EDISON

BONESUPPORT

Initiation of coverage

Innovative orthobiologics company

Pharma & biotech

BONESUPPORT is commercialising synthetic bone graft substitutes. The company invests in R&D to support continued development of innovative products that command premium pricing and differentiate them in a competitive market. Following recent issues with the exclusive, long-standing distributor in the US, BONESUPPORT terminated the agreement and US sales are expected to recover via an independent distributor network and a more hands-on approach to growing sales. After a successful IPO in June 2017 raising SEK520m, the company is well funded. We value BONESUPPORT at SEK1.13bn or SEK22.2/share.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/16	104.6	(108.4)	(4.22)	0.0	N/A	N/A
12/17	129.3	(126.7)	(3.21)	0.0	N/A	N/A
12/18e	113.8	(164.0)	(3.26)	0.0	N/A	N/A
12/19e	210.9	(128.6)	(2.54)	0.0	N/A	N/A

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

Investing in product differentiation and salesforce

BONESUPPORT's investment case rests on three strategic pillars: effective commercial organisation, products backed by clinical data and R&D innovation. The company is investing in the expansion of its sales organisation, which could sustain rapid growth seen over the past few years (2014-17 CAGR of 47%). BONESUPPORT's products are very profitable, with gross margin of c 85%. To differentiate CERAMENT from competitors, the company has gathered data and is undertaking clinical trials to support the claims of its marketed products. Several other innovative synthetic bone graft substitute solutions are in R&D.

Three products in two key markets

BONESUPPORT's three main marketed products are CERAMENT bone void filler (BVF), CERAMENT G (gentamicin) and CERAMENT V (vancomycin). In Europe BONESUPPORT either sells directly or uses distributors. In the US, BONESUPORT's exclusive distributor Zimmer Biomet experienced internal supply problems in 2017, which also affected CERAMENT sales. BONESUPPORT decided to reshape its business model in this key market and is now switching to a potentially more economically beneficial independent distributor network once Zimmer Biomet's exclusivity ends in October 2018. CERAMENT G and V are both high growth products in Europe, but not available in the US. BONESUPPORT has established an R&D programme and could bring CERAMENT G to the US market in 2021, substantially expanding its potential.

Valuation: SEK1.13bn or SEK22.2/share

Based on our DCF model, we value BONESUPPORT at SEK1.13bn or SEK22.2/share. Our model reflects organic growth in existing markets, for which we estimate that existing funds are sufficient to reach profitability by 2021. We also include risk-adjusted (70%) CERAMENT G profits in the US market from 2021. Continued strong sales growth in Europe, rebound in the US and results from the CERTiFy trial are key share price drivers in the near term.

21 June 2018

Price	**SEK10**
Market cap	**SEK508m**

Net cash (SEKm) at end-Q118	397.2
Shares in issue	50.8m
Free float	50%
Code	BONEX
Primary exchange	Nasdaq Stockholm
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(17.1)	(34.2)	N/A
Rel (local)	(15.1)	(35.7)	N/A
52-week high/low	SEK32	SEK9	

Business description

BONESUPPORT is an orthobiologics company that has commercialised three synthetic bone graft substitutes and has several other projects in R&D. The marketed products, CERAMENT BVF, CERAMENT G (gentamicin) and CERAMENT V (vancomycin), are intended to help orthopaedic surgeons manage bone voids and defects after injuries or diseases affecting bones.

Next events

Q218 report	26 July 2018
CERTiFy study results	H218
New investigator-initiated studies	2018

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Edison profile page

Investment summary

Company description: Innovative bone graft substitutes

BONESUPPORT, founded in 1999, is an orthobiologics company that has commercialised three synthetic bone graft substitutes and has several other projects at the R&D stage. The marketed products, CERAMENT bone void filler (BVF), CERAMENT G and CERAMENT V, are intended to help orthopaedic surgeons manage bone defects after injuries or bones diseases. CERAMENT G and CERAMENT V also have the property of eluting antibiotics to reduce the rate of infection complications. BONESUPPORT has a nine-year track record of patients being treated with its products and the company estimates that some 30,000 procedures have been performed to date. R&D strategy centres on clinical evidence gathering for existing products, but also the development of novel products based on patented CERAMENT technology, which could elute other drugs, such as a growth factor that promotes bone healing or bisphosphonates, popular osteoporosis drugs that reduce bone resorption rate. BONESUPPORT underwent an IPO in June 2017, listing its shares on Nasdaq Stockholm and raising a total of SEK520m (net). BONESUPPORT maintains a flat organisation structure with key personnel responsible for specific areas ranging from R&D to commercialisation, reporting directly to the CEO. The team has been substantially reinforced over the last 18 months with experienced key hires such as Helena L Brandt (HR), EVP R&D Dr Jerry Chang, CMO Michael Diefenbeck PhD, CFO Björn Westberg and CEO Emil Billbäck.

Financials: Investing in sales and R&D, profits likely by 2021

BONESUPPORT achieved a CAGR of 47% to SEK129.3m over 2014-17. FY17 sales were SEK129.3m, up 23.6% y-o-y, with gross margin of 87.0%. FY17 sales growth in the US was 13%, substantially below 75% in FY16 and 46% in FY15. This was due to the sole US distributor, Zimmer Biomet, experiencing internal supply issues associated with its hardware products sold in a bundle with CERAMENT BVF. BONESUPPORT discontinued the collaboration with Biomet Zimmer and is in the process of establishing an independent distributor network in the US. We expect sales growth in the US to pick up again in 2019. Our FY18 and FY19 total sales estimates are SEK113.8m and SEK210.9m, respectively, with an operating loss of SEK167.5m and SEK131.5m as the company invests in its sales organisation and clinical trials. We forecast that the company will be profitable by 2021 with the current cash position. CERAMENT G could be launched in the US in 2021.

Valuation: SEK1.13bn or SEK22.2/share

We value BONESUPPORT at SEK1.13bn or SEK22.2/share, based on our DCF model using a 10% discount rate, forecast period until 2027 and end-Q118 cash position of SEK397.2m (no debt). Our model reflects organic growth in existing markets and risk-adjusted (70%) cash flows from CERAMENT G product in the US starting from 2021. At end-2017 BONESUPPORT had SEK604m in tax losses carried forward, which offsets taxes during our forecast period.

Sensitivities: High spending, high growth expectations

BONESUPPORT is subject to sales and marketing, regulatory, R&D, reimbursement and contract suppliers of product materials, among other risks. Since the US is the largest market for BONESUPPORT and the company is undertaking changes to its distribution model in this market, the successful establishment of an effective independent distributor network is key to the investment case. BONESUPPORT has been growing its sales rapidly over the past few years and because of the forecasted high sales growth, our valuation is highly sensitive to near-term estimate changes. Any unforeseen market headwinds, such as a delay in the expected rebound of US sales, could result in larger downward revisions to our valuation. According to our current projections, we do not forecast the need for additional funds to reach profitability.

Outlook: Innovating synthetic bone graft substitutes

BONESUPPORT's products can be used whenever there is a need to manage bone voids. The most common causes are revision arthroplasty (after a joint prosthesis fails due to loosening of periprosthetic infection), trauma and osteomyelitis (bone infection) including diabetic foot infections and bone tumours. If treated properly bone is a tissue that can regenerate completely without leaving any scar in the long term (in the short term the healed fracture forms bone callus). This is due to constant remodelling of the bone, a balance maintained by osteoblasts (bone-producing cells) and osteoclasts (cells breaking down and resorbing bone tissue). In certain cases, this process falters and surgical intervention is needed.

- **Trauma**. If the defect is too large or fragments are two far apart, the void will not heal. Complex fractures will often require multiple procedures. Open fractures present a higher risk of infection. In the case of underlying osteoporosis, even simple fractures can be difficult to treat. An estimated c 3.1m procedures to manage simple or complex traumas are performed annually in the US and EU5, with 15-17% involving synthetic bone graft substitute (source: Apex Global Market Study 2016 on behalf of BONESUPPORT).
- **Osteomyelitis** is a difficult-to-treat bacterial infection of the bone tissue. Osteomyelitis can be a primary disease, but will often be a complication of an underlying condition, such as bone fixation procedure after trauma, especially open fracture. If not managed during the acute phase, osteomyelitis can become chronic. An estimated c 80k procedures to manage chronic osteomyelitis are performed annually in the US and EU5, with 22-23% involving synthetic bone graft substitute (source: Apex Global Market Study 2016).
- **Revision arthroplasty** can be subdivided into aseptic loosening and periprosthetic joint infections, both of which are complications of joint replacement procedures. Aseptic loosening can happen over time after the first arthroplasty and revision procedure involves replacing the prosthesis, which often is associated with significant bone loss and difficulties anchoring the new prosthesis. Arthroplasty procedures still carry a small risk of periprosthetic infection (1-2%), which means the prosthesis has to be removed, the infection treated, the bone loss restored with grafting and a new prosthesis implanted. An estimated c 276k revision arthroplasty procedures are performed annually in the US and EU5, with 27-36% involving synthetic bone graft substitute (source as above).
- **Infected diabetic foot** is a specific subtype of osteomyelitis resulting from chronic foot wounds, which are contaminated and colonised by bacteria, which leads to repeated infection and chronic osteomyelitis. Often this results in multiple partial amputations. A total of c 320k procedures involving diabetic foot complications are performed in the US and EU5, with 13-21% involving synthetic bone graft substitutes (source as above).
- **Tumours and metastases** can invade and destroy the bone leaving large voids and weakened bone structure. The treatment can require bone void filling or strengthening the bone with fixators.

