EDISON

# Carmat

Outlook – clinical overview

## Back on track as pivotal study resumes

Healthcare equipment & services

**Carmat resumed the EU pivotal trial of its artificial heart after addressing regulator concerns. We anticipate that the study could be completed in mid-2019, leading to a potential EU launch in 2020. The Carmat device could potentially fill a significant need among those waiting for human transplants and/or with terminal heart failure (HF) or acute myocardial infarction (MI). Our valuation is €627m, down from €747m previously.**

| Year end | Revenue (€m) | PBT* (€m) | EPS* (€) | DPS (€) | P/E (x) | Yield (%) |
|---|---|---|---|---|---|---|
| 12/15 | 0.0 | (20.6) | (3.81) | 0.0 | N/A | N/A |
| 12/16 | 0.3 | (25.7) | (3.80) | 0.0 | N/A | N/A |
| 12/17e | 0.0 | (22.1) | (3.67) | 0.0 | N/A | N/A |
| 12/18e | 0.0 | (26.3) | (4.36) | 0.0 | N/A | N/A |

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

## Carmat heart intends to replicate human function

The Carmat heart is the first biocompatible, biventricular mechanical heart, and is designed to act like a human heart as closely as possible, by applying technology involving self-regulatory mechanisms and biocompatible materials. The Carmat heart aims to provide a permanent solution to patients suffering from advanced biventricular HF or potentially terminal acute MI, for whom no human transplant is available and who have exhausted all remaining treatment possibilities.

## French regulator allows resumption of EU pivotal trial

Carmat began a 20- to 25-patient EU pivotal trial in July 2016, but recruitment was suspended by ANSM (the French health regulator) in Q416 following the death of the study's first enrolled patient. ANSM permitted resumption of the trial in Q217. We expect the study to be completed in mid-2019, which could lead to potential EU launch in 2020 (vs our previous estimate of H218).

## Funded to Q218

Carmat finished FY16 with €28.0m in net cash (€31.2m gross cash minus €3.2m in long-term debt), and its FY16 cash burn rate was €21.2m. We assume H117 net cash of €18.1m, and that its burn rate will increase as the pivotal study proceeds, and as it prepares the other costs associated with a potential launch. Our model assumes that the firm will raise €50m each year for three years starting in 2018. As per our usual policy, we assign these financings (totalling €150m) to long-term debt.

## Valuation: Risked NPV of €627m

We value Carmat using a risk-adjusted NPV approach, employing a 12.5% cost of capital. While we have slightly raised the target market size estimates, given the issues raised by regulators following the first patient's death in the pivotal study and the pace of recruitment to date, we are applying a lower (25%) probability of success in the EU market (vs 35% previously). We now obtain an rNPV valuation of €627m, down from €747m previously. After including €18.1m estimated H117 net cash, we derive a per-share equity valuation of €106.98.

**31 July 2017**

| | |
|---|---|
| **Price** | **€26.23** |
| **Market cap** | **€157m** |
| Estimated net cash (€m) at H117 | 18.1 |
| Shares in issue | 6.0m |
| Free float | 37% |
| Code | ALCAR |
| Primary exchange | Alternext |
| Secondary exchange | N/A |

### Share price performance


| % | 1m | 3m | 12m |
|---|---|---|---|
| Abs | (2.7) | (2.1) | (20.9) |
| Rel (local) | (1.4) | (1.1) | (32.7) |
| 52-week high/low | | €42.2 | €25.9 |

### Business description

Carmat is developing a biocompatible, artificial heart to satisfy the lack of donor hearts available for terminal biventricular heart failure patients. It completed a feasibility study in early 2016, and first received authorisation to start a European pivotal study in July 2016.

### Next events

| | |
|---|---|
| H117 results | August 2017 |
| Finish recruitment for EU pivotal study | H218e |

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***CarmatCarmat is a research client of Edison Investment Research Limited***

# Investment summary

## Company description: Bioprosthetic heart development

Founded in 2008, Carmat and its bioprosthetic heart project are the result of a collaboration between technology firm, Matra Défense (now part of Airbus Group), and Professor Alain Carpentier, a cardiac surgeon. The device is the first biocompatible, biventricular mechanical heart, and is intended to treat end-stage heart failure (HF) and potentially terminal myocardial infarctions (MI), and to help compensate for the significant shortfall in the availability of human donor hearts. Carmat completed a four-patient feasibility study (first implantation in late 2013) in January 2016, and began an EU pivotal trial in July 2016, which was temporarily suspended in late November 2016 following the death of the study's first enrolled patient (implanted in August 2016) in October 2016. The study resumed in May 2017. Carmat received €33m in subsidies and repayable advances from French government institution Bpifrance in 2008, and has also raised c €123m in equity, including a €50m financing secured in 2016 directed towards a pivotal EU study for the Carmat heart.

## Valuation: rNPV valuation of €627m

Our risk-adjusted net present value (rNPV) valuation, using a 12.5% discount rate, is €627m, or €106.98m per share after including €18.1m estimated net cash at H117. The EU market opportunity is the primary driver of our valuation. Given the c seven-month pause in recruitment for the EU pivotal trial and the pace of enrolment to date, we have pushed back our potential EU launch timeline to 2020 (from H218 previously) and we also are revising our US market entry timeline estimate, under a Humanitarian Use Device (HUD) approach, to 2021 (vs 2020 previously).

## Financials: Funded into Q218

Carmat secured €50m in funding in early 2016 (the issue of 1.35m shares at €37.06 per share), with the objective at the time for the funding to be sufficient to proceed with a 20- to 30-patient CE Mark-enabling pivotal trial. However, we believe the c seven-month pause in study recruitment following the first patient death in October 2016 will require the company to obtain additional funding to complete the trial, which we now expect to finish in mid-2019. Carmat finished FY16 with €28.0m in net cash (€31.2m gross cash minus €3.2m in long-term debt), and its FY16 cash burn rate was €21.2m. Given such trends, we expect its cash on hand to last into Q218. We assume, consistent with company guidance, that it will need an additional €150m to complete the regulatory, manufacturing and commercial activities and investments to bring the Carmat heart to sustainable profitability. As per our usual methodology, we assign these financings to long-term debt.

## Sensitivities: Clinical risk, competition, financing

The main investment sensitivity and driver would be future results from Carmat clinical trials, including safety and tolerability. The company met the objective of a 30-day survival in 75% of implanted patients from the four-patient feasibility study, and we believe it is aiming for a 90-day survival in the pivotal study, given that subjects may be recruited with less severe stages of disease than during the feasibility study. Risks inherent in the Carmat device include the range of different technologies, including biomaterials, micro-mechanics and self-regulatory electronics, which add to the complexity of the device. Should the Carmat heart obtain regulatory approval, the firm will need to build confidence among physicians for them to select the Carmat implant over alternative mechanical circulatory support devices. Carmat will require further investor funding to support the pivotal trial and commercial launch in CE Mark territories.

