

# ***Company presentation***

*VFB Happening*

*16 April 2016*



 **Bone** Therapeutics

# FORWARD-LOOKING STATEMENTS

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This document and the accompanying oral presentation contain information on Bone Therapeutics SA' markets and competitive position, and more specifically, on the size of its markets. This information has been drawn from various sources or from Bone Therapeutics SA own estimates. Investors should not base their investment decision on this information. This document and the accompanying oral presentation also contain certain forward-looking statements. These statements are not guarantees of the Company's future performance. These forward-looking statements relate to the Company's future prospects, developments and marketing strategy and are based on analysis of estimates not yet determinable. Forward-looking statements are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future.

Bone Therapeutics SA draws your attention to the fact that forward-looking statements cannot under any circumstance be construed as a guarantee of the Company's future performance and that the Company's actual financial position, results and cash flow, as well as the trends in the sector in which the Company operates may differ materially from those proposed or reflected in the forward-looking statements contained in this document and the accompanying oral presentation. Furthermore, even if Bone Therapeutics SA financial position, results, cash-flows and developments in the sector in which the Company operates were to conform to the forward-looking statements contained in this document and the accompanying oral presentation, such results or developments cannot be construed as a reliable indication of the Company's future results or developments. Certain figures and numbers appearing in this document and the accompanying oral presentation have been rounded. Consequently, the total amounts and percentages appearing in the tables are therefore not necessarily equal to the sum of the individually rounded figures, amounts or percentages.

# KEY INVESTMENT HIGHLIGHTS

1

## LARGE TARGETED MARKETS

(12M PATIENTS<sup>(1)</sup>, 30% OF A \$34Bn MARKET<sup>(2)</sup>)  
WITH SIGNIFICANT  
HIGH UNMET MEDICAL  
NEEDS



2

CELL THERAPY  
APPROACH  
ENABLES  
FRACTURE REPAIR  
AND PREVENTION



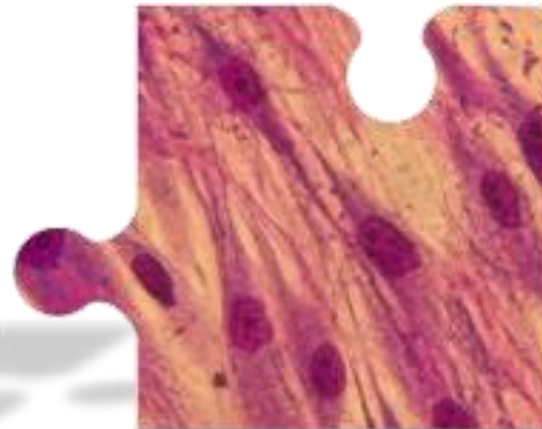
4

WITH STRONG  
CLINICAL  
RESULTS -  
2 ONGOING  
PHASE III trials



3

BONE  
THERAPEUTICS  
A LEADER IN  
BREAKTHROUGH  
BONE CELL  
THERAPY



(1) Europe, US, Japan (Company estimates) (2) For the global fracture repair and prevention market: Transparency Market Research: Osteoporosis Drugs Market (2013) & The orthopaedic industry annual report (2013)

# MANAGEMENT TEAM

## Enrico Bastianelli, MD, MBA

### *Chief Executive Officer & co-founder*



- ▶ 21 years experience in pharma/biotech
  - Founder & VP Corporate Development at ProSkelia/ProStrakan
  - Consultant at McKinsey & Company
  - Marketing at Procter & Gamble

## Wim Goemaere, MAE

### *Chief Financial Officer*



- ▶ 26 years experience in finance
  - CFO Devgen (sold to Syngenta for €400m)
  - Finance Director at Flanders Institute for Biotechnology (VIB)
  - Finance & control at BP

## Thomas Lienard, MBA

### *Chief Business Officer*



- ▶ 15 years of experience in sales & marketing
  - Managing Director at Lundbeck (BE&LU)
  - Various position at Eli Lilly and Company, including Sales Director Belgium
  - Consultant at McKinsey & Company

## Valérie Gangji, MD, PhD

### *Chief Medical Officer & co-founder*



- ▶ 21 years experience in rheumatology and medical research
  - Head of the Rheumatology Dept. of Erasme University Hospital (Brussels, Belgium)
  - Responsible for bone cell therapy program and pain clinic

## Guy Heynen, MD

### *Chief Clinical & Regulatory Officer*

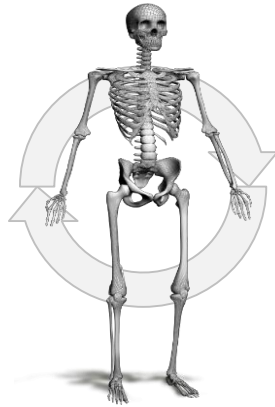


- ▶ 35 years experience in medical & regulatory
- ▶ Rheumatologist
  - Clinical & Medical research at Pfizer
  - European team leader for Alzheimer's drugs & US team leader for anti-inflammatory drug franchise

