BRYAN, GARNIER & CO

CORPORATE RESEARCH

13th January 2015

Bone Therapeutics

Cell therapy: The new backbone for orthopaedics

Healthcare

Fair Value Between EUR96m and EUR109m **CORPORATE**

Bloomberg	BOTHE FP
Reuters	BOTHE.PA
Enterprise Value (BG estimates M€)	96-109
3y EPS CAGR	ns
Gearing (12/14)	NM
Dividend yield (12/15e)	NM

YE December	12/14e	12/15e	12/16e	12/17e
Revenue (EURk)	2,908	2,327	1,861	1,489
EBIT(EURk)	-5,277	-7,367	-10,130	-13,646

Bone Therapeutics develops innovative cell therapy products capable of restoring bone tissues and administered through a minimally invasive approach. The company targets two major orthopaedics markets: Fracture Repair and Prevention. Bone Therapeutics has already achieved strong clinical results and has a broad, late-stage pipeline including two pivotal phase III and 3 phase II. Those products are strongly positioned and game changers in those large orthopaedics markets (12 million patients). As a result, Bone Therapeutics has the potential to establish a global leadership. We value Bone Therapeutics at Between EUR96m and EUR109m.

- **Why Bone Therapeutics cell therapy products are game changers?** Bone Therapeutics has succeeded in producing differentiated bone cells and has proved clinically their ability to initiate bone formation and amplify the natural bone regeneration process. The company has by far the most advanced programs. Existing standard of care have considerable limitations (e.g. risk of serious complications) and have virtually no effect on bone formation.
- **What is the revenue potential?** The Fracture Repair franchise represents revenues of almost EUR500m in 2025e based on the two leading indications non-union and delayed union fractures. The lead indication in Fracture Prevention, Osteonecrosis, is projected to generate sales of EUR100m in 2025e. We see osteoporosis and spine fusion indications as a huge upside potential (EUR600m cumulative sales in 2025e).
- **Why Bone Therapeutics has an attractive risk/reward profile?** Our sum-of-the-part valuation leads to a pre-money equity value of Between EUR96m and EUR109m for a late-stage biotech company that has unmatched clinical results, a de-risked pipeline with favourable phase III trial design and innovative treatments offering a compelling value proposition.

Analyst:
Hugo Solvet
33(0) 1 56 68 75 57
hsolvet@bryangarnier.com

Sector Analyst Team:
Pierre Corby
Eric Le Berrigaud

BRYAN, GARNIER & CO HAS BEEN APPOINTED TO ACT AS LEAD MANAGER IN RELATION TO THE PROPOSED OFFER OF SHARES IN BONE THERAPEUTICS SA (THE COMPANY).

THIS DOCUMENT IS CONFIDENTIAL AND IS BEING FURNISHED TO YOU SOLELY FOR YOUR INFORMATION AND MAY NOT BE REPRODUCED OR REDISTRIBUTED, IN WHOLE OR IN PART, DIRECTLY OR INDIRECTLY, TO ANY OTHER PERSON. IN PARTICULAR, NEITHER THIS DOCUMENT, IN WHOLE OR IN PART, NOR ANY COPY THEREOF MAY BE TAKEN OR TRANSMITTED INTO THE UNITED STATES, CANADA, JAPAN OR AUSTRALIA OR BE DISTRIBUTED, DIRECTLY OR INDIRECTLY, IN THE UNITED STATES OR TO ANY US PERSON (AS DEFINED IN REGULATION S UNDER THE US SECURITIES ACT OF 1933, AS AMENDED) OR DISTRIBUTED OR REDISTRIBUTED IN CANADA, JAPAN OR AUSTRALIA OR TO ANY RESIDENT THEREOF. ANY FAILURE TO COMPLY WITH THESE RESTRICTIONS MAY CONSTITUTE A VIOLATION OF THE SECURITIES LAWS OF THE UNITED STATES, CANADA, JAPAN OR AUSTRALIA.

THIS DOCUMENT IS FOR DISTRIBUTION IN THE UNITED KINGDOM ONLY TO (I) PERSONS WHO HAVE PROFESSIONAL EXPERIENCE IN MATTERS RELATING TO INVESTMENTS FALLING WITHIN ARTICLE 19(5) OF THE FINANCIAL SERVICES AND MARKETS ACT 2000 (FINANCIAL PROMOTION) ORDER 2005 (THE ORDER), OR (II) PERSONS FALLING WITHIN ARTICLE 49(2)(A) TO (D) (HIGH NET WORTH ENTITIES) OF THE ORDER OR (III) PERSONS WHO ARE PROFESSIONAL CLIENTS UNDER COBS 3 OF THE CONDUCT OF BUSINESS SOURCEBOOK OF THE UK FINANCIAL CONDUCT AUTHORITY (ALL SUCH PERSONS TOGETHER BEING REFERRED TO AS RELEVANT PERSONS). THIS DOCUMENT IS DIRECTED ONLY AT RELEVANT PERSONS AND OTHER PERSONS SHOULD NOT ACT OR RELY ON THIS DOCUMENT OR ANY OF ITS CONTENTS.

THE DISTRIBUTION OF THIS DOCUMENT IN OTHER JURISDICTIONS MAY BE RESTRICTED BY LAW, AND PERSONS INTO WHOSE POSSESSION THIS DOCUMENT COMES SHOULD INFORM THEMSELVES ABOUT, AND OBSERVE, ANY SUCH RESTRICTIONS. ANY FAILURE TO COMPLY WITH THESE RESTRICTIONS MAY CONSTITUTE A VIOLATION OF THE LAWS OF SUCH OTHER JURISDICTION. BY ACCEPTING THIS DOCUMENT, YOU AGREE TO BE BOUND BY THE FOREGOING RESTRICTIONS.

THIS DOCUMENT DOES NOT CONSTITUTE OR FORM PART OF AN OFFER TO SUBSCRIBE FOR OR PURCHASE, OR AN INVITATION OR SOLICITATION OF AN OFFER TO SUBSCRIBE FOR OR PURCHASE, ANY SECURITIES NOR SHALL IT, OR ANY PART OF IT, FORM THE BASIS OF, OR BE RELIED ON IN CONNECTION WITH, ANY CONTRACT OR COMMITMENT WHATSOEVER. ANY DECISION TO PURCHASE OR SUBSCRIBE FOR SECURITIES IN THE COMPANY SHOULD BE MADE SOLELY ON THE BASIS OF THE INFORMATION CONTAINED IN THE PROSPECTUS AND ANY SUPPLEMENTARY PROSPECTUS TO BE PUBLISHED IN RESPECT OF THE OFFER AND NOT ON THE BASIS OF THE CONTENTS OF THIS DOCUMENT.

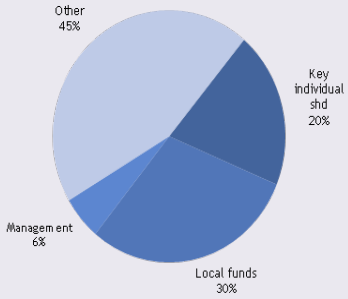
THIS DOCUMENT HAS BEEN PREPARED BY BRYAN, GARNIER & Co. INDEPENDENTLY OF THE COMPANY IN ORDER TO PROVIDE BACKGROUND

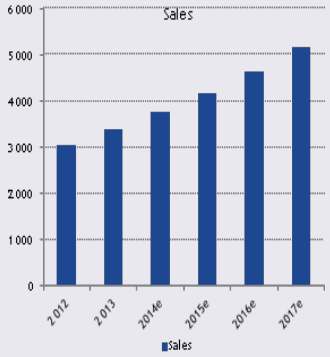
INFORMATION ABOUT THE COMPANY. THE INFORMATION, FORWARD-LOOKING STATEMENTS, OPINIONS AND EXPECTATIONS CONTAINED HEREIN ARE ENTIRELY THOSE OF BRYAN, GARNIER & Co AS PART OF ITS INTERNAL RESEARCH COVERAGE AND NOT AS AN UNDERWRITER OR MANAGER OF ANY OFFERING OF SECURITIES. ACCORDINGLY, NONE OF THE COMPANY, ANY SPONSOR, ANY UNDERWRITER OF SECURITIES OF THE COMPANY, OR ANY OF THEIR RESPECTIVE DIRECTORS, OFFICERS OR EMPLOYEES, SHALL BE IN ANY WAY RESPONSIBLE FOR THE CONTENTS HEREOF, OR SHALL BE LIABLE FOR ANY LOSS ARISING FROM USE OF THIS REPORT OR OTHERWISE ARISING IN CONNECTION THEREWITH.

THIS DOCUMENT DOES NOT PURPORT TO BE A COMPLETE DESCRIPTION OF THE MATTERS REFERRED TO IN THE DOCUMENT. THE INFORMATION ON WHICH THIS DOCUMENT IS BASED HAS BEEN OBTAINED FROM SOURCES WHICH BRYAN, GARNIER & Co BELIEVES TO BE RELIABLE, BUT NONE OF BRYAN, GARNIER & Co, KEPLER CHEUVREUX AND BANK DEGROOF THE COMPANY OR ANY OTHER PERSON HAS INDEPENDENTLY VERIFIED SUCH INFORMATION. NO REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, IS MADE AS TO THE FAIRNESS, ACCURACY, COMPLETENESS OR CORRECTNESS OF THE INFORMATION AND OPINIONS CONTAINED IN THIS DOCUMENT AND NO RELIANCE SHOULD BE PLACED ON SUCH INFORMATION OR OPINIONS. THE INFORMATION AND VIEWS GIVEN IN THIS DOCUMENT ARE SUBJECT TO CHANGE WITHOUT NOTICE AND MAY NOT CONTAIN ALL MATERIAL INFORMATION CONCERNING THE COMPANY. NONE OF THE COMPANY, KEPLER CHEUVREUX AND BANK DEGROOF OR ANY OF THEIR RESPECTIVE MEMBERS, DIRECTORS, OFFICERS OR EMPLOYEES OR ANY OTHER PERSON ACCEPTS ANY LIABILITY WHATSOEVER FOR ANY LOSS HOWSOEVER ARISING FROM ANY USE OF THIS DOCUMENT OR ITS CONTENTS OR OTHERWISE ARISING IN CONNECTION THEREWITH. BRYAN GARNIER & CO. AND THEIR RESPECTIVE AFFILIATES AND/OR THEIR DIRECTORS, OFFICERS AND EMPLOYEES MAY FROM TIME TO TIME PURCHASE, SUBSCRIBE FOR, ADD TO OR DISPOSE OF, ANY SECURITIES OF THE COMPANY (OR MAY HAVE DONE SO BEFORE PUBLICATION OF THIS DOCUMENT) OR MAKE A MARKET OR ACT AS PRINCIPAL IN ANY TRANSACTIONS IN SUCH SECURITIES.

[THERE CAN BE NO ASSURANCE THAT ACTUAL RESULTS WILL NOT DIFFER MATERIALLY FROM THOSE SET OUT IN ANY FORWARD-LOOKING STATEMENTS CONTAINED IN THIS DOCUMENT OR THAT FUTURE RESULTS OR EVENTS WILL BE CONSISTENT WITH ANY OPINIONS, ESTIMATES, PROJECTIONS OR FORECASTS CONTAINED IN THIS DOCUMENT. NEITHER BRYAN, GARNIER & CO., NOR THE COMPANY, NOR ANY OF THEIR MEMBERS, DIRECTORS, OFFICERS OR EMPLOYEES NOR ANY OTHER PERSON ACCEPTS ANY LIABILITY WHATSOEVER FOR ANY LOSS HOWSOEVER ARISING FROM ANY USE OF THIS DOCUMENT OR ITS CONTENTS OR OTHERWISE ARISING IN CONNECTION THEREWITH. BRYAN, GARNIER & CO. MAY IN THE FUTURE PARTICIPATE IN AN OFFERING OF THE COMPANY'S SECURITIES FROM TIME TO TIME.]

BY ACCEPTING THIS REPORT YOU AGREE TO BE BOUND BY THE FOREGOING LIMITATIONS, INSTRUCTIONS AND RESTRICTIONS.





Company description

Bone Therapeutics is a biotechnology company developping cell therapy products for bone fracture repair and fracture prevention. The innovative platform relies on minimally-invasive treatments in areas with a high unmet medical where competition is limited despite large markets. Its two lead compounds are autologous cell products (PREOB) indicated in Non-Union Fractures and Osteonecrosis and currently evaluated in phase IIb/III. Other compounds studied at a less advanced development phase are allogeneic cell products which should enable the company to significantly broaden its addressable patient base in other indications (Delayed-Union Fractures, Lumbar Spine Fusion and Osteoporosis).

