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# ARECOR: Improved Biotherapeutics Through Smart Formulation Technology

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**Abstract:** Arecor is a fast growing startup that has a proven track record in developing superior biopharmaceuticals through the application of its innovative formulation technology platform. Arecor is leveraging this platform to develop a portfolio of proprietary products enabling improved treatments for diabetes care via the innovative reformulation of approved proteins and peptides. It was founded in 2007 in the Cambridge ecosystem as a very small team of five people.

**Keywords**: formulation, biopharmaceuticals, vaccines, diabetes, stability, patient convenience

## 1. The success story

Arecor, a Cambridge based biotechnology company founded in 2007, is a world leader in formulation technology innovation and has a proven track record of delivering superior biopharmaceuticals by application of its proprietary technology (Arestat™) to a broad range of therapeutic proteins and peptides. The technology enables development of products that have superior stability and other advantages such as low viscosity or compatibility with state-of-the-art delivery devices, providing considerable benefits both for the patients and for the healthcare professionals. For example, Arecor has developed heat stable vaccines that do not require refrigeration and can be delivered to remote parts of sub-Saharan Africa where they are most needed. Other products developed by Arecor allow convenient self-administration of therapeutic products by eliminating the need for reconstitution prior to their use and enabling sufficient stability of the products outside the cold-chain. So, whilst Arecor is not directly involved in the discovery of new drugs, it can apply its technology to improve existing products, giving them a considerable commercial advantage. Arecor has established commercial licensing partnerships with many of the world's leading pharmaceutical and biotech companies to

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ensure its smart technology is converted into products that will benefit patients. In addition, Arecor is leveraging its technology platform to develop an in-house portfolio of proprietary products enabling improved treatments for diabetes care via the innovative reformulation of approved proteins and peptides with the view to licensing these high-value assets at a later point.

## 1. Where did we start?

As it is often the case, Arecor came into existence not by design, but by a gradual, organic development. The company is a spin-out from another start-up company called Insense Ltd, which was set up in 2001 by a biotechnology entrepreneur, Prof. Paul Davis, with initial backing from Unilever Ventures to develop novel wound care products to improve the treatment of venous and diabetic ulcers. During the successful development of these products, it was essential to stabilize proteins that were critical components of these novel medical devices. A considerable effort was invested into solving this problem and several interesting discoveries were made. Ironically, many of these discoveries were most likely made because none of the scientists involved in this process was specifically trained to be protein formulators and a lot of unusual conditions and excipient combinations were thus tested. It is quite possible that a trained formulator would simply follow the textbook formulation optimization processes and the discoveries would thus not be made. Importantly, apart from solving the immediate problem of protein stability for the wound care products, the discoveries raised an intriguing possibility of improving the stability of other important proteins and peptides, particularly those used as therapeutic products. Therefore, the team, with the backing of the shareholders, embarked on a new journey aimed at securing a supply of important therapeutic proteins and vaccines, learning about the stability requirements of therapeutic products and assessing what improvements the newly discovered formulation principles could make. Support from UK grant-funding bodies as well as Bill Gates Foundation was invaluable during that time. As expected, it was a steep learning curve and not a completely straightforward journey, but eventually, the team demonstrated that it can create a significant improvement in the quality of the selected products which can improve the life of patients and that is also commercially meaningful. It was subsequently an easy decision to set up a new company that would focus entirely on the further technical development of the novel formulation technology as well as its commercial exploitation. This is how Arecor was born.

## 2. Our technology

The Arestat™ technology includes several unique formulation platforms that define specific combinations of excipients and other conditions resulting in a reduced rate of protein degradation. Whilst some of these platforms are specific to controlling chemical degradation pathways such as hydrolytic processes or deamidation, other platforms control various physical aspects of stability such as the formation of soluble aggregates and particles. On a physicochemical level, the platforms are based on a unique understanding of how structural features of excipients interfere with detrimental interactions between proteins; including hydrophobic interactions, ionic interactions, interactions with metals via coordinate bonds,

