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Introducing the MarketVector™ Bioproduction Tech and Tools ESG Index

Biologic Breakthroughs Begin Here

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Investing in the Bioproduction Tools & Tech Industry

The healthcare sector landscape is swiftly changing. Largely unheralded, biologics-based treatments are quietly but increasingly taking the spotlight in the biopharmaceutical segment. This trend is allowing Bioproduction Tools and Tech companies to emerge with a distinctive position in the broader field, playing a catalytic role in achieving scale, efficiency, and precision in biologics production. At the same time, the nature of these bioproduction companies can sidestep the high-risk nature typically associated with drug development companies themselves. This sets the stage for a discussion around the investment opportunity created by the thematic isolation of these companies from the broader industry of biopharmaceuticals.

Biologics refers to medications that are sourced from living cells or produced using biological processes. These relatively large and complex molecules have critical use cases for tackling formerly untreatable diseases. Biologic compounds have become the foundation for specialized immunotherapy, gene therapy, and regenerative medicine products. Moreover, they are breaking new ground in treating a range of conditions, from cancers to rare genetic disorders[1]. While biologics are produced by drug-makers, the value add of bioproduction companies revolves around working with these producers to expedite drug discovery, amplify production, and ensure more precise treatments. This industry serves not just as a distinct and key pillar of the biopharmaceutical sector, but as a portal to the innovative regimens that hold the promise to revolutionize healthcare.

In the vanguard of technological innovation, companies in the Bioproduction Tools and Tech sector have demonstrated their leadership through initiatives like the early adoption of AI and big data analytics. This development reflects an industry-wide trend rather than just a strategic maneuver, setting them apart as key suppliers in the high-demand technology market. Their influence is particularly significant for emerging biopharmaceutical drug makers, who depend on these technological advancements to enhance their processes and establish a level playing field in the arena of innovation. Utilizing methodologies such as neural networks, hybrid modeling, and mechanistic modeling, such solutions diligently analyze and predict patterns within vast amounts of cellular data points, often reaching into the trillions. Beyond analysis, bioproduction machine learning applications are capable of intelligently scheduling, executing, and optimizing experiments for researchers, leveraging previous insights and past dataset experiences. As a result, the potential of these technologies grows exponentially with each use, allowing existing systems to unlock new developmental capabilities as time goes on.[1]

The MarketVector™ Bioproduction Tools & Tech ESG Index (MVBIOP) sets a precedent as a pioneering index dedicated to providing pure-play exposure to companies that obtain the majority of their revenue from products and services utilized in the research, development, and production of biologic drugs specifically. The index stands apart from more expansive biopharmaceutical indexes by distinctively excluding firms that are themselves drug manufacturers. Using a thematic approach to dissect multiple broader sectors, the index incorporates five sub-themes collectively referred to or related to the “Bioproduction” industry: Bioproduction, Laboratory Technologies, Clinical Diagnostics, Contract Research, and Contract Manufacturing.

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1 Sarkar C, Das B, Rawat VS, "Artificial Intelligence and Machine Learning Technology Driven Modern Drug Discovery and Development, 10.3390/ijms24032026, Int J Mol Sci., 2023

Industry Growth & Drivers

Growth of Biologic Therapeutics

Over the past several years the world has become familiarized with biologic drugs due to the COVID-19 vaccination. Buzzwords like 'mRNA' and 'spike protein' related to the vaccines circulated widely. They sparked a conversation about the difference between the traditional mechanisms of daily use of small molecule drugs - like ibuprofen - and this seemingly new class of medicine.

In contrast to popular perceptions, Biological drugs have a history stemming back several decades. Concepts such as serum therapy, where serum from animals was injected in humans to produce antibodies, had already been established by the 1970s, and a "biologic revolution" that occurred over the next 20-30 years led to breakthroughs in discoveries of key biologics like monoclonal antibodies[2].

