N°3 - January 2013

shareholder newsletter

A word from the CEO

Dear shareholders,

In this early part of the year, I am delighted to be able to address you through this third CARMAT Shareholder Newsletter*. 2012 was an intense year during which we simultaneously carried out numerous essential activities for our project. We trust that this Newsletter will help you get a good understanding of the diversity of these activities, as well as some of the talented people who have come onboard to help us pursue this unique project.

This Newsletter includes an interview with Professor Daniel Duveau, Medical Director at the Thorax Institute and Professor of Thoracic and Vascular Surgery at the Nantes Nord Laennec university hospital. Professor Duveau has been a part of the evolution of circulatory support systems and artificial hearts since their beginnings 30 years ago, and is a world-renowned expert in this field. His advice and support have been invaluable in validating medical regulation algorithms and setting up the in-vivo validation protocol, in collaboration with ONIRIS, the national college of veterinary medicine in Nantes.

CARMAT has adopted the aeronautical sector's integration model based on the coordination of a large number of suppliers and service providers. With this in mind, a considerable number of suppliers had to be incorporated within the value chain and trained to meet even higher standards than those governing the aeronautical sector. This sometimes meant tests and adjustments that caused delays. This is why we felt that it was necessary to pay tribute to an exemplary partner, a French SME that has always supported us since the very first micro-pump system mock-up 12 years ago: Vignal-Artru Industries. Its Chairman & CEO, Mr Laurent Le Portz, tells us about the long-term collaboration between our two companies.

Lastly, the CARMAT artificial heart project incorporates a number of breakthrough innovations such as the use of biological tissue and the automatic adjustment to the patient's physiological requirements. This latter feature is based on extremely sophisticated embedded software programmes that are considered to be medical devices in their own right insofar as they are vital for the patient. We would like to make the most of this Newsletter to acknowledge the considerable work carried out by our software development team.

Our project is moving forward and reaching further technical and regulatory milestones each day that are bringing us closer and closer to our first human implant. On behalf of the CARMAT team, I would like to thank all of our shareholders for their trust, their patience and their support. I wish you all a very happy and successful 2013, and look forward to addressing you again in our fourth Shareholder Newsletter and in the Company's future press releases.

Marcello Conviti
CEO

** Readers are invited to consult the caution note included in the Company's press releases*

Contents

The CARMAT motor-pump system:
facts and figures

The true heart of the CARMAT heart, the system consists of 2 connected electro-hydraulic pump units that displace an activating fluid that in turn displaces the biosynthetic membranes.

Characteristics:

- 200 grams
- Can run continuously for up to 12 years
- 7 years of R&D (2001-2008) to obtain the final prototype
- More than 100 people, researchers, technicians, engineers and operators, have contributed to this product
- 10 companies* have been working with CARMAT on the product's development, fine-tuning, validation and production

* CARMAT thanks the OSEO partners (Dedienne Santé, Ireis and Vignal Artru Industries), its suppliers (Arnold Magnetics, Invibio, Matra Electronique, Mecaplast and Precilec) and its service providers (LRA and Phimeca) for their contribution.

H2 2012 key events

July Satisfactory in-vivo implants and encouraging intermediary results for the endurance tests added to the ANSM file.

September Publication of the 2011 reference document.
2012 half-year results show a cash position of €16.6m at end-June 2012.

October The Company participates in the French American Biotech Symposium (FABS 2012) in Nice.
The Company participates in the Techno College of the 26th Annual Meeting of the European Association for Cardio-Thoracic Surgery (EACTS) in Barcelona.

The point of view of the clinician:
fascinating dialogue between technology and physiology

Interview with Prof. Daniel Duveau, Medical Director of the Thorax Institute and Professor of Thoracic and Vascular surgery at the Nantes CHU Nord Laennec university hospital.*

When did you first hear about the CARMAT project?

Over a decade ago, during a conference by Prof. Carpentier at the SFCTCV**. I'd always been drawn to the possible use of artificial components in heart surgery to repair or replace elements. Prof. Carpentier asked me to become involved in CARMAT's Scientific Committee, and I immediately accepted: coming onboard an adventure such as this is not something you turn down! When we created the transplant programme in Nantes in 1984, we were quickly faced with a divergence between the limited number of donors and the need for grafts. We therefore turned our attention to solutions enabling patients to wait for transplants in the best possible conditions. By 1986 we were already using the first artificial ventricles, initially external and then implanted within the abdomen 5 or 6 years later.

So you have participated in the entire evolution of this sector?