# Company description: Biocompatible artificial heart

Carmat is developing an innovative, biventricular bioprosthetic heart, differentiated from previous generations of artificial hearts to make the prosthesis function as closely as possible to a human heart, by applying technology involving self-regulatory mechanisms, and biocompatible materials. Carmat's bioprosthetic heart aims to provide a long-term (permanent) therapeutic solution, or destination therapy (DT), to patients suffering from advanced biventricular heart failure (HF) or acute myocardial infarction (MI, commonly referred to as heart attack), for whom no human transplant is available and who have exhausted all remaining treatment possibilities.

After the completion of a four-patient feasibility trial in early 2016, Carmat started a 20- to 25-patient CE Mark-enabling pivotal trial in July 2016, for which enrolment was paused in November 2016 following the death of the first recruited patient. The company received approval in May 2017 to resume this pivotal study which, if successful, should lead to commercialisation in Europe and advances towards seeking US registration. We expect the pivotal trial to be completed in mid-2019, which could allow the device to be launched in Europe in 2020 (from H218, previously), to meet the significant clinical need for a permanent alternative for the patients on heart transplant waiting lists. The lack of any accepted biventricular implant for permanent use (DT) in either the EU or the US is potentially a significant commercial advantage.

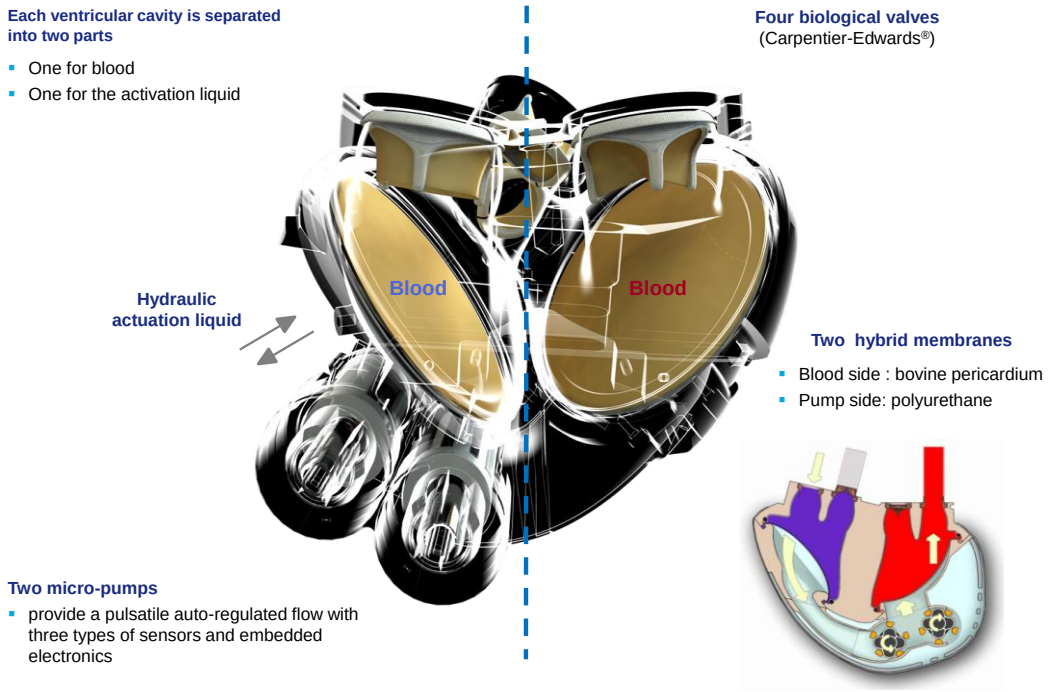
## Carmat heart and the cardiac transplant indication

The Carmat artificial heart is being developed as a permanent replacement, or DT, for biventricular HF or acute MI patients who do not have access to viable or compatible human donor hearts. It is designed to replicate as closely as possible the functionality and morphology of the human heart. Its key potential benefits compared to prior artificial implantable hearts are as follows:

- It is intended to function similarly to a natural heart and as a self-regulating device, thus delivering blood flow at differing rates in response to differing physiological needs. This is unlike earlier mechanical hearts, such as the SynCardia Total Artificial Heart (TAH), which focused on restoring blood flow and tended to pump blood at a fixed rate.
- The surfaces of the prosthesis (the only portions that come into contact with the blood) are made from biocompatible, haemocompatible and non-thrombogenic materials (bovine pericardium treated to become chemically inert, and medical-grade ePTFE), which allow continuous proteinic surface coverage, thereby reducing the risk of complications including blood clotting or haemolysis. Carmat suggests that the metals and polymers used in existing competitors' mechanical circulatory support (MCS) products generally do not cause continuous surface proteinization (as do the Carmat surface materials described above) and are thus thrombogenic (ie activate the coagulation system and therefore create blood clots which can either block a pump/motor, or migrate elsewhere and cause strokes or pulmonary embolisms).

The Carmat implant consists of a prosthetic heart and an electrical connection to a power supply (battery). The prosthesis reproduces the operation of the natural heart by using hydraulic actuation, with an activation liquid used as an intermediary to push the blood. The natural cardiac rhythm consists of two periods: systole (where blood is pumped out of the heart) and diastole (when the cardiac ventricles fill up with blood).

**Exhibit 1: Diagram of Carmat biventricular heart**




Source: Carmat company documents

Like the human heart, the prosthesis comprises two ventricular cavities. Each cavity is separated into two volumes (one for blood, one for the actuation liquid) by a flexible hybrid membrane. This membrane aims to reproduce the viscoelastic nature of cardiac muscle, and pump blood as it contracts. A motor-pump group (consisting of two miniature pumps) moves the actuation liquid to the ventricles, thus generating systole or, by working in reverse, it moves this fluid towards an external pouch (reproducing diastole). This mechanism aims to provide a pulsatile heartbeat to eject and admit blood and mimic the natural flow action of the heart.

The blood flow rate is governed by an internal electronic device and microprocessor (auto-regulation), controlled by embedded sensors and software algorithms that adjust flow rate in accordance with the patient's physiological and metabolic requirements, varying both the rate and the strength at which the blood is pumped.

The heart is accompanied by a portable system (weighing 3kg) with lithium-ion batteries, which provides over five hours of independent operation (the patient can carry additional batteries to extend independent utility, or can also connect to a power outlet). Carmat is also working on implementing a second-generation power supply developed by PaxiTech that employs fuel cell technology and can potentially provide more than 12 hours of independence while weighing below 3kg. We believe the firm intends to introduce this power source after the Carmat heart obtains CE Mark approval.

## Manufacturing and sourcing initiatives

Carmat sources most of the many individual components of the heart from external suppliers and assembles them onsite. The company has an agreement with Edwards Lifesciences to use Carpentier-Edwards valves. In May 2017 Carmat announced that it is preparing a new production facility to increase automation in the manufacturing process, and appointed a director of manufacturing in July 2017. It expects the new site to be operational by year-end 2017 and that it could eventually be used for the first commercial launch phases.

