

EVALUATING NANOMEDICINE IN ACUTE MYELOID LEUKEMIA: THERAPEUTIC ADVANCES AND PATIENT-CENTERED OUTCOMES IN THE CONTEXT OF HEALTHCARE ACCESSIBILITY AND SOCIAL DETERMINANTS OF CANCER CARE

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Abstract

Acute myeloid leukemia (AML) is an aggressive and biologically heterogeneous hematological malignancy in which therapeutic resistance, relapse, treatment-related toxicity, and persistent disease within the bone-marrow microenvironment continue to limit long-term outcomes. Molecularly directed therapies, venetoclax-based combinations, immunotherapeutic approaches, and liposomal formulations have expanded the therapeutic landscape, but treatment effectiveness remains dependent on disease biology, patient fitness, treatment tolerance, and access to specialized care. Nanomedicine has emerged as a potential strategy for addressing several of these limitations through controlled drug release, altered pharmacokinetics, combination delivery, cellular targeting, and bone-marrow-directed delivery. This narrative review examines the development of nanomedicine in AML while extending the discussion beyond drug-delivery efficacy to patient-centered outcomes, healthcare accessibility, and clinical translation. Evidence indicates that lipid-based, polymeric, biomimetic, and ligand-functionalized nanoparticles can improve delivery characteristics in preclinical AML models, while the clinical success of the liposomal cytarabine–daunorubicin formulation CPX-351 demonstrates that nanomedicine can reach routine clinical practice. However, most actively targeted AML nanoplateforms remain preclinical, and important barriers include biological heterogeneity, limited predictability of nanoparticle distribution in hematological malignancy, manufacturing complexity, regulatory uncertainty, cost, and inadequate patient-centered evidence. Quality of life, treatment burden, convenience, financial toxicity, geographical access, and equitable availability therefore need to become explicit considerations in nanomedicine development. Future AML nanomedicine research should integrate molecular patient selection, human-relevant models, standardized manufacturing, health-economic evaluation, patient-reported outcomes, and implementation science. Nanomedicine should consequently be evaluated not only according to whether it can deliver a therapeutic payload, but also according to whether that delivery

Introduction

Acute myeloid leukemia (AML) is a rapidly progressive hematological malignancy characterized by abnormal proliferation and impaired differentiation of myeloid precursor cells. Its biological heterogeneity encompasses diverse cytogenetic and molecular abnormalities, which have increasingly become central to diagnosis, prognostication, measurable residual disease assessment, and treatment selection (Döhner et al., 2022).

Despite major therapeutic advances, AML remains difficult to treat. Intensive chemotherapy, targeted inhibitors, hypomethylating agents, venetoclax-based combinations, antibody-drug conjugates, maintenance therapy, and hematopoietic stem-cell transplantation have expanded available treatment options. Targeted therapies have produced clinically meaningful improvements in genetically defined patient groups, while lower-intensity combinations have expanded treatment options for patients who cannot tolerate intensive induction (Stone et al., 2017; Perl et al., 2019; DiNardo et al., 2020).

Nevertheless, treatment remains limited by systemic toxicity, pharmacokinetic variability, treatment resistance, relapse, and the persistence of disease within protective bone-marrow environments. These limitations have encouraged investigation of nanomedicine as a strategy for modifying drug delivery, cellular uptake, biodistribution, and controlled release. Nanomedicine encompasses engineered systems capable of transporting therapeutic compounds or biological molecules at the nanoscale. In AML, investigated platforms include liposomes, polymeric nanoparticles, micelles, dendrimers, inorganic nanoparticles, biomimetic systems, and cell-membrane-coated nanoparticles (Li et al., 2024; Wang et al., 2025).

A particularly important distinction between AML and solid tumors is that AML does not form a conventional solid tumor mass. Disease involves circulating malignant cells and specialized bone-marrow niches. Therefore, assumptions concerning passive tumor accumulation may not translate directly to leukemia. Current research increasingly

emphasizes active targeting of AML cells and bone-marrow microenvironments (Tang et al., 2026).

The patient dimension is equally important. Treatment decisions in AML are influenced not only by response and survival but also by age, comorbidities, functional status, treatment tolerance, hospitalization, quality of life, treatment preferences, and access to specialized care.

