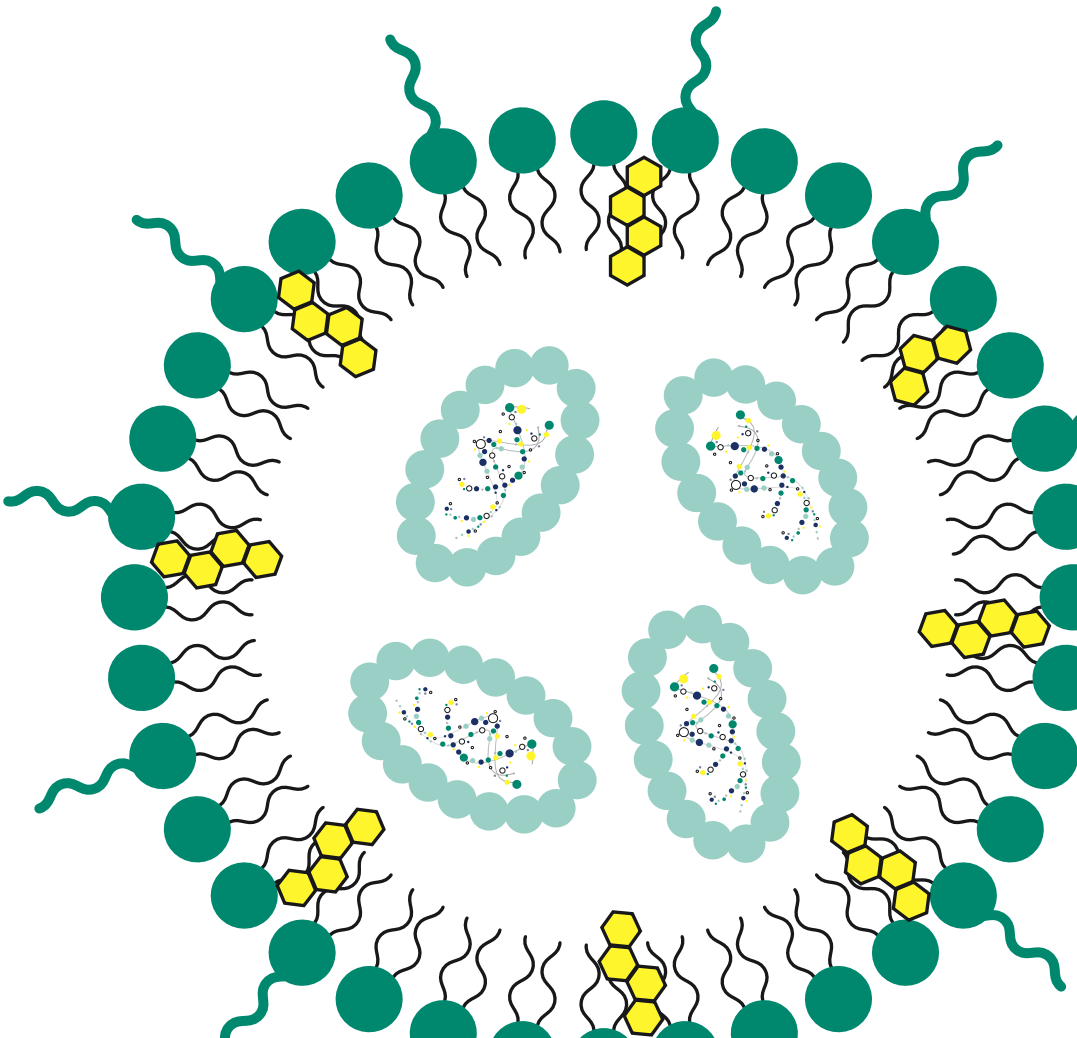
cytiva

Accelerating innovation: Replicate Bioscience and Cytiva collaborate to deliver srRNA-LNP vaccines

Imagine a world where cutting-edge science meets nanomedicine expertise.

