FROST & SULLIVAN

Helio Genomics

2022 COMPANY OF THE YEAR

North American Liver Cancer Early Detection with Liquid Biopsy Industry

Best Practices Criteria for World-Class Performance

Frost & Sullivan applies a rigorous analytical process to evaluate multiple nominees for each award category before determining the final award recipient. The process involves a detailed evaluation of best practices criteria across two dimensions for each nominated company. Helio Genomics excels in many of the criteria in the liver cancer early detection with liquid biopsy space.

Diagnostics Challenges for Early Cancer Detection and Surveillance

To address the unmet clinical needs for patient-centric healthcare delivery in cancer requires advancing precision diagnostics capabilities, including instrument, assay, technology, and informatics. Conventional tissue biopsy techniques are invasive, require hospitalization, and do not represent the tumor heterogeneity appropriately, limiting targeted patient selection for clinical trials for personalized therapies. Furthermore, traditional diagnostic imaging modalities are inconvenient, expensive, and poor predictors of early-stage cancer. In contrast, next-generation sequencing-based liquid biopsy (LBx) advances precision medicine for cancer. It empowers individuals to check and detect the disease at a treatable stage, improving the survival rate significantly. Additionally, linking automation to digital technologies improves efficiency and productivity; this includes leveraging artificial intelligence (AI) to enhance workflow and accuracy.

However, tissue-based testing and imaging still operate as the gold standard in cancer care, making liquid biopsies a complementary tool. Additionally, most regulatory bodies that set cancer screening guidelines require clinical utility studies conducted on large population sets, which can take up to seven years, limiting LBx market growth. Government support poses another challenge, arising from the limited reimbursement (non-coverage for panel-based tests) due to variation in coverage policies by private payers. Besides, the lack of a standardized framework for approving LBx tests for different analytes limits clinical adoption. Clinical sensitivity appears to be an immediate challenge in detecting LBx analytes compared to hematological markers in the blood sample.

Frost & Sullivan estimates the LBx market will reach $7,015.6 million by 2025, with a compound annual growth rate of about 14% from 2019 to 2025.[1] Precision oncology-related applications constitute the predominant segment during the forecast period. Helio Genomics (Helio) uniquely leverages its technology to meet its customer's needs. It is well-positioned to capitalize on new growth opportunities, cementing its leadership in the AI-enabled LBx market.

Founded in 2014 and headquartered in California, the United States (US), Helio is a cancer diagnostics technology and tests developer. Recently renamed (previously Helio Health), the company's new identity reflects its consistent focus on developing (from concept) and advancing cutting-edge AI-enabled technologies in genomics to detect and screen cancer at its earliest stage. Helio provides the healthiest and safest diagnostic technologies for the medical community to drive curative precision medicine for cancer.

Helio Genomics Mission: Simple and Accurate Early Cancer Detection

Helio's vision centers on detecting cancer early with the stated purpose of saving lives. It connects deep-seated domain and operational knowledge with advanced technology to facilitate individuals to check for cancer quickly, early, and often, enabling them to ensure the wellness of their everyday health. The company's scientific team employs a multi-dimensional approach. It leverages AI and machine learning to recognize distinctive and proprietary DNA signatures and combine them with protein biomarkers to predict cancer presence as early as stage I.

Innovative Technology Design

Helio's breakthrough technology design involves two primary concepts. Firstly, the wet-lab platform component ECLIPSE™ covers entire steps from cell-free DNA (cfDNA) extraction from plasma to the library preparation and next-generation sequencing (on the Illumina platform). Secondly, the company employs a unique enzymatic DNA conversion approach, gentler and more efficient than traditional bisulfite DNA conversion methods used by competing LBx technologies known to damage the DNA and signals.

Hence, Helio's technology provides a higher quantity and quality of converted DNA that heightens the sensitivity and specificity of its LBx test versus other commercially available LB methods. Furthermore, the process leverages a cellular heterogeneity-adjusted clonal methylation technique that accurately identifies methylation patterns and improves test diagnostic performance compared to standard methods.[2]

HelioLiver™: First-of-its-kind Early Liver Cancer LBx

With incidence (more than tripled) and mortality (doubled) rapidly growing since 1980,[3] Helio realized the high clinical need to test for liver cancer early. The company employed its decade-old robust research and development (R&D) and novel AI-enabled technology to develop the first-of-its-kind liver cancer test, HelioLiver™, holding a soft launch (with a selected customer group) in December 2021. The multianalyte test detects liver cancer early, addressing the challenges of existing surveillance and diagnostic methods.

