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Paras Biopharmaceuticals Finland Oy

2014 European Biopharmaceuticals Technology Innovation Leadership Award

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50 Years of Growth, Innovation & Leadership

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Technology Innovation Leadership Award

The Biopharmaceuticals Industry

EUROPE

Background and Company Performance

Industry Challenges

The two major challenges in the production of biopharmaceuticals are upstream and downstream processing, accounting for nearly 60% of manufacturing costs. The choice of optimised expression systems which turn cells into more efficient production systems and developments in culture media, including feed strategy, are crucial to yield increased biomass content. Given a maximum of 40% bio-manufacturing costs represented by downstream processing activities, Frost & Sullivan notes that the most crucial challenge faced by biopharmaceutical manufacturers is insufficient downstream processing technologies, due of a lack of proper funding and investment. Downstream processing technologies follow two different trends specific to monoclonal antibodies (mAbs) and recombinant proteins. As mAbs are high-dosage drugs, requiring large scale manufacturing, filtration steps need to cope with high biomass content in initial stages, and purification resins must offer higher capacity while maintaining or improving the purification effect. Thus, a two-step purification process is employed for mAbs. Most recombinant proteins are produced in smaller quantities, and each protein is different, requiring the use of four purification steps. As such, the focus is on using steps with higher selectivity than reducing the number of steps involved. For all proteins, flow-through mode steps where impurities are adsorbed represent a major trend in purification strategies and help to keep column and buffer volumes small.

Furthermore, Frost & Sullivan points out that product stability and bio-activity is hugely dependent on proper folding of recombinant proteins. In the case of large therapeutic proteins such as GLPs, the protein refolding process is quite laborious, often causing a loss of a large quantity of the product. Disulphide bond formation is a post-translational modification required for the proper refolding and functioning of approximately one-third of human proteins. Being a complex multi-factorial process, native disulphide formation has not been possible in the cytoplasm of E.coli due to the presence of two reducing pathways. Nevertheless, the conventional methods employed in the periplasm of bacteria, or by using in-vitro oxidative refolding methods, pose limitations in terms of cost and efficiency.

Therefore, Frost & Sullivan firmly believes that any company that truly strives to adequately address these challenges and develop novel, innovative technologies for the enhanced expression of biologics and long therapeutic peptides in the most economical way - without compromising on quality - deserves appreciation and recognition in the healthcare society.

Technology Excellence and Visionary Innovation of Paras Biopharmaceuticals

Commitment to Innovation

As a fast-growing biopharmaceutical technology development company, Paras Biopharmaceuticals has built a robust portfolio of proprietary technologies for the high-level expression of biosimilars and long therapeutic peptides in specially designed genetically stable clones. The novel technologies developed by Paras Biopharmaceuticals include: a) Diabrid technology® that enables higher production of biologics compared to traditional methods and enhances the quality and effectiveness of molecules, in addition to significantly reducing the cost of production; b) Noble Cleav® technology that facilitates high-level production of authentic biologics by combining high specificity and activity of processing of recombinant therapeutic peptides and therapeutic proteins; and c) Biomultifold® Microbial High Expression technology that enables to achieve expression levels of multigrams of therapeutic proteins per litre of fermentation using E.coli. Furthermore, the company has an unrestricted license to use Cytoplasmic Oxidative Protein Folding technology for the high-level expression of homogeneously folded disulphide bond containing proteins in the cytoplasm of E.coli.

Best Practices Example: Paras Biopharmaceuticals has developed proprietary expression vectors based on the most optimum genetic codes selected for each amino acid of the therapeutic product. A selective combination is then developed using the most advanced optimization programs available in the industry in order to achieve the highest levels of protein expression. Genes are coupled with suitable Diabrid partners to achieve a unique combination of therapeutic proteins and peptides.

