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Systematic Review of Smart Nanoplatforms in Liver, Breast, Kidney, and Brain Cancers: Targeted Delivery, Omics, and Therapy Response

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Abstract:

Background: Liver, breast, kidney, and brain cancers remain major contributors to global cancer morbidity and mortality. Conventional therapies are limited by systemic toxicity, drug resistance, and tumor heterogeneity. Smart nanoplatforms offer targeted delivery, controlled release, and theranostic capabilities to address these challenges. **Objective:** This systematic review evaluates the development and clinical translation of smart nanoplatforms between 2019 and 2024, focusing on their design, omics integration, therapy response, and clinical outcomes in liver, breast, kidney, and brain cancers. **Methods:** Studies published between 2019 and 2024 were systematically analyzed, encompassing preclinical research, clinical trials, and multi-omics-guided nanoparticle strategies. Nanoplatforms were categorized into lipid-based, polymeric, inorganic, and hybrid/bioinspired systems. The review highlights therapy response, biomarker monitoring, and adaptive approaches informed by omics data. **Results:** Lipid-based and polymeric nanoparticles demonstrated enhanced tumor targeting and reduced systemic toxicity. Inorganic and hybrid/bioinspired platforms enabled imaging-guided therapy and immune evasion. Integration of genomics, transcriptomics, proteomics, and metabolomics with AI-driven analytics facilitated personalized therapy and adaptive treatment strategies. Clinical trials reported improved patient tolerability, quality of life, and preliminary survival benefits, though translational barriers—including tumor heterogeneity, blood–brain barrier penetration, manufacturing, and regulatory hurdles—remain significant. **Conclusions:** Smart nanoplatforms represent a transformative approach to precision oncology. The combination of targeted delivery, multi-omics guidance, and AI-driven therapy optimization has the potential to enhance treatment efficacy and patient-specific outcomes. Future research should focus on scalable manufacturing, regulatory standardization, and integration of innovative trial designs to accelerate clinical adoption.

Keywords:

Cancer nanomedicine; Targeted delivery; Smart nanoplatforms; Omics; Precision oncology; Therapy response

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1. Introduction

Cancer remains a leading cause of morbidity and mortality worldwide, contributing to millions of deaths annually and imposing a significant burden on healthcare systems. Liver, breast, kidney, and brain cancers, in particular, account for a substantial proportion of global cancer-related mortality, with late diagnosis, aggressive progression, and treatment resistance exacerbating patient outcomes [1]. Despite substantial advancements in conventional therapies such as surgery, chemotherapy, and radiotherapy, these approaches are often limited by systemic toxicity, multidrug resistance, and intratumoral heterogeneity, which compromise therapeutic efficacy and patient quality of life.The rise of nanotechnology in oncology offers a paradigm shift, introducing smart nanoplatforms capable of targeted delivery, controlled release, and multi-functional theranostic applications. By leveraging nanoscale properties, these systems can improve drug solubility, enhance tumor selectivity, and integrate diagnostic and therapeutic functionalities in a single platform [2]. Lipid-based, polymeric, inorganic, and hybrid bioinspired nanoparticles have shown considerable promise in preclinical and clinical studies, marking the transition of nanomedicine from experimental proof-of-concept to translational relevance.This systematic review aims to provide a comprehensive analysis of smart nanoplatforms developed between 2019 and 2024, focusing on their application in liver, breast, kidney, and brain cancers. Specifically, it examines the design and functionality of various nanocarriers, the integration of multi-omics approaches for personalized therapy, and clinical trial outcomes in terms of efficacy, safety, and therapy response. By synthesizing current knowledge, this review highlights both the achievements and challenges in advancing nanomedicine toward routine clinical implementation [3]. (Figure 1)