# A GAME CHANGER IN ORTHOPAEDICS

## *Rationale for bone cell therapy in orthopaedics and bone diseases*

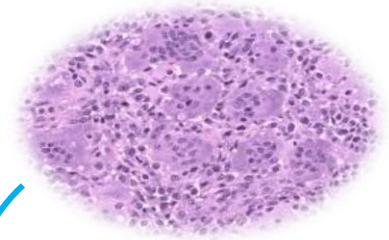
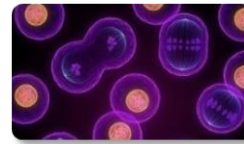
**Skeleton: a naturally  
regenerative system**



**Limitations of standard  
orthopaedic approaches**



**Production of bone-forming cells**



**Minimally invasive administration**



# UNIQUE MODE OF ACTION FOR NEW TREATMENT PARADIGM

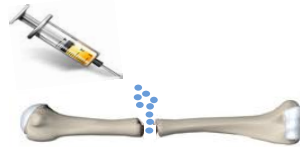
Unique expertise of Bone Therapeutics in manufacturing osteoblasts



Few months process

## IMPLANTATION

MINIMALLY  
INVASIVE



- ▶ One single and local percutaneous injection
- ▶ Fast (20 min.) & ambulatory

## INITIATION

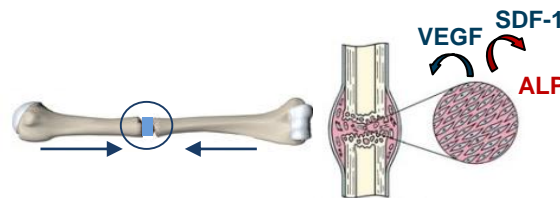
OF BONE  
FORMATION



- ▶ Local action at fracture site
- ▶ Replacement of defective / missing bone cells

## AMPLIFICATION

OF NATURAL  
REGENERATION  
PROCESS



- ▶ Recruitment of dedicated patient's cells
- ▶ Re-creation of a healthy bone environment

# OUR TARGET MARKETS

## FRACTURE REPAIR

*Severe unhealed fractures*



**Non-union**

**Delayed-union**

Addressable Pop.  
(~0.3M)

Addressable Pop.  
(~1.0M)

## FRACTURE PREVENTION

*Bone fragility conditions at increased fracture risk*



**Osteonecrosis**

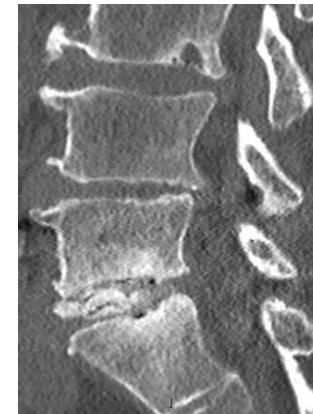
**Severe osteoporosis**

Addressable Pop.  
(~0.2M)

Addressable Pop.  
(~10M)

## SPINAL FUSION

*Degenerative diseases of the spine*



**Spinal fusion**

**Revision spinal fusion**







Addressable Pop.  
(~0.5M\*)

Addressable Pop.  
(~0.12M\*)

*\*Only lumbar spine fusion procedures*

# PIPELINE

Two products: autologous (PREOB®) & allogeneic (ALLOB®) in six indications

Indication	Platform	Preclinical	Phase I/IIA	Phase IIB/III
Non-Union Fractures	PREOB®			
Delayed-Union & Multiple Fractures	ALLOB®			
Osteonecrosis	PREOB®			
Osteoporosis	PREOB®			
Spinal Fusion	ALLOB®			
Rescue Spinal Fusion	ALLOB®			





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## CLINICAL HIGHLIGHTS 2015

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# CLINICAL HIGHLIGHTS SINCE IPO

Significant progress in ongoing **Phase II** clinical trials

- ALLOB® Phase I/IIA in **delayed-union**:
  - 8 patients safely treated; first 4 patients achieving primary endpoints
  - Extension of the delayed-union program for ALLOB® into multiple delayed-union fractures
- ALLOB® Phase IIA in **spinal fusion**:
  - ALLOB® Phase IIA spinal fusion trial: 75% of patients treated; successful fusion demonstrated in first patient
- PREOB® Phase IIA in **severe osteoporosis**:
  - Demonstration of safety of intravenous administration and of cells migration of towards the bones most prone to osteoporosis-related fractures
  - Positive efficacy results from the PREOB® Phase IIA trial in severe osteoporosis of the first patient cohort



Initiation of pioneering ALLOB® Phase IIA trial for the minimally invasive treatment of **failed spinal fusions**

