EDISON

CARMAT

Initiation of coverage

Brave heart

Healthcare equipment & services

Carmat is at a critical stage of CE-mark clinical studies for its bio-prosthetic heart, having gained authorisation to implant the second patient. The device is being developed as a permanent replacement for up to 50,000 late-stage heart failure patients on donor heart waiting lists outside the US. There is no existing European standard for a permanent implant, providing significant commercial potential. Clinical studies could be completed in 2015, leading to CE-mark award in 2016 and confirmation of the US strategy. Our valuation is €533m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/12	0.0	(21.9)	(403.8)	0.0	N/A	N/A
12/13	2.9	(16.2)	(336.5)	0.0	N/A	N/A
12/14e	5.4	(14.7)	(280.3)	0.0	N/A	N/A
12/15e	0.3	(27.5)	(535.6)	0.0	N/A	N/A

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

Green light to resume clinical trials for CE mark

Carmat started its first-in-man feasibility study in December. The first patient, in end-stage heart failure, survived for 74 days satisfying the 30-day survival success measure. The study was paused for three months to determine whether there had been a malfunction of the heart. No data have been disclosed; however, the DSMB and ethics committee have granted approval to resume the study, being satisfied of the device's safety. Contingent on the outcomes of this first study, Carmat will move onto a pivotal trial in c 25 patients. The heart could be CE marked in 2016.

US strategy to be confirmed after CE-mark award

Carmat's options to obtain US regulatory approval include first going down the humanitarian use device (HUD) route, a narrower market but a more cost-effective approval route requiring only safety data, or the longer pre-market PMA approval route (addressable market ≤ 50,000 patients) requiring a large-scale clinical trial. Carmat will seek a partnership with a larger US med-tech company.

Funded to early 2015

We estimate that Carmat is funded until early 2015, including end-December 2013 net cash of €16.1m, together with grant payments and tax credits of c €7.3m due in 2014. We estimate that Carmat will have a funding requirement of c €15m in 2015 to get to CE-mark certification and will require additional funds for the launch.

Valuation: DCF valuation of €533m

Our DCF valuation is €533m, or €125 per share, with a 12.5% discount and FY13 net cash of €16.1m, based on the company taking the humanitarian use device route in the US. If it opts for a PMA, taking into account the longer timeline, higher risk and costs, either for V1 or a follow-on version, the indicative valuation would be €911m. Carmat will require additional funding or a partnership for the US.

11 August 2014

Price	**€76.5**
Market cap	**€329m**
Net debt (€m) at 31 December 2013	16.1
Shares in issue	4.3m
Free float	32%
Code	ALCAR
Primary exchange	Alternext
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	4.9	(9.4)	(36.3)
Rel (local)	10.3	(1.6)	(38.2)
52-week high/low		€123.6	€70.0

Business description

Carmat is developing a biocompatible, artificial heart to satisfy the lack of donor hearts available for terminal heart failure patients. The development process combines the expertise of a wide range of technical and medical experts. Carmat initiated its first clinical study in man in 2013.

Next events

Recruitment of second patient for feasibility study	Q314
Initiation of pivotal trial	H115

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Investment summary

Company description: Developing a bio-prosthetic heart

Carmat was founded in 2008 and the heart project is the result of a collaboration combining the technological expertise of Jean-Luc Lagardère of MATRA Défense (now part of Airbus Group) and the medical expertise of Professor Alain Carpentier. The device is the first biocompatible bi-ventricular mechanical heart, designed to treat terminal heart failure and myocardial infarction, and to help compensate for the significant shortfall in donor hearts. Following extensive in vivo studies, the first human implantation was performed in December 2013. Paris-based Carmat floated on the Paris Alternext exchange in June 2010, raising €16.5m. Carmat is in receipt of grant funding from French government investment institution Bpifrance (formerly OSEO Innovation) and was granted a €33m subsidy from the organisation based on reaching a range of development milestones. The company has raised a further €42m by means of capital funding.

Valuation: DCF valuation of €533m

Our risk adjusted DCF valuation is €533m or €125 per share. We use a 12.5% discount rate and a long-term growth rate of 2% and add FY13 net cash of €16.1m. The EU opportunity is the key part of the valuation as this is at a more advanced stage and we assume the heart could be launched in 2017 if clinical trials progress as planned. In the US our valuation assumes that the company pursues humanitarian use device (HUD) status. If Carmat develops the heart, or any potential follow-on version, via the broad PMA route, our valuation would increase to €911m in line with the larger addressable market, including the additional R&D costs for the larger trial.

Financials: Project funding in place

The company held cash and equivalents of €16.9m as at the end of December 2013. In FY13, Carmat received €2.9m in subsidies from OSEO. During 2014, the company is due to receive additional OSEO payments totalling €5.5m on passing through the final stages of the project, together with a research tax credit of €1.8m, providing a cash reach into early 2015. We estimate that Carmat will have a funding requirement of c €15m in 2015, on top of the current equity line, which could be from a partnership with a med-tech company or via equity or debt funding (NB our valuation per share is on a pre-diluted basis, excluding any potential new equity funding).