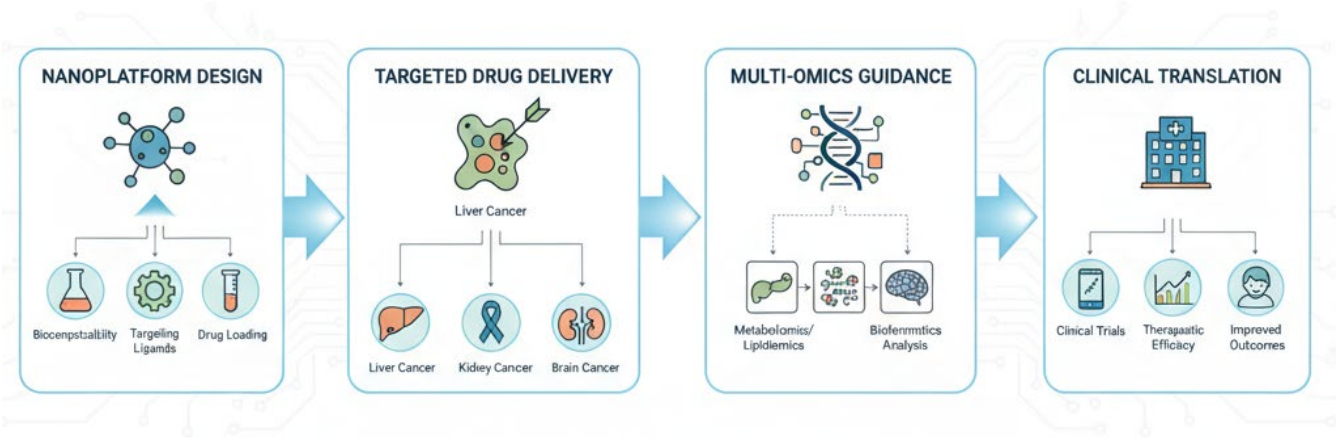

Figure 1. Conceptual roadmap of smart nanoplatforms in cancer therapy: illustrating the integration of targeted delivery, multi-omics guidance, and clinical translation for liver, breast, kidney, and brain cancers.

2. Smart Nanotechnology Therapeutic Platforms

Nanotechnology has revolutionized cancer therapy by enabling the development of smart nanoplatforms that improve drug delivery, reduce systemic toxicity, and incorporate multimodal functionalities such as imaging and therapy. These platforms can be broadly categorized into lipid-based, polymeric, inorganic, and hybrid/bioinspired systems, each with unique physicochemical properties and therapeutic advantages [4].Lipid-based nanocarriers, including liposomes and solid lipid nanoparticles, represent some of the earliest clinically translated nanomedicines. Liposomes are biocompatible, capable of encapsulating both hydrophilic and hydrophobic drugs, and can be surface-modified for active targeting. Solid lipid nanoparticles offer improved stability and controlled release properties. These systems have been successfully applied in liver, breast, kidney, and brain cancers, providing reduced systemic toxicity and enhanced drug accumulation in tumor tissue.Polymeric nanocarriers such as micelles, dendrimers, and nanogels offer high drug loading capacity and tunable release kinetics. Micelles are effective for solubilizing poorly water-soluble drugs, while dendrimers allow precise multivalent functionalization with therapeutic agents, imaging probes, and targeting ligands. Nanogels provide stimulus-responsive drug release and improved biocompatibility, making them versatile platforms for personalized therapy [5].

Inorganic nanoparticles, including gold, silica, and iron oxide nanoparticles, bring additional theranostic functionalities. Gold nanoparticles can serve as photothermal agents, converting near-infrared light into heat to ablate tumor tissue, while iron oxide nanoparticles facilitate magnetic resonance imaging (MRI)-guided therapy. Silica nanoparticles provide high surface area for drug loading and controlled release. These platforms enable integration of therapeutic and diagnostic modalities in a single system.Hybrid and bioinspired systems, including exosomes, cell membrane-coated nanoparticles, and virus-like particles, combine the advantages of synthetic and natural carriers [6]. Bioinspired designs improve biocompatibility, immune evasion, and tumor-targeting efficiency. For example, red blood cell membrane-coated nanoparticles prolong circulation time, and exosome-based carriers exploit natural intercellular communication for precise delivery [7]. (Table 1)

