

Choosing the Right Particle-Based Delivery System

A Practical Decision Guide: LNP vs. PNP vs. Polymeric Microsphere

PHOSPHOREX PRACTICAL DEVELOPMENT TOOL

There is no single “best” particle platform. The delivery problem should drive the selection. Payload properties, physiological target, route of administration, desired duration of exposure, intracellular delivery needs, targeting strategy, and manufacturability all influence whether an LNP, polymeric nanoparticle (PNP), or polymeric microsphere is the most appropriate starting point.

At-a-Glance Comparison

Consideration	LNP	PNP	Polymeric Microsphere
Primary strength	Efficient non-viral delivery, especially nucleic acids	Tunable polymer chemistry, targeting, protection and extended exposure	True long-acting / sustained release
Common payload fit	Nucleic acids and other payloads suited to lipid-based encapsulation	Small molecules, peptides, proteins; emerging nucleic-acid applications with appropriate polymers	Small molecules and peptides where potency/loading support long-duration dosing
Intracellular delivery	Strong fit for many nucleic-acid applications	Can support intracellular delivery; cationic polymers such as PBAEs are being explored for nucleic acids	Generally not well suited for intracellular nucleic-acid delivery
Release / exposure	Often shorter exposure; formulation dependent	Can provide extended half-life and controlled release	Designed for sustained release over extended periods
Targeting options	Passive and active targeting; ligand-conjugated approaches	Surface chemistry supports passive and active targeting, including ligand conjugation	Primarily driven by depot/ release strategy rather than intracellular targeting
Administration considerations	Depends on formulation and target; widely used for parenteral delivery	May support parenteral and selected alternative-route strategies depending on formulation	Commonly suited to SC or IM depot administration
Sterile processing consideration	Process-specific; filtration and aseptic strategy depend on product	Nanoparticles can often be compatible with 0.2-micron sterile filtration	Too large for standard 0.2-micron filtration; may require fully aseptic processing or terminal sterilization depending on cargo
Key development focus	Composition, particle size/PDI, encapsulation, biodistribution, downstream processing, scale-up	Polymer chemistry/MW, loading, release, size, stability, solvent/process selection, scale-up	Polymer selection, loading, burst release, release kinetics, morphology, aseptic manufacture, scale-up

Start with the Delivery Problem

1. What is the payload?

Consider molecular properties, sensitivity, required loading, and whether intracellular delivery is required. Payload class alone does not dictate the platform, but it strongly shapes the formulation strategy.

2. Where does the therapeutic need to go?

Define the physiological target, cell/tissue uptake requirements, biodistribution objective, and whether passive or active targeting is needed.

3. How long should the payload be exposed or released?

If the goal is true long-acting release, polymeric microspheres may offer a strong starting point. If extended circulation or controlled release is desired without a depot, PNPs may provide useful flexibility.

4. Is intracellular nucleic-acid delivery central to the program?

LNPs are a foundational option for nucleic-acid delivery. PNPs may also be considered where polymer chemistry can support nucleic-acid binding, uptake, and endosomal escape. Microspheres are generally not suited to this objective.

5. Is a targeted surface architecture required?

Both lipid and polymeric nanoparticles can support ligand-based targeting. For PNPs, polymer and surface chemistry can provide additional design flexibility for conjugation.

6. What route and dose are required?

Dose, injection-volume limits, administration route, and required drug loading can materially influence particle-class selection.

7. Can the platform be manufactured at the required scale?

The formulation should be evaluated with scalable unit operations, material use, sterile processing, downstream purification, reproducibility, and future GMP transfer in mind.

A Useful Rule of Thumb

Do not select the delivery system by platform popularity alone. Define the delivery problem first, then empirically evaluate the chemistry, particle characteristics, biological performance, and manufacturing strategy needed to achieve the target product profile. In some programs, evaluating lipid and polymeric nanoparticle approaches in parallel can reveal the strongest path forward.

How Phosphorex Approaches Platform Selection

Phosphorex has more than 20 years of experience with polymeric delivery vehicles and also supports lipid and ligand-conjugated nanoparticle systems. Our teams connect formulation science, analytical development, process design, scale-up, and CMC considerations so platform decisions are made with both therapeutic performance and clinical translation in mind.

Use this tool as a discussion framework, not as a substitute for program-specific scientific, quality, regulatory, or manufacturing assessment.

Particles Engineered for Drug Delivery



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