Simplified Profit & Loss Account (EURk)	2013	2014e	2015e	2016e	2017e	2018e	2019e
Revenues	3,394	2,908	2,327	1,861	1,489	1,191	11,520
Change (%)	*11.0%*	*-14.3%*	*-20.0%*	*-20.0%*	*-20.0%*	*-20.0%*	*867%*
R&D expenses	6,816	6,904	8,285	9,941	11,930	14,316	17,179
SG&A expenses	*621*	*1,081*	*1,189*	*1,308*	*1,439*	*1,583*	*1,741*
Adjusted EBITDA	(3,636)	(4,678)	(6,646)	(9,327)	(12,762)	(17,053)	(15,004)
EBIT	(4,043)	(5,277)	(7,367)	(10,130)	(13,646)	(18,000)	(16,008)
Change (%)	*-10.4%*	*-30.5%*	*-39.6%*	*-37.5%*	*-34.7%*	*-31.9%*	*-11.1%*
Financial results	(41.0)	(615)	(979)	(40.0)	(40.0)	(40.0)	(40.0)
Pre-Tax profits	(4,065)	(5,891)	(8,346)	(10,170)	(13,686)	(18,040)	(16,048)
Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net profit	(4,065)	(5,891)	(8,346)	(10,170)	(13,686)	(18,040)	(16,048)
Restated net profit	(4,065)	(5,891)	(8,346)	(10,170)	(13,686)	(18,040)	(16,048)
Change (%)	*-9.9%*	*-44.9%*	*-41.7%*	*-21.9%*	*-34.6%*	*-31.8%*	*-11.0%*
Cash Flow Statement (EURk)							
Operating cash flows	(3,272)	(5,339)	(6,316)	(9,492)	(12,679)	(17,094)	(14,984)
Change in working capital	251	(661)	330	(165)	82.6	(41.3)	20.6
Capex, net	(1,710)	(1,122)	(1,416)	(1,269)	(1,342)	(1,305)	(1,324)
Financial investments, net	2,640	13,795	(1,691)	510	(430)	(362)	(430)
Dividends	0.0	0.0	0.0	0.0	0.0	0.0	1.0
Net debt	8,001	8,171	6,531	17,332	31,393	49,833	66,180
Free Cash flow	(7,983)	(9,480)	(10,674)	(13,676)	(16,936)	(21,315)	(19,222)
Balance Sheet (EURk)							
Tangible fixed assets	11,418	11,278	20,088	11,179	1,709	(12,217)	(30,429)
Intangibles assets	60.0	60.0	60.0	60.0	60.0	60.0	60.0
Cash & equivalents	2,440	9,926	654	(9,447)	(23,748)	(42,360)	(58,947)
current assets	8,087	16,234	6,631	(3,304)	(17,688)	(36,259)	(52,867)
Total assets	12,811	21,481	12,572	3,102	(10,824)	(29,036)	(45,324)
L & ST Debt	5,561	18,097	7,185	7,885	7,645	7,473	7,233
Others liabilities	4,279	4,279	4,279	4,279	4,279	4,279	4,279
Shareholders' funds	64.0	(3,803)	(1,799)	(11,970)	(25,656)	(43,696)	(59,744)
Total Liabilities	12,748	25,284	14,372	15,072	14,832	14,660	14,420
Capital employed	NM	NM	NM	NM	NM	NM	NM

Source: Company Data; Bryan, Garnier & Co ests.

Table of contents

1. Investment Case

Why the interest now?

The reason for writing now

Bone Therapeutics' story is at a turning point with the interim results of both a pivotal phase IIb/III and phase III study of its flagship product, due to report in 2016 in the fracture repair and fracture prevention markets respectively. In the meantime, we expect a dense newsflow in 2015 with Blockbuster potential for PREOB® and ALLOB® in a broad range of indications should lead to value creation whether on a standalone basis or via a sale to a big Pharma.

Cheap or Expensive?

Valuation

We value Bone Therapeutics at Between EUR96m and EUR109m (pre-money) via a SotP valuation. We assume a 16.2% WACC and have applied probability of success rates associated with the various indications.

When will I start making money?

Catalysts

While the two major catalysts are clearly the interim results of the two phase III trials due to report in 2016, other events could have a positive impact on Bone Therapeutics' in the meantime (Delayed Union and Osteoporosis in 2015). Favourable study designs should bring dense clinical newsflow in 2015 alongside two US trials expected to start in 2016 which could trigger partnership opportunities.

Could I lose money?

Risks to our investment case

The company's valuation is focused on phases IIb/III and III results. A negative outcome from the interim phase IIb/III and phase III results expected in 2016 could hit hard on the value of Bone Therapeutics'. The sales potential and adoption rates of the company's products are dependant from commercial execution and it is to note that the company is about to bring its first product to the market upon approval. Clinical development in the US is also a risk factor. Moreover, scaling up of manufacturing and regulatory process of stem cell therapy leading to approval could take a longer time than expected.

2. Valuation: Between EUR96m and EUR109m

We consider that Bone Therapeutics' development model based on both a standalone strategy and an out-licensing of its products depending on geographical area or market size is particularly relevant for a discounted cash flow valuation. We have therefore used a sum of the parts calculation adjusted for risk on a project by project basis. This valuation of Bone Therapeutics works out at Between EUR96m and EUR109m.

Fig. 1: Valuation of Bone Therapeutics

Growth rate \ WACC	15,2%	15,7%	16,2%	16,7%	17,2%
-2,0%	111	104	98	92	87
-1,0%	113	106	100	94	88
0,0%	116	109	102	96	90
1,0%	119	112	104	98	92
2,0%	123	115	107	100	94

Source: Bryan, Garnier & Co ests.

2.1. Sum of the parts valuation

The use of this type of valuation method by project requires a closer look how the discount rate is calculated. The discount rate enables us to take account of risk in the valuation, since it integrates a time value (risk-free rate = 2.3%) and the reduction in value associated with the inherent risk of a biotech company (β of 2.1). As such, we have applied to each of our projects a normalised discount rate, taking account of current market parameters and the risk associated with the company's asset category (biotechnology). This discount rate (WACC) works out at 16.2%.

Fig. 2: Discount rate assumptions

Risk free rate (10-yr yield bond) %	2,3%
Equity risk premium %	6,6%
Beta	2,1
terminal growth rate	0,0%
WACC	**16,2%**

Source: Bryan, Garnier & Co ests.

Various probabilities of success depending on indications and regions

A project's specific risk rate is associated with the probability of success for each project considered. As such, a phase I project (around 10% probability of success) does not present the same likelihood of reaching the market as a phase II project (in the 15-20% range) or a phase III (in the 50-60% range). Averages have been established, although values can differ considerably depending on the therapeutic field in question as well as the study design.

Fig. 3: Average success rate for new molecules depending on their stage of clinical development

Development Phase	Average success rate
Pre clinical	5%
Phase I to phase II	10%
Phase II to phase III	15%-20%
Phase III success rate	50%-60%
Phase III to approval	80%

Source: BioMed Tracker 2012.

2.1.1. The fracture prevention market

Osteonecrosis and non-union fractures are the highest value projects

Osteonecrosis

We assume a 50% probability of success (PoS) in Europe. The US trial is expected to be initiated in 2016 and considering strong phase II clinical results in EU as well as a design compliant with FDA requirements, we assume a 10% PoS in the US.

Osteoporosis

We assume a 10% PoS. Although studied in phase II, the studiy aims to evaluate the biodistribution of Bone Therapeutics' products. Only secondary endpoints will evaluate the efficacy.

2.1.2. The fracture repair market

Non-union

We assume a 50% probability of success (PoS) in Europe. The US trial is expected to be initiated in 2016 and considering strong phase II clinical results in EU, we assume a 5% PoS.

Delayed-union

We assume a 15% PoS.

Lumbar spine fusion (LSF) and rescue lumbar spine fusion (RLSF)

We assume a 10% of success as we do not have any clinical data in this indication yet.

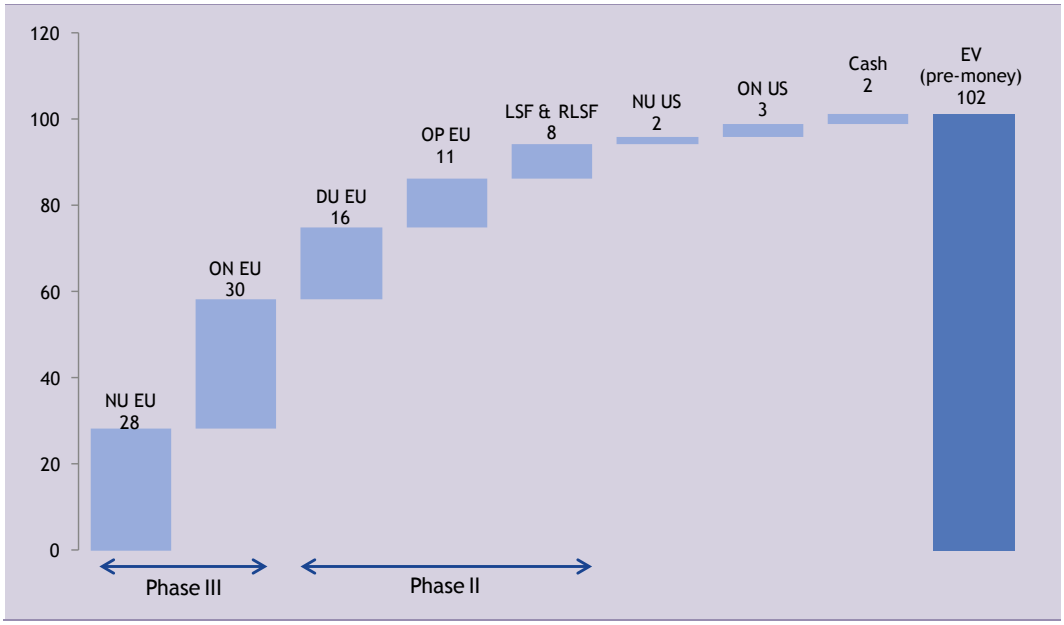
2.1.3. Valuation by projects

Fig. 4: Valuation by the r-NPV method (in EURm)

Project	Development phase	PoS	EV	% of EV
NU EU	Phase IIb/III	50%	28,1	26%
ON EU	Phase IIII	50%	30,3	28%
DU EU	Phase I/IIa	15%	16,4	15%
OP EU	Phase I/IIa	10%	11,2	10%
LSF & RLSF	Phase I/IIa	10%	8,1	7%
NU US	set to enter the clinic in 2016	5%	1,8	2%
ON US	set to enter the clinic in 2016	10%	3,0	3%
(Net Debt) / cash excluding OC as of 12/31/2014			2,2	10%
EV (pre-money)			**102**	

Source: Company Data; Bryan, Garnier & Co ests.

Fig. 5: Breakdown of Bone Therapeutics' valuation by project (EURm)



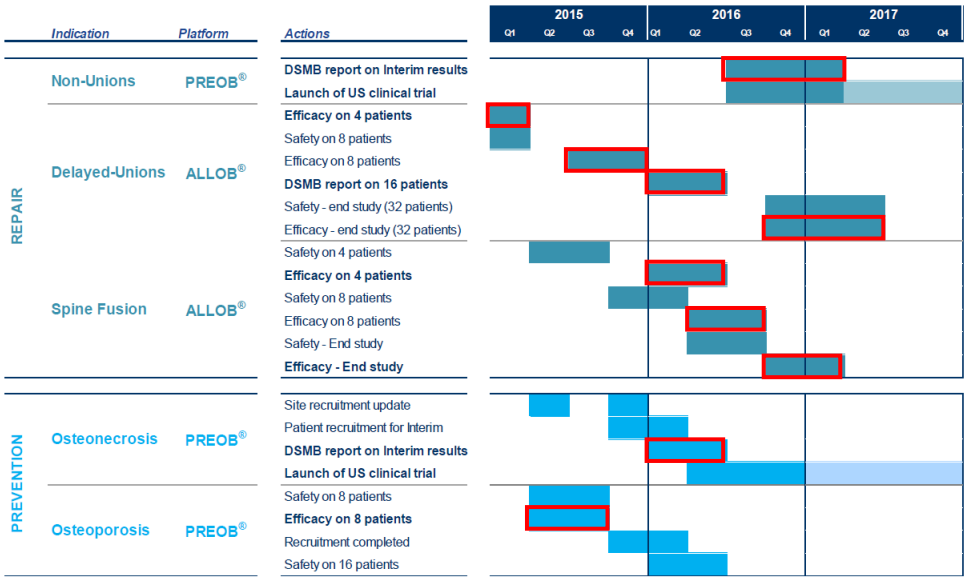
Source: Company Data; Bryan, Garnier & Co ests.

