

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

FROST & SULLIVAN BEST PRACTICES AWARD

ESSENTIAL TREMOR TREATMENT - NORTH AMERICA

Technology Innovation 2019



FROST & SULLIVAN

2019

BEST
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AWARD

Contents

Background and Company Performance	3
<i>Industry Challenges</i>	3
<i>Technology Attributes and Future Business Value</i>	3
<i>Conclusion</i>	6
Significance of Technology Innovation.....	7
Understanding Technology Innovation	7
<i>Key Benchmarking Criteria</i>	8
Best Practice Award Analysis	8
<i>Decision Support Scorecard</i>	8
<i>Technology Attributes</i>	9
<i>Future Business Value</i>	9
<i>Decision Support Matrix</i>	10
Best Practices Recognition: 10 Steps to Researching, Identifying, and Recognizing Best Practices	11
The Intersection between 360-Degree Research and Best Practices Awards.....	12
<i>Research Methodology</i>	12
About Frost & Sullivan	12

Background and Company Performance

Industry Challenges

Essential tremor (ET) is a type of neurological condition that is characterized by rhythmic trembling or shaking in the hands and other parts of the body. People affected with the condition often experience difficulty in performing normal tasks such as writing, dressing, eating, and drinking. ET is one of the most prevalent neurological disorders among adults. According to the National Organization for Rare Disorders (NORD), ET is estimated to affect about 7 million people in the United States alone. The condition exhibits an age-associated rise in prevalence; individuals aged 40 to 60 years have an incidence of 4% to 5%, and people aged 60 and above have the highest incidence of the disorder at 6.3% to 9%.

Although there is no effective cure for ET, several medications have been traditionally used as first-line of treatment for the condition, including propranolol, primidone, atenolol, sotalol, gabapentin, and topiramate, which have been modestly effective in reducing tremors in patients. However, most of these drugs belong to additional drug classes such as beta blockers, antidepressants, and anticonvulsants that have been approved for indications other than ET. Generally a single drug is administered initially at lower doses followed by gradual increase in the doses until complete response, and tolerance is attained. Other medications may be subsequently introduced and increased in an effort to achieve maximum benefit. Unsuccessful drugs that do not elicit sufficient response are gradually tapered down. Frost & Sullivan notes that sustained increase in the medication doses to achieve requisite benefits often leads to undesirable side-effects in patients - including decreased blood pressure and heart rate, nausea, fatigue, dizziness, and weight loss.

Surgery is often used as a second-line of treatment for managing the condition in patients who do not respond to medication. Surgical procedures such as deep brain stimulation (DBS) and thalamotomy are performed to provide relief to patients from tremors. However, these procedures are quite invasive and cause severe anxiety among many patients, who consequently become averse to such treatment options. Moreover, these therapies carry significant post-procedure risks, such as intracerebral hemorrhage, wound infection, and implant-related complications that include component malfunction and lead migration.

Ultimately, patients are increasingly seeking alternative modalities that offer effective treatment managing ET - while at the same time cause minimal side effects. Frost & Sullivan research reveals that treatment methods that are less invasive, simpler to use, and able to properly address patients' safety concerns are bound to witness rapid adoption.

Technology Attributes and Future Business Value

Industry Impact

Founded in 2014 and headquartered in Burlingame, California, Cala Health properly identified the unmet need tied to the limitations of current ET treatment methods and has

developed a breakthrough product for better managing the condition. The company has emerged as a pioneer in use of peripheral nerve stimulation for the upper limbs through its Cala Trio™, a prescription-only, wrist-worn device. The device was launched in the United States in September 2019 to deliver precise electrical pulses to the median and radial nerves in the wrist that target the central tremor network, in turn addressing the underlying cause of ET. The 40-minute therapy session delivers meaningful reduction in hand tremors after a single use, thus offering a more convenient method for managing the condition without systemic side effects.



