Project:
Georgian National NanoInnovation Initiative
NANOTECHNOLOGY plan

Presenter: Tamar Chachibaia, Tbilisi, Georgia

Nanotechnology - A POWERFUL RESEARCH ENABLER

NANOTECHNOLOGY –
looks like the next big thing

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NANOTECHNOLOGY - BRIDGE TO THE FUTURE

Apple recently introduced tiny iPod Nano music player

- 'Nano" is a term creeping into our vocabulary and our culture these days, and it's likely to be one of the buzzwords of the future, the way "cyber" was in the '90s.
- There should be major advances in medical technology.
- Nanotechnology is widely expected to be one of the most important industrial innovations of the 21st century. U.S. Sen. Ron Wyden, Democrat from Oregon, has said, "My own judgment is that the nanotechnology revolution has the potential to change the world on a scale equal to, if not greater than, the computer revolution.

NANOTECHNOLOGY - BRIDGE TO THE FUTURE

Apple recently introduced tiny iPod Nano music player

- The term "nano" refers to the measurement of a *nanometer* — one nanometer equals one thousandth of a micrometer, or one millionth of a millimeter, or one billionth of a meter.
- Nanotechnology is a process of building things at the nanometer scale, usually 100 nanometers or less in size. This is microscopic. A swatch of Nano Care fabric, for example, resists stains and liquids because it is layered with billions of microscopic hairs that act like the fur on a seal. But these hairs are so small that Nano Care fabric looks no different than plain cotton.
- Nanotechnology is expected to produce an immense new wave of novel products and improved versions of what we have now. Scientists envision materials with several times the strength of steel but a fraction of its weight. Developments in data storage could put nearly all the world's information on a single tiny chip. There should be major advances in medical technology.

Strategic Initiative

Nanotechnology - Implication in Medicine

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Near-term Nanoparticle Delivery Therapeutics

- Autoimmune Diseases
- Cardiovascular Medicine
- Cancer Therapy
- Musculoskeletal
- Vaccines
- Emerging Markets
- Existing/Approved Drugs
- New Drug Discovery
- DNA-based Therapies

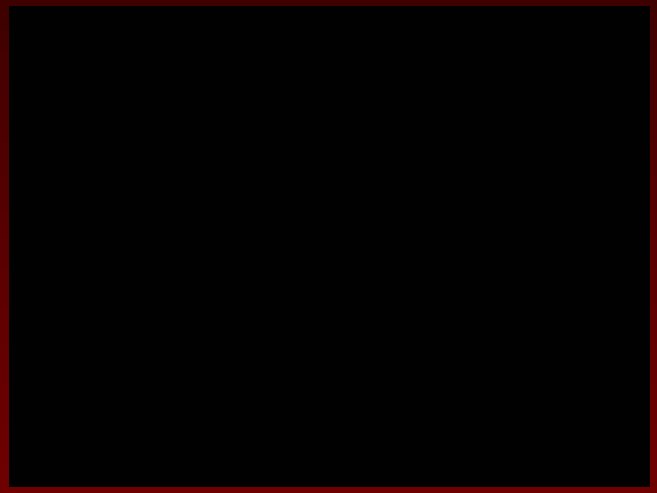
Nanotechnology will change the very foundations of disease diagnosis, treatment, and prevention

- These nanodevices are evaluated in clinical trials, researchers envision that nanotechnology will serve as multifunctional tools that will not only be used with any number of diagnostic and therapeutic agents, but will change the very foundations diagnosis, treatment, and prevention.
- Novel nanodevices capable of one or more clinically important functions, including detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are killing malignant cells.

NANOTECHNOLOGY AND CANCER

By the year 2015 National Cancer Institute plan to meet the goal of eliminating death and suffering from cancer. The National Cancer Institute is engaged in efforts to harness the power of nanotechnology to radically change the way we diagnose, image, and treat cancer.

The NCI Alliance for Nanotechnology in Cancer represents an investment of $144.3 million over five years.

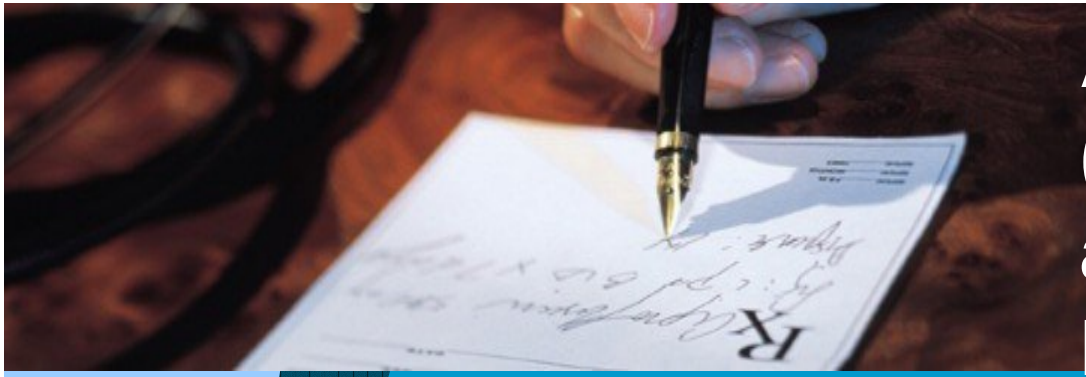


Nanotechnology is Here

- Nanoscale drug delivery devices are being developed to deliver anticancer therapeutics specifically to tumors. Liposomes are one such "first generation" nanoscale device. Liposomal doxorubicin is used to treat specific forms of cancer, while liposomal amphotericin B treats fungal infections often associated with aggressive anticancer treatment. Commercialization of these liposome encapsulated drugs produced by **Nexstar** with sales over $20 million in 1999.
- Recently, a nanoparticulate formulation of the well-known anticancer compound taxol was submitted as a new treatment for advanced stage breast cancer.

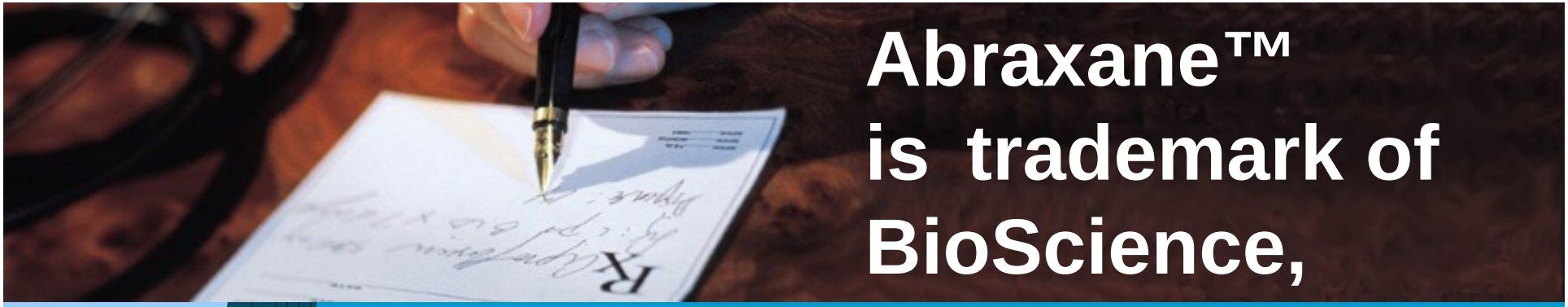
Nanotechnology Could Be The Solution To Chemotherapy Solutions

- As terrible as cancer can be, chemotherapy treatments can make one think that the disease might be the lesser of two evils. The basic premise behind chemotherapy is to poison the patient's system with a cocktail of drugs. Not only does the cancer get attacked but so too does the entire body.
- If the drugs aren't water soluble the need to be dissolved in another solvent so they can be injected. Often this solvent is highly toxic and causes strong side effects. American Pharmaceutical Partners have announced that its cancer-fighting drug Abraxane (consisting of 130-nanometer spheres of protein and paclitaxel) has demonstrated greater tumour reduction and fewer side effects when compared to a solvent-dissolved equivalent.



