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Reimagining precision medicine for rare diseases—a clinical perspective on the promise of NANOSPRESSO

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An Editorial on the Frontiers in Science Lead Article

NANOSPRESSO: toward personalized, locally produced nucleic acid nanomedicines

Key points

- Patients with rare diseases often fall outside the economic logic of the pharmaceutical industry, remaining "therapeutic orphans" despite existing incentive structures and expedited regulatory pathways.
- The NANOSPRESSO project fundamentally challenges the dominant paradigms of pharmaceutical development and healthcare delivery by offering a disruptive reimagining of how we might produce and deliver nucleic acid therapeutics for patients with rare and ultra-rare diseases.
- Both revolutionary and necessary, such initiatives could ignite the long-overdue transformation of precision medicine into a truly equitable, patient-centered practice delivered by collaborative ecosystems and driving innovation in regulatory, ethical, and reimbursement frameworks.

The completion of the Human Genome Project ushered in the era of precision medicine and targeted therapies (1). Enabled by breakthroughs in sequencing technology and rapid gains in computational power, deciphering the genome and transcriptome of cells and tissues soon became a reality and provided a foundational framework for a new era of precision medicine. Nucleic acids have emerged as a versatile and highly customizable therapeutic platform. Unlike proteins, all nucleic acids share a conserved chemical backbone, with functional specificity dictated by the nucleotide sequence. This enables modular, scalable manufacturing and rapid redesign for new targets, making them particularly attractive for personalized interventions (2, 3).

In the rapidly evolving landscape of biomedical innovation, it is rare to encounter a concept that fundamentally challenges the dominant paradigms in pharmaceutical development and healthcare delivery. Estapé Senti et al. offer precisely such a concept with their NANOSPRESSO project (4)—a disruptive reimagining of how we might produce and deliver nucleic acid therapeutics, particularly for the most underserved patient populations with rare and ultra-rare diseases (5). The interdisciplinary team of authors does not merely present a technical innovation—rather, they set out to overhaul and re-sculpt the ecosystem of care. At the heart of this initiative lies the stark realization that the current industrial model for drug development is neither scalable nor sustainable for patients with rare diseases. While we celebrate the scientific triumphs of modern pharmacology, we must also confront the ethical void it leaves behind when entire patient populations remain invisible to the system (6).

Pediatric and adult patients with rare diseases often fall outside the economic logic of the pharmaceutical industry. Although incentive structures have been devised that may grant therapies targeting rare diseases market exclusivity and expedited regulatory pathways, patients with rare diseases remain "therapeutic orphans". Developing a new therapeutic—particularly a gene- or nucleic acid-based drug—requires not only enormous financial investment but also navigation of an increasingly rigid regulatory environment. As a consequence, the cost of emerging drugs is often prohibitive for both patients and healthcare systems (7).

In this context, innovative, decentralized point-of-care models are both revolutionary and necessary. By marrying microfluidic precision with proven lipid nanoparticle (LNP) delivery platforms, the NANOSPRESSO initiative proposes a return to the concept of magistral preparation: a modern revival of the pharmacist's art of personalized compounding. Their technological core, building on decades of nanomedicine development, including the LNP underlying messenger (m)RNA COVID-19 vaccines, appears robust and clinically sound. The innovation here is not the novelty of the LNPs themselves, but rather their operational flexibility: small-batch, on-demand synthesis at or near the bedside. This shift is potentially transformative. It means that once a molecular target is identified, a therapy can be generated swiftly, tailored to the patient's genetic makeup, and produced without the logistical complexities or regulatory inertia associated with industrial manufacturing.