Accordingly, this review examines AML nanomedicine through four interconnected dimensions: therapeutic development, patient-centered outcomes, healthcare accessibility, and translational feasibility.

Literature Review

Contemporary AML Therapy and the Need for Improved Delivery

Modern AML treatment is increasingly molecularly informed. FLT3-mutated disease can be treated with FLT3-directed agents, while IDH1- and IDH2-mutated AML can be addressed using targeted inhibitors in appropriate clinical settings. Midostaurin improved outcomes when combined with chemotherapy for FLT3-mutated AML, while gilteritinib improved survival compared with salvage chemotherapy in relapsed or refractory FLT3-mutated disease (Stone et al., 2017; Perl et al., 2019).

For patients unable to tolerate intensive chemotherapy, azacitidine plus venetoclax represents an important treatment approach. The VIALE-A trial reported longer overall survival with azacitidine plus venetoclax compared with azacitidine alone, although clinically important cytopenias and infections remained common (DiNardo et al., 2020).

These developments illustrate an important principle: improved therapeutic efficacy does not necessarily eliminate treatment burden. Nanomedicine may therefore contribute by modifying how therapeutic compounds are delivered.

Nanomedicine Platforms in AML

Lipid-based systems are among the most clinically mature nanomedicine platforms.

CPX-351, a fixed-ratio liposomal formulation of cytarabine and daunorubicin, provides an important clinical example. In older patients with newly diagnosed secondary AML, CPX-

351 improved median overall survival compared with conventional 7+3 chemotherapy (Lancet et al., 2018).

Stage	Technology	Main purpose	Evidence context
1	Conventional systemic chemotherapy	Systemic cytotoxic treatment	Established clinical practice
2	Liposomal delivery	Alter drug exposure and delivery characteristics	Clinical
3	Polymeric/micellar nanocarriers	Controlled release and drug protection	Mainly experimental
4	Active ligand targeting	Recognition of specific cellular targets	Predominantly preclinical
5	Bone-marrow targeting	Target leukemic niches	Predominantly preclinical
6	Biomimetic/cell-membrane systems	Biological recognition and delivery	Preclinical
7	Nanomedicine-enabled immunomodulation	Modify immune/tumor microenvironment interactions	Emerging/preclinical

