Diane I Blumenthal, MSE

President, Dianthus Biopharma Consulting, LLC

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CMC executive with nearly 40 years of experience in leading teams in the areas of process and product development, clinical and commercial manufacturing, quality control, scientific facilities, program management and CMC regulatory for the biopharmaceutical industry. Former SVP/Head of Technical Operations for Spark Therapeutics. Provided strategic direction and operational leadership to achieve regulatory approval for Luxturna®, the first gene therapy product approved for the treatment of a genetic disorder. This included the first viral vector facility approved and licensed in the United States. Former VP, Manufacturing Sciences and Technology for Eli Lilly and Company. Played a leadership role in the approval of Erbitux® and Cyramza® two monoclonal antibody therapies to treat cancer. Member of Board of Directors for ValSource Inc., a company that provides consulting and advisory services to the pharmaceutical industry, advanced therapy medicinal products, biologics and medical device industries. Member of the Science and Technology Board Subcommittee at Code Biotherapeutics.

Biographical Overview

Diane has a well-respected track record of nearly 40 years in the biopharmaceutical industry as a leader in process and product development and clinical and commercial manufacturing. Her depth and breadth of knowledge also includes quality control, scientific facilities, program management and CMC regulatory. She has extensive expertise in building and transitioning companies from a start-up research and development organization to a fully integrated biopharmaceutical company with approved commercial manufacturing operations and products. Throughout her career, Diane has played a key role in the development and commercialization of six well-known pharmaceutical products, including Erbitux® and Cyramza® and most recently Luxturna®.

At Spark Therapeutics, Diane built and led the Technical Operations team which was responsible for the late-stage technical development and ultimate approval of Luxturna®, the first gene therapy product approved for the treatment of a genetic disorder. This included licensure of the first viral vector facility in the United States. Diane joined Spark Therapeutics in October 2014 as employee #38. She led the technology transfer of the research process and test methods from Children's

Hospital of Philadelphia to Spark Therapeutics (CHOP). In only 2.5 years, she and her team delivered a successful CMC (Chemistry, Manufacture and Control) package to FDA following on shortly thereafter with a marketing authorization application to EMA. These packages were required to demonstrate a reproducible manufacturing process, product comparability to the CHOP clinical product, as well as deliver robust and validated analytical methods to support the release and development of commercial specifications and assure acceptable product shelf-life to support marketable supply chain logistics. Equally as important was the successful completion of a Pre-Approval inspection (PAI) for the first commercial Gene Therapy Manufacturing Facility in the United States. Diane was a critical team member representing Spark at the Advisory Committee meeting with the FDA, which led to the approval of Luxturna®.

Prior to joining Spark Therapeutics, she served as Vice President of Manufacturing Sciences and Technology for Eli Lilly and Company, following the acquisition of ImClone Systems. While in this role, Diane was responsible for leading a multi-disciplinary team of scientists, statisticians and engineers tasked with providing technical support to manufacturing, development, quality control, quality assurance and regulatory teams. Diane has well-honed know-how in the transfer and scale-up of processes from the laboratory bench to commercial scale manufacturing with proficiency in both microbial and mammalian cell culture expression systems and the corresponding downstream purification processes.

Before her time at Lilly, Diane served as a scientific and manufacturing consultant to multiple start-up biotechnology companies and held scientific leadership positions at ZymeQuest, Inc., Scios, Inc. and the Eastman Kodak Company.

She received her M.S.E. in Chemical Engineering from Lehigh University and a B.S.E. in Bioengineering at the University of Pennsylvania.

SPARK THERAPEUTICS, INC.
(A Member of the Roche Group)

January 2018 – September 2020
SVP/Head, Technical Operations

October 2014 – January 2018
VP/Head, Technical Operations

- Built and led the Technical Operations team which delivered the first gene therapy product approved for the treatment of a genetic disorder and licensure of the first viral vector facility in the United States.
- Directed the advancement of Spark Therapeutics' Hem A and Pompe programs through the development and tech transfer of a next generation viral vector manufacturing process required to support larger patient populations.

