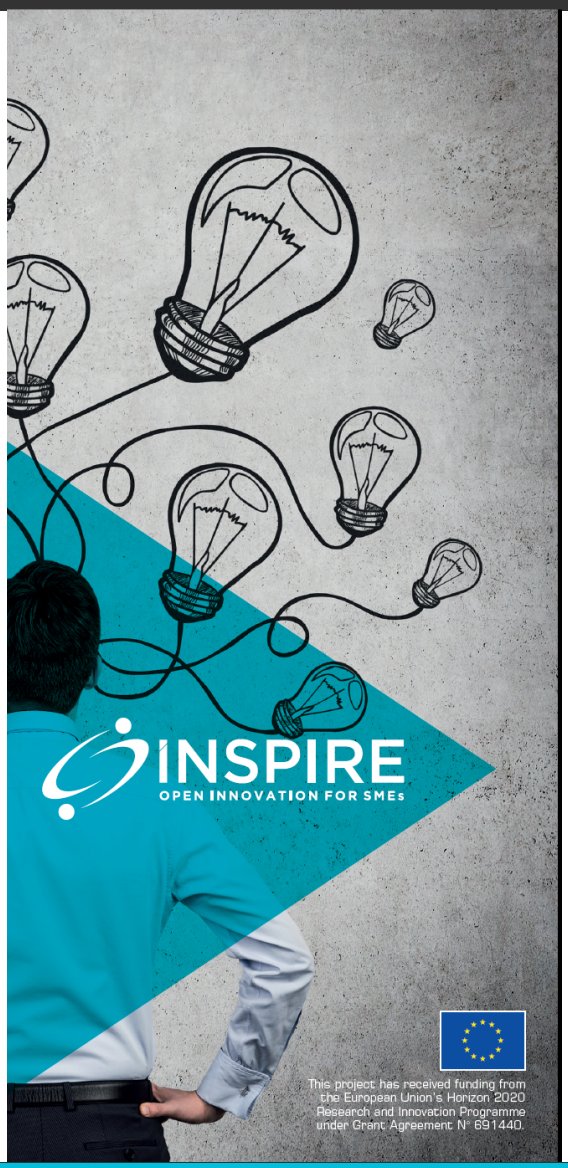

ANONYMOUS

United Kingdom

A university spin-out company collaborated with both a UK-based PSR and a non-European PSR in Brazil which undertook clinical tests for it. The case shows how the partners overcame logistical, technical and regulatory challenges to develop a novel product which meets a strong clinical need

Executive Summary

This is the story of a medical technology spin-out company from a UK university which develops regenerative solutions for the problems of ageing and disease. The company's value proposition is that it has been developing solutions which do not need to be cryogenically stored and that potentially adapt to younger patients who are still growing. The company has successfully performed implantation testing to ascertain the functionality of its heart valves in collaboration with university partners in the UK and South America. The OI project has been an important step to undertaking full clinical trials of its heart valve products.ing.

CASE N°: UKI07

SECTOR: MEDICAL

TECH INTENSITY: HIGH-TECH

LIFE CYCLE STAGE: EARLY STAGE

INNOVATION VECTORS: PRODUCT

OI PARTNERS: PUBLIC SECTOR RESEARCH

KEYWORDS: Medical technology, heart valves, licensed-in technology, university spin-out, partnerships with global PSR organizations

BACKGROUND

The company was formed in 2006 as a spin-out from the University of Leeds. Its focus is on commercializing academic research conducted by its partners. Its products are medical devices for use in regenerative medicine and are based on patented decellularization (dCELL) technology. The dCELL technology removes DNA and cellular materials from animal and human tissue; the tissue scaffold can then be implanted in patients to repair worn-out or diseased body parts. This technology can be applied in a wide range of potential applications from the treatment of vascular disease to knee repair.