**ODD** granted to ALLOB® by the EMA and FDA for the treatment of osteogenesis imperfecta

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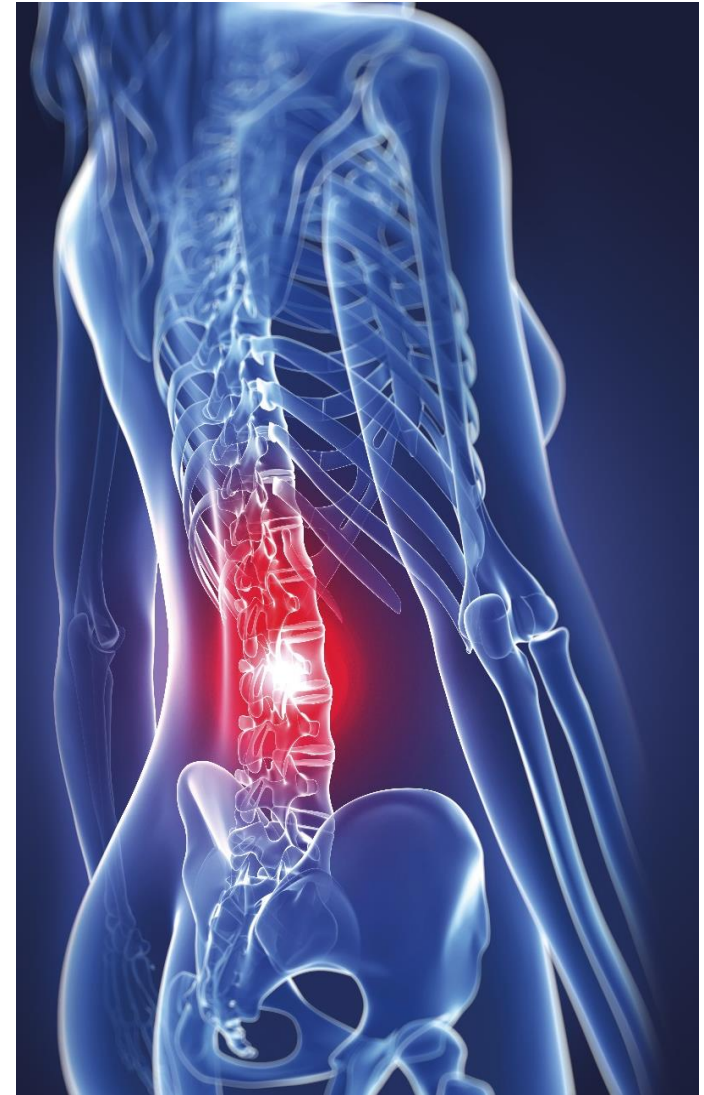


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**ODD** granted to ALLOB® by the EMA and FDA for the treatment of osteogenesis imperfecta

# NEW OPPORTUNITIES IN ORTHOPAEDICS – SPINAL FUSION

- ▶ Seizing the opportunity in spinal fusion (18% of orthopaedics market)
  - Characterized by strong growth (5-6% p.a.) and large unmet need
  - Current standard-of-care applied with limited success: up to 25% of patients unsatisfied with their surgery
- ▶ Bone Therapeutics' innovative bone-forming cell therapies can potentially enhance current treatments
- ▶ Creating a market in spinal fusion
  - Now in two Phase IIA trials with ALLOB®
  - No safety issues so far and first efficacy results due



# ALLOB<sup>®</sup> IN SPINAL FUSION – PHASE IIA TRIAL

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**23 March 2015:**

**Bone Therapeutics treats first patients in ALLOB<sup>®</sup> Phase IIA spinal fusion trial**

**Four patients requiring spinal fusion surgery have now been treated with Bone Therapeutics' allogeneic osteoblastic cell therapy product**

**15 December 2015:**

**Bone Therapeutics completes recruitment of the first half of patients in ALLOB<sup>®</sup> Phase IIA spinal fusion trial**

***ALLOB<sup>®</sup>'s positive safety profile confirmed at mid-point in trial***

**17 February 2016:**

**Bone Therapeutics treats 12 patients without safety concerns in ALLOB<sup>®</sup> Phase IIA spinal fusion trial**

**Recruitment almost complete with four patients left to treat**

**24 February 2016:**

**Bone Therapeutics presents ALLOB<sup>®</sup> pre-clinical and early clinical efficacy data in spinal fusion at the 'Clinical Applications of Stem Cells' Conference**

**Successful spinal fusion achieved in first patient within 12 months**

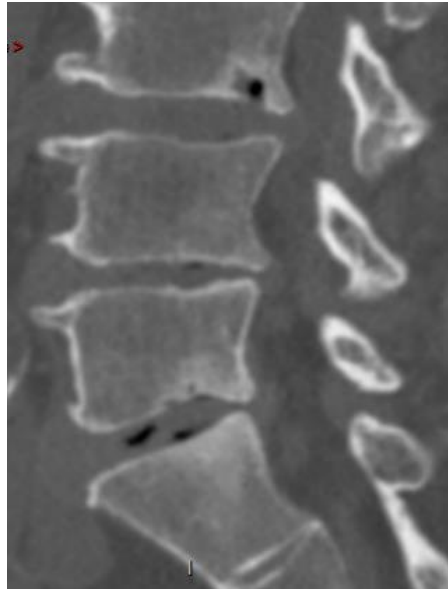
# PHASE IIA ALLOB<sup>®</sup> SPINAL FUSION TRIAL