Bone graft substitutes

Bone voids are treated with bone graft. Initially, this was done using the patient's own bone from a different location, most often from iliac crests, and remains popular. While such an approach works well, autograft provides a limited amount of bone and requires a separate surgical intervention, which carries risks such as blood loss, infection and pain. Allograft or bone harvested from living or deceased donors could partly solve the quantity issue, but supply is not straightforward as it requires infrastructure (bone banking) and carries risks of disease transmission or bacterial contamination. Bone tissue can also be harvested from animals (xenograft) but, due to concerns about the transmission of infection and other issues related to allografting, it is not very popular.

Synthetic bone graft substitutes appeared as a novel alternative and are gaining market share with improving technology.

In addition to providing structure, there are three biological mechanisms for bone grafts involved in bone formation: **osteoconduction** (graft acts as a scaffold for new bone), **osteoinduction** (turning undifferentiated cells into osteoblasts) and **osteogenesis** (new bone tissue production by osteoblasts).

- The majority of all bone grafting procedures involve **autologous grafts** as they work well and historically have been considered the 'gold standard' since they are osteoconductive, osteoinductive and osteogenic. However, harvesting involves a second surgical intervention with associated risks such as infection and pain, in addition to the cosmetic effect. Another disadvantage is the limited amount of bone tissue that can be taken.
- **Allografts** are taken from deceased donors or living donors, for example bone banks store femoral heads taken from primary hip arthroplasty procedures. Allografts are osteoconductive, but there is insufficient evidence that osteoinduction and osteogenicity is still present after the processing of the grafts in order to keep them in the bone bank. Other disadvantages include the required infrastructure and potential for disease transmission. Demineralized bone matrix (DBM) is a processed form of allograft retaining much of the protein content of the bone, while reducing mineral content. The original idea was that the protein content, such as growth factors, will act as potent osteogenic/osteoinductive agents. While there are data to some extent supporting better DBM properties compared to allografts, DBM lacks mechanical strength because it is soft and cannot therefore act as a mechanical support.
- **Synthetic bone graft** substitutes are an attractive option as they can be manufactured in unlimited amounts and their mechanical and chemical properties can be tailored, so use is more predictable. Historically, the perceived downside was that they lack the signalling cues present in naturally derived materials, having only an osteoconductive function. BONESUPPORT's R&D pipeline explores the potential of combining its technology with growth factors to increase osteoinduction and osteogenicity.
  - While a variety of materials can be used for synthetic bone graft, ceramic materials are the most common choice and are based on forms of calcium sulfate, calcium phosphate or combinations. Calcium sulfate was the first material used in synthetic bone graft substitutes. However, the main drawback was quick resorption over six to eight weeks and lack of bone growth support. The addition of calcium phosphate substantially improved resorption time and during the last two decades different combinations of these materials have been explored in various forms. CERAMENT is 60% calcium sulfate and 40% hydroxyapatite (a form of calcium phosphate). BONESUPPORT has shown a clinically balanced resorption rate (see CERAMENT BVF section below) that matches the formation of new bone tissue, allowing time for bone remodelling.
  - Other materials used less frequently for synthetic bone graft substitution include bioglass, degradable and non-degradable polymers and other biomaterials.

Innovation in bone graft substitution: Managing infections

Risk of infection in trauma and orthopaedic surgery is a particular concern. Around 30% of open fractures and 2-5% of closed fractures treated surgically become infected. The percentage is much smaller in joint replacement procedures (1-2%), although this is still a major issue. For example, if a joint prosthesis becomes infected after the primary replacement operation, the common two-stage treatment involves complete removal of the device, debridement of the necrotic tissue, leaving an antibiotic-loaded cement spacer, treatment of the infection with systemic antibiotic therapy and then repeated arthroplasty. This means primary arthroplasty is wasted, which is costly, as well as highly invasive for the patient, and repeated arthroplasty is complicated as a significant amount on bone can be lost while removing the primary prosthesis, which has been firmly anchored in the bone.

In the case of infection, antibiotics can be delivered systemically or/and locally. While there are various materials used for the delivery of antibiotics locally, in situations where bone grafting is needed, the combination of a bone graft substitute is a natural solution. Osteoset-T (Wright Medical) was the first synthetic bone graft substitute based on calcium sulfate with added antibiotic tobramycin and was CE marked in the late 1990s. However, as discussed above, standalone calcium sulfate is not an ideal synthetic bone substitute. It is minimally osteoconductive, quickly resorbing and not injectable. BONESUPPORT's two products with added vancomycin and gentamicin, CERAMENT V and CERAMENT G, have the same properties of the backbone CERAMENT technology in addition to an antibiotic-eluting property. According to the company and to our knowledge, currently these two products are the only ones available with in an injectable form and a CE mark.

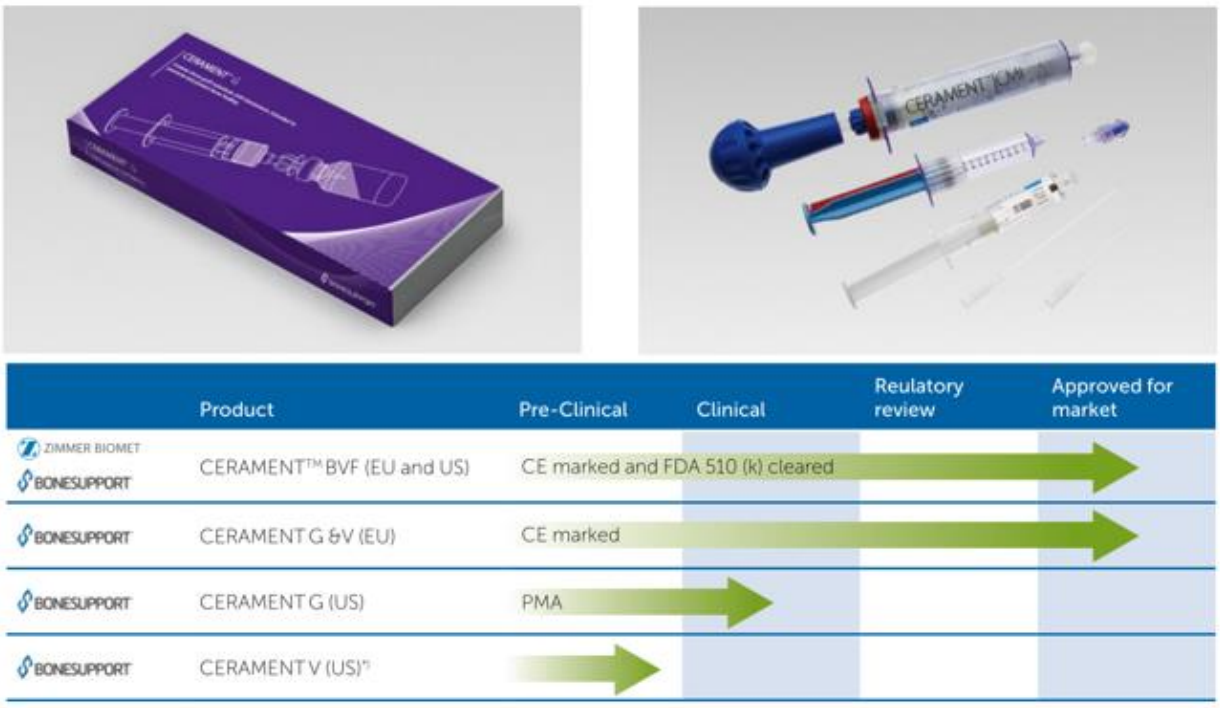
Macro trends to support synthetic bone graft market growth

We believe that prevailing macro trends are beneficial for BONESUPPORT in the long run. Longer life expectancy and increasing prevalence of chronic diseases put pressure on healthcare system. Improving technology is viewed as one way of controlling increasing health costs. Synthetic bone graft substitutes are likely to gain market share from auto/allografts due to inherent limitations of the latter and improving technology coupled with the convenience of the former. Further innovation with synthetic substitutes (eg combination with growth factors) should also support the growth of the market. The innovation aspect is specifically applicable to BONESUPPORT, as the current synthetic bone substitute market has many players with a number of products. However, the majority of those are bone void fillers, which are little differentiated. Accumulating clinical data and innovation in bone substitution is one of the core strategic directions for BONESUPPORT.

Product portfolio

CERAMENT is a patented synthetic bone graft substitute technology, which consists of a powder component and a liquid component. The powder consists of 60% calcium sulfate and 40% hydroxyapatite. The liquid component contains a contrast agent, which is useful for visualisation during medical imaging studies. During the procedure, the two are mixed together to form a paste which, once injected into a bone void, stabilises the bone structure and forms a scaffold for an osteoblast (bone-producing cells) to produce a new bone tissue. This initiates the bone remodelling process, repairing the defect. Based on the CERAMENT technology platform, BONESUPPORT is commercialising three distinct products: CERAMENT BVF, CERAMENT G (elutes gentamicin) and CERAMENT V (elutes vancomycin). In addition, the company is developing four new CERAMENT-based products.