ABRAXANE™ (Paclitaxel) was approved in February 2005 by the FDA.

- **ABRAXANE™ - for Injectable Suspension is the first and only approved taxane for the treatment of metastatic breast cancer in a new class of albumin-bound nanotechnology that is free of solvents.**
- **As a solvent-free chemotherapy agent, ABRAXANE increases the convenience of administration.**
- **For the first time, the anticancer drug paclitaxel can now be delivered using the protein albumin rather than a chemical solvent.**

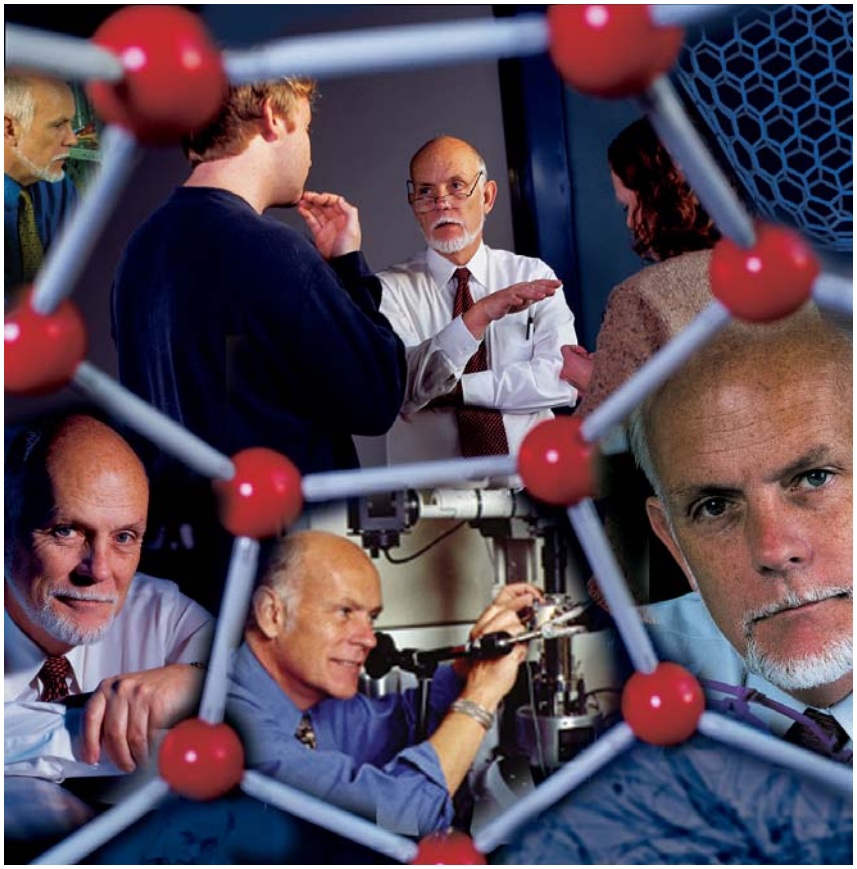


Abraxane™ is trademark of BioScience, Inc.(USA)

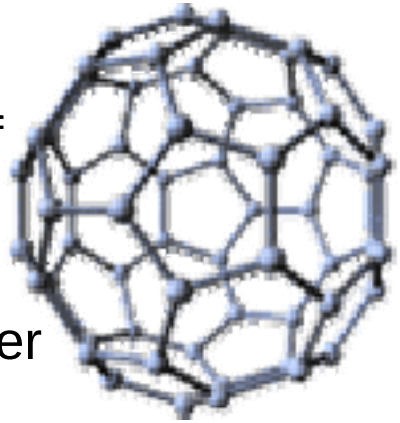
- American Pharmaceutical Partners have announced that its cancer-fighting drug Abraxane (consisting of 130-nanometer spheres of protein and paclitaxel) has demonstrated greater tumour reduction and fewer side effects when compared to a solvent-dissolved equivalent.
- ABRAXANE ™ for Injectable Suspension launched by Abraxis Oncology, the proprietary drug division of (APP) American Pharmaceutical Partners, Inc.

Carbon 60 (C60) - Buckminsterfullerene

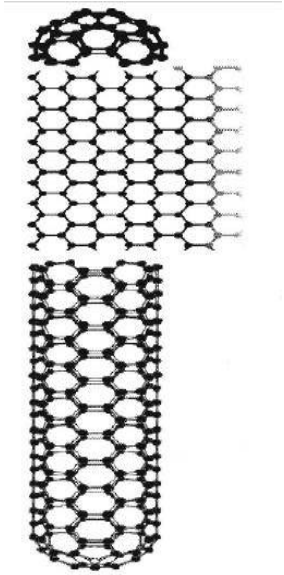
- **Buckyball was discovered in 1985 among the byproducts of laser vaporization of graphite in which the carbon atoms are arranged in sheets.**
- **Though C60, referring to the number of carbon atoms that make up one sphere, is the most common fullerene, researchers have found stable, spherical carbon structures containing 70 atoms (C70), 120 (C120), 180 (C180), and others.**
- **Robert F. Curl Jr. and Richard E. Smalley and Harold W. Kroto won the 1996 Nobel Prize for Chemistry for their discovery of buckminsterfullerene, the scientific name for buckyballs.**



Buckyball or Fullerene or C60

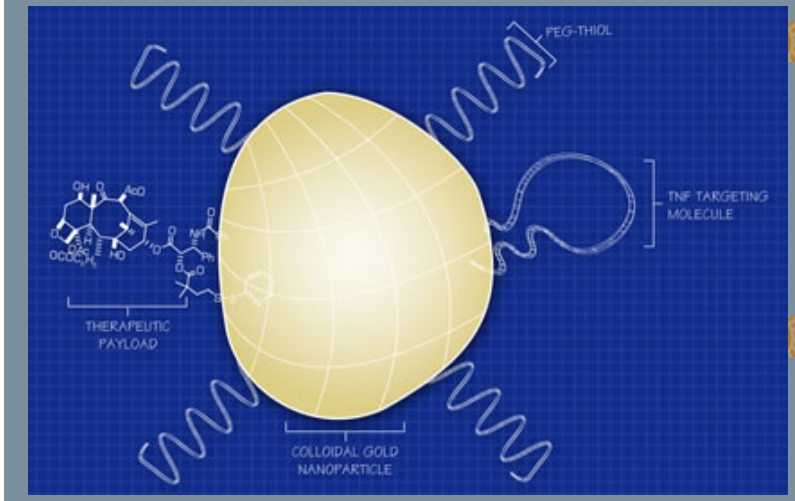


- One of three known pure forms of carbon (graphite and diamond being the other two) Carbon-60, a molecule of 60 carbon atoms that form a hollow sphere one nanometer in diameter. The molecule was named buckminsterfullerene, or fullerene, because of its similarity to the geodesic dome designed by Buckminster Fuller.
- A form of carbon related to fullerenes, except that the carbon atoms form extended hollow tubes instead of closed, hollow spheres. Carbon nanotubes can also form as a series of nested, concentric tubes. Carbon nanotubes can be used as nanometer-scale syringe needles for injecting molecules into cells and as nanoscale probes for making fine-scale measurements. Carbon nanotubes can be filled and capped, forming nanoscale test tubes or potential drug delivery devices. Carbon nanotubes can also be “doped,” or modified with small amounts of other elements, giving them electrical properties that include fully insulating, semiconducting, and fully conducting.