.

2.1.4. Bone Therapeutics' dense upcoming newsflow

Numerous newsflow elements should create value

Fig. 6: Bone Therapeutics' newsflow



Source: Company Data.

- **Q1 2015:**
  - Delayed-union (Ph I/IIa), first efficacy interim data (4/32 patients).

- **Q2/Q3 2015**
  - Osteoporosis (Ph IIa), interim efficacy data (8/20 patients).
- **H2 2015**
  - Delayed-union (Ph I/IIa), second interim efficacy data (8/32 patients).
- **H1 2016**
  - **Osteonecrosis (Ph III): DSMB report on interim results (35% of patients with 6 months follow-up).**
  - **Delayed-union (Ph I/IIa): DSMB report (16/32 patients). Study could be prematurely stopped upon positive results.**
  - Lumbar spine fusion (Ph IIa): first interim efficacy results (4/16).
- **H2 2016/early 2017**
  - **Non-union (Ph IIb/III): DSMB interim report on efficacy (50% with 6 months follow-up).**
  - **Delayed-union (Ph I/IIa): topline study results, except if prematurely stopped.**
  - **Spine fusion (Ph IIa): topline study result.**

In addition to the newsflow listed above, the company plans to initiate two phase III trials in the US in osteonecrosis (design approved by the FDA) and in non-union fractures respectively in 2016.

3. Breakthrough technology

Regenerative therapy which promotes bone formation

Bone Therapeutics is a biotech company focused on regenerative therapies for unmet medical needs in the field of orthopaedics. The company develops cell products for bone fracture repair and fracture prevention and brings to this field an efficient, safe and minimally invasive treatment as opposed to current standard of care treatments (heavy surgery and long recovery periods). Its technology is based on differentiated bone-forming cells, osteoblasts.

3.1. Poor standard of care (SoC) in fracture prevention and fracture repair

In normal and healthy people, bone, which is a living tissue, has the capacity to repair itself thanks to a balance between bone formation (osteoblasts, i.e. bone-forming cells) and bone resorption (osteoclasts, i.e. bone-resorbing cells) aimed at continuously replacing old by newly-formed bone. In adults, it takes usually seven to ten years to completely renew one's skeleton. However, this balance, between bone formation and bone resorption, may be disrupted in two principal situations:

- Traumatic situations like severe bone fractures
- Non-traumatic situations like bone diseases (osteoporosis, osteonecrosis, rheumatoid arthritis, etc)

In such situations, the bone formation capacity is overrun by the bone resorption capacity leading to bone disorders.

3.1.1. SoC in fracture repair: bone graft surgery

Highly invasive SoC in fracture repair

As there is no efficient treatment on the market, bone graft surgery could be needed after a trauma (severe/complex fracture or fracture not healing well after a previous treatment), in certain cases of joint problems or in order to reconstitute bone around implanted devices. The origin of the bone used in the grafting could be:

- **Autograft**: from one's own body, usually from the hips or ribs,
- **Allograft**: from a deceased donor, tissue bank or synthetic (manmade bone substitute).

Under general anaesthesia, the surgeon performs an incision and positions the already-shaped bone graft next to the patient's bone. The graft is then held in place with screws, plates or pins. After stitching the wound, a splint or a cast will be used to keep the graft in place.

The process is invasive, hence the risks of serious complications cannot be ruled out (persistent pain, nerve injury, rejection of the graft, inflammation...). Moreover both the hospital stay and the recovery process are long and there is usually poor efficacy in terms of tissue regeneration.

3.1.2. SoC in fracture prevention: little innovation to date

The fracture prevention field is wide. It spans from the huge market of osteoporosis to rare diseases such as osteonecrosis, Paget's disease, osteomalacia or osteopetrosis to name but a few.

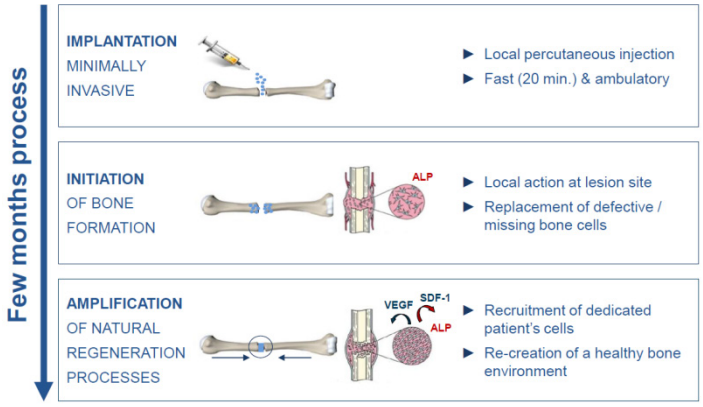
Little innovation and not efficient SoC in fracture prevention

Bone Therapeutics is targeting first the osteonecrosis market and then the osteoporosis market. As mentioned earlier there is no treatment available for osteonecrosis, the only option being surgical intervention know as "core decompression". This old technique (1964) may not be efficient in some patients in the early stages but only delays the progression of the disease.

For osteoporosis there is a myriad of treatments with the first-line option being the biphosphonates class which has an anti-resorptive activity, i.e. slowing or stopping the process of bone destruction. As noted in the chapter on markets, no drug currently mimics the normal function of the bone (normal balance between bone formation and bone resorption), hence the need for a breakthrough therapy based on this principle is high. It is acknowledged that roughly one-third of moderate to severe osteoporotic patients are non responders to existing therapies.

3.2. Bone Therapeutics' brings innovation

Fig. 7: Bone Therapeutics' technology for fracture repair



Source: Company Data.

Bone Therapeutics' brings efficacy over current SoC

Bone Therapeutics has developed a breakthrough technology in the field of orthopaedics. Its technology is based on cell therapy products, more specifically differentiated osteoblastic cells administered directly at the damaged bone site and which will immediately begin to restore a bone to normal *in-situ*. The two first-in-class cell therapy products currently under development, **PREOB®** (autologous) and **ALLOB®** (Allogeneic), are unique in the space of bone disorders for the following reasons:

- **Better efficacy** of its engineered osteoblasts compared to non-differentiated Mesenchymal Stem Cells (MSC; used by competitors) thanks to a specific and proprietary differentiation process. MSCs extracted from bone marrow are multipotent stem cells, meaning that they can differentiate into only few specific cells: osteoblasts, chondrocytes and adipocytes. Bone Therapeutics uses bone-specialised cells dedicated to bone regeneration. Starting the differentiation from an already bone specialised stem cell allows for a more potent treatment (faster and better bone-forming capacity).

Enhanced safety due to a mini-invavise procedure

- **Better safety** as the differentiation process starts from bone specialised stem cells. There is no risk of obtaining a "mix" of different cells at the end of the differentiation procedure (no

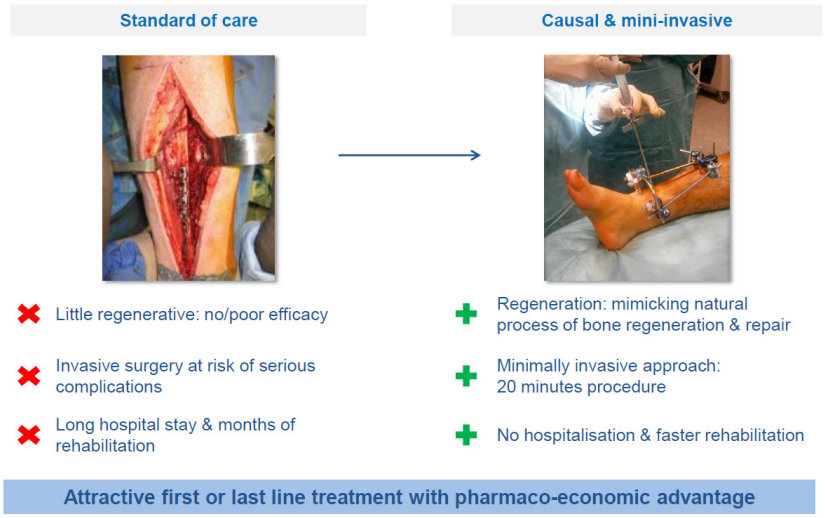
unwanted cells, only specific bone-activity) as opposed to starting the differentiation process with a multipotent stem cell (which has the potential to differentiate into any type of tissue). Using undifferentiated cells may lead to uncontrolled proliferation of different types of cells and cancer.

- **Minimally invasive technique implying shorter hospital stay and faster rehabilitation** in the case of fracture repair. As opposed to bone graft surgery which implies open surgery, Bone Therapeutics' technology only requires a quick (about 20 minutes) single ambulatory percutaneous injection to implant the osteoblastic cells.

Short manufacturing time scaling up

- **Manufacturing process is short, robust, reproducible and specific.** According to management, it takes only three weeks to manufacture PREOB® and four weeks to manufacture ALLOB® using specific culture media. Full process to go from bone marrow to ALLOB® is split into two parts. Two weeks are necessary to produce an intermediate product which is cryo-preserved. When an order comes in, it takes a two weeks process to produce ALLOB® from the cryo-preserved product. Thus, time to delivery only takes two weeks.

Fig. 8: SoC (graft surgery) vs. Bone Therapeutics' technology in fracture repair



Source: Company Data.

PREOB®, Bone Therapeutics' lead product is an autologous osteoblastic cell product (cells come from the patient) whereas, **ALLOB®** is an allogeneic osteoblastic cell product (cells come from a universal donor) offering scaling-up opportunities to address larger patients base's indications. Indeed, a single bone marrow harvest enable the company to make multiple batches of final products while for PREOB®, one marrow harvest will give one single batch.

Both products have the potential to be a major force in the bone disorders space as they mimic the natural process of bone formation as opposed to current standard of care treatments.

3.2.1. PREOB®, the autologous lead product

This first-in-class autologous osteoblastic cell product is currently in two phase III clinical trials in Europe for both osteonecrosis and non-union fractures, and in a phase II study in osteoporosis.

This product targets niche markets with high unmet medical needs, offering the advantage of an absence of competition. As a consequence, the development risk associated with this project is low.

Triple mechanism of action of PREOB

The product has demonstrated a triple mechanism of action in trials, PREOB® combines osteoblastic, osteoclastic and angiogenic properties. PREOB® is safe as, in terms of biodistribution in preclinical trials, the osteoblastic cells do not migrate out of the fracture site, and there is no problem of tumourigenicity issues. The first patient treated with PREOB® was injected in 2003 and has not shown any complication to date.

Orphan drug designation in Osteonecrosis

Note that PREOB® has already received orphan drug status for osteonecrosis in both the US and Europe.

3.2.2. ALLOB®, the allogeneic product

This allogeneic cell product is currently in phase I/IIa clinical trials for delayed-union fractures (DU) and in phase IIa for the Spine Fusion indication.

Allogeneic product to address larger populations

The markets for this product are more important compared to PREOB®'s targeted indications (more than 1 million patients per annum) however, the risk for the company is limited as there is no (or scarce) competition in theses indications.

The ALLOB® product offers the advantage of the PREOB® product combined with an allogeneic product profile. ALLOB® cells present the same properties as the PREOB cells, i.e. osteoblastic, osteoclastic and angiogenic properties and, in addition, they are immunoprivileged. This means that they won't trigger an immune response after injection in a patient's body. ALLOB® cells present the same characteristics as PREOB® cells in terms of biodistribution (no migration) and tumourgenicity (no tumour development). There are no pharmacology or toxicity issues in animal models.

Note that ALLOB® has also received the orphan drug designation from the EMA and the FDA for the osteonecrosis indication. ALLOB® is classified as a tissue-engineered product under the ATMP (Advanced-Therapy Medicinal Product) in Europe.

4. Large market opportunities stemming from two markets

Bone Therapeutics is focusing on two main markets:

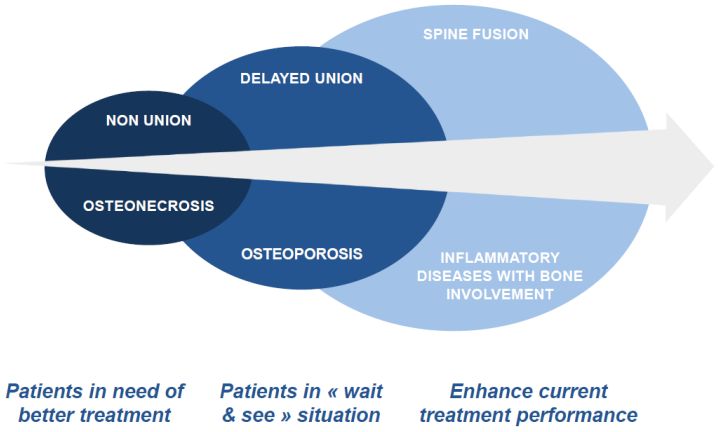
- **Fracture repair:** severe unhealed fractures, delayed-union and non-union fractures (niche markets with no efficient treatment option) and followed by spine fusion (large market and increased competition)

- **Fracture prevention**: Bone fragility conditions at increased fracture risk, osteonecrosis (orphan disease with a high unmet medical need) and osteoporosis (large market but with a somewhat competitive environment).