Exhibit 1: BONESUPPORT's product portfolio



Source: BONESUPPORT. Note: *Planned PMA pathway.

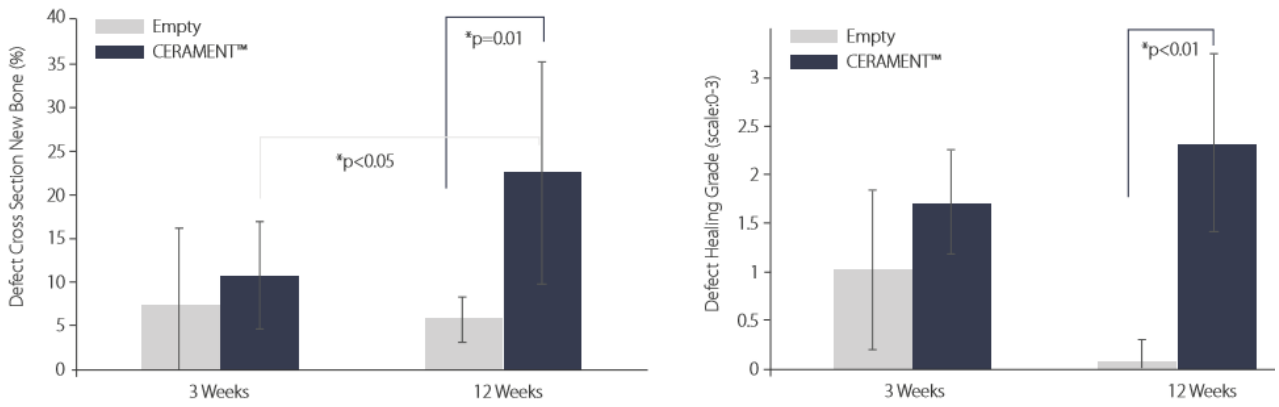
CERAMENT

CERAMENT BVF is a versatile synthetic bone substitute, which can be used for a variety of bone defects resulting from either surgical intervention or trauma. The powder and liquid components are mixed together just before injection in a closed mixing system (30 seconds), then injected into the void (up to five minutes) and can be moulded for up to two minutes thereafter. CERAMENT sets within 10 minutes. After 15 minutes the CERAMENT structure can be drilled if required with no cracking. In our view, one of the key differentiating aspects of CERAMENT BVF and other synthetic bone substitutes is that, according to the company and to our knowledge, CERAMENT BVF is the only commercially available synthetic bone substitute on the market that has been shown to remodel to host bone with six to 12 months. As summarised in CERAMENT's technical monograph, the technology has been shown in multiple preclinical studies to be:

- **Biocompatible with no inflammatory reaction.** Good tissue response in contact with bone and with surrounding muscles. The new bone tissue completely surrounds and embeds hydroxyapatite particles. No inflammatory reactions or scarring were observed after three and six weeks.
- **Osteoconductive.** Calcium sulphate resorbs faster than hydroxyapatite turning the graft into a porous scaffold. This allows bone-forming cells to enter the structure and slowly remodel the whole structure into a bone.
- **Improves new bone formation.** Because of the ability to form a porous scaffold, CERAMENT technology improved new bone formation. In one in vivo study (Exhibit 2) the researchers compared bone healing with CERAMENT versus open void in rabbit distal femurs with critical defect.[1] After three and 12 weeks both the amount of new bone formation and the healing grade were substantially improved in the CERAMENT group.

[1] M. Voor et al. Cancellous Bone Defect Healing with a Novel Calcium Sulfate – Hydroxyapatite Composite Injectable Bone Substitute. 56th annual meeting of the Orthopaedic Research Society, New Orleans, 2010.

Exhibit 2: Bone defect healing with CERAMENT versus open void in rabbits with distal femoral defects (n=12)



Source: BONESUPPORT

Over the years BONESUPPORT has also accumulated clinical evidence of CERAMENT's use, mainly from investigator-initiated studies and clinical cases (Exhibit 3). BONESUPPORT continues to support investigator-initiated studies and mentioned that the interest from surgeons in gaining access to CERAMENT products is high. While investigator-led studies tend to be smaller, the high value of supporting them comes from increasing awareness of CERAMENT products and gaining data in a variety of different settings. A recent example is Ferguson et al's presentation at the British Limb Reconstruction Society meeting, 15-16 March 2018. The researchers compared the use of CERAMENT G in 160 patients with chronic bone infection (mean follow up 1.4 years) versus Osteoset T in 137 patients with chronic bone infection (mean follow up 2.5 years). CERAMENT G demonstrated significantly better bone healing (73.2% versus 40.0%) and was associated with a lower rate of recurrent infections (4.4% versus 11.7%).

Exhibit 3: Overview of completed CERAMENT BVF studies

Study title	Trial start	Number of patients	Indication	Notes
Osteotomy of Distal Radius Fracture Malunion Using a Fast Remodeling Bone Substitute Consisting of Calcium Sulphate and Calcium Phosphate	2005	15	Distal radius fractures (malunion)	Prospective, single-arm study with 15 patients having distal radius fractures. During surgery they were treated with CERAMENT in addition to external fixation devices. Patients were followed for 12 months. All osteotomies healed and patients showed improved grip strength.
Augmentation of tibial plateau fractures with an injectable bone substitute: CERAMENT Three-year follow-up from a prospective study	2010	24	Tibial plateau fractures	Prospective, single-arm study with 24 patients having tibial plateau fractures. Patients were treated with CERAMENT BVF as the bone graft substitute during their surgical procedure, then assessed at 1, 3, 9, 12, 24 and 36 months for radiographic analysis and Rasmussen system analysis. Joint alignment was satisfactory, mean Rasmussen knee function 26.5.
Complete 12-month bone remodelling with a bi-phasic injectable bone substitute in benign bone tumours: a prospective pilot study		14	Benign bone tumours	Prospective, single-arm study with 14 patients having bone cysts or solid benign tumours were treated with CERAMENT BVF using a minimally invasive technique. The patients were followed for 12 months. Full remodelling was seen in 11 patients.

Source: BONESUPPORT Prospectus

CERTiFy

To further differentiate CERAMENT technology from other competing products BONESUPPORT is supporting a relatively large clinical study, CERTiFy (CERament Tibia Fracture study). The trial aims to demonstrate non-inferiority of CERAMENT BVF in tibial fractures compared with the 'gold standard' bone autograft. The study will compare pain, quality of life and cost of care measured by established endpoints (see Exhibit 4). The trial is currently ongoing in 14 orthopaedic centres in Germany. The last patient was enrolled on 13 December 2017, the follow up is ongoing and data are expected in 2018. If results from this trial are positive, the company expects to see improved clinical uptake of CERAMENT BVF.

Exhibit 4: Overview of the CERTiFy clinical study	
Aim	To demonstrate non-inferiority of CERAMENT BVF in tibial fractures compared with autologous bone graft.
Summary design	Prospective, open-label, multi-centre, randomised, controlled trial.
Design details	136 patients with acute traumatic depression fractures of the proximal tibia; patients received either autologous iliac crest bone graft or CERAMENT BVF; patients are treated and assessed during seven visits over a 26-week period.
Patients	Male or female; aged between 18-65; having solitary, acute, traumatic, closed depression fracture of the proximal tibia requiring reconstruction; no longer than one week since fracture occurred.
Endpoints	Primary: SF-12 v2 Physical Component Summary (PCS, health assessment questionnaire) score at week 26 after the intervention. Co-primary: pain measurement using standard visual analogue scale. Secondary: SF-12 v2 Mental Component Summary (MCS), costs of care-related resources.
Completion date	Last patient to be enrolled December 2017, publication end 2018.

Source: BONESUPPORT CERTiFy study protocol, Prospectus

CERAMENT G and V

Both products are based on CERAMENT technology and therefore have similar mechanical properties in addition to antibiotic-eluting features. The preparation and use is therefore similar to CERAMENT BVF, but CERAMENT G and V are especially suited where infection is already present or there is increased likelihood of infectious complications. Even though systemic antibiotics are a treatment option, they cannot easily reach these areas in a high enough concentration to kill all bacteria and can cause systemic toxicity. It is necessary to ensure that antibiotics are released above the minimum inhibitory concentration (MIC) level for a certain period of time. CERAMENT G and V have been shown to release the antibiotics initially in high burst concentrations followed by sustained delivery above MIC for at least 28 days.