Replicate Bioscience is striving to revolutionize therapeutics for infectious diseases, cancer, and autoimmune conditions. So, with a ground breaking self-replicating RNA (srRNA) platform set to open new clinical doors, they sought a collaborator that could help them navigate the complex journey to patients quickly and effectively. That's where Cytiva came in.



"Cytiva offers a diverse, ionizable lipid library with advantages in terms of licensing and pricing, and they also offer the formulation side and end-to-end service. They can do all of the preclinical work, the scale up for you and you can focus on your biology and in vivo testing and accelerate your program forward."

Andy Geall, PhD, Board Chair of the Alliance for mRNA Medicines (AMM) and Chief Development Officer, Replicate Bioscience

There's much buzz around mRNA and pDNA therapeutics in the fast-evolving world of vaccine development, but the potential for srRNA to change the clinical landscape shouldn't be overlooked. Due to a unique ability to create more of itself, srRNA can offer sustained protein expression with lower dosing requirements, fewer side effects, a smaller manufacturing footprint, and reduced costs. However, as is true with any RNA vaccine, srRNA technology's promise will hinge on a precise delivery system to efficiently bring active payloads to target cells.

Replicate Bioscience is a biotechnology company that is working to develop srRNA therapeutics for complex diseases such as cancer and autoimmune disorders. Their advanced srRNA platform stands apart from conventional RNA-based technology by offering improved efficacy with fewer doses.

Recognizing the critical importance of both payload and delivery to srRNA therapeutic success, Replicate Bioscience formed a strategic collaboration with Cytiva. Through the integration of their innovative srRNA payload with our advanced LNP technology, proprietary ionizable lipid portfolio, and extensive LNP experience, we've been able to drive advances that will accelerate the development of next-generation RNA therapeutics with the potential for improved delivery, reduced dosing frequency, and enhanced patient outcomes.

A collaboration that drove the success of the RBI-4000 program

While approximately 59 000 lives are lost to rabies viral infections annually, death is preventable if exposed individuals are treated with an effective vaccine before the virus spreads to the central nervous system and clinical symptoms appear. Current vaccine options are effective, but they require 3 to 5 doses and are subject to supply shortages due to complicated manufacturing processes that can affect accessibility and make administration complex in resource-limited settings.

RBI-4000 is a flagship clinical initiative of Replicate Bioscience, utilizing srRNA and LNP delivery technology to create a vaccine tailored to stimulate virus-neutralizing immune responses against rabies.

Recently published data from the program's Phase 1 study (1) demonstrates immunogenicity from an srRNA vector encoding the rabies glycoprotein at all doses tested, including a single-dose regimen. Furthermore, there were no serious adverse events reported in any of the study cohorts.

Fig 1. Tailored to a program's unique needs, our BioPharma Services team leverages innovative technology, deep industry expertise, and regulatory support to help you cut through the complexity and accelerate toward the next milestone.