4.1. A sound market strategy: from niche to large indications

Bone Therapeutics' strategy is to focus first on niche markets with high unmet medical needs for both types of market, i.e. fracture repair and fracture prevention. These niche markets (Non-union and osteonecrosis) are characterised by an absence of competition, hence increasing the probability of success. Then the company will target larger indications (delayed-union and osteoporosis followed by spine fusion and bone-based inflammatory diseases) with still limited competition and/or unsatisfactory treatments.

Fig. 9: Bone Therapeutics' strategy to broaden its addressable market in fracture repair and prevention



Source: Company Data.

4.2. The fracture repair market, strong opportunities in a >USD6.5bn market

To start, Bone Therapeutics will focus on the severe unhealed fractures market. This means patients who suffer from a high energy fracture which is not healing well, hence requiring osteosynthesis, i.e. a

surgical operation with the fixation of medical devices such as screws, plates or nails. According to the orthopaedic industry, the osteosynthesis market is valued at USD6.5bn, representing around three million severe fractures per annum in the US, Europe and Japan.

Strategy is to move up earlier in the treatment paradigm to address larger population

After three months, about two-third of the severe fractures cases are still unhealed, and these cases are called delayed-unions. Typically, the approach adopted here is "wait and see", i.e. patients will remain without any treatment implying a heavy socio-economic burden as the patient is disabled. The number of patients is estimated at 750 000 per annum in the major territories.

6-7 months after the fracture, approximately 30% of delayed-unions fracture patients will need invasive surgery (allogeneic or autologous bone graft surgery) as their fracture is still unhealed; these cases are referred to as non-union. Out of the patients who will undergo invasive surgery, 20% will suffer from severe complications with an extended hospital stay and a long recovery process. There is no reported development programme for these cases, making this condition an unmet medical need with a heavy socio-economic burden. A little over 200 000 patients per annum are considered as non-union per annum in the US, Europe and Japan.

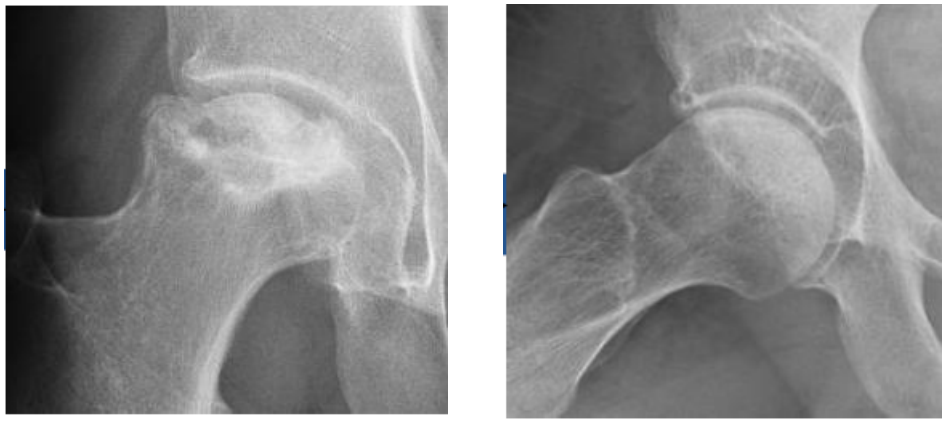
Bone Therapeutics also targets degenerative disorders of the spine with high unmet medical needs. Lumbar spinal fusion is a surgical operation in which at least two vertebrae are bridged in order to stabilise a portion of the spine. In about 25% of cases, the bone graft is unsuccessful, eventually leading to non-union and persistent pain. According to the company, there are on average 0.5 million surgeries at lumbar level per annum in Europe and North America.

4.3. The fracture prevention market

To start, the company will focus on the de-risked niche osteonecrosis market and then move on to the large osteoporosis market.

Osteonecrosis (or avascular necrosis) is a rare disease characterised by the loss of blood supply to the bones ending in the death of the bone tissue. Most of the time, it affects the epiphysis of the femur, the hip or sites close to joints and usually appears in young adults. The natural evolution of osteonecrosis leads in less than two years to femoral head collapse and a total replacement is required. There is no efficient treatment for this disease, and consequently a surgeon may perform a technique called "core decompression" after the diagnosis is confirmed through an X-ray or Magnetic Resonance Images (MRI) scan. This procedure involves making a small hole (drilling) into the sick bone in order to release the pressure and enhance tissue regeneration and vascularisation in the hole. This technique dates back to 1964, is only fairly-efficient at the early stages of the disease and is not a curative technique (unmet medical need).

Fig. 10: Osteoporosis of the femoral head (left) vs. normal femoral head (righ)



Source: Company Data.

The company estimates the market at around 180 000 individuals in the US, Europe and Japan and, as there is no treatment available, the potential is high for a newcomer.

Osteoporosis is a large indication characterised by the progressive loss in bone mass and density which makes the bone more fragile and prone to fractures. The disease is diagnosed by X-ray radiography by measuring the Bone Mineral Density (BMD) and it is a common disease in women after the menopause. Note that the bone still has the capacity to repair itself like in healthy people in six to eight weeks. The bones most commonly affected by osteoporosis-induced fractures are the wrists, hips and spinal bones. Current SoC treatments, in addition to calcium and vitamin D, include the bisphosphonate class as first-line treatment (Fosamax/Merck, Boniva/Roche, Actonel/Actavis, Aclasta/Novartis) and used in patients who have already experienced a fracture in order to decrease the risk of further fractures. Other available treatments include hormone-based treatments like parathyroid hormone (Forteo/Lilly - USD1.2bn of sales in 2013) and selective oestrogen receptor modulators (SERM) and monoclonal antibodies (Prolia/Amgen – USD0.7bn in 2013) blocking osteoclasts. Basically these drugs either slow down the bone loss or increase the rate of bone formation. There is currently no drug available on the market which restores the normal function of bone cells, in other words re-establishing the normal balance between functional osteoblasts and osteoclasts.

Non-responders to first line treatment are estimated at 10 million in the US, Europe and Japan. The osteoporosis market is estimated at around USD7-8bn in 2014 and is expected to grow at a 4% CAGR over the period 2013-18 thanks to the aging population mainly (volume growth).

There is a current unmet medical solution for osteonecrosis and the treatments available for osteoporosis are insufficient due to a lack of major innovation in this field for decades.

5. Reshuffling the cards in fracture repair treatments

5.1. Bringing an innovative treatment option in non-union fractures

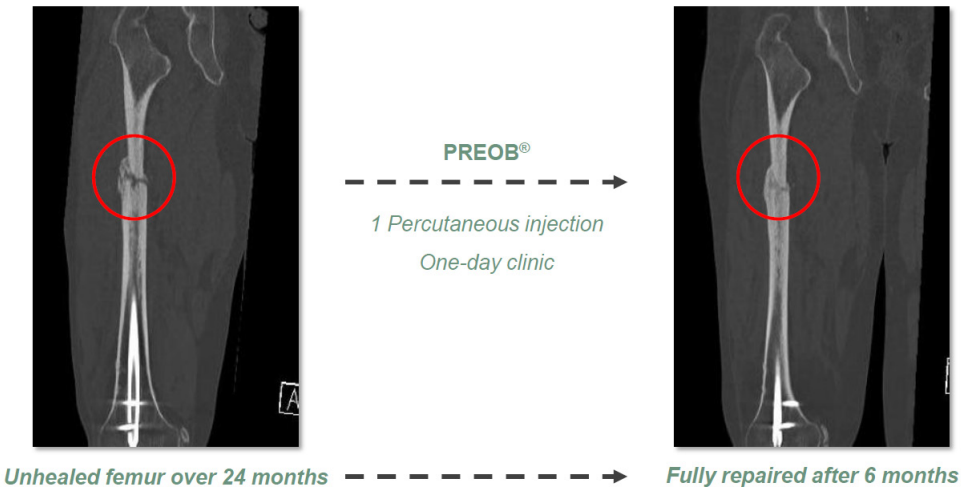
5.1.1. Phase I/IIa sets the bar high!

Strong phase I/IIa results

The 12-months study enrolled 28 patients who have fractures (i.e. non-union fracture) that have not healed within a minimum of six months. The mean non-union duration in the patients' group was 21.8 months before treatment with PREOB® (ranging from 7 to 137 months). Out of these patients, 13 had to have at least one or more additional surgeries after initial osteosynthesis. Co-primary endpoints of the study were the clinical symptoms and radiological score improvements from baseline after a single percutaneous injection of PREOB® avoiding the need for rescue surgery. Clinical symptoms were measured by a Global Disease Evaluation (GDE) score scale (>25% improvement threshold) while the radiological score was assessed by a CT-scan and X-ray (>2 points improvement scale).

As highlighted by the figure below which assesses the radiological improvement in fracture healing in one patient, phase I/IIa results set the bar high. Within six months after a single percutaneous injection of PREOB at the fracture site, the femur fracture has totally healed.

Fig. 11: PREOB phase I/IIa clinical results in non-union Fractures (radiographic data)



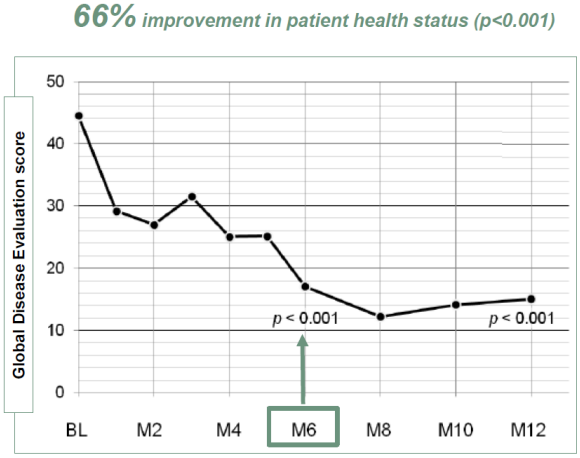
Source: Company Data.

Topline data from the trial showed that 85% (25/28) of patients treated with PREOB® met the primary endpoints with an improvement in their health status of 66% ($p<0.001$; statistically significant) and a mean increase in CT scan score of 56% (3.3 points; from 5.9 to 9.2; $p<0.01$). The chart below shows the improvement in patient's health status which pinpoints a two-step process. In the first month after treatment, there is observed an immediate improvement followed by a gradual

one over the eleven remaining months. Above all, we can see that the improvement was maintained at 12 months.

Improvement maintained at 12 months

Fig. 12: PREOB phase I/IIa clinical results in non-union fractures



Source: Company Data.

Three patients (15%) did not respond to treatment (need for a rescue surgery). Feedback from surgeons suggested that instability of osteosynthesis (which is performed immediately post-trauma (i.e. 24-48 hours) during the study follow-up period could explain these unsatisfactory results as two out of the three non-responders to PREOB® had this condition. The study showed no safety concerns as adverse reactions were mainly related to the implantation procedure and were limited to fever and inflammation.

Fig. 13: PREOB in non-union fractures, phase I/IIa results

	Global success	Rescue surgery	Failed score improvement
6 months	27/28 (96.4%)	1/28 (3.6%)	0/28 (0.0%)
12 months*	17/20 (85.0%)	3/20 (15.0%)	0/20 (0.0%)

** From the baseline pop., 8 pts had not a valid Intend Consent Form for the 8 to 12 months follow-up period*

Source: Company Data.

The company decided to build on these strong results to carry the product further to a pivotal phase IIb/III study initiated in Q3 2012.

5.1.2. Pivotal phase IIb/III study

Study design

The Phase IIb/III study is based on the earlier study. Over a 12-month period, 176 patients will be randomised (on a 1:1 basis) to either receive a single percutaneous administration of PREOB® or bone autograft (i.e. reference treatment; SoC). The non-inferiority design mans that PREOB® has to show similar efficacy to reference treatment.

As in the phase I/IIa study, co-primary endpoints have been defined has a minimum improvement in GED and CT-scan scores of at least 25% and 2 points respectively.

