

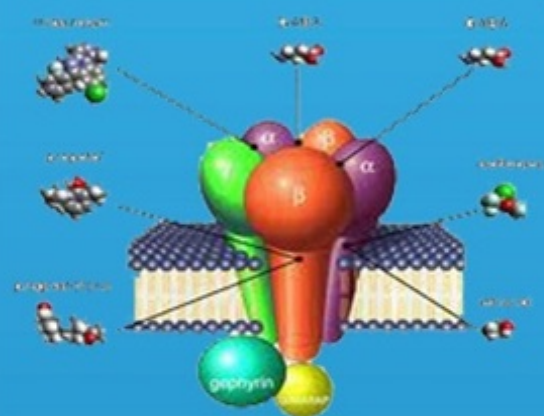


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The Recent Clinical Trends Of The Drugs Developed By Nanotechnology

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Abstract:

In view of scenario pharmaceutical industries are focusing towards their research on nanotechnology because developing new chemical entity is very time consuming and expensive affair and most of drugs will be off patent very soon causing huge revenue loss. Applications of nanotechnology to pharmacy that provide intelligent and smart drug delivery systems is expected to emerge as most important and powerful tool as alternate to conventional dosage form. These nano-intelligent drug delivery systems need little investment while expected to be a high profit making deal due to new patent-protection for current or soon-to-be off-patent drugs. Therefore most of industrial research interest lies in fact to exploit the newer technology to develop drug delivery system of available drugs in order to reduce or overcome their shortcoming like high toxicity, instability in biological environment, poor bioavailability, and low therapeutic concentration at site of action, which rendered them poor candidates in currently available dosage forms.

Keywords : Nanoparticles, Application, Marketed products of nanomedicine.

Introduction:

Nanotechnology in medical field:

Nanomedicine, an emerging new field, is an outcome of fusion of nanotechnology and medicine. Nanomedicine is the medical

application of nanotechnology. It covers areas such as nanoparticle drug delivery and possible future applications of molecular nanotechnology (MNT) and nanovaccinology.¹ 1974- Taniguchi uses the term Nanotechnology for the first time. In 1999 – “Nanomedicine” – 1st nanomedicine book by

R. Freitas. Nanotechnology is defined as the study and use of structures between 1 nanometer and 100 nanometers in size. Nanotechnology deals with the creation of useful materials, device and systems and systems through control of matter on the nanometer length scale and exploitation of novel phenomena and properties at that length scale.^{2,3} With advancements in nano science and technology, a large number of materials and improved products may be available with a change in the physical properties when their sizes are shrunk. Nanotechnology-based delivery systems can also protect drugs from degradation. These properties can help reduce the number of doses required, make treatment a better experience and reduce treatment expenses.^{4,5},⁶

Nanotechnology's promise to improve our quality of life has attracted worldwide investment from both private and public sources. Nanotechnology applications are coming to market rapidly; the worldwide nano product market is estimated to reach \$1 trillion dollars by 2015 ^{7,8}. In 2005, nearly \$10 billion dollars were spent on nanotechnology research and development alone . Nanotechnology-enabled applications in medical imaging, diagnosis, drug delivery and anticancer therapy offer exciting new possibilities for significantly advancing medical science in the 21st century .^{9,10,11} In 2004, the National Institute for Occupational

Safety and Health (NIOSH) established a Nanotechnology Research Center to identify the risk implications of nanotechnology for worker health, and to devise ways to protect workers from any identified adverse health effects from working with nanomaterials.^{12,13,14}

Nano-Definitions

Important nano-definitions are described below:

Nanoscience can be defined as study of phenomenon and manipulation of materials at atomic and molecular scales.¹⁵

Nanotechnology is related to design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale.¹⁶

Pharmaceutical nanotechnology

embraces applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor.

