# *Annual Results 2016*

***16 March 2017***

Bone Therapeutics

***New frontiers in orthopaedic and bone diseases***

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# AGENDA

- Welcome and introduction
- 2016 at a glance: key highlights and financials
- 2016 highlights
  - Strong progress in ALLOB® programmes
  - Validation Bone Therapeutics' cell therapy approach by PREOB®
- Strategy and outlook 2017
- Q&A



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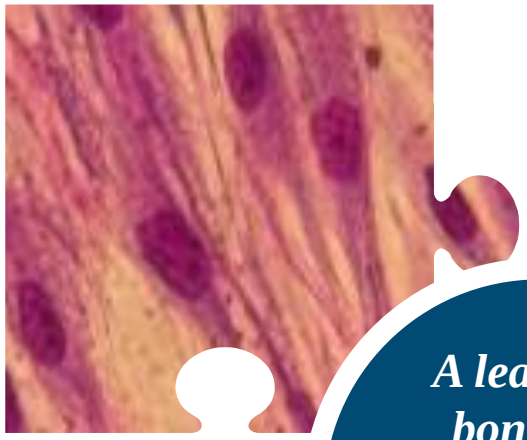
# INVESTMENT HIGHLIGHTS

1

**UNIQUE TECHNOLOGY**
DIFFERENTIATED CELLS & MINIMALLY INVASIVE



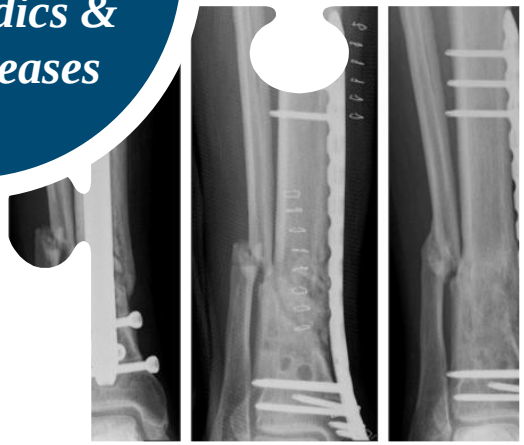
2

**BROAD AND DIVERSIFIED PIPELINE**
(MULTIPLE INDICATIONS)

***A leader in bone cell therapy for orthopaedics & bone diseases***

4

**AHEAD OF COMPETITION IN ITS MARKETS**
(ONLY COMPANY IN PHASE III)



3

**MARKETS WITH SIGNIFICANT UNMET MEDICAL NEEDS**



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# KEY HIGHLIGHTS 2016

**Pipeline**

- Streamlined strategic priorities with **primary focus** on **allogeneic pipeline**
- **Strong progress** in clinical development of allogeneic platform **ALLOB®**
  - Delayed Union
    - Positive safety & efficacy results for first 8 patients in ALLOB® in Phase I/IIA trial
    - 16 patients for interim analysis recruited and safety confirmed by Monitoring Committee (pp)
  - Spinal fusion
    - Completed patient recruitment for interim analysis for ALLOB® Phase IIA study
    - Preliminary positive safety and efficacy data for first 8 of 16 patients
- Further demonstration of **clinical potential** of Bone Therapeutics' bone cell therapy products in autologous PREOB® programmes
  - Osteonecrosis
    - Demonstrated superiority of PREOB® in Phase IIB study (presented at EULAR)
  - Osteoporosis
    - Preliminary beneficial effects on pain and blood markers following administration of PREOB®
    - Open to partnership for the development of an allogeneic approach

**Financial**

- **Cash** at end of 2016: **€20.3M** (giving runway into Q2 2018)

**Corporate**

- **Strengthening** of the **management team:** Thomas Lienard (CEO), Benoît Champluvier (CTMO) and Miguel Forte (CMO) (pp)



