


# Voices of Nanomedicine: Blueprint Guidelines for Collaboration in Addressing Global Unmet Medical Needs

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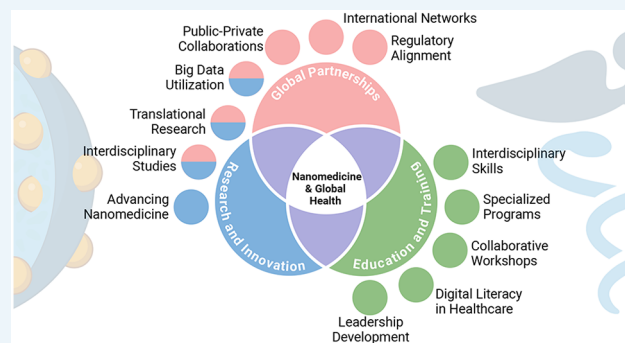
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**ABSTRACT:** The “Voices” under this Perspective underline the importance of interdisciplinary collaboration and partnerships across several disciplines, such as medical science and technology, medicine, bioengineering, and computational approaches, in bridging the gap between research, manufacturing, and clinical applications. Effective communication is key to bridging team gaps, enhancing trust, and resolving conflicts, thereby fostering teamwork and individual growth toward shared goals. Drawing from the success of the COVID-19 vaccine development, we advocate the application of similar collaborative models in other complex health areas such as nanomedicine and biomedical engineering. The role of digital technology and big data in healthcare innovation is highlighted along with the necessity for specialized education in collaborative practices. This approach is decisive in advancing healthcare solutions, leading to improved treatment and patient outcomes.

**KEYWORDS:** nanomedicine, healthcare, laboratory research



Bringing translational research into healthcare policies and practices is a major challenge.<sup>1</sup> To bridge the gap between laboratory research, industrial manufacturing, and clinical implementation, coordinated efforts must be made among multiple communities including bioengineers, medical doctors, computational scientists, regulatory bodies, and investors. Collaborations not only help to identify and understand complex factors affecting public health but are also needed to improve biopharma solutions, such as drug discovery, design, and manufacturing. The primary purpose of this Perspective is to highlight the opinions and knowledge of leading academic experts regarding the current multi- and interdisciplinary collaborative framework for solving healthcare concerns. While the modern perception of collaboration involves sharing ideas and knowledge to advance scientific and clinical progress, the practice of collaboration is continually evolving and can be further improved to

deconstruct critical medical issues. Multiple global projects, such as the development of the COVID-19 vaccine,<sup>2</sup> the Global Alliance for TB Drug Development,<sup>3</sup> and the Human Genome Project,<sup>4</sup> have shown that collaboration is key to solving healthcare problems. From this Perspective, we revisit how foundational nanomedicine and biomedical engineering research has stimulated the collaborative development and global deployment of COVID-19 mRNA vaccines<sup>5</sup> for an example. Reflecting on the successful principles of COVID-19

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**Figure 1. Spectrum of possibilities:** The diverse and interconnected fields of nanomedicine encompass an array of disciplines, each contributing unique insights and innovations to healthcare. With the development of advanced diagnostic tools for the engineering of tissues and biomaterials and the integration of nanotechnology for targeted therapies, nanomedicine is at the forefront of medical advancement. This spectrum spans fundamental research on the application of clinical solutions and driving progress in medical devices, prosthetics, and personalized medicine. The synergy between these fields underlines the collaborative nature of healthcare technology with the aim of improving patient care.

multidisciplinary collaborations, it is evident that these strategies can be effectively translated to address the challenges of nanomedicine,<sup>6</sup> (bio)medical implants,<sup>7</sup> organ transplantation,<sup>8</sup> and other public health concerns, as well as to build trust and combat disinformation.<sup>9</sup> The pandemic response showcased the power to integrate diverse expertise, as exemplified by the synergistic efforts of virologists, public health experts, and data scientists. This model of interdisciplinary cooperation can be mirrored in cancer research and organ transplantation. For instance, a blend of oncologists, radiologists, biomedical

engineers, biochemists/biochemical engineers, nanotechnologists, surgeons, and immunologists can generate innovative solutions and accelerate advancements in these fields by fostering open communication and collaboration. By applying these principles, we can enhance our approach to address complex health challenges, resulting in more effective therapies and better patient outcomes. The pandemic has highlighted the role of collaboration in bringing innovation to the market to solve real-life healthcare challenges. Several key factors have contributed to this remarkable achievement and marked a

significant shift in how we think about collaborative research among academia, industry, clinical medicine, and governments.