Nanomedicine is defined as submicron size (<1 μ m) modules, used for treatment, diagnosis, monitoring, and control of biological system.¹⁷

Properties of nanoparticles:-

A good physicochemical understanding of the formulation is an absolute necessity for rational formulation design. Size, surface characteristics, particle morphology, structure, and drug release are all relevant topics each of which will be briefly discussed below.¹⁸ Size is a central focus of nanotechnology as defined above, so its measurement is significant from that perspective. More importantly the size of a nanoparticle will determine its behavior both in vitro and in vivo, hence quantitative data on this characteristic is indispensable.^{19,20,21} Particle sizing can be broken down into three classes, ensemble, counting, and separation. Ensemble techniques, which include many of the spectroscopies such as light scattering and acoustic, make a single measurement of the system and then apply appropriate mathematics to extract a size population.^{22,23}

Surface properties

Contact of the particle surface with its environment will determine the particles' interaction with one another and may strongly influence their in vivo behavior, e.g., clearance. Charge, usually measured as zeta potential, is a primary descriptor and is determined most easily using techniques such as electroacoustic and electrophoretic light

scattering.²⁴ These particular methods are ensemble in nature and so have the same advantages and limitations as those listed above. Measurements of zeta potential based upon counting also exist. Using electrophoreses to analyze bound proteins extracted from plasma-treated nanoparticles is a useful means of better understanding the interaction of nanoparticles with blood components.^{25,26,27}

Particle morphology

In some cases the interest is in the shape of the particle and the nature of its surface. In other cases interest focuses on the particle disposition, such as aggregation state or location within a matrix. Particularly when the objects to be analyzed have a high aspect ratio, such as the case with nanotubes, an actual picture is a valuable complement to instrumental methods.²⁸

Given the size of the particles, scanning electron microscopy, either in transmission or scanning mode, are the primary tools of the analyst.^{29,30} The magnifications are much higher in the former mode, but the 2-D appearance of the images and the extensive sample preparation serve as

Draw backs. Freeze-fracture sample preparation, where a cast is taken of the sample of interest and then examined in turn is valuable in those instances where the sample is fragile, but it is a laborious

procedure that requires a high level of skill to properly utilize.³¹ Recently there has been a great interest in applying atomic force microscopy (AFM) to the analysis of pharmaceutically relevant nanoparticles. Very high-resolution images of particles in their native environment can be obtained using AFM, albeit at the expense of time since it is a rastering method.^{32,33} Depending on the interaction established between the probe tip and the sample, a wide range of material characteristics can be mapped on the nano-scale, e.g., electrostatic potential or hardness. The particles must be located on a solid support like mica, so understanding the effect that the latter has on the former, flattening for example, is important, and constitutes one reason that experience of the analyst with AFM is necessary. Optical microscopy can be quite valuable, even though the size of the particles is below the resolution of the technique. For example, darkfield methods allow the presence of nanoparticles, and hence their number-weighted concentration, to be detected even though the particles themselves are not imaged directly.^{34,35}

Structure

The arrangement of components within the nanoparticle can determine its behavior and stability. A number of common methods are appropriate such as differential scanning calorimetry and powder X-ray diffraction if

one is interested in overall structural characteristics such as crystal form or extent of amorphous character. Given the small size of nanoparticles, particular structural features such as layers, may be on the molecular scale.^{36,37} In such cases, establishing the orientation of molecules requires higher energy scattering methods such as small-angle neutron and X-ray scattering. Needless to say such techniques require highly specialized equipment and operators. When the nanoparticle in question has a fluid component or when there is interest in measuring free drug levels, NMR is a good technique since the magnitude of instrumental response depends upon molecular motion. Combining chemical speciation and diffusion measurement in 2-D gradients NMR can be very informative.^{38,39,40}