Over the past decade, biologics have continued to gain market share on their small molecule counterparts, growing from ~27% of the total biopharmaceutical pipeline in 2012 to ~45% in 2022[3]. Though partially attributed to COVID-19, biologic drugs have also been known to portray different capabilities for treatments of serious diseases, including the ability to effectively recruit the body's immune system to fight against cancer cells. Therapies like GLP-1, a biologic treatment for obesity and diabetes, grew in projected 2028 total product sales nearly 5-fold from 2021 to 2022, citing Evaluate Pharma's revised estimate of $50B.[2] U.S. President Biden in Autumn 2022 signed an executive order that invested $2B of federal funding in bio-manufacturing infrastructure, while the Office of Therapeutic Products announced plans of increasing headcount by +30%.[3] [4]

Mitigating Risk: Diversifying Revenue Streams Beyond the Traditional Drug Pipeline

Despite the biotechnology industry´s recent growth relative to that of small molecule pharmaceuticals, it still faces many challenges. Regulations set by the U.S. Food and Drug Administration (FDA) and other international government entities pose a major obstacle common between the two industries. For all clinical drug development candidates from 2011-2020, the overall likelihood of approval for strictly Phase 1 clinical trials was just 7.9%. Furthermore, the average timeline of a Phase 1 development candidate will spend 10.5 years progressing to final regulatory approval.[5] As a result of the tight regulation, investors are made aware of the inherent volatility and uncertainty associated with biopharmaceutical stocks, which contributes to their reputation as high-risk reward investments.

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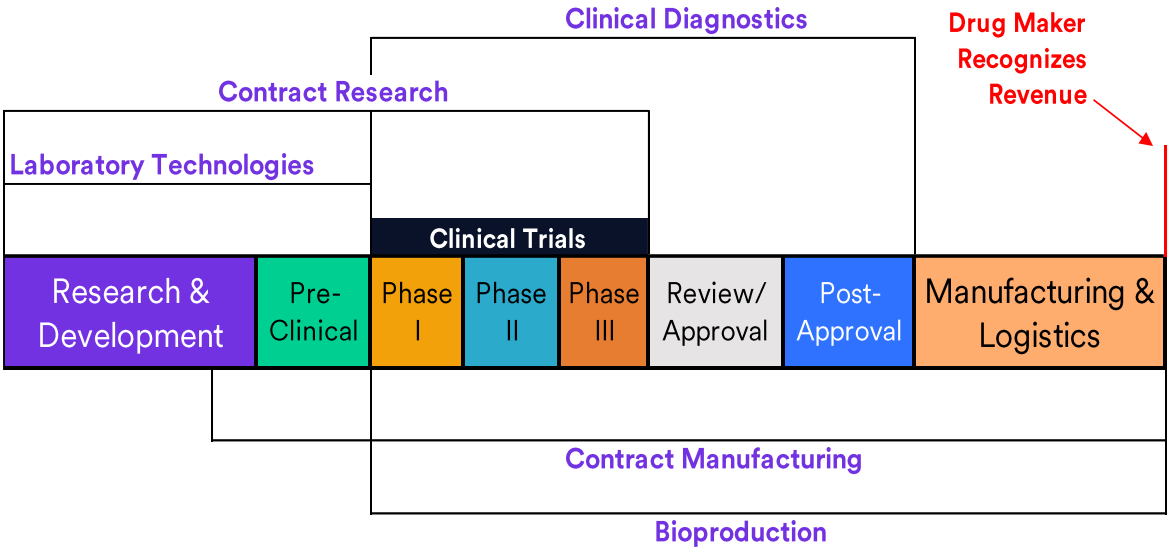
[2] https://www.evaluate.com/vantage/articles/analysis/spotlight/lilly-and-pfizer-fight-new-territory-obesity-and-diabetes
[3].https://www.whitehouse.gov/briefing-room/statements-releases/2022/09/14/fact-sheet-the-united-states-announces-new-investments-and-resources-to-advance-president-bidens-national-biotechnology-and-biomanufacturing-initiative/
[4].https://www.federalregister.gov/documents/2022/09/28/2022-20997/statement-of-organization-functions-and-delegations-of-authority
[5] David Thomas, "Clinical Development Success Rates and Contributing Factors 2011–2020", Informa Pharma Intelligence, 2021

Importantly, these obstacles are more acutely felt by companies that derive revenue potential from product pipelines themselves. While these challenges add risk to drug makers, they also create value for those companies that can help optimize and scale these processes throughout the drug development phase. While drug makers may have to wait more than a decade to realize any revenue from their products, companies that provide raw materials, technology, and services to those drug makers can generate revenue regardless of whether their customer's drugs pass regulatory approvals.