Sensitivities: Clinical outcomes

The main investment driver is the outcome of clinical studies. While rigorous preclinical testing has been carried out, it is too early to draw conclusions from one patient on how well the heart will function in man. Following the death of the first patient, there has been a three-month pause to analyse data and verify if there was a malfunction of the heart. Carmat has obtained approval to resume the study, having satisfied safety conditions (although no detail was disclosed). Additional delays in the clinical trials could result in the CE mark award/launch timeline being pushed back further. The range of different high-end technologies, including biomaterials, micro-mechanics and electronics, adds to the complexity of the device. These components are procured from a variety of sources, which could affect timely production. Carmat is likely to depend on the support of investors to fund the EU pivotal trial and commercial launch in CE mark territories. Further down the line, Carmat will repay €14.5m in grants plus additional payments to OSEO subject to receipt of the CE mark and achieving sales milestones. Access to the US market is dependent on the outcome of CE mark studies and on securing a partner or independent funding for development and launch. Carmat's US options include developing the heart through the HUD and/or PMA route. If it chooses to go first through the HUD route, it could enable Carmat to access the market more quickly, generate sales and develop partnerships, although initially restricting the size of the addressable market.

Outlook: Brave heart

Carmat is developing an innovative bio-prosthetic heart, differentiated from previous generations of artificial hearts through pioneering use of technology to make the prosthesis function as closely as possible like a human heart. A successful outcome in the ongoing CE mark clinical trials could allow the device to be launched outside the US in 2017 to meet the significant clinical need for a permanent alternative for the patients on heart transplant waiting lists in CE mark regions; our peak sales estimate is €1.2bn. The lack of any accepted implant for permanent use in either the EU or the US is potentially a significant commercial advantage. Carmat is funded to early 2015 and is likely to require financing to complete the pivotal study, to achieve CE mark and to commercialise the device. It plans to subsequently finalise its US strategy. Our valuation is €533m.

Carmat heart and the cardiac transplant market

The Carmat artificial heart is being developed as a permanent replacement or destination therapy (DT) for chronic heart failure or acute myocardial infarction patients, who do not have access to a human donor heart. Carmat initiated the first-in-man feasibility study in December as part of the CE mark certification process. The study will recruit a total of four patients from three domestic cardiac centres. The company plans to start the US regulatory process subsequent to obtaining CE mark.

The Carmat heart is designed to replicate as closely as possible the functions, size and shape of the human heart. It is a self-regulating device unlike earlier mechanical hearts, which focused on restoring blood flow and tend to pump blood at a fixed rate. In addition, the surfaces of the prosthesis that interface with the blood are made from biocompatible materials to help overcome complications including blood clotting.

Having completed the preparation phase of development, the first patient in the feasibility study, a 76-year-old man in the terminal stages of heart failure, was implanted in December. The patient survived 74 days, which satisfied the success criteria of the study: survival at 30 days, or successful bridge to transplant. However, Carmat halted the trial for three months to establish if there had been a malfunction of the heart. No further data have been disclosed, although independent review bodies[1] have authorised the study to continue, being satisfied of the safety of the prosthesis. Carmat expects to implant the second patient in the coming weeks. Carmat will subsequently seek approval to start a pivotal study in c 25 patients, planned for H115. This study could take six months or more depending on the rate of recruitment, the number of centres and the time for the follow up.

Care of end-stage heart failure patients

Transplantation with a human heart is the gold standard for end-stage heart failure patients. The average adult survival rate following transplantation is 10 years[2] and this has improved over the past decade due to improvements in follow-up care, including advances in the expertise of cardiac surgeons, post-operative care and immunosuppressant therapy.

Transplantation has extended the lives even of patients with a very poor prognosis. The one-, five- and 10-year average survival rates are approximately 88%, 75% and 56% respectively, and the outcome is notably improved for lower-risk patients, for example those who are infection-free and have no previous implantation with any mechanical support device.

The cost of transplantation including assessment, medication and post-surgical care is estimated at $1m in the US, with additional costs for ongoing care and medication. Extensive screening excludes patients with significant comorbidities that can increase either short-term risk or long-term

1 DSMB Data and Safety Monitoring Board, comité de protection des personnes (ethics committee).

2 Society of Thoracic Surgeons.

survival. Preference is given to patients who are likely to survive the longest after transplantation and those who have waited longest.