1,000,000 surgeries p.a. in EU & US, of which 500,000 at lumbar level

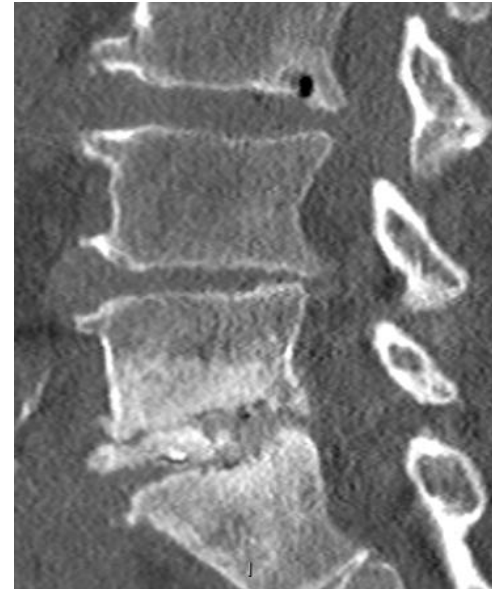
Slow progression to fusion and treatment failure (no fusion) in 5% to 35% of procedures

Declining sales of Infuse (BMP2) – FDA warning and safety concerns

- ▶ Phase IIA proof-of-concept
- ▶ 16 patients with symptomatic lumbar degenerative disc disease, requiring a spinal fusion procedure
- ▶ Objectives: safety & efficacy (functional disability and fusion)
- ▶ Duration: 12 months follow-up



***Before procedure***



***21 months***



# PHASE IIA ALLOB® SPINAL FUSION TRIAL

**Local administration of ALLOB®**  
intended to promote faster & better  
bone formation in lumbar interbody  
fusion



## ALLOB®



## Standard-of-Care

Interbody cages  
Bioceramic granules



- ▶ Standard-of-care surgical approach combining cage and bioceramic granules/ALLOB® mix
- ▶ Add-on to standard-of-care
- ▶ Single application
- ▶ **75% of patients treated**
- ▶ **No safety issues** reported

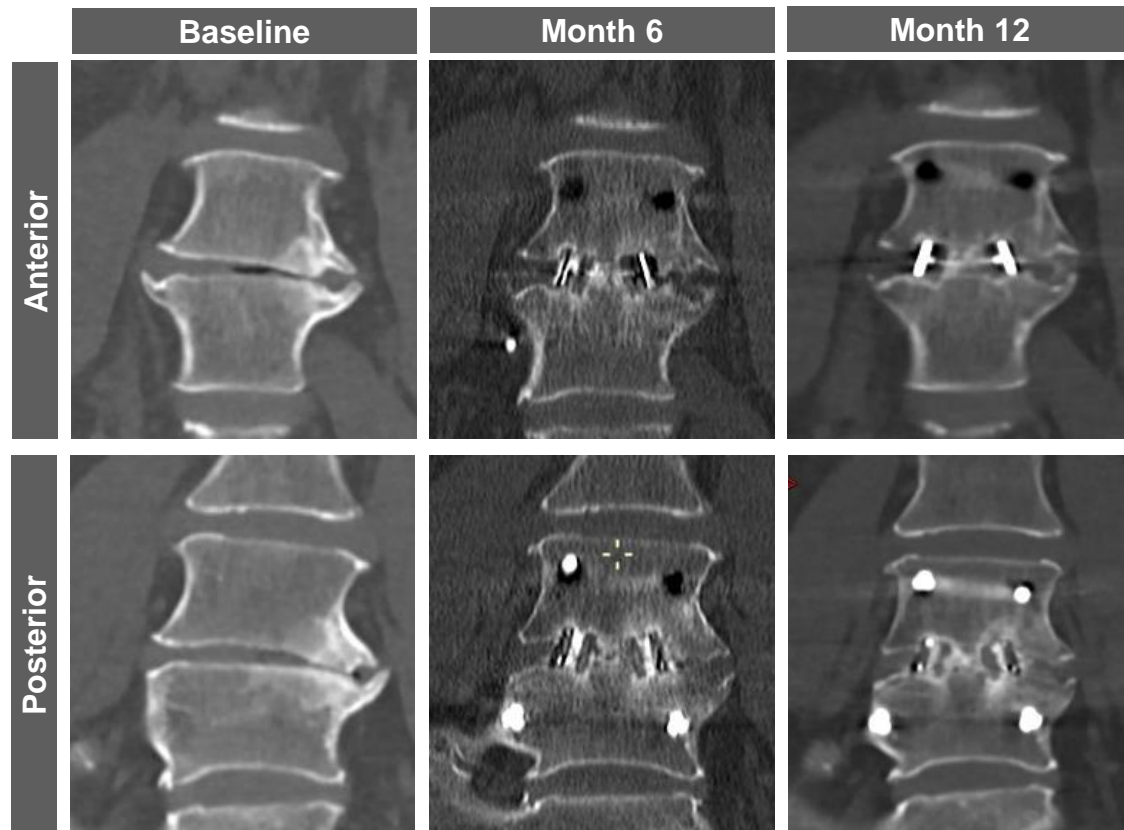
# PHASE IIA ALLOB<sup>®</sup> SPINAL FUSION TRIAL