Exhibit 1: Points of Revenue Recognition for Bioproduction Tools & Tech Companies Throughout Biopharmaceutical Timeline by Subtheme*



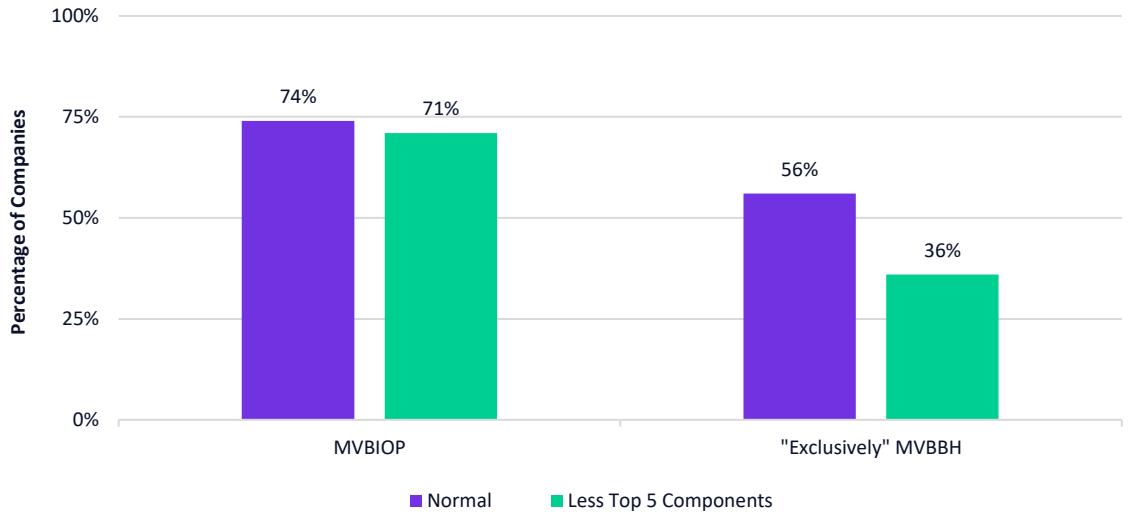
*The Biopharmaceutical Timeline is complex and variable. Companies in given subthemes may recognize revenue from more or less points in the timeline, as well as specialize in processes unmentioned in this exhibit.

Source: MarketVector Indexes™ ("MarketVector"), Adapted from Kesik-Brodacka, M. (2018), Progress in biopharmaceutical development. Biotechnology and Applied Biochemistry, 65: 306-322. https://doi.org/10.1002/bab.1617

Moreover, the unique nature of biologic compounds further incentivizes these very drug makers to seek help from technologies and services that Bioproduction Tools and Tech companies provide. Biologics are derived from living organisms and consist of larger molecular compounds, as such they oftentimes require extensive diligence and caution throughout the manufacturing and research process compared to their synthetically derived counterparts. Two noteworthy embodiments of this can be exhibited through the requirement of practices such as cryostorage to transport raw materials used in biologic development, and the requirement of fill-and-finish services to create administrable therapeutics that frequently require injection instead of oral delivery.

In essence, Bioproduction Tools and Tech companies' position in the Biopharmaceuticals value chain – as a provider of capital goods and consumables - is linked to their track record of year-on-year revenue growth and their ability to generate positive net income, generally speaking. To demonstrate this point, one could consider the components exclusively in a subset of the top 15 biopharmaceutical drug makers by free-float market capitalization, and compare them with the MarketVector™ Bioproduction Tools & Tech ESG Index (MVBIOP) composition:

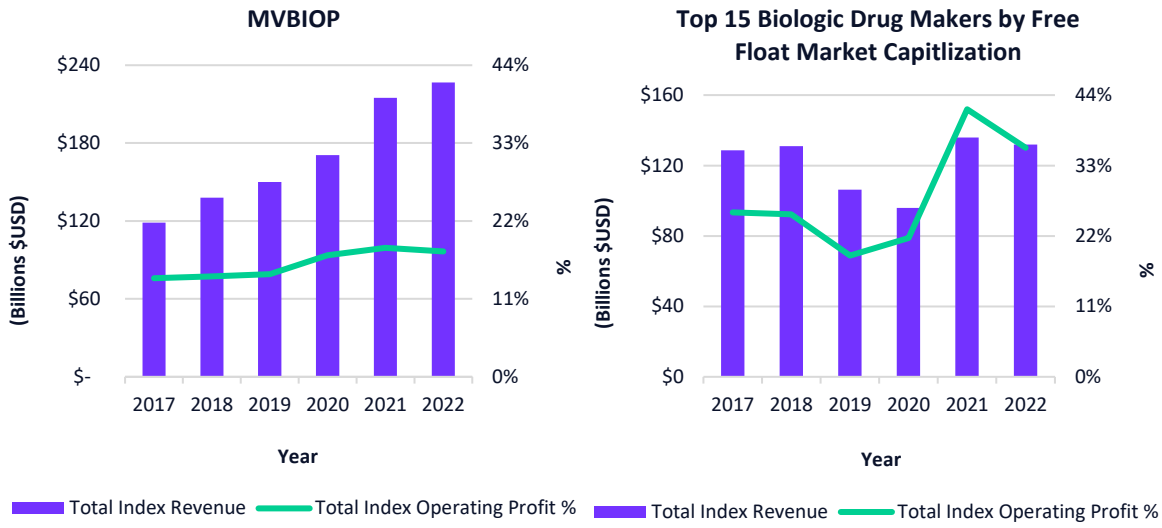
Exhibit 2: Percentage of Companies with Positive Net Income - MVBIOP vs. Top 15 Biopharmaceutical Drug Makers by Free Float Market Capitalization – FY2022



Source: Refinitiv

A comparison of these baskets reveals that in FY2022, 74% of the companies in MVBIOP recorded positive net income, as opposed to 60% of those in the top 15 drug maker category. If the five largest components by market cap are excluded from both subsets, the discrepancy widens even more drastically. Specifically, 71% of companies in MVBIOP alone registered positive net income, contrasting starkly with 40% of those in the top 15 drug makers.

Exhibit 3: Index Level Operating Margin (%) – MVBIOP vs. Top 15 Biopharmaceutical Drug Makers by Free Float Market Capitalization



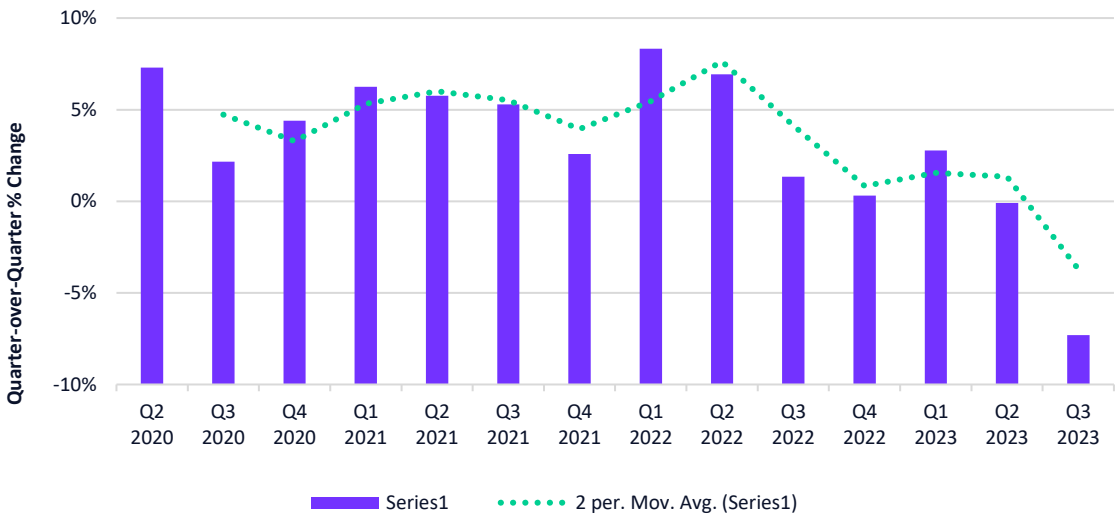
Source: Refinitiv

Additionally, MVBIOP companies show notable differences when comparing the index-level operating profit margin against the same top 15 drug maker subset. From 2018 to 2022, MVBIOP's operating profit margin saw a relatively consistent variability of no more than -0.51% to +2.86% YoY. In contrast, the drug makers' portfolio experienced more variability, with YoY changes oscillating anywhere from -6.4% to +20.1%.