For patients undergoing invasive surgical procedures such as DBS that involve implants placed in the brain, patients are typically apprehensive regarding the outcome of the procedure and its impact on their health. Consequently, patients may prefer to avoid undergoing these procedures when seeking remedial treatment against the condition. To address this challenge, Cala Trio was designed as a neuromodulation treatment, a non-invasive therapy patients can use from the comfort of their homes. Frost & Sullivan believes that this user-friendly, non-invasive, and at-home approach will drive further product adoption among patients.

Product Impact

Traditionally, the cost of surgery for treating ET is considerably high; a single procedure may incur more than \$40,000 in treatment expenses for patients. Moreover, tremor recurrence may necessitate additional surgeries, leading to enormous financial burden. Also, for patients undergoing these procedures, the recovery period ranges between 3 to 5 days. In contrast, the therapy offered by Cala Trio is provided at a modest cost and causes no patient downtime, offering a relatively cost-effective and convenient treatment method when compared to surgical procedures.

A major area of concern for patients seeking treatment for ET regards the health risks of medication-associated adverse reactions as well as procedure-related complications. On the contrary, therapy provided through Cala Trio causes no systemic side-effects, and the wrist-worn therapy delivers low intensity stimulation that leads to mild-tingling sensation in the fingers. Patients can easily control the pulses intensity based on their comfort level.

Application Diversity

In addition to ET, Cala Health is planning to expand the application of neuromodulation therapy to other therapeutic areas. Cala Health is actively licensing technologies from academic medical centers to incorporate them into the company's neuromodulation platform that can be used in the treatment of other chronic diseases. For instance, in March 2019, the company licensed Partners Healthcare and its affiliate Massachusetts General Hospital's neuromodulation technology that is based on the research on respiratory-gated vagal afferent nerve stimulation and transcutaneous vagus nerve stimulation. The company is aiming to use this technology to develop novel therapies for treating diseases in the areas of neurology, psychiatry, and cardiology.

Customer Acquisition

Clinical studies carried out to evaluate the effectiveness and safety of Cala Trio have demonstrated positive outcomes in patients. According to the results of the PROSPECT study presented in September 2019 during the International Congress of Parkinson's Disease and Movement Disorders, the study showed that physician-rated, patient-rated and objective motion sensors all showed statistically significant improvement in tremor during 3 months of daily use. 62% of the patients had reduction in tremor severity according to physician-rated scales, while 68% of them witnessed reduction in tremor severity according to patient-rated assessment scales. Endpoint analysis of motion sensor data highlighted that 54% of patients experienced more than 50% improvement in tremor power during the study period. The study also highlighted minor device-related adverse events in the patients - but none of them required any medical intervention. These promising results have impressed both the medical community and Frost & Sullivan regarding the device's ability to provide safe and effective treatment to patients suffering from ET.

Brand Loyalty

Cala Health was founded in 2014 by Kate Rosenbluth with the objective to develop bioelectronic devices through the amalgamation of innovations in neuroscience and technology. Within a few years of its inception, the company has managed to receive regulatory approval from the US Food and Drug Administration (FDA) to facilitate commercial rollout in the country.

Frost & Sullivan is impressed with Cala Health's novel digital business model of direct-to-consumer solutions that allows patients to receive Cala Trio at their doorstep once a prescription is sent to the company. Moreover, Cala Health actively engages with patients during the course of the therapy, allowing them to make necessary modifications to the electrical stimulation, which in turn empowers them to more effectively manage their condition. Frost & Sullivan expects this unique approach aimed at facilitating greater convenience for patients to play a pivotal role in driving market adoption of the device.

Visionary Innovation

Cala Trio is a first-of-its-kind wearable device that provides individualized therapy for managing ET in patients. Due to its best-in-class engineering, the device is able to capture the frequency of hand tremors during tasks that are assigned to patients at the onset. The accelerometers in the device measure the patients' motion, which is used by the onboard software to characterize the tremors, allowing it to provide electrical pulses that are calibrated to the users' tremor frequency. This development demonstrates the company's unwavering commitment to innovation and its resolve to develop an ingenious product for improving management of ET. The company's vision has received wide interest from investors, including some of the largest venture capital firms who have vigorously channeled funding of around \$84 million since Cala Health's inception.