Mechanisms of action for these smart nanoplatforms include:

- Targeted delivery via passive (EPR effect) or active (ligand-receptor) targeting
- Controlled release triggered by pH, enzymes, or redox gradients
- Photothermal and photodynamic therapy for energy-based tumor ablation

Table 1. Summary of nanoplatforms, functional attributes, and advantages

Platform Type	Examples	Advantages	Mechanisms of Action	Reference
Lipid-based	Liposomes, Solid Lipid Nanoparticle	Biocompatible, drug solubilization, surface modifiable	Targeted delivery, controlled	8

	s		release	
Polymeric	Micelles, Dendrimers, Nanogels	High drug loading, multifunctionalization, tunable release	Stimulus-responsive release, ligand targeting	9
Inorganic	Gold, Silica, Iron Oxide	Imaging + therapy, photothermal/photodynamic effects	Thermotherapy, imaging-guided therapy	10
Hybrid/Bioinspired	Exosomes, Cell membrane-coated, Virus-like particles	Immune evasion, biomimicry, prolonged circulation	Targeted delivery, natural cellular uptake	11

3. Omics Integration in Smart Nanomedicine

The integration of omics technologies into nanomedicine has opened new avenues for personalized cancer therapy, allowing the design of smart nanoplatforms tailored to the molecular profile of individual tumors. By leveraging genomics, transcriptomics, proteomics, and metabolomics, researchers can identify actionable targets, predict therapy response, and monitor treatment outcomes in real time.Genomics plays a pivotal role in identifying molecular targets for nanoparticle-based interventions [12]. Whole-genome and exome sequencing allow detection of driver mutations, copy number variations, and other genetic alterations that underlie tumorigenesis and progression. Nanocarriers can then be engineered to deliver small-molecule inhibitors, siRNA, or CRISPR-Cas9 components specifically to cells harboring these alterations. For instance, lipid nanoparticles delivering KRAS-targeting siRNA have shown promise in preclinical models of pancreatic and liver cancers [13].Transcriptomics and proteomics provide complementary layers of information on tumor biology, particularly in identifying biomarkers of drug resistance. RNA sequencing uncovers differential gene expression patterns, while proteomic profiling reveals signaling networks and post-translational modifications that may mediate therapeutic escape. Smart nanoplatforms can be designed to co-deliver chemotherapeutics along with modulators of resistance pathways, enhancing treatment efficacy and reducing recurrence risk.Metabolomics captures dynamic changes in tumor metabolism, offering real-time insights into therapy response. Alterations in glycolysis, glutamine utilization, or lipid metabolism can serve as indicators of treatment effectiveness or emerging resistance [14]. Nanocarriers can be functionalized to exploit these metabolic vulnerabilities or to incorporate sensors that monitor treatment response at the molecular level.The true power of multi-omics integration emerges when these diverse datasets are fused using artificial intelligence and machine learning algorithms. Predictive models derived from integrated genomics, transcriptomics, proteomics, and metabolomics data allow researchers to design nanocarriers

optimized for a patient's unique tumor profile. This approach enables adaptive and highly personalized therapeutic strategies, moving beyond empirical treatment selection toward precision-guided nanomedicine [15]. (Figure 2)