- Identified and selected the contract development and manufacturing organization required to support the larger scale production needs of Spark's pipeline products.
- Organizational functions included: manufacturing (internal and external), manufacturing sciences and technology, qualify control, supply chain & logistics, scientific facilities (metrology, engineering, validation, environmental health and safety) non-clinical statistics, CMC regulatory, program management.

ELI LILLY AND COMPANY
(Formally ImClone Systems Incorporated)

October 2000 – October 2014
Advancing Roles to Vice President, Technical Services/Manufacturing Sciences

- Built and lead the Manufacturing Technology Organization for a leading biologics cancer therapeutics company. Marketed products included Erbitux® for the treatment of refractory colon cancer and head and neck cancer and Cyramza® for the treatment of gastric cancer.
- Areas of responsibility included: process sciences, process validation, CMC regulatory support as well as non-clinical statistics and quantitative sciences, clinical manufacturing and equipment and facilities validation.
- Developed a broad pipeline of products from preclinical to late Phase III/pre-registration and ultimately commercialization. Marketed products included Erbitux® for the treatment of refractory colon cancer and head and neck cancer and Cyramza® for the treatment of gastric cancer.
- Delivered technical support to Eli Lilly and Company's Branchburg clinical and commercial manufacturing operations for API and drug product.
- Facilitated the transfer of processes and process improvements. Coordinated large scale process validation efforts.
- Supplied statistical support for analyzing and trending manufacturing data, implementation of Quality by Design (QbD) for streamlined filings and key experimental strategies for process optimization.
- Prepared the Chemistry, Manufacturing and Controls sections for all clinical, commercial, and post-marketing regulatory filings.

BIOPROCESS TECHNOLOGY CONSULTANTS
November 1998 – May 2000

Worked with nearly a dozen clients to develop cost-effective, reproducible biopharmaceutical manufacturing processes. Products included monoclonal antibodies, viral vaccines, and recombinant therapeutic proteins.

- Provided guidance in choosing the appropriate expression system for manufacturing, scale-up, validation and testing.
- Aided with securing cell banking services, development of manufacturing strategies, renovation of existing facilities, design, construction, and validation of new facilities and selection and management of contract manufacturers.
- Prepared required CMC sections for product licensure.
- Assisted with inspection readiness. Conducted mock cGMP audits.
- Prepared answers to product license application questions and audit observations.

ZYMEQUEST, INC.
February 1998 - November 1998
Director, Manufacturing

Responsible for developing and implementing a manufacturing strategy to produce a medical device designed to convert A, B, and AB red blood cells to universal donor O red blood cells. The device consisted of a series of recombinant enzymes, a mechanical device, and a set of sterile disposable components.

SCIOS, INC. (formerly California Biotechnology and Scios Nova, Inc.
May 1987 - February 1998
Advancing Roles to Director, Manufacturing and Fermentation Process Development

Responsible for the manufacture of all of Scios' recombinantly derived therapeutic proteins. This included the project management of the contract manufacture of Natrecor®. Supervised the manufacturing operation at Scios, Inc., which included responsibility for the fermentation, purification, and manufacturing support groups. Responsible for maintaining the manufacturing facility in compliance with current Good Manufacturing Practices. Coordinated the equipment, process and cleaning validation required to bring and maintain the manufacturing facility in compliance with current Good Manufacturing Practices. Prepared the CMC sections for all regulatory filings. Participated in required regulatory inspections. Additional responsibilities included the development of scalable fermentation processes for all new recombinantly derived human therapeutic proteins including Natrecor®.