The total costs of caring for patients in the terminal stages of the disease awaiting transplantation is estimated at up to $35bn pa in the US due to the dependence of these patients on intensive care and medication. Furthermore, the worldwide prevalence of heart failure is forecast to rise by up to 50% by 2030, which could double the costs of treatment.[3] However, the shortfall in donor hearts is such that only around 3,800 human heart transplants were performed globally in 2013 compared to c 100,000 patients currently on the active transplantation waiting lists.[4]

Mechanical circulatory support

Mechanical circulatory support devices and artificial hearts are an important bridge to transplant, recovery or decision on future treatment as an alternative to heart transplant where the patient is ineligible or there is no donor heart available. They provide an immediate stopgap for patients and are designed to extend the life expectancy of late-stage heart failure patients awaiting heart transplantation. The type of device used depends on the stage of heart failure and whether a single or both ventricles are affected.

Patients are categorised according to the classification system developed by INTERMACS, the Interagency Registry of Mechanically Assisted Circulatory Support created in 2006 by the FDA, CMS and the NHLBI. The registry is used to record, classify and improve the outcomes for patients implanted with durable MCS devices and to stratify risk and monitor the outcomes of these patients.

Exhibit 1: INTERMACS classification system

NYHA Class	Profile level	Patient profile	Time to intervene
IV	1	Critical cardiogenic shock	Hours
	2	Progressive decline	Days
	3	Stable, inotrope dependent	Weeks
	4	Resting symptoms	Months
	5	Intolerant to exertion	
	6	Limited activity	
III	7	Advanced Class III	

Source: INTERMACS

Patients who suffer mono-ventricular failure (the left is the most susceptible to failure due to around five times the pressure workload of the right) in profile three or four would usually be implanted with a ventricular assistance device (VAD). These devices include left and right ventricular assistance devices – LVADs and RVADs – that were developed as a bridge to transplant (BTT) and work in parallel with the natural heart to support a failing ventricle. Despite relatively good outcomes for patients implanted with an LVAD, up to 30% of patients go on to develop right ventricular failure. In addition, these devices are mechanical and pump blood at a set rate and in some cases require the patient to remain hospitalised. In general, the patient requires long-term anti-coagulation treatment.

A small proportion of these level three or four patients suffering from or susceptible to bi-ventricular failure go on to be implanted with a combination of a left and right assistance device known as a BiVAD, to support both ventricles. However, a BiVAD is a temporary solution and most are approved for use inside the hospital and many pumps are worn outside the body, which restricts patient mobility. So far there is limited data with which to assess the risk benefit of the procedure.

The main treatment for patients in INTERMACS profile 1 or 2 suffering bi-ventricular failure, is a bridge to transplant with the Syncardia total artificial heart where no donor heart is immediately available. The Syncardia heart is approved as a bridge to transplant and replaces the human heart while the patient waits for a donor heart.

3 CDC, Centers for Disease Control and Prevention.

4 National Heart Lung and Blood Institute statistics.

There have been over 1,300 implantations with the Syncardia heart, and the longest implanted patient has lived for nearly four years. However, the device was designed for use in a hospital setting and the air compressor is positioned externally to the body. A portable driver is now CE marked and available in the US on an investigational basis. It has limited adaptability to the cardiac output needs of the patient as it is a mechanical heart. Also, anti-clotting medication is required long term, which excludes patients unable to tolerate such medication.

The Carmat heart has been developed to provide significantly better outcomes for terminal heart failure patients who otherwise might be considered for a total artificial heart or a BiVAD due to the lack of human donors. Specifically, its features are designed to provide improved outcomes compared with approved MCS devices.

