

Commercial Opportunity



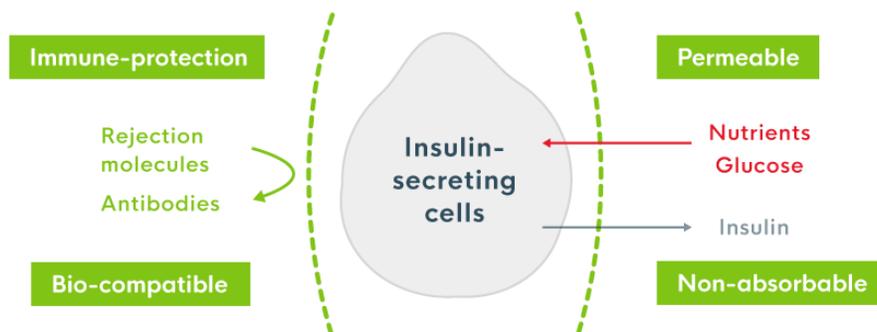
Title	MailPan®, a cell macro-encapsulation device developed to fight current unmet medical needs of diabetic patients
Challenge	<p>The current main therapy to treat diabetes is to provide patients with exogenous insulin. The main administration route is sub-cutaneous insulin injection using syringes, pens, pumps and artificial pancreas which couples a continuous glucose monitoring system with an external pump which injects the right amount of insulin according to the measured glycaemia. Despite the advantages of such devices, they deliver insulin subcutaneously, which is far from being the best physiological solution for insulin efficacy. To treat Type 1 Diabetes physiologically, human islets allo-transplantation allows patients to reach a stable normoglycaemia without exogenous insulin therapy. Indeed, this therapy still faces many problems such as the lack of human donor pancreases for islet isolation and the need for immunosuppression. The use of stem-cell derived insulin secreting cells is a good alternative to the lack of human cells but the risk of uncontrolled cell replication in the recipient organism and the need for immunosuppression limited the development of this therapy. To answer this, Defymed developed an innovative macro-encapsulation device, named MailPan®.</p>
Technology	<p>MailPan® is a bio-artificial pancreas developed to fight current unmet medical needs of diabetic patients. This cell macro-encapsulation device is designed to encapsulate new sources of insulin-secreting cells, available in unlimited sources, without the need for immunosuppressive therapy. MailPan® shall autonomously and physiologically regulate the blood glucose level because the cells detect the level of glucose in the blood and release automatically the required amount of insulin.</p> <p>This breakthrough innovation shall bring millions of diabetic patients close to a curative treatment which shall be fully autonomous (absence of daily management), non-painful (no more daily insulin injections and daily glucose monitoring) without need to take any medication (i.e. immune-suppressors), discreet (implantable, without need to wear a device (i.e. pump or Continuous Glucose Monitoring)), physiologic and efficient (absence of severe hyper/hypoglycemic episodes).</p> <p>Today treating patients with cell therapy is no longer a dream but a reality. The strong research on stem cells and gene therapy has opened up the field of possibilities. However, using them free presents a major risk for the patient (i.e. teratoma ...). MailPan® device shall allow this cellular therapy to be considered for a large number of pathologies, such as hemophilia or adrenal insufficiency. Finally, any pathology presenting a deficiency in protein production could be eligible for the encapsulation of cells producing this protein.</p>