To expand the current discussion, it is necessary to explore the transformative role of digital technologies and big data in bridging the gap between translational research and healthcare practices. The integration of AI and machine learning algorithms into biomedical research can significantly help understand the huge amount of preclinical data generated in recent decades, thus accelerating the development of clinically successful platforms.<sup>10</sup> Furthermore, the emergence of global health informatics networks facilitates the continuous sharing of research data and enhances the efficiency of clinical trials. For example, during the COVID-19 public health crisis, there was a call for global AI and machine learning researchers to establish data-mining techniques to maintain COVID-19-related research and findings. Currently, several efforts have been made to design cost-effective and novel diagnostic protocols/routes using machine learning algorithms, including neural networks and deep learning-based approaches or procedures that were developed for the detection and monitoring of COVID-19 patients by validating computed tomographic scans/images. Overall, artificial intelligence and machine learning-based rapid and automated diagnostic approaches not only help in diagnostic accuracy but also protect healthcare workers/professionals from contact with COVID-19 patients. Ethically employing such data requires careful consideration of the ethical dimensions of data usage and patient privacy. The regulation of AI varies significantly across different regions, making it crucial to have a clear understanding of the regulatory frameworks in place.<sup>11</sup> Recently, European policymakers approved the Artificial Intelligence Act, which focuses on high-risk AI applications in healthcare and imposes penalties for noncompliance. In Latin America, Brazil's General Data Protection Law plays a key role in regulating AI, whereas China's New Generation Artificial Intelligence Development Plan outlines the country's approach to AI governance in Asia.

Another key aspect of the effective use of big data is the need for specialized education and training programs to equip future researchers and healthcare professionals with interdisciplinary collaboration skills.<sup>12</sup> The conduction of translational workshops and courses would establish a new junction/bridge for the multidisciplinary professionals to work together, such as setting integrated degree programs (e.g., MD-PhD, MS-PhD, M.Tech.-PhD) would initiate effective communication skill between academic and non-academic workers who are dealing with patients on day-to-day basis. In medical education, adaptability of the curriculum, incorporation of technology, professional growth of the faculty, comprehensive student support, and cross-disciplinary teamwork are becoming increasingly important. These elements are key to nurturing resilience and maintaining the quality of education during potential future crises.<sup>13</sup> However, it may go further into specific barriers to this kind of cooperation, such as cultural disparities, communication breakdowns, and conflicting resource priorities, which can impede advancement. There is also a road blocker in terms of regulatory concerns, but it should go into further detail about problems, including a regional lack of uniformity, sluggish approval procedures, and the challenge of keeping up with rapidly changing technologies. This focus on thorough procedures and ongoing cooperation will guarantee that the potential of AI and ML in healthcare is a long-lasting, revolutionary force rather than a passing fad.<sup>14</sup>

In addition to collaborative models and data use, government policies, including funding and regulatory frameworks, should be developed to foster an environment conducive to translational research. Recognizing the importance of international health diplomacy in strengthening global partnerships is necessary to address the widespread health challenges.

The future of global health must reflect the multidisciplinary nature and scope of nanomedicine in which the entire spectrum of possibilities (Figure 1) represents a distinct but interconnected specialty within the field. From nanomedicine to bioinformatics, tissue engineering, and biophysics, this symbolizes the unity and diversity of research areas that contribute to comprehensive healthcare solutions. This underscores the field's commitment to innovation through collaboration, which is essential for the full spectrum of advancements in medical technology and patient care.

### SYNERGY IN SCIENCE: REFORMING HEALTHCARE WITH PUBLIC-PRIVATE PARTNERSHIPS

Over the last 30 years, synergy between manufacturer-driven research has advanced nanocarrier research, with manufacturer collaboration evolving with the integration of innovative practices in nanotechnology and pharmaceutical development. The success of the rapid development of mRNA vaccines against COVID-19 should be expanded to incorporate a more sustainable approach toward equitable global health solutions, emphasizing the need for shared resources, technology transfer, and transparent public-private partnerships (PPPs) that prioritize global health needs over individual corporate interests. PPPs play a central role and are characterized by openness and resource sharing, which can enhance the availability of health services, particularly in isolated regions. Governments are encouraged to develop enduring strategies and policies for initiating PPPs in healthcare, with careful consideration of unique local demands and circumstances.<sup>15</sup> For example, Machine Learning Ledger Orchestration for Drug Discovery (MELLODDY) project consists of 10 pharmaceutical partners and 7 public partners, including European Federation of Pharmaceutical Industries and Associations (EFPIA) companies, universities, research organizations, public bodies, non-profit groups, small and medium-sized enterprises, and non-EFPIA companies.<sup>16</sup> The consortium was able to deliver an unprecedented cross-pharma data set of 2.6+ billion confidential experimental activity data points, documenting 21+ million physical small molecules and 40+ thousand assays in on-target and secondary pharmacodynamics and pharmacokinetics. The MELLODDY project delivered insights to advance drug development by carrying out the first successful federated learning run using this new predictive modelling platform. Nanomedicine (imaging, therapeutics, and theranostics) has evolved into a multifaceted discipline that encompasses immune therapies, precise drug delivery, and advanced diagnostics. The development of nanoparticles for drug delivery, the cornerstone of this evolution, is crucial for the rapid deployment of mRNA vaccines. These collaborations were marked by a shift in traditional practices, with technology transfers and relaxed licencing agreements catalyzing global vaccine production. This model of cooperation exemplifies how shared objectives and resource pooling can lead to rapid advancements in crisis situations, thereby establishing a new standard for future collaboration in nanomedicine.

