/07	171.46	26.54-256.45	13,360.00	Hold
Enabling Technologies *Tools and instrumentation that enable critical science and technology discoveries*					
Veeco [VECO]	3/02	13.23	15.47-22.28	420.30	Buy
FEI Company [FEIC]	1/03	21.81	24.01-39.25	791.40	Buy
Accelrys [ACCL]	3/02	6.25	5.51-8.24	166.80	Buy
Investment Vehicles *Funds that have investments in promising emerging technology companies*					
Harris & Harris Group [TINY]	5/02	6.99	8.00-14.32	163.40	Buy
PowerShares Lux Nanotech Portfolio [PXN]	8/07	13.94	15.21-18.75	127.10	Buy
PowerShares WilderHill Clean Energy [PBW]	8/07	21.55	16.61-26.53	1,310.00	Buy

Word on the Street

GE: General Electric was down 5% for the month. It reported a 4% increase in Q4 earnings to $6.7 billion (or $0.66 per share), from $6.44 billion (or $0.62 per share) from the previous year. Sales grew robustly across all business units, with the infrastructure group posting a 26% increase in revenues. The company said it installed over 2.3 GW of wind power equipment in 2007 and raised its renewable energy investment target to $6 billion by 2010, a 50% jump. GE reiterated its guidance for $2.42 in 2008 EPS.

HPQ: Hewlett-Packard fell 11.8%, even as it became the world's largest PC maker in 2007. HP founder William Hewlett's philanthropic foundation said it would create a fund dedicated to fighting global warming, spending over $500 million a year. HP issued 2009 fiscal year guidance for EPS of $3.79 and revenues of $118 billion, and also said it was developing PCs that would consume 25% less power.

IBM: Big Blue held steady in a turbulent month for the markets, moving up by 2.3%. It issued preliminary Q4 revenues at $28.9 billion, beating analyst estimates of $27.7 billion. IBM's T.J. Watson Research Center also partnered with the Cancer Institute of New Jersey and Rutgers University to develop diagnostic tools for cancer detection. IBM has undertaken a significant restructuring of its hardware group, and is even rumored to be making a bid to acquire **AMD** [AMD].

SMMX: Symyx Technologies wilted by 11.1%, as it said it expected a loss of $0.28-$0.34 per share in fiscal 2008, with revenues between $165-175 million. The outlook was way below analyst expectations of profits of $0.03 per share on revenues of $168 million. Symyx also launched a new screening pressure reactor for selecting catalysts and opt mizing catalyst processes.

IVGN: Invitrogen ended the month 7.9% lower. It acquired Research Triangle Park, NC-based CellzDirect for $57 million in cash. CellzDirect provides hepatocyte-based cell products and services for drug testing. It also entered into a global marketing partnership with the Netherlands-based PamGene International for its nuclear receptor-targeted drugs, a $50 billion market worldwide.

NSPH: Nanosphere remained flat for the month, successfully navigating the financial market turmoil. There was no new information about the company.

NVEC: NVE Corporation trumped the broader market to register 8.3% gains for the month, enabled by strong quarterly earnings of $1.70 million ($0.36 per share) on revenues of $4.7 million, besting analyst expectations of $0.30 in EPS. The results boosted the stock by over 35% in a single day. Broadpoint Capital upgraded the stock to a Buy rating from Neutral.

FSLR: First Solar deflated by 26%, ending its dream run on the bourses. The solar bellwether is down some 35% from its peak price of $280 reached in late December.

VECO: Veeco Instruments collapsed 17.6%, caused by tough market conditions and expectations of weak Q4 earnings. It also released a new automated 3-D atomic force microscope, the only one of its kind capable of non-destructive, high-resolution, 3-D imaging at the 32nm and 45nm length scales.

FEIC: FEI Company fell 12.3%. FEI also established a NanoPort in Shanghai, China. The NanoPort serves as collaboration centre between FEI's product developers and end-use customers, and is the fourth of its kind after locations in North America, Europe and Japan.

ACCL: Accelrys fell a precipitous 16.5% despite lack of news flow. The company will be reporting quarterly earnings on February 5.

TINY: Harris & Harris Group fell another 12.8%, adding to last month's sharp drop and turbulent market conditions made exits for its portfolio companies through the initial public offering route harder. We expect NAV to climb in the next quarter as TINY reprices its portfolio companies valuations on new financings.

PXN: The PowerShares Lux Nanotech Portfolio ended the month lower by 8.8%, the fall assuaged in part by NVE Corp.'s surge. Major fund holdings such as Altair Nanotechnologies and Arrowhead Research suffered because of unfavorable market conditions.

PBW: The PowerShares WilderHill Clean Energy Portfolio contracted by 14%, despite a new law requiring lower fossil fuel use and expansion of alternative energy by four times over the next 15 years. Many of the alternative energy and cleantech stocks that had seen dramatic run-ups over the previous months, particularly in solar, saw corrections.

Stock prices as of January 24, 2008

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