



# INTEGRUM

Sweden, [www.integrum.se](http://www.integrum.se)

A small medical company with close connections to universities and hospitals made intelligent use of public grants to fund development projects which have put it in the enviable position of obtaining FDA approval for its revolutionary prostheses

## Executive Summary

Integrum makes innovative systems for bone-anchored prostheses that have been improving the lives of people with amputations since 1990. The implant system has been proven in several clinical studies and has been used by patients around the globe. The innovative technology is based on osseointegration, enabling the direct connection of an artificial limb to the skeleton. Several benefits, such as increased prosthetic use, improved mobility and enhanced quality of life, have been demonstrated.

For this type of company, it is vital to find a good collaboration between industry, academia and health care. It is important to network with key people who are able to open doors and help build the business. Integrum has participated in several open innovation projects, often funded by public grants.

**CASE N°: SC31**

**SECTOR: MEDICAL**

**TECH INTENSITY: HIGH-TECH**

**LIFE CYCLE STAGE: RENEWAL**

**INNOVATION VECTORS: PRODUCT, CUSTOMERS & MARKETING**

**01 PARTNERS: PSR, LEAD CUSTOMERS/USERS, HOSPITALS**

**KEYWORDS:** Research-based company, open innovation projects, FDA approval, academic publishing, public funding, collaboration with universities and hospitals

- BACKGROUND FRAMEWORK
- INNOVATION CHALLENGE & MARKET OPPORTUNITIES
- OI TRAJECTORY
- BUSINESS IMPACT
- LESSONS LEARNED



## BACKGROUND

Integrum makes innovative systems for bone-anchored prostheses that have been improving the lives of people with amputations since 1990. The history of the company started in 1962 when a Swedish professor, Per-Ingvar Branemark, used a titanium implant chamber to study blood flow in a rabbit bone and noted that the titanium implant could not be removed at the end of the experiment. He later coined the word "osseointegration" to describe the phenomenon when bone cells grow in direct contact with a titanium implant.

The discovery was initially used for the prosthetic replacement of teeth, but it has since been further developed and is nowadays also used for e.g. facial prosthetics and the anchorage of hearing aids. The discovery has since led to the creation of several new companies, many of them in the Gothenburg region. Jointly their annual sales are over €3 billion.

The implant system has been proven in several clinical scientific studies and has been used by patients around the globe. The innovative technology is based on osseointegration, enabling the direct connection of an artificial limb to the skeleton. Several benefits, such as increased prosthetic use, improved mobility and enhanced quality of life, have been demonstrated

In 1990 Dr Per-Ingvar Branemark and Dr Bjorn Rydevik performed the world's first surgery in which a patient was implanted with a transfemoral osseointegrated prosthesis\* in Gothenburg, Sweden. Integrum was established the same year, but did not start operations until 1998. The founders were Per-Ingvar Branemark and Rickard Branemark, father and son. Both father and son had been professors at Sahlgrenska University Hospital, but in different ways they also had connections to Chalmers University (in the same town).

In 2013, Dr Rickard Branemark led the world's first surgery in which neuromuscular electrodes were permanently implanted in an amputee. And in 2015, the U.S. Food and Drug Administration (FDA) announced that the OPRA Implant System was approved for adults who have amputations above the knee. Integrum is the first company in the world with a bone anchored prosthesis to be approved by the FDA for use in the USA.

\*Transfemoral amputation, is an amputation above the knee. Osseointegration is a method for anchoring the prosthesis directly to the bone.

In 2015 Integrum had 12 employees and a turnover of around €2 million. The company has been profitable most years, and is still owned by the founding family. It is expected that the company will start to grow considerably now that FDA approval has been secured. A new CEO, Jonas Bergman, was recruited. With a background at the School of Entrepreneurship at Chalmers University of Technology, Jonas joined Integrum in 2014 and became CEO in 2015.

Integrum's vision is to remain the world leader in the emerging industry of implanted prostheses. They want to make "natural" arms and legs for amputees that are controlled by the brain. They are already the world leader, but want to retain their position as competition increases. To do so they must continue to innovate. Today, their technology is revolutionary, and no other competitor has access to historical clinical tests. This makes it hard for others to catch up. In 10 years' time, Integrum wants to be a big Swedish med tech company and expect sales to reach €15–20 million by 2020.

