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pharma TECH OUTLOOK

CONTRACT MANUFACTURING ORGANIZATION EDITION

WHERE MANUFACTURING MEETS MOBILITY:
INNOVATING & SECURING THE PHARMACEUTICAL SUPPLY CHAIN

BIOSPECTRA INC.

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The pharmaceutical industry is a complex and dynamic enterprise that blends scientific innovation with commercial acumen, resulting in the development of life-enhancing and often life-saving medicines and treatments. In this landscape, pharmaceutical companies must navigate intricate regulatory requirements, patent laws, and market forces to successfully launch their products. To be successful, drug manufacturers must rely on a vast, global supply chain of goods and services that demands constant oversight, innovation and increased security due to ever-changing trends and challenges to keep up with ever-changing industry narratives.

BioSpectra Inc. (BSI), a privately owned, US-based, manufacturer of premium pharmaceutical ingredients and bulk cGMP fine chemicals (as part of the larger BioSpectra Organization), is a key player in fulfilling these critical requirements offering innovative purification and synthetic capabilities, with products produced in its expanding gloabal manufacturing platform in Asia, India, US and Canada and further synthesized and or purified, tested and packaged under cGMP at its FDA registered and cGMP facilites in Renessalaer NY, Stroudsburg and Bangor Pennsylvania.

BSI is a leader in manufacturing cGMP pharmaceutical-grade ingredients, including biological buffers, actives, excipients, cGMP process.

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chemicals, as well as new chemical entities (NCEs) at IPEC & ICH Q7 regulatory compliance levels. It specializes in small molecule synthesis and true, phase-change multi-step purifcation, providing solutions for various key ingredient issues at various stages of the drug manufacturing process that its clients face.

"We support key biopharmaceutical companies for a unique range of critical cGMP products used upstream and downstream, including ingredients for the final drug product," says Paul DiMarco, SVP of commercial operations at BSI.

This flexible cross-functional model allows BSI to focus on the small molecule needs for highly varied, critical cGMP requirements, streamlining the supplier base, and reducing redundant work and operational costs. This includes synthesized / re-purified cGMP bulk biological buffers and a wide range of synthesized and purified functional excipients and NCEs that meet strategic product applications and regulatory demands. Depending on the specific needs of the client, these products can be produced in multiton quantities down to kilo-scale volumes based on the cGMP facility where they are manufactured. For instance, API synthesis is focused on smaller volumes for orphan drug applications rather than high-volume generic drugs, whereas cGMP biological Buffers are produced in much larger multiton quantities.

Tromethamine, a.k.a. "Tris" or "Tris base", serves as an excellent example, being utilized upstream as a key bulk, cGMP biological buffer, as well as a key excipient in other drug products. Further purified, BSI offers the highest quality API grade of Tromethamine on the market today for downstream, final drug use. BSI's multi-step proprietary purification processes combined with a robust regulatory support package through to the DMF submission, showcases its experience and manufacturing capabilities. Other key biological buffers that have made way downstream into the final drug product include highly purified ICHQ7 cGMP versions of MOPS, MES Monohydrate, HEPES Free Acid, and TRIS HCl. BSI's recent expansion of cGMP Tris HCL synthesis and purification makes them one of the world's largest synthetic producers of this key biological buffer that is surpassing the use of Tris in new drug platforms.

A Unique Three-Tiered Approach Supporting Pharmaceutical Drug Manufacturing

BSI's approach to providing biopharma manufacturing services is centered on a three-tier manufacturing platform that encompasses multiple scales of manufacturing (from kilo to multi-ton lots) as well as a range of applications, upstream, midstream, and downstream, that include but are not limited to cGMP biological buffers, functional excipients and NCEs, custom cGMP solutions and small volume APIs. These are supported by an ever-expanding global manfacturing base that includes three cGMP manufacturing facilities in PA and NY, a newly aquired polymer production facility in Canada, a new cGMP manufacting facility in Sarigam, India as well as expanded R&D facilities outside of Mumbai and in the US.

BSI works with biopharma companies as a synthetic manufacturer, providing comprehensive support throughout the entire drug manufacturing process. Biological buffers play a critical role in the upstream purification of biological drug products, as well as downstream, ensuring consistent and precise pH conditions through to drug delivery. Its functional excipients are custom molecules designed to enhance the stability and efficacy of biological and synthetic drug products. Regardless of the application, the BSI manufacturing process employs proprietary and precise purification steps that remove specific impurities that may adversely impact the effectiveness of the final drug product.

An expert in small molecule purification, BSI has acquired synthetic capabilities in its nearly 30-year tenure, expanding its manufacturing platform for contract synthesis of kilo-scale and multi-ton quantities of small molecules. Since by definition, NCEs used as excipients are not registered in any Compendial Monograph (USP, EP, JP), they must undergo multiple purification processes and robust regulatory support before being included in the final drug product. With this wide range of manufacturing, synthesis and purification expertise, BSI can provide various compendial and unique molecules to aid biopharma companies in bringing their products to market.