Non-inferiority vs. SoC : a favourable design

Non inferiority in phase IIb/III should be achievable

The non inferiority of PREOB® over bone autograft will be considered with the percentage of responders using a 15% non-inferiority margin. Considering the phase I/IIa results, PREOB® could achieve these co-primary endpoints. Indeed, phase I/IIa results showed an 85% responder rate while the estimated percentage of responder to bone autograft based on the literature is ~82%. A first DSMB report including safety as well as efficacy data is expected in H1 2016 and should confirm the efficacy and onset of action of PREOB® shown in the phase I/IIa study.

In this indication, we believe that beyond efficacy results, the strong advantage of Bone Therapeutics is its mini-invasive percutaneous injection administration route. Thus, we believe that similar results from the PREOB® arm over the autograft arm at the end of the study should not be a drag on the PREOB® adoption rate in the non-union fracture indication.

5.1.3. PREOB® in non-union fracture sales estimates

EUR300m in sales in EU and the US in 2025

Based on strong phase I/IIa results from the European study, the company intends to start a phase III in the US in H2 2017/early 2017. In the US, we have modelled a partnership agreement (12.5% royalty rate) based on phase III results expected in 2020 (below are total sales details).

Fig. 14: PREOB® – Non-Union fracture sales estimates EU & US (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Non-union fractures																	
Europe patients	89	89	90	90	91	91	92	92	93	93	94	94	94	95	95	96	96
US patients	84	85	86	87	88	89	90	91	91	92	93	94	95	96	97	98	99
Europe - Acces to Healthcare	80	80	81	81	82	82	83	83	83	84	84	85	85	85	86	86	87
US - Acces to Healthcare	72	73	73	74	75	75	76	77	78	79	79	80	81	82	83	83	84
Europe - Treated patients	72	72	73	73	74	74	74	75	75	75	76	76	77	77	77	78	78
US - Treated patients	61	62	62	63	64	64	65	65	66	67	67	68	69	69	70	71	72
Europe - Market share	0%	0%	0%	0%	0%	1%	3%	6%	8%	10%	13%	15%	15%	15%	15%	15%	15%
Europe - Treated NU patients	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,7**	**2,5**	**4,2**	**6,0**	**7,8**	**9,6**	**11,4**	**11,5**	**11,5**	**11,6**	**11,7**	**11,7**
US - Market share	0%	0%	0%	0%	0%	0%	0%	2%	5%	7%	10%	12%	15%	15%	15%	15%	15%
US - Treated NU patients	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**0,0**	**1,3**	**3,0**	**4,8**	**6,6**	**8,4**	**10,3**	**10,4**	**10,5**	**10,6**	**10,7**
EU Non Union - PREOB®	**0**	**0**	**0**	**0**	**0**	**8**	**27**	**47**	**66**	**86**	**106**	**126**	**127**	**127**	**128**	**129**	**129**
US Non Union - PREOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**23**	**53**	**86**	**124**	**167**	**214**	**227**	**229**	**232**	**234**

Source: Company Data; Bryan, Garnier & Co ests.

Based on strong phase I/IIa results from the European study, the company intends to start a phase III in the US in H2 2017/early 2017. In the US, we have modelled a partnership agreement based on phase III results expected in 2020.

5.2. Moving up earlier in the treatment of fractures with ALLOB® in delayed-union

5.2.1. Broadening the patient base

As mentioned in *Chapter 4* Bone Therapeutics' plans to gradually broaden the patients base by moving toward an allogeneic technology platform in larger markets that could not be addressable by autologous technology, not scalable and too costly to address larger markets. In the case of the fracture market, this involves moving upstream in the fracture treatment, i.e. delayed–union, described as patients suffering from fractures unhealed within 3 to 7 months post trauma. This enables Bone Therapeutics' to address patients who are currently in a "wait-and-see" situation.

5.2.2. Phase I/IIa design with two cherries on top

Study design

Initiated in June 2014, this proof of concept study aims to assess the efficacy and safety of ALLOB® in patients suffering from unhealed fractures after a minimum three months and maximum seven months. 32 patients will be enrolled in the 6-month trial which will include an additional 24-month follow-up. Co primary endpoints have been set in accordance with the EMA as an improvement in the GDE as perceived by the patients of at least 25% or an improvement in CT-scan score of at least 2 points.

Open label should offer dense newsflow

Open label study design and 4 patients' cohort should offer strong newsflow

The study benefits from an open label design. This is a crucial advantage for Bone Therapeutics as it will enable the company to communicate often on the advancement of the study rather than waiting for the complete set of data to be available. Hence, the company decided to give interim results for each four patient group having completed the study (*see newsflow*) which we believe could create strong value for shareholders.

Premature study stop as an attractive free option

Strong upside potential upon premature stop

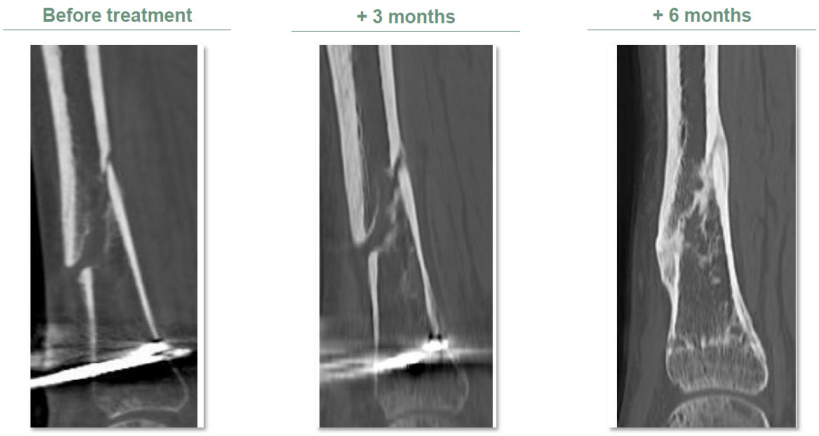
Moreover, and in accordance with the study design, the study could be prematurely stopped upon positive results from the DSMB report (16/32 patients) expected in H1 2016. This could significantly accelerate the development of the allogeneic technology.

Preliminary results from first patients show encouraging results

First results showed encouraging data

As illustrated below by radiologic data from the first patient suffering from delayed-union fracture, reported data are strongly supportive for a positive outcome of the phase I/IIa trial in delayed-union fractures. The radiological score of this patient increased by 5 points (at month 3) and 7 points (at month 6) to 12 (the maximum union score). On December 16th, 2014, the Safety Monitoring Committee unanimously recommended the continuation of the enrolment following positive safety data at 2 weeks from the first cohort (4 patients)

Fig. 15: ALLOB® – delayed-union fracture first patient's radiologic data



Source: Company Data.

5.2.3. ALLOB® – delayed-union fractures sales estimates

EUR250m in sales in 2025 in the US and Europe

Although we do not take into account any sales from the US in our model we indicate them in the table below.

Fig. 16: ALLOB® – Delayed-Union fractures sales estimates in Europe (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Delayed-union																	
Europe patients	297	298	300	301	303	304	306	307	309	310	312	313	315	316	318	320	321
US patients	282	284	287	290	293	296	299	302	305	308	311	314	317	320	324	327	330
Europe - Acces to Healthcare	267	268	270	271	272	274	275	276	278	279	281	282	283	285	286	288	289
US - Acces to Healthcare	239	242	244	247	249	252	254	257	259	262	264	267	270	272	275	278	281
Europe - Treated patients	160	161	162	163	163	164	165	166	167	168	168	169	170	171	172	173	173
US - Treated patients	144	145	147	148	149	151	152	154	156	157	159	160	162	163	165	167	168
Europe - Market share	0%	0%	0%	0%	0%	0%	0%	1%	3%	5%	6%	8%	10%	10%	10%	10%	10%
Europe - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	1,7	4,7	7,7	10,8	13,9	17,0	17,1	17,2	17,3	17,3
US - Market share	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	2%	4%	5%	7%	8%	10%	10%
US - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	3,2	5,8	8,4	11,1	13,9	16,7	16,8
EU Delayed Union - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**18**	**52**	**85**	**119**	**153**	**188**	**189**	**190**	**191**	**192**
US Delayed Union - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**60**	**114**	**175**	**242**	**302**	**363**	**367**

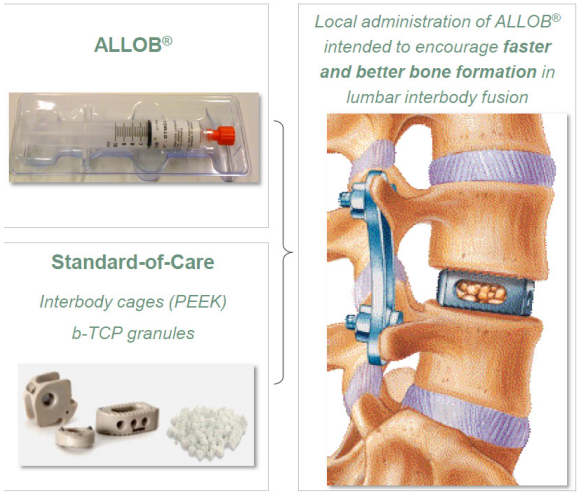
Source: Company Data; Bryan, Garnier & Co ests.

5.3. Lumbar spine fusion

In spinal fusion whether about it is lumbar spine fusion (LSF) or rescue lumbar spine fusion (RLSF), in the 25% cases in which LSF failed, Bone Therapeutics will be used on top of the use of traditional granules (in a fusion cage) to boost the fusion process.

As such, Bone Therapeutics haspartnered with Kasios, a European medical device company specialised in synthetic bone substitute.

Fig. 17: ALLOB® in spine fusion



Source: Company Data.

5.3.1. Lumbar spine fusion (LSF)

Initiated in September 2014, Bone Therapeutics' phase I/IIa study which aims at enrolling 16 patients will evaluate the efficacy and safety of ALLOB® administered concomitantly to an interbody fusion cage. Safety and efficacy will be assessed at 12 months by the change from baseline in disability and a radiological evaluation followed by a 24-month follow-up study.

Although highly competitive, strong sales potential in LSF

Although we do not take into account any sales from the US in our model, we indicate them in the table below

Fig. 18: ALLOB® – LSF sales estimates in Europe (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Lumbar Spine Fusion																	
EU LSF patients	166,8																
US LSF patients	253,4																
EU Spinal Fusion growth rate	3,5%	3,2%	2,8%	2,5%	2,2%	1,9%	1,5%	1,2%	0,9%	0,5%	0,2%	-0,1%	-0,5%	-0,8%	-1,1%	-1,5%	-1,8%
US Spinal Fusion growth rate	3,5%	3,0%	2,5%	2,0%	1,5%	1,0%	0,5%	0,0%	-0,5%	-1,0%	-1,5%	-2,0%	-2,5%	-3,0%	-3,5%	-4,0%	-4,5%
Europe - Acces to Healthcare	166,8	172,1	177,0	181,5	185,4	188,8	191,7	194,0	195,7	196,7	197,1	196,8	195,9	194,4	192,2	189,4	186,0
US - Acces to Healthcare	253,4	261,0	267,6	272,9	277,0	279,8	281,2	281,2	279,8	277,0	272,8	267,4	260,7	252,9	244,0	234,3	223,7
Europe - Market share	0%	0%	0%	0%	0%	0%	0%	0%	1%	2%	4%	5%	6%	8%	8%	8%	8%
Europe - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	2,0	4,5	7,1	9,6	12,1	14,6	14,4	14,2	14,0
US - Market share	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	2%	3%	4%	5%	6%	8%
US - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	5,3	8,1	10,6	12,9	15,0	16,8
EU LSF - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**22**	**50**	**78**	**106**	**134**	**161**	**159**	**157**	**154**
US LSF - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**106**	**168**	**231**	**282**	**327**	**366**

Source: Company Data; Bryan, Garnier & Co ests.

5.3.2. Rescue Lumbar Spine Fusion (RLSF)

Better growth prospects in RLSF. A new SoC?

Considering the high failure rates in RLSF, ALLOB® could be found to be a cost-effective alternative to second surgeries (i.e. revision procedures) often leading to greater complication rates.

16 patients will be recruited in this phase I/IIa study aiming at evaluating the efficacy and safety of a single percutaneous injection of ALLOB® in patients requiring second surgery 15 months after the failure of an initial LSF. Safety and efficacy will be assessed at 12 months by the change from baseline in disability and a radiological evaluation.