## Review of heart failure and MI characteristics

MI occurs when there is insufficient blood flow to a portion of the heart, leading to damage and cellular death to the affected heart muscle. The US Centers for Disease Control and Prevention (CDC) estimates that 735,000 Americans have an MI each year[1] and the European Heart Network estimated that there are at least 750,000 cases in the EU (>2.0 per 1,000 for males and >1.0 per 1,000 for females in a 500 million population).[2]

HF occurs when the myocardium (cardiac muscle) is not fully capable of performing its essential function as a blood "pump" to provide a sufficient cardiac output and oxygenated blood to meet an individual's metabolic needs. HF can occur in either the left (targeting the primary systemic circulation) or right ventricle (which pumps bloods to the lungs and pulmonary circulation), or in both (biventricular HF). HF is primarily caused by coronary disease or other cardiovascular disorders including hypertension,[3] and is one of the possible consequences following an MI.

HF is estimated to affect nearly 38 million people worldwide, including 20 million across the US and Europe, and total medical care costs in the US have been forecast to rise from $21bn in 2012 to over $53bn by 2030.[4] The US CDC estimates that 5.7 million Americans have HF. HF can be classified using the New York Heart Association (NYHA) scale, show below.

**Exhibit 2: NYHA Heart failure grading system**

| | Class I | Class II | Class III | Class IV |
|---|---|---|---|---|
| Symptoms | No symptoms | Tiredness, palpitations, shortness of breath after sustained effort | Symptoms or discomfort on the least effort | Symptomatic even at rest |
| Activity | No limitations | Modest limitations | Marked reduction | Inability to perform nearly all activities; permanently confined to bed |

Source: Company reports

## Current treatment approaches for HF

Class I and II stages are often treated with medical therapy (including anticoagulant/anti-platelet aggregation medications, angiotensin-converting enzyme inhibitors, beta-blockers, diuretics, etc).

Between Class II and Class III marks a significant shift for patient's quality of life, reflecting the transition between a virtually normal life and one with considerably reduced activity, potentially involving a loss of independence. Class IV patients represent about 2.3% of heart failures[5] or approximately 500,000 people in the US and EU.

Starting in Class III, surgical options and the implantation of supportive medical devices are considered, such as mono or biventricular pacemakers, implantable defibrillators, intra-aortic balloon pump procedures and stents. Generally, these procedures can restore or increase blood flow to the heart or slow the progression of the disease. Further advanced cases (within Class III or Class IV) can be treated with HHT or with MCS devices.

### HHT traditionally reserved for most severe cases but supply very limited

For the most severe cases of HF, human heart transplantation (HHT) is considered the best treatment for patients who are refractory to management with medical therapy, or less invasive options. The cost of HHT, including surgery, assessment, admission costs, medication (eg

1 www.cdc.gov/heartdisease/heart_attack.htm

2 European Heart Network. http://www.ehnheart.org/component/downloads/downloads/2452

3 High blood pressure causes an increased workload to cardiac muscle, leading to enlargement and less efficient functioning.

4 Ziaeian B, Fonarow GC.Nat Rev Cardiol. 2016 Jun;13(6):368-78. doi: 10.1038/nrcardio.2016.25. Review.

5 Jhund PS et al. Circulation. 2009; 119:515-523

immunosuppressants) and postoperative care has been estimated by the Milliman Risk Institute at over $1m per patient.[6] Extensive screening is done prior to surgery to exclude those with comorbidities that can increase complications, to ensure that the patients chosen for surgery are those who are likely to survive the longest after transplantation.

It has been estimated that up to 20,000 US patients could benefit from heart transplantation each year,[7] but due to a shortage in donor organs, in recent years (2013-16) only about 2,500-3,200 heart transplants have been performed each year in the US.[8] These are generally reserved for younger candidates with fewer comorbidities. A similar supply/demand mismatch exists in Europe (across France, Germany and the UK there are only c 900 transplants per year[9]). Reasons for the shortage of donors relative to need include the strict criteria for donors (ie aged under 61 years, not suffering from certain infectious diseases, etc) and a reduction in motor vehicle accident-related fatality rates. The limited number of human hearts available provides a need for alternative approaches including MCS devices to restore cardiac function to maximise advanced HF patient survival.

## Types of MCS device and usage patterns

MCS devices considered for patients with advanced HF include ventricular assistance devices (VADs) and total artificial hearts (TAH). The type of device used depends on the stage of HF and whether a single or both ventricles are affected. Currently, the SynCardia device is the only approved TAH on the market (the Carmat heart, if approved, could be the second). VADs, also called implantable heart pumps, are more commonly used than TAHs and are implanted in parallel to the native heart, and they assist the existing ventricles to pump blood, reducing the cardiac workload in patients with HF. The left ventricle (which pumps oxygenated blood to the general circulation) is most susceptible to failure as it has around five times the pressure workload of the right. Left VADs (LVADs) are most commonly implanted in patients with monoventricular failure.

## MCS device use categories: BTR, BTT, DT

The intended usage of MCS devices falls into three categories: bridge-to-recovery (BTR), bridge-to-transplantation (BTT) or destination therapy (DT). BTR refers to scenarios when the HF scenario is temporary (ie a recovery from heart surgery) and an MCS can be implanted for a few weeks or months to assist the heart during its recovery period. In the vast majority of advanced HF cases where MCS is indicated, the damage is permanent and BTT or DT treatment may be required.

BTT (or pending transplantation) refers to the intent to implant the device temporarily until an organ transplant is available, or until the patient's condition improves sufficiently to tolerate such surgery. The patient's MCS device (often an LVAD) may remain in place for several years until a donor heart becomes available for transplant. Destination therapy (DT) refers to the MCS being implanted permanently, or effectively for patients who are not expected to be eligible for or compatible with a heart transplant. DT aims for an improvement of at least two classes on the NYHA scale.[10]

### VAD technology improvements have improved its market penetration

[6] Milliman Report 2014 - Table 2: Estimated US Average 2014 Billed Charges Per Transplant. www.milliman.com/uploadedFiles/insight/Research/health-rr/1938HDP_20141230.pdf

[7] Khush KK, Zaroff JG, Nguyen J, et al. Am J Transplant. 2015 Mar;15(3):642-9. doi: 10.1111/ajt.13055. Epub 2015 Feb 10.

[8] Statistics from Organ Procurement and Transplantation Network. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

[9] Using statistics from Agence de la biomédecine (for France), Eurotransplant (for Germany), and NHS Organ Donation and Transplantation (for UK).

[10] The NYHA Functional Classification scale for HF places patients in four symptomatic (I-IV) and objective categories (A-D) classifying the severity of the disease.

VAD technology has also improved since the first VADs were approved in the 1970s, leading to devices with improved flow rates and with lower risks of infection and thrombosis, making them capable of long-term or permanent circulatory support (rather than BTRs, which were the first-generation VADs). Frazier et al.[11] showed a 34% increase in survival to transplantation in patients supported with a VAD compared with those treated with medical therapy, and several other studies also suggest that LVADs provide excellent outcomes in advanced HF compared to medical therapy.[12] Between 2007 and 2013, the number of LVADs implanted in the US alone each year increased over 600% to over 2,500.