## INNOVATION CHALLENGE & MARKET OPPORTUNITIES

Integrum already had experience of selling amputation prostheses anchored in the bone by titanium screws, when this project was initiated in 2006. The overall challenge and aim of the project was to develop an implant system with a higher-strength titanium alloy in addition to the pure titanium that was used at this time. They had seen that there were mechanical limitations when patients used their prostheses, which meant that they were not suitable for physically active people. The company's vision was to provide prostheses for very active people, such as war veterans, and for that they needed to undertake a study of how a higher-strength titanium alloy would work.

The company's vision was therefore to address very active people, such as war veterans, thereby opening up a much larger market niche for the company.

## OPEN INNOVATION TRAJECTORY

### Concept development

The project was divided into three different parts:

- Screening of existing alloys
- Surface modification for higher biomechanics
- Histological and biomechanical evaluation of titanium alloy

The end goal of the project was to have a well-documented biomechanical and histological evaluation of bone healing in connection with the laser surface modified pure titanium and a titanium alloy in comparison with untreated pure titanium and titanium alloy.

The expected results also had to achieve an unchanged biocompatibility and increased biomechanical anchoring for the laser surface-modified implants compared with reference implants.

## The development process, IPR and competition strategy

The project investigated which type of alloy would be most suitable. One material was identified and tested on animals with good results. During the project, Integrum collaborated with the Department of Biomaterials at Chalmers University. Integrum was also successful in attracting a Vin nova grant (the Swedish Agency for Innovation) for the development of the project. The company was relatively confident that the project would succeed. It was more about actually doing the work that needed to be done, but the company did not have enough of its own resources to do so. The funding helped Integrum to hire good staff. One example was a Masters student from Chalmers, who went on to play a major role in the development of the company.

The cooperation with the Department of Biomaterials at Chalmers was extremely important for the development of the product. The strong links have remained in place after this project. The collaboration was important for understanding biocompatibility and healing processes. This represented an important advance on earlier basic technology research. In turn, this has also led to a number of different patents. On another level, Chalmers University has also been an important source for recruiting new engineers for the company.

The challenge for Integrum has been less the development of the material itself, as the company is a world leader in titanium. The hard part has been the business side. Not only is it difficult to introduce new technology in this market, it has taken a long time to understand how the market

functions.

The industrial challenges have also been numerous, including:

- connecting suppliers to production
- increasing volumes; to go from small scale to a larger series is a challenge, but it is possible with proper verification
- developing the commercial organization and professionalism

Integrum has made a point of focusing a lot on building strong relations with hospitals. This has helped the company to obtain access to clinical data going back in time, and to be able to undertake retrospective studies. This is crucial in this industry, and creates a competitive advantage. No other amputation companies have access to similar clinical data. The fact that Integrum was able to do retrospective studies contributed to the FDA approval, which no other amputation company has yet managed.

The institutional framework (including regulations), and payment models via "reimbursements" are very complex in this industry. It is necessary to build good relations with, for example, insurance companies and various authorities, who are ultimately the ones who pay. Lead times are therefore long.

Integrum has been granted 8 patents and they have currently filed 11 more patent applications.

The company saw early on that the project would open up new market opportunities. Improved healing created new market segments, i.e. that the company could take a larger share of the potential market. Integrum has a niche-market strategy. They focus on three market niches: orthopaedic implants, brain-controlled prosthesis and treatment against phantom pain. Brain-controlled prosthesis and treatment against phantom pain are still in the R&D phase, while orthopaedic implants are more mature.

In this case, orthopaedic surgery is a key skill and it is the surgeons who make decisions about their patients. Without collaborating with surgeons at hospitals, Integrum would not have access to any patients or any clinical studies. Integrum's USP is to be a world leader with clinical studies (and academic publishing) supporting the product. It is extremely important for Integrum to have patients who are happy and enjoying an improved quality of life.

## Commercialization and follow-up

Traditionally research staff like to focus on research activities, and less so on business

opportunities. Generally, this leads to a mismatch between research and business activities. Integrum has tried to solve this by bringing in people who have a sales profile. It is difficult for researchers themselves to change into salesmen. Integrum therefore needs people who have a passion for selling. When Integrum sought funding for a second time from Vinnova, in the "robotics project", they had a good discussion just about commoditization, which was very valuable.