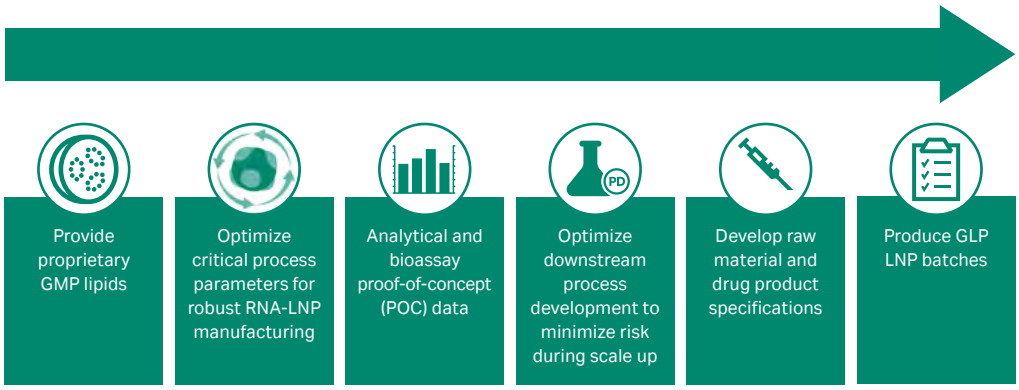
Assessing RNA-LNP manufacturing needs

As Replicate Bioscience ventured deeper into srRNA vaccine development, they sought a collaborator with advanced delivery technologies and the scientific insight needed to achieve clinical success. Across all development stages, Cytiva was able to provide the broad LNP application experience, analytical methodologies, and manufacturing solutions that Replicate Bioscience was seeking. Our NanoAssemblr™ technology and proprietary ionizable lipids — along with extensive experience in GMP manufacturing and regulatory submissions — come with a track record of helping drive innovation in genomic medicine and LNP applications.

Access to a proprietary lipid library

Collaborating with Cytiva gave Replicate Bioscience access to a proprietary ionizable lipid portfolio, allowing their team to quickly perform multiple rounds of *in vitro* and *in vivo* studies using a diverse range of pre-screened and well-characterized ionizable lipids before finalizing their lead drug candidate. This streamlined approach to developing potent lipid formulations accelerated the clinical advancement of their srRNA therapeutics and vaccine program.

Analytical support and lead srRNA-LNP formulation development



Our analytics team provided Replicate Bioscience with the methods needed to optimize their srRNA-LNP formulation. Given that srRNA is significantly larger than mRNA, we developed tailored methods to assess srRNA purity and integrity during the manufacturing runs for their drug product. Our team also developed methods to assess lipid purity and identity testing, ensuring the chosen lipids met the stringent criteria required for their therapeutic formulation.

With custom assays that accurately assessed particle characteristics like size, polydispersity index (PDI), and encapsulation efficiency, our analytics team offered crucial support during Replicate Bioscience's preclinical studies. Early identification of potential risks for downstream processes also helped to drive efficiency and confidence on their development journey.

Fueled by shared goals and collaborative efforts, this rigorous and careful approach to analytics and formulation led to Replicate Bioscience identifying a lead srRNA-LNP formulation and advancing their clinical program forward with the manufacture of a Phase 1 clinical drug product batch.

Analytical activities are crucial for formulation development. By leveraging our in-house datasets and analytics, we collaborated with the Replicate Bioscience team to develop custom assays early on to optimize formulations and validate the formulation process during scale-up.

"Two days of analytics, weeks saved!"

Adam Crowe, PhD, Senior Manager, Analytical Development, Cytiva

Scale-up process development and GMP manufacturing

Once a lead srRNA-LNP candidate was identified, Replicate Bioscience shifted focus toward scaling up their manufacturing process. The team at Cytiva was ready to lend a hand.

Using the NanoAssemblr Blaze system, we transferred process defined parameters from preclinical studies to GMP-scale production. The scale-up effort included validating the process with flow mapping studies to optimize the flow rate ratio (FRR), testing to verify the dilution ratio and process, and monitoring pressure to confirm the formulation could scale effectively.
Filterability is also a key concern for LNPs in the final formulation stages, so optimizing downstream processing and tangential flow filtration (TFF) was a top focus area for our analytical team. Leveraging broad experience in selecting appropriate TFF consumables, we were able to maximize process efficiency while maintaining product quality. Using a single-use fluid path design reduced cross-contamination risks, facilitating efficient changeovers between batches and enabling a smooth transition from small-scale research to large-scale clinical production. Incorporating single-use components within the manufacturing process also helped to address extractables and leachables (E&L) considerations while following United States Pharmacopeia (USP) chapter <665> guidelines and the BioPhorum Operations Group (BPOG) protocol for testing of product-contacting plastic components.

Ultimately, all of the data from these processes and evaluations was provided to Replicate Bioscience to select the strongest formulation for clinical trial evaluation. Acceptance criteria and specifications for the drug substance (provided by Curia), reagents and buffers, and the drug product release criteria were established and documented so the program was ready for transfer to a GMP environment.

