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NANOTECHNOLOGY-ENABLED TARGETED DRUG DELIVERY SYSTEMS FOR PRECISION CANCER THERAPY: ADVANCES, CHALLENGES, AND CLINICAL TRANSLATION

Pooja Khatri, Preeti Singh*

School of Pharmacy, Sharda University, Plot No. 32-34, Knowledge Park III, Greater Noida, Uttar Pradesh.

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Corresponding Author:** **Preeti Singh
School of Pharmacy, Sharda University, Plot No. 32-34, Knowledge Park III, Greater Noida, Uttar Pradesh.
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ABSTRACT

The treatment of cancer is often constrained by lack of specificity of drugs used, systemic toxicity, multiple drug resistance and insufficient therapeutic effect of traditional methods of treatment. The targeted drug delivery systems that are possible with nanotechnology have become promising approaches to enhancing precision oncology by means of better targeting of the tumor, controlled release of drugs, better pharmacokinetics, and fewer adverse effects. There are several nanocarriers such as liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, and biomimetic nanoplatforms that have shown high potential in delivery of chemotherapy, immunotherapy, gene therapy, photothermal therapy, and theranostic. More complex methods of targeting like ligand-mediated delivery, antibody-conjugated nanoparticles, and stimuli-responsive systems also improve therapeutic selectivity and intracellular accumulation of drugs. Although considerable advances have been achieved, nanotoxicity, biological barriers, mass production, and regulatory acceptance issues still present a hurdle to clinical translation. In the future, the application of AI-based nanomedicine, CRISPR-based delivery platforms, and customized nanotherapeutics are predicted to speed up the oncology field of precision and the development of safer and more effective cancer therapy.

KEYWORDS: Nanotechnology; Targeted drug delivery; Precision oncology; Nanomedicine; Cancer therapy; Nanoparticles; Theranostics; Personalized medicine.

1. INTRODUCTION

Cancer still has a significant clinical, social and economic burden on the health system, and is one of the major causes of death and morbidity globally (Tarekegn et al., 2026). The latest cancer statistics reveal millions of new cancer cases

and cancer deaths reported every year, and with a growing aging population, environmental exposure, lifestyle changes, and genetic susceptibility, it is believed that the number of new cancer cases each year will continue to rise (Gambhir et al., 2026). While the survival of patients has greatly improved with the use of traditional therapeutic methods, including surgery, radiotherapy, and traditional chemotherapy, traditional chemotherapy has disadvantages including poor tumor selectivity, high side effects for healthy tissues, rapid drug degradation, multidrug resistance, unfavorable pharmacokinetics, and high toxicity (Smith et al., 2026). The majority of cytotoxic anticancer agents are non-specific with respect to their biodistribution, thus causing damage to the rapidly dividing bone marrow, gastrointestinal epithelium and hair follicles, which limits the therapeutic efficacy and compliance of the patient (Dai et al., 2026). In addition, the multi-clonally heterogeneous tumor, the deregulation of molecular signaling pathways and immune evasion mechanisms render it difficult to achieve therapeutic success and prevention of disease recurrence (Veleva et al., 2026). These restrictions have driven the shift towards the new paradigm of precision oncology, which focuses on individual tumor molecular and genetic traits and phenotypes to better tailor cancer treatment (Ismailov et al., 2026).

Precision oncology is a constellation of new strategies that combines genomic profiling, identification of biomarkers, molecular diagnostics, and targeted therapeutics to increase the specificity of care and improve clinical outcomes with reduced systemic toxicity (X. Li et al., 2026). Against this background, nanotechnology has been introduced as a revolutionizing delivery system for specific drugs and precision cancer therapy (X. Li et al., 2026). Nanotechnology-based drug delivery systems involve the use of nanocarriers (typically 1-200 nm), which enhance the solubility, stability, pharmacokinetics, tumor accumulation and controlled release of the drug (Ward et al., 2026). Different nanocarriers such as liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, solid lipid nanoparticles, mesoporous silica nanoparticles and biomimetic nanovesicles have shown great potential to overcome biological barriers and improve therapeutic efficacy (Gu et al., 2026). Surface modification with ligands, antibodies, peptides, aptamers, or receptor specific molecules can enable active targeting of tumor cells and the tumour microenvironment, while the enhanced permeability and retention effect (EPR) can be used for passive targeting of nanoparticles (B. Zhang et al., 2026). Furthermore, site-specific drug release and intracellular drug uptake have been further enhanced by stimuli-responsive smart nanoparticles which can respond to pH, temperature, enzymes, hypoxia or redox conditions (S. Wang et al., 2026). Nanotechnology also enables co-delivery of chemotherapeutic agents, nucleic acids, immunotherapeutics and imaging probes, to facilitate theranostic and multimodal therapeutic strategies (Han et al., 2026). Although major improvements have been made, a number of barriers still exist such as nanotoxicity, immune clearance, manufacturing challenges, regulatory issues, scale-up and clinical translation barriers (R. Wang et al., 2026).

Thus, the purpose of this review is to discuss recent developments in nanotechnology-based targeted drug delivery systems for precision cancer therapy, highlighting the design of nanoparticles, targeting strategies, therapeutic applications, translation barriers, regulatory hurdles and future perspectives in the clinical applications of precision cancer therapy in the modern era of oncology (S. Kumar et al., 2026; Mousavi-Kiasary et al., 2025).

2. Fundamentals of Nanotechnology in Cancer Therapy

Nanotechnology has become a groundbreaking platform in contemporary oncology due to its ability to deliver therapeutic agents to tumor tissues in a precise, controlled, and targeted manner with a reduced systemic toxicity (Gupta et al., 2026). Generally, nanocarriers in cancer therapy can be described as nanoscale delivery systems (1-200 nm) that are designed to enhance the pharmacodynamics and pharmacokinetics of anticancer agents (Saifullah et al.,

2026). Lipid-based systems (liposomes and solid lipid nanoparticles), polymeric nanoparticles, dendrimers, metallic nanoparticles, mesoporous silica nanoparticles, carbon-based nanomaterials, micelles, and biomimetic vesicles (exosomes) are the broad categories of nanocarriers based on their composition and structural features (Chauhan et al., 2026). In the nanocarrier systems, every system has its own distinct strengths in terms of drug loading capacity, stability, biodegradability, controlled release behavior, and targeting efficiency (Yao et al., 2026). The physicochemical properties of nanoparticles such as particle size, shape, surface charge, hydrophobicity, surface functionalization, and colloidal stability are critical factors influencing the therapeutic performance of nanoparticles (Alkan et al., 2026).