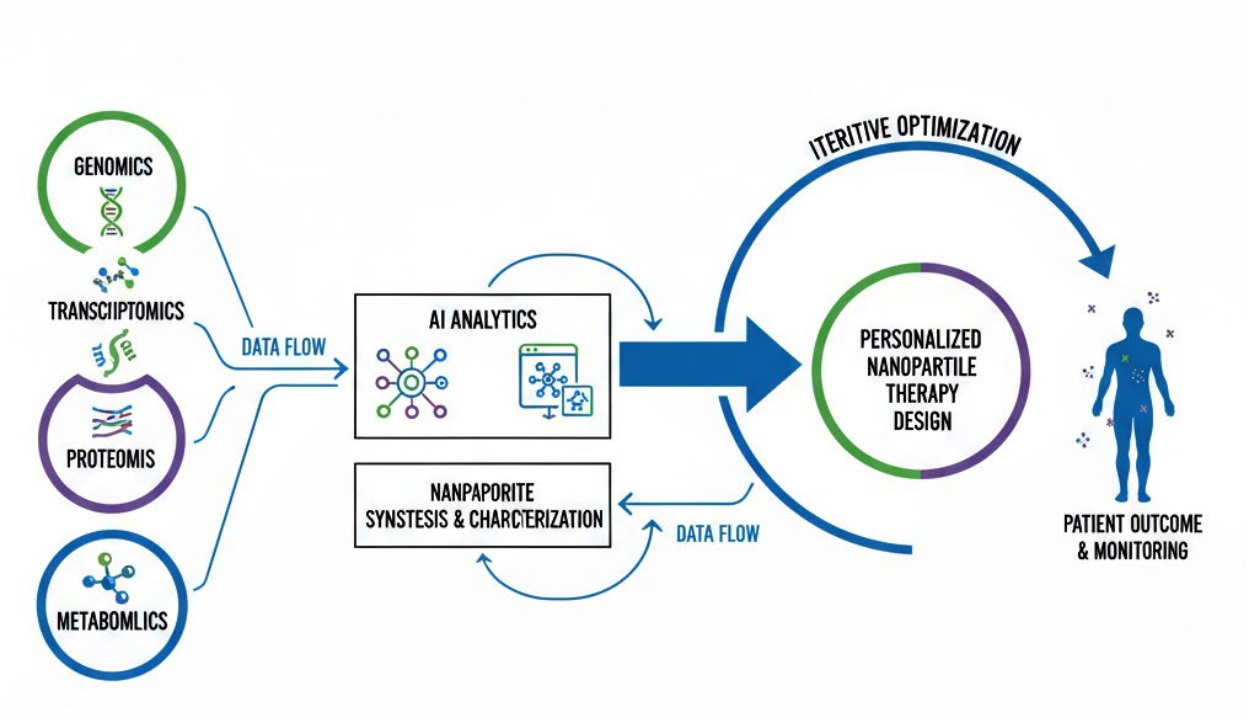

Figure 2. Omics-guided smart nanomedicine development pipeline: integrating genomics, transcriptomics, proteomics, and metabolomics with AI-driven analytics to inform the design and optimization of personalized nanoparticle therapies.

4. Clinical Trial Progress

Between 2019 and 2024, the clinical translation of smart nanoplatforms in oncology has gained considerable momentum, particularly in liver, breast, kidney, and brain cancers. The global landscape reflects a combination of early-phase and advanced clinical trials evaluating diverse nanocarriers, ranging from lipid-based and polymeric systems to inorganic and hybrid/bioinspired platforms. These trials aim to assess not only therapeutic efficacy but also safety, patient survival, and quality-of-life improvements compared to conventional treatments [16].

Lipid-based nanoparticles, such as liposomal doxorubicin and solid lipid carriers, have been widely tested across liver, breast, and kidney cancers. Clinical data indicate enhanced tumor accumulation and reduced systemic toxicity, resulting in improved tolerability and patient-reported outcomes. For instance, liposomal formulations in hepatocellular carcinoma demonstrated prolonged progression-free survival while minimizing cardiotoxicity and myelosuppression [17].Polymeric nanocarriers, including micelles and dendrimer-based systems, have been explored for co-delivery of chemotherapeutics and nucleic acids in breast and kidney

cancers. Early-phase trials show promising results in overcoming multidrug resistance and improving drug bioavailability. These carriers also enable combination therapy strategies, delivering multiple agents simultaneously to enhance tumor response.Inorganic nanoparticles, such as gold and iron oxide nanoparticles, have been primarily investigated in brain tumors for their theranostic potential. Studies demonstrate feasibility in imaging-guided therapy and selective tumor ablation via photothermal or magnetic approaches, though clinical efficacy remains in early evaluation stages due to challenges in blood brain barrier penetration [18].

