Building a first-of-its kind gene therapy facility, commercializing one of the first gene therapies, and industrializing the largest gene therapy footprint in the world ($500MM over 5 years)

Situation:

- In 2015, client was a clinical-stage company focused on bringing their gene therapy from the lab into a clinical setting for patients and families devastated by rare neurological genetic diseases. Today, client is a leading, global gene therapy company with one of the first-ever commercialized, FDA, EMA and other regulatory agency-approved gene therapies
- Client was looking to pioneer the industrialization of gene therapies and build a cutting-edge manufacturing facility using modular cleanrooms, emerging bioreactors and single-use technologies for the clinical and commercial manufacture of a life-saving gene therapy for a rare neurological disease. At the time, this disease was the leading cause of infant death from genetic disorders
- Client had a team of less than ten employees with product being manufactured at an academic hospital. Client had no further external or internal manufacturing capability, no facility selected, no facility design, no technical operations infrastructure, no long-term plan or execution strategy and an accelerated timeline of fifteen months from board approval to facility startup

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Task: Provide a manufacturing strategy and build a first-of-its-kind gene therapy facility using cutting-edge technologies within 15 months.

- Project Farma collaborated with client on the strategic effort to secure board approval and funding for a manufacturing facility in Illinois after conducting a thorough Make Vs. Buy analysis including a ten-year EBITDA and ROI model, sample organizational chart and resource model
- While facility build was underway, the team evaluated and selected CDMOs (domestic and international), tech transferred process from academic center to CDMOs and internal facility to ensure clinical supply was met
- Client selected Project Farma to fill key technical operations roles: Capital Portfolio Manager, Program and Validation Director, Quality Management Program Director and various project management, engineering, validation, and reliability and maintenance roles
- Project Farma provided critical, strategic roles in building a functional cGMP compliant manufacturing facility using many early-stage and innovative technologies and techniques not commonly utilized at that time (2016) in advanced therapies including:

> **“Project Farma was a true partner from the beginning, providing the right cross-functional resources with the right level of expertise which ensured that critical milestones were met, and life-saving medicines were manufactured for the patients.”**

Task: (continued)

- First-of-its-kind standalone single-use emerging bioreactors, TFF skids, chromatography skids, and vial filling system. Project Farma provided valuable input into the design and optimization of many of these systems and executed full engineering, automation and validation testing and integration
- Project Farma assisted in the design and optimization of GMP modular cleanrooms which were built offsite, shipped to the facility, and commissioned and qualified as capital equipment
- To reduce cleaning validation timelines and mitigate contamination risks in the manufacturing process, single-use disposable technology was implemented throughout the process including all upstream and downstream operations

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Actions: Provide an innovative approach to build a first-of-its-kind gene therapy facility.

Project Farma mobilized several tactical teams and identified and created various project team swim lanes to divide, organize, and execute the overall scope. Project Farma provided each work stream project management, engineering, automation, validation and quality support. Project Farma also provided project execution teams across the various swim lanes.

To meet the aggressive timeline, Project Farma provided strategies to expedite engineering, automation and validation programs using quality-by-design, GAMP, ASTM E2500 risk-based approach principles:

Project Farma created engineering, automation and validation programs that reflected engineering and validation efforts that were commensurate with the complexity of the GMP asset, software or system.

- Project Farma implemented and executed a phase-appropriate engineering and qualification program based on three phases: pre-clinical, clinical and commercial

Project Farma delivered qualified GMP assets, asset maintenance and training on schedule, in order to meet GMP production timelines. The complete project from site selection to facility release was delivered in the original fifteen-month goal.

Results: One of the first FDA-approved commercial gene therapy facilities is established. Project Farma and Client kickstart our next mission to build the largest gene therapy manufacturing footprint in the world

- Project Farma's success and proven track record led to the continued industrialization of over one million square feet of gene therapy manufacturing for client totaling over $500MM in capital spend

Results: (continued)

- The initial 55,000 sq. ft. facility was expanded twice to over 100,000 sq. ft. Below are the expansion highlights:
  - A 50,000+ sq. ft. expansion for the design and construct of a warehouse, cold rooms, hazardous rooms, dock, offices, equipment cages, freezer farm and more
  - The design and construct of an additional biochemistry lab, packaging and thaw room, production suites, and more
- Project Farma supports design, construction and multiple expansions of quality control and process development labs in San Diego, California totaling $65MM
- Project Farma supports building a 180,000+ sq. ft. greenfield gene therapy facility in Durham, North Carolina totaling $230MM+
- Project Farma supports retrofitting a 680,000+ sq. ft. brownfield gene therapy facility build in Longmont, Colorado totaling $200MM.
- Project Farma was selected by client to lead CDMO expansion efforts including project management, CDMO management, equipment engineering and procurement and validation in Baltimore, Maryland

- Client's drug becomes one of the first-ever gene therapies using intravenous delivery to be approved by the FDA, EMA and other regulatory agencies
- Project Farma and Client presented this case study at various cell and gene therapy conferences to other industry leaders
- Project Farma remains a key partner for client today (2021) as they work together to bring these life-saving therapies to every patient and family globally

PRECISION ADVANCE the cell & gene therapy collective™

PRECISION ADVANCE, a collection of interconnected services and complementary teams uniquely focuses on the complexities of clinical, regulatory, manufacturing and commercial needs to successfully bring a cell or gene therapies to market.

Develop and manufacture your therapy, prepare the market, position your brand. Contact us at info@precisionmedicinegrp.com

To learn more about Precision Medicine Group, visit **www.precisionmedicinegrp.com.**

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