- Nanotubes may one day be used in transdermal drug delivery patches as nanoscale needles that can inject substances into the body. In fact, developing nanotubes as nanoscale, intravenous or intradermal, drug delivery devices is medically significant because
- a) it increases the mechanical and sensing functionality of the resultant nanoneedle, which makes it precise.
- b) it is a less invasive and less painful drug administration. Nanotubes offer the potential of targeted drug delivery, for example to muscles, with molecular amounts of material, which maximizes efficiency by permitting lower doses, thereby minimizing possible toxicity and harmful side effects.
- Nanotubes could even be used as nanoneedles that inject drugs directly into individual cells, as developed at Purdue University. Indeed, many drugs destroy infectious bacteria by poking holes in their cellular membranes and leaking out their nutrients, just like pricking a hole in a balloon. The nanotubes developed by Purdue University could also act in this manner, but in addition, they can be targeted and thus lure bacteria with “a bait” that guides the nanotubes to the bacterial cell membrane where they can start destroying the cell.

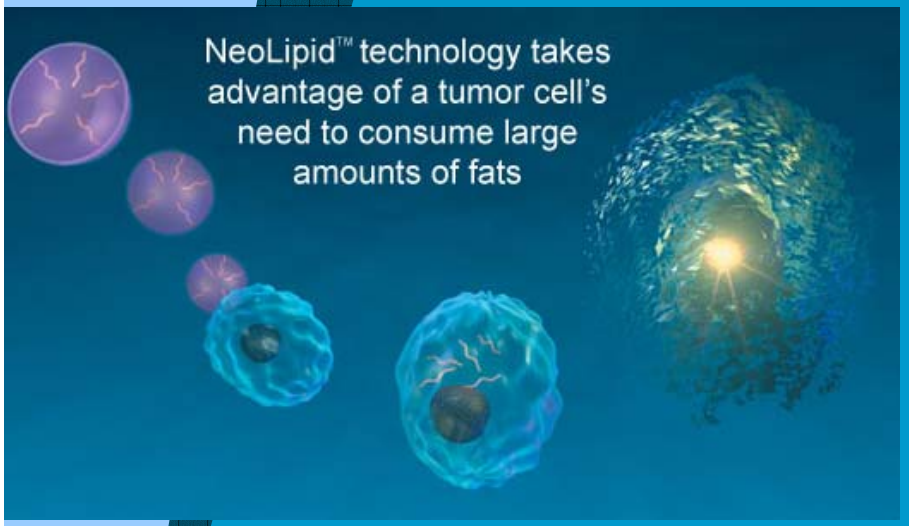
How works Colloidal Gold?

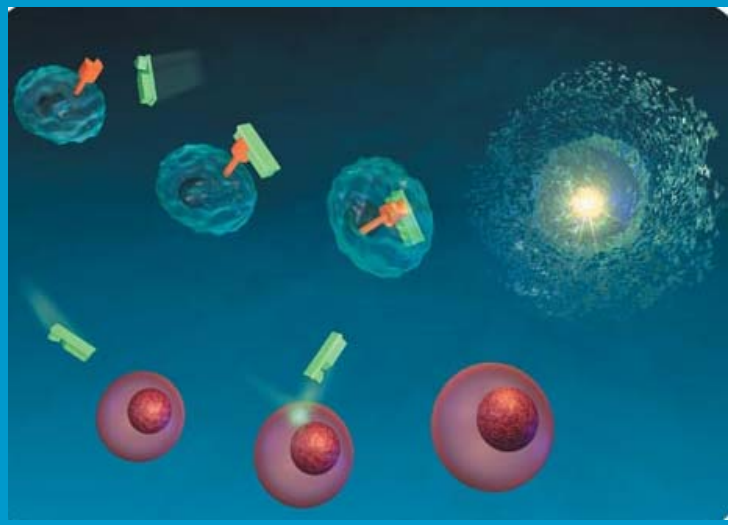


- Polyethylene glycol (PEG) masks particles from immune recognition preventing uptake by liver and spleen
- Nanoparticles exit circulatory system only at the tumor neovasculature due to leakiness of blood vessels
- Particles too large to exit circulation elsewhere
- TNF targeting molecule on particle's surface binds to receptors causing rapid absorption of drug in and around tumor.

Please Switch Appendix Flash file!

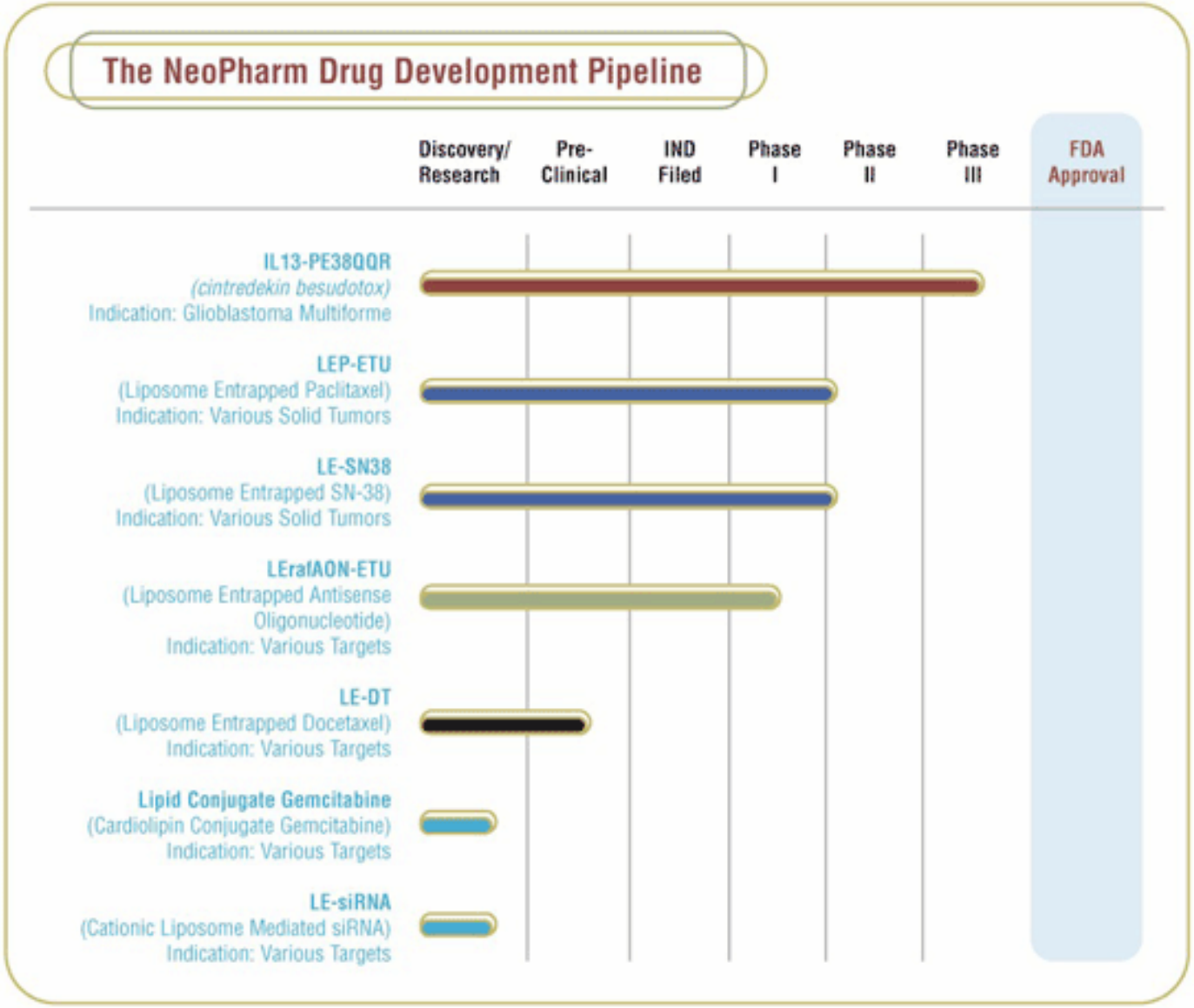
NeoPharm has built its drug portfolio based on its two novel proprietary technology platforms: a tumor-targeting platform and the NeoLipid® drug delivery system.