Hybrid and bioinspired systems, including exosome-based carriers and cell membrane-coated nanoparticles, are emerging in trials for liver and breast cancers. These platforms offer enhanced circulation time, immune evasion, and targeted delivery, marking a shift toward more biomimetic and personalized therapy approaches.Despite these advances, several barriers continue to impede widespread clinical adoption [19]. Complex trial designs, particularly for multi-agent or adaptive studies, slow recruitment and extend timelines. Regulatory hurdles remain substantial, with strict requirements for nanoparticle safety, biodistribution, and long-term monitoring. Manufacturing scalability and cost also pose challenges, limiting broader accessibility, especially in resource-limited settings.Overall, the 2019 2024 clinical trial period demonstrates that smart nanoplatforms can improve tolerability, patient quality of life, and in some cases survival outcomes. However, addressing translational and regulatory challenges is critical to achieving the full clinical potential of nanomedicine [20]. (Table 2)

Table 2. Clinical trialsof smart nanoplatforms in liver, breast, kidney, and brain cancers

Cancer Type	Nanoplatform	Trial Phase	Primary Outcomes	Findings	Reference
Liver	Liposomal doxorubicin	Phase II	PFS, toxicity	Reduced systemic toxicity, improved PFS	21
Breast	Polymeric micelles + siRNA	Phase I/II	Safety, response rate	Enhanced drug bioavailability, overcame resistance	22
Kidney	Solid lipid nanoparticles	Phase I	Safety, QoL	Improved tolerability, reduced side effects	23

Brain	Gold nanoparticles	Early Phase I	Feasibility, imaging	Demonstrated BBB penetration and photothermal potential	24

5. Translational and Technical Challenges

Despite substantial progress in smart nanomedicine, translating these innovations from bench to bedside remains a major challenge. Several biological, technical, and regulatory barriers hinder the routine clinical implementation of nanoplatforms in liver, breast, kidney, and brain cancers.Tumor heterogeneity and delivery limitations pose one of the most significant obstacles [25]. Variability within and between tumors including differences in vascularization, extracellular matrix density, and cellular composition affects nanoparticle penetration and accumulation. Consequently, the enhanced permeability and retention (EPR) effect, often relied upon for passive targeting, shows inconsistent performance across patients and tumor types, reducing therapeutic efficacy.Blood brain barrier (BBB) penetration remains a critical limitation for brain cancer therapies. While certain nanoparticles, such as transferrin-conjugated or exosome-based carriers, have shown the ability to cross the BBB, efficiency is often low and heterogeneous [26]. Achieving safe, noninvasive delivery of therapeutic payloads to central nervous system tumors without off-target effects continues to be a formidable challenge.Manufacturing, scalability, and cost considerations further impede translation. Complex multi-step synthesis processes, batch-to-batch variability, and stability issues complicate large-scale production under Good Manufacturing Practice (GMP) standards. High production costs limit accessibility, particularly in low- and middle-income regions, and may constrain widespread clinical adoption even for successful platforms.Ethical, regulatory, and safety aspects also represent significant barriers. Regulatory agencies require extensive preclinical and long-term safety data for novel nanomaterials, including biodistribution, clearance, and potential immunogenicity. Ethical considerations arise in first-in-human trials, where uncertainties about toxicity or long-term effects must be clearly communicated [27.] Additionally, the lack of standardized guidelines for evaluating nanomedicine safety and efficacy across global regulatory frameworks can slow approval and commercial translation.Addressing these challenges will require interdisciplinary solutions, including innovative delivery strategies, scalable manufacturing technologies, harmonized regulatory pathways, and predictive preclinical models that better represent human tumor heterogeneity [28]. (Figure 3)