Yes, and much progress has been made over the last 30 years. At first, we only implanted devices for a few weeks, 3 months at the most. These days, there are a significant number of patients who keep their system for more than a year. We've also learned a lot about selecting patients to obtain better results. In 70% of cases, heart failure only affects the left ventricle, whence the development of a number of systems that solely assist the left side, and these systems have become increasingly miniature, easier to implant and more energy efficient. For the remaining 30% of cases, i.e. patients with terminal biventricular failure, there is currently just one solution – an artificial heart using pneumatic technology, which we were among the first centers to implant in the 1980s. However, this system has not evolved, it doesn't provide a response to effort and is noisy because of the compressor. With current systems, there are numerous complications because the blood circulates in non-biological systems where there are no endothelial cells. Furthermore, it is difficult to optimise anticoagulant treatment.

With the CARMAT heart, we have the ability to reduce these complications. It's more than plausible with our hindsight and experience of Carpentier-Edwards biological valves. Of course there will always be a risk, because this isn't a natural human organ, but we are confident.

How have you collaborated with CARMAT?

I didn't participate in the design or development at the start of the project, but I have been involved in the validation of physiological response algorithms and of course the in-vivo validation. It was really very interesting: at the very start of our collaboration, the engineers – essentially from the aeronautical sector – didn't know about cardiac physiology. A heart isn't exactly the same as a rocket! For example, when there's a haemorrhage the heart doesn't stop, instead it accelerates in order to continue supplying an appropriate blood flow. Similarly, one should always bear in mind that it's a patient who will use and live with the system: everything therefore has to be designed for a layman. We thus allowed the engineers to meet with and talk to people who are ill about their daily lives, their needs (sleeping, showering, getting dressed) and the way in which they use the batteries, fuel supply, alarms etc.

Could you tell us about the in-vivo validation?

CARMAT has carried out numerous bench tests, but there comes a time when surgical actions are necessary. In-vivo validation is an area in which we have a lot of experience thanks to our longstanding collaboration with ONIRIS, the national college of veterinary medicine in Nantes. There is real symbiosis between Prof. Gauthier's veterinary teams and our own surgical teams. The technical facilities and the teams' motivation have enabled a rapid pace of implants, an animal a week, which is a good performance on a French level, and indeed a European level. We have thus carried out a number of series of implants on calves, firstly to practice the surgical procedure and secondly to check that the prosthesis works properly. Although successful animal implants are not an absolute guarantee of safety for our first patients, this in-vivo validation, even short term, helps reassure both the regulatory authorities and clinicians.

Are you ready to implant the CARMAT prosthesis into patients?

As soon as we receive authorisation, of course.

* *Centre Hospitalier Universitaire (university hospital)*

** *Société Française de Chirurgie Thoracique et Cardio-Vasculaire (French Society of Thoracic and Cardiovascular Surgery)*

Focus on software development

What software is used for the CARMAT heart?

It would be more appropriate to talk of the CARMAT system's software, which is a set of specific developments spread between the implantable prosthesis and the external equipment. The first category concerns software directly "embedded" within the implanted prosthesis, and which steers it to ensure the flow of blood. This is this software that our division is responsible for. The Equipment division develops software for the external equipment, i.e. the console used at the hospital and patients' portable systems. They enable the remote exchanging of data and provide the alarm settings and displays.

What is the purpose of this embedded software?

Just like in a computer, there is software that steers the electronic components, software that controls the physical environment like a BIOS* and application software that ensures the steering of the prosthesis, medical regulation. The application software uses incremental logic for enhanced security. For example, one software package ensures a fixed flow defined by doctors via the external console. This is the software used during the implant, and also the software that takes over if there is a problem in order to ensure a minimum flow. Other software programmes enable the operational downloading of new features or versions, for example the software enabling automatic adaptations to the patient's metabolic requirements, on the basis of information provided by the sensors, which is downloaded when the patient leaves the hospital.

So this software ensures critical functions?

Yes; it ensures vital functions, and indeed its development is subject to strict norms, standards and controls. Software whose purpose is to be used by people to diagnose, control or treat an illness is considered to be a medical device in itself, and must therefore be developed in accordance with

Focus on the industrial model:
a partnership that is as demanding as it is rewarding

Interview with Laurent Le Portz, Chairman and CEO of the Pack'Aéro group.

What is the Pack'Aéro group's field of business?

Pack'Aéro is a French family-owned business backed by an investment fund specialising in non-listed companies called Entrepreneur Venture. Through our five subsidiaries including Vignal Artru Industries (VAI) we employ almost 220 people. We are a global tier-1 supplier of components and sub-assemblies essentially to the European aerospace industry, and directly deal with major clients and integrators such as Safran, Eurocopter and Dassault. More specifically, we are based around three divisions: precision mechanical engineering, surface treatment of metals and mechatronics, i.e. products combining mechanics, hydraulics and electromagnetism, either standard or custom-made, such as the high-precision electro-hydraulic pump system that we have developed with CARMAT.