Exhibit 5: Overview of completed CERAMENT G and V studies

Study title	Trial start	Number of patients	Indication	Notes
Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate/hydroxyapatite biocomposite	2013	100	Chronic osteomyelitis (variety of locations including tibia)	Prospective, single-arm study in 100 patients with chronic osteomyelitis. Patients were treated with CERAMENT G as a bone void filler after the usual surgical techniques including debridement. No other local antibiotic was given, although systemic vancomycin was given during surgery. Patients were followed for 12-34 months, 96% of patients had no infection.
Pharmacokinetics of gentamicin eluted from a regenerating bone graft substitute		11 / 8 / 13	Hip fractures/ bone tumour resection/ chronic osteomyelitis	This study investigated the pharmacokinetics of CERAMENT G in 11 patients with trochanteric fracture and uncemented hip revision, 8 patients with bone tumour resection, and 13 patients with chronic osteomyelitis. The study found that the release pattern of antibiotic in the patients was similar to the in vitro studies, and that infection was eradicated in the osteomyelitis group after 18 months.
Calcium-Based, Antibiotic-Loaded Bone Substitute as an Implant Coating: A Pilot Clinical Study	2013	20	Hip or knee revision prosthesis	Prospective, observational pilot study in 20 patients having revision surgery for periprosthetic joint infection. Patients were treated with CERAMENT G or V during surgery. 95% of patients had no infection at 12 months.

Source: BONESUPPORT Prospectus

FORTIFY

In order to obtain the PMA from the FDA to market CERAMENT G in the US, BONESUPPORT is conducting a clinical FORTIFY study (NCT02820363), which aims to demonstrate the safety and efficacy of CERAMENT G in open tibial mid-shaft fractures compared to current standard of care (surgical treatment using fixation with intramedullary nails). The study will compare presence of infection, secondary procedures and functional health and wellbeing measured by established endpoints (see Exhibit 6). The trial is currently recruiting in 26 study centres in the US and Europe (Germany, the UK, Poland) but plans to open 30 sites. The first patient was recruited in May 2017 and the last is expected to be recruited by end 2019. A broad label has been accepted by the FDA, but the final label will be negotiated with the FDA based on the results.

Exhibit 6: Overview of the FORTIFY clinical study	
Aim	To demonstrate safety and efficacy of CERAMENT G in open tibial mid-shaft fractures compared to current standard of care.
Summary design	Prospective, multi-centre, randomised controlled trial.
Design details	230 patients; patients receive either CERAMENT G or tibial fracture fixation with intramedullary nail; 12 months.
Patients	Male or female; aged between 22-75; patients having open tibial shaft fracture that can be fixated with an intramedullary nail; 5-26.5mm bone loss gap; no longer than 10 days since fracture occurred.
Primary, co-primary endpoints	Primary: after 12 months, absence of deep infection at fracture site, absence of secondary procedures intended to promote fracture union, improvement in SF-36 v2 PCS. Secondary: serious device-related adverse events.
Dates	Start 14 February 2017; completion December 2019.

Source: Clinical trials.gov (NCT02820363), BONESUPPORT Prospectus

Sales & marketing

Several sources calculate the global bone graft substitute market to be around $2.7-3.4bn (excluding autograft procedures). In terms of volume, the company estimates that its target market (when any bone graft is used in procedures for trauma, revision arthroplasty, osteomyelitis including diabetic foot infection) is around 3.8m procedures annually in the US and top 5 European (EU5) countries (source: Apex Global Market Study 2016 on behalf of BONESUPPORT). Autograft and allograft account for the bulk of the procedures, but associated limitations mean a growing market opportunity for innovative synthetic bone substitutes, which are currently used in around 650,000 procedures, implying a 17% penetration rate.

Overhauling the US business

BONESUPPORT has established two business segments: North America and Europe, and Rest of World. Sales in the North America segment come mainly from the US, which is a key market for the company and accounted for 60% of total sales in 2017. Since mid-2017 BONESUPPORT's distributor Zimmer Biomet, with which it has had an exclusive agreement since 2012 in the US, began experiencing internal hardware supply problems. Since CERAMENT BVF is sold together with Zimmer's products, this had a substantial impact on the US sales, which decreased from a peak of SEK23.5m in Q217 to as low as SEK12.6m in Q417, with a slight rebound to SEK15.9m in Q118. This prompted BONESUPPORT to reconsider its US distribution model. Another reason for the change was the fact that BONESUPPORT would build an independent network of distributors that could access a larger part of the US market than that reached by Zimmer Biomet currently. Lastly, BONESUPPORT views the new set up as the best platform to launch CERAMENT G in the US; if the FORTIFY trial is successful, this could rapidly become a high-value product based on the experience in Europe.

Several other circumstances also pointed towards the benefit of having an independent network in the US. Zimmer Biomet acquired ETEX Holdings in 2014, which had its own synthetic bone graft substitute products line and could be considered a competing product to CERAMENT in certain indications, and incentives in promoting BONESUPPORT product could therefore be compromised. In addition, BONESUPPORT's CEO, Emil Billbäck, who joined the company in March 2018, has several years of direct work experience in the US orthopaedics market, and is therefore able to leverage this knowledge in creating an effective distributor network supported by the company's own local personnel.

BONESUPPORT has now terminated the agreement with Zimmer and the exclusivity period ends in October 2018. In May 2018, BONESUPPORT detailed a new strategic plan covering a changed distribution model in the US. As per the new plan, around 18 independent distributors will be engaged by end 2018, increasing to around 25 over time. These will be supported by the company's own personnel, which will increase from 14 currently to 23 by year-end. By comparison, Zimmer Biomet works with a network of 53 different distributors in the US ranging from independent

to wholly owned. However, according to BONESUPPORT, 70% of total US CERAMENT BVF sales were achieved via around 13 of the most active distributors. Changing the way a product is distributed typically raises the risk that existing customers may be lost and winning new ones may take time. However, the company cited the strong loyalty of surgeons who use CERAMENT, and therefore the likelihood of regaining access to those currently using the product can be perceived as relatively high, in our view. Existing relationships with surgeons and hospital is also one of the selection criteria BONESUPPORT is using screen for the right distributors.

Another strategic element of the new US commercial platform is the envisioned expansion of the product portfolio through strategic collaborations. BONESUPPORT is seeking to gain access to third-party products that are complementary to CERAMERNT with osteoinductive/osteoconductive properties. These bundled offerings would improve BONESUPPORT's competitive position as a "one-stop-shop" for buyers. The first example is the recently signed agreement with Collagen Matrix, with which BONESUPPORT acquired rights to market Collagen Matrix bone graft substitute products under its own brand in the US. Collagen Matrix synthetic bone graft substitutes can have osteoinductive and osteogenic features when combined with patient's bone marrow.

Mixed business model in Europe/RoW

In Europe BONESUPPORT has a commercial team of 20 people and markets all three of its products directly in five countries: the UK, Germany, Switzerland, Sweden and Denmark. In Italy, Poland, Spain, Benelux, Finland, Norway and Austria the company has established agreements with national distributors. Outside the US and Europe, BONESUPPORT has distributors in Oman, Singapore, India and Malaysia. The company seeks to further expand its geographical footprint and signed a distribution agreement to market its products in France. While direct selling requires an in-house salesforce, which takes time and capital to grow, such a model allows the company to maintain higher margins at operating level than a typical distributor model (CERAMENT products are very profitable, with an 85% gross margin). BONESUPPORT indicated that it is willing to increase its direct selling presence and announced in May 2018 that it will add 13 sales representatives in 2018 alone, with primary focus on the antibiotic-eluting CERAMENT products. We believe BONESUPPORT could eventually shift from a distribution model to direct selling depending on available resources and increasing knowledge of different markets. The company has outsourced all manufacturing activities.

Regulatory and reimbursement strategy

In the US, CERAMENT BVF has been cleared via a 510(k) pathway and marketed since 2005, while the CE mark was received in 2009. Both CERAMENT V and G are CE marked as well, but in the US the products are subject to premarket approval (PMA). If the FORTIFY study is successful, BONESUPPORT plans to file for CERAMENT G approval in the US. The company also plans to initiate a similar study for CERAMENT V. In Europe, all three marketed products have a CE mark.

BONESUPPORT's clients are healthcare providers, such as hospitals or clinics that have the capacity to perform orthopaedic procedures. The reimbursement of the company's products varies on a country-by-country basis. The products can be reimbursed through hospital budgets (eg Scandinavian countries) or via diagnosis-related groups (DRG, eg Germany and the US). Under the DRG-based system all activities related to treating a patient in the hospital are grouped according to diagnosis. The hospital is then reimbursed a fixed amount for the DRG-coded activities rather than being paid what it actually spent. These amounts are usually calculated based on the average cost of the specific activity, with some adjustments for complexity. Such a system incentivises the rational use of resources and discourages overtreatment.

BONESUPPORT considers that the current reimbursement level is not reflective of the innovative nature of CERAMENT G and CERMANT V. According to the company, hospitals and payors are

increasingly requesting more health economics and outcomes research (HEOR) data to justify the use of the products. BONESUPPORT's strategy is to continue to accumulate HEOR data to demonstrate improved clinical outcomes due to reduced rates of infection (shorter hospital stays, fewer revision procedures). The associated cost savings would allow the company to negotiate premium pricing and increase market penetration.