Smaller nanoparticles are more effective tumor penetrators with increased circulation time and surface functionalization with polyethylene glycol (PEG) or targeting ligands can minimize immune clearance and increase tumor cell selectivity (Thakare et al., 2026). Moreover, morphology and surface chemistry of nanoparticles have a major influence on cellular internalization, biodistribution, protein corona formation, and biological events in the tumor microenvironment (Mazumdar et al., 2025; Swarn et al., 2026). The tumor microenvironment is a very complex and heterogeneous ecosystem with the presence of abnormal vasculature, hypoxia, acidic pH, high interstitial pressure, dense extra-cellular matrix, inflammatory mediators, immune cells, and stromal fibroblasts, which control the nanoparticle transport and therapeutic efficacy. Such pathological abnormalities result in special possibilities of drug delivery because the nanoparticles can concentrate in malignant tissues (Ahmad & Usmani, 2026). The enhanced permeability and retention (EPR) effect, initially proposed by Matsumura and Maeda, is among the most thoroughly characterized mechanisms of nanomedicine where a defective tumor blood vessels with large endothelial orifices has been identified to facilitate selective extravasation of nanoparticles into tumor tissues with the defective lymphatic drainage facilitating extended retention in the tumor microenvironment (Hussain et al., 2026; Mousavi-Kiasary et al., 2025). Passive targeting is largely reliant on this EPR effect and allows non-specific concentration of nanocarriers in tumor areas without molecular recognition. Nevertheless, the heterogeneity of the tumor vascularization and disparate expression of EPR in patients may restrict the uniformity of therapy (Chen et al., 2026). To address these issues, active targeting has been conceived by surface functionalizing nanoparticles with antibodies, peptides, aptamers, folic acid, transferrin or receptor specific ligands which specifically receptor overexpressing cells of the cancer cell, thus leading to receptor-mediated endocytosis and increased delivery of drugs into the cell (Albatsh, 2026). Active targeting does not only lead to better therapeutic specificity, but also increase cellular uptake, drug bioavailability, and anticancer efficacy and decrease off-target toxicity (Khambete et al., 2026; Omidian & Gill, 2025). In addition, contemporary multifunctional nanoparticles are able to integrate passive and active targeting strategies as well as stimuli-responsive release of drugs to attain enhanced accuracy in cancer therapy (Liu et al., 2026). Passive targeting is mainly partially mediated by the EPR effect caused by leaky tumor vasculature and ineffective lymphatic drainage, and active targeting is mediated by ligand-receptor interaction, which serves to increase the selective accumulation and intracellular internalization of nanoparticles in tumor tissues (as shown in **Figure 1**)(Salaudeen & Akinniranye, 2024). These innovations emphasize the importance of nanotechnology in addressing biological impediments and enhancing precision oncology clinical efficacy (Zhu et al., 2026).

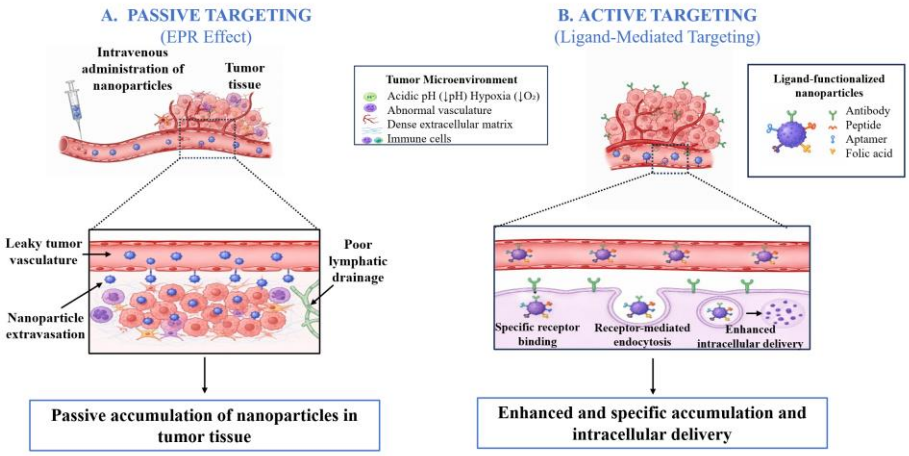

Figure 1: Schematic representation of passive and active nanoparticle targeting mechanisms in tumor tissues.

3. Types of Nanotechnology-Based Drug Delivery Systems

Nanotechnology is a drug delivery system that has revolutionized precise cancer therapy by enhancing the solubility, stability, bioavailability, targeting efficiency, and therapeutic index of anticancer agents with minimal systemic toxicity and multidrug resistance (S. Kumar et al., 2026). There is a broad range of nanocarriers that have been engineered to possess unique structural and physicochemical characteristics, which facilitate targeting of tumors and targeted drug delivery (Razavi et al., 2026). Liposomes represent one of the oldest and most effective systems in the clinic as a nanocarrier of phospholipid bi-layers that have the ability to encapsulate both hydrophilic and hydrophobic drugs, therefore, increasing the circulation time and decreasing off-target toxicity (Gupta et al., 2026). Various liposomal preparations like doxorubicin-impregnated liposomes have shown considerable clinical benefits in various cancers (Rathour et al., 2026). Polymeric nanoparticles, made of biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA), chitosan, polyethylene glycol (PEG), provide controlled and sustained drug delivery with enhanced stability and adjustable surface characteristics to be used in active targeting (Abualsoud et al., 2026). Dendrimers are branched three-dimensional macromolecules with defined molecular structure, large drug-loading capacity, and various surface functional groups, which enable ligand conjugation, and gene delivery (Wei, 2026). Nano-sized lipid particles offer the benefits of lipid-based delivery systems, alongside increased physical stability and biocompatibility, rendering them attractive as vehicles to deliver hydrophobic chemotherapeutics (Othman et al., 2026). Metallic nanoparticles, especially, gold, silver, and iron oxide nanoparticles have distinctive optical, magnetic, and photothermal characteristics, which are useful in imaging, photothermal therapy, radiosensitization, and theranostics (Anand et al., 2026). Mesoporous silica nanoparticles have high surface area, controllable pore size and high loading efficiency, which allow drugs, proteins, nucleic acids and imaging agents to be delivered with controlled release properties (Ahmad & Usmani, 2026). Nanomaterials based on carbon nanotubes and graphene have outstanding electrical, thermal and mechanical characteristics that enable the effective cellular delivery and multifunctional therapy including photothermal therapy and gene delivery, but the issue of long-term toxicity and biocompatibility has become a major concern (Singhai et al., 2026). Exosomes and biomimetic nanocarriers have attracted much attention more recently due to their natural source, immune evasion capacity, intrinsic targeting capacity, and enhanced biocompatibility. Exosome-mediated delivery systems have the ability to deliver proteins, RNA, and chemotherapeutic agents across biological barriers with minimal immunogenicity and increased uptake into cells (Ge et al., 2026). Moreover, hybrid