The primary MCS devices for advanced HF patients are intracorporeal[13] VADs (ie those placed using highly invasive open-heart surgery with implantation in the surgery suite) or TAHs. The market intracorporeal LVAD leader are Abbott's (ABT:NYSE) HeartMate line[14] and Medtronic's HVAD line.[15]

### Thrombosis, right heart failure a risk in LVADs

LVADs are not without risk, as up to c 20% of patients implanted with LVADs generate right ventricle heart failure (RVHF)[16] and may require right VADs (RVADs), although the more recent LVADs, such as those with continuous flow (eg HeartMate II) or centrifugal/electromagnetic-based mechanisms (eg HeartMate III or HVAD) have lower RVHF and mechanical failure risks. While RVADs can be used in some cases in RHVF, in addition to surgical risks, there can be technical complications involved with using non-integrated VADs for different ventricles (such as ensuring proper synchronization or communication between both, as imbalance of flows can lead to thrombosis or pulmonary edema). In cases of biventricular failure, biventricular VADs (BiVADs[17]) can be implanted (in place of LVAD or RVAD) to provide biventricular support, but these are more complicated to manage[18] and are less commonly used than LVADs (a TAH or HT could be more suitable for such patients).

VADs have also been associated with an increased risk of thrombosis and blood clots, and patients generally require long-term anticoagulant therapy. In August 2015, the FDA issued an alert indicating that the HeartMate II was associated with an increased rate of pump thrombosis (blood clots inside the pump), and that patients implanted with the HeartWare HVAD had a markedly higher rate of stroke (>28%) at two years than those implanted with the HeartMate II (<13%) in the ENDURANCE study (n=446). In the case of the HeartMate II, some studies have shown a higher pump thrombosis rate than what was observed in the pivotal studies conducted to support its approval in BTT (2008) and DT (2010). Starling et al. (2013) found a pump thrombosis rate of 8.4% at three months, and Kirklin et al. (2014) found a 6% rate at six months; this compares to a 1.6% rate at one year in the BTT clinical trial and 3.8% at two years during the DT clinical trial. Abbott is

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11 Frazier OH, Rose EA, Oz MC et al. J. Thorac. Cardiovasc. Surg. 122, 1186–1195 (2001).

12 Makdisi G,Makdisi PB, Bittner HB et al. J Thorac Dis. 2017 Apr; 9(4): 932–935. doi: 10.21037/jtd.2017.03.139

13 Intracorporeal VADs differ from percutaneous VADs; percutaneous assist devices (examples include Abiomed's Impella line and Abbott's HeartMate PHP) are inserted through a small skin puncture in the leg and allow for much less invasive placement and removal. However, percutaneous VADs are indicated to support the heart for short period (ie generally up to six days) for high-risk percutaneous coronary intervention (PCI) procedures and thus are not indicated as potential long-term treatments for HF.

14 Abbott recently acquired St. Jude Medical, which obtained the HeartMate line as part of its 2015 acquisition of Thoratec Corp.

15 Medtronic acquired HeartWave International, in August 2016; HeartWave developed and marketed the HVAD System at the time of the acquisition.

16 Argiriou M, Kolokotron SM, Sakellaridis T, et al. J Thorac Dis. 2014 Mar; 6(Suppl 1): S52–S59. doi: 10.3978/j.issn.2072-1439.2013.10.26

17 Abbott/Thoratec's pVAD, an earlier-generation VAD, offers biventricular support.

18 Sen A, Larson JS, Kashani KB. Crit Care. 2016 Jun 25;20(1):153. doi: 10.1186/s13054-016-1328-z.

developing HeartMate III, a follow-on device to the HeartMate II and designed to lower thrombosis risk, which is currently in a pivotal US study and received a CE Mark in late 2015.

The Carmat heart could have a potential advantage vs existing VADs in reducing thrombosis risk given that it was designed such that only biocompatible or bioinert materials would come into contact with a patient's blood, in order to reduce thromboembolic risks.

### TAH, like SynCardia, a potential alternatives in biventricular failure

"Total" artificial hearts (TAH) are alternative MCS treatments to VADs for advanced HF patients. A TAH comprises two ventricular volumes and is designed to fully replace an existing heart. The only TAH currently on market in the US and Europe is produced by privately held SynCardia. TAH are more likely to be employed in cases of biventricular failure (where LVADs would not be sufficient as both ventricles require support), and could be used instead of BiVADs. While no head-to-head randomized trials have compared the SynCardia TAH to BiVAD mechanical circulatory support, one retrospective study (Kirsch et al, 2012; n=383, including 90 TAH implants) showed no difference in mortality for patients implanted with a TAH compared with BiVADs.[19] It also found that TAH patients had a substantially reduced rate of stroke, and that among patients who experienced prolonged support (≥90 days), those with the SynCardia TAH showed a trend towards improved survival. Kirsch et al. (2013)[20] reviewed data on the 90 SynCardia TAH implantations performed at Hôpital Universitaire de la Pitié Salpêtrière (Paris, France) between 2000-10 with a BTT intent on patients with cardiogenic shock[21] and determined that actuarial survival on the device was 74% ± 5%, 63% ± 6% and 47% ± 8% at 30, 60 and 180 days after implantation.

### Being reserved for more severe cases, TAH use rates well below those of LVADs

While well over 28,000 HeartMate II LVAD implants have been performed worldwide since its launch, only about 1,600 SynCardia TAH implantations have been made thus far, in part due to the more invasive nature of TAH implantation compared to an LVAD (or even BiVAD) and a higher rate of surgical complications such as infections with the SynCardia TAH. Further, while a DT study is currently underway, the SynCardia device is only approved for BTT in the EU and US.

The design of the SynCardia TAH is over 40 years old and, like some earlier-generation LVADs, its mechanics are driven by pneumatic (compressed air) actuation, and as such it requires the constant use of an external compressor or driver (weighing about 6kg), which is itself powered electrically with lithium-ion batteries. Newer-generation LVADs use continuous flow or centrifugal/magnetic designs for pumping blood, and the Carmat device uses hydraulic actuation; these approaches use power sources that involve fewer mobility encumbrances than the external driver required by the SynCardia device. With its biocompatible materials, a more convenient power source and a differing mechanical approach, the Carmat heart has several potential advantages over the SynCardia device.

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[19] Kirsch M, Mazzucotelli JP, Roussel JC, et al. J Heart Lung Transplant 2012;31:501-8.

[20] Kirsch ME, Nguyen A, Mastroianni C, et al. Ann Thorac Surg. 2013 May;95(5):1640-6.

[21] A potentially fatal condition, often resulting from a severe MI that leads to sustained low blood pressure and poor tissue perfusion. The overall in-hospital mortality rate was estimated by Kolte et al. (2014) at approximately 40%.