Developed ten scalable fermentation processes for the production of recombinantly derived human therapeutic proteins. Nine of the processes developed utilize *Escherichia coli* as the host organism. One product was expressed in two yeast systems: *Saccharomyces cerevisiae* and *Pichia pastoris*. Responsibilities included the selection of an appropriate host/vector system as well as conducting the required studies for optimizing growth, protein expression while maintaining both product and genetic stability.

Prepared material in compliance with current Good Manufacturing Practices for those protein products used in clinical trials. This included the preparation and maintenance of the required

master and working cell banks. Responsible for the design and construction of the fermentation area in a new facility used for the manufacture of clinical trial material. Established the company's first fermentation facility. Included the specification, design and installation of all fermentation equipment, upstream recovery equipment and corresponding process vessels. This facility was used for the development of fermentation processes and the production of Phase I and Phase II clinical trial material.

Responsible for identifying, coordinating, and executing large scale fermentations at contract manufacturing facilities when required. Developed and transferred the Natrecor® fermentation process to for commercial manufacturing.

Collaborated in the development of in-process assays used for measuring expression level as well as the monitoring of any process related heterogeneity.

Expertise in the use of statistical experimental design for optimizing processes.

EASTMAN KODAK COMPANY - Life Sciences Research Laboratories
December 1984 - May 1987
Research Engineer and Supervisor, Screening Laboratory

Manager of a small-scale fermentation. Responsibilities included the transfer of technology from shake flask to fermentation tank, evaluation of pathway engineered mutant strains for optimal product production, media optimization and preliminary process optimization.

Small scale process optimization. Responsibilities included the detailed evaluation of several of our most promising production strains and the development of an optimum fermentation strategy using these strains.

EDUCATION

LEHIGH UNIVERSITY - M.S.E. - BIOCHEMICAL ENGINEERING
UNIVERSITY OF PENNSYLVANIA - B.S.E. - BIOENGINEERING

RECENT PRESENTATIONS AND PANELS

"Making Gene Therapy A Reality – Challenges and Opportunities – A CMC Perspective" @

- BioPhorum (formally BPOG) – March 10-12, 2020
- American Manufacturing Summit - June 18 -19, 2019
- Pharma Centaur – July 16-17, 2019
- Basal Life – September 9-12, 2019
- Biomanufacturing World Summit – June 29, 2018

- CASSS Cell and Gene Therapy – July 10-12, 2018

"Gene Therapy Manufacturing and Technical Development", 3rd Annual BioProcessing Summit Europe, July 20-23, 2020.

"The Future of Pharma/BioPharma Manufacturing and Supply", Presentation and Panel Discussion, DCAT, March 19, 2019

Women in Leadership Panel – American Manufacturing Summit – June 18-19, 2019

International Alliance of Biological Standardization – 7th Annual Statistics Workshop – November 8, 2022 – Plenary Lecture – Making a Difference in the Biotechnology Journey – A CMC Perspective

NEWS ARTICLES

K.R. Poudel, Zenobia Taraporewala, Diane Blumenthal, Deep Shah, Kathy Francissen, "Comparability for Cell and Gene Therapy Products: A Challenge and an Opportunity", Bioprocess International, 22(1-2), January - February 2024.
https://secure.viewer.zmags.com/publication/157a0a62#/157a0a62/19

Vivienne Raper, PhD, A Paradox? Gene Therapy Manufacturers Should Learn Lessons from the Past, Genetic and Engineering, July 27, 2020.
https://www.genengnews.com/topics/bioprocessing/a-paradox-gene-therapy-manufacturers-should-learn-lessons-from-the-past/

Blumenthal, Diane I, Manufacturing the Next Gene Breakthrough in Gene Therapy, STAT Plus "First Opinion", December 18, 2019.
https://www.statnews.com/2019/12/18/manufacturing-the-next-breakthrough-in-gene-therapy/

Parrish, Meagan, Gene Therapies: On the Rise, Pharma Manufacturing, September 17, 2019.
https://www.pharmamanufacturing.com/articles/2019/the-rise-of-gene-therapies/