The company went about hiring business-oriented staff to offer more of a balance with the research-focus of existing staff.

The project has resulted in patents, which in turn has created a larger market through licensing opportunities. Integrum is targeting the US market, where the need for this type of product is high and the ability to pay for it is good, especially when it comes to helping war veterans. The most important customers are now the US Defence and the University Hospital in San Francisco. 6-7 other leading US university hospitals want to join as "collaborating customers". Hospitals are important collaboration partners, as they are research partners (clinical testing) and customers at the same time. It is not possible to succeed without collaborating with hospitals.

Integrum competes primarily with the older type of prosthesis which is placed on the outside of the stump. There are a few competitors moving in their direction, but none of them has done any studies yet. DARPA has funded a project in robotics, but with wireless transmission of data, and it involves some significant problems. Integrum is therefore in an interesting position: their customers have money and through partnerships with the US military they also have a direct link into health care funds, which is otherwise hard to achieve.

Integrum has received funding from Vinnova for several projects, covering various areas of development. One project involved sending light onto the titanium and forming free radicals to kill bacteria. It was an interesting idea but the project did not result in any conclusive results.

Another project concerned robotics. In this project wires are connected to the implants so that the patient can control the prosthesis with the brain. It was not possible to carry out such a project without public funding. The project has attracted much attention, and the founder has since had meetings with American scientists and DARPA has expressed an interest. Another example that can be highlighted is called Biomatcell. The only thing missing in this project is good industrial momentum. Without involving a partner with strong market drive, it will lead to too much development and too few sales.

## BUSINESS IMPACT

The project created new products and new innovations as a result. Integrum is now a small business with several product areas. In addition, the project and the Vinnova funding helped Integrum gain a broader understanding of their product, which is very important in such a sensitive market as the US. The new robotics project will, in turn, revolutionize the treatment of amputees and what people can do.

For this type of company, it is vital to find a good collaboration between industry, academia and health care. It is important to network with key people who are able to open doors and build the business. Integrum will continue to depend on its collaboration partners in the future. The market segments for brain-controlled prosthesis and treatment against phantom pain are still in a very early phase, with a need for further research and development. Integrum wants to continue to develop these segments in close collaboration and interaction with others.

In terms of impact on the business, the effect has been very positive. However, as far as sales are concerned, it is still too early to advance figures, but sales should start increasing soon. The titanium alloy is now approved in both Europe and the US and the effects on the business are expected to materialize after the FDA approval. Until now Integrum has not had a department for marketing and sales.

## LESSONS LEARNED

Integrum's development has taken a long time and cost huge investment. The company was successful in attracting public funding from Vinnova. It is important for Integrum to have adequate resources so that they can take appropriate action when there are problems or opportunities.

For this type of company, it is vital to find a good collaboration between industry, academia and health care/hospitals. Because of its long history (dating back long before the company started), Integrum is today the only amputation company in the world that has access to clinical data going back in time, thereby enabling the firm to undertake retrospective studies (together with hospitals and researchers).

The academic publishing which has resulted from these projects and studies has been important for Integrum. It has created scientific legitimacy, which has also helped Integrum with obtaining FDA

approval.

Integrum has participated in several open innovation projects, often funded by public grants, and will continue to do so in the future. One of the key issues for the company's development has been to find a balance between research and business oriented staff. After the recent FDA approval for its product, the company now expects to start expanding and growing.

#### Main lessons learned:

1. Integrum's development has benefited substantially from Vinnova funding. Vinnova has been visionary in funding six different projects over time which have helped to strengthen the company's position. It is important to have adequate resources so that appropriate action can be taken when there are problems or opportunities. Having too much money is not always good, but sufficient funding has allowed Integrum to aim high in their development work and not be forced to take the cheap solution which implies poorer quality.
2. Recruitment of staff is a key issue. Integrum often found high quality staff to hire through its collaborative open innovation projects (as in this case from Chalmers University).
3. Another result of the projects (for universities as well as hospitals) has been the academic publications which have helped to raise the profile of Integrum in a highly competitive niche market.