Navigating Through Post-Pandemic Challenges & Emerging Trends in 2024

Faced with the short-term issues of destocking and R&D budgets that were misallocated due to COVID-19 projections, MVBIOP finished 2023 returning -1% YTD. In contrast to what one would expect after a down year, the biopharmaceutical drug and biotechnology pipeline continues to grow larger, with half of the research pipelines predicted to consist of biologics as of December. In 2023, the FDA approved 23 biologics (a record), and GLP-1 growth continued to incentivize companies to adopt to the changing landscape of biopharmaceutical pipelines. As far as inventory issues are concerned, recent stagnation in inventory levels followed by a markedly sharper decrease in the latest quarter for which data is available, suggests that inventory may be beginning to normalize. More significantly, the emphasis on inventory and R&D spending is shifting away from COVID-19-related products to biologics that are in far higher demand, leading to a more consolidated inventory that aligns with the current state of this burgeoning biologic revolution.

Exhibit 4: Index-Level Total Inventory % Change by Quarter – MVBIOP



Source: Refinitiv

Sub-Themes Included in MVBIOP

Bioproduction

The Bioproduction sub-theme consists of companies that provide a broad range of instruments, consumables, raw materials, technologies, and services that are used by customers to **manufacture** new biological therapeutics and vaccinations. Companies within this sub-theme focus on providing their products and services to the production side of the biopharmaceutical industry, with some overlap in research and development.

Example products and services in this sub-theme include but are not limited to:

- High-quality "Raw" DNA, mRNA, and plasmids used as the building blocks of biopharmaceuticals
- Gene and Cell Delivery Vectors designed to deliver genetic material directly into a cell accurately while simultaneously increasing manufacturing yields
- RNA Service solutions designed to optimize formulas and ratios for unique gene editing processes
- Bio-Filtration Mechanisms, Cell Cultures, and Fermentation Equipment designed to remove contaminants, increase scale of manufacturing, and minimize rejects
- Panels of disease, antibodies, and antigens that aid manufacturers in identifying and testing quality and immune response to biopharmaceuticals as they are created on a scale
- Hypothermic and Cryopreservation Services used to transport and control the highly volatile biological materials used in therapeutics

Laboratory Technologies

The Laboratory Technologies sub-theme consists of companies that focus on specialty products, devices, technologies, and services for the research and development of Biopharmaceuticals. These products and services are highly specialized in R&D processes and laboratory research, and serve the purpose of detection, quantification, automation, and enhanced analysis for highly specific biological research on cells and their attributes.

Example products and services in this sub-theme include but are not limited to:

- Automated Electrophoresis Systems designed to separate DNA, RNA, or protein molecules and their electrical charge
- Cloning Vector Kits designed to generate and clone cells with extremely high precision and optimization to the researcher's specific case
- Modifying Enzymes which are used as raw inputs designed for cloning and duplication of cell components
- Silicon Chip Microarray Technology for Oligo Pools that are capable of producing millions of unique single-stranded segments of DNA

Contract Research

The Contract Research sub-theme consists of companies that derive a majority of their revenue from operating as third-party research and development contractors for biologics. Companies within this segment are contracted by Biopharmaceutical drug makers and have focused on services that aid in the research of biopharmaceutical prospects (discovery services), and the analysis of clinical research/trials (analytical services). In addition, companies within this sub-theme also have a focus on services that provide aid in regulation, safety, and good laboratory practice (lab safety assessment services).

Example services in this sub-theme include but are not limited to:

- Phase I-IV Clinical Development Services that provide developmental plan design, coordinated central laboratory services, project management, regulatory guideline affairs, clinical monitoring, and clinical data analysis and management
- Biologic Compound Discovery Services which are non-regulated services to assist clients with the identification, screening, and selection of the lead compound for drug development
- Biopharmacovigilance Services designed to assess, understand, and prevent adverse side effects to a clinical patient population
- Good Laboratory Practice (GLP) Services designed to aid companies in adhering to the guidelines of GLP, a detailed set of laboratory conduct regulations enforced by regulatory bodies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA)

Contract Manufacturing

The Contract Manufacturing sub-theme consists of companies that act as third-party custom development and manufacturing of predominately biologic drugs or drug delivery systems for biotherapeutics. Companies within this subtheme are contracted by Biopharmaceutical drug makers and research institutions to aid in or handle, end-to-end production of biologic medicines and administration systems to enhance scale, efficiency, and regulatory compliance.