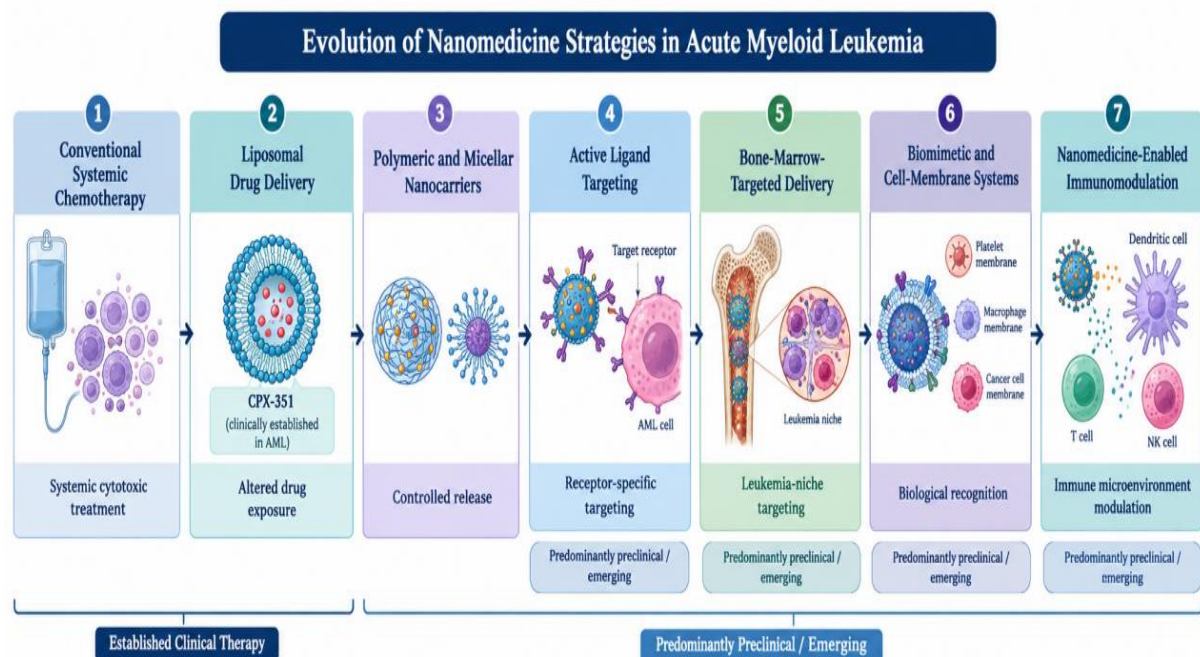


Figure 1. Evolution of nanomedicine strategies relevant to acute myeloid leukemia, progressing from conventional systemic treatment toward liposomal delivery, active cellular targeting, bone-marrow targeting, biomimetic systems, and nanomedicine-enabled immunomodulation.

Active Targeting and the Bone-Marrow Microenvironment

The next generation of AML nanomedicine increasingly emphasizes active targeting.

Antibodies, peptides, aptamers, nanobodies, and other ligands may be attached to nanoparticle surfaces to recognize receptors

expressed by leukemic cells or components of the bone-marrow environment.

Current literature broadly describes two approaches: targeting aberrantly expressed receptors on AML cells and targeting

components of the bone-marrow microenvironment (Tang et al., 2026).

This distinction is particularly relevant to leukemia stem cells, which may persist within protective bone-marrow niches and contribute to relapse.

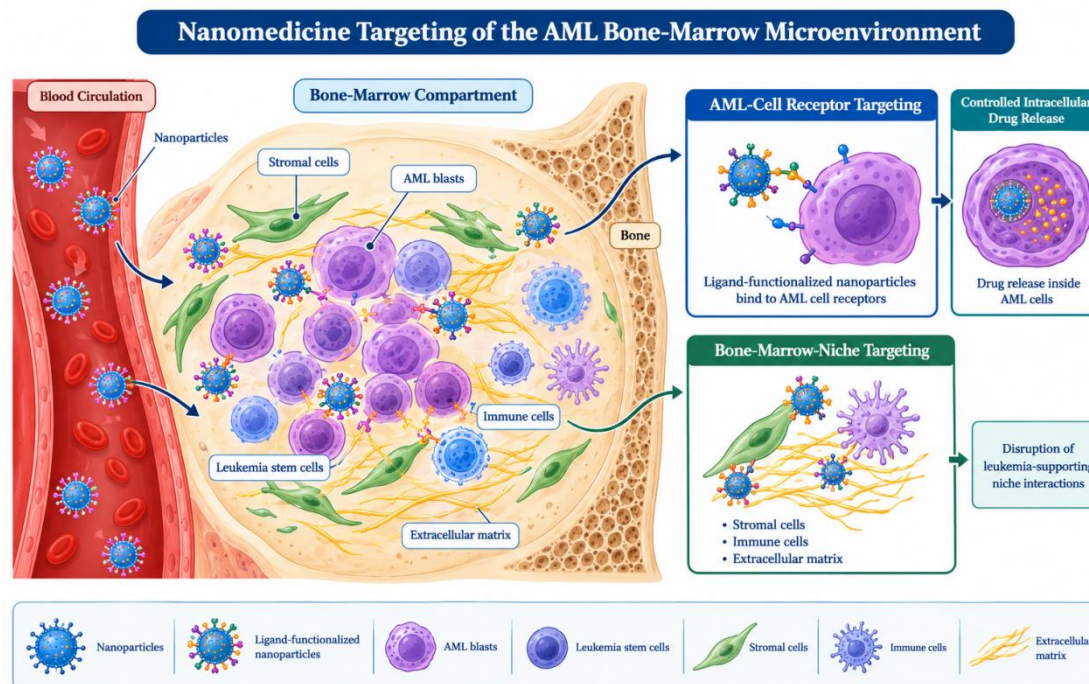


Figure 2. Conceptual representation of nanomedicine targeting strategies within the AML bone-marrow microenvironment. Nanoparticles may be engineered for recognition of AML-associated cellular targets or components of the leukemia-supporting niche.

Nanomedicine and Immunotherapy

Nanomaterials may also be used to modify the immune microenvironment. AML develops within a specialized bone-marrow niche in which immune suppression, abnormal cellular interactions, and metabolic changes can influence therapeutic response. Recent research has therefore explored nanomaterial-mediated immunomodulation and targeted delivery of immune-active agents.