"Our focus on functional NCEs and other critical cGMP process chemicals requires multiple and unique purification steps to remove unwanted contaminants with exceptional lot to lot consistency. In that sense, we specialize in purification pathways with a robust regulatory support program," says DiMarco.

With its precise attention to market trends and flexible operations toward customer needs, BSI has geared itself with foresight, allowing it to identify emerging issues and obstacles. As a notable example, DiMarco underscores the U.S. pharmaceutical sector's dependence on foreign manufacturing and the hurdles to increase drug ingredient and fine chemical manufacturing capacity in North America.

Recognizing the current reliance on foreign, generic drug imports, and drug product ingredients BSI's long-standing program to onshore and reshore key pharmaceutical ingredients have helped to bring finished drug manufacturing back to North America. The recent pandemic highlighted the country's own awareness of its tenuous dependence on foreign sources of finished drug products and drug ingredients, resulting in federal initiatives to address supply chain security. Unlike others, BSI would not accept any Federal, State or Local grants or money to confront the problem with its massive expansion of its manufacturing capabilities thus, helping to strengthen North American-based drug manufacturing and driving local economic growth.

Regarding supply chain security of critical, crude raw materials, with over 25 years of on-site inspections and management of vendor relationships with overseas raw material manufacturers, BSI has acquired an unparalleled understanding of the risks associated with offshore chemical procurement. This resulted in securing redundant, qualified supply for these critical chemicals, reducing the dependency of its clients on foreign manufacturers, thereby reducing operational redundancies, increasing efficiencies, and overcoming supply chain obstacles while fostering more secure and sustainable manufacturing of finished drug products. Its unwavering dedication to the pharmaceutical industry is exemplified by its continued investment in facilities, capacity expansion and innovative technologies in areas of analytical support, purification and finished product manufacturing as well as Sustainability initiatives.

Considering BSI's track record of supplying fully cGMP products and improving the competitive stature of its clients, it is natural to wonder how it achieves this success. The answer lies in its adaptability, customer-centric operational models, and exceptional customer care and support. These pillars empower it to exceed client expectations.

An Unmatched Ally

BSI is well-known for its manufacturing agility and dedication to staying true to its operational model. Founded in 1993 at Shawnee on the Delaware, Pennsylvania (PA), after initial research and development in biological buffer purification, the company began manufacturing reagent grade buffers and laboratory chemicals in Sciota, PA. Later, it established its first dedicated manufacturing facility for cGMP biological buffers in Stroudsburg, PA being the first company in the U.S. to re-purify biological buffers under a fully cGMP-compliant system. In 2011, BSI expanded its chemical manufacturing portfolio by acquiring and renovating a much larger cGMP facility in Bangor, Pennsylvania.

Since then, the firm has made multiple facility acquisitions to house its fleet, operational and administrative services, opening its new Corporate Services Center in Wind Gap, Pennsylvania. These acquisitions allowed for further expansion of its cGMP manufacturing footprint at its Bangor and Stroudsburg facilities. In addition, the company began renovating a Kilo-scale cGMP facility in Rensselaer, New York to complement its small molecule CMO services. In early 2023, BSI opened a massive cGMP warehouse in Stroudsburg PA, allowing for significant expanded production space at its Bangor facility while simultaneously completing renovations and officially launching its Kilo-Scale Rensselaer site.

The new cGMP Warehouse is located adjacent to a second, much larger facility that will be completed in 2024/2025 and will allow the firm to relocate additional storage and other quality services from its Bangor location, creating further room for expansion in synthetic manufacturing operations there. The Rensselaer facility will continue to act as the kilo-scale cGMP facility to feed the larger manufacturing facilities as products move up into larger-scale production. In August of 2023, BioSpectra completed the acquisition of Dextran Products in Scarborough, Ontario Canada that will add yet another manufacturing facility to help expand its line of key excipients and critical NCE's for the Biopharma industry with specialized focus on dextran polymers.