R&D: Broadening the innovative portfolio

At the IPO the aim was to launch existing products in new markets (like CERAMENT G in the US). Portfolio expansion was planned to come from the products developed internally. This meant that there were no new product offerings envisaged in the mid-term. The recruitment of managers such as Patrick O'Donnell (US), Michael Diefenbeck (CMO) and Jerry Chang (R&D) has increased the team's expertise. The company then reviewed its short and mid-term opportunities with the aim of expanding its product portfolio over the next several years. The opportunities that BONESUPPORT is considering include CERAMENT in other formulations, CERAMENT plus other complementary products, making the solution attractive in certain indications, and developing CERAMENT as part of a combination kit for a specific treatment. Acquiring external products is also being considered. A recent example of this strategy is the signed deal with Collagen Matrix, which creates both an expanded offering but could also be supportive of the CERAMENT BVF sales in the US.

BONESUPPORT's internal pre-clinical stage R&D programme focuses on CERAMENT technology in combination with various other substances which, when eluted, could be beneficial for certain conditions. The company's know-how in powder technology is one of its competitive advantages, as the addition of other substances mostly prolongs the setting time of the paste, which needs to be carefully considered. BONESUPPORT's three existing products address conditions where void filling and infections treatment/prevention is needed. However, the company has identified a number of conditions that still represent an unmet need because of the complexity of bone defects. The three major challenging areas are bone fracture non-union, critical-size bone voids and osteoporosis.

- **Non-union** is a serious fracture complication, following which the bone fails to heal. This could result from inefficient immobilisation, poor blood supply or infection. If the fracture persists after six months, specific treatment (eg surgery) will be required. Prevalence of non-union depends on a number of risk factors and which bones are affected, but on average the reported rate is 5-10% of all fractures.[2]
- **Critical-size bone voids** are a result of prosthetic loosening, periprosthetic infections or complicated traumas and other extensive orthopaedic interventions.
- **Osteoporosis** is the most common metabolic bone disease with a characteristic progressive loss of bone mass and is most often associated with ageing. Women are especially at high risk, with an estimated 30% of all postmenopausal women meeting osteoporosis criteria. Advanced osteoporosis presents a fracture risk due to weakening bone structure, which also complicates the healing process.

All these conditions involve extensive damage to the bone structure. Osteoinduction is needed to effectively manage this. During osteoinduction mesenchymal cells are transformed into osteoblasts, which produce bone material (osteogenesis). BONESUPPORT's pre-clinical R&D efforts focus on several directions (Exhibit 7) to achieve this.

[2] R. Zura et al. Epidemiology of Fracture Nonunion in 18 Human Bones. JAMA Surg. 2016;151(11):e162775.

Exhibit 7: BONESUPPORT's R&D programmes

	Product candidate	Pre-clinical	Clinical	Regulatory review	Approved for market
BONESUPPORT	CERAMENT + bisphosphonate	→			
BONESUPPORT	CERAMENT + bisphosphonate + bone morphogenic protein	→			
BONESUPPORT	CERAMENT + bone morphogenic protein	→			
BONESUPPORT	CERAMENT + bone marrow aspirate / stem cells	→			

Source: BONESUPPORT

- **CERAMENT in combination with bisphosphonate**. Systemic oral treatment with bisphosphonates, which inhibit bone resorption by osteoclasts, is currently the standard treatment for osteoporosis. Combination with CERAMENT would mean that bisphosphonates are delivered locally, which would be a new approach. In addition, substantial side effects (mainly GI, rarely osteonecrosis of the jaw) have been associated with the use of systemic bisphosphonate therapy, therefore local administration is of interest. BONESUPPORT has conducted feasibility and in vivo efficacy studies with zoledronic acid (generic API), a potent bisphosphonate. In one in vivo study, the company demonstrated that the addition of zoledronic acid enhanced bone healing, increased bone mineral density and mineralized tissue volume.[3] Due to patent expirations the bisphosphonate market is expected to contract rapidly from $6.8bn in 2009 to a still solid $1.7bn by 2022 (source: EvaluatePharma), indicating popularity. BONESUPPORT is continuing in vivo studies.
- **CERAMENT in combination with bone morphogenic proteins**. Bone morphogenetic proteins (BMP) are a group of proteins that act as growth factors or osteoinductive agents. BMPs also play a role in other tissues such as limb, kidney, skin, hair and neural development. Recombinant BMPs have been approved by the FDA (BMP-2 and BMP-7) for use as an alternative to bone autograft in certain indications such as long bone non-unions. Although BMPs gained widespread recognition, an increasing amount of data shows that besides being bone growth inducers, BMPs also induce bone resorption, which tends to be premature during the healing process. BONESUPPORT's in vivo data showed that the addition of BMP-2 to CERAMENT led to improved bone healing and increased mineralized tissue volume.[4]
- **CERAMNENT in combination with bisphosphonate and bone morphogenic proteins.** The rationale for this project follows from the feature that BMPs act as inducers of bone growth (via osteoblast activation), but also increase resorption (via osteoclast activation). Bisphosphonates, being osteoclast suppressors, can tilt the balance towards improved bone production. BONESUPPORT's animal studies have shown that CERAMENT in combination with BMP and zoledronic acid improved bone healing better than a combination with BMP or zoledronic alone.[4]
- **CERAMENT with stem cells from bone marrow**. This preclinical project is at a very early stage and relies on stem cell property to restore tissues including bones. Several third-party studies have shown that bone marrow aspirate alone used in conjunction with bone auto/ allograft can influence new bone formation. BONESUPPORT is conducting feasibility studies.

[3] P. F. Horstmann et al. Composite Biomaterial as a Carrier for Bone-Active Substances for Metaphyseal Tibial Bone Defect Reconstruction in Rats. Tissue Eng Part A. 2017 Dec;23(23-24):1403-1412.

[4] Raina et al. A biphasic calcium sulphate/hydroxyapatite carrier containing bone morphogenic protein-2 and zoledronic acid generates bone. Sci. Rep. (2016) 6, 26033.

Competitive landscape

The market is fragmented, with most products offering the same advantages: osteoconductive, bioresorbable, injectable, set in a wet environment. In terms of composition, most bone void fillers are ceramics, variations of calcium-containing compounds: calcium sulphate, calcium phosphate, hydroxyapatite (HA), tricalcium phosphate (β-TCP). Some DBM products are also used as bone void fillers (eg DBX). The composition of the material determines its properties. For example, one of the biggest effects of the composition is the resorption rate. Products containing calcium phosphate should have slow resorption rates, which means that subsequent remodelling is also slow (eg PRO-DENSE Graft, HydroSet Injectable HA Bone Substitute, Norian Drillable, EquivaBone BGS). CERAMENT BVF and chronOS Inject Bone Void Filler claim a faster resorption time of 6-12 months and six to18 months respectively. Zimmer Biomet has its own range of bone healing products, such as ETEX range on synthetic bone substitutes. After reviewing we believe that CERAMENT technology is at least not inferior, but potentially superior in certain cases.

In order to achieve differentiation and a higher acceptance and pricing in this market, products must set themselves apart in other ways, eg to be osteoinductive as well as osteoconductive. BONESUPPORT is differentiating itself via clinical studies and remodelling time. A robust body of clinical evidence around CERAMENT BVF would give the product an advantage over competitors since very few have well designed clinical studies.

There are several products on the market with the aim of treating or preventing infections in the bone void. Some are antibiotic-eluting like BONESUPPORT's products, eg Osteoset-T and Herafill. However, some are not antibiotic-eluting. BonAlive claims that the bioactive glass in their material gives an antibacterial effect when it reacts with body fluids, while at the same time being osteostimulative, whereas Stimulan is mixed with an antibiotic prior to use. However, this is considered off-label usage according to Biocomposites' website. According to BONESUPPORT, CERAMENT V and G are the only CE-marked injectable, antibiotic-eluting bone void fillers.

Potential competitive advantages of CERAMENT technology

- Proprietary, patent-protected composition of the company's CERAMENT technology related to the composition of calcium sulfate, hydroxyapatite and liquid phase enables remodelling to host bone in combination with the property to elute drugs.
- BONESUPPORT's preclinical and clinical data show that CERAMENT BVF remodels to host bone in six to 12 months, providing support for healing bone structures. In addition, CERAMENT G and CERAMENT V have the property to locally elute antibiotics, reducing the risk of infection. In *in vitro* studies both products have been shown to elute antibiotics above the MIC level for at least 28 days.
- CERAMENT is the only commercially available bone graft substitute that has been clinically proven to remodel into host bone within six to 12 months and elute effective doses of antibiotics. BONESUPPORT believes that these clinical data will sufficiently differentiate its products and attract support from KOLs.
- CERTiFy and FORTIFY studies, if successful, will further cement CERAMENT's competitive edge.
- Potential to build on CERAMENT technology to develop new products. Four products in the pipeline.

Sensitivities

BONESUPPORT is subject to sales and marketing, regulatory, R&D, reimbursement and contract suppliers of product material, among other risks. Since the US is the largest market for BONESUPPORT and the company is undertaking changes to its distribution model in this market, the successful establishment of an effective independent distributor network is key to the investment case. BONESUPPORT has been growing its sales rapidly over the past few years and because of the forecast high sales growth, our valuation is highly sensitive to near-term estimate changes. Any unforeseen market headwinds, such as a delay in the expected rebound of US sales, could result in larger downward revisions to our valuation. The ramp-up phase to 2020-22 will require an increasing cost base but, according to our current projections, we do not foresee the need for any additional funds to reach profitability.