[1] *United States Liquid Biopsy Growth Opportunities*, (Frost & Sullivan, February 2022)
[2] https://www.nature.com/articles/d43747-022-00065-x#ref-CR3, accessed June 2022
[3] https://www.cancer.org/cancer/liver-cancer/about/what-is-key-statistics.html, accessed June 2022

> *"The multianalyte test incorporates cfDNA methylation patterns (77 methylation sites) and three serum protein markers to indicate whether early-stage (stage I and II) hepatocellular carcinoma (HCC) is present. Hence, HelioLiver informs providers and patients to initiate curative treatment early, heightening HCC's survival rate multifold."*
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> ***- Supriya Lala,***
> ***Best Practices Research Analyst***

With several studies pointing to early cancer detection improving clinical outcomes and survival rates 12 times higher than late detection, HelioLiver is a groundbreaking discovery. The multianalyte test incorporates cfDNA methylation patterns (77 methylation sites) and three serum protein markers to indicate whether early-stage (stage I and II) hepatocellular carcinoma (HCC) is present. Hence, HelioLiver informs providers and patients to initiate curative treatment early, heightening HCC's survival rate multifold.[4]

With first mover advantage, Helio's compelling value proposition underpins its sustained success. Rich biological data-trained algorithms support its performance. As a result, the multianalyte test's reliability and quality are unmatched by ultrasound, the current standard of care that suffers from low sensitivity.

HelioLiver's sensitivity outperformed other detection tools (alpha-fetoprotein and the GALAD model) as per the data presented at The Liver Meeting® in 2021. It demonstrated 76% early-stage sensitivity and 85% overall HCC sensitivity at 91% specificity, thus, establishing the test's promise to advance the standard of care for early-stage liver cancer detection.

"Sequencing at scale and advanced AI/deep-learning techniques have enabled valuable insights from biomarkers in our blood. Helio has proven this with its first test, HelioLiver, which can detect small-lesion hepatocellular carcinomas (HCC) where traditional imaging tools fall short."[5]

Justin Chen Li, CEO of Helio Genomics

Roadmap to Success: Customer-centric, Continuous, Proactive Approach to Screening

With its customer-centric corporate philosophy, Helio operates on the central tenet that its success depends on customer satisfaction. This philosophy permeates the company's daily practices. Helio's patient-first commitment drives its personalized approaches to early cancer testing, enabling regular surveillance for people at a high risk of cancer development. Furthermore, its testing solution helps providers and patients proactively manage the disease on time.

High cost and low convenience deter patients from undergoing regular cancer surveillance. Hence, the company ensures that its test is universally accessible, affordable, and easy to use. The high-throughput automated technology enhances customer (payers, providers, patients) experience by providing a seven-day turnaround time, easily-readable results, and understandable science.

Diagnostic imaging (e.g., ultrasound, computed tomography, magnetic resonance, colonoscopy, and mammography) involves individuals visiting a specialist. In contrast, any nurse practitioner or mobile phlebotomist can conduct Helio's test from a simple blood draw during a patient's routine check-up. It thus removes diagnostic barriers to routine screening and improves patient adherence.

[4] https://heliohealth.com/solutions, accessed June 2022
[5] https://www.nature.com/articles/d43747-022-00065-x

At the same time, the company's bioinformatics platform, namely multimodal epigenetic signatures, analyses several types of markers (nucleosome occupancy, methylation, and fragmentation markers) in a single laboratory workflow, lowering costs.

> *"HelioLiver provides richer biological data than competing technologies, delivering greater test sensitivity and specificity. Simultaneously, by enabling early cancer detection, the test eliminates the potential need for expensive therapies and diagnostics (at late-stage detection), lowering the overall cost burden of the healthcare economy."*
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> ***Best Practices Research Analyst***

Without increasing the turnaround time and cost, HelioLiver provides richer biological data than competing technologies, delivering greater test sensitivity and specificity. Simultaneously, by enabling early cancer detection, the test eliminates the potential need for expensive therapies and diagnostics (at late-stage detection), lowering the overall cost burden of the healthcare economy. Operational convenience, affordability, and restricted care expenses will spur HelioLiver's adoption in the mainstream medical community enabling it to emerge as the new standard of care for liver cancer diagnostics.