Conclusion

Based on Frost & Sullivan's exhaustive analysis of the essential tremor treatment market, Cala Health has completely revolutionized treatment provided to ET patients through body-worn electronic devices.

Frost & Sullivan salutes the company's ability to bring to market a device that is non-invasive, patient-friendly, causes minimal side-effects, and is more cost-effective when compared to current ET treatment methods. The wrist-worn device empowers patients to get on-demand relief from tremors anywhere, including at home, in social settings, or at work. Moreover, by providing electrical stimulation based on the individual tremor patterns, the device is taking personalized therapy to the next level, which is expected to help in providing better outcomes for patients.

For its strong overall performance, Cala Health has earned the 2019 Frost & Sullivan Technology Innovation Award.

Significance of Technology Innovation

Ultimately, growth in any organization depends on finding new ways to excite the market and maintaining a long-term commitment to innovation. At its core, technology innovation, or any other type of innovation, can only be sustained with leadership in 3 key areas: understanding demand, nurturing the brand, and differentiating from the competition.



Understanding Technology Innovation

Technology innovation begins with a spark of creativity that is systematically pursued, developed, and commercialized. This spark can result from a successful partnership, a productive in-house innovation group, or a bright-minded individual. Regardless of the source, the success of any new technology is ultimately determined by its innovativeness and its impact on the business as a whole.

Key Benchmarking Criteria

For the Technology Innovation Award, Frost & Sullivan analysts independently evaluated 2 key factors—Technology Attributes and Future Business Value—according to the criteria identified below.

Technology Attributes

- Criterion 1: Industry Impact
- Criterion 2: Product Impact
- Criterion 3: Scalability
- Criterion 4: Visionary Innovation
- Criterion 5: Application Diversity

Future Business Value

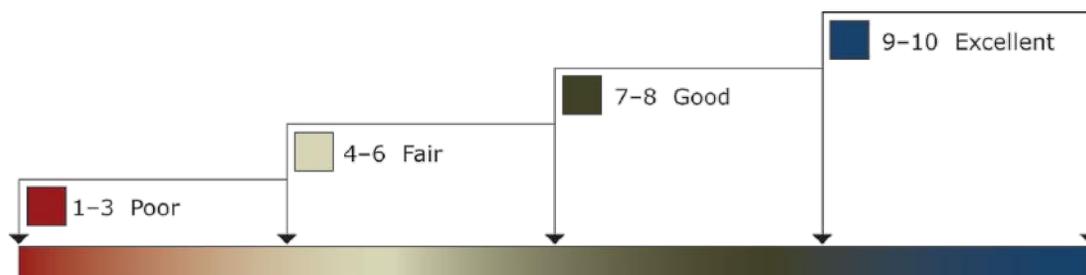
- Criterion 1: Financial Performance
- Criterion 2: Customer Acquisition
- Criterion 3: Technology Licensing
- Criterion 4: Brand Loyalty
- Criterion 5: Human Capital

Best Practices Award Analysis for Cala Health

Decision Support Scorecard

To support its evaluation of best practices across multiple business performance categories, Frost & Sullivan employs a customized Decision Support Scorecard. This tool allows research and consulting teams to objectively analyze performance according to the key benchmarking criteria listed in the previous section, and to assign ratings on that basis. The tool follows a 10-point scale that allows for nuances in performance evaluation. Ratings guidelines are illustrated below.

RATINGS GUIDELINES



The Decision Support Scorecard considers Technology Attributes and Future Business Value (i.e., the overarching categories for all 10 benchmarking criteria; the definitions for each criterion are provided beneath the scorecard). The research team confirms the veracity of this weighted scorecard through sensitivity analysis, which confirms that small changes to the ratings for a specific criterion do not lead to a significant change in the overall relative rankings of the companies.

The results of this analysis are shown below. To remain unbiased and to protect the interests of all organizations reviewed, Frost & Sullivan has chosen to refer to the other key participants as Competitor 2 and Competitor 3.