Table 1. Global Highlights Multidisciplinary Research with Key Collaborative Projects Across Continents<sup>a</sup>

Project name	Year launched	Key contributors	Description	Outcomes
Human Genome Project <sup>41</sup>	2000	International consortium of researchers	An international scientific research project to map and understand all human genes	Complete mapping of human genome, foundation for much genetic research
Global Alliance for TB Drug Development <sup>42</sup>	2000	Public-private partnership	Partnership aiming to discover and develop new, faster-acting tuberculosis drugs	Development of new TB treatments and improved drug protocols
International HapMap Project <sup>43,44</sup>	2002	Multiple international research institutions	Develops a haplotype map of the human genome for genetics and disease studies	Provided valuable data on human genetic variation and disease
ENCODE Project <sup>45</sup>	2003	International consortium, led by NHGRI	Project to identify all functional elements in the human genome sequence	Identification of key genomic elements, advancing understanding of human genetics
1000 Genomes Project <sup>46</sup>	2008	International consortium of genomic researchers	A global research project to map genetic variation in the human genome	Detailed map of human genetic variation across multiple populations
International Cancer Genome Consortium <sup>47,48</sup>	2008	International consortium of cancer researchers	A global effort to map the genetic changes in 50 different types of cancer	Extensive genetic data on cancer, aiding in personalized medicine
The BRAIN Initiative <sup>49</sup>	2013	NIH, DARPA, NSF, private partners	Aims to enhance understanding of the brain and improve treatments for brain disorders	Advancements in neural imaging and understanding of neurological diseases
Cancer Moonshot Initiative <sup>50</sup>	2016	NIH, private companies, research institutions	Accelerates cancer research through collaboration among researchers, industries, and agencies	Enhanced cancer research, new treatments, and diagnostic technologies
All of Us Research Program <sup>51</sup>	2018	NIH, various research institutions	An ambitious NIH initiative to gather data from one million or more people living in the USA	Rich database for personalized medicine and understanding of diverse populations

<sup>a</sup>TB: Tuberculosis. NHGRI: National Human Genome Research Institute. NIH: National Institutes of Health. DARPA: Defense Advanced Research Projects Agency. NSF: National Science Foundation.

## ACADEMIC ALLIANCES: PIONEERING OPEN RESEARCH FOR GLOBAL HEALTH INNOVATION

As with companies, universities often fight hard for intellectual property to maximize returns and monetization. Although competition can create an environment for innovation, it can also hinder collaboration. In academic research, the COVID-19 pandemic has fostered a unique environment for collaboration, as well as competition. Many research institutions worldwide have adopted a cooperative approach that shares key data, such as genetic sequences and clinical insights. This shift has facilitated a deeper and quicker understanding of viruses. Collaborative platforms, such as *CEPI*<sup>17</sup> and the *WHO Organization's Solidarity Trial*,<sup>18</sup> exemplify global coordination, accelerating the vaccine development process. This period marked an unprecedented level of data exchange and communication, offering a blueprint to address future global health emergencies. This positive experience underlines the potential for multidisciplinary collaboration in biomedical research and demonstrates how shared research findings, data, and resources across institutions can lead to breakthroughs in public health. Moving forward, this model should be further developed to encourage a more integrated global research community that focuses on sharing knowledge and resources to tackle broad public health challenges with an emphasis on open-source data and cross-institutional research projects. Rapid data exchange and communication through international networks have been crucial in keeping researchers informed about the virus's mutations, epidemiological trends, and vaccine efficacy across different populations. An example of this success is the *Europe COST* (European Cooperation in Science and Technology) *Actions*. This framework facilitates collaboration and knowledge-sharing between scientists and researchers across Europe. Through *COST Actions*, experts in various fields were able to rapidly exchange data and insights, contributing significantly to the understanding and management of the virus on a continental scale. This collaborative effort not only enhanced the response to the pandemic but also set a precedent for

future international cooperation in addressing global health challenges.

## CLINICIANS UNITED: SETTING GLOBAL STANDARDS IN PATIENT CARE

Worldwide clinician response to the pandemic has been essential, marking a new era of global health collaboration. Multicentric trials across continents represent more than just a mechanism for assessing vaccine safety and efficacy; they represent a fundamental change in how clinicians approach global health crises. By incorporating diverse patient populations, these trials offer a comprehensive view of the impact of the virus, establishing a basis for tailored treatment strategies across demographics. Furthermore, the clinician community went beyond sharing of the treatment protocols. They created a dynamic knowledge exchange network, rapidly adapting to new information on virus management, and thereby significantly improving patient outcomes. This network has become a model for real-time global collaboration in healthcare.

This collaborative model offers a blueprint for a future health crisis response. Establishing structured global clinician networks that influence digital platforms for real-time data sharing and disease surveillance is imperative. Such networks can expedite global responses to emerging health threats and ensure timely and effective treatment. Additionally, integrating lessons from the pandemic into the education and training of health care professionals can further strengthen this collaborative approach. The challenges of the pandemic have underscored the need for a robust and globally coordinated health-surveillance system.<sup>19</sup> This system tracks disease patterns and treatment outcomes and incorporates predictive analytics to anticipate and mitigate future health crises. Integration of biomedical engineering and nanomedicine into this system can further enhance its ability to respond swiftly and effectively to global health emergencies. The level of international clinical cooperation during the pandemic has set a precedent for future medical crises, highlighting the need for ongoing collaboration and information-sharing among clini-

cians in the rapidly evolving fields of biomedical engineering and nanomedicine. Such cooperation should be expanded to include a more structured global network of clinicians sharing real-time data, treatment strategies, and patient outcomes to enhance global health responses. This network would facilitate a more rapid and coordinated response to future health crises, emphasizing the need for a global surveillance system that tracks disease patterns and treatment outcomes in real-time.