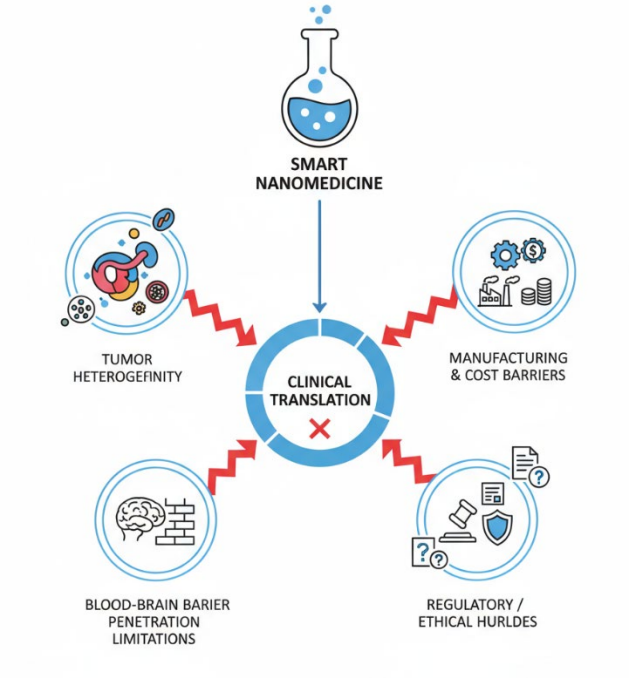

Figure 3. Translational challenges schematic: illustrating tumor heterogeneity, blood brain barrier limitations, manufacturing and cost barriers, and regulatory/ethical hurdles affecting the clinical translation of smart nanomedicine.

6. Therapy Response and Biomarker Monitoring

Smart nanoplatforms not only deliver therapeutics efficiently but also play a pivotal role in modulating and monitoring therapy response. By integrating drug delivery with diagnostic and imaging capabilities, these platforms enable real-time evaluation of treatment efficacy, early detection of resistance, and adaptive therapeutic strategies tailored to individual patients.Role of nanoplatforms in modulating therapy response:Nanoparticles can enhance drug accumulation within tumors, overcome multidrug resistance, and alter the tumor microenvironment to improve therapy outcomes [29]. For example, co-delivery of chemotherapeutics with RNA interference molecules via polymeric micelles or liposomes can suppress resistance pathways in breast and liver cancers, increasing overall treatment sensitivity. Stimuli-responsive carriers can also release drugs in a spatiotemporally controlled manner, maximizing tumor cell killing while minimizing systemic toxicity.Biomarker-driven assessment of treatment efficacy:The integration of molecular biomarkers into clinical monitoring allows early assessment of therapy response. Circulating tumor DNA (ctDNA), exosomal RNA, and protein signatures can be tracked in real time to determine whether a patient is responding or developing resistance. Nanoplatforms can be engineered to either deliver therapeutic payloads based on biomarker profiles or provide simultaneous biomarker sensing, enabling dynamic adjustment of therapy.Imaging-guided therapy and theranostic approaches:Inorganic and hybrid nanoparticles facilitate imaging-guided treatment through modalities such as magnetic resonance imaging (MRI), computed tomography

(CT), and near-infrared (NIR) fluorescence [30]. Theranostic nanoparticles combine therapeutic and diagnostic functionalities, enabling clinicians to visualize drug delivery, monitor tumor regression, and fine-tune therapy in a minimally invasive manner. This approach has been successfully applied in preclinical and early-phase clinical trials for liver, brain, and breast cancers.Integration of omics with response monitoring for adaptive therapy:Combining multi-omics data (genomics, transcriptomics, proteomics, metabolomics) with nanomedicine-enabled monitoring allows for adaptive, personalized therapy. AI-driven models can analyze longitudinal biomarker data to predict treatment response, identify emerging resistance, and recommend adjustments in nanoparticle formulation or dosing. This closed-loop system represents a critical step toward fully personalized, precision-guided nanomedicine [31].