interactions at liquid/air or liquid/solid interfaces and many others. Arecor uses proprietary structural parameters and computational approaches that allow prediction of how an excipient of a given structure will interact with proteins and thus prevent a specific detrimental interaction between protein molecules. For example, one specific platform is based on the use of small amphiphiles in low ionic strength that was found to have a strong stabilizing effect with respect to the hydrophobicity-driven aggregation of proteins by masking hydrophobic patches at the protein surface. Thus, the use of a benzoate anion, a preferred small amphiphile, in specifically defined ionic strength compositions is an example of a proprietary formulation (protected by granted patents - EP2283027B1 and US9005611B2) that has been used to achieve significant improvement in the stability of commercially important proteins and peptides. Applications of this formulation platform to therapeutic proteins and peptides are shown in Figures 1 and 2. In a different platform, novel combinations of buffering species (denoted as “displaced buffers”) have been developed by Arecor for any given pH that lead to a considerably lower rate of aggregation and hydrolytic degradation due to limited proton exchange at the protein surface. This represents another patented proprietary formulation platform (EP2114456B1, US20150071879A1). These are just two examples of Arecor’s extensive proprietary formulation technology platforms that can be applied in this grant work. Many of the above platforms have been patented although some are also kept as trade secrets. The technology also comprises considerable know-how and computational algorithms for efficient screening of the platforms to enable Arecor to find unique stabilizing formulations most efficiently against strict time-lines often associated with collaborative projects with pharmaceutical companies.

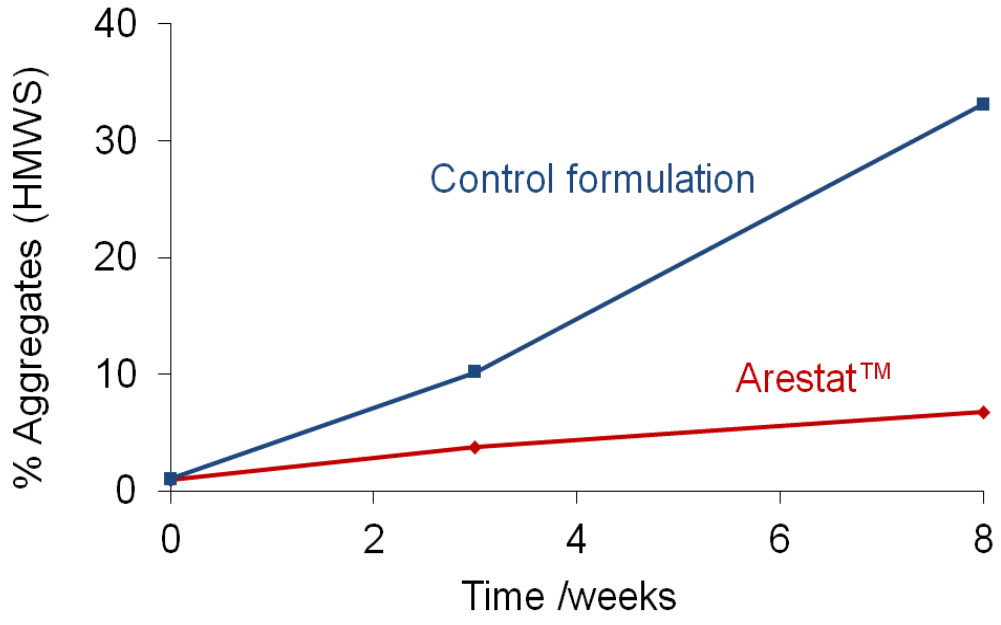


**Figure 1.** Stability of a therapeutic protein (25 mg/ml) at 40°C measured by SEC. Control formulation = optimised formulation developed by the partner company.

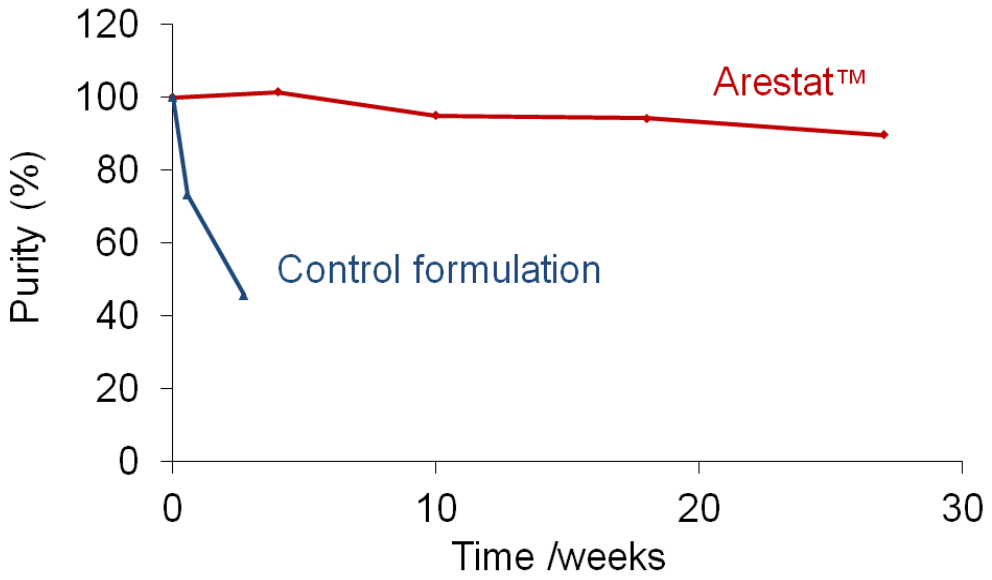


**Figure 2.** Stability of aqueous glucagon (1 mg/ml) at 25°C measured by RP-HPLC. Control formulation = reconstituted marketed product.