Example services in this sub-theme include but are not limited to:

- Process Development Services that aid biopharmaceutical companies with process optimization, scale-up, technology transfer, and process characterization
- Bioprocessing Services designed to aid companies in large-scale processes like cell cultures, fermentation, and downstream processing using facilities, technology, equipment, and expertise
- Good Manufacturing Practice (GMP) Services designed to aid companies in adhering to the guidelines of GMP, a detailed set of manufacturing conduct regulations enforced by regulatory bodies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA)
- End-to-End Manufacturing Services that operate the entire manufacturing process of biologic drugs and/or biologic drug delivery systems as a third-party contractor

Clinical Diagnostics

The Clinical Diagnostics sub-theme is somewhat distinctive as it overlaps with the research/clinical trial aspect of biologic therapeutics as well as the healthcare services industry. Companies within this sub-theme provide technology and services that provide the biological testing of individuals for researcher and medical practitioner use cases. Clinical Diagnostics companies may focus on analysis of clinical trial patient results and testing, specialty genetic tests for diagnosis of healthcare patients, or custom biologic tests for research or diagnosis of rare diseases.

Example products and services in this sub-theme include but are not limited to:

- Hereditary Cancer Test Panels designed to use NGS technology to provide information to patients about the presence and absence of mutations in the tested genes, assessing the risk of an individual's likelihood of a genetic cancer
- Carrier Screenings that can be used to target correct patient populations for clinical trial use or optimizing strategies for treating patient populations
- Biomarker Testing Services designed to assess residual and genetic risk within patients using the analysis of the components of the blood and other biological samples

Example Companies in MVBIOP

Agilent Technologies, Inc. (Laboratory Technologies)

Based in California, Agilent Technologies Inc. specializes in providing high-tech instruments and software for life science laboratories. Their product range covers the entire laboratory workflow and includes spectrometry instruments, automated machine-learning processes, and application-centric platforms. They also offer diagnostics and genomics services focused on DNA and gene analysis. Their global presence and advanced technologies like NGS products and CRISPR solutions position them as leaders in Laboratory Technologies.

Charles River Laboratories International, Inc (Contract Research)

Founded in 1947 in Massachusetts, Charles River Laboratories offers drug discovery services, specializing in in vivo research, and sells biologic research models. Their services target pharmaceutical companies, academic institutions, and government labs, providing end-to-end research and development outsourcing. They also provide safety assessment services and a variety of research models, including genetically engineered mice and human-derived cellular material. Their focus is on reducing costs and accelerating development for clients.

Lonza Group AG (Contract Manufacturing)

Lonza Group AG is a leading contract development and manufacturing organization for Biopharmaceuticals, supporting processes from late discovery to commercial manufacturing. They specialize in various manufacturing areas including mammalian, microbial, bio conjugates, and mRNA drug substances. They offer innovative technologies like GS PiggyBac and mRNA commercialization technology, used in Moderna's COVID-19 vaccine. Their services extend to regulatory consulting, bioassay qualifying, and advanced bioprocessing solutions.

Repligen Corporation (Bioproduction)

Repligen Corporation supplies technology and raw inputs for biopharmaceutical production, including monoclonal antibodies and vaccines. They have four main franchises: Filtration, Process Analytics, Chromatography, and Proteins. Their technologies include XCell ATF Cell Retention Systems and TangenX Flat Sheet Cassettes for bioprocessing, and sensors for maintaining optimal production conditions. Repligen's comprehensive expertise makes it a key partner for biotech companies in scaling and setting new manufacturing standards.

Quest Diagnostics Incorporated (Clinical Diagnostics)