Exhibit 2: Comparison of mechanically assisted circulatory support devices

Company/ device	Approval status	Technology/Portability of energy source	Adaptability/Haemocompatibility	Data
Carmat/ Bio-prosthetic artificial heart	In development: CE mark DT/US-PMA or HUD as DT pending	Electro-hydraulic pulsatile flow contained within the body. First-generation lithium-ion batteries (3-4 hours of autonomy). Second-generation fuel cell battery (<3kg, >12 hours of autonomy).	Self-regulating, miniaturised device. Algorithms mimic the reactions of the cardiac muscle to BP, aortic pressure and patient posture changes, detected by embedded sensors. All blood-facing surfaces haemo-compatible.	Durability of five years under bench conditions. Preclinical testing completed to ISO 9001. First-in-man transplantation Dec 2013. Duration of first human implantation procedure - 2 hours 49 minutes. Feasibility stage of clinical development is ongoing, pivotal stage to start H115.
Syncardia/ Total artificial heart	Approved: BTT US, Europe, Canada/US HUD status aims for HDE as DT	Pneumatic, pulsatile, biventricular support, polyurethane ventricles. Hospital console in US. Portable Freedom Driver CE marked FDA trial due to complete May 2014.	Ventricles adjust to increase in blood flow during exercise. Blood-facing surfaces are non-biocompatible including mechanical Medtronic Hall valves, pyrolitic carbon in titanium housing. Thrombogenetic, long-term use of anti-coagulation medication is required.	FDA approval study n=81, 79% survived to transplantation vs 46% control group n=35. One-year survival 70% and 31% respectively. Over 1,250 implants as BTT since approval.
Ventricular assistance devices				
Thoratec, HeartMate II/ LVAS	Europe/US/Can BTT/BTR or DT	An axial-flow rotary ventricular assist device that generates flows up to 10 litres/per minute. Lithium battery up to 10 hours autonomy. Pocket Controller recently launched.	Diverts blood from the weakened left ventricle and propels it to the aorta. Flow rate set externally by patient or physician. Reduced risk of thrombotic events, higher incidence of haemorrhagic events in the long term.	BTT approval study demonstrated non-inferiority 76% vs objective performance criterion of 75% defined by survival to transplantation or recovery within 180 days of LVAD support.
HeartWare/ HVAD	Europe/US/Can BTT/BTR	Non-pulsating miniature device. Blood pump with an integrated inflow cannula, gel-impregnated polyester outflow graft, and a percutaneous driveline. Portable power unit with battery and mains adapter.	Estimates blood flow rate using characteristics eg blood viscosity – calculated from the patient's haematocrit – which are entered into the monitor. Flow estimation used as a trending tool only, as device cannot adapt to changing fluid conditions.	Non-inferiority vs primary endpoint, survival, transplanted, or explanted for recovery at 180 days compared to INTERMACS registry. 90.7% success rate vs 90.1% control group in safety cohort, 92% vs 90.1% control group in per protocol cohort.
ThoratecIVAD/ BiVAD	Europe/US/BTT or post-cardiotomy	Blood pump, left, right, or biventricular assist device. A titanium alloy case containing a blood-pumping sac composed of proprietary polyurethane multi-polymer.	Mechanical valves mounted in the inflow and outflow ports of the blood pump control the direction of blood flow. Effective stroke volume of 65ml pumps approx 6.5L/min at a rate of 100bpm.	69% of patients successfully supported to cardiac transplantation or explantation, with no device failures.

Source: Edison Investment Research, Carmat, Syncardia,Thoratec, HeartWare. Note: DT = destination therapy, BTT = bridge to transplant, HUD = humanitarian use device, HDE = humanitarian device exemption, BTR = bridge to recovery, PMA = pre-market approval.

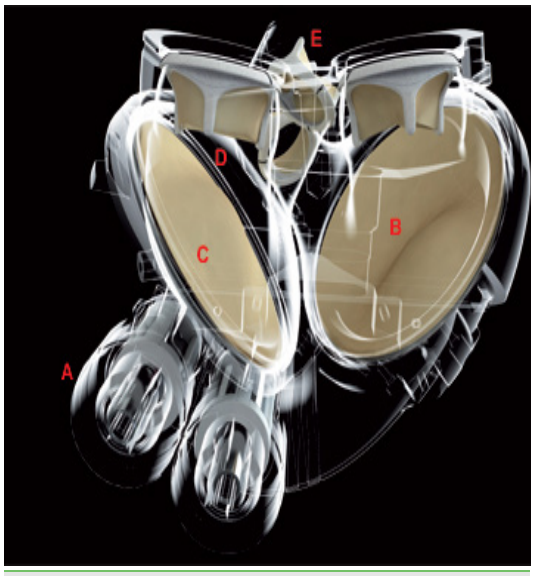
The potential main clinical advantages of the Carmat Heart

The specific features of the Carmat heart include pulsating, auto-regulatory pump; biocompatibility, greater autonomy for the patient; durability; and optimised transplantation process.

The external wall of each ventricle is contained by a bio-membrane creating two volume spaces. Within the external volume space is a flexible sac containing hydraulic activation fluid. Two motor units provide a pulsatile heart beat and displace the flexible bio-membrane to eject and admit blood, mimicking the natural flow action of the heart. The flow rate is governed by an internal electronic device, controlled by embedded sensors that adjust flow rate in accordance with the patient's physiological requirements, varying both the rate and the strength at which the blood is pumped. Auto-regulation is governed by software algorithms that replicate cardiac characteristics and

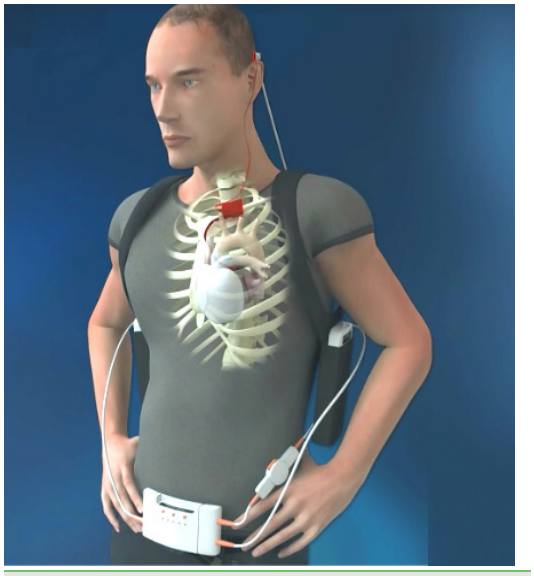
respond to changes in posture and to the physiological and haemodynamic requirements of the patient.

