

F R O S T & S U L L I V A N

FROST & SULLIVAN BEST PRACTICES AWARD

LIQUID BIOPSY FOR PRECISION ONCOLOGY  
ASIA-PACIFIC

Growth Excellence Leadership  
2019



FROST & SULLIVAN

2019

BEST  
PRACTICES  
AWARD

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## Background and Company Performance

### *Industry Challenges*

Cancer is a serious public health concern. The International Agency for Research on Cancer reported nearly 18.1 million new cancer diagnoses globally in 2018 and expects newly diagnosed cases to reach 29.5 million by 2040.<sup>1</sup> Worldwide, one in six deaths is cancer-related, 9.6 million in 2018.<sup>2</sup> Global patterns depict nearly half of the new cases are from Asia—recorded about 8.8 million cases in 2018, growing to 14.5 million by 2040.<sup>3</sup> China alone totaled 4.3 million newly diagnosed cancers the same year—close to a quarter of all new global cases.<sup>4</sup>

Cancer's cost burden over the care continuum spreads across diagnostics, treatment, and survivorship. The global financial impact estimated at \$ 1.16 trillion in 2010 is consistently growing due to rising cancer incidence and prevalence. Based on surveys done by National Cancer Institute (US) and Chinese Journal of Cancer Research (China), Frost & Sullivan estimates direct medical costs of cancer in the United States (US) at \$147 billion and in China at \$39 billion in 2017.<sup>5</sup>

In an era of value-based care, focus on low-cost and improved patient outcomes is profound, driving precision oncology. Genomic and epigenomic data provide better insights into the tumor's molecular characteristics to determine targeted therapies across the care pathway. However, tissue biopsy, the current gold standard, does not fully realize precision oncology's potential, having several limitations—invasive, associated with complications, time-consuming (several weeks), delays treatment, costly, tumor site-specific.

In comparison, liquid biopsy (LB) is a minimally invasive diagnostic tool to identify cancer-specific biomarkers and has the potential to detect the presence of cancer at its earliest stages. In the US alone, the breast and colorectal cancer (CRC) screening expenditure was nearly \$9 billion in 2018, denoting tremendous potential for early cancer screening tests in these segments.<sup>6</sup> The technology is rapid, and provides a holistic tumor profile. Thus, blood-based circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) are emerging as a new frontier in cancer diagnostics given the advantages over traditional tissue-based methods and applicable for early cancer detection, therapy identification, and recurrence monitoring.

These biomarkers are gaining momentum in clinical care, advancing precision oncology through improved healthcare outcomes while lowering care expenses.

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<sup>1</sup> International Agency for Research on Cancer. "Estimated number of incident cases from 2018 to 2040, all

<sup>2</sup> Ibid

<sup>3</sup> Ibid

<sup>4</sup> International Agency for Research on Cancer. "Estimated number of incident cases from 2018 to 2040, all cancers, both sexes, all ages." 2018. Cancer Tomorrow - IARC. August 2019 <[https://gco.iarc.fr/tomorrow/graphic-bar?type=0&population=900&mode=population&sex=0&cancer=39&age\\_group=value&apc\\_male=0&apc\\_female=0#collapse-group-0-3](https://gco.iarc.fr/tomorrow/graphic-bar?type=0&population=900&mode=population&sex=0&cancer=39&age_group=value&apc_male=0&apc_female=0#collapse-group-0-3)>.