NeoLipid® technology entraps anticancer agents inside liposomes, which are microscopic membrane-like structures created from lipids (fats). Because tumor cells need to consume large amounts of fats to sustain their rapid growth, they eat the liposome, while at the same time absorbing the anticancer agents.

NeoLipid® DRUG DELIVERY PLATFORM



BioDelivery Sciences International, Inc.

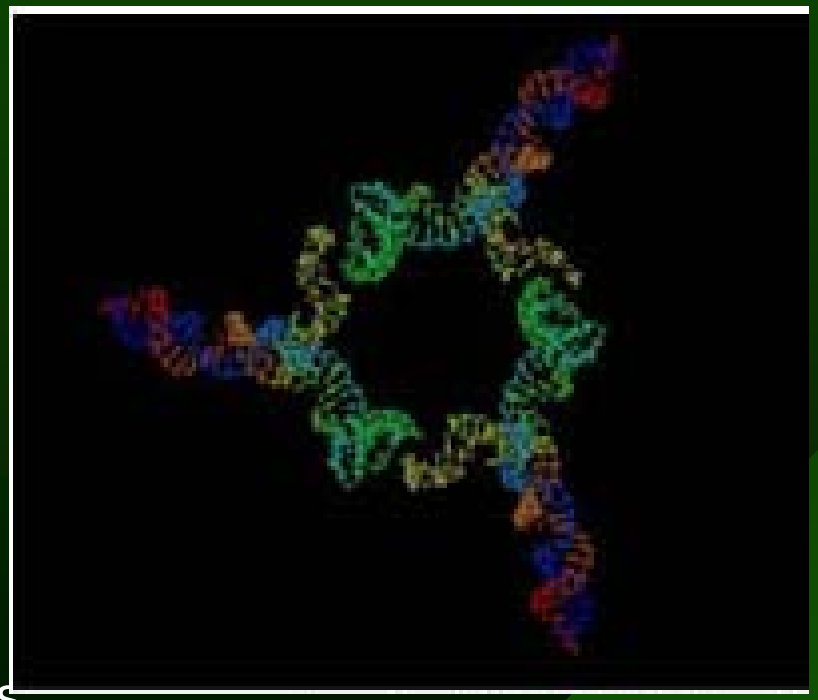
Drug	Indication	Status
Emezine	Nausea/Vomiting	Partnered
BEMA Fentanyl	Breakthrough pain	Proprietary
Bioral Amphotericin B	Fungal infections	Proprietary
Bioral NSAID	Pain	Licensed
Bioral paclitaxel	Oncology	Avail. for Licensing
Bionasal Amphotericin B	Chronic rhinosinusitis	Partnered
Biorazyme	Gauchers Disease	Avail. for Licensing
Bioral siRNA	Infectious disease/cancer	Avail. For Licensing

Aphios Corporation is developing enhanced therapeutics for health maintenance and the treatment of human diseases with a focus on infectious diseases, cancer and quality-of-life medicines

- Aphios has utilized its patented *SuperFluids™CFN* technology to form nanosomes (small, uniform liposomes) of paclitaxel. Liposomes are microscopic vesicles of phospholipid bilayers comprised of single or multiple lipid bilayers. Most liposomes are non-toxic, non-antigenic and biodegradable in character since they have the molecular characteristics of mammalian cell membranes. Hydrophobic compounds are trapped inside the lipid bilayers, masking the toxic nature paclitaxel and permitting a biocompatible formulation to be administered.

Purdue Scientists Treat Cancer with RNA Nanotechnology

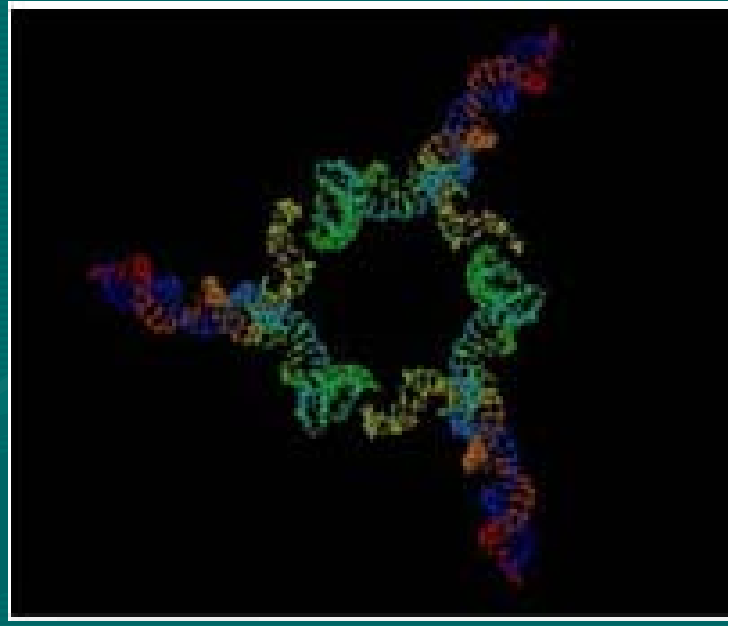
- The researchers developed some of their RNA-manipulation techniques in 2003 by building an RNA nanomotor. (Controllable Self-Assembly of Nanoparticles for Specific Delivery of Multiple Therapeutic Molecules to Cancer Cells Using RNA Nanotechnology, Nano Letters, September 14, 2005)
- Using strands of genetic material, Purdue University scientists have constructed tiny delivery vehicles that can carry anticancer therapeutic agents directly to infected cells, offering a potential wealth of new treatments for chronic diseases