Drug release

A central reason for pursuing nanotechnology is to deliver drugs, hence understanding the manner and extent to which the drug molecules are released is important. In order to obtain such information most release methods require that the drug and its delivery vehicle be separated. The simplest case is separating dissolved from undissolved drug in a traditional solid formulation.^{41,42,43} In this example, a filtration step is sufficient to produce the separation. However, what happens when the drug containing particles

are sufficiently small to slip through the filter pores? This is easily the case with nanoparticles and the result is an inability to distinguish between free (available) and bound (unavailable) drug. In such situations the distinction can be brought about via size discrimination or spectroscopy. The former case is just an extension of conventional methodology although rather than using standard filters, diffusion membranes or

spectroscopic characteristics. In this way the increase in released drug can be quantified as a measurement of release. Because of its sensitivity to molecular structure and mobility, NMR is one way of taking this approach. On the other hand, the spectroscopic method has to have a sufficient limit of quantitation. Since nanotechnology is frequently applied to poorly soluble

Types and description of nanoparticles:- Table: 1 Brief descriptions of nanosystems

Types of Nanoparticles	Size (range)	Characteristics	Applications
Polymeric nanoparticles	10-1000 nm	Biocompatible, biodegradable, offer complete drug protection	Excellent carrier for controlled and sustained delivery of drugs. Stealth and surface modified nanoparticles can be used for active and passive delivery of bioactives. ⁵⁰
Nanocrystals Quantum dots ultracentrifugation can be employed instead. While effective at separating released drug from the nanoparticles, this approach takes a long time and thus makes it impossible to measure fast release rates. ^{44,45,46} One can also	2–9.5 nm	Semi conducting material synthesized with II-VI and III-V column element; Size between 10-100 Å; Bright fluorescence, narrow emission, Broad UV excitation and high photo stability	Long term multiple color imaging of liver cell; DNA hybridization, immunoassay; receptor mediated endocytosis; labeling of breast cancer marker Her ₂ surface of cancer cells

take advantage of the fact that bound and released drug may have different

Carbon nanotubes	0.5–3 nm diameter and 20–1000 nm length	Third allotropic crystalline form of carbon sheets either single layer (single walled nanotube, SWNT) or multiple layer (multi-walled nanotube, MWNT). These crystals have remarkable strength and unique electrical properties (conducting, semi conducting, or insulating)	Functionalization enhanced solubility, penetration to cell cytoplasm and to nucleus, as carrier for gene delivery, peptide delivery
Dendrimer	<10 nm	Highly branched, nearly monodisperse polymer system produced by controlled polymerization; three main parts core, branch and surface	Long circulatory, controlled delivery of bioactives, targeted delivery of bioactives to macrophages, liver targeting
Metallic nanoparticles	<100 nm	Gold and silver colloids, very small size resulting in high surface area available for functionalization, stable	Drug and gene delivery, highly sensitive diagnostic assays, thermal ablation and radiotherapy enhancement
Polymeric micelles	10-100nm	Block amphiphilic copolymer micelles, high drug entrapment, payload, biostability	Long circulatory, target specific active and passive drug delivery, diagnostic value
Liposome	50-100 nm	Phospholipid vesicles, biocompatible, versatile, good entrapment efficiency, offer easy surface functionalization	Long circulatory, offer passive and active delivery of gene, protein, peptide and various other bioactives
Iron oxide nanocrystal	4–5 nm with a hydrodynamic radius of 15–25 nm	Superparamagnetism	Magnetic resonance imaging (disease detection such as cancer, arthritis, and atherosclerosis); intracellular monitoring
Silica Nanoparticles	10 nm–50 μ m	Silanised and coated with oligonucleotide. Observable by fluorescence method.	Efficient nucleic acid hybridization Detection of DNA Nanobiosensor for trace analysis

Nanoshells	Nanoshells typically have a silicon core that is sealed in an outer metallic core. By manipulating the ratio of wall to core, the shells can be precisely tuned to scatter or absorb very specific wavelengths of light	Gold encased nanoshells have been used to convert light into heat, enabling the destruction of tumors by selective binding to malignant cells. ⁵¹
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compounds, this can become problematic. Note that in either approach it might make more sense to look for the disappearance of drug from the nanoparticle than it does to measure its appearance in the release media.^{47,48,49}