From an ethical perspective, such disruptive initiatives to design novel delivery tools for nucleic acid-based therapies give tangible form to the four foundational principles of medical ethics—beneficence, non-maleficence, autonomy, and justice—through their design, implementation, and intended use (8). Beneficence, or the obligation to promote patient well-being, is realized through a patient-centric approach to therapy development. By enabling the creation of bespoke nucleic acid therapeutics at the point of care, the project empowers clinicians to act swiftly on actionable genetic insights of pathomechanisms. For a child diagnosed with a rare metabolic disorder, this could mean receiving a potentially life-saving treatment weeks or months earlier than if development followed traditional industrial timelines. Non-maleficence, or "*primum nil nocere*", is addressed through the system's intrinsic safeguards. Point-of-care systems for drug delivery operate as a closed, automated, cartridge-based system, minimizing contamination risk and human error. By relying on well-characterized lipid nanoparticle components—many of which are already validated in approved mRNA vaccines—the platform benefits from a demonstrated safety profile (9). Moreover, quality control methods such as real-time particle analysis and batch validation are built into the production process. Autonomy, i.e., respecting the patient's right to make informed choices, is supported by the tailored nature of these therapies. Since treatments can be rapidly customized to match an individual's needs and genetic profile, patients and their guardians are more directly involved in the decision-making process. This reintroduces a level of personalization that is easily endangered in industrial medicine, where treatment options are limited by regulatory and commercial constraints rather than individual needs. Justice, or the principle calling for fair access and distribution, is perhaps the most powerful driver behind decentralized motors of therapeutic innovation. This bioethical principle finds expression in the project's efforts to dismantle structural inequities in access to cutting-edge care. By lowering the costs and logistical barriers to production, the platform enables hospitals around the world to produce their own nucleic acid therapies. For patients with rare metabolic diseases—e.g., Crigler-Najjar syndrome or methylmalonic acidemia, which serve as paradigms for Estapé Senti et al. (4)—for which effective molecular blueprints exist, but market-driven incentives are absent, such an approach could be key to closing the gap between knowledge and the cure of patients.

This framework of ethical vigilance is not theoretical. Estapé Senti et al. proactively engage with regulatory bodies and offer a roadmap for integrating local production within existing legal structures, such as the European Union's magistral exemption and hospital exemption pathways (4). This engagement ensures that the innovation is not merely aspirational, but implementable and actionable.

The NANOSPRESSO project challenges us to think beyond product pipelines and imagine ecosystems instead: networks of clinicians, pharmacists, engineers, and regulators co-producing care and ultimately striving for definitive cures. In this ecosystem, knowledge is not sequestered in silos but rather flows freely between research and bedside care, and between design and delivery. This reorients the entire value chain—from molecule to medicine—toward the patient. It is a profound decentralization of power, shifting it away from the monopoly of pharmaceutical giants and into the collaborative hands of hospitals and academic centers. In doing so, it paves the way for innovation in reimbursement strategies and ethical and regulatory frameworks.

Of course, such disruption comes with its inherent challenges. There are risks related to standardization, training, liability, and scalability. The idea of complex nanomedicines being produced outside of industrial cleanrooms will be unsettling to some and appalling to others. However, Estapé Senti et al. are careful to

preempt such concerns by citing both historical precedents in hospital compounding and modern advancements in closed-system microfluidics (4). Moreover, the platform's success during the response to the COVID-19 pandemic lends both technical credibility and a sense of urgency to the proposal.

Ultimately, as with all bold ideas, the NANOSPRESSO project will be judged not only by its feasibility, but by its alignment with human needs. Here, the verdict seems clear. As rare disease patients and their families wait—often for years, sometimes generations—for a therapy that may never come, innovative and disruptive projects rekindle hope. They remind us that translational science is not only about discovery, but more importantly about delivery and catering to the needs of patients.

We are invited to reimagine the boundaries of our roles in academia, industry, and healthcare systems. As co-creators of new models of patient care, we are called upon to think and speak not only in the language of symptoms, diseases, and pathomechanisms, but also to appreciate the expectations of patients and societies, and to learn the languages of systems and mutual respect. Innovation for patients with rare diseases cannot wait for the market to catch up. It must be led by science, guided by ethics, and implemented by those closest to the patient. The NANOSPRESSO project could be a spark to ignite the long-overdue transformation of precision medicine into a truly equitable, patient-centered practice.

Statements

Author contributions

DP: Conceptualization, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing.

CK: Conceptualization, Formal Analysis, Investigation, Project administration, Writing – original draft, Writing – review & editing.

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Conflict of interest

CK is a co-founder of Prism Ingenuity and Dioscuri Biopharmaceuticals.

CK declared that they were an editorial board member of Frontiers at the time of submission. This had no impact on the review process and the final decision.

The remaining author declared that this work was conducted in the absence of financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declared that generative AI was used in the creation of this manuscript. ChatGPT4.0 was used to screen background information and to generate a first outline of a draft for defined paragraphs. Final wording was done by DP and CK.

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