How did your collaboration with CARMAT come about?

Although our presence is mainly in aeronautics, we have already worked on a medical device; an experimental trileaflet mechanical heart valve (Triflo Medical Inc.). We have over 50 years of experience in precision mechanics and an excellent grasp of people's demands. It was therefore quite natural that we should be approached within the framework of the OSEO contract to supply the moto-pump system, which lies at the very centre of the heart. Personally, I am fascinated by the biotech and medical device sector, as these devices are very similar to those within the aeronautical sector in many critical aspects such as their traceability and reliability. Being a tier-1 benchmark supplier in the aeronautical sector involves manufacturing critical elements where the slightest defect can send an aircraft plummeting to the ground, thus putting hundreds of lives at risk. Likewise, for CARMAT's artificial heart project, a defect in the pump system (the two electro-hydraulic pump units propel an activating fluid that displaces the biosynthetic membranes) can result in the patient's death. We therefore have the same criteria in terms of requirements and the same level of responsibility.

What specific challenges have you faced?

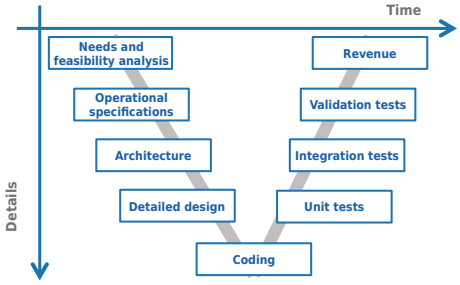
The development and production were the result of a real long-term collaborative process between CARMAT and VAI. The standards required are high and absolute, and regulatory constraints are even more drastic for an implantable medical device than they are for an aircraft. As with some parts of an aeroplane, the CARMAT heart's pump units are produced in small series and can tolerate only minute discrepancies with micron accuracy. We worked with other CARMAT partners such as a tribology specialist to reduce friction and optimise the units' performance. Within the framework of the CARMAT project, we do not manufacture simple components, but qualified comprehensive sub-systems, which entails their in-house manufacturing, putting together and checking. The traceability and validation requirements necessary for each part of an implantable medical device are much higher than those necessary in aeronautics: we therefore adjusted our quality management systems and set up specific validation and running-in benches. This requires not only manufacturing, but also engineering, and we have strengthened our research department in order to position ourselves as an equipment manufacturer in our own right, not only in aeronautics but also for complex life-support systems. We also created a specific decontaminated building for this purpose with teams of qualified operators.

What has this partnership with CARMAT brought you?

On a human level, it's an inspiring project, the flagship project for our teams: the operators working on the CARMAT project know that patients' lives will be dependent on their work. On a business level, the project has also led us to develop new skills and expertise in engineering and system qualification, thus strengthening our positioning and our growth prospects. Strategically, this is a very important project for us. We're in the starting blocks and have the ability to rapidly increase production as soon as the clinical trials are completed.

Vignal-Artru Industries – Chabeuil site (26 – Drôme)

– interview with Mohamed-Tahar Zaghdoud, Head of CARMAT's software division



V-shape development cycle from IEC 62304

norm IEC 62304, in class C. That's the level with the highest level of requirements used for software that could result in a patient's death. Each of the CARMAT system's software programmes, whether embedded or external, i.e. around a dozen, has been developed and tested in strict accordance with this norm, which describes the regulatory requirements for each stage of the development cycle as well as every activity and task that should be carried out to produce safe and reliable software. In particular, development and verification activities are clearly separated. The design teams are not involved in development and the development teams are not the same as those who carry out the tests.

Isn't this very consuming in terms of time and resources?

It took more than 5 years to design the first model software and then allocate the necessary resources to separating the teams. Each software programme is executed on embedded electronic components, so of a very restricted size in order to limit congestion and consumption. Maximum optimisation is therefore required to meet operational constraints. Furthermore, the physiological regulation algorithms have to provide real-time responses, i.e. in under a millisecond. We therefore validated, optimised, corrected and revalidated until we obtained a version presenting no risk to the patient.

No doubt one of the greatest professional challenges!