Applications of Pharmaceutical

Nanotools in health care :-

1.As nanomaterials for tissue engineering:

Nanotechnology offered numerous smart materials that are used for tissue repair and replacement, implant coatings, tissue regeneration scaffolds, structural implant materials, bone repair, bioresorbable materials, some implantable devices (sensory aids, retina implants etc.), surgical aids, operating tools, and smart instruments.^{54,55}

Table: 2 Applications of nanosystems in tissue regeneration, growth and repair

Nanosystems	Property	Applications
Nano engineered prosthetics	Increased miniaturisation; increased prosthetic strength & weight reduction; improved biocompatibility	Retinal, auditory, spinal and cranial implants
Cellular manipulation	Manipulation of cellular systems	Persuasion of lost nerve tissue to grow; growth of body parts

2. As drug carrier system:

Nanotechnology enabled drug delivery system with optimized physical, chemical and biological properties can serve as effective delivery tools for currently available bioactives.⁵⁶ Some nanobased drug delivery tools are polymeric nanoparticles, liposome, dendrimer, polymeric micelles, polymer-drug conjugates, antibody- drug conjugates, which can broadly be classify as

- (i) sustained and controlled delivery system,
- (ii) stimuli sensitive delivery system,
- (iii) functional system for delivery of bioactives,
- (iv) multifunctional system for combined delivery of therapeutics, biosensing and diagnostic, and
- (v) site specific targeting (intracellular, cellular, tissue) .^{57,58,59}

Cancer treatment:

Nanotechnology can have a revolutionary impact on cancer diagnosis and therapy. Available therapies commonly employed in cancer treatment include surgery, chemotherapy, immunotherapy, and radiotherapy.⁶⁰ Nanotechnology offers tremendous opportunities to aid and improve these conventional therapies by virtue of its nanotools. Some nanotools that have played key role in cancer therapy are listed below .^{61,62}

	protein biomarker detection
Dendrimers	Controlled release drug delivery, image contrast agents ⁶³
Nanocrystals	Improved formulation for poorly-soluble drugs ⁶⁴
Nanoparticles	MRI and ultrasound image contrast agents, targeted drug delivery, permeation enhancers, reporters of apoptosis, angiogenesis, etc.
Nanoshells	Tumor-specific imaging, deep tissue thermal ablation
Nanowires	Disease protein biomarker detection, DNA mutation detection, gene expression detection
Quantum dots	Optical detection of genes and proteins in animal models and cell assays, tumor and lymph node visualization.

Table: 3 Applications of various nanosystems in cancer therapy

Nanosystem	Applications in cancer therapeutics
Carbon nanotubes	DNA mutation detection, disease

Implantable delivery systems:

Nanotechnology is opening up new opportunities in implantable delivery ,Some pharmaceutical novel nano drug vascular carriers like liposome, ethosome and trnaserosome and some implant chips have been envisaged recently, which may help in minimizing peak plasma levels and reduce the risk of adverse reactions, allow for more predictable and extended duration of action,

reduce the frequency of re-dosing and improve patient acceptance and compliance.,^{65,66,67,68}

Site specific drug delivery:

Several approaches are now being tested for better site-specific delivery using liposomes, polymeric micelles, dendrimers, iron oxide, proteins using manipulation in passive and active uptake of drug.^{69,70} The tumor targeting of drugs with passive delivery using enhanced permeation and retention (EPR) effect is thought to be one intelligent approach using these carrier system taking the advantages of leaky vasculature of tumor. Some surface modification approaches using various site-specific ligands via covalent binding or adsorption with carrier system enhanced their site specificity and make them intelligent tools for active delivery.^{71,72,73}

Gene therapy:

In gene therapy, a normal gene is inserted in place of an abnormal disease-causing gene using a carrier molecule. Conventional uses of viral vectors are associated with adverse immunologic, inflammatory reactions and diseases in the host.^{74,75} Nanotechnology enabled delivery systems have currently emerged as potential vector and are shown to be effective and promising tool in systemic gene treatment.⁷⁶ Various polymer based nanoparticles like chitosan, gelatin and poly-l-lysine and modified silica nanoparticles have

been reported to have increased transfection efficiency and decreased cytotoxicity. It is well established that nanotechnology provides viable option as ideal vector in gene delivery.^{77,78,79,80}

3. Molecular Diagnostics :

Molecular imaging is the nanoscience of representing, characterizing, and quantifying subcellular biological processes in intact organisms.⁸¹ These processes include gene expression, protein-protein interaction, signal transduction, cellular metabolism, and both intracellular and intercellular trafficking. Some nanoparticles, which have inherent diagnostic properties, are quantum dots, iron oxide nanocrystal and metallic nanoparticles.⁸² They have been successfully utilized in various magnetic resonance imaging, optical imaging, ultrasonic imaging and nuclear imaging .^{83,84,85}

Table: 4 Approved nanoparticles as imaging agents and drug carriers

Modality	Compound	Status	Use
Imaging Agents	superparamagnetic iron oxide nanoparticle	Market Phase III	MRI agent
	Endorem®		MRI agent
	Gadomer®	clinical trial	cardiovascular
	Dendrimer-based MRI agents		

Drug delivery Abraxane®	Albumin nanoparticle containing paclitaxel	Market	Breast cancer
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4 .Biosensor and biolabels:

A number of analytical tools have been developed with application of this smart and potential technology.^{86,87} These tools are employed for determination of various pathological proteins and physiological-biochemical indicator associated with disease or disrupted metabolic conditions of body. Various nanoenabled technologies, techniques and their analytical applications are listed below.^{88,89}

Table: 5 Nanoenabled technologies, techniques and their analytical applications

Technology	Technique	Application
Bioarrays and Biosensors	Nanofabrication	Nano-Objects Detection
DNA Chips	Lab on Chip Nanotubes	Electrochemical Detection
Protein-Chips	Pill on Chip Nanowires	Optical Detection
Glyco-Chips	Nanofluidics Nanoparticles	Mechanical Detection
Cell-Chips	Nanostructured Surfaces	Electrical Detection ⁹⁰

Table: 6 Applications of various nanosystems as biosensor and biolabels

Nanosystem	Applications
Gold Nanoparticle-s	For sDNA detection; in immune-histochemistry to identify protein-protein interaction. ⁹¹
Iron oxide nanocrystal	Monitor gene expression; detect the pathogens such as cancer, brain inflammation, arthritis and atherosclerosis. ⁹²
Nanopores	Sensing single DNA molecules by nanopores .
Cantilever array	Diagnosis of diabetes mellitus, for detection of bacteria, fungi, viruses; for cancer diagnosis .
Carbon nanotube	Blood glucose monitoring; sensors for DNA detection.
Nanowire	Electrical detection of single viruses and biomolecules.
Nanoparticle-based biodetection	Detection of pathogenic biomarkers, Ultra-sensitive detection of single bacteria.

Hormone Deficiency

Aging is associated with changes in the levels of many hormones; perhaps the best known example is menopause, which is caused by a reduction in estrogen. It is likely that treating

glands against aging at the cellular level would restore age-appropriate hormone production.⁹³ However, if this is not enough to bring the body to a younger state, artificial glands could be built that would maintain the desired hormone levels.⁹⁴ In fact, different hormone levels could be supplied to different organs -something that the body cannot do for itself. This would be an example of heterostasis.^{95,96}

ADVANTAGES OF NANOTECHNOLOGY TECHNIQUES

1. Nanotechnology-based delivery systems can also protect drugs from degradation.
2. Improved products may be available with a change in the physical properties when their sizes are shrunk.
3. Reduce the number of doses required.
4. Make treatment a better experience and reduce treatment expenses.
5. Nano-based systems allow delivery of insoluble drugs.
6. Allowing the use of previously rejected drugs or drugs which are difficult to administer.
7. Drug targeting can be achieved by taking advantage of the distinct pathophysiological features of diseased tissues.
8. An ideal targeting system should have long circulating time, it should be present at appropriate concentrations at the target site.