Exhibit 3: Internal layout of the prosthesis



Source: Carmat SA

Exhibit 4: Prosthesis and control system



Source: Carmat SA

The biocompatible materials used by Carmat include four Carpentier-Edwards bovine pericardium heart valves, which are proven to be durable and to reduce the need for anticoagulants compared to mechanical valves. Other blood-contacting surfaces are medical-grade ePTFE, which has low shear stress rates, reducing clotting.

The energy source consists of two lithium batteries, which can be charged to provide up to four hours of power. A lighter weight (<3kg) fuel cell alternative is currently being developed by Carmat's partner Paxitech, the first time a fuel cell has been developed for medical use, to provide over 12 hours of power. A console serves as the power source for the heart while the patient is in hospital. Data are transmitted externally from the device to the hospital console during the post-operative period. After discharge, the patient system is a portable control box, which relays information remotely to the transplant centre and is carried in a back pack together with the energy supply.

The target durability of the device and its component parts is up to five years under bench conditions. The company aims to improve this over time and is conducting long-term durability testing.

The surgical procedure for implanting the Carmat heart is similar to that for a heart transplant; the prosthesis is clicked into an interface device, which is sutured to the atria after removal of the diseased heart. The first human implantation with the Carmat heart took 132 minutes compared to six hours for a human heart transplant.

Scaling up the production process

Carmat sources most of the many individual components of the heart from external suppliers and assembles them onsite, except the bio-synthetic components, which are sourced internally. The company has an agreement with Edwards Life Sciences, automatically renewable on an annual basis, to use Carpentier-Edwards valves. Around 80% of its suppliers are France-based aeronautic and medical suppliers. The company is in the process of identifying back-up sources for all the suppliers of the critical components, as required for CE mark certification, and is scaling up its production capability ahead of launch. Carmat targets a reduction in the duration of the currently largely manual assembly and testing process. These efficiencies can be achieved by automating

parts of the process and by sourcing some elements ready sub-assembled and by means of other production efficiency measures.

Development and commercial strategy in EU

For Europe and outside the US, the route to market is via CE mark certification. The development plan is divided into the preparation, clinical and development stages. The preparation phase is complete, including validating and testing the design and the manufacturing process for the prosthesis and its component parts. CE mark certification requires completion of a technical dossier and a clinical data dossier in up to c 25 patients. Carmat plans for a potential approval in 2016 and launch in 2017 contingent on a satisfactory outcome from its pivotal trial.

During the preparation stage, Carmat completed assessments and validation for the components, sub-assemblies, prosthesis and software systems. This included ex vivo, in vivo and haemo-compatibility testing. The results of an in vitro case study demonstrated limited platelet adhesion and minor blood cell deposits using proprietary biocompatible materials.[5] Carmat received authorisation from the ANSM to commence clinical trials starting in France last December, after successful completion of preclinical testing; the results of animal studies in calves demonstrated pulsatile flow of up to 9l/min and restored tissue perfusion.[6]

The clinical validation stage is in two parts, a feasibility study in four patients (INTERMACS 1 and 2) and a six-month pivotal study in c 25 patients. Once the feasibility study and analysis of the dataset is complete, Carmat will seek regulatory approval to commence the pivotal study in H115.

The pivotal study requires implantation into patients over a period of 180 days. It is likely to include patients with better prognosis than those included in the feasibility stage, depending on final analysis of the data from the first four patients. The safety, efficiency and performance of the prosthesis and its control systems will be validated during this stage. The key endpoints of the pivotal study have not yet been defined, although they are likely to include survival or bridge to transplant at 180 days, cardiac pumping volumes, normal functioning of kidneys/liver and non-inferiority survival rates versus INTERMACS as control.

In addition to the three French centres, the pivotal study will recruit patients from other countries in Europe and potentially the four centres announced at the start of the clinical phase in 2013. In parallel with the pivotal study, Carmat will complete the third and final development stage, using the results and data obtained to make systems modifications. It will implement further refinements of the manufacturing process including validating secondary suppliers for all key components and amending all the necessary documentation. The portable fuel cell is being developed to coincide with planned CE mark.

Commercialisation prospects and strategy in the EU

Carmat is preparing the ground for planned launch in CE mark territories in 2017 by forming partnerships and training key centres of excellence in heart transplantation and developing relationships with the key opinion leaders. Its strategy is to launch the prosthesis in France first and then to extend to the four international centres. The detailed plan for CE mark territories is not yet confirmed, but it is likely to be done on a phased basis. After the initial launch, Carmat plans to extend into other key territories, approaching the highest volume and value markets in the first instance. These secondary territories could include Germany, Switzerland, Austria, Italy, Spain, the Netherlands, Gulf territories, Russia and Turkey.