**Exhibit 3: Comparison of selected mechanical-assisted circulatory support devices**

| Device | Manufacturer | Approval status | Characteristics | Data |
|---|---|---|---|---|
| **Artificial heart** | | | | |
| Bioprosthetic artificial heart | Carmat | In development (CE Mark study suspended) | Self-regulating electro-hydraulic pulsatile flow contained within the body; uses external (lithium-ion, potentially fuel cell in second gen) batteries. Algorithms mimic reactions of cardiac muscle to BP and postural changes. All blood-facing surfaces biocompatible. | EU feasibility study successful (n=4) with 75% surviving more than 30 days; CE Mark study on hold following death of first patient. |
| Total artificial heart | SynCardia | Approved: BTT in US/Europe; 19-pt DT Pivotal US study underway (NCT02232659); HUD designation for DT in US | Ventricles adjust to increase blood flow during exercise; Blood can contact non-biocompatible surfaces including Medtronic-Hall valves (titanium and pyrolytic carbon); anticoagulant therapy required post-implantation. Offered in two sizes. | In BTT pivotal study, one-year survival (n=81) was 70% vs 31% in control arm (n=35). Over 1,400 implants since approval. |
| **Intracorporeal ventricular assistance devices** | | | | |
| HeartMate II LVAS | Thoratec (Abbott) | Approved for BTR/BTT and DT in US and Europe | LVAD with continuous flow, rotary pumps with axial flow, generating a net pressure rise across the pump. External system driver connected by a percutaneous lead to lithium-ion battery providing up to 10 hours of autonomy. Requires anticoagulant therapy. | In DT pivotal study (n=200) in advanced HF patients, survival of 68% and 58% at one and two years, respectively. Over 20,000 implants worldwide. |
| HVAD | HeartWare (Medtronic) | Approved for BTR/BTT in US and Europe; ENDURANCE supplemental study (NCT01966458) for DT completed in April 2017 | Centrifugal LVAD that uses hydrodynamic and magnetic forces to hold the impeller in place. The impeller spins at high speed to create suction that pulls blood into the pump, changes its flow direction, and then pushes it out of the pump. Portable power unit with battery and mains adapter. | Non-inferiority vs HeartMate II shown in DT ENDURANCE study (n=446), where HVAD arm had 55.0% stroke-free survival at two years, vs 57.4% for Heartmate II. Supplemental study (n=465) did not meet primary endpoint of non-inferiority vs HeartMate II in all neurologic events at 12 months, but secondary data showed 76.4% of patients survived on original device and free of stroke, vs 66.9% for HeartMate II. |
| HeartMate III LVAS | Thoratec (Abbott) | Approved for BTR/BTT in Europe; US registration study (MOMENTUM 3/ NCT02224755) underway | Centrifugal LVAD that uses magnetic levitation to hold the impeller in place. Designed to reduce thrombosis risk (vs HeartMate II). | CE Mark-enabling study (n=50) had 92% six-month survival and 80% one-year survival; with no occurrences of pump thrombosis, malfunctions, or haemolysis. Interim six-month data (n=289) of MOMENTUM 3 US IDE study (NCT02224755; n>1000) reported in Q217 showed less pump thrombosis and nondisabling strokes vs HeartMate II |

Source: Edison Investment Research, Medscape, company reports. Note: DT = destination therapy; BTT = bridge-to-transplant; BTR = bridge-to-recovery.

### Bivacor, Cleveland Heart developing TAH competitors

Besides Carmat, at least two private companies have their own proprietary TAH devices in the development stages. Texas-based Bivacor is developing a centrifugal rotary pump-based TAH using a single moving part and which applies magnetic levitation (to reduce mechanical wear). Like the Carmat device, it adapts the pump's operation to changes in activity levels. Similar to the Bivacor device, Cleveland Heart's SmartHeart TAH uses centrifugal pumps with a single moving part and is in preclinical testing. Both the Bivacor and Cleveland Heart devices are in preclinical testing (having both been implanted in calves), and they are both intended to be small enough to be implantable in men, women and children.

## INTERMACS classification system for MCS implantations

The INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) register, established in 2009, intends to record all MCS implantations in North America across over 150 participating hospitals. INTERMACS uses a seven-level profile scale reflecting the general clinical description of patients receiving MCS devices (generally primary LVAD or TAH implants).

**Exhibit 4: INTERMACS classification system**

| NYHA Class | Profile level | Patient profile | Description |
|---|---|---|---|
| IV | 1 | Critical cardiogenic shock | Life-threatening hypotension |
| | 2 | Progressive decline | Dependent on ionotropic support but shows signs of deterioration (eg renal function, fluid retention, etc) |
| | 3 | Stable but inotrope dependent | Stable but requires mild-moderate doses of intravenous inotropes (or has temporary circulatory support device) |
| | 4 | Resting symptoms | Patient who is at home on oral therapy but has frequent symptoms of congestion at rest or with daily living activities |
| | 5 | Exertion intolerant | Patient who is comfortable at rest but unable to engage in activities, and is predominantly housebound |
| | 6 | Exertion limited | Patient is able to do some mild activity |
| III | 7 | Advanced NYHA Class III | Patient is clinically stable with reasonable level of comfortable activity (ie can walk for more than a block) |

Source: INTERMACS

Generally speaking, patients with mono-ventricular failure in profile 3 or 4 or later are more likely to be implanted with a VAD than a TAH. We estimate that c 33% of the c 500,000 US and EU Class IV HF patients have biventricular failure and could be potential candidates for a BiVAD or a TAH (if approved for DT and if all other eligibility criteria are met). Since the SynCardia TAH is not yet approved for DT, we believe it is primarily oriented as a BTT for patients with biventricular failure in INTERMACS profile 1 or 2 where no human donor heart is available.

Carmat believes that its self-regulating artificial biventricular heart could be a superior solution in biventricular failure to BiVADs or LVAD/RVAD combinations, as it can synchronize the pumps between the pulmonary (right ventricle) and the systemic (left ventricle) circulation and instantaneously respond to physiological changes in demand.

## Carmat completed a four-patient feasibility study in early 2016

Carmat began a four-patient feasibility study in late 2013, and completed it in January 2016. There was a minor delay in recruitment after the second patient's death in May 2015 as, despite a survival of nine months post-implantation, the device malfunctioned due to a disruption in micro-steering electronics following a micro-leak. Carmat identified the cause of the malfunctioning and then worked on corrective measures, including a software tool predicting malfunctions, and received authorisation from French regulators to resume the study in November 2015. Carmat's analyses confirmed that the malfunctioning was not due to an inherent flaw in product design, but rather issues stemming from the early stage of production. The death of the fourth patient was due to complications unrelated to the performance of the bioprosthetic heart itself.