9. It should not lose its activity or therapeutic efficacy while in circulation.

10. Tumors allow an enhanced permeability and retention effect.

11. Passive targeting of drugs to the macrophages present in the liver and spleen.⁹⁷

12. Nanotechnology offers a solution for using the numerous chemical entities for treating brain disorders that are not clinically useful because of the presence of the blood-brain barrier.⁹⁸

13. Improve the oral bioavailability of the agents that are not effectively used orally.⁹⁹

Market product of Nanomedicine :

Drug	Ingredient	Marketed
AVINZA	Morphine sulphate	U.S. ¹⁰⁰
TRICOR	Fenofibrate	U.S. by Abott
NAPRELAN	Naproxen(s.r.)	U.S. ¹⁰¹
THEODUR	Theophyllin(s.r.)	Japan
VERELAN	Verapamil(s.r.)	World wide
VERELAN PM	Chronotherapeutic verapamil	U.S. ¹⁰²
HERBESSER	Diltiazem (s.r.)	Japan and other Asian markets
FOCALIN XR	Dexmethyl phenidate HCL	U.S.
ROPAMUNE	Sirolimus	U.S.
RITALIN LA	Methyl phenidate	U.S.
MEGACE ES	Conc. Oral suspension	U.S.
EMEND	Oral suspension	U.S. ¹⁰³

Other nanotherapeutics by different companies:

DRUG	NANOPARTICLE COMPONENT/ ACTIVE INGREDIENT	DELIVERY ROUTE	COMPANY	INDICATION	FDA APPROVAL
DOXIL CAELYX	Pegylated Doxorubicin (Adriamycin) HCL, liposome	i.v.	ortho biotech	Metastatic ovarian cancer	nov-1995 ¹⁰⁴
ABRAXANE	Paclitaxel bound albumin nanoparticle	i.v.	Abraxis bioscience, Astrazeneca	Metastatic breast cancer	Jan- 2005
AM BISOME	Ampho.B liposome	i.v.	Gilead sciences	Fungal infction	Aug-1997 ¹⁰⁵
DIPRIVAN	Propofol liposome	i.v.	Zeneca pharma	Anaesthtic	Oct-1989
TRIGLIDE	Nanocrystalline fenofibrate	Oral tab.	Skye pharma	Lipid disorder	May-2005 ¹⁰⁶
MYOCET	Liposome encapsulated Doxorubicin citrate	i.v.	Zeneus pharma	Cardio protective, metastatic breast cancer	Approve in Europe & canada