Combination platforms could potentially deliver cytotoxic drugs, molecular inhibitors, nucleic acids, or immune modulators within coordinated systems. However, combination platforms also increase formulation complexity and introduce additional safety, manufacturing, and regulatory considerations.

Conceptual Framework

This review adopts a patient-centered translational nanomedicine framework. The framework conceptualizes clinical value through four interconnected domains:

- Therapeutic performance
- Patient-centered benefit
- Healthcare accessibility
- **Clinical translation**

The framework extends beyond conventional drug-delivery efficacy because a technically successful nanoparticle may have limited clinical value if it is excessively toxic, unaffordable, difficult to manufacture, inaccessible to patients, or impractical for routine clinical use.

Patient-Centered Translational Framework for Nanomedicine in Acute Myeloid Leukemia

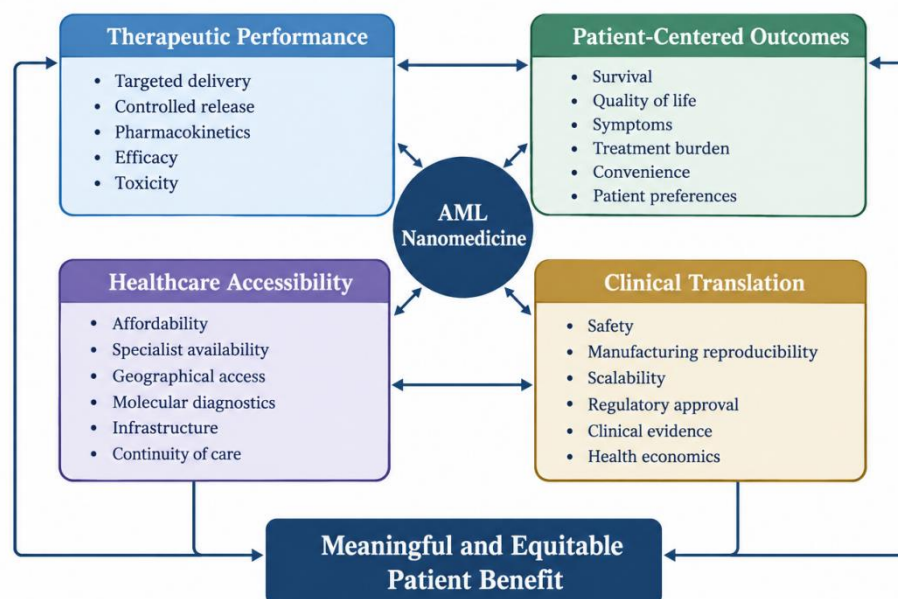


Figure 3. Patient-centered translational framework for evaluating AML nanomedicine across therapeutic performance, patient-centered outcomes, healthcare accessibility, and clinical translation.

Methodology

Study Design

This study was designed as a narrative literature review to critically examine the development, clinical relevance, patient-centered evaluation, and translational challenges of nanomedicine-based therapies for acute myeloid leukemia (AML). The review integrates evidence from clinical, translational, and patient-centered research to provide a comprehensive understanding of how AML nanomedicine can be evaluated beyond conventional measures of treatment efficacy and safety.

Literature Identification

The review was informed by peer-reviewed literature indexed through PubMed and publisher databases, together with authoritative regulatory information. Priority was given to AML-specific nanomedicine reviews, clinical trials involving nanomedicine-based AML treatment, studies addressing quality of life and patient preferences, and literature examining translational barriers.

Analytical Approach

Evidence was organized thematically into: AML therapeutic challenges; nanoparticle and nanocarrier technologies; active targeting and bone-marrow delivery; patient-centered outcomes; healthcare accessibility and equity; manufacturing and regulatory translation. Because the evidence is heterogeneous, no pooled meta-analysis was undertaken.

Results

Therapeutic Advances

The literature demonstrates substantial progress in AML treatment. Targeted therapies have provided clinically meaningful options for genetically defined subgroups, while lower-intensity approaches have expanded treatment options for patients who are unsuitable for intensive chemotherapy.

Nanomedicine contributes most clearly where drug formulation becomes a therapeutic variable. CPX-351 provides the strongest established clinical example. Its randomized clinical evidence demonstrates that a liposomal formulation can produce a clinically meaningful difference in AML treatment.