<i>Measurement of 1-10 (1 = poor; 10 = excellent)</i>			
Technology Innovation	Technology Attributes	Future Business Value	Average Rating
Cala Health	9.7	9.6	9.7
Competitor 2	6.6	5.7	6.2
Competitor 3	4.5	5.0	4.8

Technology Attributes

Criterion 1: Industry Impact

Requirement: Technology enables the pursuit of groundbreaking ideas, contributing to the betterment of the entire industry.

Criterion 2: Product Impact

Requirement: Specific technology helps enhance features and functionalities of the entire product line for the company.

Criterion 3: Scalability

Requirement: Technology is scalable, enabling new generations of products over time, with increasing levels of quality and functionality.

Criterion 4: Visionary Innovation

Requirement: Specific new technology represents true innovation based on a deep understanding of future needs and applications.

Criterion 5: Application Diversity

Requirement: New technology serves multiple products, multiple applications, and multiple user environments.

Future Business Value

Criterion 1: Financial Performance

Requirement: Potential is high for strong financial performance in terms of revenue, operating margins, and other relevant financial metrics.

Criterion 2: Customer Acquisition

Requirement: Specific technology enables acquisition of new customers, even as it enhances value to current customers.

Criterion 3: Technology Licensing

Requirement: New technology displays great potential to be licensed across many verticals and applications, thereby driving incremental revenue streams.

Criterion 4: Brand Loyalty

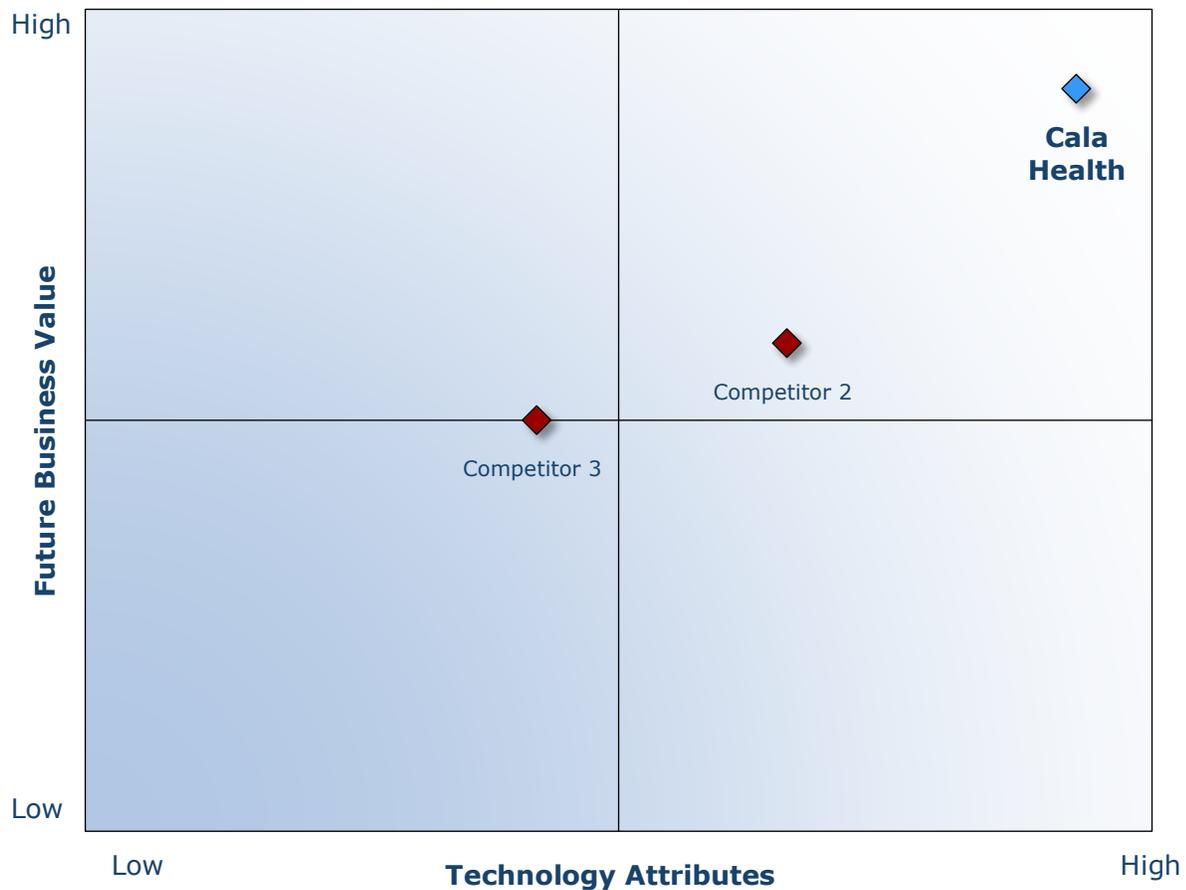
Requirement: New technology enhances the company’s brand, creating and/or nurturing brand loyalty.