### COOPERATION BETWEEN MANUFACTURERS, GOVERNMENT AGENCIES, AND REGULATORS

The last 30 years have brought about several innovations in nanocarrier research for medical applications, such as immune checkpoint therapy, drug delivery,<sup>20,21</sup> disease diagnostics and imaging, and theranostics.<sup>20–22</sup> Although an initial goal of this nanocarrier research was to deliver potentially toxic anticancer drugs, the ability to design and manufacture nanoparticles laid the groundwork for the rapid delivery of mRNA vaccines to patients. Public and private corporations are already well versed in the design, optimization, and large-scale manufacture of lipid nanoparticles.<sup>23</sup> This prior foundation led to the establishment of transparent public-private partnerships that facilitate collaboration to expedite vaccine development. In fact, the advanced manufacturing observed here provided skill maps for many industries to training institutions, including polytechnics, universities, and commercial vendors. In addition to evaluating talent and developing training plans, it is crucial to inform individuals of accessible training opportunities. Efforts to help the community, whether public or private, often fail to reach their intended audience. It is important to involve the workforce, unions, and universities by highlighting the efforts of institutions and governments to develop materials and courses that prepare workers for the future. This will promote cooperation among manufacturers, government agencies, and regulators.

In the face of the COVID-19 pandemic, significant synergies have emerged among manufacturers, government agencies, and regulatory bodies. Understanding the urgency of regulatory agencies worldwide has streamlined their processes and led to fast-track approvals of COVID-19 vaccines. This nimbleness, virtually unseen in regulatory frameworks, was critical in granting emergency authorization and full approval at an unprecedented pace. However, this collaboration has not stopped at the national borders. International regulatory bodies broke down traditional barriers, shared information, and harmonized approval processes across countries. Initiatives such as the Access to COVID-19 Tools Accelerator (ACT-A)<sup>24</sup> and WHO's Emergency Use Listing (EUL)<sup>25</sup> embodied this new spirit of global regulatory cooperation. This era of cooperation has served as a testament to the seamless integration of academic research, clinical practice, and regulatory supervision. From laboratories where basic and applied research converges, pushing the boundaries of medical science to frontline healthcare workers, this period has exemplified the strength of diverse medical backgrounds uniting under a common goal.<sup>26</sup>

This success extends beyond the rapid development of the COVID-19 vaccines. In the field of personalized medicine, we have witnessed the fusion of genomics and data analytics to redefine treatment methodologies.<sup>27</sup> Similarly, the field of bioengineered tissues and organs demonstrates interdisciplinary collaboration, merging cell biology, materials science, and surgical expertise.<sup>28–30</sup> In nanomedicine,<sup>31–38</sup> collaborations

among institutions such as the *National Cancer Institute's Center of Cancer Nanotechnology Excellence (CCNEs)*, the *Alliance for Nanotechnology in Cancer*,<sup>39</sup> and the *Nanotechnology Characterisation Laboratory (NCL)*<sup>40</sup> have been instrumental. These partnerships have supported the development of groundbreaking cancer nanotherapies such as liposomal doxorubicin, albumin-bound paclitaxel, and gold nanoparticles, highlighting the critical role of collaboration in achieving healthcare breakthroughs. This enhanced cooperation among various sectors is not merely a response to a crisis; it is also a blueprint for future advancements in healthcare, emphasizing the necessity of collaborative efforts for significant medical breakthroughs. The examples listed in Table 1 further illustrate the extensive global collaboration that has been pivotal to these advancements.

### UNITING FOR INNOVATION: EXPLORING THE DIVERSITY AND VISION OF NANOMEDICINE AND NANOTECHNOLOGY

Collaboration not only helps us solve immediate public health concerns, as demonstrated by the COVID-19 response, but also enables us to identify key questions and limitations in other areas of research. For instance, advances in nanotechnology and our understanding of tumor biology have driven the development of nanoparticles to improve diagnostics and therapeutic efficacy and to minimize the off-target toxicity of conventional anti-cancer drugs. However, critical gaps remain in the detection, modeling, and treatment of cancer. In the field of cancer nanomedicine, the modest clinical success rate of nanomedicines targeting tumors underscores the importance of critically evaluating the actual clinical benefits of engineering innovations.<sup>52</sup> Tremendous funding over decades of research has led to numerous discoveries in biomaterials science; however, increasing drug accumulation in solid tumors to improve anticancer efficacy remains poorly understood. The complexity and heterogeneity of cancer make it difficult to create a one-size-fits-all solution. Personalized cancer vaccines represent a promising approach in this regard. This strategy exemplifies the multidimensional approach already mentioned, integrating advanced biomaterial science (for vaccine delivery), an understanding of tumor microenvironments (to identify unique tumor antigens), and patient-specific factors (personalized immune response). Moreover, the complexity of tumor biology and heterogeneity of cancer types call for more personalized, targeted nanomedicine strategies<sup>21</sup> that are already being produced using mRNA technology.<sup>5</sup> For instance, *Moderna* and *Merck's* melanoma mRNA vaccine (V940/mRNA-4157 - NCT03897881), designed for adjuvant treatment of patients with resected high-risk melanoma, and *BioNTech's* pancreatic cancer mRNA vaccine (autogene cevumeran, an individualized neoantigen vaccine based on uridine mRNA-lipoplex nanoparticles),<sup>53</sup> which encodes up to 20 neoantigens tailored for different pancreatic ductal adrenal cancer patients. This type of therapeutic development requires a multidimensional approach that integrates advancements in biomaterials science, tumor microenvironments, and patient-specific factors. The role of academia, industry, healthcare, and government in this collaborative framework is crucial for overcoming current limitations and steering the future course of cancer nanomedicine research toward more effective and individualized therapies. This clearly suggests the need for new guidelines governing nano-delivery drug design and reporting as well as