RNA Nanotechnology Purdue study: RNA “motor” transports DNA

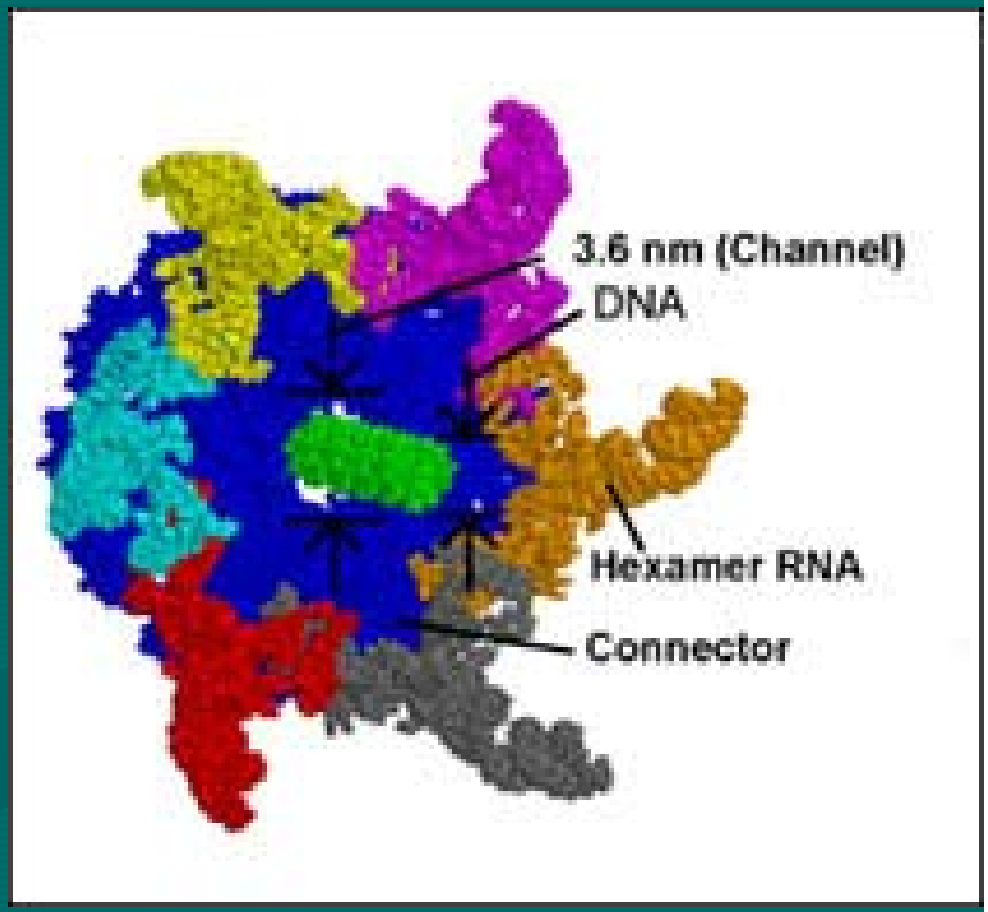
Purdue Scientists Treat Cancer with RNA Nanotechnology

- Purdue Universitie's researchers developed some of their RNA-manipulation techniques in 2003 by building an RNA nanomotor.
- The team sorted through a variety of RNA forms that have shown promise for disease treatment and found three that could perform each of the desired tasks.
- One example is "small interfering RNA," or siRNA, which deactivates certain genes in cells.
- The others are RNA aptamers, which bind to cancer cell surface markers, and
- ribozymes, which can be designed to degrade specific RNA in cancer cells or viruses.



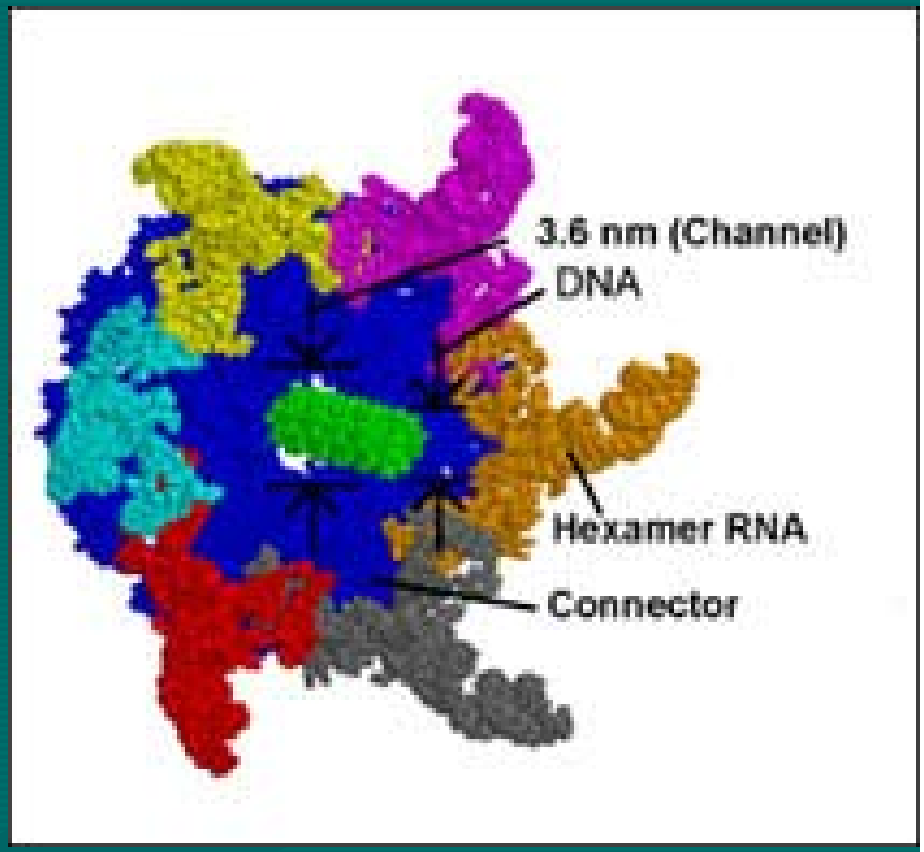
The nanoparticles have already proven effective against cancer growth in living mice as well as lab-grown human nasopharlyngeal carcinoma and breast cancer cells. [Shu, D., Moll, W.-D., Deng, Z., Mao, C., and Guo, P. (2004). Nano Lett. 4:1717–1724]

- In 1987, Guo discovered this "transporting" RNA species and provided the first evidence that RNA played a role in packaging DNA in Phi 29. This new type of RNA was dubbed "pRNA" for "packaging" RNA.
- Subsequent reports by Guo and others have since established the presence and molecular structure of pRNA.