multifunctional nanoplatforms encompassing several therapeutic and diagnostic elements into a single nanosystem have become new advanced approaches to precision oncology. These bifunctional systems can be used to concomitantly integrate chemotherapy, immunotherapy, photothermal therapy, gene therapy, and imaging modalities to obtain synergistic anticancer activity and real-time monitoring of therapy (X. Zhang et al., 2026). Targeting ligands, antibodies, aptamers, peptides, and stimuli-responsive parts can also be engineered on the surface of these multifunctional systems to further provide specificity and therapeutic efficacy. In summary as can be seen in **Table 1**, all nanocarrier systems have unique compositions, strengths, weaknesses and clinical uses that determine their applicability to particular oncological indications (Youssef et al., 2026).

Table 1: Major nanocarrier systems used in cancer therapy: composition, advantages, limitations, and clinical applications.

Nanocarrier System	Composition	Major Advantages	Limitations	Clinical Applications in Cancer Therapy
Liposomes	Phospholipid bilayer vesicles with aqueous core	Biocompatible, reduced systemic toxicity, prolonged circulation, capable of carrying hydrophilic and hydrophobic drugs	Drug leakage, limited storage stability, high production cost	Breast cancer, ovarian cancer, Kaposi's sarcoma, metastatic cancers
Polymeric Nanoparticles	Biodegradable polymers such as PLGA, PEG, chitosan, PLA	Controlled drug release, enhanced stability, tunable surface modification, targeted delivery	Complex synthesis, possible polymer toxicity, burst release	Targeted chemotherapy, gene delivery, combination therapy
Dendrimers	Highly branched synthetic macromolecules	High drug-loading capacity, precise architecture, multiple functional groups for targeting	Cytotoxicity at higher generations, expensive synthesis	Gene therapy, targeted drug delivery, imaging applications
Solid Lipid Nanoparticles (SLNs)	Solid lipid core stabilized by surfactants	High biocompatibility, improved drug stability, controlled release	Limited drug-loading capacity, risk of drug expulsion during storage	Delivery of hydrophobic anticancer drugs, oral chemotherapy
Metallic Nanoparticles	Gold, silver, iron oxide, titanium dioxide nanoparticles	Unique optical and magnetic properties, photothermal activity, imaging capability	Potential long-term toxicity, bioaccumulation concerns	Photothermal therapy, MRI imaging, radiosensitization
Mesoporous Silica Nanoparticles (MSNs)	Silica-based porous nanostructures	Large surface area, high drug-loading efficiency, tunable pore size	Slow biodegradation, possible inflammatory response	Controlled drug delivery, theranostics, gene delivery
Carbon Nanotubes (CNTs)	Cylindrical graphene sheets composed of carbon atoms	High surface area, efficient cellular penetration, thermal conductivity	Biocompatibility and toxicity concerns, poor biodegradability	Photothermal therapy, drug and gene delivery
Graphene-Based Nanomaterials	Single or multilayer carbon sheets	Excellent drug adsorption, photothermal properties, multifunctionality	Oxidative stress, potential cytotoxicity	Cancer imaging, photodynamic and photothermal therapy
Exosomes and Biomimetic Nanocarriers	Cell-derived extracellular vesicles or membrane-coated nanoparticles	Natural targeting ability, immune evasion, superior biocompatibility	Difficult large-scale production, purification challenges	Personalized medicine, RNA delivery, immunotherapy

Also, **Figure 2** shows how large nanocarrier systems are categorized in targeted cancer therapy, and the variety of organic, inorganic, biomimetic, and hybrid nanosystems that are being explored at this time as precision drug carriers (Z. Li et al., 2026). In spite of the spectacular progress, nanotoxicity, complexity of manufacturing, scalability, immune clearance, and regulatory issues still represent barriers to large-scale clinical translation (S. Kumar et al., 2026).

However, recent advancements in nanoparticle development, surface engineering and multifunctional therapeutic development will greatly increase the future clinical utility of nanotechnology-enabled targeted cancer therapy (Kimta et al., 2026).