the need for new cancer models.<sup>54</sup> In a multidisciplinary collaboration framework, close coordination between academia, industry, healthcare, and government agencies is vital for identifying shortcomings in current cancer nanomedicine solutions as well as conceptualizing future designs. Addressing these challenges will not only improve therapeutic outcomes but also lay the groundwork for innovation in other areas of nanomedicine, reinforcing the importance of sustained and diverse collaborative efforts.

## NANOMEDICINE: WHERE ARE WE COMING FROM AND WHERE ARE WE GOING?

In nanomedicine, there has been a growing focus on refining nanoparticle drug delivery<sup>21</sup> systems. The current strategy

crucial for obtaining high-quality fresh tumor samples that preserve patient-derived cell features for inclusion in *in vitro* models to better understand tumor heterogeneity. In addition, new imaging technologies developed by biophysicists may provide better feedback regarding *in vivo* targeting and biodistribution.<sup>58–60</sup>

Moreover, the use of nanomedicine (imaging, therapeutics, theranostics, etc.) for cancer<sup>61,62</sup> treatment has expanded significantly. Nanocarriers are used in conjunction with immune checkpoint inhibitors and adoptive cell-transfer therapies. They also play a role in stabilizing mRNA vaccines, thereby offering new possibilities for combination therapy. This evolving landscape underscores the importance of collaboration between cancer immunologists, scientists, and bioengineers to optimize treatment combinations, scheduling, and dosages, adapting to the complexities of cancer treatment in the era of personalized medicine.

The field of nanomedicine encompasses an array of applications, from diagnostics to targeted drug delivery, leveraging the unique properties of nanoparticles. The small size and large surface-area-to-volume ratio of nanoparticles enable precise interactions at the molecular level, making them ideal for targeting specific tissues or cells, such as cancerous tumors. Advances in nanotechnology have led to the development of various types of nanoparticles, each with distinct characteristics and applications (Table 2). In clinical trials, nanomedicines have demonstrated significant potential, particularly in cancer treatment. The high success rates of the Phase I trials highlight their safety and efficacy. However, the decreased success rates in Phase II and III trials indicate that significant challenges remain in translating lab-based successes to effective clinical treatments. To better understand why laboratory success frequently does not translate into effective treatments, a more thorough examination of the lower success rates in Phase II and III clinical trials, which are frequently attributed to the limitations of preclinical models, patient heterogeneity, and inadequate biomarkers, is also necessary.

Applications of nanoparticles in health include a relatively wide range of interdisciplinary fields including biology, chemistry, physics, engineering/technology, and medical science. However, nanomedicines are not only related to the diagnosis and treatment of diseases but also related to safety and efficacy in biological systems. Nanomedicines can be classified into three main categories: inorganic, organic, and biological. Biological particles are derived from tissues and cellular components and are known as biomimetics.<sup>63</sup> Significant progress in nanomedicine engineering and characterization has been achieved since the *Food and Drug Administration* (FDA) approved *Doxil* (1995) for cancer treatment, which allows for longer drug retention and targeted release in tumors using a temperature-sensitive phosphatidylcholine and cholesterol bilayer for stable doxorubicin delivery.<sup>64</sup> Globally, 15 nanomedicines have been approved for cancer treatment, 75 of the 190 cancer nanomedicines are in clinical trials.<sup>65</sup> In phase I, 48 trials were completed in 91 trials, 59 were completed from 78 phase II trials, and 11 were completed in phase III trials. It is interesting to note that phase-I showed an ~94 % success rate with 45 positive results and only one negative result in terms of safety and efficacy, and 2 terminated because of adverse effects. However, the success rate of clinical trials has decreased to ~48 % in phase II and ~14 % in phase III, and nanomedicines face various immunological and translational barriers. These challenges

