

Technology Innovation Award Stem Cell Technologies North America, 2013

Frost & Sullivan's Global Research Platform

Frost & Sullivan is in its 50th year in business with a global research organization of 1,800 analysts and consultants who monitor more than 300 industries and 250,000 companies. The company's research philosophy originates with the CEO's 360-Degree Perspective™, which serves as the foundation of its TEAM Research™ methodology. This unique approach enables us to determine how best-in-class companies worldwide manage growth, innovation and leadership. Based on the findings of this Best Practices research, Frost & Sullivan is proud to present the 2013 North American Technology Innovation Award in Stem Cell Technologies to Xcelthera, Inc. (Xcelthera).

Significance of the Technology Innovation Award

Key Industry Challenges Addressed by Xcelthera Inc.

Pluripotent human embryonic stem cells (hESC) have unrestrained capacity for long-term, stable undifferentiated growth in culture, as well as the intrinsic potential for differentiation into all somatic cell types in the human body. These characteristics show that hESC has tremendous potential for restoring human tissue and organ function.

A persistent challenge for scientists and researchers is to enable a well-controlled and efficient induction of hESC exclusively to a specific, clinically relevant lineage. These aspects play a key role not only for tissue/organ engineering and regenerative cell-based therapy, but also for drug discovery and development. Indeed, human stem cell therapy products today constitute a new conception of a drug as a cellular entity capable of offering pharmacological activity associated with human tissue and function restoration.

Over the past decade, notable advancements have taken place in stem cell research related to the differentiation of hESC into specific lineages by small molecule induction. Among such small molecules, retinoic acid can be cited, which potentially induces the specification of neuroectoderm directly from hESC, while triggering progression to neuronal progenitors. Nicotinamide, on the other hand, induces the specification of cardiomesoderm directly from pluripotent hSCs, thus triggering progression to cardiac precursors, among many others. These two instances among many others constitute clinically representative progress in both human neuronal and cardiac therapeutic products for central nervous system (CNS) and myocardium repair, respectively.

Nonetheless, a limiting factor in stem cell research is present because of the lack of a clinically suitable source of engraftable human stem/progenitor cells with adequate neurogenic potential. Novel solutions to this issue are crucial for developing safe and

effective cell-based therapies for regeneration of the damaged CNS structure and circuitry evidenced in various neurological disorders. Regarding cardiovascular research, the absence of a clinically suitable human cardiomyocyte source with adequate myocardium regenerative potential is also a major drawback for achieving damaged human heart regenerative solutions.

The limited capacity of these two cell systems—neuron circuitry and cardiomyocytes—for self-repair makes them suitable for stem cell derivative-based neuronal and heart therapies. Clinical applications of stem cell therapy derivatives have demonstrated successful alternatives for a wide range of incurable or hitherto untreatable neurodegenerative and heart diseases. Neurodegenerative and heart diseases cost the worldwide healthcare system more than \$500 billion annually.

Key Benchmarking Criteria for Technology Innovation Award

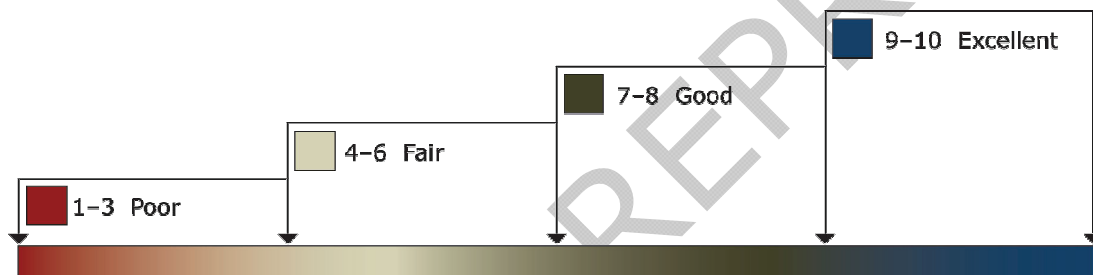
For the Technology Innovation Award, the following criteria were used to benchmark Xcelthera's performance against key competitors:

- Uniqueness of Technology
- Impact on New Products/Applications
- Impact on Functionality
- Impact on Customer Value
- Relevance of Innovation to Industry

Decision Support Matrix and Measurement Criteria

To support its evaluation of best practices across multiple business performance categories, Frost & Sullivan employs a customized Decision Support Matrix (DSM). The DSM is an analytical tool that compares companies' performance relative to each other with an integration of quantitative and qualitative metrics. The DSM features criteria unique to each Award category and ranks importance by assigning weights to each criterion. The relative weighting reflects current market conditions and illustrates the associated importance of each criterion according to Frost & Sullivan. Fundamentally, each DSM is distinct for each market and Award category. The DSM allows our research and consulting teams to objectively analyze each company's performance on each criterion relative to its top competitors and assign performance ratings on that basis. The DSM follows a 10-point scale that allows for nuances in performance evaluation; ratings guidelines are shown in Chart 1.

Chart 1: Performance-Based Ratings for Decision Support Matrix



This exercise encompasses all criteria, leading to a weighted average ranking of each company. Researchers can then easily identify the company with the highest ranking. As a final step, the research team confirms the veracity of the model by ensuring 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.

Chart 2: Frost & Sullivan's 10-Step Process for Identifying Award Recipients



Best Practice Award Analysis for Xcelthera

The Decision Support Matrix, shown in Chart 3, illustrates the relative importance of each criterion for the Technology Innovation Award and the ratings for each company under evaluation. To remain unbiased while also protecting the interests of the other organizations reviewed, we have chosen to refer to the other key players as Competitor 1 and Competitor 2.

Chart 3: Decision Support Matrix for Technology Innovation Award

Measurement of 1–10 (1 = lowest; 10 = highest)	Award Criteria					
	Uniqueness of Technology	Impact on New Products/Applications	Impact on Functionality	Impact on Customer Value	Relevance of Innovation to Industry	Weighted Rating
Relative Weight (%)	20%	20%	20%	20%	20%	100%
Xcelthera	9.7	9.5	9.6	9.5	9.6	9.6
Competitor 1	6.2	5.8	5.5	5.0	6.0	5.7
Competitor 2	6.5	5.5	4.8	4.9	5.2	5.0

Criterion 1: Uniqueness of Technology

Xcelthera has been a pioneer in stem cell therapeutics and its technology platform—PluriXcel—is currently the only available human cell source offering products with the pharmacological capacity to regenerate neurons and contractile heart muscles that allow restitution of function of the CNS and heart repair in the clinic.

Along with a group of researchers working at the San Diego Regenerative Medicine Institute, an independent biomedical research institute focused on human stem cell-based regenerative medicine, Xcelthera has specifically worked on the development of a novel technology platform for efficiently converting pluripotent hESC uniformly into a particular clinically relevant lineage by small molecule induction. Overcoming some major issues in bringing hESC therapy derivatives toward clinical applications, these investigations have resulted in remarkable advances and breakthroughs. One of the major achievements was the establishment of unique human stem cell technology platforms. PluriXcel technology has been developed for defined culture systems for *de novo* derivation and maintenance of clinical-grade pluripotent hESC, through the PluriXcel-DCS technology platform, and for lineage-specific differentiation of pluripotent hESC by small signal molecule induction via

PluriXcel-SMI. The main goal is to achieve a highly efficient direct conversion of pluripotent hESC into a large supply of high-purity clinical-grade neuronal cells or heart muscle cells (Xcel), conserving their adequate capacity to regenerate neurons and contractile heart muscles.

Frost & Sullivan recognizes the exemplary efforts of Xcelthera in building the foundation for the development of safe and effective stem cell therapies, thus addressing major concerns in the healthcare industry.