<sup>5</sup> *Growth Opportunities in the Global Liquid Biopsy Market, 2018* (Frost & Sullivan, October 2018)

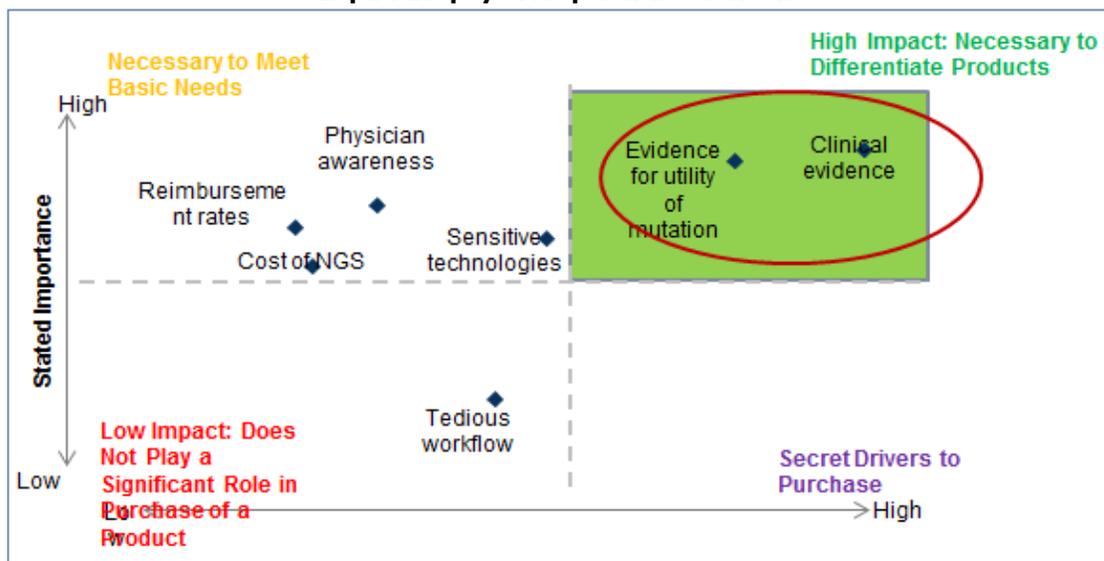
<sup>6</sup> Ibid

### Adoption Barriers

There are significant barriers to LB adoption. Several assays designed on high-cost next-generation sequencing (NGS) technology lack test reimbursement, inhibiting market uptake. Price points will enable access to a larger population in India, China, and Japan, which rely heavily on out-of-pocket costs and for the procedure to be reimbursed by payers. Payers within geography must agree to cover the test and reimburse at a level that will allow stakeholders in the value chain to be successful.<sup>7</sup>

Moreover, establishing clinical utility and clinical evidence are substantial bottlenecks. Tissue-based testing and imaging are still the standards of care, leaving LB as surrogate testing complementary to tissue biopsy. Furthermore, ctDNA detection is dependent on the biology of the tumor and the amount of tumor DNA that is shed. In some cases, the concentration of ctDNA in the blood is too small to be detected. Globally, East Asia is second in terms of active clinical trials in the area of liquid biopsy, with China reporting the maximum number of trials. Hence, companies must design and develop randomized

**Liquid Biopsy—Adoption Bottlenecks**



Source: Frost & Sullivan

controlled trials and inclusion in guidelines to promote broader adoption and favorable payer coverage in Asia Pacific. The market in China will also show early adoption, prior to clinical utility, with a large population of self-paying patients potentially willing to afford the full cost of the tests prior to a national insurance decision.

Companies leveraging cutting-edge technology to develop a highly specific and sensitive, guideline-integrated, blood-based test will potentially reduce cancer care costs, can effectively displace tissue-based methods and emerge as market leaders. Frost & Sullivan’s end-user interviews with clinicians and oncologists reinstate the critical need for establishing clinical validity and utility for broader adoption. Vendors must emphasize regulatory and reimbursement strategies, payers and physician awareness, and affordable prices for more widespread adoption.