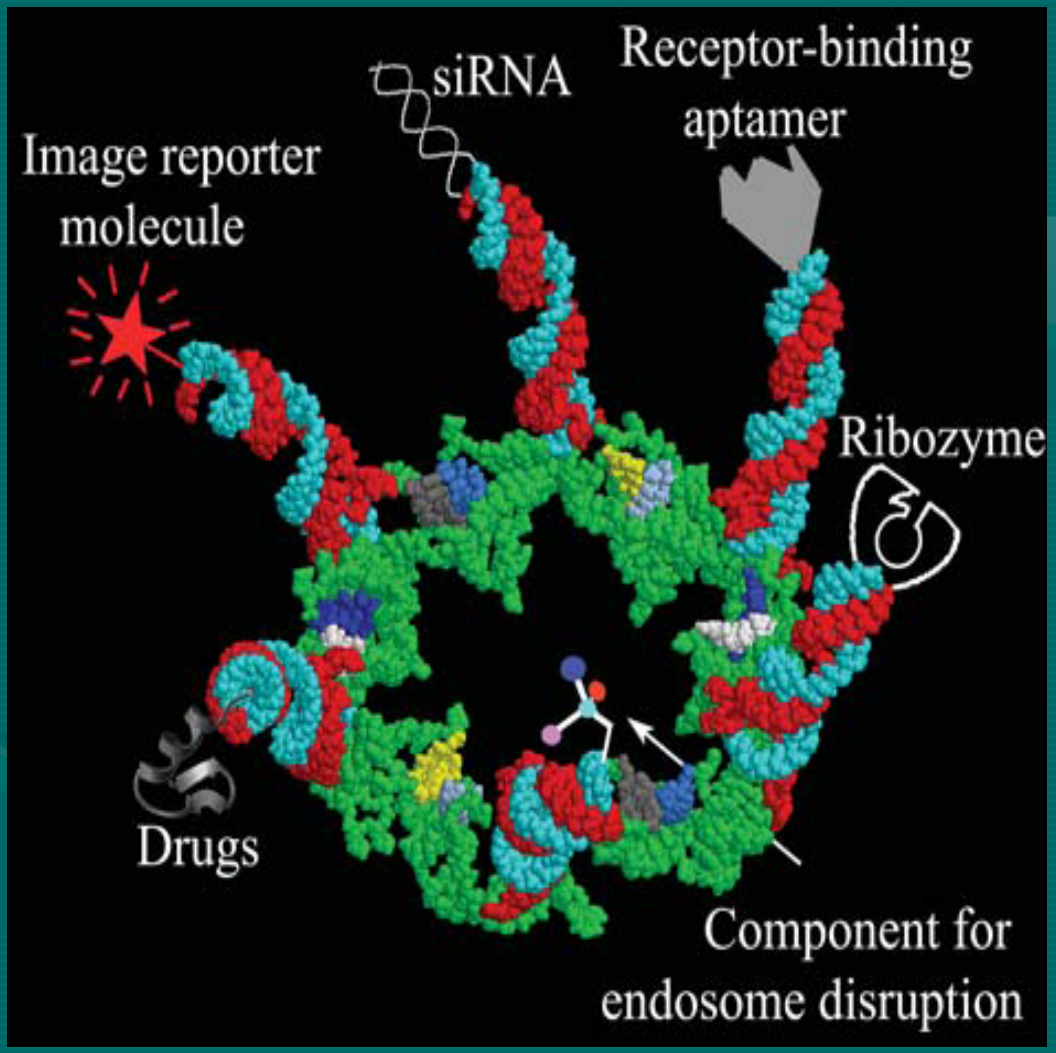
- Guo says that Bacteriophage Phi 29 is typical of double-stranded DNA viruses in that its genetic material is packaged into its protein shell, or capsid, during maturation.
- "All linear double-stranded DNA viruses, including herpes viruses, adenoviruses, pox viruses and the double-stranded DNA bacteriophages, package their genomic DNA into a pre-formed protein shell," he says. "What makes Phi 29 unique is that it is the first virus to be reported to use RNA as a component of the transportation machine to drive this process." .

- Peixuan Guo, professor of molecular virology at Purdue University, has found that a virus known as Bacteriophage Phi 29 uses six RNAs strung together in the shape of a hexagon to create a motor that transports DNA in the virus.
- Guo's findings represent the first example of a hexagonal-shaped RNA complex. It is also the first example of transportation vehicles using RNA as building blocks.
- The motor measures about 25 nanometers long, which is less than one hundredth the size of a red blood cell. It is made from six strands of RNA surrounding a center strand of DNA. In the presence of ATP, the RNA strands push the DNA axle in succession, spinning it around.



This produces 50 to 60 piconewtons, or trillionths of a newton of force. A falling apple exerts about one newton of force.

The successful use of small RNA for therapeutic purposes requires a safe and efficient delivery system capable of targeting specific cells.
These protein-free 25-nm nanoparticles will allow for repeated and longterm administration escaping immunoresponse and avoid the short retention time of smaller molecules and the undeliverability of larger molecules.



• Nanoparticle Delivery Technology Platforms

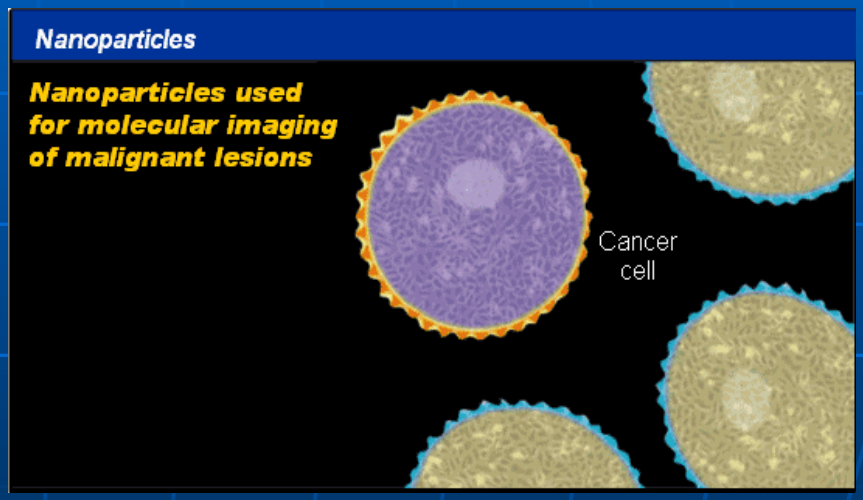
- CAP (BioSante)
- Cyclosert (Insert Therapeutics)
- Emulsiphan (Cornerstone)
- Hydroplex (ImaRx)
- LiPlasomes (LiPlasome Pharma)
- Medusa (Flamel)
- Micellular Nanoparticles (Novavax)
- NanoBiodrugs (Nanobiotix)
- Nanocrystal (Elan)
- NanoCure (Advectus)
- Nanoparticle Aggregate Technology (Access)
- Nanosomes (Molecular Therapeutics)
- Smarticles (Novosom)
- TargeTran (Intradigm)
- TransDrug (BioAlliance)
- VivaGel (Starpharma)

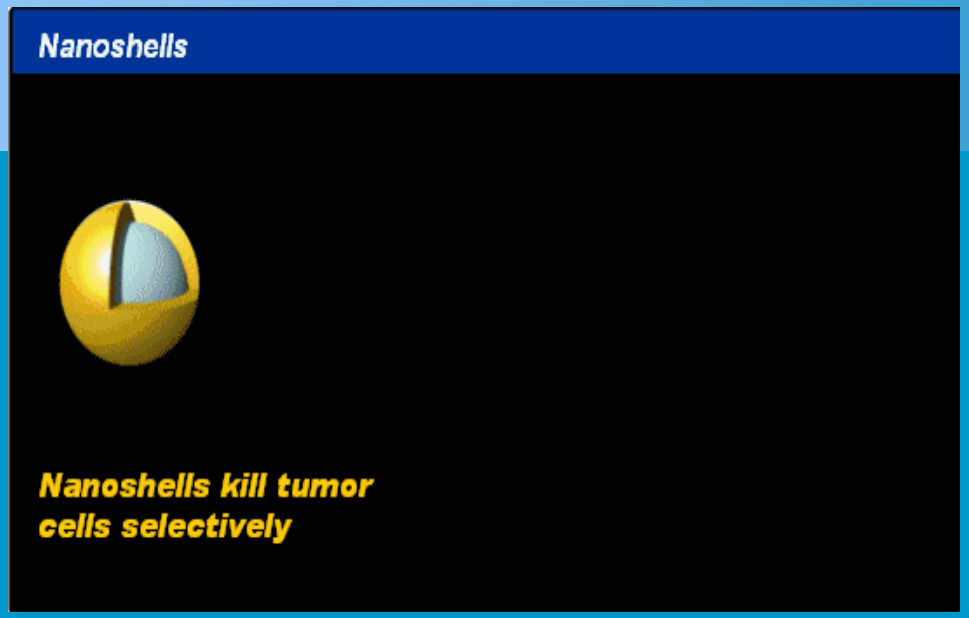
BioSante Pharmaceuticals **Announces CAP** (calcium phosphate-based nanotechnology) **Nanotechnology Product Development**