**Exhibit 5: Summary of feasibility study outcomes for Carmat bioprosthetic heart**

| Patient | Centre | Date of implantation | Primary outcomes |
|---|---|---|---|
| 1 | Hôpital Européen Georges-Pompidou | 18 December 2013 | Patient survived until March 2014 (75 days). An electrical component fault caused the bioprosthesis to malfunction. Approval to resume study from the French National Agency for Medicines and Health Products Safety (ANSM). |
| 2 | Nantes University Hospital | 5 August 2014 | Patient survived nine months, of which four months were at home. Malfunction caused by fault with steering motors led to circulatory insufficiency and hospitalisation on 1 May 2015. Patient re-implanted the next day but died later that same day due to multiple organ failure. |
| 3 | Hôpital Européen Georges-Pompidou | 8 April 2015 | Patient discharged in September 2015, but was hospitalised in November 2015 and died due to respiratory failure following a chronic renal failure. |
| 4 | Hôpital Universitaire de la Pitié Salpêtrière | 22 December 2015 | Patient died on 11 January 2016, but the severity of their underlying condition (patient had biventricular heart failure and required continuous life support) was deemed responsible for their death. Carmat heart believed to have functioned optimally during implantation. |

Source: Company reports

Overall, while the sample size was low, the first three patients (75%) met the company's targeted success of a survival duration of at least 30 days post-implantation. The Agence de la biomédecine,

a French organisation overseeing transplant procedures and organ donations, reported in 2015[22] that the 30-day survival rate (between 1993 and 2014) in human heart transplants (the 'gold standard' comparator for an artificial heart) is approximately 80% for patients above age 60 (reflecting about 20% of transplant recipients), and 85% for patients between 18 and 60 (about 75% of recipients). The 12-month survival rate drops to about 68% and 77%, respectively, and the median survival durations are about 100 months and 150 months, respectively. A Swedish study group also found that median survival (across all ages) after HHT is approximately 10-11 years.[23]

A favourable finding from the feasibility study is that there were no causes of thrombosis in a cumulative period of use of nearly two years, which suggests the biocompatibility of the product's materials that are in contact with blood or human tissue.

### EU pivotal study started in July 2016 and resumed in May 2017

Carmat began a 20- to 25-patient EU pivotal trial in July 2016, for which recruitment was suspended by ANSM in late November 2016 following the death of the study's first enrolled patient (implanted in August 2016) in October 2016. Carmat maintained that the death was not due to a prosthesis malfunction, but to poor handling of the batteries by the patients. Following a favourable review by ANSM of the actions and analyses taken by Carmat on this incident, ANSM permitted resumption of the trial in May 2017, and requested that Carmat provide an intermediate analysis on the next five patients to be involved in the pivotal study. Given the pause in the pivotal study's enrolment until Q217 and the pace of recruitment to date, we now assume completion of this study will occur in mid-2019 (vs H217 previously).

## Market opportunity and commercial assumptions

The commercial case for the Carmat bioprosthetic heart primarily lies in a general lack of available human heart transplants for patients who need them. There are approximately 0.5 million people in the US and EU with Stage IV heart failure. We currently view the EU market as the primary opportunity for the Carmat heart, as the product is currently in EU pivotal studies and Carmat's US regulatory strategy is still under evaluation. We estimate that the target potential market opportunity of the Carmat bioprosthetic heart can be broadly based as falling within two conditions. In both groups, the Carmat heart would only be implantable in patients under age 70, and for anatomical/size compatibility, in about 86% of otherwise eligible men and 14% of such women.

The two conditions we assume the Carmat bioprosthetic heart will be targeting are:

- Patients with Class IV (end-stage) HF, with biventricular failure; estimated EU market size of about 21,500.[24]
- Patients suffering from acute MIs whose severity or circumstances lead to an expected survival time of under 30 days with conventional management (estimated EU market size of about 60,300).

Altogether, we estimate that the EU target treatment population is around 82,000 (up from 74,000 previously). The American Heart Association assumes that the US HF population will rise by c 2.1% pa over the next two decades,[25] and our model assumes a more conservative 1.5% growth rate.

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22 Agence de la biomédecine (Biomedicine Agency) – Rapport d'information au Parlement et au Gouvernement – Summary 2015 : http://www.agence-biomedecine.fr/annexes/bilan2015/donnees/organes/03-coeur/synthese.htm

23 Nilsson J, Ohlsson M, Höglund P, et al. PLoS One. 2015 Mar 11;10(3):e0118644. doi: 10.1371/journal.pone.0118644. eCollection 2015

24 Previously we excluded the approximately 8,000 EU patients awaiting human heart transplant surgery form this eligible patient pool, but we now believe it is more appropriate to include them within the pool.

Given the revision in our timing expectations for completion of the pivotal trial, we now assume potential EU launch and commercialisation in H120 (from H218 previously). We continue to assume an initial average per-device market price of €160,000 (in the mid-range of company guidance of €140,000-180,000), rising 2% per year. We estimate that peak market share of 15% of this target market will be realised by 2024, with EU sales of €2.2bn in that year. This is higher than our prior peak EU sales estimate of €1.9bn, with the primary difference driving our new forecast being our assumption for a larger target pool (potential market) of 82,000 patents per year.

For the US market, our base case continues to assume that product introduction will be attempted using the HUD programme, instead of a Premarket Approval (PMA) process. The HUD approach is less onerous and would shorten the amount of clinical data required for commercialisation, but could limit product usage to 8,000 patients per year.[26] Under an HUD approach, Carmat would need to provide safety evidence but, unlike a PMA, there would be no necessity to provide rigorous efficacy data. We consider the rationale under HUD would be an orphan subset of severe HF patients reflecting patients in INTERMACS categories 1 and 2, where an HHT is unavailable and where the patient would otherwise be expected to only have days to live.

**Exhibit 6: Comparison of PMA and HUD approval processes for medical devices**

| Process | Size of clinical trial | Clinical data requirements | Timeline | Addressable market |
|---|---|---|---|---|
| PMA | Over 100 patients | Safety, efficacy | Minimum two years | 50,000 |
| HUD | 10-20 patients | Safety, probable evidence of benefit vs risk | 180 days | 8,000 |

Source: Edison Investment Research

Given our expectation that a Humanitarian Device Exemption (HDE) enabling study would only commence as the EU pivotal programme reaches its final stages, we have pushed back our US HUD commercialisation launch timeline to 2021 (from 2020 previously), while maintaining our US market price of $200,000 per device. As the US has broadened the potential market size of products seeking HDE approval, we have also raised our potential US market size for the Carmat device to 8,000 (from 4,000 previously), but for conservatism we have reduced our peak US market share assumption to 40% (from 70% previously). We now assume peak US sales of $731m by 2025 under this scenario (vs $625m by 2024 previously). Should Carmat proceed in the US via the PMA route instead of HUD, we would adjust our forecasts accordingly, but this would entail a higher risk adjustment, a later launch date due to the longer/larger study and additional R&D costs of over €35m (for a >100 patient clinical trial), although the addressable market would be larger.

# Sensitivities

**Development and regulatory risk.** Much development risk remains within the Carmat heart. While the feasibility study was successful, deaths in two of the first five human implantations to date (four from feasibility trial, first from pivotal study) prompted the regulators to suspend the involved trials. Any residual concerns involving battery safety, haemocompatibility and mechanics efficacy will need to be demonstrated through the pivotal clinical trial for commercial approval.