<sup>7</sup> Growth Opportunities in the Global Liquid Biopsy Market, 2018 (Frost & Sullivan, October 2018)

## *Growth Performance and Customer Impact of Guardant Health AMEA*

Guardant Health (GH) partnered with SoftBank to form Guardant Health AMEA (GH AMEA), a joint venture (JV) to scale commercial capabilities in Asia, the Middle East, and Africa (AMEA), with an initial focus on Japan. GH AMEA established its Singapore headquarters in November 2018 to meet cancer management needs in the region. The company's clinical trial studies on Asian patients aim to advance precision oncology for lung, breast, gastric, and colorectal cancers, all highly prevalent in Asia. GH AMEA offers its flagship LB test, Guardant360<sup>®</sup>, for clinical and biopharma customers (research use).

### **Comprehensive Genomic Profiling and Rapid TAT Instituting a Blood-First Paradigm for Standard of Cancer Care**

The Guardant360<sup>®</sup> test reached the market in 2014. The test enables oncologists in treatment selection in advanced cancers and assists pharmaceutical companies in bringing novel therapeutics to market quickly. Till-date, more than 6,000 oncologists have ordered the test over 100,000 times.<sup>8</sup> In addition, over 50 biopharmaceutical companies and 28 US-based National Comprehensive Cancer Network (NCCN) institutions use Guardant360<sup>®</sup>. Till-date, the test's performance has been reported in more than 130 peer-reviewed publications—establishing the analytical and clinical validity and clinical utility of the assay for several solid tumors.

Guardant360<sup>®</sup> successfully introduced in Japan with GH AMEA conducting two large clinical trials for lung and gastrointestinal tract cancers

Guardant360<sup>®</sup> analyzes 74 cancer-related genes for targeted therapy selection in advanced-stage cancer patients with solid tumors, comprehensively testing all targeted mutations in a single test. The test identifies all four classes of genomic alterations (point mutations, insertions/deletions, fusions, and amplifications) and microsatellite instability (MSI) at high-sensitivity levels detecting mutations in plasma with ultra-low variant frequency. Guardant360<sup>®</sup> demonstrated a 99.6% test success rate in a study comprising 10,593 real-world clinical specimens with 85.9% ctDNA detection rates.

Guardant has clinical research collaborations with South-Korea based Samsung Medical Centre investigators to conduct various studies. Together with researchers from MD Anderson Cancer Center and the Samsung Medical Center, the company established Guardant360<sup>®</sup> assay to detect MSI. Comparing the data from 1,145 Guardant360<sup>®</sup> samples to MSI status found in tissue biopsies found the assay to deliver the same results in 98.4% of cases. The robust MSI biomarker of response to checkpoint inhibitors in multiple cancer types guides immunotherapy. Enabling MSI detection through a simple blood test will increase the number of patients benefitting from immunotherapy quicker.<sup>9</sup>

The test platform leverages a proprietary digital sequencing technology that incorporates biochemistry, NGS, signal processing, bioinformatics, and machine learning (ML). The integration of molecular barcoding lowers sequencing error rates by 30-fold over other methodologies, which ML lowers sequencing error rates by 1000-fold over other NGS

<sup>8</sup> <https://investors.guardanthealth.com/news-releases/news-release-details/nile-study-results-demonstrating-guardant360s-high-concordance>

<sup>9</sup> <https://www.biospace.com/article/guardant-health-s-blood-test-could-replace-biopsy-for-certain-types-of-cancer/>

assays. In a randomized study, the median turnaround time (TAT) for results from Guardant360<sup>®</sup> was 9 days from the date of blood draw, compared to 15 days from order date for tissue-based assays (Leighl 2019). Current median TAT for Guardant360<sup>®</sup> is seven days from the date of receipt of a blood specimen in the laboratory.

Frost & Sullivan notes that the LB test's shorter TAT, ease-of-use, and broad genomic profiling enables a blood-based sequencing ahead of tissue biopsy. This directs the negatively tested patients for tissue-biopsy quickly—allows a comprehensive and faster biomarker testing in first-line non-small-cell lung carcinoma (NSCLC) patients. The blood-first paradigm, thus, drives precision oncology to maximize therapy success, eliminating the need for costly and complication-prone repeat tissue biopsies, reducing overall treatment costs.