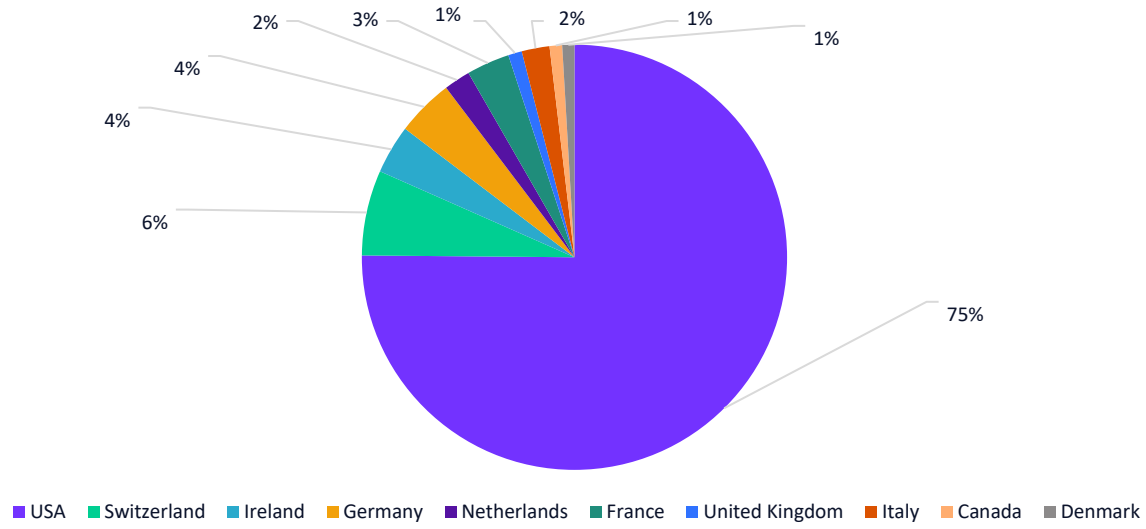
Quest Diagnostics Incorporated, a leader in diagnostic information services, provides critical biological testing services for healthcare providers and laboratories. Their services include routine and advanced diagnostics, with the latter focusing on genetic and molecular testing for precision medicine. They also offer Diagnostic Services to enhance healthcare efficiency and support population health initiatives. During the COVID-19 pandemic, Quest Diagnostics has been instrumental in providing diagnostic and antibody serology tests.

Exhibit 5: Top 25 Components by Subtheme

Company Name	Country	Weight (Capped)	SubTheme
Thermo Fisher Scientific Inc.	USA	5.00%	Laboratory Technologies
Danaher Corporation	USA	5.00%	Bioproduction
Lonza Group AG	Switzerland	5.00%	Contract Manufacturing
IQVIA Holdings Inc.	USA	5.00%	Contract Research
Agilent Technologies Inc.	USA	4.50%	Laboratory Technologies
West Pharmaceutical Services Inc.	USA	3.84%	Bioproduction
Mettler-Toledo International Inc.	USA	3.75%	Laboratory Technologies
Illumina Inc.	USA	3.49%	Bioproduction
ICON Public Limited Company	Ireland	3.31%	Contract Research
Laboratory Corporation of America Holdings	USA	2.93%	Clinical Diagnostics
Hologic Inc.	USA	2.60%	Clinical Diagnostics
Waters Corporation	USA	2.31%	Laboratory Technologies
Sartorius Aktiengesellschaft Preferred	Germany	2.28%	Bioproduction
Quest Diagnostics Incorporated	USA	2.28%	Clinical Diagnostics
Avantor Inc.	USA	2.20%	Laboratory Technologies
Exact Sciences Corporation	USA	2.17%	Clinical Diagnostics
Bio-Techne Corporation	USA	2.14%	Laboratory Technologies
Charles River Laboratories International Inc.	USA	2.00%	Contract Research
QIAGEN N.V.	Netherlands	1.88%	Laboratory Technologies
Revvity Inc.	USA	1.88%	Clinical Diagnostics
Sartorius Stedim Biotech S.A.	France	1.78%	Bioproduction
Repligen Corporation	USA	1.76%	Bioproduction
Bio-Rad Laboratories Inc.	USA	1.74%	Clinical Diagnostics
Catalent Inc.	USA	1.56%	Bioproduction
Natera Inc.	USA	1.56%	Clinical Diagnostics

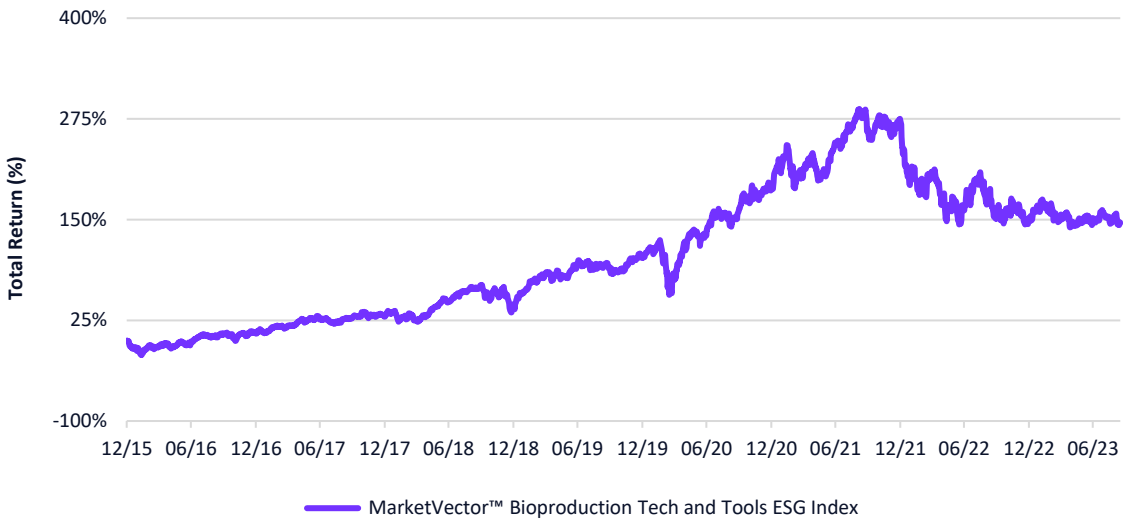
Source: MarketVector.