Stage Gate Efficiency

Paras Biopharmaceuticals has several biopharma active pharmaceutical ingredients (APIs) under development based on its novel, proprietary manufacturing technologies targeting therapeutic areas such as osteoporosis, rheumatoid arthritis, metabolic disorders (diabetes), and oncology. Those in advanced stages of development include PB-Osteo-1010, biosimilar Teriparatide API for use in post-menopausal women with osteoporosis subjected to a high risk of fracture or with history of osteoporosis fracture, PB-RA-2010, biosimilar Anakinra, a soon-to-be off-patent product for rheumatoid arthritis, biosimilar long acting insulin (Aspart), and biosimilar rapid-acting insulin (Aspart) for the treatment of type 1 and type 2 diabetes. In addition, the company also has 2 early-stage compounds, PPB (CT)-4010 and PB (CT)-4020 under development for oncology.

Best Practices Example: Paras Biopharmaceuticals offers a comprehensive technology package for the production of APIs of biosimilars, including proprietary designed robust production clones, reports on cloning, cell line development techniques, media optimization, fermentation, scale-up, product optimization, purification development, analytical methods (biosimilars fingerprinting with detailed report with MS/proteomics),

and product API characterization.

Application Diversity

The technology platforms invented and developed by Paras Biopharmaceuticals offer innovative and highly efficient processes that multiply the production of biopharmaceuticals in E.coli, resulting in significantly high biomass content. Given the very high levels of product titers, there is no need to change the clone frequently, which, in turn, is expected to simplify the regulatory process. Best suited for robust scale-up and commercial production, the Biomultifold® and Diabrid® technologies are applicable for a wide range of biopharmaceuticals, including its suitability for the production of monoclonal antibody fragments in E.coli.

Best Practices Example: Currently, the company has 6 major biosimilar product candidates in the pipeline based on its proprietary Diabrid technology platform, all of which target high-growth, high-value therapeutic areas with multiple products coming out of patent over the next 6 years. The company also plans to enter into strategic collaborations with industry participants for the clinical development of its oncology products.

Unmet Need

Frost & Sullivan independent analysis indicates that Paras Biopharmaceuticals' proprietary Diabrid technology® addresses the 2 key challenges in the biologics and therapeutic peptides industry, namely higher cost of biologics production and large-scale production of long therapeutic peptides - which is quite difficult, if not impossible, to achieve by chemical synthesis. Likewise, the Biomultifold® E.coli based technology comprises of a tightly regulated expression system induced by a low-cost, non-toxic, proprietary inducer that leads to a simplified post-production phase of protein purification, thereby significantly decreasing the purification costs.

Furthermore, the company's technology platform addresses cost and efficiency related issues in case of proper folding of lengthy recombinant therapeutic proteins containing disulphide bonds, including antibody fragments and other therapeutics.

Best Practices Example: Unlike eukaryotic and other prokaryotic systems, the Paras technology platform works in any E.coli strain. The system also works for all kinds of media and does not require any supplementation of media, thereby reducing costs. So far, the technology has been successful for the production and purification of a number of eukaryotic proteins, in high yields. Paras technologies has enabled high level production of an osteoporosis generic biologic which expects to deliver affordable healthcare in its true effectiveness. With 200 million people affected by osteoporosis worldwide, economical and quality therapeutics are expected to create better options for patients.

Blue Ocean Strategy

With most other competing technologies in the market focusing on the periplasmic folding of proteins, Paras Biopharmaceuticals is the only company worldwide to have demonstrated profound benefits with its patented propriety technologies. It provides all of the cost benefits of expression in E.coli rather than in eukaryotic systems, while still retaining the high yields obtained in cytoplasmic expression. Nevertheless, the biopharmaceuticals produced are of the highest quality and possess maximum biological activity in contrast to the activity levels obtained for various secreted proteins folding.

Moreover, Paras Biopharmaceuticals is one among very few companies that has managed to achieve a significantly high biomass yield of 6 g/L in E.coli and rendered molecular proteins non-toxic by virtue of its novel Diabrid® technology.

Best Practices Example: The resulting proteins based on the company's technology platform are homogenously folded and have native disulphide bonds and full biological activity. Eliminating the time-consuming process, Paras' technology platform significantly reduces production costs and development time.