<p>Competitive Advantage</p>	<p>MailPan® main advantages are:</p> <ul style="list-style-type: none"> - Possibility of replacing the cells without the need for surgery, thanks to an input and output connection to the device. - Physiologic: insulin-secreting cells are cell clusters in suspension mimicking endogenous ones. Mailpan® is implanted in a physiologic site which allows release of insulin in the portal system (important for rapid and efficient activity of insulin). <p>The USP of our combination is to treat physiologically and autonomously several pathologies in order for patients to be able to forget their disease.</p>
<p>Market Potential</p>	<ul style="list-style-type: none"> - Big Pharma/Big Medtech. Defymed has already collaborated and/or performed service contracts with some of these potential targets (identities are confidential for business reasons). The objective is to out-license MailPan® for the Diabetes application to a big Pharma or a Big Medtech. For this out-licensing process, Defymed is supported by an M&A consultancy company. - Diabetic patients, which are the end-users of the device. All type 1 and 20% of type 2 (who need insulin injection) diabetic patients should benefit from MailPan® due to total autonomy and physiological management of the disease. In 2017, this population is estimated to 425 million diabetic patients (€665 billion in 2017 spent on diabetes-related expenses). There is a high unmet need for autonomous management of glycaemia without need of daily control of blood glucose level and daily injection of insulin to significantly improve patients' quality of life. Defymed's objective is to develop the BEST solution to fight diabetes.
<p>Developmental Status</p>	<p>Several collaborative projects were fundamental to help Defymed to develop MailPan® in an open innovation environment and these projects raised more than 15 M€ for the development of MailPan® (public funds) plus 3.2 M€ in series A funding. Based upon the principle of bio-artificial pancreas, a prototype was validated in rodents under the BARP, and BARP+ projects coordinated by the Ceed (of which Defymed is a spin-off) and co-funded by the European Commission under FP4 and FP6, respectively. From 2013 to 2017, BIOSID project (FP7) allowed Defymed to validate several milestones on MailPan® (function and safety of pancreatic islet in the device).</p> <p>Several milestones have been achieved and are of prime importance for Defymed to obtain the authorization to enter clinical trials with MailPan® in Europe:</p> <ul style="list-style-type: none"> - Safety and bio-integration in 3 animal models - Immuno-protection in 2 animal models - Biocompatibility and sterility under ISO10993 - Function validated in diabetic rats - Surgical procedures for implantation and explantation are validated and safe - Filling and emptying procedure validated - Industrialization capacity in response to ISO13485:2016 standards
<p>IP Situation</p>	<p>Defymed's intellectual property protecting the cell macro-encapsulation device includes several owned or exclusively licensed patents, one trade-mark (MailPan®) as well as unique know-how. A Freedom to Operate search was conducted and has shown no obstacles hampering the exploitation rights of MailPan® in diabetes but also in other applications. In order to secure its value chain, Defymed signed exclusive manufacturing</p>

	<p>contracts with unique subcontractors. Defymed also performed market studies which clearly show the economic viability of its medical devices.</p>
Further Reading	<p>Website: https://defymed.com/mailpan/</p> <p>Publications:</p> <ol style="list-style-type: none"> 1. Bouaoun, <i>et al.</i> Le pancréas bioartificiel, un espoir pour les diabétiques de type 1? Mise à jour. Infusystems France, Vol.31, N°3, (2014) 43-48. 2. Rodriguez-Brotos <i>et al.</i> Impact of Pancreatic Rat Islet Density on Cell Survival during Hypoxia. J. Diabetes Res. 2016; 2016: 3615286. <p>Latest awards:</p> <ul style="list-style-type: none"> - Winner of the Medstartup- GalienAwards 2016 – Category “Best Innovative trial design leading to quicker and better therapeutic outcome” (2016) - Winner of the INPI award (2017)
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Figure(s)

Mailpan®



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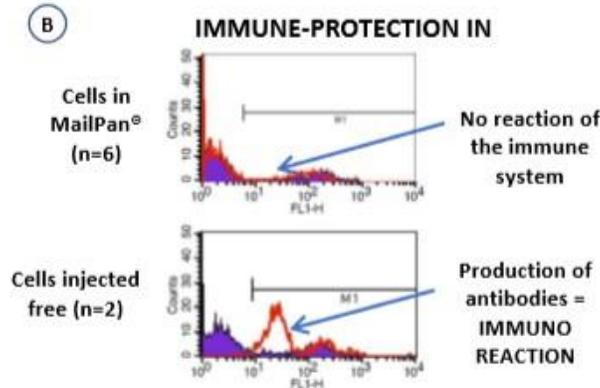
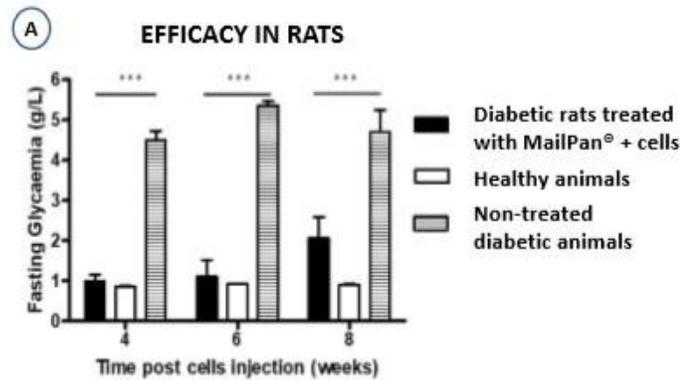
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Main results of MailPan®

A) Mean fasting glycaemia for diabetic rats with MailPan® filled with cells (black group), non-treated diabetic rats (striped group) and healthy control (white group).