Exhibit 6: Components by Country - MVBIOP



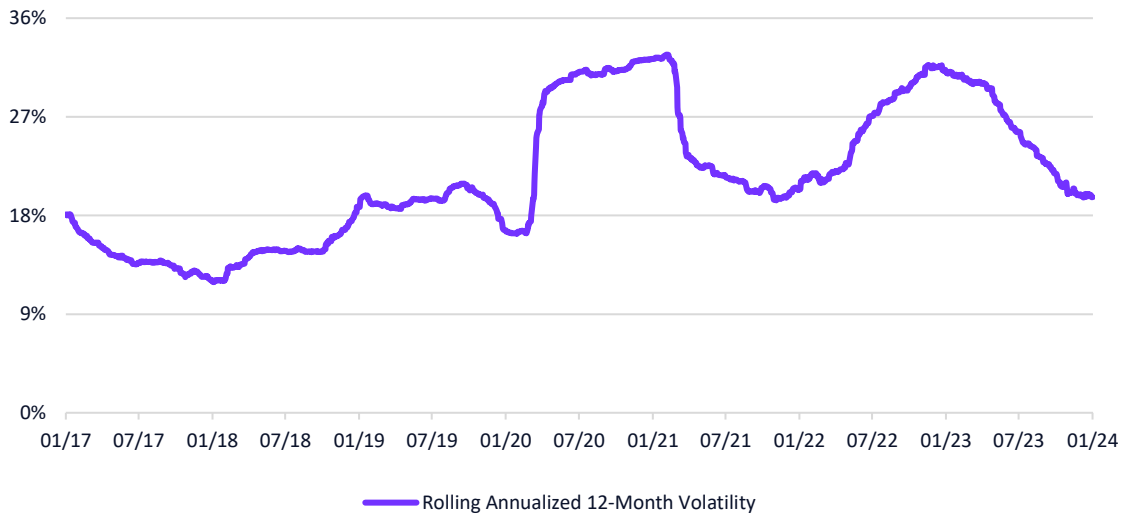
Source: MarketVector.

Exhibit 7: Historical Return – MVBIOP (TR)



Source: MarketVector.

Exhibit 8: Rolling Annualized 12-Month Volatility - MVBIOP (TR)



Source: MarketVector.

Important Definitions and Disclosures

It is not possible to invest directly in an index. Exposure to an asset class represented by an index is available through investable instruments based on that index. MarketVector does not sponsor, endorse, sell, promote, or manage any investment fund or other investment vehicle that is offered by third parties and that seeks to provide an investment return based on the performance of any index. MarketVector makes no assurance that investment products based on the index will accurately track index performance or provide positive investment returns. MarketVector is not an investment advisor, and it makes no representation regarding the advisability of investing in any such investment fund or other investment vehicle. A decision to invest in any such investment fund or other investment vehicle should not be made in reliance on any of the statements outlined in this document.

Prospective investors are advised to invest in any such fund or another vehicle only after carefully considering the risks associated with investing in such funds, as detailed in an offering memorandum or similar document that is prepared by or on behalf of the issuer of the investment fund or other vehicle. The inclusion of a security within an index is not a recommendation by MarketVector to buy, sell, or hold such security, nor is it considered to be investment advice.

All information shown prior to the index launch date is simulated performance data created from backtesting ("Simulated past performance"). Simulated past performance is not actual but hypothetical performance based on the same or fundamentally the same methodology that was in effect when the index was launched. Simulated past performance may materially differ from the actual performance. Actual or simulated past performance is no guarantee for future results.