## 3. The journey so far

Arecor started as a very small team of five people and there was a lot to do. Firstly, we had to continue refining the novel approaches to formulating biopharmaceuticals we had discovered up to this point. This meant not only improving our understanding of interactions between proteins and excipients but also finding the most meaningful ways of how these unique insights can address the stability problems of different classes of therapeutic products and vaccines in a way that matters. In other words, we had to make sure that we did not become an "academic boutique" that is doing interesting science that has no real application – we had to make sure that what we do is useful in the real world. Secondly, we had to start generating meaningful IP to protect the increasing number of discoveries, insights, and applications related to protein stability. This required a lot of discipline and collaboration with patent agents both in the UK and in the US. Both our technology portfolio and our IP portfolio has been steadily growing and it will undoubtedly keep growing in the future. Our team has slowly grown to 18 members of staff, mainly hands-on scientists, and most importantly, our confidence has grown with it. The third critical component of the journey was to identify and implement a plan for commercial exploitation of our technologies – we needed a solid business plan! We knew from very early on that since we are not a drug discovery company and do not, therefore, have any products of our own we had to start establishing partnerships with pharmaceutical companies, particularly those that are interested in innovation and seek external partners for that. Therefore, we started an intensive business development on both sides of the Atlantic. Early collaborations led to good results which further contributed to our confidence that we can make a meaningful difference in many therapeutic products. Today, we have several multi-product licensing agreements with many pharmaceutical companies and products at various stages of development. As always, the journey has not always been smooth, but a combination of good science, determination, and the ability to learn from our mistakes took us to a very

good position where we are now. The year 2015 was an important milestone in Arecor's journey. Whilst the partnering business was going very well at that point, we decided to develop a portfolio of our own products. We went through a rigorous process of selecting specific commercially attractive differentiated product concepts of off-patent molecules that we believed our technology can deliver. We then managed to get hold of sufficient quantities of the active ingredients and started our own in-house development. This was by no means a sudden decision. The possibility of developing our own products has always been discussed internally at numerous meetings and a lot of intellectual effort was invested into identifying the best process to achieve this, identifying the best product candidates and preparing a realistic business plan that recognizes the value as well as potential risks, both technical and commercial, of such enterprise. However, 2015 was the year when we made the final decisions and started working on three separate in-house development programmes. All of them are going extremely well and we will be entering Phase 1 clinical trials with one of them in 2017. All three product concepts are in the area of diabetes and we have been very fortunate to receive a significant financial, as well as, technical support from the Juvenile Diabetes Research Foundation. We also keep an active dialogue with several possible future large Pharmaceutical licensees, including the three major companies in the diabetes space. From this dialogue, we can be certain that we have made the right choices and we also receive invaluable technical support from them.

## 4. Looking to the future

Arecor is built on a solid foundation of a validated proprietary technology, excellent contacts with pharmaceutical companies and a robust business plan that includes a lower risk partnering business and higher risk development programmes. Since founding the company we have accumulated an enormous amount of experience and expertise, both technical and commercial, in the area of differentiated biopharmaceutical products formulation. Both sides of the business are progressing very well. Although the world of biotechnology is fast-changing and notoriously difficult to predict, we know exactly where we are aiming and are very confident about our future.

## The company

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Jan Jezek is the Chief Scientific Officer at Arecor Ltd. He has been trained as a biophysical chemist and holds a Master's degree from the University of Chemical Technology in Prague and Ph.D. from the University of Bedfordshire (UK). He continued his carrier as a post-doctoral scientist developing novel biosensors for measurement of water quality, and then at Insense Ltd where he was the principal scientist behind the development of a range of novel wound dressings, leading the product development from the proof-of-concept all the way to market. During his time at Insense, he and his team developed a novel formulation platform to achieve superior stability of proteins and other biological molecules. His inventions related to protein stabilisation led to inception of Arecor Ltd as a separate company focusing on commercialisation and further development of the stabilisation platform. He is the author of several papers and a number of patents which underpin Arecor's technology.