12.5x Titer Boost Accelerates CAR-T Program to IND Filing

Minaris Advanced Therapies

Case Study

SUMMARY:

Optimizing CAR LVV

A biotechnology innovator focused on cell therapies faced a significant hurdle in the development of their flagship CAR-T program. While the therapeutic potential of their candidate was high, the original lentiviral vector (LVV) construct yielded titers that were variable and low, placing a challenge on vector manufacturing as well as cell therapy drug product production.

By partnering with Minaris Advanced Therapies, the client utilized plasmid engineering and parallel process development services to achieve a 12.5-fold increase in infectious titer. This technical breakthrough allowed the company to maintain its clinical timeline and successfully file an Investigational New Drug (IND) application.

THE CHALLENGE:

Construct Insufficiency and IND Pressure

The client's project was stalled by a common but difficult obstacle in advanced therapy development: a candidate CAR LVV construct that performed poorly during viral packaging. Low infectious titers typically lead to larger or multiple batch demands ultimately translating to high manufacturing costs and, in some cases, threats to program viability. With pressure to file their IND, the client needed a molecular engineering solution that could optimize the genetic architecture of the vector itself. The challenge was to redesign the LVV genome cassette to maximize output without altering the therapeutic function of the gene of interest (GOI) and without significant delays to IND filing.

THE STRATEGY:

Molecular Engineering for Enhanced Packaging

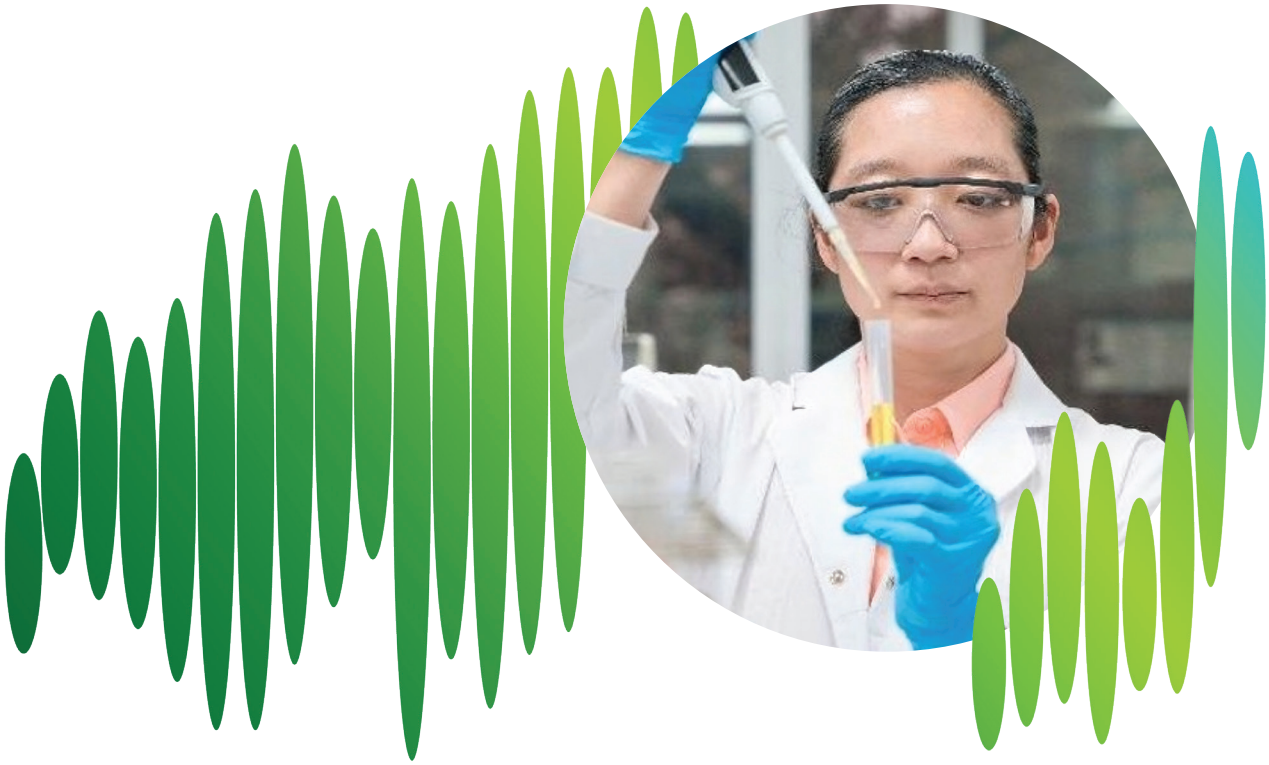
To address the titer deficit, Minaris's molecular biology team used the SnapFast® pSF-Lenti backbone. This third-generation, self-inactivating (SIN) lentiviral packaging system features low homology between expression cassettes to enhance safety and reduce recombination risk. Furthermore, its strategically placed multiple cloning sites allow for easy insertion or exchange of gene sequences, providing flexibility and efficiency in construct generation. The engineering team tailored the transfer plasmid to optimize gene expression, vector production, and safety, in line with the client's GOI-specific requirements.