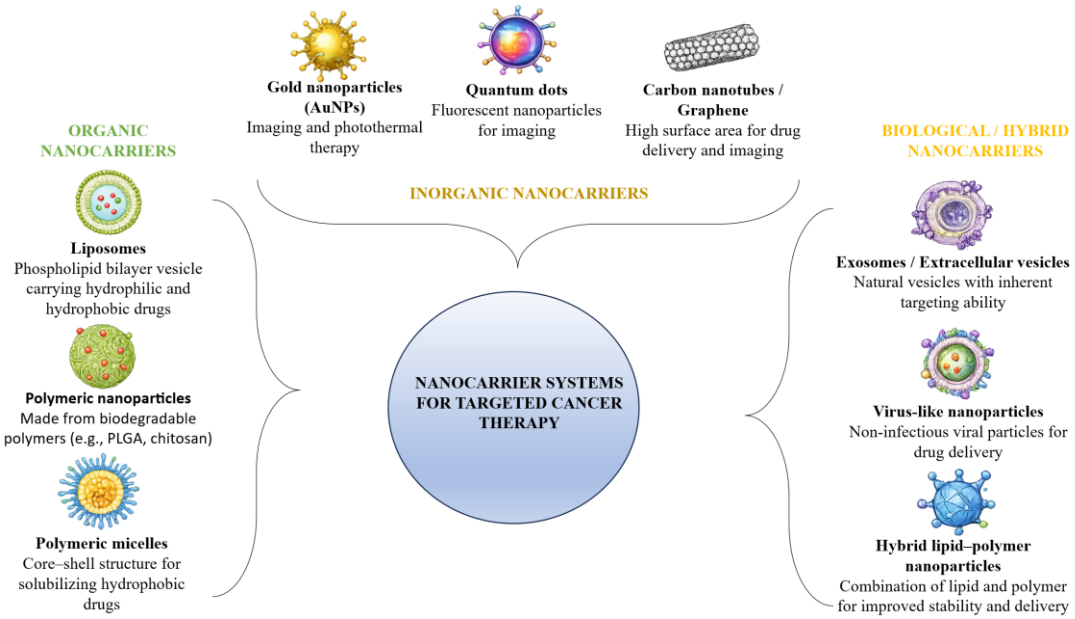

Figure 2: Classification of nanocarrier systems employed in targeted cancer therapy.

4. Targeting Strategies in Precision Cancer Therapy

Precision cancer therapy has greatly advanced with the development of nanotechnology that allows the delivery of therapeutic agents to tumor tissues selectively so that the curative therapy has fewer systemic toxic effects and greater therapeutic efficacy (Q. Sun et al., 2026). Ligand-mediated targeting is one of the most extensively studied methods, in which ligands, including folic acid, transferrin, peptides, carbohydrates and small molecules, that specifically bind overexpressed receptors on cancer cells are conjugated to the surface of nanoparticles (Kimta et al., 2026). This specific interaction with receptors results in increased cellular uptake via receptor-mediated endocytosis and increased intracellular accumulation of drug (Lionadi & Payam, 2026). The antibody-conjugated nanoparticles also increase specificity of the targeting by the use of monoclonal antibodies that specifically target the tumor-associated antigens like HER2, EGFR and CD44, allowing selective targeting and destruction of malignant cells with minimal off-target effects (Gupta et al., 2026). These immunonanoparticles have been found to have promising uses in targeted chemotherapy, immunotherapy and diagnostic imaging (S. Kumar et al., 2026). Nucleic acid aptamers have also become an innovative approach to nanomedicine because of the high affinity, specificity, low immunogenicity, and low cost of production of aptamers (Razavi et al., 2026). Aptamers are able to specifically target tumor biomarkers and deliver drugs, genes and imaging agents efficiently to cancer cells. Besides ligand-based targeting, stimuli-responsive drug delivery vehicles have also received significant interest due to their capability to deliver therapeutic cargo in response to particular tumor-related internal or external cues (Chauhan et al., 2026). pH-responsive nanoparticles take

advantage of the acidic tumor microenvironment and endosomal compartments to achieve an active release of drugs into tumor tissues (Hussain et al., 2026). Temperature responsive systems make use of phase changes in hyperthermia to enable site-specific delivery of drugs in response to higher temperatures typically encountered in tumor areas or during external thermal therapy (El-Khawaga et al., 2026). Nanoparticles that are enzyme-responsive are engineered to react to tumor-associated enzymes like matrix metalloproteinases, cathepsins, and phospholipases to allow selective breakdown of nanoparticle matrices and targeted drug delivery (Nathan S et al., 2026). On the same note, redox-reactive systems also utilise the high levels of intracellular glutathione and oxidative stress levels found inside the cancer cell to initiate rapid intracellular release of drugs by cleaving redox-reactive linkages (Z. Wang et al., 2026).

These intelligent nanocarriers considerably enhance the precision of therapeutic delivery and reduce premature drug leakage in the system circulation (Xiao et al., 2026). Moreover, gene-targeted and RNA-based nanotherapeutics have revolutionized contemporary oncology as they allow to modulate cancer-related genes and signaling pathways in a targeted fashion (Sharma et al., 2026). Nanocarriers are useful in delivery of small interfering RNA (siRNA), messenger RNA (mRNA), microRNA, plasmid DNA, and CRISPR-Cas gene-editing systems and shield these nucleic acids against enzymatic degradation and improves intracellular delivery (Y. Sun et al., 2026). Nanotherapeutics based on RNA have demonstrated considerable potential in silencing oncogenes, overcoming multidrug resistance, and augmenting immune-mediated anticancer functions (Siddalingegowda et al., 2026). Individual nanomedicine solutions go a step further in incorporating molecular profiling, genomic and biomarker discovery to create custom nanoparticle systems based on the biological properties of the specific tumor. Precision-controlled nanotherapeutics allow the selection of drugs optimally, delivery to specific locations, decreased toxicity, and enhanced clinical results (Hsu et al., 2026).

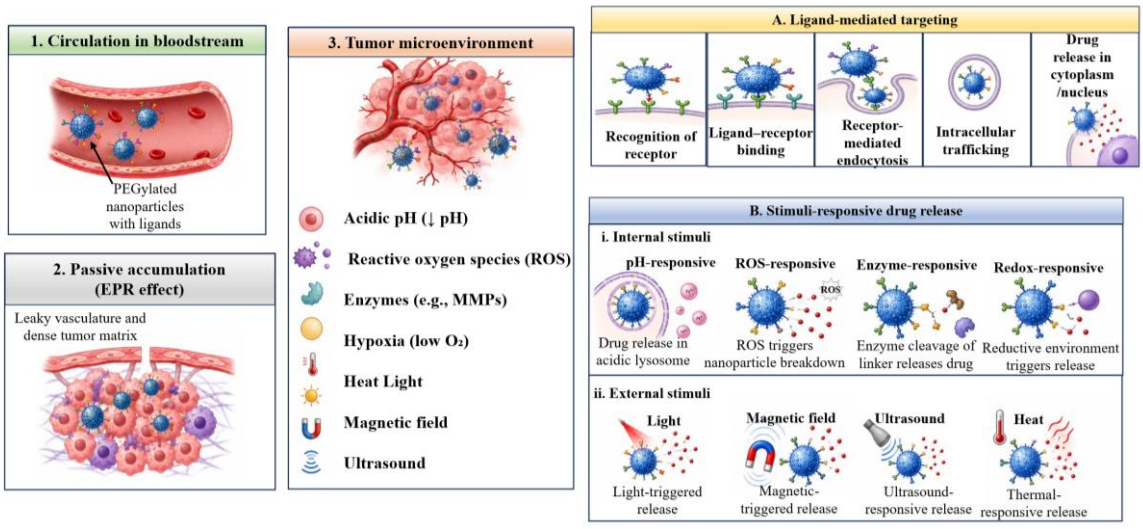

Figure 3: Mechanisms of stimuli-responsive and ligand-mediated targeted nanoparticle delivery.