## Highlights

- 75% of patients treated
- No safety issues reported
- Positive preliminary results of first patient:
  - Back and leg pain relief
  - Promotion of interbody fusion:

*Evidence of fusion as from 6 months*

*Dynamic x-rays show no motion at 12 months*

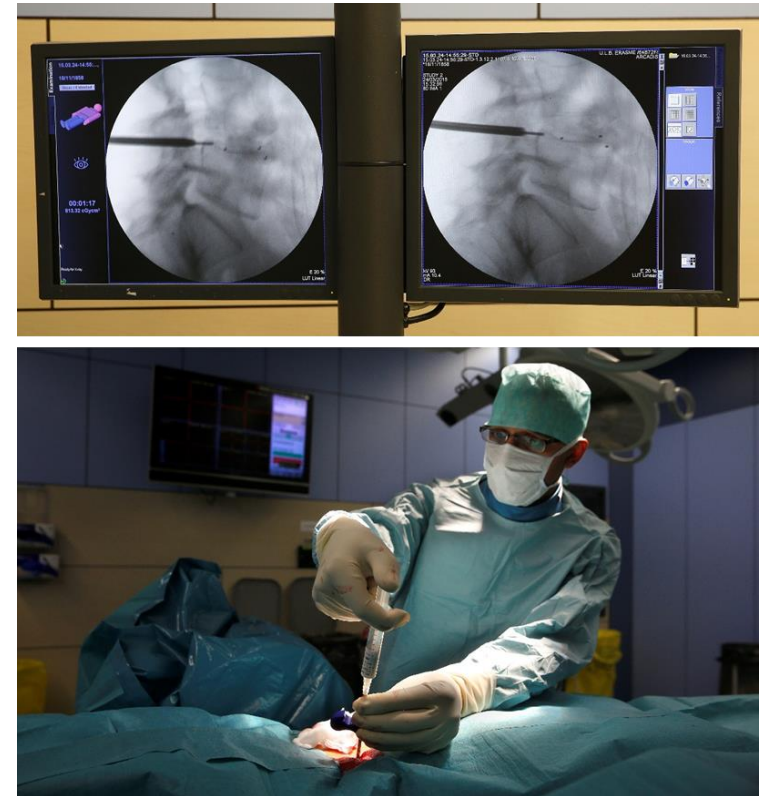


# PHASE IIA ALLOB<sup>®</sup> RESCUE SPINAL FUSION TRIAL

Up to 25% failure after initial spinal fusion surgery with non-union and persistent pain

Standard-of-care revision surgery: open, additional difficulties and associated with complications

- ▶ Phase IIA, open, multicentre, proof-of-concept
- ▶ Single minimally invasive (percutaneous) implantation into the failed fusion site
- ▶ 16 patients with a failed lumbar spinal fusion (15 months after the initial fusion procedure)
- ▶ 12-month study follow-up
- ▶ Study endpoints: clinical symptoms (pain & disability) and radiological healing



22 June 2015:

## **Bone Therapeutics reports first results of its Phase IIA trial for PREOB<sup>®</sup> in severe osteoporosis**

**Preliminary results show migration of intravenously injected  
cells to the bones and no treatment-related safety concerns  
reported in first patient cohort**

