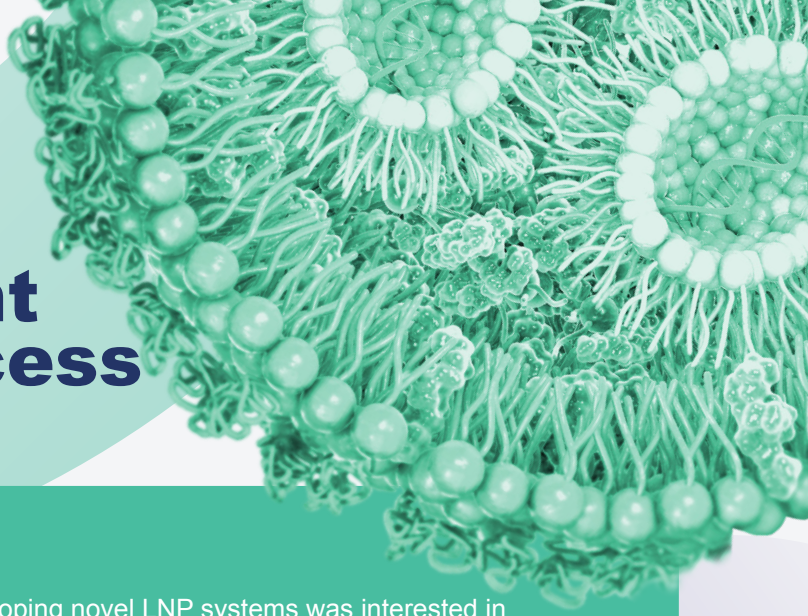
phosphorex

SUCCESS STORY

Clinically Relevant Downstream Process Optimization



⚠ Problem

An ionizable lipid chemistry innovator company developing novel LNP systems was interested in developing an effective, scalable downstream process to reliably maintain LNP critical quality attributes. Due to the unique formulation composition, the LNP demonstrated shear sensitivity in standard tangential flow filtration (TFF) protocols.

Solution

Phosphorex optimized the quality of the novel, shear-sensitive LNP formulation after mixing process scale-up and transfer of batch downstream purification from dialysis to tangential flow filtration (TFF) by:

- Determining the optimal TFF membrane chemistry, molecular weight cut-off, and surface area
- Optimizing the transmembrane pressure, feed pump flow rate, and column loading
- Determining the optimal concentration factor before diafiltration
- Optimizing the downstream buffer pH and ionic strength

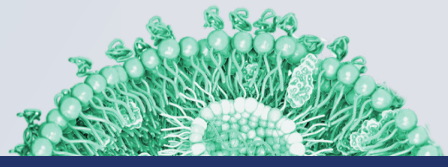
Outcome

The LNPs resulting from the optimized TFF method demonstrated>90% cargo yield, a mean particle size of 96 nm, a low PDI of 0.11, and an encapsulation efficiency of 92% following successful concentration to the target range. The final TFF method was qualified for batch fabrication to support an NHP study.

At Phosphorex, we are committed to helping our partners navigate the complexities of precision drug delivery and advance their programs with confidence. We adapt to your modality, delivery target, and mission, bringing together comprehensive expertise through our Drug Delivery Engine to support every stage of development.

With payload-agnostic, non-viral delivery capabilities, deep experience, and an adaptive approach, we move at the pace of your program; iterating, refining, and aligning as needed. Through close collaboration and clear communication, we serve as a true extension of your team, focused on delivering meaningful progress.

Let's Solve Your Delivery Challenge ›



Engineer Particles for Precision Drug Delivery with Phosphorex

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Behind the Solution

Our partner required a robust tangential flow filtration (TFF) process to support the scale-up of their proprietary lipid nanoparticle (LNP) formulation for rat and non-human primate (NHP) toxicology studies. Following successful demonstration of scalability for the upstream microfluidic mixing process, Phosphorex transitioned the downstream purification workflow from dialysis/Amicon-based processing to a TFF-based approach. This process was subsequently optimized using Phosphorex's established TFF development and scale-up methodology, resulting in a greater than twofold reduction in processing time.

Importantly, the optimized TFF process maintained the critical quality attributes (CQAs) of the LNP formulation while achieving the target final LNP concentration following sucrose addition. In addition, a high overall process yield (>90%) was maintained, which was essential given the limited availability of RNA for producing the toxicology study batches.

Using the optimized TFF process, Phosphorex successfully manufactured the LNP toxicology batches and, through the LNP Alliance, supported the execution of rat and NHP toxicology studies at Neosome and Envol, respectively. Completion of these studies represented a critical milestone, enabling our partner to make informed strategic decisions regarding the further development and advancement of their proprietary LNP formulations.

Matthew Freeman, PhD

Senior Scientist

Matthew Freeman holds a PhD in Chemical Engineering from the University of Rhode Island. He specializes in nanoparticle and microparticle drug delivery systems, with publications and presentations spanning synthesis and physicochemical characterization work.

> "This project came down to time and material. Our partner had a limited supply of RNA, so we couldn't afford a process that wasted product, and we were on a tight timeline. Moving from dialysis and Amicon-based processing to a TFF approach, then optimizing it with our scale-up methodology, cut processing time by more than half while keeping yield above 90%. The formulation reached its target concentration after the addition of sucrose and retained the quality attributes that mattered for the studies. That gave our partner the data they needed to make decisions about the next phase of their program."