Financials

Investing in the near term for high future growth

BONESUPPORT's sales grew at a CAGR of 47% to SEK129.3m over 2014-17 (Exhibit 8), while the operating loss increased from SEK39.3m to SEK99.3m. This can be attributed mainly to the company's strategic decisions to invest in innovation and take a more hands-on approach to sales. BONESUPPORT intends to grow its organisation to increase direct sales in Europe. This is attractive as the CERAMENT products are highly profitable with a c 85% gross margin. In addition, a temporary increase in loss is expected in 2018 as the company builds the independent distributor network in the US. Another strategic step was the recognition that there is a need to differentiate CERAMENT products in a market that is filled with similar products. As a result, the company is supporting clinical studies to gather data on CERAMENT products. The most recent initiative is to expand its product portfolio by establishing partnerships with third parties such as Collagen Matrix.

BONESUPPORT reports as two business segments: North America and Europe and ROW. It is building a network of independent distributors in the US, which will start to operate after Zimmer Biomet's exclusivity ends in October 2018. In Europe it markets directly in several key markets and has established local distributors in several other countries.[5] In Europe the S&M team consists of 20 people, but BONESUPPORT has indicated that it intends to increase direct sales efforts substantially, which will allow it to maintain higher margins. The intention is to increase the direct salesforce by 13 representatives in 2018.

Products and markets

BONESUPPORT's revenues currently come from three CERAMENT products. All three are marketed in Europe and ROW, while only CERAMENT BVF is marketed in the US. If the FORTIFY trial is successful, CERAMENT G will be filed for FDA approval, which could happen in 2020 and so launch is feasible by 2021. While the FDA requires a clinical study to prove the efficacy of the drug-device combo, we believe the positive outcome of the study likely (we use a 70% success probability). This is because CERAMENT G (and V) is already established product among the surgeons in Europe. Looking beyond Europe and the US, BONESUPPORT currently sells via distributors in Oman, Singapore, India and Malaysia (exact sales not disclosed). The company mentioned that there is potential in the medium term to access other large markets, such as Japan and China. For the time being those represent an upside to our forecasts, as we do not include

[5] Direct sales in the UK, Germany, Switzerland, Sweden and Denmark. Distributors in Italy, Poland, Spain, Benelux, Finland, Norway, Austria and recently signed an agreement for the French market.

them in our model, but will we will revisit this if BONESUPPORT makes the steps to enter new markets.

There is a substantial difference in pricing in the US and Europe. According to the company, the average end-user selling price is $822 per unit in existing European markets and $3,100 in the US. CERAMENT G and V cost $1,800 (outside the US). Potential pricing for CERAMENT G and V in the US is not yet clear, but if we apply the ratio of the CERAMENT BVF price in the US vs Europe, the theoretical pricing level could be around $6,800 (we use $6,000 in or model).

In terms of product mix, CERAMENT BVF accounts for 70% of total 2017 sales and we continue to expect that it will remain the largest product for the foreseeable future, mainly supported by the expected rebound in the US sales. After the CERAMENT G launch in the US, if the CERTiFy trial is successful, we expect this product will grow rapidly and total share of the portfolio will exceed CERAMNET BVF by the end of our forecast period. Our long-term sales forecast and volumes are summarised in Exhibit 11.

Market size

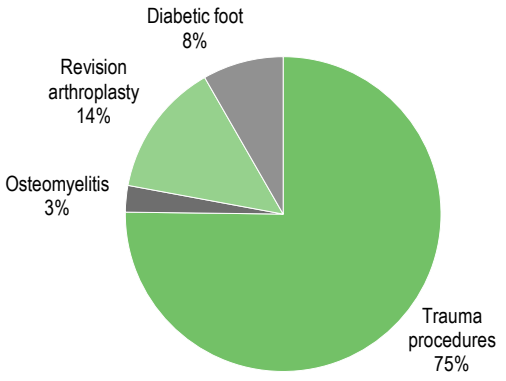
According to the Apex Global Market Study, November 2016, commissioned by BONESUPPORT, the number of procedures relevant for its products is c 3.8m in 2017 in the US and EU5. The total number of procedures where synthetic bone graft substitutes are used was estimated at c 17% or c 653,000. Extrapolating these numbers for all markets where BONESUPPORT has a presence, we use a total of 4.1m relevant procedures as the target market and 703,000 procedures that involved synthetic bone graft substitution (Exhibit 8 and Exhibit 9). We include only minimal procedure growth, as underlying conditions and trauma are stable in Western markets although, according to the company, market penetration of synthetic bone graft substitutes is growing. Our projections show that BONESUPPORT could grow its market share from c 1.7% in 2017 to 4.2% in 2022 (Exhibit 8 and Exhibit 10). We do not include expansion to other countries for the time being but, as discussed above, the company indicated expansion potential to other markets globally, which could ultimately results in target population being much larger than in the countries where BONESUPPORT has presence currently.

Exhibit 8: Assumptions and simplified P&L statement

SEKm, except pricing	2014	2015	2016	2017e	2018e	2019e	2020e	2021e	2022e
1 Total sales	**41.0**	**61.8**	**104.6**	**129.3**	**113.8**	**210.9**	**333.4**	**502.1**	**607.5**
2 Growth %		51%	69%	24%	-12%	85%	58%	51%	21%
3 CERAMENT BVF sales, SEKm	**31.6**	**47.0**	**79.1**	**90.8**	**55.6**	**128.7**	**219.2**	**319.7**	**380.1**
4 - Growth %		48.6%	68.4%	14.8%	-38.8%	131.6%	70.3%	45.9%	18.9%
5 - Units sold (volume)	2,943	4,448	7,100	8,390	6,011	7,676	11,518	15,626	18,111
6 CERAMENT G&V sales, SEKm	**9.3**	**14.8**	**25.5**	**38.5**	**58.2**	**82.2**	**114.2**	**182.4**	**227.3**
7 - Growth %		58.1%	72.6%	51.0%	51.3%	41.2%	38.9%	59.7%	24.7%
8 - Units sold (volume)	801	1,275	2,081	3,342	4,724	6,393	8,589	11,269	13,162
9 - North America sales	**26.9**	**39.4**	**68.9**	**78.1**	**39.1**	**109.4**	**196.9**	**335.8**	**418.9**
10 - Growth %		46.4%	74.8%	13.4%	-50.0%	180.0%	80.0%	70.6%	24.7%
11 - Europe and RoW sales	**14.1**	**22.4**	**35.7**	**51.2**	**74.7**	**101.5**	**136.5**	**166.3**	**188.6**
12 - Growth %		59.0%	59.8%	43.2%	46.1%	35.8%	34.5%	21.8%	13.5%
13 Target market*, '000s				4,083.8	4,407	4,416	4,424	4,433	4,442
14 Procedures involving synthetic grafts, '000s				702.8	707	718	728	739	750
15 Growth %					0.6%	1.5%	1.5%	1.5%	1.5%
16 BONESUPPORT's market share					1.7%	1.5%	2.0%	2.8%	3.6%
Simplified P&L									
17 Revenues	**41.0**	**61.8**	**104.6**	**129.3**	**113.8**	**210.9**	**333.4**	**502.1**	**607.5**
18 - Gross margin %	84%	85%	84%	87%	85%	85%	85%	85%	85%
19 Gross profit	**34.6**	**52.2**	**88.3**	**112.4**	**96.7**	**179.3**	**283.4**	**426.8**	**516.4**
20 S&M costs	-37.4	-56.2	-79.8	-92.9	-128.4	-174.8	-214.7	-270.1	-308.6
21 - Growth %		50%	42%	16%	38%	36%	23%	26%	14%
22 R&D costs	-17.0	-19.0	-38.2	-60.6	-69.7	-69.7	-69.7	-34.9	-17.4
23 - Growth %		12%	101%	59%	15%	0%	0%	-50%	-50%
24 G&A costs	-23.5	-31.7	-60.7	-57.5	-66.7	-66.7	-66.7	-66.7	-66.7
25 - Growth %		35%	91%	-5%	16%	0%	0%	0%	0%
26 EBIT	**-39.3**	**-53.9**	**-88.7**	**-99.3**	**-167.5**	**-131.5**	**-67.7**	**55.5**	**123.9**
27 - EBIT %								11%	20%

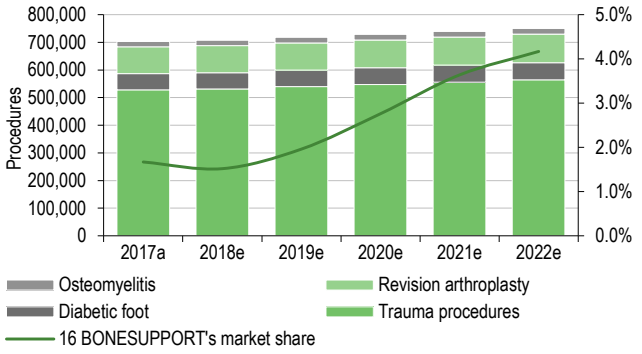
Source: Company data (including Apex Global Market Research data for BONESUPPORT), Edison Investment Research. *11.2%