### **High Impact Studies Establishing Clinical Utility to Support Regulatory Approval**

The landmark NILE study established Guardant360<sup>®</sup>'s clinical evidence and utility for the blood-first paradigm by comparing Guardant360<sup>®</sup> performance to tissue-testing for guideline-recommended biomarker detection in 282 advanced NSCLC patients. Both testing methods were in agreement in greater than 90% of cases—Guardant360<sup>®</sup> detected actionable genomic biomarkers at a similar rate to tissue testing, supporting conducting blood-based biomarker testing before tissue biopsy for all newly identified advanced NSCLC patients.<sup>10</sup>

### **SCRUM Japan Initiative**

In the AMEA region, the company supports two large cancer programs through the SCRUM initiative – a public-private partnership in Japan. In December 2017, GH and National Cancer Center East (NCCE), Japan joined forces to study the Guardant360<sup>®</sup> assay in the nationwide genomic screening network LC-SCRUM Japan. The LC-SCRUM-Japan screening network accelerates precision medicine by matching metastatic lung cancer patients with approved drugs and experimental therapies in clinical trials. Likewise, in February 2018, the NCCE launched research on liquid biopsy in advanced gastrointestinal (GI) cancers. GI-SCREEN (part of SCRUM-Japan) is the nationwide genomic screening project for several GI cancers. Within GI-SCREEN is the sub-study GOZILA, in which Guardant360<sup>®</sup> is used to evaluate and match advanced stage GI cancer patients to innovative treatments targeting specific gene alterations. Similarly, the SCRUM Japan MONSTAR SCREEN 'ctDNA monitoring and microbiome transition in all solid tumors' is ongoing (enrolled 2,000 patients with solid tumors for GI and non-GI cancer types). MONSTAR SCREEN aims to advance new drug and device discovery and development, screen patients for clinical trials targeting resistant mechanisms, and promote SCRUM Japan prospective registry for regulatory approval applications.

These projects within SCRUM Japan are aimed to establish that ctDNA analysis enables quicker TAT, detects intratumoral heterogeneity, identifies potential germline mutations, and eliminates complication-prone risky tissue biopsy. Frost & Sullivan notes that with more than 14000 NGS tests conducted, 400 plus patients enrolled in 50 clinical trials across 270 hospitals, 17 pharma companies' participation, and six approved drugs and

<sup>10</sup> <http://www.guardant360.com/publications/clinical-cancer-research-feature-publication/>

companion diagnostics (CDx), SCRUM is highly successful. As the initiative enables on-time clinic-pathologic-genome data sharing with academia and pharmaceutical companies to accelerate research, drug and CDx development, patient screening, and clinical trial enrollment; Frost & Sullivan believes that the SCRUM JAPAN results will quicken regulatory approval, drive reimbursements and post-approval commercialization—enabling extensive growth in the AMEA region.

Results from one clinical sub-study within GOZILA were presented at the 2019 European Society of Medical Oncology conference. The TRIUMPH study was a prospective, multi-center phase II clinical trial of patients with metastatic colorectal cancer (mCRC) found to have tumor HER2 amplification according to Guardant360<sup>®</sup> or by standard tissue testing. The detection rate of HER2 amplification was similar with both methods. Furthermore, Guardant360<sup>®</sup> better identified patients most likely to benefit from HER2-targeted therapy (a combination of trastuzumab and pertuzumab).<sup>11</sup> Frost & Sullivan notes that initial study data confirm ctDNA-based analysis likely to enroll more patients into clinical trials without compromising efficacy.

### **Focusing on MRD and Early Screening through LUNAR Program,**

Guidelines recommend periodic follow-up testing as vital to monitoring and detecting minimal residual disease (MRD). To that end, the company is establishing ctDNA's role in detecting MRD through the LUNAR-1 program. Available to biopharma and academic researchers to advance new MRD-related new drug development, the LUNAR assay will focus on colorectal, lung, breast, and ovarian cancers. The assay detects genomic variations at 0.01% allele frequencies and combines ctDNA's genomic and epigenomic analyses to improve assay performance, overcoming low sensitivity, and biological noise mutation problems.