Fig. 19: ALLOB® – LSF sales estimates in Europe and the US (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Rescue Lumbar Spinal fusion																	
EU SF failure rate patients	33,4	34,4	35,4	36,3	37,1	37,8	38,3	38,8	39,1	39,3	39,4	39,4	39,2	38,9	38,4	37,9	37,2
US SF failure rate patients	50,7	52,2	53,5	54,6	55,4	56,0	56,2	56,2	56,0	55,4	54,6	53,5	52,1	50,6	48,8	46,9	44,7
Europe - Acces to Healthcare	8,3	8,6	8,9	9,1	9,3	9,4	9,6	9,7	9,8	9,8	9,9	9,8	9,8	9,7	9,6	9,5	9,3
US - Acces to Healthcare	12,7	13,1	13,4	13,6	13,9	14,0	14,1	14,1	14,0	13,8	13,6	13,4	13,0	12,6	12,2	11,7	11,2
Europe - Market share	0%	0%	0%	0%	0%	0%	0%	0%	1%	3%	5%	6%	8%	10%	10%	10%	10%
Europe - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,1	0,3	0,5	0,6	0,8	1,0	1,0	0,9	0,9
US - Market share	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	2%	4%	6%	8%	10%	10%
US - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,3	0,5	0,8	1,0	1,2	1,1
EU RLSF - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**3**	**5**	**7**	**9**	**11**	**11**	**10**	**10**
US RLSF - ALLOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**5**	**11**	**17**	**21**	**26**	**24**

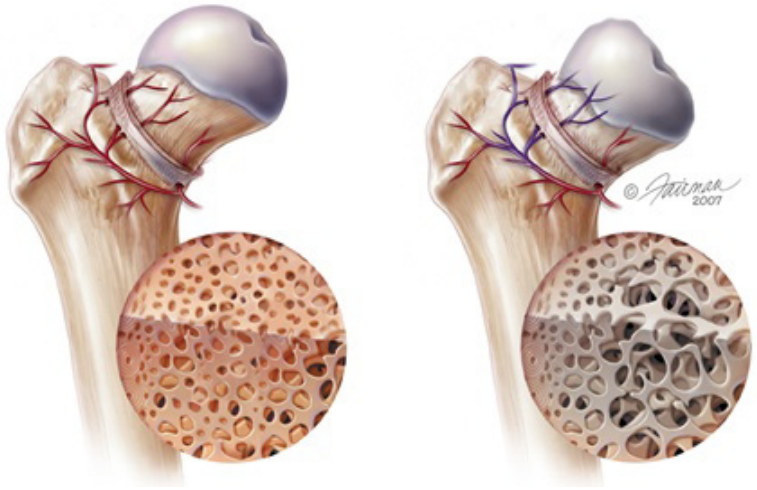
Source: Company Data; Bryan, Garnier & Co ests.

6. Better patient outcomes in fracture prevention

6.1. Osteonecrosis, an orphan disease indication to uphold the PoC

Osteonecrosis of the hip is characterised by the death of bone tissues. Although the disease often materialises in hips, where this induces pain, arthritis, and collapse of areas of bone and can lead to joint replacement surgery, it can occur in any bone of the body. Osteonecrosis could be a result of long-term high dose corticosteroid use but it has also been linked to excessive alcohol consumption, blood disorders or serious trauma. More recently osteonecrosis has been suggested as a disease of bone or mesenchymal cells as their levels significantly decrease in suffering patients.

Fig. 20: Healthy femur bone head (left) and with osteonecrosis (right)



Source: https://www.rheumatology.org.

2/3 patients go undiagnosed

It is estimated that roughly two-third of patients with osteonecrosis go undiagnosed as only X-ray examinations (which are not sensitive enough) are performed in these patients (at the time when they experience pain and movement with the hip become more and more limited). An MRI scan, which allows for 100% certain diagnosis, is too rarely performed.

Highly invasive treatment when fracture… poor efficacy of current treatments to prevent from it

Total hip arthroplasty of the femoral head (which is bilateral in 90% of the cases) caused by osteonecrosis can be prevented when the patient is at an early stage (non-fractural) of the disease i.e. stage I or II. Out of these patients, 55% undergo core decompression of the femoral head which has been widely recognised as the standard of care over past decades. Based on phase IIb results, the company's product could become a new standard of care and we estimate that it could gain access to 30% of the diagnosed patients undergoing core decompression as an add-on surgery. Core decompression alone is not very efficacious and/or is very controversial. Although not accurate, reported second surgery rates are in the 25% to 85% range. Bone decompression consists of drilling into the femoral head to promote vascularisation during the bone reconstruction process.

Fig. 21: Clinical and radiological description of osteonecrosis (ARCO classification)

Stage	Pain	Function	X-ray
I	Nil or slight	Slight or no loss	Normal
II	Slight intermittent	Moderate loss	Patchy Sclerosis, cysts
III	Severe	Severe loss	Sequestrum; loss of femoral head sphericity
IV	Permanent	Total stiffness	Osteoarthritis or head collapse

Source: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323428/.

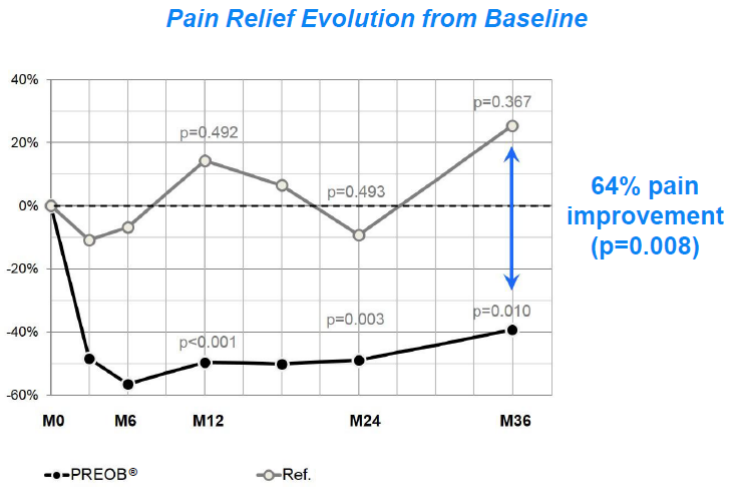
6.1.1. Strong pivotal phase IIb results

Impressive phase IIb results

53 patients suffering from early pre-fractural stage osteonecrosis of the hip (described above as stage I and II osteonecrosis) were enrolled in this, double blind study conducted at two Belgian sites, in which the 36-month follow-up was completed in March 2014. Core decompression alongside with PREOB® administration was compared to core decompression with bone marrow graft (active reference). Among these patients, 43 were treated at one hip while 10 others were treated at both hips. The first arm of the clinical trial evaluated the safety and efficacy of core decompression (SoC) with PREOB® in 32 hips while the second arm evaluated the safety and efficacy of core decompression (SoC) with bone marrow graft (active treatment) in 31 hips. Note that bilateral-treated patients received core decompression and PREOB® in one hip and core decompression and reference treatment in the other hip.

The primary endpoint of the study assessed the efficacy and safety of PREOB® compared to bone marrow graft at 24 and 36 months as measured by clinical and radiological improvements compared to baseline. Clinical change was measured by the Pain Visual Analogue Scale which ranges pain felt by the patient on a scale from 0 to 10 (0 = none; 1-3 = mild; 4-6 = moderate; 7-10 = severe). Radiological score was measured by the progression to fractural stage.

Fig. 22: PREOB® in osteonecrosis, phase I/IIa clinical symptoms data (Pain VAS scale; in months)

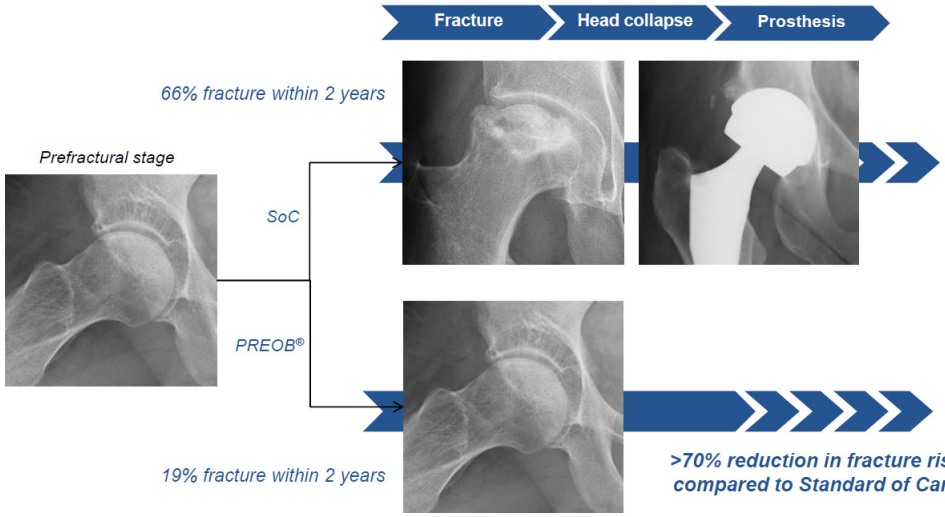


Source: Company Data.

As highlighted in the chart above, pain as well as function was reduced by 40% compared to baseline and by 64% compared to reference treatment (p=0.008) at the end of a 36month follow-up. Although we notice a slight increase in pain over the course of the treatment from a ~55% decrease at peak (6 months after treatment), a minimum 40% decrease has been maintained with PREOB® during the study. Radiographic data also shown an impressive 41.9% and 43.4% improvement in fracture risk compared to reference treatment at 24 months and 36 months respectively.

Two years after being treated with PREOB®, we would highlight that only 19% of the patients who received Bone Therapeutics' product experienced a fracture at the hip compared to 66% as reported for the patients treated with standard-of-care.

Fig. 23: PREOB® in osteonecrosis, phase IIb radiographic data



Source: Company Data.

As mentioned earlier, 10 patients (20 hips) were treated with both core decompression/PREOB® at one hip and core decompression/bone marrow graft at the other hip. In these patients, none experienced a fracture at either hip compared to 54.5% in patients treated at one hip alone with core decompression and bone marrow graft. The latter unexpected data suggest a contralateral effect of product which could increase its adoption rate in patients suffering from a unilateral osteonecrosis of the hip (i.e. 40% of patients).

The safety profile of PREOB® showed no emergence of treatment-related serious adverse advents (SAE). In the PREOB® group, only two patients experienced adverse events (AE) which resolved quickly (fever and inflammatory symptoms after implantation).

These data support further development of PREOB® in phase III.

6.1.2. A de-risked phase III study design

Study design

Study design compliant with EMA and FDA requirements

Initiated in Q2 2012, the phase III study should deliver interim top-line data (35% of patients with a 6 month follow-up) in H2 2016 and final results should be available in 2018. Thus, we expect an approval of the product in 2019 by the EMA.

Recruitment of this European study which is expected to enrol 130 patients has begun and approximately 17 patients have already been treated. Accelerating patient recruitment is part of the use of the proceeds from the IPO.

The 24-month study follows a superiority design. The 130 patients will be randomised on a 1:1 basis and are included either in the placebo arm (n=65) or the PREOB® arm (n=65). As in the phase IIb study, eligible patients have an early pre-fractural stage osteonecrosis of the hip (ARCO score I & II). 32 of the 43 sites planned by Bone Therapeutics are already open and 38 have approval from the competent authorities.

Co-primary endpoints will be 1) the change from baseline in the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain subscale, the WOMAC also assesses pain, stiffness and physical function in patients, as well as 2) the percentage of patients progressing to fractural stage as measured by X-rays with reference to the ARCO staging (i.e. stages III and higher) at 24 months.

Why it is de-risked?

We view this study as de-risked with regards to the use of a placebo arm. This has been required by the double-blind design required by the EMA. Indeed, it is impossible to have a double blind study while using core decompression and/or bone marrow graft which is an invasive procedure compared to a mini-invasive percutaneous administration of PREOB®.

Although we do not rule out a negative outcome in these phase III results, it is likely that PREOB® will show an increased efficacy over placebo, in our view, considering the strong effect shown in the phase IIb study by the PREOB® arm over the reference treatment arm (bone marrow graft).

Compliant with FDA requirements

To note is that the study design is compliant with FDA requirements which should enable the company to start a phase III in the US as soon as of 2016 for approval which we estimate in 2021. Although Bone Therapeutics will finance this phase III in the US, management expects to ink in a commercial deal with a pharmaceutical company. Thus, this will allow the company to derive royalty streams from the sales of its partner in the country.