- Current business and product development agreements:
- Corixa Corporation: (non-exclusive) for use of CAP in cancer, and infectious and autoimmune disease vaccines.
- U.S. Navy: (CRADA) for evaluation and development of a malaria vaccine.
- U.S. Army: (CRADA) for evaluation and development of needle-free biodefense vaccines including anthrax, staph, ricin and bubonic plague.
- DynPort: U.S. DOD subcontract ($658,000) for evaluation and development of a needle-free anthrax vaccine.
- NIH: SBIR grant ($100,000) for oral insulin development.

Nanoparticles

- Nanoscale devices have the potential to radically change cancer therapy and dramatically increase the number of highly effective therapeutic agents.
- In this example, nanoparticles are targeted to cancer cells for use in the molecular imaging of a malignant lesion. Large numbers of nanoparticles are safely injected into the body and preferentially bind to the cancer cell, defining the anatomical contour of the lesion and making it visible.
- These nanoparticles give us the ability to see cells and molecules that we otherwise cannot detect through conventional imaging.





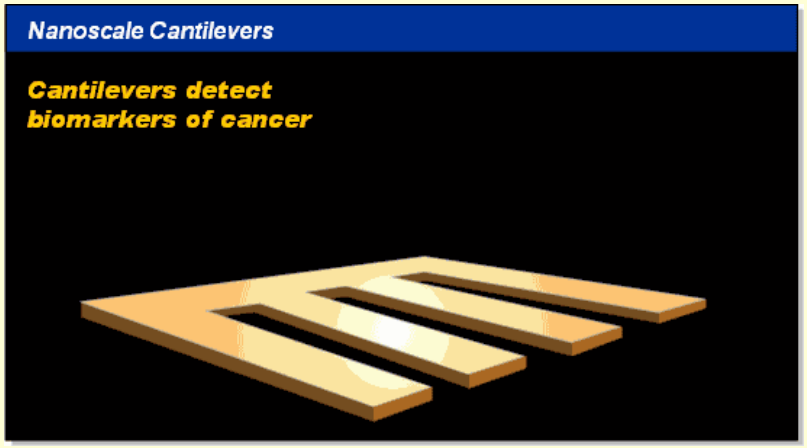
Nanoshells have a core of silica and a metallic outer layer. Nanoshells will preferentially concentrate in cancer lesion sites.

As shown in this example, scientists can then externally supply energy to these cells. The specific properties associated with nanoshells allow for the absorption of this directed energy, creating an intense heat that selectively kills the tumor cells. The external energy can be mechanical, radio frequency, optical - the therapeutic action is the same.

The result is greater efficacy of the therapeutic treatment and a significantly reduced set of side effects.

Cantilevers

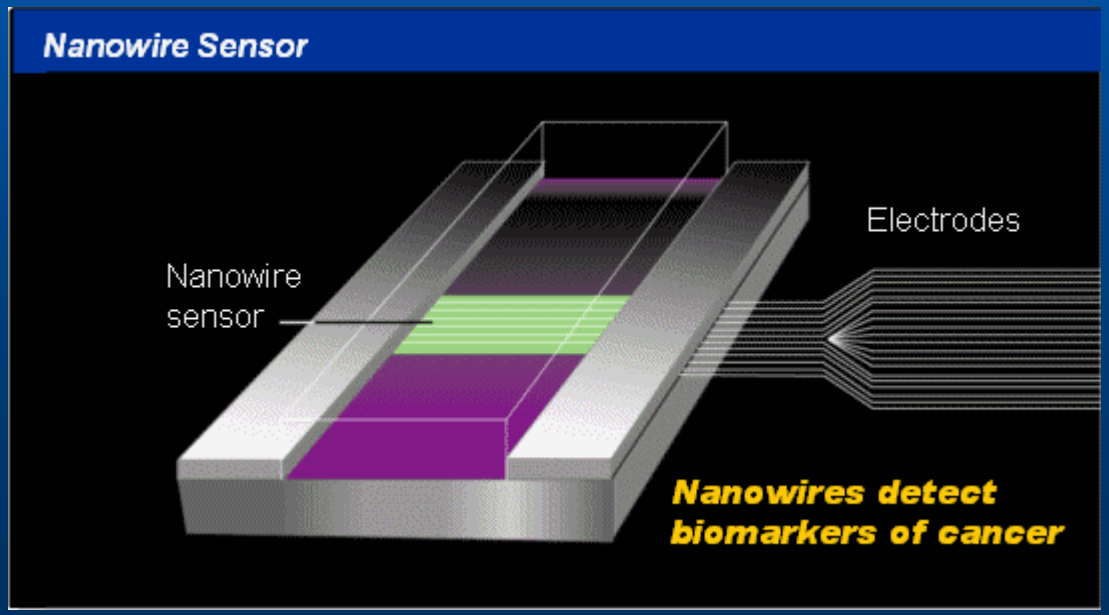
Nanoscale cantilevers - microscopic, flexible beams resembling a row of diving boards - are built using semiconductor lithographic techniques. These can be coated with molecules capable of binding specific substrates-DNA complementary to a specific gene sequence, Nanoscale cantilevers, constructed as part of a larger diagnostic device, can provide rapid and sensitive detection of cancer-related molecules.



Nanowires

In this diagram, nano sized sensing wires are laid down across a microfluidic channel. As particles flow through the microfluidic channel, the nanowire sensors pick up the molecular signatures of these particles and can immediately relay this information through a connection of electrodes to the outside world.

They can detect the presence of altered genes associated with cancer and may help researchers pinpoint the exact location of those changes.



Drug Delivery Leader - Nektar Therapeutics

- Nektar is a leader in three broadly applicable technology platforms: Molecule Engineering, Particle Engineering, and Delivery Solutions for oral, injectable, and pulmonary administration. We have partner collaborations with more than 25 pharmaceutical and biotechnology companies, including Pfizer, Roche, Amgen, Bristol-Myers Squibb, Scherig-Plough, UCB Pharma, Chiron, InterMune, Serono. This technologies are essential to six drugs approved in the United States and/or Europe.
- The combination of technology leadership and development expertise allows Netar to capitalize on the rapidly expanding market for drug delivery solutions, which is estimated to grow from $50 billion in 2000 to more than $100 billion by 2005.

Nektar Advanced PEGylation

Nectar Therapeutics September 8 , 2005, San Carlos, California

- **Nektar Reports that FDA Advisory Committee Recommends Approval of Exubera® for Use in Adults with Type 1 and Type 2 Diabetes**
- Nektar Therapeutics (Nasdaq:NKTR) today reported that Pfizer Inc and the Sanofi-Aventis Group said that a U.S. Food and Drug Administration (FDA) advisory committee panel has recommended the approval of Exubera® (insulin [rDNA origin] powder for oral inhalation), an inhaleable, rapid-acting, dry powder insulin for the treatment of adults with type 1 and type 2 diabetes.