To advance early screening testing, in collaboration with various cancer center investigators, Guardant's LUNAR-2 R&D program is developing an accurate and affordable early cancer detection blood test for high-risk asymptomatic individuals (benchmarking the LUNAR assay's clinical utility on early-stage CRC detection). Such an assay will provide a considerable cost advantage to healthcare systems by identifying a larger at-risk population through early cancer screening—enables significant drug and diagnostics savings. By detecting cancer early in with high-risk asymptomatic populations would propel preventive medicine strategies to contain the disease before the occurrence.

Frost & Sullivan observes that GH AMEA is the only company to set best practices with its offerings across staging, therapy selection, prognosis, and monitoring in the competitive landscape.

### **Strong Global Performance Metrics and KOL Relationships Bolstering Growth**

Guardant360<sup>®</sup>'s massive commercial adoption translated to \$90.6 million in revenues globally in 2018, accounting for 82% year-over-year growth.<sup>12</sup> Relationships with key opinion leaders (KOLs) and academic researchers generate LB awareness to support the

<sup>11</sup> <https://guardanthealth.gcs-web.com/news-releases/news-release-details/data-presented-esmo-show-metastatic-crc-patients-her2>

<sup>12</sup> Guardant Annual Report; <https://investors.guardanthealth.com/node/6761/html>

company's testing-as-a-service business model. Its biopharma partners educate research groups on the test's utility. Additionally, integration with NCCN guidelines fortifies physician and patient awareness for LB adoption into the care continuum. Granted breakthrough device designation by the US Food and Drug Administration (FDA) in 2018, Guardant360<sup>®</sup> tests do not require approval to market. However, Guardant intends filing the USFDA premarket approval application. Frost and Sullivan concur that strong results from SCRUM studies, FDA approval of Guardant360<sup>®</sup> with a pan-cancer tumor profiling label, pan-cancer Medicare coverage is driving the test's commercial adoption.

Through distributorships in Southeast Asia, South Korea, Hong Kong, Taiwan, and India, GH AMEA is building region-specific expertise (collaborated with CORE diagnostics to introduce Guardant360<sup>®</sup> to India).<sup>13</sup> With expertise in medical and regulatory affairs, business development, bioinformatics, lab operations, and sales in the AMEA region, the company is strategizing on clinical trial design. Frost & Sullivan believes that by replicating its public-private initiative across other Asian markets, the company will fortify clinical utility studies, advance precision oncology bringing down the cost of cancer care to ensure broader adoption and propel unprecedented growth in AMEA.

## Conclusion

Tissue-based cancer diagnostics is invasive, costly, lengthy, and complication-prone. On the other hand, molecular tests are inadequately sensitive and challenged by biological noise. Guardant Health AMEA addresses vital cancer diagnostic challenges across the care continuum through liquid biopsy for both clinical and research use.

Company's proprietary ctDNA NGS-based Guardant360<sup>®</sup> assay is improving patient outcomes, rationalizing healthcare economics, and spearheading precision oncology by enabling comprehensive genomic profiling. Company's LUNAR assay combines ctDNA's genomic and epigenomic analyses. The tests are intended to offer improved, timely insights to optimize oncology therapeutics. With a disruptive seven-day test turnaround time, Guardant360<sup>®</sup> allows oncologists to design appropriate targeted therapies for patients with advanced cancers. Driven by impactful clinical studies in Japan, Guardant360<sup>®</sup> is accelerating clinical development programs in precision medicine. Ongoing studies focus on accurately determining minimal residual disease for cancer recurrence monitoring and early cancer screening. Through its best-in-class LB tests and diagnostics, GH AMEA is advancing personalized cancer therapeutics, growing at an astonishing pace, and augmenting its total addressable market for long-term, sustained success.

