



Accelerating Ultra-Rare Disease Development Through Strategic Manufacturing Partnership

Executive Summary

The development of therapies for ultra-rare diseases requires manufacturing partners capable of balancing speed, quality, and long-term program continuity. This white paper describes how Puresyn supported The Progeria Research Foundation (PRF) through an accelerated plasmid DNA manufacturing strategy designed to meet immediate research needs while preserving future clinical flexibility.

Using a dual-batch approach, Puresyn first generated an INDReady® glycerol stock to establish continuity across development and clinical stages before manufacturing ResearchReady material. This strategy enabled PRF to advance critical development activities while maintaining a clear path toward future clinical manufacturing.

Puresyn successfully delivered qualified ResearchReady plasmid DNA products within 26 days and 21 days, respectively, of receiving starting materials for two candidate plasmids. These results demonstrate how a collaborative manufacturing model can significantly reduce development timelines while maintaining rigorous quality standards and operational control.

About Progeria and the Progeria Research Foundation

Hutchinson-Gilford Progeria Syndrome, known as Progeria, is an ultra-rare and fatal genetic condition that causes children to age at an accelerated rate. Caused by a point mutation in the LMNA gene, it leads to a buildup of a toxic protein called progerin, resulting in cardiovascular disease and other complications of aging in childhood. An estimated 400 children worldwide are living with Progeria today, and without treatment average life expectancy is approximately 14.5 years.

PRF is the driving force behind the global effort to understand, treat and ultimately cure children and young adults with Progeria. Founded by the family of Sam Berns after his diagnosis in 1999, PRF has enabled or led major scientific breakthroughs in the field, from discovery of the causative gene mutation, to Progeria's first and only FDA-approved treatment, lonafarnib, to the advancement of gene-editing approaches now in development. For more information, please visit www.progeriaresearch.org.

The Challenge

Developing therapies for ultra-rare diseases presents unique operational challenges. Limited patient populations, constrained resources, and compressed timelines create

pressure to make rapid progress without compromising scientific rigor or manufacturing quality.

For The Progeria Research Foundation, advancing potential therapies required a manufacturing partner capable of supporting immediate research objectives while helping establish a foundation for future clinical development. Traditional manufacturing approaches can introduce delays, duplicate activities, or create discontinuity between development and clinical phases. PRF sought a strategy that would minimize these risks while preserving flexibility as the program evolved.

The Puresyn Solution

Puresyn developed a manufacturing strategy designed to support both near-term execution and long-term development goals.

The program began with creation of an *INDReady*® glycerol stock, establishing a foundation for future clinical manufacturing activities before production of *ResearchReady* plasmid DNA. This dual-batch approach enabled PRF to proceed rapidly with research activities while maintaining continuity between development stages.

By integrating future manufacturing considerations into early-stage production planning, the strategy reduced potential transition challenges and helped preserve development momentum.

Accelerated Execution Without Compromising Quality

Execution speed was a defining feature of the collaboration.

Following receipt of starting materials, Puresyn manufactured, tested, quality reviewed, and released the first *ResearchReady* candidate plasmid DNA product within 26 days. A second candidate product was completed and released within 21 days.

These timelines supported PRF's downstream development activities, including vector manufacturing and program advancement, while maintaining established quality review and release processes. The ability to accelerate delivery without sacrificing quality or process control demonstrates the value of aligning manufacturing operations with program-specific development needs.

Impact on Program Development

Manufacturing strategy plays a critical role in determining how efficiently a development program advances. Delays in critical raw materials can affect downstream activities, increase costs, and postpone important development milestones.

By implementing a proactive supply strategy, Puresyn helped PRF preserve development continuity, maintain operational flexibility, and support future program progression. The dual-batch approach provided both immediate utility and long-term value, reducing friction between research-stage activities and future clinical development requirements.

For organizations pursuing therapies in ultra-rare disease settings, where timelines are particularly consequential, these advantages can have a meaningful impact on overall program execution.

Partnership Beyond Manufacturing

The collaboration between Puresyn and PRF illustrates the value of a partnership-based manufacturing model. Beyond product delivery, the engagement emphasized communication, responsiveness, technical rigor, and strategic planning.

This collaborative approach enabled manufacturing decisions to align closely with program objectives, supporting both immediate research requirements and future development planning. The result was a supply strategy designed not only to meet specifications but also to advance broader program goals.

Conclusion

The collaboration between Puresyn and The Progeria Research Foundation demonstrates how thoughtful manufacturing strategy can help accelerate development programs in ultra-rare diseases. Through a dual-batch approach, rapid execution, and a commitment to quality, Puresyn provided PRF with qualified plasmid DNA materials while preserving continuity for future development stages.

The program highlights how strategic manufacturing partnerships can help organizations reduce timelines, maintain flexibility, and advance therapies more efficiently toward the patients who need them.

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