The technical approach involved cloning the client's payload into Minaris's proprietary backbone and developing three distinct new designs. These constructs were engineered for optimal packaging and transduction of the LVV genome. By testing these three novel configurations in parallel with the original candidate, the team could rapidly identify the most efficient architecture for viral production.

EXECUTION:

From Bench to Bioreactor

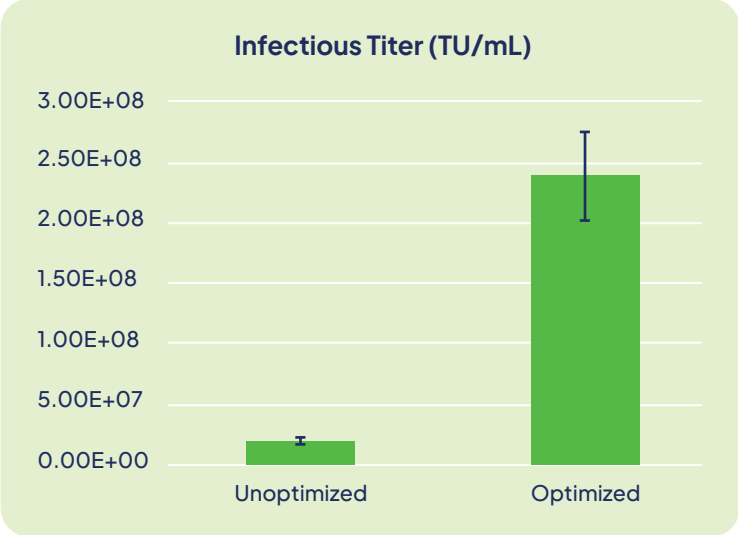
The project followed a two-phase acceleration model. The first phase focused on small-scale demonstration, where concentrated lentiviral vectors were produced in shake-flasks to confirm yield improvements. Once the high-performing constructs were identified, the project transitioned into process development using 1L stirred-tank bioreactors with established ranges for key process parameters such as dissolved oxygen, pH, and temperature.



EXECUTION:

The Path to GMP

Following the successful scale-up, the project moved into the GMP-readiness phase. This involved the characterization of three lentiviral packaging plasmids and the optimized transfer plasmid. To lock in the manufacturing process, the team conducted upstream fermentation optimization and downstream purification verification runs, ensuring long-term plasmid quality and storage stability.



- Three new plasmid designs engineered and tested to identify the optimal configuration.
- 12.5-fold increase in infectious viral titer of the best new design compared to the original construct.
- 100% consistency across IVCN, p24 ELISA, and RT-qPCR analytical assays.
- Full IND support provided, including all stability studies and template batch record reports.

IMPACT:

Advancing Life-Saving Therapies

The successful optimization of the plasmid system provided the client with a reproducible, high-yield manufacturing process. By resolving the technical bottleneck through both plasmid optimization and process development, the client was able to produce the GMP material required for their clinical studies. Most importantly, the 12.5X titer increase helped the company advance its candidate, filing its IND application with no timeline delays and moving one step closer to providing new treatment options for patients.

Contact Minaris Advanced Therapies to learn more about designing and optimizing plasmids for superior transgene expression, expression control, yield and safety.

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