Criterion 2: Impact on New Products/Applications

According to Frost & Sullivan, Xcelthera is shaping the future of medicine by providing novel, unique solutions at a clinical grade. With its exclusive rights in proprietary human stem cell technology and therapy products to provide cellular medicines for neurological and heart diseases, the company has high growth potential, targeting major health problems related to neurological and cardiovascular diseases in the biotechnology and therapeutic sectors. A strong patent portfolio, including not only North America and Europe, but also the Asia Pacific region (AU2011338711) is evidence of the commitment of the company to translate its innovations to the industry.

Frost & Sullivan recognizes Xcelthera as a major innovator in the stem cell research market. A flexible business model, open to partnerships, alliances, and investment opportunities, places this company in an optimal position for paving the way to personalized medicine.

Xcelthera's technology platforms have demonstrated tremendous potential for tissue and organ regeneration and function restoration. In fact, untreated diseases or diseases currently considered incurable could now find a strong alternative through the clinical applications of pluripotent hESC therapy derivatives.

Holding a worldwide therapeutic market of over USD 10 billion annually, Xcelthera's business strategy is focused on the preclinical and clinical development of human stem cell technology platforms and cell therapy products using pluripotent hESC. Furthermore, the company is developing cell therapeutics for neurological and cardiovascular diseases, including heart disease and failure, Parkinson's diseases, amyotrophic lateral sclerosis (ALS), Alzheimer's disease, neurodegenerative diseases, and brain and spinal cord injuries.

Human stem cell technology and cell therapy products represent a new type of drug of cellular medicine capable of providing new pharmacological utility, including tissue and function restoration. PluriXcel technology, Xcelthera's proprietary human stem cell technology platform comprises PluriXcel-DCS, the defined culture system for derivation and maintenance of clinical-grade hESC lines, and PluriXcel-SMI, the highly efficient lineage-specific differentiation of pluripotent hESCs. PluriXcel-SMI utilizes small molecule induction for direct conversion of pluripotent hESC into large sources of high purity neuronal/heart muscle cells, highly suitable for developing novel, safe, and cost-effective stem cell

therapies.

Among the company's products for neurological and cardiovascular applications, Xcel, clinical-grade hESC neuronal cell therapy products for CNS neuron regeneration, Xcel-hNuP and Xcel-hNu, can be mentioned. Similarly, Xcel-hCardP and Xcel-hCM represent the analog, clinical-grade hESC heart muscle cell therapy products for heart regeneration.

Criterion 3: Impact on Functionality

The company's technology allows the efficient production of human neuronal progenitors and human neuronal cell types and subtypes from pluripotent hESC for neuronal regeneration and replacement therapies for a wide range of neurological disorders. Similarly, the efficient production of human cardiac precursors and human cardiomyocytes for myocardium regeneration and replacement therapies for heart disease and failure has also been addressed.

Frost & Sullivan recognizes Xcelthera's technological breakthrough—enabling the well-controlled induction of pluripotent hESC. Such enhancements allow the achievement of more efficient results by only mediating the simple provision of a series of small molecules, ensuring the proliferation of undifferentiated hESC, exclusively to a particular clinically relevant lineage.

As a demonstration of that, a recent publication of Parsons in the Annual Review & Research in Biology, titled: "Embedding the Future of Regenerative Medicine into the Open Epigenomic Landscape of Pluripotent Human Embryonic Stem Cells," the investigators focused their attention on the human stem cell epigenome landscape that helps to elucidate the intrinsic plasticity and regenerative potential of human stem cell derivatives with reference to neural and cardiac lineage-specific differentiation.

Criterion 4: Impact on Customer Value

In regenerative medicine, pluripotent hESC research holds huge promise for treating major human diseases challenging traditional medicine. Neurodegenerative disorders, injury and paralysis, diabetes, heart failure, and cardiovascular diseases represent the major issues.