The company CE marketed its first product, a dCELL Porcine-based Vasular patch, in 2010, the same year as it was listed on the London Alternative Investment Market. In 2014, the company's second product was launched, a dCELL-based human dermis for distribution in the US, for use in chronic and complex wounds. In 2016, the company moved from a bio-incubator to its own facility in Leeds, thereby enabling the company to undertake its own manufacturing on-site.

Sue Smith joined the company in 2008 after completing a PhD in Tissue Engineering at the University of Leeds. Her role in the company has been in product development and she is currently the Technical Manager, managing collaborations with third parties and transferring technology from product development to the manufacturing stage.

The process of commercializing biotechnology products is a relatively long process. The company is in the process of taking porcine products developed in the laboratory into manufacturing, scaling-up production and seeking approvals for its products' use in Europe and at a later stage in the US. In 2017, the company plans to launch its porcine-based dCELL tendon for anterior cruciate ligament reconstruction.

INNOVATION CHALLENGE & MARKET OPPORTUNITIES

The development of decellularization technology for use in clinical applications is a long and costly process, particularly when the clinical trials stage is reached. The company has limited funds to undertake the whole process in-house and therefore needs to build on-going relationships with partners to undertake strategically important collaborative projects.

A commercial director at the company had identified a large market opportunity for both pulmonary and aortic heart valves. Currently the two-types of heart valve products have notable limitations. Mechanical valves require patients to be on lifelong medication after implementation and for younger patients who are still growing, heart surgery is required every few years to replace the valves. On the other hand, bioprosthetic valves have a limited lifetime of around 10 years. This has created a strong market drive for regenerative heart valve products.

OPEN INNOVATION TRAJECTORY

Concept development

The company believed its dCELL technology would be ideal for developing a regeneratitive heart valve. Initial laboratory testing of a porcine pulmonary valve had been performed with successful results; however the company needed to perform further testing before undertaking clinical trials. The gold standard for longer-term testing of heart valves is their implantation in juvenile sheep.

The company approached the University of Leeds to collaborate on the project, as they had previous experience in this type of study. The company was introduced by the University of Leeds to a multi-disciplinary academic and clinical research group in Curitiba, Brazil. The group was seen as a potentially useful partner as it was headed-up by a cardiac surgeon, had its own tissue bank and had expertise in implantation in sheep models.

A grant application was submitted for the project consortium by the University of Leeds to undertake a functional animal study of the company's dCELL heart valve technology. The company part-funded the project but most of the funding was received from WELMEC (a Wellcome Trust and EPSRC funded Centre of Excellence in Medical Engineering) and the Medical Technologies Innovation and Knowledge Centre.

The development process, IPR and competition strategy

The project partner in Brazil implanted the company's heart valve into a sheep model for a period of 12 months. After 12 months the valve was removed and analyzed. As part of the analysis process, the researchers looked for signs of regeneration in the valve and at its bio-mechanical functionality. The aim of the study was to demonstrate that the dCELL-based valve was the same or better than the current best solution of a cryopreserved valve. This was successfully demonstrated; in addition the valve showed signs of potential regeneration.

As expected, project partners working across very different time-zones create several communication, regulatory and logistical challenges. The valves were made in the UK and shipped to Brazil for the study and then sent back to the UK; this required specific import and export approvals to be in place. An unexpected challenge arose around the restrictions in shipping dry ice. While UK carriers accept shipments involving dry ice, it was discovered that Brazilian carriers generally did not. This was overcome when one Brazilian carrier accepted the shipment.

A technical challenge arose when the juvenile sheep grew more quickly than expected during the study's 12 month period, leading to the requirement to replace the valves with new ones of an appropriate size.

The company's technology is based on IP developed and patented by the University of Leeds. The company has partial rights to use the university's IP.

There are several competitors developing decellularization heart valve technology but no products are available on the market. One of the main competitors is based in Germany and is currently undertaking clinical trials with a human decellularization heart valve; they are also looking at porcine versions.

As no decellularization-based heart valves are available on the market, there is a perceived race to be the first company to deliver a product. The company's USP for all their devices is two-fold. They have a potential to regenerate after implementation leading to a long service life in the patient. Secondly, they can be stored at room temperature rather than requiring cryopreservation, hence lowering storage costs and requiring less clinical preparation before implantation.