Throughout this journey, BSI has been at the forefront of developing bulk cGMP biological buffers and other fine chemicals that continuously evolve with industry needs and will continue to do so in the future with several new product launches in 2022/23 & into 2024. That will include but not limited to the following products: 2022/23 & into 2024, that will include but not limited to the following products:

- (2022)
    - High purity, cGMP, excipient grades of Galactose and Trehalose Dihydrate
    - cGMP L-Cystine Di HCl
    - Excipient grade of Cysteamine HCl (2MEA)
- (Q4 2023)
    - Excipient grade Uridine & Bis Tris
    - cGMP fine chemical, Dextran Sulfate 8000 (polymer)
    - Excipient grade water-for-injection (WFI)
    - L-Arginine HCl
    - Bis Tris HCl
    - L-Glutamine
- (Q1 2024)
    - L-Histidine Monohydrochloride, Monohydrate
    - A fully Synthetic Parenteral grade of Glycerin;
    - Rx, API version of Uridine, Cytidine & 2MEA
    - Excipient grade of Dextran 70,000

BSI will also be relaunching Sodium Decanoate, a functional excipient and NCE at a greater scale backed by USFDA Type IV DMF, that enhances the bioavailability of many APIs its combined with in final drug formulations. While BSI may have begun by purifying biological buffers, it has since become the primary supplier of purified cGMP Tris Base and one of the largest synthetic producers of purified, cGMP Tris Hydrochloride to the biopharmaceutical industry.

This trajectory, marked by a relentless pursuit of innovation in cGMP purification and manufacturing capabilities, highlights BSI's dedication to meeting client demands and making their operations a success.

Elaborating on this, DiMarco says, "We understand our chemistry, capabilities, and capacities very well helping our customers select the best path for their projects as we are very transparent about what we can or cannot accomplish in the cGMP manufacturing space."

The firm relentlessly cultivates a culture of open and honest communication with clients, providing detailed project quotations within reasonably short periods of time. Its commercial team acts as a holistic resource center, gathering critical insights from all internal Divisions and Departments in order to respond to client inquiries quickly and efficiently.

BSI promotes a seamless and hassle-free collaboration with meticulous organization and monitoring, eliminating bottlenecks and ensuring a smooth experience. This approach is bolstered by its remarkable customer care and support services throughout the product lifecycles, which ensure client satisfaction and the delivery of top-quality, pharmaceutical ingredients and cGMP process fine chemicals. Given the dynamic nature of the U.S. pharma sector, BSI keeps its finger on the pulse of changing market narratives and client demands. Since many of these changes require a quick turnaround, it strives to maintain its mobility and agility through the growth of the organization. Private ownership has allowed it to analyze risks and overcome unforeseen challenges in remarkable time frames–an atypical feature in larger corporate environments. Its experienced team has a wealth of knowledge, including the full range of European and US, FDA, and cGMP compliance requirements. This model of customer-oriented products and services has allowed BioSpectra to service and supply products to many of the industry's leading global Pharma and Biopharmaceutical companies.

With their products and contract services, BSI has helped with thee ever-evolving needs of the pharmaceutical industry and highlighted how BSI is unique to the cGMP manufacturing space.

Commitment to Sustainability and Ethics

BSI is fully engaged in all aspects of the current sustainability movement.

"We constantly improve our facilities and workers' environment, adopting new technologies and ensuring education and vocational opportunities for our employees. And we continue a tireless effort to expand our qualified, global supply base of raw materials to sustain supply chain security, all while upholding and supporting the major principles of regulatory compliance and Corporate Social Responsibility and Global Sustainability initiatives," says DiMarco.

BSI is committed to investing tens of millions of dollars as part of a multi-year program to upgrade and centralize all utility systems at its manufacturing facilities, making them more energy efficient and environmentally friendly. To mitigate the potential risks of sourcing raw materials from a single source and to ensure supply chain security, it actively qualifies and works with manufacturers across different regions of the globe to create a sustainable and secure supply network. BSI continues to invest in critical analytical and manufacturing technologies with the expansion of its ICP-MS and ICP-OES labs for critical elemental impurity analysis, electron microscopy for identification of contaminants and a series of (massive) nitrogen based, electron-pulse spray dryers, to help usher in the next generation of drying capabilities for larger and more sensitive polymers, small-molecules and NCE's and enhanced free-flowing capabilities for existing and future biological buffers.

In its ongoing endeavors, BSI will be introducing a series of chemically altered and purified carbohydrate polymers for upstream and downstream applications for biological pharmaceutical products. BSI continues to expand critical technologies by investing in advanced electron pulse nitrogen spray drying and other advanced analytical instrumentation.

DiMarco firmly believes that biological buffers will remain significant in supporting the next generation of cell therapies and genomics. The pandemic cemented the validity and efficacy of mRNA vaccines and the investment in genomics and cell therapies continues at a rapid pace. Armed with decades of experience, expanding manufacturing facilities and product portfolio, massive capital investment in facilities and Sustainability programs, BSI endeavors to play a critical role in the success of existing drug producing technologies and products as well as the next wave of innovative drug therapies. Ph

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BIOSPECTRA INC.

> “ OUR FOCUS ON FUNCTIONAL NCEs AND OTHER CRITICAL GMP PROCESS CHEMICALS REQUIRES MULTIPLE STEPS OF PURIFICATION TO REMOVE UNWANTED CONTAMINANTS.