Aspirational Ideals

Paras Biopharmaceuticals activities were initiated in 2009 by a team of scientists and technologists with extensive knowledge and experience in the development of biologics and biosimilar technologies. Today, Paras Biopharmaceuticals strives to offer innovative solutions for the effective and economic production of recombinant proteins. The company utilizes the most advanced understanding of protein purification, thereby achieving the highest purification standards and product quality. The company is actively seeking to partner with biopharmaceutical companies to offer its core strengths to shorten the time-to-market of products. Currently, discussions are ongoing for technology out-licensing in the United States, Asia, Europe, Russia, Africa, GCC countries, and CIS countries.

Best Practices Example: The Paras team not only possesses exceptional process development skills to achieve the highest levels of production, but also has extensive experience of handling different kinds of chromatography columns and the most advanced column packaging systems. Core strengths of the company range from media selection and development, optimization of process parameters, screening of resins to minimizing aggregation concepts in purification and scale-up/scale-down approaches in determining the most economic outcome.

Conclusion

Paras Biopharmaceuticals is one of the very few biopharmaceutical manufacturing technology providers that has developed a comprehensive portfolio of technology platforms to solve critical bioprocess issues in the most effective and economical manner, while still maintaining and improving product quality. Based on the aforementioned

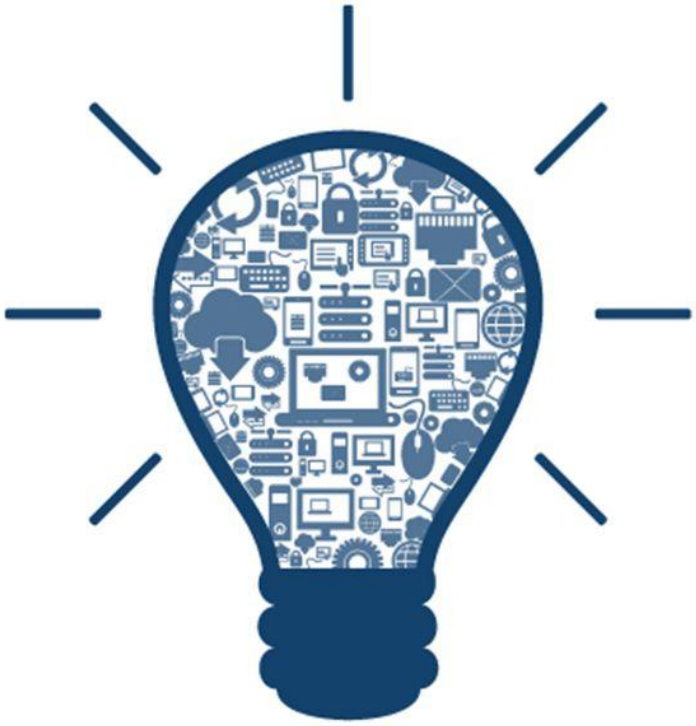
factors as measured through Frost & Sullivan independent analysis, Paras Biopharmaceuticals is the recipient of the 2014 Technology Innovation Leadership Award.

Significance of Technology Innovation Leadership

Ultimately, growth in any organization depends upon finding new ways to excite the market, and upon maintaining a long-term commitment to innovation. At its core, Technology Innovation Leadership is therefore about three key things: understanding demand, nurturing the brand, differentiating from the competition.

Understanding Technology Innovation Leadership

Deman forecasting, branding, and differentiation all play a critical role in achieving growth through technology innovation leadership. This three-fold focus, however, is only part of the journey. Ultimately, technology innovation leadership begins with an idea: with a spark of creativity that is systematically pursued, developed, and commercialized.



Key Benchmarking Criteria

For the Technology Innovation Leadership Award, Frost & Sullivan analysts independently evaluated the total client experience and strategy implementation excellence according to the criteria detailed below.

Technology Excellence

- Criterion 1: Commitment to Innovation
- Criterion 2: Commitment to Creativity
- Criterion 3: Stage Gate Efficiency
- Criterion 4: Commercialization Success
- Criterion 5: Application Diversity

Visionary Innovation

- Criterion 1: Unmet Needs
- Criterion 2: Use of Mega Trends
- Criterion 3: Pioneering Best Practices
- Criterion 4: Blue Ocean Strategy
- Criterion 5: Aspirational Ideals

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 players and for identifying those performing at best-in-class levels.