Ligand-mediated targeting **(Figure 3)** entails selective recognition of receptors and receptor-mediated endocytosis, whereas stimuli-responsive nanoparticles exploit tumor specific conditions (e.g., acidic pH, enzymatic activity, high temperature, redox imbalance) to induce controlled and localized drug delivery in cancer tissues (S. Wang et al., 2026). These enhanced targeting approaches, jointly, have significantly enhanced the treatment efficacy of nanotechnology-based cancer therapy and have served to spearhead the creation of next-generation precision cancer therapeutic systems (Sheikh et al., 2026).

5. Applications of Nanotechnology in Cancer Treatment

Modern cancer treatment has been greatly influenced by nanotechnology, as it has made it possible to have highly efficient, targeted and multifunctional therapeutic approaches, which address the limitations of conventional anticancer therapies (S. Kumar et al., 2026). Nanoparticles are used in the delivery of chemotherapy, a highly significant field of nanotechnology, whereby chemotherapy agents increase solubility, bioavailability, pharmacokinetics, and tumor-specific accumulation of chemotherapeutic agents and reduces systemic toxicity and adverse effects (Lionadi & Payam, 2026). Polymeric nanoparticles, liposomes, dendrimers and solid lipid nanoparticles have been widely used to encapsulate cytotoxic drugs like doxorubicin, paclitaxel, cisplatin and docetaxel to increase therapeutic efficacy and minimize toxicity of healthy tissues (P. Kumar et al., 2026). Drug delivery mediated by nanoparticles makes it possible to achieve controlled and sustained release profiles, enhanced uptake into cells, and increased penetration of tumor tissues (Kimta et al., 2026). Over the past few years, nanotechnology has proven to be an effective means of immunotherapy augmentation by enabling the effective delivery of immune checkpoint inhibitors, cytokines, tumor antigens and vaccine adjuvants to immune cells and tumor micro environments (Chauhan et al., 2026). Nanocarriers have the potential to enhance antigen delivery, tumor-associated macrophages, cytotoxic T lymphocytes, and immune-mediated antitumor responses and reduce systemic immune-related toxicities (Barik et al., 2026). Also, gene therapy and siRNA delivery have received significant interest because of the capability of nanoparticles to protect nucleic acids against enzymatic degradation and intracellular delivery of the nucleic acid across biological barriers (Zhu et al., 2026).

Lipid nanoparticles, polymeric nanoparticles, and exosomes are among the widely studied nanocarrier systems to deliver siRNA, miRNA, mRNA, plasmid DNA, and CRISPR-Cas gene-editing systems to target silencing of oncogenes and activating cancer-related signaling pathways (T. Li et al., 2026). Another field of nanotechnology in oncology that is rapidly developing is photothermal therapy and photodynamic therapy. Nanoparticles like gold nanoparticles, carbon nanotubes, graphene oxide, and other photothermal agents are photothermal agents made up of metals that can transform near-irradiation into localized heat, resulting in selective tumor ablation and improved therapeutic outcomes (Saifullah et al., 2026). On the same note, photodynamic therapy employs nanoparticles that are loaded with photosensitizers that form reactive oxygen species when activated with light that induces targeted destruction of cancer cells with limited harm to other tissues (Domínguez et al., 2026). Theranostics and image-guided therapy has further diversified the nanosystem with therapeutic and diagnostic capabilities in one nanosystem.

Multifunctional nanoparticles with imaging agents including magnetic resonance imaging contrast materials, fluorescent probes, radionuclides, or computed tomography enhancers allow the simultaneous imaging of tumors, delivery of drugs, therapeutic monitoring, and real-time evaluation of treatment outcome (Ganguly & Margel). In fact, combination therapy strategies of co-delivery of chemotherapeutic reagents, immunotherapeutics, gene therapies, and photothermal reagents to a single nanoparticle system have shown synergistic anticancer effects and enhanced therapeutic responses because they target multiple pathways concomitantly (Zhou et al., 2026). Moreover, nanotechnology has demonstrated a high potential in metastatic cancer therapy by increased targeting of circulating tumor cells, prevention of tumor invasion and tumor angiogenesis, and increased penetration at the metastatic lesions (Dharne et al., 2026). Nanoparticles surface-functionalized to identify metastatic biomarkers and tumor microenvironment factors can greatly enhance treatment specificity in more advanced cancers (L. S. Singh et al., 2026).

As discussed in **Table 2**, a wide variety of nanotechnology-based therapeutic approaches have shown promising preclinical and clinical results in a wide range of cancer types, indicating the growing clinical applicability of nanoparticles in oncology (Lu et al., 2026). Although this has been achieved to a great extent, issues of nanotoxicity, immune clearance, high-scale production, and regulatory clearance remain as impediments to widespread clinical translation (J. Li et al., 2026). However, continued efforts to develop multifunctional nanoplatform engineering, precision targeting, and personalized medicine will continue to transform cancer treatment and achieve better patient outcomes in the long term with precision oncology (Shevtsov et al., 2026).

Table 2: Recent nanotechnology-enabled therapeutic strategies evaluated in preclinical and clinical cancer studies.