Exhibit 9: Synthetic bone graft substitute market



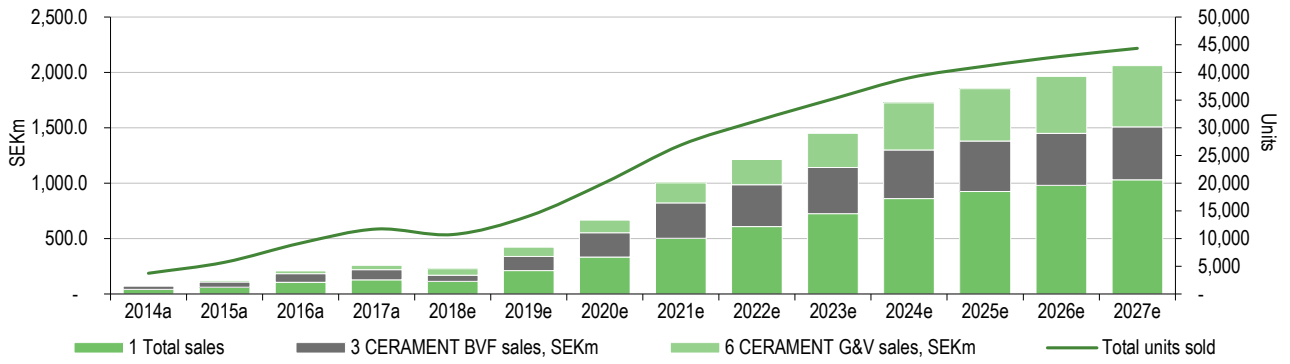
Source: Company data, Edison Investment Research

Exhibit 10: BONESUPPORT's market share



Source: Company data, Edison Investment Research

Exhibit 11: Product sales and volumes



Source: BONESUPPORT (actual data), Edison Investment Research

Short-term and long-term estimates

2017-19

BONESUPPORT achieved a CAGR of 47% to SEK129.3m over 2014-17. The company reported FY17 sales of SEK129.3m, up 23.6% y-o-y and gross margin of 87.0%. FY17 sales growth in the US was 13% to SEK78.1m, substantially below 75% in FY16 and 46% in FY15. This was due to Zimmer Biomet experiencing internal supply issues associated with its hardware products sold with CERAMENT BVF. FY17 sales in Europe/RoW increased by 43% to SEK51.2m, indicating strong organic growth in the areas unaffected by the issues with Zimmer Biomet. Total Q118 sales were SEK31.1m, largely in line with Q117 and indicating the continuing effect of Zimmer Biomet internal supply issues and destocking, as ex-US sales continued to demonstrate strong growth of 26.7% to SEK15.2m. Notably, the growth was driven by the antibiotic-eluting products, which constituted 78% of the total in Europe/RoW (up 51% y-o-y). Q118 sales in the US were SEK15.9m, down 22% y-o-y.

Zimmer Biomet has exclusivity until October 2018 and BONESUPPORT indicated that orders from the US distributor will be lower in Q218. Zimmer cancelled the majority of orders starting June 2018, which was not surprising, in our view, given the need to destock. Therefore, although in FY18 we forecast strong organic growth in Europe/RoW to continue at 46% to SEK74.7m, we estimate FY18 US sales at SEK39.1m, down 50% y-o-y. Given the company's confidence in establishing a large enough independent distributor network by the end of the year, we expect US sales to return to growth from FY19 (Exhibits 8 and 12). Of note is that top-line growth in the US will also reflect the change in how BONESUPPORT accounts for sales through the new US distributor network. Until now the company has booked part of the end-user sales in the US, c 50%, while going forward all end-user sales will be booked as income and commissions to distributors will be accounted as sales and marketing expenses. We therefore forecast a sharp increase in recognized sales, but also a substantial increase in sales and marketing expenses in 2018 and 2019. The company indicated that it expects the economics of the new arrangement to be better than those with with Zimmer Biomet.

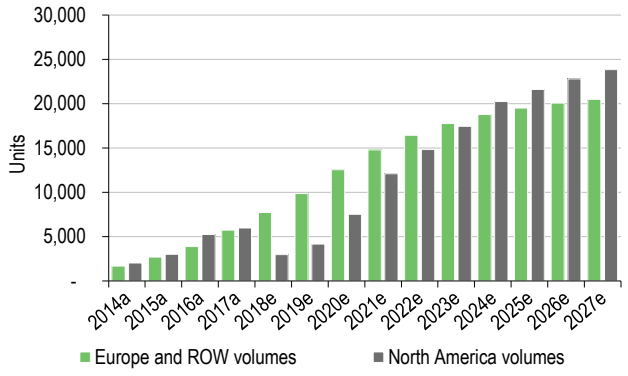
FY17 operating costs were SEK211.7m, up 20% mainly due to increased R&D activities (SEK60.6m in FY17). We expect that opex will continue to rise, with the two key components being R&D costs (the FORTIFY study), but also new hires (as explained above) with commissions to distributors being reflected in the P&L. We calculate total opex of SEK264m and SEK311m in FY18 and FY19 and an operating loss of SEK168m and SEK132m in 2018 and 2019.

2019-27

Our expectation is that the profitability on EBIT will be reached in 2021 with a profit of SEK55m (on sales of SEK502m). We maintain a stable gross margin over the whole period (the company guides to more than 85%), while the EBIT margin reaches 11% in 2021 and peaks around 30% by the end of the forecast period 2018-27. We base our long-term forecasts until 2027 on a detailed breakdown of volumes in both segments and for both sales channels. We use average growth rates over the last four years taking into account new changes to the business model. We assume CERAMENT G launch in the US in 2021. According to our scenario (Exhibit 14), sales could achieve a CAGR of 37% over 2017-22 and 20% over 2017-27. Additional potential upside could come from a number of the company's other R&D initiatives such as the addition of new complementary products to the portfolio or expansion to new markets and indications or any of the R&D projects currently in the preclinical stage. We keep our pricing assumptions flat.

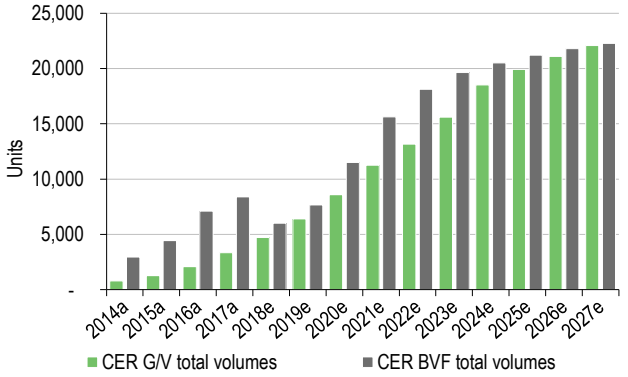
Following the IPO in June 2017 (which raised a total of SEK520m net), the cash position at end-Q118 was SEK397.2m, which according to our model is sufficient to reach profitability.

Exhibit 12: Volume projections per segment



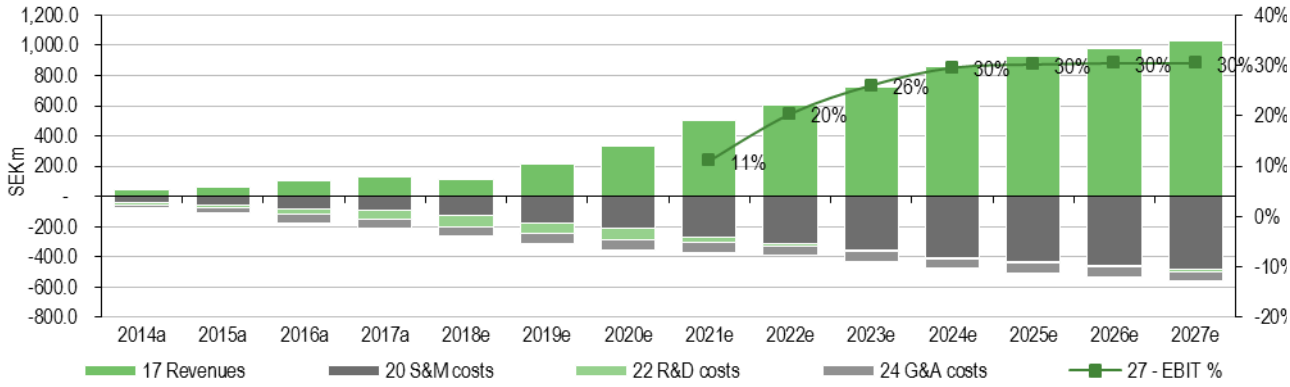
Source: Company data, Edison Investment Research

Exhibit 13: Volume projections per product



Source: Company data, Edison Investment Research

Exhibit 14: BONESUPPORT's revenue and expenses forecast



Source: BONESUPPORT (actual data), Edison Investment Research

Valuation

We value BONESUPPORT at SEK1.13bn or SEK22.2/share. This is based on our DCF model using a 10% discount rate. The forecast period is until 2027, as described above. Terminal value assumes a long-term 2.0% growth rate. At end 2016 BONESUPPORT had SEK604m in tax losses carried forward. We calculate that this should be more than sufficient to offset taxes until the end of our forecast period. The main catalysts for the share price in the near term include the results of the

CERTiFy study expected by end-2018, any new investigator-initiated studies and an update on the progress of building the independent distributor network in the US. Results of the FORTIFY trial are expected in 2020. In the case of success this will open the US market for CERAMENT G, which is already performing well in Europe. We expect this to be a substantial boost to BONESUPPORT's revenues. Given that it is currently undergoing clinical testing, yet also noting widespread use and positive feedback in Europe, we adjust income from CERAMENT G and associated commissions to distributors by 70%. With a success probability of 100%, our valuation would be SEK1.47bn or SEK28.9/share.