Decision Support Scorecard and Matrix

To support its evaluation of best practices across multiple business performance categories, Frost & Sullivan employs a customized Decision Support Scorecard and Matrix. This analytical tool compares companies' performance relative to each other. It 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. This tool allows our research and consulting teams to objectively analyze performance, according to each criterion, and to assign ratings on that basis.

Best Practice Award Analysis for Paras Biopharmaceuticals

Decision Support Scorecard: Technology Excellence

The Decision Support Scorecard illustrates the relative importance of each criterion and the ratings for each company under evaluation for the Technology Innovation Leadership Award. 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.

Finally, to remain unbiased and to protect the interests of all organizations reviewed, we have chosen to refer to the other key players in as Company 2 and Company 3.

Decision Support Scorecard: Visionary Innovation

DECISION SUPPORT SCORECARD FOR TECHNOLOGY INNOVATION LEADERSHIP AWARD (ILLUSTRATIVE): TECHNOLOGY EXCELLENCE

Measurement of 1–10 (1 = poor; 10 = excellent)	**Award Criteria**					
Technology Excellence	Commitment to Innovation	Commitment to Creativity	Stage Gate Efficiency	Commercialization Success	Application Diversity	**Weighted Rating**
Relative Weight (%)	**20%**	**20%**	**20%**	**20%**	**20%**	**100%**
Paras Biopharmaceuticals	**9.6**	**9.5**	**9.5**	**9.0**	**9.7**	**9.5**
Company 2	9.3	9.1	9.0	8.8	9.1	9.1
Company 3	8.9	8.9	8.5	8.3	9.2	8.8

Criterion 1: Commitment to Innovation

Requirement: Conscious, ongoing development of an organization culture that supports the pursuit of groundbreaking ideas

Criterion 2: Commitment to Creativity

Requirement: Employees known for pushing the limits of form and function, and who are unafraid to pursue "white space" innovation

Criterion 3: Stage Gate Efficiency

Requirement: A process that moves creative, groundbreaking concepts quickly and profitably from early-stage investments to late-stage prototyping

Criterion 4: Commercialization Success

Requirement: A proven track record of taking new technologies to market with a high rate of success

Criterion 5: Application Diversity

Requirement: The development of technologies that serve multiple purposes and can be embraced by multiple user types

Decision Support Scorecard: Visionary Innovation

DECISION SUPPORT SCORECARD FOR TECHNOLOGY INNOVATION LEADERSHIP AWARD (ILLUSTRATIVE): VISIONARY INNOVATION

Measurement of 1–10 (1 = poor; 10 = excellent)	**Award Criteria**					
Visionary Innovation	Unmet Needs	Use of Mega Trends	Pioneering Best Practices	Blue Ocean Strategy	Aspirational Ideals	**Weighted Rating**
Relative Weight (%)	**20%**	**20%**	**20%**	**20%**	**20%**	**100%**
Paras Biopharmaceuticals	**9.7**	**9.1**	**9.6**	**9.7**	**9.7**	**9.6**
Company 2	9.0	8.5	9.2	8.9	9.3	9.0
Company 3	9.0	8.6	8.7	8.5	9.0	8.8

Criterion 1: Unmet Needs

Requirement: A clear understanding of customers' desired outcomes, the products that currently help them achieve those outcomes, and where key gaps may exist

Criterion 2: Use of Mega Trends

Requirement: Ability to incorporate long-range, macro-level scenarios into strategic plans, thereby anticipating and preparing for multiple futures that could occur

Criterion 3: Pioneering Best Practices

Requirement: A nothing-ventured-nothing-gained approach to strategy implementation that results in processes, tools, or activities that generate a consistent and repeatable level of success

Criterion 4: Blue Ocean Strategy

Requirement: Proven track record of creating new demand in an uncontested market space, rendering the competition obsolete

Criterion 5: Aspirational Ideals

Requirement: A willingness to look beyond the simple goal of generating a profit to embrace a more powerful ideal of bringing greater value to customers

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 almost 50 years of experience in partnering with Global 1000 companies, emerging businesses and the investment community from 31 offices on six continents. To join our Growth Partnership, please visit http://www.frost.com.