5 In vitro Haemocompatibility of a Novel Bioprosthetic Total Artificial Heart

6 Sub-Acute Animal Implantation of a Novel Bioprosthetic Artificial Heart

Carmat aims to appoint a direct sales team for the domestic market and on a selective basis for the next largest markets. In the first phase, it is thought that one rep could target a key account on a monthly basis so that a relatively small team would be needed for France.

The company intends to appoint distributors on a selective basis to approach the next phase of territories. Its choice of launch will be driven by the reimbursement policy of the individual countries and the company plans to appoint a reimbursement specialist during the latter stages of the clinical trial.

We estimate that the market opportunity in CE mark territories is up to 50,000 eligible late-stage chronic and acute heart failure patients a year, with a device price range of between €140,000 and €180,000 per unit.

Development and commercial strategy in the US

The US is a significant market and the vast majority of cardiac transplants are performed in the region, approximately 2,000 out of a worldwide total in 2013 of 3,800 (Source: NIH). There are around 150 specialist transplant centres with a high number of key opinion leaders driving the volume of transplants. In addition, the market value is higher than EU and RoW as the pricing of medical devices is up to 50% higher in the region. Additionally, the US is more homogenous in terms of its reimbursement policies. Carmat is already developing links with the key opinion leaders with a view to establishing accredited transplantation centres and the heart has generated significant levels of interest among cardiac surgeons.

Two possible non-exclusive routes

The CE mark is not sufficient to launch the heart in the US; the approval process is distinct. In addition to the CE mark, Carmat is likely to pursue sequentially one of two regulatory pathways required for an active implantable medical device. It might choose to follow the full pre-market approval (PMA) route or apply first for the less onerous humanitarian device exemption (HDE) to market the device as a humanitarian use device (HUD), defined as a device intended to benefit patients affected by a condition manifested in fewer than 4,000 patients a year. The rationale for use in an orphan subset might be to target the sickest patients in INTERMACS categories 1 and 2, with only days to live.

Exhibit 5: Features of the PMA and HUD approval process for medical device

Heading Left	Size of clinical trial	Clinical data requirements	Timeline	Addressable market
PMA	≥100 patients	Safety, efficacy	Two years minimum	Up to 50,000 pts
HUD	10-20 patients	Safety, reasonable evidence of risk vs benefit	Six months	4,000 pts

Source: Edison Investment Research

The HUD route means Carmat would be required to provide safety evidence. However, unlike a PMA, there is an exemption from providing efficacy data. The device will be approved if there is a reasonable assessment of the benefit versus risk, compared to existing forms of treatment and approved devices. This would mean HUD approval might be faster to achieve and that the clinical trial is likely to be shorter with 10-20 patients over a three- to six-month timeframe. Any follow-on, next-generation version of the heart would need to be developed through the HUD or PMA route; an abbreviated 510k would not be sufficient for approval.

US market opportunity

The choice of route would affect the addressable market. It would be much quicker and more cost-effective to seek marketing approval as an HUD. However, sales would be limited to 4,000 patients a year and such patients are likely to be the 5% at the terminal heart failure stage.

A PMA would be more lengthy and costly to complete, although this would provide a much larger potential market, up to 50,000 heart failure patients in the US in the end-stage chronic and acute

heart failure group, who would be potentially eligible for a Carmat heart. Patients with significant co-morbidities, aged over 70 years and those with access to a human donor heart would be excluded. The price for the device in the US in either case is likely to be towards the top of the range indicated by the company at c US$280,000.

The choice of development route is likely to become clearer after achievement of the CE mark and it will depend on whether the company wants to push through a follow-on version of the heart, for example a lighter device, and the company might decide to invest in a PMA for a follow on. However, our default assumption is that Carmat will pursue HUD approval for V1 of the heart.

Carmat intends to form a partnership with a large med-tech company to develop the prosthesis in the US. It is possible that it will initiate the US development process in parallel to the CE mark process, although it is likely to wait until after the product has been launched in Europe and other CE mark countries so that the earliest launch date for the US might be 2019 via the HUD route.

Sensitivities

The key driver is achievement of CE mark and with the preparation stage complete this is dependent on a successful outcome of clinical trials. There has been a delay to complete the data analysis after the death of the first patient to establish if there was a malfunction. No cause has been disclosed, although the review bodies are now satisfied that the device is safe to be implanted in the next patient. Additional delays to the clinical trials could result in a later CE mark award and launch.

The scale-up process requires the company to locate back-up suppliers for all components and to put in place efficiencies to increase production while maintaining high-quality standards.

Successful commercialisation depends on clinical results and positioning and rate of progress of competing companies. While the heart project has generated an extremely high level of interest, particularly at the start of first-in-man studies, it is unknown how quickly the device will be adopted by the medical community after launch. The rate of adoption is also strongly related to the rate of progress in selecting, training and developing new specialist centres and on Carmat's ability to engage with key opinion leaders.

The choice of development route in the US affects the cost of development, positioning of the product and the eventual size of this market and potential returns. This is a decision that remains to be made, potentially based on the rate of progress and outcome of the CE mark certification process.