**Table 2. Clinical Status of Cancer Nanomedicine Solutions<sup>a</sup>**

Nanomedicine formulation	Status	Application
Liposomal Paclitaxel	NCT0300210/ ongoing	Breast Cancer
Liposomal VCL-1005 plasmid	NCT0039507/ completed	Melanoma
Hafnium-oxide nanoparticle	NCT0237984/ ongoing	Sarcoma
Irinotecan PEG conjugate	NCT0291574/ ongoing	Breast Cancer
Paclitaxel micellar	NCT0164489/ completed	Breast Cancer
Cisplatin micellar	NCT02043288/ unknown	Pancreatic Cancer
Thermally sensitive liposomal doxorubicin	NCT00617981/ completed	Hepatocellular Carcinoma
Lipid nanoparticle-MYC siRNA	NCT02191878/ complete	Hepatocellular Carcinoma
Superparamagnetic iron oxidenanoparticles	NA/complete	Glioblastoma
Docetaxel micellar	NCT03742713/ ongoing	Ovarian Cancer
Cisplatin micellar	NCT0091074/ completed	Pancreatic Cancer
Paclitaxel polyglumex conjugate	NCT00522795/ completed	Esophageal Cancer
Doxil/Caelyx ( <i>Johnson &amp; Johnson</i> )	Approved	Kaposi's sarcoma
Glutathione PEGylated liposomal doxorubicin	NCT01386580/ complete	Solid Tumors and Brain cancer
Liposomal irinotecan and floxuridine	NCT0036184/ completed	Colorectal Cancer

<sup>a</sup>ClinicalTrials.gov.

primarily utilizes enhanced permeability and retention (EPR), which is still under debate<sup>55</sup> concerning efficiency in humans, and aims to prolong systemic circulation to improve tumor targeting while minimizing off-target effects.<sup>56</sup> However, there is a need for more personalized approaches that consider variability in cancer types, tumor locations, tumor progression, and patient-specific factors. Collaboration between clinicians and researchers is crucial to advancing this field of research. Physicians' insights into cancer pathology are invaluable for tailoring nanoparticle designs to individual patient needs. Additionally, the effectiveness of nanoparticles observed in preclinical models, such as xenograft cancer mouse models, often does not translate directly into human tumors. This gap highlights the need for better *in vitro* models and more accurate organotypic cancer models or organoid implantation in *in vivo* models, necessitating further interdisciplinary partnerships.<sup>57</sup> Here, close multidisciplinary collaboration is

include immunogenicity, in which the body's immune system reacts unpredictably to nanoparticles, and issues related to targeted delivery and off-target effects. Further research in nanomedicine should focus on enhancing the biocompatibility of nanoparticles, improving targeting accuracy to reduce off-target effects and developing more representative preclinical models that better mimic human pathophysiology. Additionally, there is a need for more robust manufacturing processes to ensure the scalability and reproducibility of nanomedicines. As the field progresses, it is crucial to maintain a balance between innovation and patient safety, continually reassessing the risk-benefit ratio as new data emerge from clinical trials.

### BLUEPRINT FOR GLOBAL PARTNERSHIP: ENHANCING TRANSPARENCY IN COLLABORATIVE RESEARCH

A comprehensive, structured approach is essential for enhancing the transparency in global collaboration between nanomedicine and health. Effective collaboration begins with understanding the problem and creating a shared vision and motivation among multidisciplinary teams. Clear and consistent communication is the key to aligning and tracking the progress of a project. It is crucial to negotiate team overlaps, valuing each member's input while avoiding redundancy and ensuring the clarity of roles. Beyond physical workspaces, creating a conducive team environment involves fostering open ideation, brainstorming, and providing constructive feedback. As observed in successful global health initiatives, this integrated approach is critical for addressing complex health challenges. It requires balancing diverse educational, training, and cultural backgrounds, aligning everyone toward common goals, and minimizing micromanagement by empowering individual ownership and responsibility. Such collaborative environments are vital for driving ambitious projects, innovations, and solutions in healthcare research.

Building successful research collaborations relies on several key factors that can enhance international and multidisciplinary collaborations in nanomedicine and global health. These tools include establishing clear communication channels, defining roles and responsibilities, fostering trust among team members, and embracing ethnographic and disciplinary diversity. Emphasizing the importance of setting common goals and shared visions and creating an environment that encourages open ideation and constructive feedback is important. Integrating these insights can further refine the approach for fostering effective and transparent collaborations in complex health research projects.

As a model for enhancing global collaboration in nanomedicine and health, we can consider collaborative efforts in developing the CRISPR-Cas9 gene-editing technology. This breakthrough shows how multidisciplinary teams from different countries and specialties, including molecular biologists, geneticists, and bioengineers, have worked together to share insights and methodologies. Such collaboration illustrates the importance of fostering an environment in which diverse expertise and cultural backgrounds converge for innovation. Another example is the international response to the Zika virus outbreak,<sup>66</sup> in which global health teams and biomedical engineers collaborated to develop rapid diagnostic tools and to explore vaccine options. This response demonstrates the power of combining epidemiological knowledge with nanomedicine to address urgent public health needs.