B) Flow cytometry results 30 days after injection of islets (Rat specie X) into the MailPan® or free in subcutaneous of rat specie Y.



I'm interested in the following (more than 1 option can be chosen):

- Outlicensing IP (the first section is sufficient for this option)
- Investments (complete the Investment Opportunity section below)
- Collaborations (complete the Collaborative Opportunity section below)

Investment Opportunity (when selected)

<p>Business Concept</p>	<p>Exploitation activity of Defymed is based on a hybrid business model:</p> <ul style="list-style-type: none"> - Short-term: Non-exclusive service contracts to validate the combination of MailPan® with cells coming from different cell producers. This opportunity will help our non-exclusive partner to validate safety and efficacy of their cells in combination with our device in <i>in vitro</i> and <i>in vivo</i> models. Our patented medical device can be combined with different cell types for many therapeutic applications. All key parameters of our devices are customizable to meet customers' requests including the type of materials, shape, pore diameter and density, thicknesses, and surface coating. Moreover, this activity will help to prove to cell manufacturers that our device is essential to bring their cell therapy to reality for diverse therapeutic applications (door is opened for exclusive out-licensing). - Mid-term: out-licensing of the device to a big medtech or a big pharma in a specific field (first application is diabetes). For this, Defymed is already looking for a potential exclusive or non-exclusive licensee. After the out-licensing of the device, expected revenues will help the company to pursue the development of devices for other pathologies (such as adrenocortical disease and hemophilia).
<p>Team</p>	<p>Defymed's main asset, its team, was put together from a scientific, quality or even regulatory point of view with the aim of combining different complementary skill sets while also being dynamic and proactive. A feature of the Defymed team is its commitment and professionalism within a rigorous yet friendly working environment.</p> <p>Core team:</p> <ul style="list-style-type: none"> - Dr Séverine Sigrist, PhD - CEO and CSO. Severine led several R&D projects at Ceed, on type 1 and type 2 diabetes, where she led the development of a macrodevice to encapsulate insulin-secreting cells (MailPan®). Severine is also the president of the competitiveness Biocluster "Biovalley France" since 2014, a cluster dedicated to promoting Regional SMEs' innovation and increasing their competitiveness worldwide. - Dr Richard Bouaoun, COO, PhD, MBA. He has joined the Alsace-based incubator, SEMIA, as a project manager where he has accompanied the MailPan® project, before joining Defymed's team in March 2011. He is in charge of establishing and following Defymed's R&D collaborations, presenting Defymed® in international meetings and establishing contract services with academics/SMEs/industrials.
<p>Requested Funding</p>	<p>The company is looking for 4 to 5 million euros. This fundraising aims to co-finance the development of its products towards clinical trials in the Diabetes field. The valuation of the MailPan® device will allow us to customize the MailPan® device in order to meet other therapeutic applications, such as Haemophilia or adrenocortical diseases.</p>

Collaborative Opportunity (when selected)

<p>Team</p>	
<p>Envisaged Collaboration</p>	<p>The MailPan® project was set around several European projects including many public and private partners specialized in different domains, thereby opening up opportunities to go</p>

HEALTH BREAKTHROUGH

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beyond the normal limits and develop innovative medical devices. **Open innovation** is important for Defymed and brings together specialists with an extensive range of skills to tackle the same goal.

Over time, Defymed has surrounded itself with a network of experts working on innovative treatments for diabetes while also working on new medical technologies. Whether it is the patients, the scientific community or the medical profession, Defymed has a large local and international pool of resources to draw from in order to achieve its ambitions.

Defymed is looking for public (university) or private (SMEs) partners for the development of new applications using MailPan[®]. **Defymed's business model is to out-license MailPan[®] and in this objective, Defymed is also looking for a potential licensee (big pharma or big medtech) to out-license (exclusive or R&D) the MailPan[®] device.**