29 March 2016:

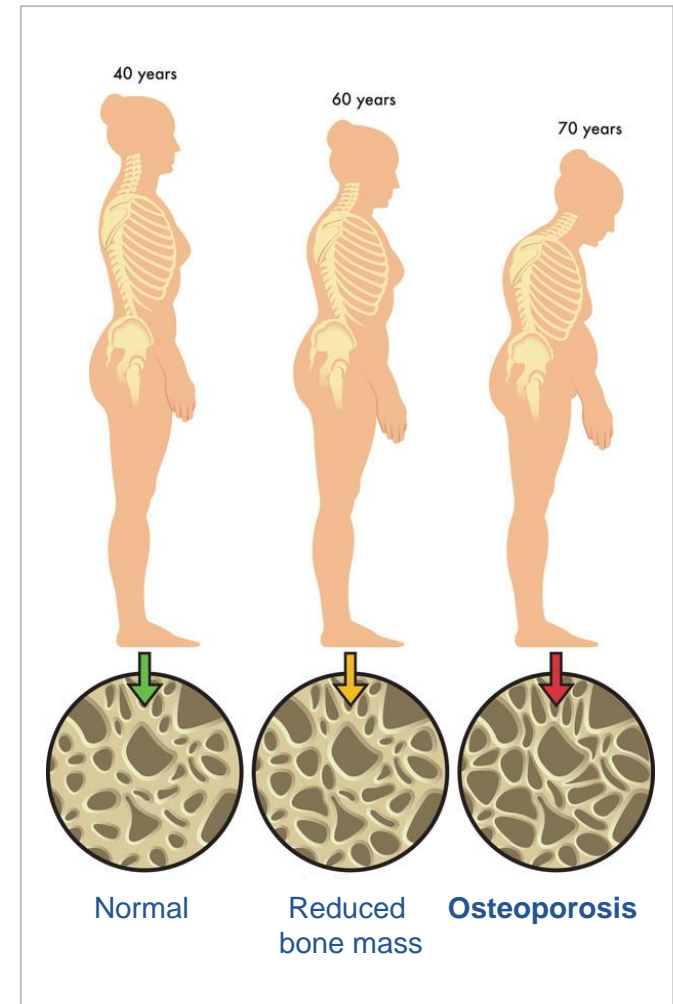
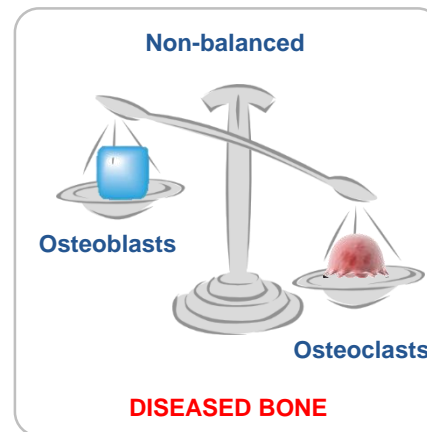
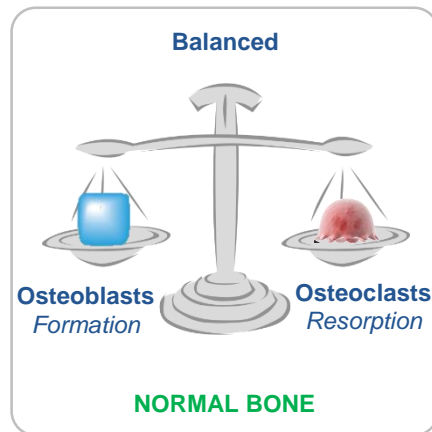
## **Bone Therapeutics reports initial efficacy results from its PREOB<sup>®</sup> Phase IIA trial in severe osteoporosis**

**Positive effects on pain and bone turnover markers in first  
patient cohort**

# PHASE IIA PREOB<sup>®</sup> OSTEOPOROSIS TRIAL

## Severe osteoporosis

- Excessive loss of bone mass due to an imbalance in bone formation and bone resorption
- Bone fragility and increased risk of fractures
- Up to 30% of osteoporosis patients do not respond adequately to currently available treatments (severe osteoporosis)<sup>1</sup>
- Existing treatments predominantly inhibit bone resorption<sup>2</sup>



# PHASE IIA PREOB<sup>®</sup> OSTEOPOROSIS TRIAL

## Phase IIA proof-of-concept

- Patients suffering from severe osteoporosis not responding to anti-osteoporotic treatment (i.e., losing bone mass)
- Single intravenous administration of PREOB<sup>®</sup>
- Objectives: to determine
  - (i) the safety and distribution of PREOB<sup>®</sup> after intravenous infusion
  - (ii) the effects on clinical symptoms (i.e., pain and general health status)
  - (iii) the effect on serum markers of bone turnover
- In total, 20 patients will be enrolled
- 12-month follow-up