Table 1. Therapeutic and Nanomedicine Developments Relevant to AML

Strategy	Principal rationale	Evidence stage	Patient relevance
Conventional intensive chemotherapy	Rapid cytoreduction	Established	Potentially curative but associated with substantial toxicity
Azacitidine + venetoclax	BCL2-mediated sensitization	Clinical	Important lower-intensity treatment option
FLT3 inhibitors	Molecular targeting	Clinical	Relevant to FLT3-mutated AML
IDH1/IDH2 inhibitors	Mutation-directed differentiation therapy	Clinical	Relevant to molecularly selected AML
CPX-351	Liposomal co-delivery	Clinically established	Demonstrates AML nanomedicine feasibility
Ligand-functionalized nanoparticles	Active cellular targeting	Mainly preclinical	Potentially improved specificity
Bone-marrow-targeted nanoparticles	Leukemic niche delivery	Mainly preclinical	Potential strategy for resistant disease
Biomimetic nanoparticles	Biological recognition	Preclinical	Potential targeting advantages

Source: Synthesis of cited literature

Patient-Centered Outcomes

Patient-centered outcomes are particularly important in AML because many patients are older and may have substantial comorbidity or functional limitations. Research has demonstrated the importance of health-related quality of life during AML treatment (Alibhai et al., 2007; Buckstein et al., 2018).

Patient preferences are also relevant to treatment decisions. Studies in older adults with AML have examined treatment attributes, quality of life, decisional regret, and perceived treatment worthiness (LoCastro et al., 2023). For nanomedicine, potentially relevant endpoints include:

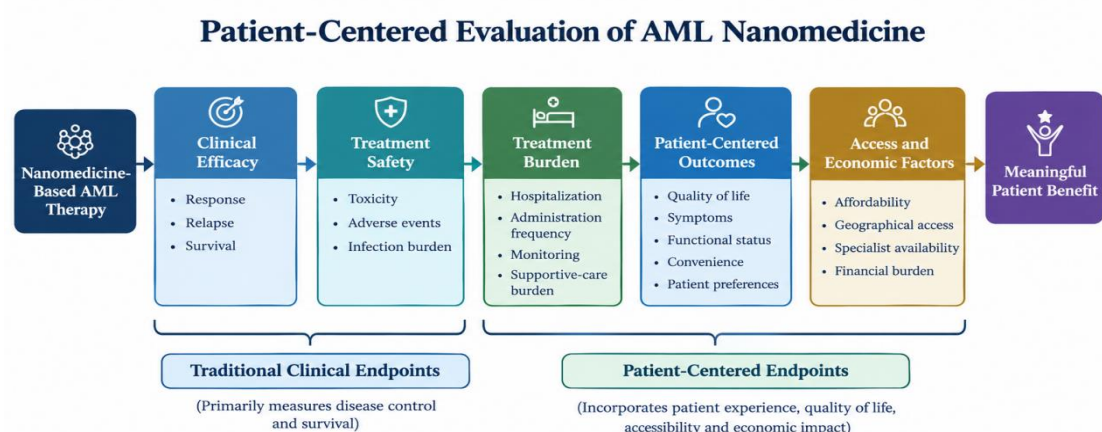


Figure 4. Patient-centered pathway for evaluating AML nanomedicine, integrating conventional clinical endpoints with treatment burden, quality of life, patient preferences, accessibility, and economic considerations.

Healthcare Accessibility

Access represents an important but comparatively underdeveloped dimension of advanced AML nanomedicine. Highly specialized cancer therapies may depend on molecular testing, tertiary hematology services, transfusion capacity, infection management, transplantation infrastructure, and prolonged monitoring.

Evidence has documented disparities in AML treatment and transplantation, demonstrating that the existence of a therapy does not necessarily guarantee equitable access.

This consideration is particularly important in low- and middle-income settings where diagnostic capacity, molecular testing, specialist availability, drug procurement, and supportive-care infrastructure may be limited.

Discussion

The reviewed evidence indicates that nanomedicine has a credible role in AML, but its clinical significance should be understood carefully. The strongest current evidence does not demonstrate that nanoparticles universally outperform conventional therapies. Instead, nanomedicine provides a platform through which established and emerging therapies can be reformulated to modify drug distribution, pharmacokinetics, toxicity, targeting, and combination delivery.