	complex				
DEPOCYT	Cytarabin liposome (s.r.)	i.v.	Skye pharma	Lymphomatus meningitis	April-1999
ESTRASORB	Estradiol hemihydrates micellar nanoparticle	transdermal	Novavax	Reduced hot flushes, night sweats in menopausal women	Oct-2003 ¹⁰⁷
MACUGEN	Pegylated anti-vegf aptamer	Intravitreal	Pfizer	Neovascular age related macular degeneration	Dec-2004
SOMAVERT	Pegvisomant	s.c.	Pfizer	Acromegaly	March-2003 ¹⁰⁸
PEG-INTRON	Peg interferon alfa-2b	s.c.	Enzon	Chronic hepatitis C, virus infection	Jan-2001
ELESTRIN	Estradiol gel (0.06%) incorporated calcium phosphate nanoparticle	Transdermal	Biosante	Moderate to severe hot flashes in menopausal women	Dec-2006
RENAGEL	Cross linked poly resin	Oral tab.	Genzyme	Control of serum phosphorus in patient with chronic kidney disease on dialysis	Oct-1998
DAUNOXOME	Encapsulated – daunorubicine citrate liposome	i.v.	Gilead science	Advanced HIV-related Kaposi sarcoma	Apr -1996
ABELCET	Ampho .B, phospholipid complex	i.v.	Enzon	Invasive fungal infection in patient who are refractory to or intolerant of conventional amphotericin therapy	Nov-1995
ADAGEN	Pegylated adenosine deaminase	i.v.	Enzon	Enzyme replacement therapy	March-1990
PEGASYS	Peg interferon alfa – 2a	s.c.	Nektar hoffmann-la - roche	Chronic hepatitis – C infection	Oct-2002
NEULASATA	Peg – g- csf or pegfilgrastim	s.c.	Amgen	Febrile neutropenia	Jan-2002
COPAXONE	Glatiramer acetate (copolymer of l- glutamine, l- alanine, l-tyrosine, l- lysine	s.c.	Teva	Relapsing remitting multiple sclerosis	Dec-1996
AMPHOTEC	Colloidal suspension	S.c.	Sequus	Invasive	Nov-1996

	of lipid – based ampho. b			aspergilosis patient who are refractory to or intolerant of conventional Ampho. B	
PEG intron	Peg interferon alfa- 2b	s.c.	Enzon	Chronic Hepatitis C	Jan-2001
ONCASPAR	pegasparaginase	s.c.	Enzon	leukemia	Feb-1994
EPAXAL	Hepatitis a vaccine	i.m.	Berna biotech	Hepatitis A	Avail. In Canada & elsewhere

Some nanotherapeutic in clinical trials-

DRUG	NANOPARTICLE/ ACTIVE INGREDIENT	ROUTE	COMPANY	INDICATION	APPROVAL STATUS
VIVA GEL	Dendrimer gel	Topical	Star pharma	Vaginal microbicidal for the prevention of HIV & genital herpes	Phase 2 , fast track ¹⁰⁹
CALAA-01	Cyclodextrin containing si rna delivery nanoparticles	i.v.	Calendo pharma.	Various cancer	Phase-1
INGN-401	Liposome fus -1	i.v.	Itrogen therapeutics	Lung cancer	Phase-1
AURIMMUNE (CYT- 6091)	Colloidal gold nanoparticle coupled to TNF and peg-triol	i.v.	Cytimmune sciences	Solid tumors	Phase-2
SGT-53	P -53 liposome	i.v.	Synergene therapeutics	Solid tumors	Phase -1
NB-00X	Nanoemulsion droplets	tropical	Nanobio	Herpes labialis caused by herpes simplex virus	Phase-2
AUROSHELL	Gold coated silica nanoparticle	i.v	Nanospectro bioscience	Solid tumors	Phase-1
XMT-1001	Fleximer camptothecin prodrug conjugate	i.v	Mersana therapeutics	Various cancer	Phase-1 ¹¹⁰

Some other companies, involved in Nanoformulation

Acrymed:

The company's SilvaSorb® products for advanced wound care and SilvaGard nanoparticle surface treatment for medical devices are among the breakthrough technologies.¹¹¹

Advanced Magnetics, Inc.:

Is a biopharmaceutical company that utilizes its proprietary nanoparticle technology for the development and commercialization of therapeutic iron compounds to treat anemia and novel imaging agents to aid in the diagnosis of cancer and cardiovascular disease. Ferumoxytol, the company's key product candidate, is being developed for use as an intravenous iron replacement therapeutic for the treatment of iron deficiency anemia in chronic kidney disease.¹¹²

Alpha Szensor:

Is developing a biomedical sensor platform for applications in the field of disease diagnostics and personalized medicine. These products will allow testing of a wide range of diseases such as Cold and Flu, Cancer, Heart Disease, Sexually Transmitted Infections, Food Contamination, and the presence of other life threatening disorders.¹¹³ Alpha Szensor technology will eliminate the costly and time consuming procedures associated

with current diagnostics technology.