**Commercial and competition risk.** Should the Carmat heart obtain CE Mark approval, the firm will need to generate confidence among physicians and stakeholders for the product to be chosen to be deployed in advanced biventricular HF or at-risk MI patients. The SynCardia TAH device and VADs will be the most immediate competitors, and we continue to anticipate that LVADs, in part due to requiring a less invasive surgical procedure, will be the preferred device in most cases of Class IV monoventricular failure. In addition, in order to obtain optimal sales penetration, the company will need to obtain reimbursement coverage with applicable payers in the targeted markets. In the

[25] Heidenreich PA, Albert NM, Allen LA, et al. Circ Heart Fail. 2013 May;6(3):606-19

[26] In late 2016, the FDA increased the population estimate required to qualify under an HUD designation from “fewer than 4,000” to “not more than 8,000”.

longer term, the company may need to compete with emerging alternative TAH heart implants should they gain approval, including but not limited to the Bivacor and Cleveland Heart product initiatives.

**Financing risk**. We estimate that Carmat's year-end 2016 net cash of €28.0m should support its runway into Q218. We assume, consistent with company guidance, that it will need an additional €150m in financing to complete the regulatory, manufacturing and commercial activities needed for the Carmat device to reach sustainable profitability. The company has €38m available as part of an equity credit line set up in early 2015 with Kepler Cheuvreux, although our model assumes, as per customary Edison policy, that Carmat's financing needs will be met through debt. We assume Carmat will raise €50m each year in the years 2018 through 2020. While our model accounts for these financings as long-term debt, the firm may need to issue equity instead, and there is the risk that pricing is not favourable for current shareholders and leads to significant dilution. We do not expect Carmat to start generating sustainable, positive, recurring operating cash flows until 2021, once Carmat sales and manufacturing efficiencies start to exceed all projected overhead costs.

# Valuation

We continue to value Carmat using a risk-adjusted NPV approach, employing a 12.5% cost of capital. We estimate the potential target market as being larger than previously (up to 82,000 EU patients versus 74,000 previously) but, given the issues raised by regulators following the first patient's death in the pivotal study and the resulting delay in recruitment, we also assume a more conservative risk adjustment (25% vs 35% previously) is warranted for the EU market. Given that approximately one year after the pivotal study's commencement in mid-2016 there has only been one implantation made, our risk-adjustment factor considers the possibility that it could take longer than our model currently estimates (mid-2019) to complete this trial.

As we believe the company places a higher priority on obtaining CE Mark clearance for the EU market than on developing the Carmat heart for the US market, we continue to apply a lower (20%) probability for commercialisation in the US.

**Exhibit 7: Carmat rNPV assumptions**

| Product contributions (net of R&D and marketing costs) | Indication | rNPV (€m) | rNPV/share (€) | Probability of success | Launch year | Peak market share | Peak WW sales (€m) |
|---|---|---|---|---|---|---|---|
| Carmat artificial heart in EU market | Terminal heart failure and myocardial infarctions | 824.9 | 136.76 | 25.0% | 2020 | 15% | 2,169 in 2024 |
| Carmat artificial heart in US market (under HUD) | Terminal heart failure and myocardial infarctions | 182.9 | 30.32 | 20.0% | 2021 | 40% | 731 in 2025 |
| Corporate costs & expenses | | | | | | | |
| G&A expenses | | (46.0) | (7.62) | | | | |
| Net capex, NWC & taxes | | (334.7) | (55.49) | | | | |
| **Total rNPV** | | **627.2** | **103.98** | | | | |
| Net cash (debt) (H117e) | | 18.1 | 3.01 | | | | |
| **Total equity value** | | **645.3** | **106.98** | | | | |
| FD shares outstanding (000s) (Q416) | | 6,032 | | | | | |

Source: Edison Investment Research

Given the above adjustments, we now obtain an rNPV valuation of €627m, down from €747m previously. We assume a mid-2017 net cash position of €18.1m. After including this net cash position, we derive an equity value of €645m, which leads to a per-share equity valuation of €106.98. This valuation does not include any additional equity offerings, as future financings may be required to prepare for commercial product launch and ramp up manufacturing.

Once Carmat bioprosthetic heart commercialisation is secured, the company plans to use its know-how in cardiac mechanics and biomaterials to expand into other cardiovascular indications or devices (such as a VAD), but until definitive R&D or clarification is made into such areas, we are not including these prospects in our valuation.

## Financials

In its 2016 annual report Carmat highlighted that it will need capital, even after it obtains CE Mark clearance, to scale up manufacturing and build commercial development, as well as support processes needed to gain US approval. It estimates that these additional requirements could reach up to €150m and our model includes significant capex, working capital and other investments and costs that are consistent with this guided requirement.

Carmat finished FY16 with €28.0m in net cash (€31.2m gross cash minus €3.2m in long-term debt), and its FY16 cash burn rate (operating cash flow excluding net interest costs minus net capex) was €21.2m. We assume H117 net cash of €18.1m.

We estimate that Carmat's net cash burn rate will increase to €23.5m in 2017, as it enrols more patients in the EU pivotal study. We anticipate that activities towards the establishment of a new manufacturing facility and preparation for commercial launch will lead to €20m in capex costs in 2018 and €25m in 2019, which will increase the burn rates to €44.7m in 2018 and €44.3m in 2019. In the first anticipated year of commercial sales (2020 in the EU), we expect initial working capital costs associated with the EU launch (and a negative profit margin on initial unit sales) and sales and marketing costs to lead to a burn rate of €54.1m.

Given the above, our model assumes the firm will raise €50m in both 2018 and in 2019 (up from €40m, previously) to effectively complete the pivotal study and prepare for the launch activities (sales and manufacturing scale-up). We also project a €50m financing requirement in 2020, as we expect initial Carmat heart sales to carry negative gross margins and we forecast G&A costs rising to €16.5m in 2020 to support the sales and marketing efforts. As per our usual methodology, we assign these financings (totalling €150m) to long-term debt. We expect gross margin for the Carmat heart to become positive by H121. We assume operating cash flows will start to run positive in 2021, as product sales rise and as manufacturing efficiency gains are realised.