7. Future Perspectives

The future of smart nanomedicine in oncology lies at the intersection of advanced nanosystem engineering, multi-omics integration, and artificial intelligence**.** As we move beyond incremental innovations, next-generation nanoplatforms are expected to offer unprecedented specificity, functionality, and adaptability, transforming cancer therapy into a fully personalized discipline [32].Emerging nanoplatforms will be AI-integrated, stimuli-responsive, and bioinspired**.** Stimuli-responsive nanoparticles can release therapeutic agents in response to tumor-specific triggers such as pH, hypoxia, or enzymatic activity, ensuring precise spatiotemporal control. Bioinspired carriers, including exosome-mimetic and cell membrane-coated nanoparticles, offer immune evasion, prolonged circulation, and enhanced tumor targeting. AI integration allows optimization of particle design, payload selection, and delivery strategies, accelerating preclinical development and reducing trial-and-error approaches. The combination of multi-omics datasets with AI-driven analytics enables adaptive, patient-specific therapy design**.** Genomic, transcriptomic, proteomic, and metabolomic data inform nanoparticle selection, dosing, and combination strategies tailored to an individual's tumor biology. Real-time biomarker monitoring can further guide adaptive interventions, adjusting therapy in response to emerging resistance patterns and ensuring maximal efficacy [33]. Future clinical evaluation will rely increasingly on basket, umbrella, and adaptive trial frameworks, which allow testing of multiple therapeutic strategies, targets, and patient subgroups simultaneously. These designs are better suited for personalized nanomedicine, reducing recruitment bottlenecks, accelerating approval timelines, and generating robust, biomarker-informed efficacy data. Achieving widespread clinical adoption requires addressing manufacturing, scalability, regulatory, and cost challenges. Standardized protocols, GMP-compliant production pipelines, and harmonized regulatory frameworks will facilitate commercialization [34]. Partnerships between academia, industry, and policy-makers will be critical to ensure equitable global access to these advanced therapies.

8. Conclusion

Over the period from 2019 to 2024, smart nanoplatforms have demonstrated significant potential in transforming cancer therapy, particularly in liver, breast, kidney, and brain cancers. By leveraging lipid-based, polymeric, inorganic, and hybrid/bioinspired nanoparticles, researchers have developed systems capable of targeted delivery, controlled release, and theranostic

functionalities, overcoming many limitations of conventional treatments such as systemic toxicity, drug resistance, and tumor heterogeneity.The integration of multi-omics approaches including genomics, transcriptomics, proteomics, and metabolomics has further enhanced the precision of nanoparticle-based therapies. Coupled with artificial intelligence, these approaches enable adaptive, personalized treatment strategies that can predict therapy response, monitor biomarkers in real time, and guide dynamic adjustments to therapy regimens. Clinical trials conducted during this period highlight improved tolerability, patient quality of life, and in some cases, enhanced survival outcomes, though challenges remain in blood brain barrier penetration, manufacturing scalability, and regulatory approval.Looking forward, the convergence of AI-driven nanosystem design, multi-omics-guided personalization, and innovative clinical trial frameworks promises to accelerate the translation of nanomedicine into routine clinical practice. Addressing translational, ethical, and regulatory challenges will be essential to ensure broad access and maximize therapeutic impact.In conclusion, smart nanoplatforms represent a transformative frontier in oncology, offering the prospect of highly effective, patient-specific therapies. Continued interdisciplinary collaboration, technological innovation, and clinical validation will be critical to fully realize their potential, marking a new era of precision-guided cancer therapy.

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