Copernicus Therapeutics, Inc.:

A privately held biotechnology company, is advancing novel nucleic acid delivery systems with broad applications in human therapeutics.¹¹⁴ The Company's delivery platform can be used to enhance the efficacy and safety of existing drugs as well as to create novel therapeutics.

Debiotech S.A:

Developer of Insulin NanopumpTM, Nanoject (micro-needle technology), Nanocoating technology for implantable devices.

Intradigm:

Is a private biotechnology company dedicated to the development of targeted, systemic RNA interference (RNAi) therapeutics for the treatment of serious diseases with an initial focus on oncology. To address the issue of effective and targeted delivery of RNAi therapeutics, Intradigm has developed its proprietary RNAi Nanoplex(TM) delivery system.¹¹⁵ This powerful combination of advanced delivery technologies is unique in its ability to offer tissue-specific targeting of siRNA and delivery against the intracellular machinery of the target tissue.

Nanobac Pharmaceuticals, Inc.:

Is dedicated to the discovery and development of products and services to improve human

health through the detection and treatment of calcifying nanoparticles (CNPs), formerly known as nanobacteria. The company's pioneering research is establishing the pathogenic role of CNPs in soft tissue calcification, particularly in coronary artery, prostate and vascular disease.

NanoMed Pharmaceuticals(R), Inc.:

Is an early-stage specialty pharmaceutical company dedicated to developing improved therapeutic and diagnostic products to treat or detect cancer and other serious diseases. The company's lead product is a nanoparticle formulation of an FDA-approved cancer drug used to treat adults diagnosed with acute myeloid leukemia.¹¹⁶ This lead product is being developed using Nanotemplate Engineering(TM), the company's proprietary nanoparticle manufacturing technology used to formulate small molecules, peptides, proteins, plasmid DNA, and diagnostic agents.

Psivida Limited:

Is a global BIO-nanotech company listed on nasdaq (psdv), Australian (PSD), and Frankfurt (PSI) stock exchanges, that is committed to the development of oncology and ophthalmology.

Tego BioSciences Corporation:

Is developing and commercializing therapeutics and other products based on the

antioxidant properties of modified fullerenes. The patent protected platform forms the basis for several products. The company is initially focused on developing products to reduce oxidative damage caused by sun exposure, radiation therapy, and chemotherapy and mitigate complications associated with organ transplantation and tissue engineering.¹¹⁷ For other applications of derivatized fullerenes such as MRI imaging or central nervous system disorders, Tego BioSciences will establish a program to license and partner the commercialization of its intellectual property to third parties.¹¹⁸

Telomolecular:

Is a nanotechnology company focused on the invention of treatments for human aging, age-associated diseases, and cancer.

Conclusion

Nanotechnology will change healthcare, and human life more profoundly than many developments of the past. As with all technologies, nanotechnology carries a significant potential for misuse and abuse on a scale and scope never seen before. However, they also have potential to bring about significant benefits, such as improved health, better use of natural resources. Current work is focused on the recent developments, particularly of nanoparticles and nanotubes. Nanomedicine needs to overcome the

challenges for its application, to improve the understanding of pathophysiologic basis of disease, bring more sophisticated diagnostic opportunities, and yield more effective therapies and preventive properties. Molecular technology is destined to become the core technology underlying all of 21st century medicine and health care.

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119. The following abbreviations are used in table, i.v.-intravenous, s.r.- sustain release, peg-hgh- pegylated human growth hormone, csf- colony stimulating factor, nm – nanometer, peg- polyethylene glycol, vegf- vascular endothelial growth factor, hdl & ldl- high & low density lipoprotein.