Founders and key shareholders hold over 68% of the shares restricting stock liquidity. A remaining 83,200 warrants are issuable through the Kepler Chevreux contingent equity facility (1:1 ratio) representing c 2% dilution at the current share price.

Valuation

Our DCF valuation of Carmat is €533m using a 12.5% WACC and a long-term growth rate of 2%. This is on an undiluted basis, before any potential equity funding needed to launch the product, and is based on Carmat launching the heart in the EU in H117 and in the US via the HUD route in 2019. We have not broken down the valuation per region at this stage as our forecasts use a blended margin, although peak sales value in the EU is around twice the value of the US. The key assumptions used are shown below.

Exhibit 6: DCF assumptions

Market	Launch date	Penetration	Peak sales	Probability	Valuation €
CE mark territories	2017	15%	1,200	35%	-
US via HUD	2019	70%	560	25%	-
Net cash (FY14)					16.1m
Total					533m
Value per share					125

Source: Edison Investment Research

If Carmat opts for the PMA route, there would be additional R&D costs of c €30m, a higher risk adjustment of 15% and a later launch date of 2021 due to the longer trial. The addressable market would be larger, although we assume lower penetration of 20%. This increases our peak sales estimate to €2bn, taking our total valuation to €911m or €213 per share. This gives an initial indication of the valuation uplift of a follow-on product designed for the US market.

Gross margin could trend towards 60% based on peer group metrics and assuming a c 50% balance between distributors and direct sales. Our gross margin assumption takes into account a 2% royalty payable annually to inventors after launch. Our long-term projection is for an operating margin of c 35% assuming US launch in 2019 as an HUD.

The following table shows a scenario analysis based on the company pursuing HUD approval, flexing risk adjustment and price showing the potential for value to increase as the project advances. We estimate that the device will be launched in Europe/RoW in 2017 at a price of €160,000 with a c 25% premium in the US, €200,000 (US$280,000).

Exhibit 7: Valuation per share (€) based on different risk adjustment and price

	Risk adjustment					
Price in Europe (€)	10%	20%	30%	50%	75%	100%
140,000	30	66	102	175	265	356
160,000	36	77	119	201	305	408
180,000	42	88	135	228	344	461

Source: Edison Investment Research

Financials

Cash and equivalents at the end of December 2013 stood at €16.9m. Carmat raised €11.9m in FY13 through the drawdown on its contingent equity line with Kepler Chevreux. It also received €6.7m in grants from Bpifrance/OSEO. We estimate that the year-end cash and equivalents, together with projected grant payments in FY14, will provide a cash reach into early 2015. A further €0.3m subsidy is receivable from Bpifrance on production of systems documentation in 2015 and €1.5m on CE mark in 2016; and 83,200 shares, which are issued at 93% of the VWAP for the preceding five days, can still be drawn down from the equity line. On this basis, Carmat will have an approximate funding need of €15m in 2015 to achieve CE mark certification. It aims to finance the commercialisation stage and US development through additional financing or with a partner. If Carmat forms a partnership for the US, it could receive an upfront payment that could be used to fund the company's ex-US development programme.

The Carmat heart project has been financed to date on the basis of a framework agreement with Bpifrance/OSEO, for total grant funding of €33m, of which €18.5m is grants and €14.5m is repayable advances, subject to it passing through the seven milestone stages of the project. The company received €2.9m in subsidies and repayable advances in FY13 and in FY14 it is due to receive a further €5.3m advance triggered by the start of the feasibility study and the final subsidy of €159k payable at the start of the pivotal study. A research tax credit of €1.8m was received in H114. We include in our projection repayment of grants to Bpifrance/OSEO, subject to CE mark certification and launch annually, starting in the year following achievement of sales over €38m and

capped at maximum cumulative sales of €50m as follows: 0.5% year one and two, 1% years three and four, 2% in year five.