Experts from science, engineering, medicine, and industry are required to develop safer nanotherapeutics and improve

**Table 3. Showcase of Indo-Global Collaborative Ventures in Healthcare Initiatives**

Collaboration	Key contributors	Description	Outcomes
Indo-US Vaccine Action Program (VAP) <sup>72</sup>	Govt. of India and US Govt.	A bilateral initiative to develop vaccines for preventable diseases, including COVID-19	Development of new vaccines and strengthening vaccine research
DBT-Wellcome Trust India Alliance <sup>73</sup>	DBT, India and Wellcome Trust, UK	A partnership to promote biomedical research and develop healthcare solutions in India	Funding and support for numerous healthcare research projects in India
IIT Bombay-Monash Research Academy <sup>74</sup>	IIT Bombay, India and Monash University, Australia	Collaboration for research in science, technology, and engineering between IIT Bombay and Monash University, Australia	Innovations in science and technology through collaborative research
Indo-German Science & Technology Centre (IGSTC) <sup>75</sup>	Govt. of India and Govt. of Germany	A joint initiative to enhance research and development in science and technology between India and Germany	Enhanced bilateral scientific cooperation and development of new technologies
DBT-BIRAC-BMGF-Wellcome Trust Grand Challenges India <sup>76</sup>	DBT, BIRAC, BMGF, and Wellcome Trust	A program supporting health research and innovation, with a focus on affordable healthcare solutions	Innovative health solutions addressing critical healthcare challenges in India
IISc Bangalore and University of Glasgow Partnership <sup>77</sup>	IISc Bangalore, India and University of Glasgow, UK	A partnership focusing on research in precision medicine, biomedical and health sciences	Joint research projects in advanced medical and health sciences
IIT Kharagpur and University of Manchester Collaboration <sup>78</sup>	IIT Kharagpur, India and University of Manchester, UK	Joint research in healthcare technologies and biomedical engineering	Breakthroughs in biomedical engineering and healthcare technologies
National Institute of Immunology and Harvard Medical School <sup>79,80</sup>	National Institute of Immunology, India and Harvard Medical School, USA	Collaboration in immunology research, particularly in areas like vaccine development and infectious diseases	Significant contributions to immunology and vaccine research
Jawaharlal Nehru Centre for Advanced Scientific Research and Japan's National Institute for Materials Science and TWAS <sup>81</sup>	JNCASR, India and NIMS, Japan	A partnership for research in material sciences with applications in biomedicine and healthcare	Advances in material sciences with biomedical applications

Table 4. Roadmap for New Leaders and Clinicians Based on the Complexities of Collaborative Nanomedicine Projects

Guideline	Strategy	Successful example/Case study
Leadership in collaborative projects	Foster an inclusive culture, promote clear communication, and encourage innovation	The leadership approach in the Human Genome Project facilitated collaboration across numerous international research groups, leading to its successful completion ahead of schedule.
Multidisciplinary team building	Engage diverse expertise from academia, industry, and healthcare to address complex problems	The development of CRISPR-Cas9 gene editing technology involved collaboration between biochemists, geneticists, and clinicians, revolutionizing genetic engineering and therapy.
Identifying unmet medical needs	Utilize patient input, clinical insights, and data analytics to guide research priorities	The use of real-world evidence (RWE) to identify gaps in cancer treatment led to the accelerated development and approval of new oncology drugs.
Translational pathways for therapeutics	Streamline the process from research to clinical application through regulatory guidance and strategic partnerships	Collaboration between academic researchers and pharmaceutical companies in the development of mRNA vaccines for COVID-19 showcased a rapid translational pathway from bench to bedside.
Enhancing interdisciplinary communication	Implement regular cross-disciplinary meetings and shared digital platforms	The creation of a centralized digital platform for the International Space Station's research teams facilitated seamless communication and data exchange across various scientific disciplines.
Promoting diversity and inclusion in team composition	Develop inclusive recruitment and retention practices targeting underrepresented groups	The diversity in Clinical Trials Initiative significantly increased participation of minority groups in clinical research, improving the applicability of health outcomes.
Leveraging data analytics for decision making	Use big data and machine learning to inform project directions and patient care improvements	Google Health's application of AI in mammogram analysis improved breast cancer screening accuracy, demonstrating the power of machine learning in enhancing diagnostic processes.
Enhancing interdisciplinary collaboration	Foster cross-disciplinary teams with shared goals and regular communication	Global Alliance for TB Drug Development: A partnership that influences diverse expertise to accelerate the development of tuberculosis treatments
Leveraging digital technology and big data	Utilize digital platforms and data analytics to drive innovation and decision-making	Human genome project: Demonstrated the power of big data in mapping the human genome, facilitating breakthroughs in genetic diseases
Specialized education for collaborative practice	Integrate collaborative skills and interdisciplinary approaches into educational programs	Bioengineering educational initiatives: Programs that combine engineering, biology, and clinical practice to prepare students for collaborative research and development
Fostering public-private partnerships	Encourage collaboration between government, academia, and industry to accelerate innovation	COVID-19 vaccine development: A prime example where public-private partnerships expedited the development and distribution of vaccines
Incorporating patient-centered design	Engage with patients and clinicians to ensure the relevance and applicability of healthcare innovations	Freestyle Libre glucose monitoring system: Improved diabetes management by incorporating user feedback into product design, enhancing user compliance and satisfaction
Streamlining regulatory pathways	Engage early with regulatory bodies to navigate the approval process efficiently	Expedited approval of Pfizer-BioNTech COVID-19 vaccine: Utilized emergency use authorization pathways for rapid approval and distribution
Incorporating end-user feedback in design	Engage patients and healthcare providers early in the design process through surveys and focus groups	The development of the Freestyle Libre glucose monitoring system, which significantly improved user compliance and satisfaction by integrating user feedback into product design
Streamlining regulatory approval processes	Early and continuous engagement with regulatory bodies to ensure compliance and expedite approval	The expedited approval of the Pfizer-BioNTech COVID-19 vaccine by engaging with regulators early in the development process to navigate the Emergency Use Authorization pathway
Fostering entrepreneurship and commercialization	Encourage translational research and support startup creation through incubators and accelerators	The success of Moderna in rapidly developing and distributing its mRNA vaccine was supported by a strong foundation in biotech entrepreneurship and public-private partnerships