Helio meets with customers to assess their specific needs and develop tailored solutions with roadmaps for seamless execution. This foundational approach establishes ongoing trust with customers for long-lasting relationships extending throughout the product's lifecycle. The company staffs a large sales force so that every individual handles only a few accounts. They identify the distinctive pain points the doctors face based on the unique logistics of every clinical setting. Simultaneously, the test purchase procedures (paperwork, blood draw, and logistics) are straightforward. By providing a seamless sales and customer service experience, Helio aims to retain customers and drive recurring business for its testing platform in line with the standard of care guidelines for cancer screening that require routine cancer testing within defined time intervals.

To acquire new customers, the company collaborates with leading scientists, physicians, cancer research centers, medical institutions, and business leaders globally to advance cancer research through multiple pivotal, multi-center clinical trials. For example, to compare HelioLiver 's sensitivity and specificity with ultrasound within a population at high risk of HCC due to liver cirrhosis, Helio is enrolling patients in its US-based CLiMB study. It is also conducting the LIVER-1 clinical trial to evaluate and validate the Helio LBx within individuals at high risk for HCC due to liver disease/cirrhosis and HCC-positive patients. Other notable studies include:

- The Victory study in China (recently concluded) analyzed HelioLiver's performance characteristics in various patient groups.
- The prospective FAST study (funded by National Cancer Institute in association with Mount Sinai and other US clinical organizations) assesses novel screening modalities and biomarkers.
- The ELITE study aimed to uncover novel colon, lung, and breast cancer biomarkers.

Positioned for Growth: Partnerships, Test Pipeline, and Branding Strategy

Since its inception, Helio's sterling reputation and customer-centric framework led to its coveted preferred partner status. Over the years, it added a range of new customers and partners to its established base. The company has an extensive laboratory infrastructure in California. It partners with FUJIFILM Medical Systems USA, Inc, a leading medical devices manufacturer that provides their 510(k)-cleared µTASWako® i30 Immunological test system for liver cancer biomarkers supporting Helio's liver test. Its technology partners include Qiagen for DNA extraction and Illumina for sequencing.

The company collaborates with over 75 US-based hospitals, such as Cedars-Sinai, Sanford, and Harvard, to further improve its technology. These organizations provide extensive patient samples and clinical data to train the company's algorithms continuously, support R&D, and expand the technology's application to other cancer types. Furthermore, it partners with several advocacy groups, such as Blue Faery, the Hepatitis B Foundation, and the American Liver Foundation, to raise awareness about its test's usability and educate patients on the need for routine cancer screening, driving wider test adoption.

With the plan to submit the Food and Drug Administration application in 2023, Helio expects approval for HelioLiver in 2024 to begin a full-fledged commercial launch and increase the size of its sales force henceforth. Although the initial focus is the US, it will work with partner organizations in Canada, Australia, China, and Japan, to navigate regulatory requirements and design distribution channels in those regions.

With its core focus on multimodal epigenetics, the company continues to advance its technology to support precision oncology. To that end, Helio pursues algorithm improvements to upgrade its current test and develop new tests, expanding its pipeline. Its technology progression covers nearly 20 other cancer modalities (e.g., breast, cervical, nasopharyngeal, and lung) and other parts of the cancer care continuum, including minimal residual disease and treatment recurrence monitoring. Its second products are a colon test and a multi-cancer detection test (focusing first on gastrointenstinal cancers), with a scheduled launch planned before the end of 2022.

Helio’s branding strategy aims to establish the company as a consumer brand and a household name for cancer testing. It works with media outlets, non-profit organizations, and physician networks to maximize awareness and leverages distribution partners to enhance brand reach. For example, its commercial partner, Fulgent Genetics, Inc, will supply HelioLiver in the US and Canada. The company's advertising campaign centers around 'peace of mind' and a vision to make cancer manageable.

Frost & Sullivan believes Helio is well-positioned to drive liver cancer early detection with liquid biopsy, leveraging the technology into its next growth phase, capturing market share, and sustaining its leadership in LBx in the coming years.

Conclusion

Helio Genomics' (Helio) artificial intelligence and machine learning-powered breakthrough technology enables the development of novel cancer detection tests to address current cancer surveillance challenges.

