

2009 North American RNAi Therapeutic Design & Delivery Technology Innovation of the Year Award

RXi Pharmaceuticals

The 2009 Frost & Sullivan North American Technology Innovation of the Year Award in the field of RNAi therapeutic design and delivery goes to RXi Pharmaceuticals in recognition of the company's development of RNAi compounds, rxRNA™, and delivery methods. RXi Pharmaceuticals implements several technologies that include self-delivering rxRNA (sd-rxRNA™), glucan encapsulated RNAi particles for local as well as systemic delivery, including delivery to the liver for metabolic diseases.

Company Background

Founded in January 2007 by Craig Mello, the 2006 Nobel Laureate for Medicine, RXi Pharmaceuticals (RXi) has positioned itself as a discovery stage Biopharmaceutical Company with a strong focus on treating inflammatory and metabolic diseases as well as many other diseases through the mechanism of RNA interference. Through a culture of innovation and research fostered by its founders, RXi has employed its existing RNAi intellectual property to build expertise and specialized therapeutics in treating inflammatory and metabolic diseases.

Technology Relevance in the Market Place

With nearly 8 million people in the United States being afflicted by inflammatory diseases, there is a constant need to develop safe and effective alternatives to conventional therapies. Moreover, inflammation is the main factor for the initiation and progression of several diseases that include rheumatoid arthritis, crohn's disease, atherosclerosis, inflammatory bowel disease, diabetes, and on the like. On the other hand, high cholesterol, obesity, and Type-2 diabetes are the main health problems affecting hundreds of millions of people globally. The WHO approximates that on a global basis, there are more than 300 million obesity cases and 159 million Type-2 diabetes cases.

Although, several genes connected to the disease have been identified, these are tough to treat with conventional medicinal chemistry. RNAi technology may have a

crucial role in targeting these genes and potentially treating diseases. The important aspect of success in RNAi therapeutics is in delivering intact RNAi compounds to the target tissue and the interiors of the target cells. At present, the various RNAi therapeutic products that are being designed need frequent intravenous injections or other forms of administrations which do not suit clinical needs and are not patient-friendly.

Technology Overview & Innovative Features

RNAi compounds are mostly duplexes of two strands of chemically synthesized RNA and they are significantly different in the efficacy, stability, and specificity. They are of different chemical modifications and lengths (i.e. with different number of nucleotide units). The combination of the length, nucleotide sequence, and the configuration of chemical modifications determine the effectiveness of RNAi therapeutics. Based on the above mentioned factors, RXi Pharmaceuticals has developed a class of rxRNA™ compounds which are optimized for a specific gene target, delivery route and disease indication. RXi's rxRNA™ compounds are different from conventional small interfering RNA (siRNA) compound used for RNAi therapeutics. The rxRNA™ compounds are up to 100x more active than conventional siRNA (depending on the target site), have increased nuclease stability with decreased toxicity levels and are readily manufactured.

RXi delivers intact RNAi compounds to the target tissue and the interiors of the target cells. The company is involved a comprehensive program that includes oral, systemic and local delivery approaches. These approaches take benefit of direct delivery of RNAi compounds and administration of RNAi compounds using an additional delivery vehicle. The GeRP technology may enable the rxRNA™ compounds to be incorporated into orally administered pills. The GeRP delivery system consists of hollow, porous, micron-sized shells, which can be filled with more than one type of RNAi compounds. When the pills are ingested, they are taken up by microfold cells in the intestinal wall and then transport to immune cells in the underlying gut associated lymphatic tissue (GALT). Once macrophages and other phagocytic cell types take up the GeRPs, the RNAi compounds are released into the cytoplasm to silence the specific target gene. The method of oral administration offers a much less invasive alternative that is also more suitable than injection, which is the current standard of care for patients with these inflammatory diseases. This results in improved compliance and potentially greater market acceptance of the product. The technology resolves the pathology of inflammation by specifically delivering the drug to macrophages, key cells involved in the progression of various inflammatory diseases.

RXi is also developing advanced systemic delivery solutions that employ nanotransporters to aid in transport of RNAi compounds to several target tissues, including the liver. This system protects the RNAi compound in the body until it reaches the target tissue.

In addition, the company is also developing a portfolio of advanced direct delivery solutions that enables rxRNA™ compounds to be administered without an additional delivery vehicle. These new compounds are called self-delivering rxRNA™ (sd-rxRNA™) and have shown promising pre-clinical results.

Best Practices

The company has a strong early intellectual property position in RNAi chemistry and delivery. The company is also an active participant in several conferences such as IBC's Oligonucleotide Therapeutics Conference, Biotech Industry Conference, Oligonucleotide Therapeutics Conference, Bio CEO & Investor Conference and so on. Employees and advisors to RXi Pharmaceuticals also have publications in several peer reviewed journals such as *Nature*, *ACS Chemical Biology*, *Molecular Cell* and *Proceedings of the National Academy of Science*.

Conclusion

In recognition of the company's development of RNAi compounds, the rxRNA™, and delivery methods in the field of RNAi therapeutic design and delivery for inflammatory and metabolic diseases, Frost & Sullivan is pleased to present the 2009 North American Technology Innovation of the Year Award to RXi Pharmaceuticals.

Award Description

Frost & Sullivan's Technology Innovation Award is bestowed upon a company (or individual) that has carried out new research, which has resulted in innovation(s) that have or are expected to bring significant contributions to the industry in terms of adoption, change, and competitive posture. This award recognizes the quality and depth of a company's research and development program as well as the vision and risk-taking that enabled it to undertake such an endeavor.

Research Methodology

To choose the award recipient, Frost & Sullivan's analyst team tracks innovation in key hi-tech markets. The selection process includes primary participant interviews and extensive primary and secondary research via the bottom-up approach. The analyst team shortlists candidates based on a set of qualitative and quantitative measurements. The analysts also consider the pace of research and technology innovation, and the significance or potential relevance of the innovation to the overall industry. The ultimate award recipient is chosen after a thorough evaluation of this research.

Measurement Criteria

In addition to the methodology described above, there are specific criteria used to determine the final rankings. The recipient of this award has excelled based on one or more of the following criteria:

- Significance of the innovation(s) in the industry, and across industries (if applicable).
- Potential of the products of innovation(s) to become industry standard(s).
- Competitive advantage of innovation vis-à-vis other related innovations.
- Impact (or potential impact) of innovation(s) on company or industry mind share and/or company bottom line.
- Breadth of intellectual property related to the innovation(s), that is, patents, scientific publications, and papers in peer-reviewed journals.

About Best Practices

Frost & Sullivan Best Practices Awards recognize companies in a variety of regional and global markets for demonstrating outstanding achievement and superior performance in areas such as leadership, technological innovation, customer service, and strategic product development. Industry analysts compare market participants and measure performance through in-depth interviews, analysis, and extensive secondary research in order to identify best practices in the industry.

About Frost & Sullivan

Frost & Sullivan, the Growth Consulting Company, partners with clients to accelerate their growth. The company's Growth Partnership Services, Growth Consulting and Career Best Practices empower clients to create a growth focused culture that generates, evaluates and implements effective growth strategies. Frost & Sullivan employs over 45 years of experience in partnering with Global 1000 companies, emerging businesses and the investment community from more than 30 offices on six continents. For more information about Frost & Sullivan's Growth Partnerships, visit <http://www.frost.com>.

www.awards.frost.com