Millions of people are pinning their hopes on stem cell research to provide novel and effective solutions for such concerns. On that note, the clinical translation of stem cell research and innovation capabilities demonstrated by hESC investigations can extend the lives of patients and reduce the burden of illness.

The PluriXcel technology platform is incomparable, providing life scientists and clinicians with novel, efficient, and powerful resources to address major health concerns. The introduction of novel developments and new business opportunities based on this technology are expected to revolutionize the biomedical industry and bring new therapeutics into the market.

Criterion 5: Relevance of Innovation to Industry

The limited capacity of neuron circuitry and cardiomyocytes for self-repair constitutes a significant challenge in both the scientific and clinical community. As neurodegenerative and heart diseases incur exorbitant costs on the healthcare system worldwide, there is a strong focus on providing newer, more efficient solutions for these therapeutic needs. The clinical applications of stem cell therapy derivatives have demonstrated an ability to provide successful alternatives for a wide range of incurable or hitherto untreatable neurodegenerative and heart diseases. Xcelthera and the SDRMI have jointly translated their developments to the clinical community.

These advancements are expected to transform the biomedical science arena and help develop groundbreaking pluripotent hESC technology platforms and innovative regenerative approaches. Xcelthera's technology platform is shaping the future of medicine by providing pluripotent human embryonic stem cell-based technology, and developing optimal regeneration treatment options for human tissue and function restoration.

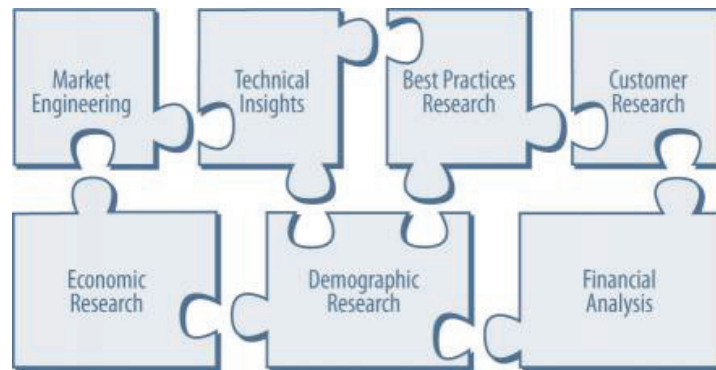
Conclusion

Xcelthera Inc. is a (bio)-pharmaceutical company committed to clinically translating human stem cell research discoveries for unmet medical challenges in major health problems, particularly neurodegenerative disorders and cardiovascular diseases.

Founded for clinical applications of pluripotent human embryonic stem cells (hESC) therapy derivatives, Xcelthera is translating its stem cell research to clinical applications through the introduction of its proprietary clinical-grade hESC neuronal and cardiomyocyte cell therapy products. In recognition of its efforts, Frost & Sullivan is proud to present the 2013 North America Technology Innovation Award in Stem Cell Technologies to Xcelthera.

Critical Importance of TEAM Research

Frost & Sullivan's TEAM 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 seven of Frost & Sullivan's research methodologies. Our experience has shown over the years that companies too often make important growth decisions based on a narrow understanding of their environment, leading to errors of both omission and commission. Frost & Sullivan contends that successful growth strategies are founded on a thorough understanding of market, technical, economic, financial, customer, best practices, and demographic analyses. In that vein, the letters T, E, A and M reflect our core technical, economic, applied (financial and best practices) and market analyses. The integration of these research disciplines into the TEAM Research methodology provides an evaluation platform for benchmarking industry players and for creating high-potential growth strategies for our clients.

Chart 4: Benchmarking Performance with TEAM Research

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 50 years of experience in partnering with Global 1000 companies, emerging businesses and the investment community from more than 40 offices on six continents. To join our Growth Partnership, please visit <http://www.frost.com>.