Exhibit 15: Assumptions, projected cash flow and DCF valuation

	2018e	2019e	2020e	2021e	2022e	2023e	2024e	2025e	2026e	2027e
EBIT* (risk adjusted)	(167.5)	(131.5)	(67.7)	78.0	149.2	193.8	215.2	211.4	204.3	195.2
Tax**	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
D&A	1.6	1.8	2.0	2.2	2.4	2.6	2.8	3.0	3.2	3.4
Change in WC	0.9	(35.7)	(45.1)	(57.6)	(36.1)	(26.3)	(18.4)	(4.4)	(2.9)	(1.9)
Capex	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)
Operating FCF	**(165.3)**	**(165.7)**	**(111.0)**	**22.3**	**115.2**	**169.8**	**199.2**	**209.6**	**204.3**	**196.4**
PV FCF	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**

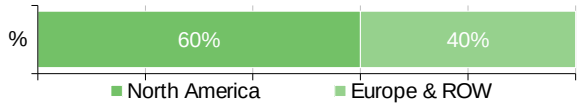
	NPV (SEKm)
Free cash flows FY18-27e	171.0
Terminal value (2.0% growth rate assumed)	560.4
Total NPV	731.4
Net cash (est end-Q118)	397.2
Valuation	**1,129**
Valuation/share (SEK)	**22.2**
Discount rate	10.0%
Tax rate (long term)	22%

Source: Edison Investment Research. *EBIT here includes risk adjusted cash flows associated with CERAMENT G launch in the US in 2021. **Tax loss carry forwards (SEK604m as end-2017) offset taxes during our forecast period.

Exhibit 16: Financial summary

SEK'000s	2014	2015	2016	2017	2018e	2019e
December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	40,961	61,755	104,599	129,301	113,813	210,917
Cost of Sales	(6,374)	(9,507)	(16,312)	(16,871)	(17,072)	(31,638)
Gross Profit	34,587	52,248	88,287	112,430	96,741	179,280
Research and development	(17,020)	(18,999)	(38,233)	(60,636)	(69,731)	(69,731)
EBITDA	(38,055)	(52,614)	(87,399)	(97,898)	(165,866)	(129,663)
Operating Profit (before amort. and except.)	(38,267)	(52,817)	(38,267)	(52,817)	(87,601)	(98,146)
Intangible Amortisation	(1,036)	(1,089)	(1,144)	(1,139)	(1,328)	(1,506)
Exceptionals	0	0	0	0	0	0
Other	(1)	0	0	0	0	0
Operating Profit	(39,304)	(53,906)	(88,745)	(99,285)	(167,495)	(131,482)
Net Interest	(11,770)	(5,509)	(20,821)	(28,600)	2,156	1,405
Profit Before Tax (norm)	(50,037)	(58,326)	(108,422)	(126,746)	(164,010)	(128,570)
Profit Before Tax (reported)	(51,074)	(59,415)	(109,566)	(127,885)	(165,339)	(130,076)
Tax	8	(140)	(625)	(1,007)	(1,007)	(1,007)
Profit After Tax (norm)	(50,030)	(58,466)	(109,047)	(127,753)	(165,017)	(129,577)
Profit After Tax (reported)	(51,066)	(59,555)	(110,191)	(128,892)	(166,346)	(131,083)
Average Number of Shares Outstanding (m)	2.5	2.5	23.5	25.8	39.8	50.5
EPS - normalised (SEK)	(20.32)	(2.49)	(4.22)	(3.21)	(3.26)	(2.54)
EPS - normalised and fully diluted (SEK)	(20.32)	(20.32)	(2.49)	(4.22)	(3.21)	(3.26)
EPS - (reported) (SEK)	(20.74)	(2.53)	(4.26)	(3.24)	(3.29)	(2.57)
Dividend per share (SEK)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	84.4	84.6	84.4	87.0	85.0	85.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET						
Fixed Assets	5,756	5,892	5,091	8,591	8,986	9,581
Intangible Assets	5,091	4,934	4,469	5,244	6,171	6,750
Tangible Assets	382	588	442	3,099	2,567	2,583
Investments	283	370	180	248	248	248
Current Assets	39,864	105,741	183,718	588,093	335,326	216,242
Stocks	9,295	15,032	14,489	22,079	15,164	28,102
Debtors	9,005	17,600	20,242	20,678	26,702	49,485
Cash	18,386	68,881	141,501	533,367	281,491	126,686
Other	3,178	4,228	7,486	11,969	11,969	11,969
Current Liabilities	(26,544)	(91,305)	(69,742)	(145,725)	(47,105)	(47,105)
Creditors	(22,341)	(28,418)	(44,639)	(47,105)	(47,105)	(47,105)
Short term borrowings	(4,203)	(62,887)	(25,103)	(98,620)	0	0
Long Term Liabilities	(62,593)	0	(84,763)	(173)	(173)	(173)
Long term borrowings	(62,593)	0	(84,599)	0	0	0
Other long term liabilities	0	0	(164)	(173)	(173)	(173)
Net Assets	(43,517)	20,328	34,304	450,786	297,034	178,545
CASH FLOW						
Operating Cash Flow	(41,187)	(58,941)	(70,184)	(95,060)	(152,382)	(152,789)
Net Interest	(4,674)	(6,302)	(11,640)	(11,737)	2,156	1,405
Tax	(62)	(49)	(109)	(737)	(1,007)	(1,007)
Capex	(424)	(497)	(67)	(2,344)	(329)	(329)
Acquisitions/disposals	0	0	0	0	0	0
Financing	0	119,606	103,714	504,833	0	0
Other	(10,433)	587	4,091	7,993	(1,695)	(2,085)
Dividends	0	0	0	0	0	0
Net Cash Flow	(56,780)	54,404	25,805	402,948	(153,256)	(154,804)
Opening net debt/(cash)	(8,370)	48,410	(5,994)	(31,799)	(434,747)	(281,491)
HP finance leases initiated	0	0	0	0	0	0
Other	0	0	0	0	0	0
Closing net debt/(cash)	48,410	(5,994)	(31,799)	(434,747)	(281,491)	(126,686)

Source: BONESUPPORT accounts, Edison Investment Research

Contact details	Revenue by geography (2017)
BONESUPPORT AB Scheelevägen 19 SE-223 70 Lund Sweden +46 46 286 53 70 info@BONESUPPORT.com	

Management team

CEO: Emil Billbäck

Emil Billbäck has more than 20 years' experience in commercial operations within the life science industry. Most recently, he was senior adviser to the merged SCA/BSN Medical. Before the merger he held multiple senior level positions at BSN Medical including executive VP EMEA and Head of Global Commercial Operations at BSN Medical. Mr Billbäck has also worked at Beiersdorf and AstraZeneca. Mr Billbäck holds a BSc in business administration from Karlstad University.

CFO: Björn Westberg

Björn Westberg joined the company as chief financial officer in January 2017 from Recipharm, one of the largest pharmaceutical contract manufacturers in the world, where he was CFO from 2007. Prior to this Mr Westberg was CFO of the Nasdaq Stockholm-listed software company Jeeves (2001-07). Before that he held senior roles at AstraZeneca, including FD, Northern Europe and controller in Astra Japan.

General manager & EVP int. commercial operations: Vikram Johri

Vikram Johri is responsible for developing and managing international sales and was previously chief commercial officer (2009-12) at BONESUPPORT. Prior to joining the company, he was VP of EMEA Wright Medical (2007-09) and international group marketing manager at Boston Scientific from 2002 to 2009. He holds an MBA in marketing from Syracuse University (1993) and a Bachelor of Commerce from Delhi University (1988).

General manager & EVP commercial operations US: Patrick O'Donnell

Patrick O'Donnell has experience in the medical device, biologics and biomaterials industries gained over the past 24 years. Mr O'Donnell most recently served as the founder and CFO of ProteoThera, an early-stage biotech company with matrix-binding protein fusion technology for local delivery of small molecules and proteins to address articular joint inflammatory diseases. Prior to this he held the position of CEO at several organisations including EndoSphere Inc, Histogenics Corporation and Prochon BioTech, and director of global marketing at Confluent Surgical.

Principal shareholders	(%)
HealthCap V LP	13.3
Stiftelsen Industrifonden	9.6
Lundbeckfond Invest A/S	9.6
Robur AB	9.1
Tredje AP-fonden	8.2
Tellacq AB	6.0
Carl Westin	5.4

Companies named in this report

Zimmer Biomet, BonAlive, Biocomposites, Stryker, Wright Medical Group, DePuy Synthes