In addition to helping finalize the drug product and optimize manufacturing processes for scale up, our project management team also coordinated the logistics of shipping the confirmation batches for biological testing, aligning with the targeted accelerated timelines defined in the drug development program.

With shared goals and an end-to-end collaborative approach, we were able to provide continuous support from early-stage formulation to GMP manufacturing, helping Replicate Bioscience focus on advancing their therapeutic candidates through clinical evaluation.

"The best part about working with Cytiva was their adaptability to changing priorities. Whether it was logistics, sourcing raw materials, or clearing roadblocks at our end, they were in constant communication with us — always a step ahead!"

Andy Geall, PhD, Board Chair of the Alliance for mRNA Medicines (AMM) and Chief Development Officer, Replicate Bioscience

RNA-LNP technology platform and regulatory support

Combining an innovative srRNA platform from Replicate Bioscience with our established LNP technology allowed for the efficient and targeted delivery of an srRNA vaccine for clinical evaluation. Optimizing the delivery system for RBI-4000 helped make sure the vaccine was stable, targeted the disease of interest, and elicited robust immune responses while minimizing adverse events, as was demonstrated by an interim dataset.

We also provided Replicate Bioscience with regulatory support, including a drug master file (DMF) submission. This comprehensive documentation was prepared by both parties and included the manufacturing process, raw materials, facilities, stability data, and supply chain information. By providing the regulators with all necessary insights into drug production and quality control, completing this crucial step in the submission process reduced the need for additional inquiries, streamlined the FDA's review, and accelerated Replicate Bioscience's journey toward filing its investigational new drug (IND) application. Having well-characterized, quality GMP ionizable lipids and LNPs with manufacturing processes documented in an FDA-reviewed DMF also helped to expedite IND submission.

"The FDA-reviewed DMF file provides a foundation for our future clients to benefit from the GMP ionizable lipids and a regulatory framework that shortens time to market and shows that Cytiva takes its regulatory support seriously."

Lloyd Jeffs, PhD, Strategic Customer Leader, Cytiva

Future programs

Encouraged by the strong immunogenicity results of the RBI-4000 program and its demonstrated safety profile, Replicate Bioscience expanded its research into additional srRNA programs, exploring a broader range of ionizable lipids for infectious disease applications. Our ability to provide lipid nanoparticle solutions for scale up and manufacturing of up to 15 srRNA therapeutics allowed Replicate Bioscience to explore new indications beyond their initial focus on rabies. This collaboration unlocked new possibilitiesfor RNA-based therapeutics, helping to set the stage for addressing other pressing healthcare needs such as endocrine therapy resistance in breast cancer,

immunotherapy resistance in solid tumors, and pandemic preparedness.

Conclusion

Our collaboration with Replicate Bioscience demonstrates the power of working together in advancing innovative RNA therapeutics. Through access to advanced LNP technology, proprietary ionizable lipids, and comprehensive analytical and regulatory support, Replicate Bioscience was able to accelerate the development of its srRNA platform and move closer to achieving its goals of bringing new treatments to complex diseases. Together, we've shown that shared goals and the right collaboration can drive scientific innovations from the lab to the clinic.

As an established service provider in nanomedicine drug delivery systems, we provide end-to-end RNA-LNP solutions, including:

- A diverse ionizable lipid portfolio that can be licensed for clinical development and applications
- Scalable NanoAssemblr instruments and BioPharma Services for the formulation, process development, and GMP manufacturing of LNP drug candidates
- Regulatory support to accelerate the clinical advancement of srRNA therapeutics

We're here to help you secure funding, reach your milestones quickly, and develop more innovative RNA-LNP therapeutic solutions.

Contact our specialists to discuss your project.

References

(1) Maine CJ, Miyake-Stoner SJ, Spasova DS, et al. Safety and immunogenicity of an optimized self-replicating RNA platform for low dose or single dose vaccine applications: a randomized, open label Phase I study in healthy volunteers. *Nat Commun*. 2025;16(1):456. Published 2025 Jan 7. doi:10.1038/s41467-025-55843-9.

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