CPX-351 illustrates this principle. Its randomized clinical evidence and regulatory approval demonstrate that a liposomal formulation can produce clinically meaningful differences in AML treatment. However, this should not be interpreted as evidence that every nanoparticle system will provide similar benefits.

One of the most important scientific challenges is the biological uniqueness of AML. Nanoparticle research in solid tumors has frequently emphasized tumor accumulation and tissue penetration. AML instead involves circulating malignant cells and specialized bone-marrow niches. Consequently, receptor-mediated targeting and bone-marrow-directed delivery may be more relevant than passive accumulation alone.

The next-generation nanomedicine literature therefore suggests increasing emphasis on active

targeting, leukemia stem-cell biology, bone-marrow niches, and microenvironmental interactions.

The patient-centered dimension is particularly important. AML treatment is experienced as a sequence of diagnosis, hospitalization, induction, complications, consolidation, transplantation where appropriate, maintenance, monitoring, and management of relapse. A successful nanomedicine should therefore be evaluated according to whether it changes this experience in meaningful ways.

Reduced systemic toxicity, fewer hospitalizations, lower administration burden, improved symptom control, or greater convenience could all represent meaningful benefits even when differences in conventional efficacy endpoints are modest.

At the same time, nanomedicine should not automatically be assumed to reduce toxicity. Nanoparticles introduce their own biological interactions, including altered biodistribution, immune recognition, metabolism, elimination, and potential long-term effects. Safety characterization, reproducible manufacturing, scalability, and regulatory requirements therefore remain major translational issues.

Manufacturing is particularly important. Laboratory formulations may be produced under controlled experimental conditions that are difficult to reproduce at commercial scale. Variability in particle size, surface properties, drug loading, release kinetics, aggregation, and stability may influence clinical performance.

Cost represents another important translational dimension. A sophisticated nanoparticle may require expensive materials, specialized equipment, extensive characterization, and complex regulatory testing. If these requirements result in a therapy that is inaccessible to health systems or patients, the population-level benefit may be limited even if efficacy is demonstrated in controlled clinical trials.

8. Practical and Theoretical Implications Researchers

Future studies should report standardized physicochemical characteristics, pharmacokinetics, biodistribution, toxicity, and manufacturing parameters.

Clinicians

Clinical evaluation should consider molecular subtype, age, comorbidity, functional status, treatment goals, patient preferences, and quality of life alongside conventional efficacy endpoints.

Patients

Patient-reported outcomes should be incorporated into clinical trials, including treatment convenience, hospitalization, symptom burden, financial effects, and perceived treatment value.

Health Systems

Implementation studies should examine whether nanomedicines can be manufactured, stored, administered, monitored, and reimbursed within real-world healthcare environments.

Policymakers

Regulatory and health-technology assessment frameworks should consider both clinical effectiveness and equitable access.

Limitations

This article is a narrative review rather than a systematic review or meta-analysis. The evidence base contains substantial heterogeneity in nanoparticle composition, payload, targeting strategy, experimental model, and outcomes. Direct comparisons between platforms are therefore difficult.

Furthermore, much of the evidence concerning actively targeted AML nanomedicines remains preclinical. Patient-centered and health-economic outcomes are considerably less developed than pharmacological and laboratory endpoints.

Conclusion

Nanomedicine represents an important translational opportunity in AML because it can modify how therapeutic agents are delivered to malignant cells and their surrounding microenvironment. CPX-351 provides clinical evidence that liposomal drug delivery can become an established component of AML treatment, while actively targeted, bone-marrow-directed, biomimetic, and

immunomodulatory nanoplateforms represent emerging areas of research.

However, most sophisticated targeted AML nanomedicines remain in preclinical development. Their future clinical relevance will depend on overcoming biological heterogeneity, targeting limitations, biodistribution challenges, toxicity concerns, manufacturing complexity, regulatory requirements, cost, and healthcare-access barriers.

The next generation of research should therefore move beyond demonstrating nanoparticle uptake or laboratory cytotoxicity. Meaningful evaluation should incorporate survival, toxicity, quality of life, treatment burden, patient preferences, affordability, accessibility, and implementation feasibility.

The ultimate value of AML nanomedicine will depend not solely on technological sophistication but on whether technological advances can be converted into safe, clinically meaningful, affordable, and equitable benefits for patients.

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