Nanotechnology-Based Strategy	Nanocarrier/System	Therapeutic Agent	Cancer Type	Study Level	Major Findings/Outcome
Liposomal Chemotherapy	PEGylated liposomes	Doxorubicin (Doxil®)	Breast cancer, ovarian cancer	Clinical	Reduced cardiotoxicity and prolonged circulation with enhanced tumor accumulation
Polymeric Nanoparticle Drug Delivery	PLGA nanoparticles	Paclitaxel	Lung cancer	Preclinical/Clinical	Improved drug stability, controlled release, and enhanced cytotoxicity
siRNA Nanotherapy	Lipid nanoparticles	siRNA targeting KRAS	Pancreatic cancer	Preclinical	Effective oncogene silencing and suppression of tumor growth
Gold Nanoparticle Photothermal Therapy	Gold nanoshells	Near-infrared photothermal agents	Prostate cancer	Clinical	Selective thermal ablation of tumor tissues with minimal normal tissue injury
Photodynamic Nanotherapy	Silica nanoparticles	Photosensitizers	Skin cancer	Preclinical	Enhanced reactive oxygen species generation and targeted tumor destruction
Immunotherapy Enhancement	Polymeric nanocarriers	PD-L1 inhibitors	Melanoma	Preclinical	Increased T-cell activation and improved immune response
Exosome-Mediated Drug Delivery	Tumor-derived exosomes	Doxorubicin/siRNA	Glioblastoma	Preclinical	Improved blood–brain barrier penetration and targeted delivery
Theranostic Nanoplatforms	Iron oxide nanoparticles	Imaging + chemotherapy agents	Breast cancer	Clinical/Preclinical	Simultaneous tumor imaging and targeted therapy monitoring
Combination Nanotherapy	Hybrid multifunctional nanoparticles	Chemotherapy + photothermal agents	Triple-negative breast cancer	Preclinical	Synergistic anticancer activity and reduced multidrug resistance

Targeted Antibody-Conjugated Nanoparticles	HER2-targeted nanoparticles	Trastuzumab-loaded systems	HER2-positive breast cancer	Clinical	Enhanced receptor-mediated targeting and therapeutic efficacy
Magnetic Nanoparticle Hyperthermia	Magnetic iron oxide nanoparticles	Hyperthermia-inducing agents	Brain tumors	Clinical	Localized heating and enhanced tumor cell sensitivity to therapy
Redox-Responsive Nanocarriers	Polymeric redox-sensitive nanoparticles	Cisplatin	Ovarian cancer	Preclinical	Controlled intracellular drug release in tumor microenvironment
pH-Responsive Nanoparticles	Mesoporous silica nanoparticles	Doxorubicin	Colon cancer	Preclinical	Selective drug release in acidic tumor tissues
Biomimetic Cell Membrane-Coated Nanoparticles	Cancer cell membrane-coated nanoparticles	Paclitaxel	Metastatic cancer	Preclinical	Enhanced immune evasion and metastatic tumor targeting
CRISPR-Cas Nanodelivery Systems	Lipid-polymer hybrid nanoparticles	CRISPR-Cas9 components	Liver cancer	Preclinical	Efficient gene editing and suppression of tumor progression

6. Clinical Translation and Regulatory Perspectives

The clinical translation of nanotechnology-based cancer therapeutics has advanced considerably over the past two decades, resulting in the development of several FDA-approved nanomedicines and a growing number of nanoformulations undergoing clinical evaluation for precision oncology applications (Gupta et al., 2026).

Nanotechnology offers substantial advantages in improving drug solubility, pharmacokinetics, biodistribution, tumor targeting, and therapeutic efficacy while reducing systemic toxicity associated with conventional chemotherapy (S. Kumar et al., 2026). Liposomal formulations such as pegylated liposomal doxorubicin, albumin-bound paclitaxel nanoparticles, liposomal irinotecan, and lipid-based daunorubicin/cytarabine combinations represent some of the most successful clinically approved nanomedicines currently utilized in the treatment of breast cancer, ovarian cancer, pancreatic cancer, leukemia, and metastatic malignancies (Zeeshan et al., 2026). These nanocarrier systems have demonstrated improved circulation time, enhanced tumor accumulation, reduced cardiotoxicity, and superior therapeutic index compared with conventional formulations (Abualsoud et al., 2026). In addition to approved products, numerous nanoparticle-based therapeutics including polymeric nanoparticles, gold nanoparticles, siRNA nanocarriers, magnetic nanoparticles, and multifunctional theranostic systems are currently being investigated in ongoing preclinical and clinical studies for targeted drug delivery, gene therapy, immunotherapy enhancement, photothermal therapy, and image-guided treatment (Lionadi & Payam, 2026). Despite these advancements, the successful clinical translation of nanomedicines remains hindered by several scientific, manufacturing, regulatory, and economic challenges. Large-scale manufacturing and reproducibility of nanoparticles continue to represent major obstacles due to the complexity of nanoparticle synthesis, batch-to-batch variability, stability concerns, sterilization requirements, and difficulties in maintaining consistent physicochemical properties during industrial production (Yadav et al., 2026). Furthermore, the pharmacokinetics and biodistribution of nanoparticles are influenced by particle size, surface charge, protein corona formation, immune clearance, and interactions with biological barriers, which may significantly alter therapeutic efficacy and safety profiles in humans compared with preclinical models (C. K. Singh et al., 2026). Nanoparticles may

also accumulate in off-target organs such as the liver, spleen, lungs, and kidneys, raising concerns regarding long-term toxicity, immunogenicity, oxidative stress, inflammation, and potential bioaccumulation (Yang et al.). Safety assessment of nanomedicines therefore requires comprehensive evaluation of physicochemical characterization, pharmacodynamics, immunotoxicity, genotoxicity, biodegradability, and long-term biocompatibility (Chahal et al., 2026). Regulatory approval pathways for nanotechnology-based therapeutics remain highly complex because conventional pharmaceutical evaluation criteria are often insufficient to fully characterize nanoscale systems (Stucchi et al., 2026). Regulatory agencies including the FDA and EMA have established evolving guidelines focused on nanoparticle characterization, quality control, manufacturing practices, safety evaluation, and clinical performance; however, the absence of globally harmonized regulatory standards continues to slow commercialization and approval processes (Gupta et al., 2026). Additionally, the high cost associated with nanoparticle development, large-scale production, quality assurance, clinical trials, and regulatory compliance presents substantial economic barriers that may limit accessibility and widespread clinical implementation (Vyas et al., 2026). Nevertheless, advances in scalable manufacturing technologies, artificial intelligence-assisted nanoparticle design, biomimetic nanocarriers, and precision medicine approaches are expected to accelerate future clinical translation and commercialization of nanomedicines (Pathak et al., 2026).

Table 3: FDA-approved nanomedicines and clinically investigated nanoformulations for cancer therapy.