Helio's first-in-line flagship product, HelioLiver™, is a multianalyte blood test. It uses cell-free DNA methylation patterns and serum protein markers to detect early-stage hepatocellular carcinoma (HCC) from a simple blood draw during routine patient screening. Easy-to-use, cost-effective, universally accessible, and more sensitive than conventional diagnostics, HelioLiver promises to redefine cancer care by identifying early-stage HCC, one of the fastest-growing and deadliest cancers worldwide. By eliminating diagnostic barriers, the multianalyte test will drive patient adherence to surveillance guidelines to better manage liver cancer and initiate life-saving treatment interventions on time.

The company addresses the unmet needs with a strong leadership focus that incorporates customer-centric strategies and exemplifies best practice implementation. Besides a rapid seven-day turnaround time and easily-readable results, HelioLiver provides richer biological insights to detect cancer presence accurately, constraining the need for potential expensive therapies and lowering the overall cancer care cost burden. Furthermore, the test is easy to order and conduct, delivering a frictionless experience for physicians and patients. Helio continues to enrich the clinical data supporting the test's clinical utility through studies and simultaneously focuses on establishing a strong brand presence for cancer management.

Helio remains a trusted partner, earning a reputation for offering the overall best in early cancer detection with liquid biopsy. With its core focus on multimodal epigenetics, the company continues to advance its technology to support precision oncology. Ongoing early cancer detection and surveillance development efforts include nearly 20 other cancer types and various parts of the cancer care continuum, such as minimal residual disease and treatment recurrence monitoring.

With its strong overall performance, Helio Genomics earns Frost & Sullivan's 2022 North American Company of the Year Award in the liver cancer early detection with liquid biopsy market.

What You Need to Know about the Company of the Year Recognition

Frost & Sullivan's Company of the Year Award is its top honor and recognizes the market participant that exemplifies visionary innovation, market-leading performance, and unmatched customer care.

Best Practices Award Analysis

For the Company of the Year Award, Frost & Sullivan analysts independently evaluated the criteria listed below.

Visionary Innovation & Performance

Addressing Unmet Needs: Customers' unmet or under-served needs are unearthed and addressed by a robust solution development process

Visionary Scenarios Through Mega Trends: Long-range, macro-level scenarios are incorporated into the innovation strategy through the use of Mega Trends, thereby enabling first-to-market solutions and new growth opportunities

Leadership Focus: Company focuses on building a leadership position in core markets and on creating stiff barriers to entry for new competitors

Best Practices Implementation: Best-in-class implementation is characterized by processes, tools, or activities that generate a consistent and repeatable level of success

Financial Performance: Strong overall business performance is achieved in terms of revenue, revenue growth, operating margin, and other key financial metrics

Customer Impact

Price/Performance Value: Products or services provide the best value for the price compared to similar market offerings

Customer Purchase Experience: Quality of the purchase experience assures customers that they are buying the optimal solution for addressing their unique needs and constraints

Customer Ownership Experience: Customers proudly own the company's product or service and have a positive experience throughout the life of the product or service

Customer Service Experience: Customer service is accessible, fast, stress-free, and high quality

Brand Equity: Customers perceive the brand positively and exhibit high brand loyalty

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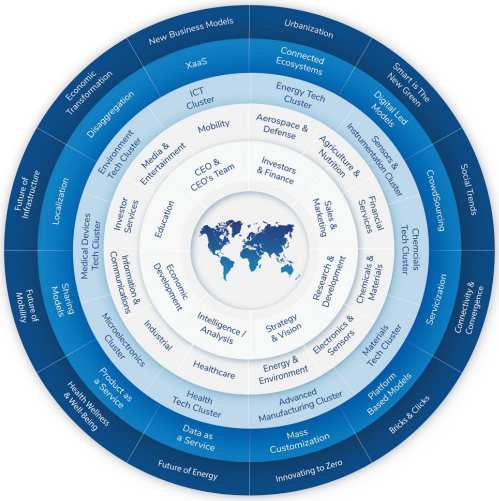
- **Growth Pipeline:** *Continuous Flow of Growth Opportunities*
- **Growth Strategies:** *Proven Best Practices*
- **Innovation Culture:** *Optimized Customer Experience*
- **ROI & Margin:** *Implementation Excellence*
- **Transformational Growth:** *Industry Leadership*

The Innovation Generator™

Our 6 analytical perspectives are crucial in capturing the broadest range of innovative growth opportunities, most of which occur at the points of these perspectives.



Analytical Perspectives:

- Mega Trend (MT)
- Business Model (BM)
- Technology (TE)
- Industries (IN)
- Customer (CU)
- Geographies (GE)