** Basic Input Output System*

CARMAT and the stock market
at December 31st, 2012

Share price (closing): **€127.38**
Number of shares: **4,157,795**
Free float: **26.7%**

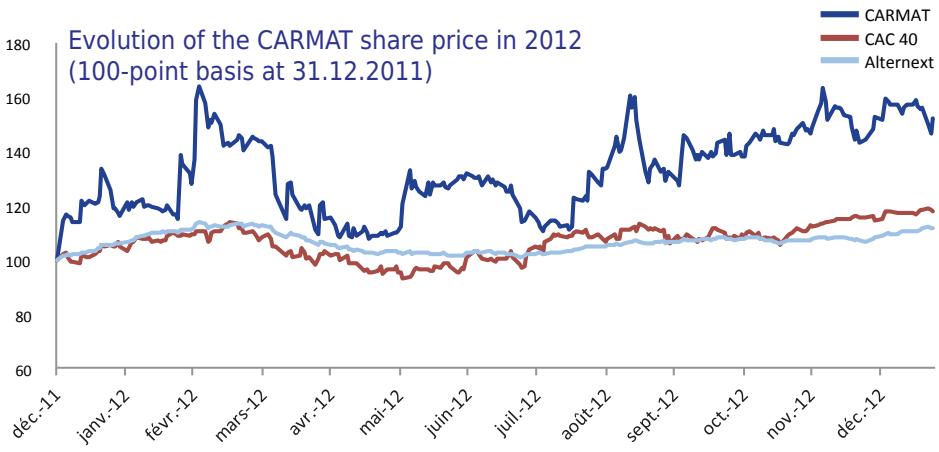
Name: **CARMAT**
Ticker: **ALCAR**
ISIN code: **FR0010907956**

ALCAR
LISTED
NYSE
ALTERNEXT.

2012 share performance

Change in share price: **+51.9**% (Alternext: +8.8% / CAC 40: +15.2%)

Liquidity: **9,800 shares a day** on average over FY 2012



Shareholders' questions

Why have there not been any more publications regarding the timetable since the reference document?
CARMAT is a listed company that scrupulously respects current rules and regulations. Within this framework, official press releases are the only ones that are binding. CARMAT bases its communication policy solely on significant proven facts likely to influence the project's progress. For example, the Company did not publish a press release in 2011 regarding its request for an opinion from the Patient Protection Committee, but did issue a press release to announce that it had received this favourable opinion. Therefore, given that there have been no new elements affecting the timetable – such as a decision from the ANSM (France's national agency for drug and health product safety) – since the publication of our reference document, there has not yet been a press release in this respect. We remind you that only press releases issued by the Company and its official representatives are binding. Private statements such as rumours, opinions, articles, headlines, accounts of interviews, minutes of meetings, analyses, blogs or comments on forums from either staff involved in the project or from people outside the Company purely reflect the personal opinions of those who publish them, and the Company does not comment on such statements.

What is your policy regarding the publication of Shareholder Newsletters?
The Company is fully aware of the importance of its artificial heart project for the financial community, and so it communicates in a transparent manner beyond the regulated mandatory information it is required to publish, through its Shareholder Newsletter for example. CARMAT's Shareholder Newsletter is an informative tool that supplements the legal information setup and allows readers to discover the project from a different perspective, better understand its technical component, which is unique in France, and get to know the various people involved in this fascinating project. It is published twice yearly, usually a few weeks after the end of each half depending on the availability of the people interviewed. In each issue of this Newsletter, CARMAT strives to provide readers with qualitative and enlightening information about its activity and those who fervently work on the project. However, it is not possible to mention, in a Shareholder Newsletter, significant new information that has not been the subject of a prior or simultaneous press release. Furthermore, a scheduled publication every six months is not suited to the announcement of new events whose occurrence, by their very nature, cannot be anticipated.

When can we expect the first human implant?
Our project is moving forward and reaching further technical and regulatory milestones each day that are bringing us closer and closer to our first human implant. Nevertheless, it remains subject to a decision from the ANSM, and CARMAT will officially inform the public by press release as soon as it receives this decision.

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Financial Agenda

Monday, March 4th, 2013
2012 full-year results

Monday, September 16th, 2013
2013 half-year results

CARMAT in the media

Les Echos

January 2013
"Following its listing in July 2010, the start-up, which has raised a total of 53 million euros and obtained 20 million euros in subsidies, essentially from OSEO, now has a market cap of almost 500 million euros."

Ca m'intéresse

December 2012
"This artificial heart has been developed by CARMAT and heart surgeon Alain Carpentier. Its microprocessor steers the pumps using information from three pressure sensors, two ultrasound sensors that detect the membrane's position and an accelerometer that determines the patient's position."

Pharmaceutiques

October 1st, 2012
"…French company CARMAT, as it awaits the go-ahead from the health authorities, is preparing to implant its artificial heart into a human being for the first time."

LE FIGARO

September 17th, 2012
"…[this] totally artificial heart is a little device weighing just 860 grams that has to meet numerous challenges. Its miniaturisation, for example, or adapting the prosthesis to the expected constraints (blood pressure, temperature) and unexpected issues (shocks, illness). However, the artificial heart's potential market is estimated at 16 billion euros, and CARMAT is aiming to get 10% of it."