Nanomedicine/ Nanoformulation	Nanocarrier Type	Therapeutic Agent	FDA Approval/Clinical Status	Cancer Indication	Major Clinical Advantage
Doxil®	PEGylated liposome	Doxorubicin	FDA-approved	Ovarian cancer, breast cancer, Kaposi's sarcoma	Reduced cardiotoxicity and prolonged circulation time
Abraxane®	Albumin-bound nanoparticles	Paclitaxel	FDA-approved	Breast cancer, pancreatic cancer, NSCLC	Improved solubility and enhanced tumor penetration
Onivyde®	Liposomal formulation	Irinotecan	FDA-approved	Metastatic pancreatic cancer	Enhanced drug stability and prolonged drug exposure
Vyxeos®	Liposomal dual-drug formulation	Daunorubicin + Cytarabine	FDA-approved	Acute myeloid leukemia	Fixed synergistic drug ratio with improved efficacy
Marqibo®	Liposomal nanoparticle	Vincristine sulfate	FDA-approved	Acute lymphoblastic leukemia	Improved pharmacokinetics and reduced neurotoxicity
DaunoXome®	Liposomal formulation	Daunorubicin	FDA-approved	Kaposi's sarcoma	Reduced systemic toxicity and improved biodistribution
Mepact®	Liposomal macrophage activator	Mifamurtide	Approved in Europe	Osteosarcoma	Immune activation and improved survival outcomes
NanoTherm®	Magnetic iron oxide nanoparticles	Hyperthermia nanoparticles	Clinical use (Europe)	Glioblastoma	Localized thermal ablation of tumor tissue
CRLX101	Polymeric nanoparticle	Camptothecin	Clinical trials	Renal cancer, ovarian cancer	Sustained drug release and tumor targeting

BIND-014	Targeted polymeric nanoparticles	Docetaxel	Clinical trials	Prostate cancer, lung cancer	PSMA-targeted delivery with enhanced specificity
CALAA-01	Cyclodextrin polymer nanoparticles	siRNA targeting RRM2	Clinical trials	Solid tumors	First targeted siRNA nanoparticle in humans
NU-0129	Gold nanoparticles	siRNA delivery system	Clinical trials	Glioblastoma	Enhanced blood–brain barrier penetration
AuroShell® Nanoparticles	Gold nanoshells	Photothermal therapy agent	Clinical trials	Prostate cancer	Near-infrared mediated tumor ablation
Lipid Nanoparticle mRNA Systems	Lipid nanoparticles	mRNA therapeutics	Clinical investigation	Melanoma and solid tumors	Efficient intracellular nucleic acid delivery
Mesoporous Silica Nanoparticles	Silica-based nanocarriers	Doxorubicin/targeted agents	Preclinical/Clinical investigation	Breast cancer, colon cancer	High drug-loading capacity and controlled release

As summarized in **Table 3**, several FDA-approved nanomedicines and clinically investigated nanoformulations have demonstrated promising therapeutic outcomes across multiple cancer types. Furthermore, **Figure 4** illustrates the translational pathway of nanotechnology-based cancer therapeutics from initial laboratory research and nanoparticle design through preclinical evaluation, clinical trials, regulatory approval, and eventual clinical application in precision oncology (Jain, 2026).

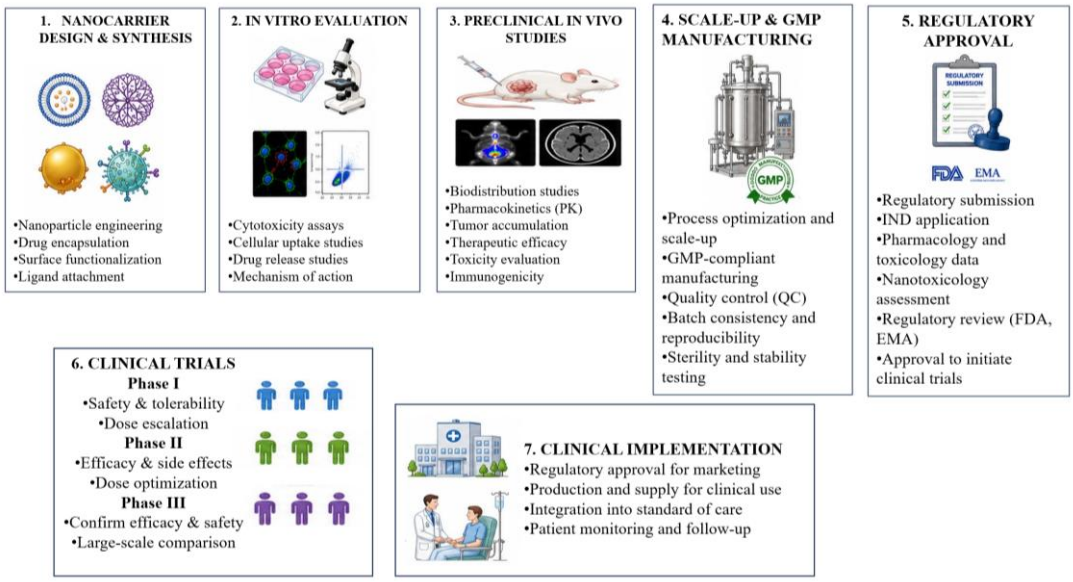

Figure 4: Pathway for clinical translation of nanotechnology-based cancer therapeutics from bench to bedside.

7. Current Challenges and Limitations

In spite of the incredible advancements in nanotechnology based cancer therapeutics, a number of significant challenges and limitations still remain that prevent their extensive clinical application and durability in the treatment of cancer (Pawar et al., 2026). Among the greatest challenges are the existence of biological barriers and quick immune elimination systems that markedly decrease the concentration of nanoparticles at tumor locations (Deorankar et al.,

2026). After systemic exposure, nanoparticles are coated by the plasma proteins to form a protein corona, which can modify their physicochemical characteristics, biodistribution, and targeting efficiency and facilitate recognition and clearance by the mononuclear phagocytic system, especially in the liver and the spleen (Mirza & Kherb, 2026).