Exhibit 8: Financial summary

€'000s	2011	2012	2013	2014e	2015e
Year end 30 June	French GAAP	French GAAP	French GAAP	French GAAP	French GAAP
PROFIT & LOSS					
Revenue	6,102	18	2,874	5,410	291
Cost of Sales	0	0	0	0	0
Gross Profit	6,102	18	2,874	5,410	291
EBITDA	(14,495)	(20,814)	(15,156)	(13,729)	(21,681)
Operating Profit (before GW and except.)	(14,495)	(22,017)	(15,885)	(14,202)	(22,145)
Intangible Amortisation	(1,496)	(271)	(191)	(58)	(45)
Exceptionals	0	(34)	0	0	0
Other	(100)	(98)	(40)	0	0
Operating Profit	(16,091)	(22,420)	(16,116)	(14,260)	(22,190)
Net Interest	97	110	(324)	(464)	(5,380)
Profit Before Tax (norm)	(14,398)	(21,907)	(16,209)	(14,666)	(27,526)
Profit Before Tax (FRS 3)	(15,994)	(22,310)	(16,440)	(14,724)	(27,570)
Tax	2,516	5,015	1,770	2,424	4,136
Profit After Tax (norm)	(11,845)	(16,787)	(14,413)	(12,242)	(23,390)
Profit After Tax (FRS 3)	(13,479)	(17,295)	(14,670)	(12,300)	(23,435)
Average Number of Shares Outstanding (m)	4.1	4.2	4.3	4.4	4.4
EPS - normalised (€)	(287.0)	(403.8)	(336.5)	(280.3)	(535.6)
EPS - FRS 3 (€)	(326.5)	(416.0)	(342.5)	(281.7)	(536.7)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0
BALANCE SHEET					
Fixed Assets	3,148	2,267	1,633	1,586	1,168
Intangible Assets	235	168	125	95	79
Tangible Assets	1,263	725	945	928	526
Investments	1,651	1,373	563	563	563
Current Assets	34,278	17,431	20,351	9,945	7,387
Stocks	0	0	48	48	48
Debtors	4,121	6,092	2,952	1,779	1,779
Cash	29,370	11,135	16,884	7,575	4,581
Other	788	204	467	544	980
Current Liabilities	(6,756)	(5,939)	(7,098)	(2,523)	(7,982)
Creditors	(6,152)	(5,327)	(6,254)	(1,112)	(1,112)
Short term borrowings	(217)	(460)	(822)	(1,389)	(6,848)
Other	(387)	(152)	(22)	(22)	(22)
Long Term Liabilities	(3,779)	(3,817)	(7,654)	(7,654)	(22,654)
Long term borrowings	0	0	0	0	(15,000)
Other long term liabilities	(3,779)	(3,817)	(7,654)	(7,654)	(7,654)
Net Assets	26,891	9,941	7,232	1,354	(22,081)
CASH FLOW					
Operating Cash Flow	(10,031)	(18,108)	(9,792)	(17,523)	(21,661)
Net Interest	0	0	0	103	79
Tax	325	154	153	2,347	3,699
Capex	(1,023)	(516)	(266)	(555)	(33)
Acquisitions/disposals	0	0	0	0	0
Financing	26,819	240	11,881	6,422	0
Dividends	0	0	0	0	0
Net Cash Flow	16,090	(18,229)	1,977	(9,206)	(17,916)
Opening net debt/(cash)	(11,337)	(29,153)	(10,675)	(16,062)	(6,185)
HP finance leases initiated	0	0	0	0	0
Other	1,725	(248)	3,409	(670)	(5,537)
Closing net debt/(cash)	(29,153)	(10,675)	(16,061)	(6,185)	17,268

Source: Edison Investment Research, company accounts. Note: The financing in FY14 assumes that the remainder of the equity line is drawn down priced at the current share price. In FY15, the €15m in long-term borrowings is indicative of the funding requirement in FY15

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

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 11-15e	N/A	ROCE 14e	N/A	Gearing 14e	N/A	Litigation/regulatory	●
EPS 11-15e	N/A	Avg ROCE 11-15e	N/A	Interest cover 14e	N/A	Pensions	◖
EBITDA 11-15e	N/A	ROE 14e	N/A	CA/CL 14e	N/A	Currency	◖
EBITDA 11-15e	N/A	Gross margin 14e	N/A	Stock days 14e	N/A	Stock overhang	●
Sales 11-15e	N/A	Operating margin 14e	N/A	Debtor days 14e	N/A	Interest rates	◖
Sales 11-15e	N/A	Gr mgn / Op mgn 14e	N/A	Creditor days 14e	N/A	Oil/commodity prices	○

Management team

CEO: Marcello Conviti	CSO: Professor Alain Carpentier
Mr Conviti worked at Sorin Biomedica for over 12 years. Before joining Carmat, he held several senior international positions with Edwards Lifesciences over a period of 17 years (most recently senior vice president for strategy and new business development).	Professor Carpentier is a founder of Carmat and a pioneer in the development of biological heart valve replacement. Grand Prize winner of the Foundation for Medical Research (1998) in 2007, he received the Albert Lasker Medical Research award 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.
COO: Patrick Coulombier	**Medical Director: Piet Jansen, MD**
Head of the project team since 2001 within the EADs group, Patrick Coulombier formerly worked at MBDA France in charge of two international defence programmes. Previously, he headed up aeronautic and space projects at Thales Avionnique. Mr Coulombier holds a degree in electronic engineering.	Dr Jansen was head of research and clinical trials at Edwards Lifesciences, where he focused on developing LVADs. Before joining Carmat, he was head of clinical trials at Jarvik Heart in Europe and the US leading to CE mark approval and medical director at World Heart USA for five years. He qualified as a medical doctor at the Catholic University of Nijmegen and has a PhD in physics from the University of Amsterdam.

Principal shareholders	(%)
Airbus	29.5
Truffle Capital	26.1
Alain Carpentier	12.8

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