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their manufacturing scale. Concerted efforts from a diverse group of experts are essential to reducing failure rates in clinical trials. These partnerships can provide academic researchers with access to manufacturing expertise, which can further inform nanomedicine design. These partnerships can be important in fostering collaboration with the industry for cost-effective healthcare solutions, as seen in initiatives at institutes such as the Indian Institute of Technology, India, Boston University, NOVA Medical School, Weizmann Institute of Science, Northwestern University, RWTH Aachen University, University of California, Tel Aviv University, Stanford University, University of Padua, University at Buffalo, Massachusetts Institute of Technology, and many others. International partnerships, such as the *Indo-US Vaccine Action Program*, for the development of vaccines other than COVID-19, such as HIV<sup>67</sup> or TB,<sup>68</sup> exemplify successful collaborations, resulting in significant achievements, such as the ROTAVAC vaccine.<sup>69–71</sup> The COVID-19 pandemic has highlighted the importance of international initiatives for rapid and effective vaccine development. These examples (Table 3) underscore the need for structured and transparent collaborations to advance the field of nanomedicine and address global health challenges.

## EMPOWERING NEW VOICES

To summarize, collaboration enables solving global problems in society with the goal of positively impacting people's lives. Significantly, creating an efficient collaborative environment does not happen overnight; it requires extensive effort and time to create a culture. Effective communication is required to bridge gaps between different teams, build trust and confidence between or within teams, and overcome challenges such as personal differences, time management, and conflicts to build an efficient and strong team that can help every team member grow and achieve their goals. The future of healthcare research is linked to the evolution of collaborative approaches at multiple levels. A next frontier in healthcare research will likely focus on integrating emerging technologies such as artificial intelligence, big data analytics, and advanced computing with traditional medical science. Multidisciplinary collaboration can potentially unlock a new understanding of disease mechanisms, diagnostics, and treatments, further reforming healthcare delivery.<sup>82</sup> Continuous investment in fostering collaborative environments, both within and across institutions, is imperative for realizing this future. Ultimately, the concerted efforts of diverse experts are important for shaping a healthier and more resilient global society. Furthermore, we should generate standards in research and reporting that are essential for advancing science and improving human health. This multidisciplinary and multidimensional approach promises cutting-edge advancements in the understanding, diagnosis, and treatment of various diseases. Continuous investment in fostering collaborative environments and supportive leaders and establishing robust research standards is the key to advancing science and improving global health outcomes. Empowering new leaders in global health and nanomedicine requires a multifaceted approach that integrates leadership development, technical expertise and collaborative innovation (Table 4). Discussing the practical steps for new leaders to initiate, manage, and lead successful collaborative projects, with an emphasis on communication, goal setting, and team dynamics, is of the utmost importance for empowering the upcoming Voices of Nanomedicine.

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### Notes

The authors declare the following competing financial interest(s): J.C. is a co-founder and shareholder of TargTex S.A. - Targeted therapeutics for Glioblastoma Multiforme. J.C. is also a member of the Global Burden Disease (GBD) consortium of the Institute for Health Metrics and Evaluation (IHME), University of Washington (US). R.P. holds various patents for nanoparticles and nanotheranostics for cancer imaging and therapy. R.S. is a part of various patents related to point-of-care diagnostics, biosensors, biomaterials, and Co-Founder for AudoSens Pvt Ltd, Clinocosis Pvt Ltd, Effecmed Pvt Ltd, Reproductive LifeSeed Pvt Ltd, Med Inno Tec Pvt Ltd. R.L. is a founder of Moderna. For a complete list of entities with which R.L. is, or has been recently involved, compensated or uncompensated, see: <https://www.dropbox.com/s/yc3xqb5s8s94v7x/Rev%20Langer%20COL.pdf?dl=0>.

W.C. declares conflict of interest with the following corporations: Actithera, Inc., Portrai, Inc., rTR Technovation Corporation, Four Health Global Pharmaceuticals Inc., and POP Biotechnologies, Inc. D.P. receives licencing fees (to patents on which he was an inventor) from, invested in, consults (or on scientific advisory boards or boards of directors), or Founder of, or conducts sponsored research at TAU for the following entities: ART Biosciences, BioNtech SE, Earli Inc., Kernal Biologics, Kerna Ventures, Geneditor Biologics Inc., Newphase Ltd., NeoVac Ltd., RiboX Therapeutics, Roche, SirTLabs Corporation, Teva Pharmaceuticals Inc. A.S.T. is a co-founder and holds stock options for Teal Health and is on the Scientific Advisory Board, received grants, or is a consultant for RespondHealth Inc, Cellular Vehicles Inc, Nephrogen Inc, ReThink64 Inc, AlloTRx Inc, Inari Inc and Genentech Inc. All other authors declare no conflicts of interest.

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### DEDICATION

We dedicate this review to the memory of the late Professor Sanjiv Sam Gambhir, a molecular imaging scientist.

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