## PREOB<sup>®</sup>



## I.V. administration

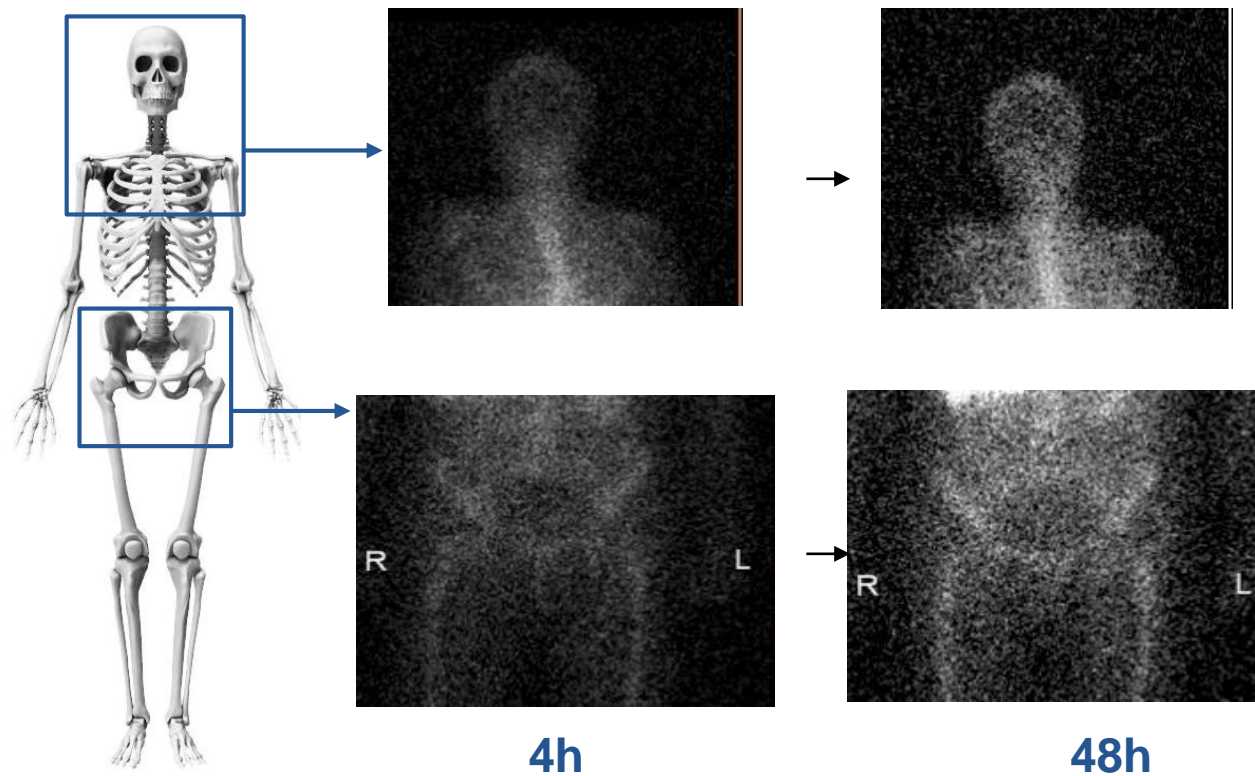




# PHASE IIA PREOB<sup>®</sup> OSTEOPOROSIS TRIAL

## Initial results of first cohort of seven patients after 12-month follow-up:

- Promising biodistribution data: migration towards the bones most prone to osteoporotic fractures
- No treatment-related safety concerns reported

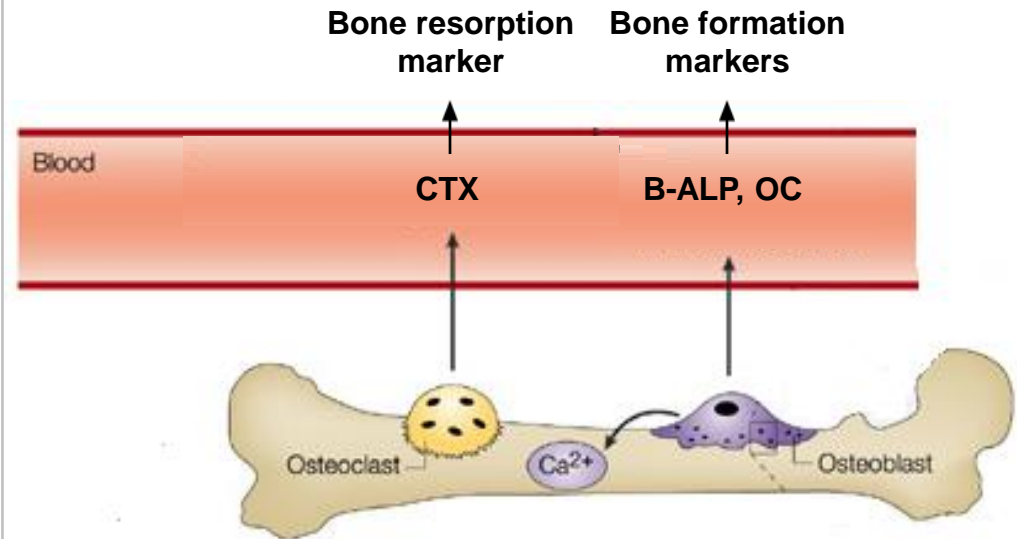


# PHASE IIA PREOB<sup>®</sup> OSTEOPOROSIS TRIAL

## Initial results of first cohort of seven patients after 12-month follow-up:

- Effect on clinical symptoms
  - Progressive, strong and clinically relevant pain relief (>40%, maximum at 6 months)
  - Improved general health status
- Effect on bone turnover markers: dual trend
  - (i) Early phase (of 12-month period): decrease bone resorption marker, unaffected or slightly increased bone formation markers
  - (ii) Later phase (of 12-month period): moderate increase bone resorption marker, continuous increase bone formation markers

## MEASUREMENT OF BONE TURNOVER IN THE BLOOD





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## **2015 CORPORATE & FINANCIAL HIGHLIGHTS AND UPCOMING CLINICAL NEWS**