## Exhibit 8: Financial summary

| €000s | 2013 | 2014 | 2015 | 2016 | 2017e | 2018e | 2019e |
|---|---|---|---|---|---|---|---|
| Year end 31 December | IFRS | IFRS | IFRS | IFRS | IFRS | IFRS | IFRS |
| **PROFIT & LOSS** | | | | | | | |
| Revenue | 2,874 | 49 | 14 | 263 | 0 | 0 | 0 |
| Cost of Sales | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| General & Administrative | (4,694) | (5,408) | (6,012) | (6,426) | (6,000) | (6,650) | (9,304) |
| Research & Development | (13,376) | (14,031) | (13,392) | (17,912) | (16,000) | (18,000) | (10,000) |
| EBITDA | (15,197) | (19,390) | (19,390) | (24,075) | (22,000) | (24,650) | (19,304) |
| Depreciation | (920) | (479) | (377) | (504) | (490) | (1,530) | (5,539) |
| Amortisation | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Operating Profit (before exceptionals) | (16,117) | (19,869) | (19,767) | (24,579) | (22,490) | (26,180) | (24,843) |
| Exceptionals | 25 | (127) | (89) | (75) | 0 | 0 | 0 |
| Other | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Operating Profit | (16,091) | (19,996) | (19,857) | (24,655) | (22,490) | (26,180) | (24,843) |
| Net Interest | (324) | (476) | (838) | (1,143) | 346 | (94) | (783) |
| Profit Before Tax (norm) | (16,440) | (20,345) | (20,605) | (25,722) | (22,144) | (26,274) | (25,626) |
| Profit Before Tax (FRS 3) | (16,415) | (20,472) | (20,694) | (25,797) | (22,144) | (26,274) | (25,626) |
| Tax | 1,770 | 2,209 | 3,149 | 2,817 | 0 | 0 | 0 |
| Profit After Tax and minority interests (norm) | (14,670) | (18,136) | (17,456) | (22,905) | (22,144) | (26,274) | (25,626) |
| Profit After Tax and minority interests (FRS 3) | (14,645) | (18,263) | (17,546) | (22,980) | (22,144) | (26,274) | (25,626) |
| Average Number of Shares Outstanding (m) | 4.3 | 4.4 | 4.6 | 6.0 | 6.0 | 6.0 | 6.0 |
| EPS - normalised (€) | (3.42) | (4.14) | (3.81) | (3.80) | (3.67) | (4.36) | (4.25) |
| EPS - normalised and fully diluted (€) | (3.42) | (4.14) | (3.81) | (3.80) | (3.67) | (4.36) | (4.25) |
| EPS - (IFRS) (€) | (3.42) | (4.17) | (3.83) | (3.81) | (3.67) | (4.36) | (4.25) |
| Dividend per share (€) | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **BALANCE SHEET** | | | | | | | |
| Fixed Assets | 1,633 | 1,377 | 1,215 | 1,751 | 2,788 | 21,258 | 40,719 |
| Intangible Assets | 125 | 254 | 218 | 196 | 196 | 196 | 196 |
| Tangible Assets | 1,508 | 1,123 | 998 | 1,555 | 2,592 | 21,062 | 40,523 |
| Current Assets | 20,351 | 12,665 | 7,435 | 35,738 | 12,557 | 17,813 | 22,726 |
| Short-term investments | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cash | 16,884 | 9,219 | 3,012 | 31,163 | 7,982 | 13,238 | 18,152 |
| Other | 3,467 | 3,447 | 4,422 | 4,575 | 4,575 | 4,575 | 4,575 |
| Current Liabilities | (6,254) | (4,750) | (4,722) | (5,195) | (5,195) | (5,195) | (5,195) |
| Creditors | (6,254) | (4,750) | (4,722) | (5,195) | (5,195) | (5,195) | (5,195) |
| Short term borrowings | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Long Term Liabilities | (844) | (1,349) | (2,246) | (3,213) | (3,213) | (53,213) | (103,213) |
| Long term borrowings | (822) | (1,349) | (2,224) | (3,213) | (3,213) | (53,213) | (103,213) |
| Other long term liabilities | (22) | 0 | (22) | 0 | 0 | 0 | 0 |
| Net Assets | 14,886 | 7,944 | 1,681 | 29,082 | 6,937 | (19,336) | (44,962) |
| **CASH FLOW** | | | | | | | |
| Operating Cash Flow | (9,314) | (18,270) | (16,349) | (20,111) | (22,000) | (24,650) | (19,304) |
| Net Interest | (324) | (476) | (838) | (1,143) | 346 | (94) | (783) |
| Tax | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Capex | (266) | (331) | (292) | (1,096) | (1,527) | (20,000) | (25,000) |
| Acquisitions/disposals | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Financing | 11,932 | 6,033 | 11,185 | 50,175 | 0 | 0 | 0 |
| Net Cash Flow | 2,029 | (13,044) | (6,295) | 27,825 | (23,181) | (44,744) | (45,087) |
| Opening net debt/(cash) | (215) | (16,062) | (7,870) | (788) | (27,951) | (4,770) | 39,974 |
| HP finance leases initiated | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 13,818 | 4,852 | (787) | (662) | 0 | 0 | 0 |
| Closing net debt/(cash) | (16,062) | (7,870) | (788) | (27,951) | (4,770) | 39,974 | 85,061 |

Source: Company reports, Edison Investment Research

| Contact details | Revenue by geography |
|---|---|
| 36 Avenue de l'Europe<br>CS 40533 - Immeuble l'Etendard<br>78941 Vélizy Villacoublay CEDEX<br>France<br>+33 (0)1 39 45 64 50<br>www.carmatsa.com | N/A |

**Management team**

**CEO: Stéphane Piat**

Stéphane Piat joined Carmat in September 2016 as chief executive officer. He started his career at Becton Dickinson and then joined J&J Cordis where he covered several management positions including European marketing director for cardiology. He then moved to Abbott Vascular as general manager for mid-size countries, EMEA and then as divisional VP of the Structural Heart division in California. He has a Bachelor's degree in economics from the Business Administration Institute (IAE) from Dijon in France and a Master's degree in quantitative marketing from the Graduate Business School (ESA) of Grenoble in France.

**Chief Scientific Officer: Alain Carpentier**

Professor Carpentier is a founder of Carmat and played a significant role in the development of biological heart valve replacement. Grand Prize winner of the Foundation for Medical Research (1998), he received the Albert Lasker Medical Research Award in 2007 for his work in developing bioprostheses and techniques for reconstructive surgery of heart valves. He was elected president of the Academy of Sciences in 2011-12.

**Medical Director: Petrus Jansen**

Petrus Jansen began his career in 1997 with Edwards Lifesciences as head of research and clinical trials, particularly in connection with the Novacor programme (a left ventricular assistance device). Before joining Carmat in December 2009, he was head of clinical trials with Jarvik Heart, responsible for obtaining the CE Mark approval for its products, and medical director at World Heart USA for five years. Petrus qualified as a medical doctor at the Catholic University of Nijmegen. He has a PhD in medicine from the University of Amsterdam and was a research fellow at the University of Rotterdam.

**Chief Financial Officer: Benoît de la Motte**

Before joining Carmat, Benoît de la Motte was the CFO at Nexeya, which provides electronic solutions for multiple industries, and which he joined in 2008. From 2000 to 2007, Benoît was financial director of Southern Europe at Diebold, a participant in the ATM business. From 1995 to 2000, he was financial controller at Thales for its German operations. He began his career as an audit manager at PwC. Benoît is a graduate of the EM Lyon business school (1988), has an MBA from Pace University in New York (1988) and is a chartered accountant (1997).

| Principal shareholders | (%) |
|---|---|
| Airbus Group | 22.1 |
| Truffle Capital | 15.4 |
| Alain Carpentier and his Association | 11.0 |
| CorNovum | 7.6 |

**Companies named in this report**

Abbott, Bivacor, Cleveland Heart, Edwards Lifesciences, Medtronic, SynCardia



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