With its strong overall performance, Guardant Health AMEA earns Frost & Sullivan's Asia Pacific 2019 Growth Excellence Leadership Award in the liquid biopsy for precision oncology market.

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<sup>13</sup> <https://www.biospectrumindia.com/news/78/12011/core-diagnostics-partners-with-guardant-health-amea-.html>

## Significance of Growth Excellence Leadership

Growth Excellence Leadership is about inspiring customers to purchase from your company and then return time and again. In a sense, then, everything is truly about the customer. Making customers happy is the cornerstone of any successful, long-term growth strategy. Companies that excel in driving growth strive to be best in class in three key areas: meeting customer demand, fostering brand loyalty, and carving out a unique and sustainable market niche.



## Understanding Growth Excellence Leadership

Companies that creatively and profitably deliver value to customers ultimately set up their businesses for long-term, rapid growth. This is what Growth Excellence Leadership is all about: growth through customer focus, fostering a virtuous cycle of improvement and success.

## Key Benchmarking Criteria

For the Growth Excellence Leadership Award, Frost & Sullivan analysts independently evaluated Growth Performance and Customer Impact according to the criteria identified below.

### *Growth Performance*

#### **Criterion 1: Growth Strategy**

Requirement: Executive team has a shared vision for the organization's growth and has created and implemented a strategy that is consistent with that vision.

#### **Criterion 2: Above-market Growth**

Requirement: Company's growth rate exceeds the industry's year-over-year growth rate.

#### **Criterion 3: Share of Wallet**

Requirement: Customers allocate a greater percentage of their total spend to purchasing products or services produced by the company.

#### **Criterion 4: Growth Diversification**

Requirements: Company is equally able to pursue organic (e.g., distribution channel optimization, new product innovation) and inorganic (e.g., acquisitions, partnerships) growth opportunities consistent with the long-term objectives of the organization.

#### **Criterion 5: Growth Sustainability**

Requirement: Company has consistently sought opportunities for growth, enabling the organization to build on its base and sustain growth over the long term.

### *Customer Impact*

#### **Criterion 1: Price/Performance Value**

Requirement: Products or services offer the best value for the price, compared to similar offerings in the market.

#### **Criterion 2: Customer Purchase Experience**

Requirement: Customers feel they are buying the optimal solution that addresses both their unique needs and their unique constraints.

#### **Criterion 3: Customer Ownership Experience**

Requirement: Customers are proud to own the company's product or service and have a positive experience throughout the life of the product or service.

#### **Criterion 4: Customer Service Experience**

Requirement: Customer service is accessible, fast, stress-free, and of high quality.

#### **Criterion 5: Brand Equity**

Requirement: Customers have a positive view of the brand and exhibit high brand loyalty.

## Best Practices Recognition: 10 Steps to Researching, Identifying, and Recognizing Best Practices

Frost & Sullivan analysts follow a 10-step process to evaluate Award candidates and assess their fit with select best practice criteria. The reputation and integrity of the Awards are based on close adherence to this process.