Furthermore, abnormal tumor vasculature, high interstitial fluid pressure, high extra-cellular matrix and low tissue penetration of nanoparticles impair successful delivery of nanoparticles in solid tumors (Selvakumar et al., 2026). The heterogeneity of tumors further complicates targeted nanotherapy, as genetic, molecular and cellular differences among tumors and even within distinct regions of tumors can cause unreliable receptor expression, uneven enhanced permeability and retention, and unreliable therapeutic responses (Anand et al., 2026). Nanotoxicity and long-term safety is another important issue. Whilst some nanocarriers are biocompatible and biodegradable, some nanoparticles can cause oxidative stress, inflammation, immunogenicity, accumulation in the body, damage of DNA, and chronic toxicity based on their composition, size, surface charge, or degradation profile (Stuempfig et al., 2026). The patterns of biodistribution and clearance in the long term are still poorly known on a variety of the advanced nanosystems of concern to bioaccumulation and delayed adverse effects. The problem of reproducibility and standardization is also a significant obstacle in the development of nanomedicine (Kummer et al., 2026). The variability in the synthesis of nanoparticles, characterization, surface modifications, drug loading performance, and storage stability has commonly led to batch-to-batch variations that can impact therapeutic performance and regulatory approval (A. Singh et al., 2026). Moreover, the lack of uniformly standardized methods of characterizing nanoparticles and assessing their safety makes it more difficult to compare studies and slow down commercialization (O'Meara & Hoskins, 2026). Ethical and regulatory issues are also of concern, especially when it comes to patient safety, long-term follow-ups, environmental issues, clinical trial strategies, and the absence of unified global regulations about nanomedicine (Rehman et al., 2026).

The identification of these multidisciplinary issues with enhanced nanoparticle engineering, scalable culture, standardized assessment procedures, and formidable regulatory guidelines will play a critical role in the future clinical realization of precision nanomedicine in cancer care (A. Singh et al., 2026).

8. Emerging Trends and Future Perspectives

Current innovative trends in nanotechnology-based cancer therapy are centered on the incorporation of more sophisticated computational technology, precision medicine approaches, biomimetic engineering, and multifunctional nanosystems to circumvent the existing limitations of therapy and to enhance clinical outcomes in cancer (Kimta et al., 2026). The addition of artificial intelligence and machine learning to nanomedicine design is one of the most promising features that can be optimally applied to nanoparticle composition, size, surface properties, drug loading efficiency, and targeting capability via predictive modeling and data-guided analysis (Gupta et al., 2026). Nanoparticles Nanoparticles can be screened much faster with AI-assisted platforms, therapeutic personalization can be enhanced, and the pharmacokinetics, toxicity, and response to treatment can be predicted (Gharti et al., 2026). The other field of fast development is the creation of CRISPR and genome-editing delivery systems based on lipid nanoparticles, polymeric nanocarriers, and exosome-based systems to deliver CRISPR-Cas components to tumor cells (He et al., 2026). Such technologies present unprecedented possibilities of targeted gene correction, silencing of oncogenes, the regulation of tumor suppressor pathways and reversal of multidrug resistance in cancer treatment (Aidhen et al., 2026). Individualized and patient-specific nanotherapeutics will also bring a revolution to precision oncology, by incorporating

genomic profiling, molecular diagnostics, and biomarker-directed selection of therapeutic regimens, to design personalized nanocarriers based on the unique biological properties of the tumor in each patient (Aili et al., 2026).

Moreover, smart multifunctional nanorobotics are another promising direction of cancer treatment, entailing nanoscale robots that can perform autonomous navigation, release drugs into the tumor microenvironment, biosensing, and real-time monitoring of therapeutic processes (Alam et al.). These intelligent systems could allow very accurate delivery of drug in the cell and minimal invasion cancer treatment in future. Biomimetic nanocarriers such as exosome-inspired vesicles, cell membrane-coated nanoparticles, and immune cell-derived nanosystems are under much consideration due to their enhanced biocompatibility, longer circulation duration, immune evasion ability, and inherent targeting capabilities (Pandey et al., 2026). These biomimetic platforms have the potential to target across biological barriers and enhance therapeutic specificity. All of these new innovations will widen the future potential of precision oncology by making it safer, more effective, highly personalized, and multifunctional with better diagnostic, therapeutic, and prognostic features, eventually leading to the full integration of precision nanomedicine into clinical oncology (Saifullah et al., 2026).

9. CONCLUSION

Targeted drug delivery systems based on nanotechnology have become one of the most transformative innovations in the contemporary precision oncology, providing new solutions to the numerous limitations of the existing cancer therapies. A combination of nanoscale delivery platforms and molecular targeting approaches has dramatically enhanced the pharmacokinetics, tumor specificity, and bioavailability of anticancer agents, as well as their therapeutic efficacy, and minimized the systemic toxicity and toxicity to normal tissues. Different nanocarrier platforms such as liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, mesoporous silica nanoparticles, exosomes, and multifunctional hybrid nanoplatforms have shown impressive promise in chemotherapy delivery, immunotherapy, gene therapy, photothermal therapy, theranostics, and management of metastatic cancer. Moreover, innovations in ligand-mediated targeting, stimuli-responsive drug delivery systems, RNA-based therapeutics and personalized nanomedicine approaches have further enhanced the role played by nanotechnology in ensuring high selectivity and patient-specific treatment of cancer. Although significant advancements have been made in preclinical research and some nanomedicines have been approved to be used in clinics, significant barriers to full clinical translation are still present such as biological barriers, immune clearance, tumor heterogeneity, nanotoxicity, reproducibility, large-scale production, regulatory complexity, and long-term safety issues. To overcome these multidisciplinary issues, researchers, clinicians, pharmaceutical industries and regulatory agencies will have to work together to develop standardized evaluation strategies, scalable manufacturing technologies and unified regulatory frameworks across the world. The development of precision nanomedicine is likely to keep gaining momentum with the emergence of new technologies like AI-assisted nanoparticle design, CRISPR-based delivery systems of genome editing, biomimetic nanocarriers, and smart multifunctional nanorobotics, which will enable more opportunities of personalized cancer treatment. Research in the future must not be limited to enhancing therapeutic efficacy and safety but must also be aimed at increasing clinical applicability, cost-effectiveness, and accessibility of advanced nanotherapeutics. In general, nanotechnology has a huge potential in changing the way cancer is diagnosed, treated, and monitored, and its further evolution is bound to be a central force in creating the advances in next-generation precision oncology and personalized cancer therapy.

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