6.1.3. Orphan Drug Designation should reduce time to approval

Orphan drug status in Europe and in the US

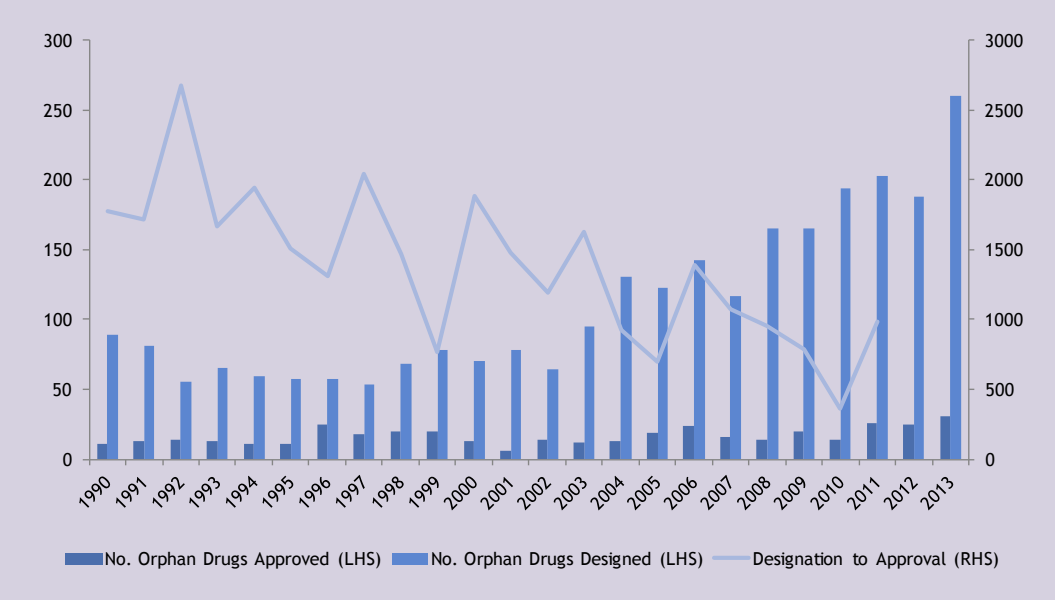
In both Europe and the US, Bone Therapeutics' PREOB product enjoys an Orphan Drug designation making it eligible for a 10-year and 7-year exclusive marketing period respectively upon approval. This designation was granted to the product by the EMA in October 2007 and by the FDA in March 2008.

Although the osteonecrosis indication represents one of the smallest addressable by Bone Therapeutics, we would highlight the growing interest from Big Pharmas' for Orphan Drug products. While the multi-blockbuster era seems to have ended, the Big Pharma groups have managed to offset this decline with a number of products with lower individual sales potential but addressing unmet medical need that enable prices and margins to be maintained at high levels. These trends have

therefore favoured the emergence of drugs addressing Orphan diseases as well as licence agreements and M&A operations.

As the same autologous product will be administrated to patients whether it is in the Osteonecrosis or in the Non-Union fracture indication and that that the company is willing to have a price per procedure, we believe Bone Therapeutics should not be able to have a higher pricing in this indication. Nonetheless, time to approval should be reduced, upon positive phase III results. In Europe, the Committee for Orphan Medicinal Products (COMP) evaluation process takes a maximum of 90 days while in the US, roughly 75% of Orphan Drug designation reviews have been completed in 90 days or less.

Fig. 24: Number of Orphan drugs designations (LHS) and designation to approval Time (in days) in the US (RHS)



Source: FDA.org.

6.1.4. Osteonecrosis of the hip sales model

EUR10,000 price in Europe, EUR15,000 in the US

The company aims to have a price per dose (i.e. percutaneous or intravenous injection) rather than a price depending on the dosage needed per patient; we have assumed a EUR10,000 price. Osteonecrosis is likely to be the first approved indication for PREOB® according to our estimates. Although it is an Orphan indication, the price of the existing SoC i.e. core decompression is EUR2,400 per procedure while that of a total hip arthroplasty (THA) is EUR9400 on average. Thus we have retained a EUR10,000 price in Europe which represents roughly 4 times that for core decompression and is still benefitting from a premium over a THA. In the US we have assumed a EUR15,000 price (USD18,000). The pricing strategy discussed above is the one we have retained for PREOB® and ALLOB® excluding osteoporosis. To note that the price is slightly lower (EUR8,000) in osteoporosis which targets different physicians as well as a much larger population.

Fig. 25: PREOB® – Osteonecrosis of the hip sales estimates in Europe and the US (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Osteonecrosis																	
Europe patients	66,0	66,3	66,7	67,0	67,3	67,7	68,0	68,3	68,7	69,0	69,4	69,7	70,1	70,4	70,8	71,1	71,5
US patients	63,0	63,6	64,3	64,9	65,6	66,2	66,9	67,6	68,2	68,9	69,6	70,3	71,0	71,7	72,4	73,2	73,9
Europe - undergoing Core dec SoC	33,0	33,2	33,3	33,5	33,7	33,8	34,0	34,2	34,3	34,5	34,7	34,9	35,0	35,2	35,4	35,6	35,7
US - undergoing Core dec SoC	31,5	31,8	32,1	32,5	32,8	33,1	33,4	33,8	34,1	34,5	34,8	35,1	35,5	35,9	36,2	36,6	36,9
Europe - Acces to Healthcare	29,7	29,8	30,0	30,1	30,3	30,4	30,6	30,8	30,9	31,1	31,2	31,4	31,5	31,7	31,8	32,0	32,2
US - Acces to Healthcare	26,8	27,0	27,3	27,6	27,9	28,1	28,4	28,7	29,0	29,3	29,6	29,9	30,2	30,5	30,8	31,1	31,4
Europe - Market share	0%	0%	0%	0%	0%	1%	6%	11%	16%	20%	25%	30%	30%	30%	30%	30%	30%
Europe - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,3	1,8	3,3	4,8	6,3	7,9	9,4	9,5	9,5	9,6	9,6	9,6
US - Market share	0%	0%	0%	0%	0%	0%	0%	2%	8%	13%	19%	24%	30%	30%	30%	30%	30%
US - Treated NU patients	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,6	2,2	3,9	5,6	7,3	9,1	9,1	9,2	9,3	9,4
EU Osteonecrosis - PREOB® Sales	**0**	**0**	**0**	**0**	**0**	**3**	**20**	**36**	**53**	**70**	**87**	**104**	**104**	**105**	**105**	**106**	**107**
US Osteonecrosis - PREOB® Sales	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**10**	**39**	**69**	**105**	**144**	**188**	**199**	**201**	**203**	**205**

Source: Company Data; Bryan, Garnier & Co ests.

6.2. PREOB®: an attractive treatment option in osteoporosis

To broaden the scope of indication in fracture prevention, the company has initiated an open label phase IIa pilot study with a 12 month follow-up in osteoporosis.

Phase IIa could trigger partnership in osteoporosis upon positive results

This phase IIa trial aims at assessing the cell distribution of PREOB® in the patient's body after a single dose intravenous infusion. As osteoporosis is a crowded indication, the company has decided to place its product as a last line treatment by evaluating the safety and biodistribution of PREOB® in 20 severe osteoporotic patients non-responding to existing treatments for more than two years.

Phase IIa study short-term follow-up results are already available for seven patients. In these patients, diffusion of the products into the patient's body following the natural distribution in bones has been proven effective at 48 hours after a transit in the lungs at 4 hours post-injection while no treatment-related serious adverse events or any side-effects were reported.

6.2.1. A potential licensing agreement...

The company expects to be able to license the product, so that it is responsible only for financing the phase IIa study. In this case, physicians will be targeted instead of surgeons but this would represent a too large sales force to be handled by Bone Therapeutics' cost structure alone.

12-month secondary endpoints especially the occurrence of new vertebral fractures and bone mineral density as assessed by X-ray and Dual-energy X-ray asbsorptiometry (DEXA) respectively should give interesting efficacy results which could trigger a partnership.

If these secondary endpoints results show encouraging results or in a blue sky scenario are found to be superior to results which have already been obtained by existing treatments, we are confident that

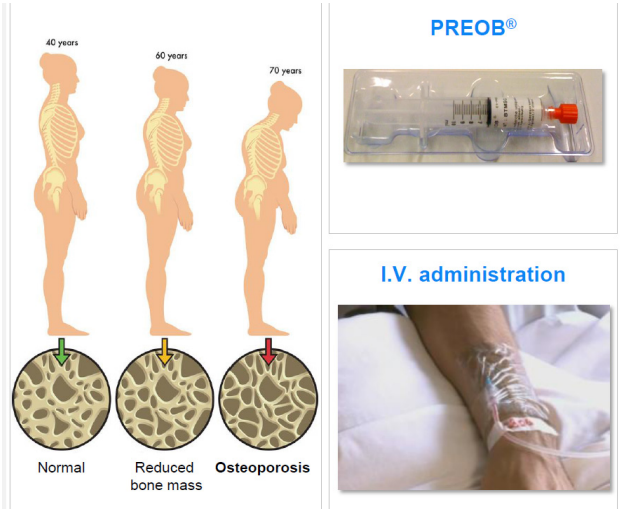
they could trigger a partnership agreement for the company with a significant upfront as well as royalties and milestone payments.

6.2.2. ... could give a strong advantage to the commercial partner

Highly innovative once-a-year I-V administration route

Indeed, even in a crowded competitive landscape, we believe that the once-a-year intravenously infusion administration route for PREOB® could be a strong competitive advantage for the product as currently commercialised treatments only offers a once-daily or/to one-every-other-week treatment option(s).

Fig. 26: A breakthrough I.V. treatment administration route in osteoporotic patients



Source: Company Data.

EUR1.1bn in sales in the US and in Europe in 2025

6.2.3. Severe osteoporosis sales model

Although we do not include any US sales in our model, we have indicated them below

Fig. 27: PREOB® – Severe Osteoporosis sales estimates in Europe and the US (in EURm)

in €m (except per patient data)	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Severe Osteoporosis																	
Europe pop >40yo	171	171	172	173	174	175	176	177	177	178	179	180	181	182	183	184	185
US pop >40yo	162	164	165	167	168	170	172	174	175	177	179	181	182	184	186	188	190
Europe patients	25,6	25,7	25,8	26,0	26,1	26,2	26,4	26,5	26,6	26,8	26,9	27,0	27,2	27,3	27,4	27,6	27,7
US patients	24,3	24,5	24,8	25,0	25,3	25,5	25,8	26,0	26,3	26,6	26,8	27,1	27,4	27,6	27,9	28,2	28,5
Europe diagnosed pts	7,67	7,71	7,75	7,79	7,83	7,87	7,91	7,95	7,99	8,03	8,07	8,11	8,15	8,19	8,23	8,27	8,31
US diagnosed pts	7,29	7,36	7,43	7,51	7,58	7,66	7,73	7,81	7,89	7,97	8,05	8,13	8,21	8,29	8,38	8,46	8,54
Europe - moderate to severe	2,69	2,70	2,71	2,73	2,74	2,75	2,77	2,78	2,80	2,81	2,82	2,84	2,85	2,87	2,88	2,89	2,91
US - moderate to severe	2,55	2,58	2,60	2,63	2,65	2,68	2,71	2,73	2,76	2,79	2,82	2,85	2,87	2,90	2,93	2,96	2,99
Europe - non-responder	0,81	0,81	0,81	0,82	0,82	0,83	0,83	0,83	0,84	0,84	0,85	0,85	0,86	0,86	0,86	0,87	0,87
US - non-responder	0,77	0,77	0,78	0,79	0,80	0,80	0,81	0,82	0,83	0,84	0,85	0,85	0,86	0,87	0,88	0,89	0,90

Europe - Market share	0%	0%	0%	0%	0%	0%	0%	0%	1%	1%	2%	2%	2%	3%	3%	3%	3%
Europe - Treated NU patients	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,03	0,04	0,05	0,06	0,07	0,08	0,09	0,09	0,09
US - Market share	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	1%	1%	2%	2%	2%	3%
US - Treated NU patients	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,03	0,04	0,05	0,06	0,07	0,08
EU Osteoporosis – PREOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**309**	**414**	**520**	**627**	**735**	**844**	**954**	**959**	**964**
US Osteoporosis - PREOB®	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**562**	**795**	**1 054**	**1 277**	**1 505**	**1 738**

Source: Company Data; Bryan, Garnier & Co ests..

7. IP & manufacturing

7.1. Strong IP protection

IP protection until 2027-2029

Bone Therapeutics has currently nine patent families covering its products as well as cell populations, methods and applications until 2027-2029.

The PREOB® product has a patent granted for the US, Japan and Singapore and the ALLOB® product is under patent protection in Japan, Australia and Singapore.

The Orphan Drug designation for PREOB® and ALLOB® in the US and Europe for osteonecrosis entitles the product to a 7-year and 10-year period of market exclusivity respectively once they reach the market.