STEP	OBJECTIVE	KEY ACTIVITIES	OUTPUT
1 <b>Monitor, target, and screen</b>	Identify Award recipient candidates from around the globe	<ul style="list-style-type: none"> <li>• Conduct in-depth industry research</li> <li>• Identify emerging sectors</li> <li>• Scan multiple geographies</li> </ul>	Pipeline of candidates who potentially meet all best-practice criteria
2 <b>Perform 360-degree research</b>	Perform comprehensive, 360-degree research on all candidates in the pipeline	<ul style="list-style-type: none"> <li>• Interview thought leaders and industry practitioners</li> <li>• Assess candidates' fit with best-practice criteria</li> <li>• Rank all candidates</li> </ul>	Matrix positioning of all candidates' performance relative to one another
3 <b>Invite thought leadership in best practices</b>	Perform in-depth examination of all candidates	<ul style="list-style-type: none"> <li>• Confirm best-practice criteria</li> <li>• Examine eligibility of all candidates</li> <li>• Identify any information gaps</li> </ul>	Detailed profiles of all ranked candidates
4 <b>Initiate research director review</b>	Conduct an unbiased evaluation of all candidate profiles	<ul style="list-style-type: none"> <li>• Brainstorm ranking options</li> <li>• Invite multiple perspectives on candidates' performance</li> <li>• Update candidate profiles</li> </ul>	Final prioritization of all eligible candidates and companion best-practice positioning paper
5 <b>Assemble panel of industry experts</b>	Present findings to an expert panel of industry thought leaders	<ul style="list-style-type: none"> <li>• Share findings</li> <li>• Strengthen cases for candidate eligibility</li> <li>• Prioritize candidates</li> </ul>	Refined list of prioritized Award candidates
6 <b>Conduct global industry review</b>	Build consensus on Award candidates' eligibility	<ul style="list-style-type: none"> <li>• Hold global team meeting to review all candidates</li> <li>• Pressure-test fit with criteria</li> <li>• Confirm inclusion of all eligible candidates</li> </ul>	Final list of eligible Award candidates, representing success stories worldwide
7 <b>Perform quality check</b>	Develop official Award consideration materials	<ul style="list-style-type: none"> <li>• Perform final performance benchmarking activities</li> <li>• Write nominations</li> <li>• Perform quality review</li> </ul>	High-quality, accurate, and creative presentation of nominees' successes
8 <b>Reconnect with panel of industry experts</b>	Finalize the selection of the best-practice Award recipient	<ul style="list-style-type: none"> <li>• Review analysis with panel</li> <li>• Build consensus</li> <li>• Select recipient</li> </ul>	Decision on which company performs best against all best-practice criteria
9 <b>Communicate recognition</b>	Inform Award recipient of Award recognition	<ul style="list-style-type: none"> <li>• Present Award to the CEO</li> <li>• Inspire the organization for continued success</li> <li>• Celebrate the recipient's performance</li> </ul>	Announcement of Award and plan for how recipient can use the Award to enhance the brand
10 <b>Take strategic action</b>	Upon licensing, company is able to share Award news with stakeholders and customers	<ul style="list-style-type: none"> <li>• Coordinate media outreach</li> <li>• Design a marketing plan</li> <li>• Assess Award's role in future strategic planning</li> </ul>	Widespread awareness of recipient's Award status among investors, media personnel, and employees

## The Intersection between 360-Degree Research and Best Practices Awards

### Research Methodology

Frost & Sullivan's 360-degree research methodology represents the analytical rigor of our research process. It offers a 360-degree-view of industry challenges, trends, and issues by integrating all 7 of Frost & Sullivan's research methodologies. Too often companies make important growth decisions based on a narrow understanding of their environment, leading to errors of both omission and commission. Successful growth strategies are founded on a thorough understanding of market, technical, economic, financial, customer, best practices, and demographic analyses. The integration of these research disciplines into the 360-degree research methodology provides an evaluation platform for benchmarking industry participants and for identifying those performing at best-in-class levels.

### 360-DEGREE RESEARCH: SEEING ORDER IN THE CHAOS



## About Frost & Sullivan

Frost & Sullivan, the Growth Partnership Company, enables clients to accelerate growth and achieve best-in-class positions in growth, innovation and leadership. The company's Growth Partnership Service provides the CEO and the CEO's Growth Team with disciplined research and best practice models to drive the generation, evaluation and implementation of powerful growth strategies. Frost & Sullivan leverages more than 50 years of experience in partnering with Global 1000 companies, emerging businesses, and the investment community from 45 offices on six continents. To join our Growth Partnership, please visit <http://www.frost.com>.