Criterion 5: Human Capital

Requirement: Customer impact is enhanced through the leverage of specific technology, translating into positive impact on employee morale and retention.

Decision Support Matrix

Once all companies have been evaluated according to the Decision Support Scorecard, analysts then position the candidates on the matrix shown below, enabling them to visualize which companies are truly breakthrough and which ones are not yet operating at best-in-class levels.



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 practices criteria. The reputation and integrity of the Awards are based on close adherence to this process.

STEP	OBJECTIVE	KEY ACTIVITIES	OUTPUT
1 Monitor, target, and screen	Identify Award recipient candidates from around the world	<ul style="list-style-type: none"> • Conduct in-depth industry research • Identify emerging industries • Scan multiple regions 	Pipeline of candidates that potentially meet all best practices criteria
2 Perform 360-degree research	Perform comprehensive, 360-degree research on all candidates in the pipeline	<ul style="list-style-type: none"> • Interview thought leaders and industry practitioners • Assess candidates' fit with best practices criteria • Rank all candidates 	Matrix positioning of all candidates' performance relative to one another
3 Invite thought leadership in best practices	Perform in-depth examination of all candidates	<ul style="list-style-type: none"> • Confirm best practices criteria • Examine eligibility of all candidates • Identify any information gaps 	Detailed profiles of all ranked candidates
4 Initiate research director review	Conduct an unbiased evaluation of all candidate profiles	<ul style="list-style-type: none"> • Brainstorm ranking options • Invite multiple perspectives on candidates' performance • Update candidate profiles 	Final prioritization of all eligible candidates and companion best practices positioning paper
5 Assemble panel of industry experts	Present findings to an expert panel of industry thought leaders	<ul style="list-style-type: none"> • Share findings • Strengthen cases for candidate eligibility • Prioritize candidates 	Refined list of prioritized Award candidates
6 Conduct global industry review	Build consensus on Award candidates' eligibility	<ul style="list-style-type: none"> • Hold global team meeting to review all candidates • Pressure-test fit with criteria • Confirm inclusion of all eligible candidates 	Final list of eligible Award candidates, representing success stories worldwide
7 Perform quality check	Develop official Award consideration materials	<ul style="list-style-type: none"> • Perform final performance benchmarking activities • Write nominations • Perform quality review 	High-quality, accurate, and creative presentation of nominees' successes
8 Reconnect with panel of industry experts	Finalize the selection of the best practices Award recipient	<ul style="list-style-type: none"> • Review analysis with panel • Build consensus • Select recipient 	Decision on which company performs best against all best practices criteria
9 Communicate recognition	Inform Award recipient of recognition	<ul style="list-style-type: none"> • Present Award to the CEO • Inspire the organization for continued success • Celebrate the recipient's performance 	Announcement of Award and plan for how recipient can use the Award to enhance the brand
10 Take strategic action	Upon licensing, company is able to share Award news with stakeholders and customers	<ul style="list-style-type: none"> • Coordinate media outreach • Design a marketing plan • Assess Award's role in strategic planning 	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 the 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, resulting in 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, helps clients 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-practices models to drive the generation, evaluation, and implementation of powerful growth strategies. Frost & Sullivan leverages nearly 60 years of experience in partnering with Global 1000 companies, emerging businesses, and the investment community from 45 offices on 6 continents. To join Frost & Sullivan's Growth Partnership, visit <http://www.frost.com>.