Above all, in the emerging cellular therapy market, secrecy and know-how are both crucial. For instance, in order to develop PREOB® and ALLOB®, the differentiation process requires several weeks and different culture media with a secret composition. Management has indicated that there are thousands of different possible combinations for these media, hence this considerably reduces the risk linked to the emergence of competitive products. Bone Therapeutics will pursue in the future its strategy of mixed protection (patents and secrecy).

7.2. Manufacturing scaling up

Manufacturing scaling up. Should be able to cover entire demand

It terms of manufacturing, the company has currently one facility in Brussels which is GMP (Good Manufacturing Practices) approved. This facility has two production lines for PREOB® and ALLOB® with a 200 batches per annum capacity.

A new manufacturing facility is under construction in Gosselies (south of Brussels). This factory is already fully financed and is expected to open by mid-2016. This state-of-the-art GMP facility will have a capacity of 5,000 batches per annum for PREOB® or 12,000 for ALLOB®. Note that the company plans to invest 5% of the amount raised at the IPO in optimising production.

The stability of the PREOB® and ALLOB® products is approximately 24 hours today. This number could be increased in the future as the company dedicates R&D resources to this goal. For the US clinical trials, in the case of PREOB®, a manufacturing facility will be built on US soil. Regarding ALLOB®, the decision has not yet been taken.

8. No competition in sight in key indications

Few if no competition

8.1. Fracture repair

8.1.1. Non-union and delayed union fully open to new players

In the fracture healing market, the only product which has already been approved, aside from bone grafting procedures which remains the gold standard, was Osigraft (Stryker). Nonetheless, this product has been withdrawn from the market.

UCB/Amgen's romosozumab development in the consolidation of fractures was interrupted in 2013, with the FDA having requested assessment of four primary efficacy criteria, which would have implied carrying out a second phase II trial. The product is currently being evaluated in phase III in post-menopausal osteoporosis.

8.1.2. Lumbar spine fusion

In lumbar spinal fusion, Bone Therapeutics' products derived from allogeneic stem cell therapy, is at the moment the only company with an ongoing phase IIa study. Mesoblast completed a phase II with its allogeneic spine fusion product but the phase III remains on hold due to a change in priorities.

Except for Mesoblast we see no potential competitors for the company but we would put the spotlight on the high innovation in the medical devices space (i.e. prosthesis) which for some patients allows him/her to regain full mobility of the cervical spine. We believe that this high innovation could be a threat to Bone Therapeutics' fusion product if such kinds of devices reach the market in the lumbar spine segment in the coming years.

8.2. Fracture prevention

8.2.1. Osteonecrosis of the hip

In this indication, only one academic collaborative project has a product under development but at an earlier stage than PREOB®. Reborne (a collaborative project name) is conducting a phase I study in Osteonecrosis.

8.2.2. Osteoporosis

Competition is fierce in the osteoporosis space with several blockbuster products (Forteo, Fosamax) and the emergence of a new treatment paradigm with anti-sclerostin slightly increasing bone mineral density. Nonetheless, considering: 1) the results of the technology platform in other indications, 2) an attractive I-V-administration route for the product as well as 3) its positioning as a last line treatment in which there is currently an unmet medical solution, we estimate that PREOB® in osteoporosis could achieve significant sales upon positive development leading to approval.

9. Further opportunities

9.1. Looking outside Europe

9.1.1. The US

Partnership will be key in the US

The road to the US market has already been paved for Bone Therapeutics with a phase III study design in osteonecrosis compliant with the FDA requirement. The company also plans to initiate a phase III study in non-union in the US. Both of these trials are expected to be initiated in 2016. Looking forward, we believe that the company will look for one development/commercial partnership for its products in each of its core markets, fracture repair and fracture prevention. Whilst we do not take into account in our model any US sales from products that have not been stated by the company as about to enter the clinic in the country, we do not rule out that this could materialise in the coming years.

9.1.2. Japan

Japan approval pathway of stem cell therapy products upon phase II results as a free option

Japan has recently shaken up its "drug lag" described as the slow process that sometimes translates into therapies reaching the market well after they have received the green light elsewhere. In 2013, Japan's Upper House parliament passed legislation which allows conditional approval for stem cell therapies based on their strong safety profile in small clinical trials that can go to market without the usual requirement of efficacy. This has been done to push regenerative medicine in the hope that the country can become a global leader in the area. We believe that there will be a rapid turnaround development timeframe in the country so that the ageing population could benefit from new treatments after only a 2-4 years development timeframe. As a reminder, none of the completed studies or ongoing studies at Bone Therapeutics has shown the emergence of serious treatment related adverse events. The company is actually working on bringing studies to be completed for registration and is looking to out-license its product in the region. As Japan's regulator has historically appeared to be cautious, and that none of the studies in the country have started yet, we have taken a conservative stance and decided not to include any royalties derived from a Japanese partner yet.

9.2. Early stage opportunities

9.2.1. MXB® preclinical programme

This addresses large bone defects described as a lack of bone tissue in a body area, where it should normally be. Although surgical procedures like bone defect reconstitution, excision and fixation, bone grafting, etc.… exist, they involve repeated highly invasive surgery. In this indication, Bone Therapeutics approach consists of injecting its product (MXB®, an injectable combined osteoblastic cell matrix) into a scaffold structure. Two weeks after injection, *in vivo* bone size almost doubled after a single administration.

9.2.2. JTA®

JTA® is an enhanced viscosupplement developed by the company for intra-articular administration into the osteoarthritic joint. The product is set to enter the clinic in a phase I/IIb study which is in preparation. The trial aims at assessing the efficacy and safety of JTA® in 75 osteoarthritic patients who will be randomised on a 1:1:1 basis to receive either two different doses of one single injection of Bone Therapeutics' product or one dose of Ostenil (SoC; marketed by TRB Chemedica; a family

owned company). The safety and efficacy will be evaluated at six months and will include an interim analysis at three months.

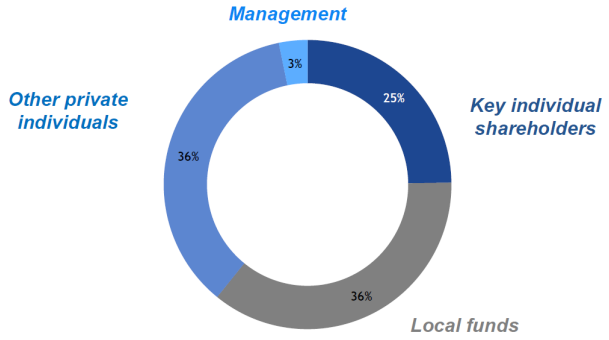
10. Shareholder's structure and management

10.1. Shareholder's structure

Long-term shareholders accounts for 74% of the capital before IPO

Bone Therapeutics' long term shareholders who reiterated their commitment to the development of the company accounted for 74% of the capital which in our view is reassuring. Moreover, only 3 key individual shareholders have 25% of the capital.

Fig. 28: Shareholder's structure (before IPO)



Source: Company Data.

10.2. Management

Management has a proven track record

Enrico Bastianelli – CEO. E. Bastianelli started his career in the public sector (Pathology Department of the Erasme University Hospital in Belgium) and then moved to the marketing department of Procter & Gamble Pharmaceuticals where he was involved in bone-related diseases. After being a consultant at McKinsey from 1999 to 2002, he became VP Corporate Development at ProSkelia (bone and hormone disorders) until 2006 when he became the CEO of Bone Therapeutics.

Wim Goemaere – CFO. W. Goemaere has over 25 years international financial experience, mainly in the biotech sector. After a role at BP, he moved to the Flanders Institute for Biotechnology as CFO. In 2008 he worked at Devgen as the CFO (Devgen was sold to Syngenta in September 2012 for EUR403m), before joining Bone Therapeutics in 2013.

Valérie Gangji – CMO. V. Gangji has a broad experience in rheumatology and bone diseases. She started her career in the public sector in 1993 at the Erasme University Hospital in Belgium. She specialised in osteo-articular disorders and rehabilitation. Since 1997 she has conducted several clinical trials in Osteonecrosis, Arthritis and Osteoporosis and she is still, each year, the main investigator in 3 to 4 clinical studies. Valérie is Enrico's spouse.

Guy Heynen – CCRO. G. Heyen started his career as a doctor at University Hospital in Liege, Belgium. He is a specialist in rheumatology and immunology. He has over 35 years' experience in medical affairs and regulatory functions. Most of his career has been at Pfizer.

Bryan Garnier stock rating system

For the purposes of this Report, the Bryan Garnier stock rating system is defined as follows:

Stock rating

BUY — Positive opinion for a stock where we expect a favourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential upside based on valuation), but also takes into account a number of elements including a SWOT analysis, positive momentum, technical aspects and the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

NEUTRAL — Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, but in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

SELL — Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements including a SWOT analysis, positive momentum, technical aspects and the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

Distribution of stock ratings

BUY ratings 55.3% NEUTRAL ratings 37.6% SELL ratings 7.1%

Research Disclosure Legend

1	Bryan Garnier shareholding in Issuer	Bryan Garnier & Co Limited or another company in its group (together, the "Bryan Garnier Group") has a shareholding that, individually or combined, exceeds 5% of the paid up and issued share capital of a company that is the subject of this Report (the "Issuer").	No
2	Issuer shareholding in Bryan Garnier	The Issuer has a shareholding that exceeds 5% of the paid up and issued share capital of one or more members of the Bryan Garnier Group.	No
3	Financial interest	A member of the Bryan Garnier Group holds one or more financial interests in relation to the Issuer which are significant in relation to this report	No
4	Market maker or liquidity provider	A member of the Bryan Garnier Group is a market maker or liquidity provider in the securities of the Issuer or in any related derivatives.	No
5	Lead/co-lead manager	In the past twelve months, a member of the Bryan Garnier Group has been lead manager or co-lead manager of one or more publicly disclosed offers of securities of the Issuer or in any related derivatives.	**NO**
6	Investment banking agreement	A member of the Bryan Garnier Group is or has in the past twelve months been party to an agreement with the Issuer relating to the provision of investment banking services, or has in that period received payment or been promised payment in respect of such services.	YES
7	Research agreement	A member of the Bryan Garnier Group is party to an agreement with the Issuer relating to the production of this Report.	No
8	Analyst receipt or purchase of shares in Issuer	The investment analyst or another person involved in the preparation of this Report has received or purchased shares of the Issuer prior to a public offering of those shares.	No
9	Remuneration of analyst	The remuneration of the investment analyst or other persons involved in the preparation of this Report is tied to investment banking transactions performed by the Bryan Garnier Group.	No
10	Corporate finance client	In the past twelve months a member of the Bryan Garnier Group has been remunerated for providing corporate finance services to the issuer or may expect to receive or intend to seek remuneration for corporate finance services from the Issuer in the next six months.	YES
11	Analyst has short position	The investment analyst or another person involved in the preparation of this Report has a short position in the securities or derivatives of the Issuer.	No
12	Analyst has long position	The investment analyst or another person involved in the preparation of this Report has a long position in the securities or derivatives of the Issuer.	No
13	Bryan Garnier executive is an officer	A partner, director, officer, employee or agent of the Bryan Garnier Group, or a member of such person's household, is a partner, director, officer or an employee of, or adviser to, the Issuer or one of its parents or subsidiaries. The name of such person or persons is disclosed above.	No
14	Analyst disclosure	The analyst hereby certifies that neither the views expressed in the research, nor the timing of the publication of the research has been influenced by any knowledge of clients positions and that the views expressed in the report accurately reflect his/her personal views about the investment and issuer to which the report relates and that no part of his/her remuneration was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in the report.	YES
15	Other disclosures	Other specific disclosures: Report sent to Issuer to verify factual accuracy (with the recommendation/rating, price target/spread and summary of conclusions removed).	YES

Summary of Investment Research Conflict Management Policy is available www.bryangarnier.com

BRYAN, GARNIER & CO

London
Heron Tower
110 Bishopsgate
London EC2N 4AY
Tel: +44 (0) 207 332 2500
Fax: +44 (0) 207 332 2559
Authorised and regulated by the Financial Conduct Authority (FCA)

Paris
26 Avenue des Champs Elysées
75008 Paris
Tel: +33 (0) 1 56 68 75 00
Fax: +33 (0) 1 56 68 75 01
Regulated by the Financial Conduct Authority (FCA) and the Autorité de Contrôle prudential et de resolution (ACPR)

Geneva
rue de Grenus 7
CP 2113
Genève 1, CH 1211
Tel +4122 731 3263
Fax+4122731 3243
Regulated by the FINMA

New Delhi
The Imperial Hotel
Janpath
New Delhi 110 001
Tel +91 11 4132 6062
+91 98 1111 5119
Fax +91 11 2621 9062