Amgen	Neulasta™ (pegfilgrastim) Neutropenia	FDA Approved
Bristol-Myers Squibb	Definity® Vial for (Perflutren Lipid Microsphere) Injectable Suspension (PEG) Hepatitis C	FDA Approved
Eyetech	Macugen™ (pegaptanib sodium) Hepatitis C	FDA Approved Filed in Europe
Pfizer	Somavert® (pegvisomant) Acromegaly	FDA Approved Approved Europe
Pfizer	Exubera® (inhaled human insulin powder)	Filed with FDA Filed in Europe
Roche	PEGASYS® (peginterferon alfa-2a)	FDA Approved Marketed Europe
Schering-Plough	PEG-INTRON® (peginterferon alfa-2b)	FDA Approved

UCB Pharma	Cimzia™ (PEG anti-TNF alpha antibody fragment)	Phase III
Roche	CERA (Continuous Erythropoiesis Receptor Activator)	Phase III
Chiron	Tobramycin Inhaled Powder (TIP)™	Phase III
Confluent Surgical	SprayGel™ Adhesion Barrier System (PEG hydrogel)	Phase II/III U.S. Marketed Europe
Solvay Pharmaceuticals	Inhaled Dronabinol	Phase II
Undisclosed	Undisclosed (PEG)	Phase II
UCB Pharma	CDP 791	Phase I
InterMune	PEG Infergen (PEG-interferon alfacon 1)	Phase I*
Pfizer	PEGylated undisclosed	Phase I
Proprietary Product	Inhaled Amphotericin B	Phase I
Proprietary Product	Inhaled ICU Antibiotics	Phase I (proof of concept)
Serono	PEG interferon beta 1a	Phase I*

Generex Biotechnology, Canada

Oral-lyn™

is pioneering contribution to diabetes management. It's a unique oral insulin formulation that is delivered directly into the mouth via our RapidMist device, where it's rapidly absorbed into the bloodstream through the buccal mucosa.

the rapidmist™ device
(click for cutaway view)

Disease Target	Candidate	Note
Diabetes	Oral-lyn™	Ecuador Approval
Pain Management	Fentanyl	Late Phase II
Pain Management	Morphine	Filed CDN IND
DVT, Blood Clots	LMW Heparin	Filed CDN IND
Breast Cancer	Vaccine	Completed PC
Melanoma	Vaccine	Phase I clinical trial
Cancer	Vaccine	$440K NIH Grant
Prostate Cancer	Vaccine	$550K Defense Grant
Ovarian Cancer	Vaccine	Late pre-clinical
HIV/AIDS	Vaccine	MGH collaboration
SARS		IBC collaboration

NOBEX

- **PRODUCT PIPELINE**
  NOBEX has an extensive product pipeline with many innovative products currently under active development. The most advanced products in development are an oral insulin for treating Type II diabetes; oral APAZA™ for treating inflammatory bowel disease; and an oral calcitonin for treating osteoporosis.
  Oral Insulin
  Currently, insulin is an injectible protein drug for treating type 1 and type 2 diabetes. NOBEX has developed a revolutionary oral version that is in Phase II clinical studies. This revolutionary oral insulin would provide medical benefits unattainable by any other method of delivery, including injectible, pulmonary, nasal or buccal (absorption from the mouth).

  • Orally delivered insulin follows the same pathway into the body as does natural insulin secreted by the pancreas, through the portal vein directly into the liver. The liver exerts considerable control over the levels of glucose in the bloodstream and thus, is the first and most important target of pancreas-secreted insulin. All peripheral dosing of insulin (injectible, nasal, pulmonary, buccal) provides little and poorly-timed insulin to the liver.

  • Insulin is necessary in the peripheral bloodstream but having excessive amounts, which can occur with injection, can cause "hypoglycemia," low blood sugar, a dangerous condition for the patient. It is possible that orally-delivered insulin will lessen the risk of hypoglycemia by lowering the amount of insulin in peripheral blood.

NANOTECHNOLOGY FUTURE INSIGHTS

- The US National Science Foundation (NSF) expects nanotechnology to account for around half of all pharmaceutical industry sales by 2010.
- As part of NCI mission to accelerate the application of nanotechnology to the major challenges in clinical oncology and basic cancer research, the NCI Alliance for Nanotechnology in Cancer is dedicating $144.3 million as part of a 5-year initiative for nanotechnology in cancer research.
- Nektar developed more than 50 products with partners . . . 19 approved, filed, or in human clinical trials, including 6 approved in the U.S. or Europe.

Nanoparticle Drug Delivery
Technology, Therapies, and Prospects.
February 2005

Greystone Associates

- At present, there are 30 main drug delivery products on the market. The total annual income for all of these is approximately US$33 billion with an annual growth of 15% (based on global product revenue).
- Advances in nanotechnology are creating a host of opportunities for drug developers.
- The number of research programs and active drug development projects has escalated as funding to nanotechnology developers has increased
- A variety of nanostructures are being investigated as functional drug carriers for a wide range of therapies
- The capabilities that evolving technologies possess will leads to a dramatic increase in the number of therapies delivered via nanoparticles
- Nanoparticles can improve therapeutic outcomes because drugs can be delivered directly to the tissue and in controlled doses related to the patient's personal requiremen.

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February 2005

Greystone Associates

is a medical technology consulting firm. Forecasts and projections cover the period from 2004 to 2008.

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Nanoparticle Drug Delivery – Company Profiles

- Access Pharmaceuticals
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- BioDelivery Sciences International
- Biophan Technologies
- BioSante Pharmaceuticals
- Capsulution Nanoscience AG
- Cornerstone Pharmaceuticals
- Dendritic Nanotechnologies
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- ImaRx Therapeutics
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- Intradigm
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- Molecular Therapeutics
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- NanoCarrier
- NanoCure
- NanoCyte
- NanoMed Pharmaceuticals
- Nanospectra Biosciences
- Novavax
- Novosom AG
- Roche
- SoluBest Technology
- Starpharma Holdings
- Transgenex Therapeutics

NANOTECHNOLOGY - A POWERFUL RESEARCH ENABLER

- Nanotechnology is providing a critical bridge between the physical sciences and engineering, on the one hand, and modern molecular biology on the other. Materials scientists are learning the principles of the nanoscale world by studying the behavior of biomolecules and biomolecular assemblies.
- In return, engineers are creating a host of nanoscale tools that are required to develop the systems biology models of malignancy needed to better diagnose, treat, and ultimately prevent cancer.

Piribo is the source for information products concerning the global biotechnology and pharmaceutical industries. Here you can browse and buy thousands of business information studies, market reports and books. Piribo has ongoing relationships with leading market research and publishing companies, so we can offer you a current and comprehensive range of specialized intelligence.

Drug Delivery Market Research, Intelligence and Forecasts (164 source).

In this section you will find information products, including market research, covering the Drug Delivery Industry, including latest technologies, company profiles, biopharmaceuticals, market data and information covering Europe, the UK, North America and Asia.

NANOTECHNOLOGY - BRIDGE TO THE FUTURE

Apple recently introduced tiny iPod Nano music player

- Nanotechnology is the science of building devices at the molecular and atomic level. For example, a single data bit might be represented by only one atom some time in the future.
- Beyond being used in computers and communications devices, nanotechnology could be used extensively in biotechnology to build devices, fight disease, and change the properties of materials.