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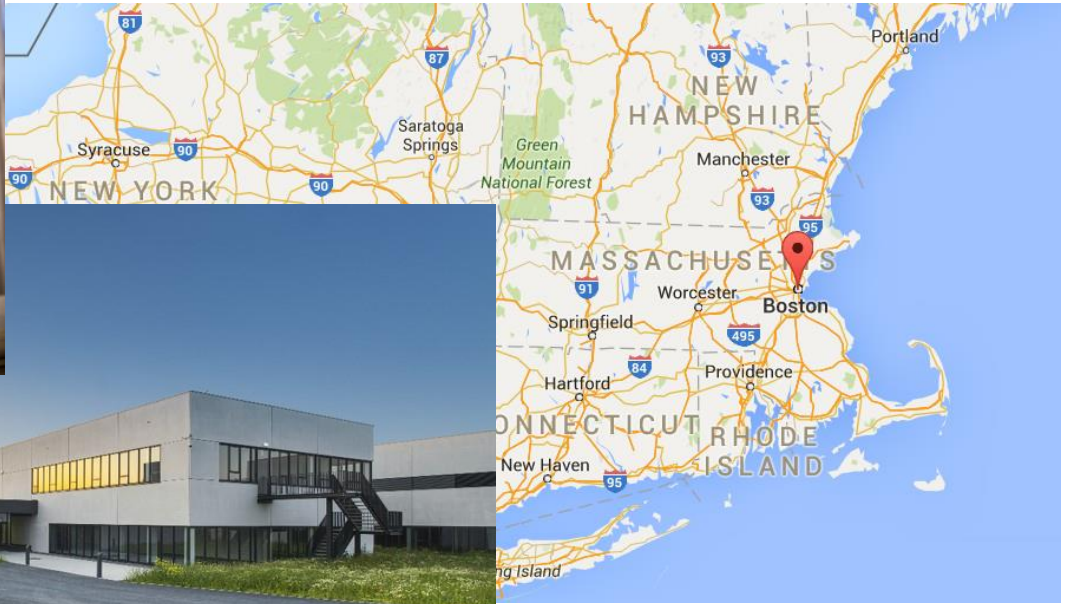
# CORPORATE & FINANCIAL HIGHLIGHTS

Established a **US subsidiary** in Boston and **new headquarters** at the Gosselies Biopark

Successful **€37M IPO** on Euronext Brussels and Euronext Paris

Awarded **€5M** in funding from the Walloon Region in 2015

Cash position at end of 2015 of **€33.6M**



# KEY FINANCIALS

<i>(€ million)</i>	<b>FY 2015</b>	<b>FY 2014</b>
<b>Operating income</b>	<b>3.82</b>	<b>3.68</b>
<b>Operating expenses</b>	<b>(16.05)</b>	<b>(9.30)</b>
R&D expenses	(12.91)	(7.96)
G&A expenses	(3.14)*	(1.35)
<b>Operating result</b>	<b>(12.22)</b>	<b>(5.63)</b>
<b>Net financial result</b>	<b>(1.80)</b>	<b>(0.19)</b>
<b>Net result</b>	<b>(14.09)</b>	<b>(5.81)</b>
<b>Net cash flow</b>	<b>22.04</b>	<b>9.14</b>
Operating activities	(11.77)	(3.52)
Investing activities	(2.98)	(3.00)
Financing activities	36.78	15.67
<b>Cash position</b>	<b>33.61</b>	<b>11.58</b>

\* Including € 1.06 million of IPO costs

# UPCOMING CLINICAL NEWS

Indication	Phase	Platform	Actions	2015					2016				2017			
				Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Non-Union	IIB/III	PREOB®	Study status for Interim/DSMB													
			<b>Launch of US clinical trial</b>	✓												
			<b>Efficacy 4 patients</b>			✓										
Delayed-Union	I/IIA	ALLOB®	Safety 8 patients													
			<b>Efficacy 8 patients</b>													
			Safety 12 patients													
Osteonecrosis	III	PREOB®	<b>Efficacy 12 patients</b>													
			Site update													
			Study status for Interim/DSMB													
Osteoporosis	IIA	PREOB®	<b>Launch of US clinical trial</b>													
			Safety 8 patients			✓										
			<b>Efficacy 8 patients</b>													
Spinal Fusion	IIA	ALLOB®	Safety 16 patients													
			Safety 4 patients		✓											
			Safety 8 patients													
Revision Spinal Fusion	IIA	ALLOB®	Safety 12 patients													
			<b>Efficacy 4 patients</b>													
			<b>Efficacy 8 patients</b>													
Revision Spinal Fusion	IIA	ALLOB®	Initiation of study													
			Safety 4 patients			✓										
			Safety 8 patients													
			<b>Efficacy 4 patients</b>													



**Enrico BASTIANELLI, MD, MBA**  
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**Wim GOEMAERE, MAE**  
Chief Financial Officer

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Wallonie