Commercialization and follow-up

Following the successful outcomes from the project, further analysis opportunities of the data have been identified. The commercialization strategy for the project outcomes is to partner with a German organization with a tissue bank with a view to forming a joint venture to develop a human dCELL version of the heart valve. This will verify that the technology works and help to gain acceptance in Europe. Due to the limited supply of human valves to create products from, this is not seen as a long-term solution. As a result, after the human dCELL valve project is completed, a follow-on, longer-term project will be undertaken with porcine dCELL valves leading to clinical trials being conducted over several years.

The company is in the process of further developing its manufacturing capability on-site. It is expected that as the company grows, it will benefit from the availability of local people already trained in harvesting and making valves, as another related company developing bioprosthetics valves is present in the same geographical area.

A major challenge in developing porcine heart valve products is that previous attempts by competing companies have failed, leading to patient deaths. This has led to scepticism in the clinical community and presents a challenge to people accepting that these products may still offer a solution.

The company is continuing to work closely with the University of Leeds to publish and present their project outcomes at important conferences and in journals.

BUSINESS IMPACT

The project has led to progress in new product development which would not have been possible without the partners and funding acquired. New high-quality data containing valuable functional performance of the dCELL porcine heart valve has been a key outcome of the project. This, in turn, has provided confidence within the company that the valves work as intended.

The project has helped to build a stronger relationship both with the University of Leeds and the Brazilian research group. As the findings from the project will be published in high-quality journals, it will assist the company in PR activities by raising its profile from a relatively unknown

company. Its association with internationally well-respected partners will also help in this regard.

The company has gained a better insight into what should be considered in future complex studies. This includes steps to manage deviations from project plans as a result of unexpected technical challenges.

As the porcine pulmonary heart valve has not been through clinical trials yet, it has not been made available for sale and therefore no income has been realized.

LESSONS LEARNED

The SME has learnt that it requires at least one designated project manager to manage OI projects and develop and deliver to a good project plan. Within this plan there should be a sufficient level of contingency planning to cope with unexpected events. It has also learnt the need to build on-going relationships with academic groups undertaking research in areas of interest to the company, rather than engaging only on a project-by-project basis. Furthermore, in building these relationships SMEs need to understand the differences in working methods between academic researchers and commercial organizations, e.g. the difference in the pace at which both work.

To assist the company undertake further OI projects, support in writing grant proposals would be helpful. The company has also found that events bringing together potential academic partners, clinicians and other companies to identify unmet needs and brainstorm ideas for solving these needs have been useful. It therefore suggests that more such events would be helpful, particularly if some form of mechanism is in place to help partners follow-up on discussions at the events.

This case offers a valuable example of an OI project involving a spin-out company which collaborates with both a UK-based PSR and a non-European PSR in Brazil. It successfully highlights how partners can overcome logistical, technical and regulatory challenges to develop a novel product which meets a strong clinical need.

This case has also highlighted that in some areas not-for-profit organizations can also collaborate strategically to help OI project consortia form and secure funding. The company has engaged with Regener8, the Medical Technologies IKC and WELMEC in the formation and funding of this project. These organizations consist of members from the UK research councils, government agencies, universities, other SMEs, large multinational companies and charities.

Main lessons learned:

1. The importance of not-for-profit organizations assisting in the formation and funding of OI projects.
2. The importance for SMEs to plan for and build on-going relationships with key PSR partners rather than engaging only on a project-by-project basis.
3. The need for a designated project manager and careful planning for contingencies.
4. The need for SMEs to understand the operational differences between commercial and PSR organizations, such as universities, to enable them to work together more efficiently.
5. Founding a company based on licensed-in technology can be the stepping stone to developing their own innovative derivative technology products.
6. Potentially valuable collaborators may be found at any distance and SMEs should seek the best partners irrespective of geographical distance.