pp: post period

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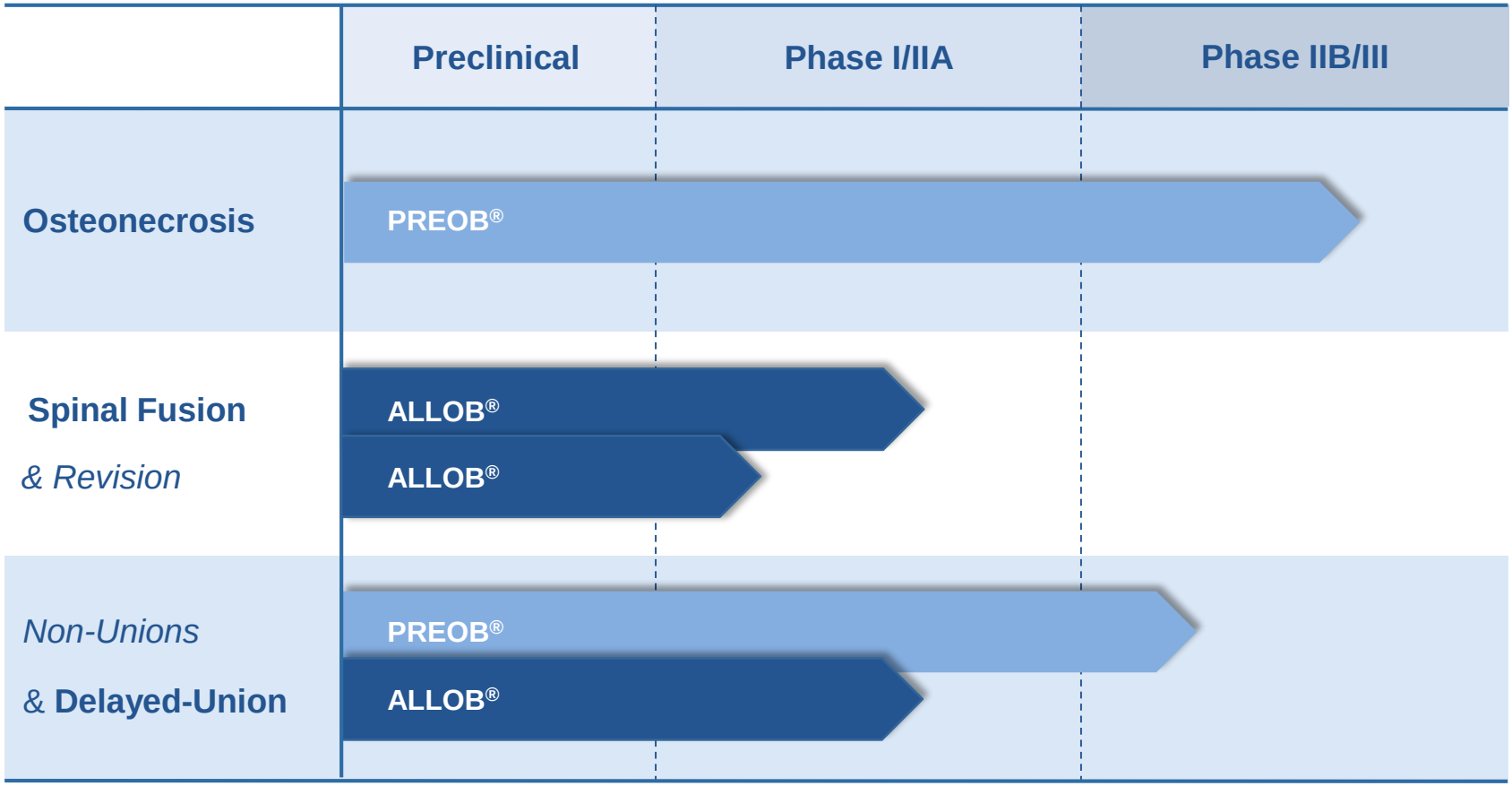
# ADVANCED AND DIVERSIFIED PIPELINE



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# FINANCIAL HIGHLIGHTS 2016

| *(€ million)* | FY 2016 | FY 2015 |
|---|---|---|
| **Operating income** | **4.01** | **3.82** |
| **Operating expenses** | **(16.81)** | **(16.05)** |
| R&D expenses | (13.65) | (12.91) |
| G&A expenses | (3.16) | (3.14)[1] |
| **Operating result** | **(12.80)** | **(12.22)** |
| **Net financial result** | **(0.28)** | **(1.80)** |
| **Net result** | **(13.02)** | **(14.09)** |
| **Net cash flow** | **(13.31)** | **22.04** |
| Operating activities | (11.37) | (11.77) |
| Investing activities | (0.58) | (2.98) |
| Financing activities | (1.36) | 36.78 |
| **Cash position** (at 31 Dec) | **20.30** | **33.61** |

[1] *Including € 1.06 million of IPO costs*

# 2016 HIGHLIGHTS

# SKILLED MANAGEMENT TO TAKE COMPANY FORWARD

**Nora Meskini**
***Director Clinical Operations***

**Miguel Forte, MD, PhD**
***Chief Medical Officer***

**Thomas Lienard**
***Chief Executive Officer***

**Wim Goemaere**
***Chief Financial Officer***

**Benoit Champluvier, PhD**
***Chief Technology & Manufacturing Officer***

**Guy Heynen, MD**
***Chief Clinical & Regulatory Officer***

- Significant expansion of leadership team over past 2 years
- Skills and industry expertise to take Bone Therapeutics through to commercialisation of first products
- Focus on clinical, regulatory, business development and manufacturing

June 2016

## Benoît Champluvier, PhD

***Chief Technology & Manufacturing Officer***

- 20y experience in driving innovation and complex bioprocesses
- Formerly Director Downstream Process Technology, Coordinator New Technologies & GMP Pilot Plant at GlaxoSmithKline Vaccines

October 2016

## Thomas Lienard

***Chief Executive Officer***

- 15y of international sales and marketing experience in pharmaceutical industry
- Formerly Managing Director BeLux at Lundbeck, Sales Director BE at Eli Lilly, Consultant at McKinsey & Company

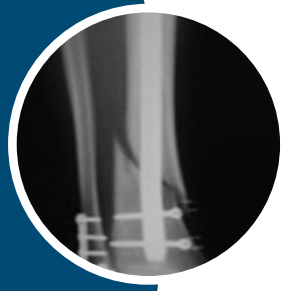
March 2017

## Miguel Forte, MD, PhD

***Chief Medical Officer***

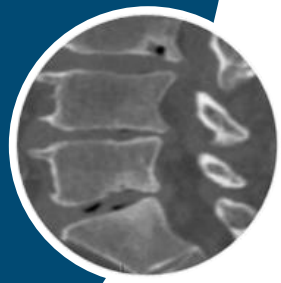
- 20y experience in medical and regulatory affairs, and regenerative medicine
- Formerly Chief Operating and Medical Officer at TxCell, Global Vice President Medical Affairs of UCB, senior positions at EMA, BMS and GSK
- Chief Commercialization Officer and Chair Commercialization Committee ISCT

# STRONG PROGRESS IN CLINICAL DEVELOPMENT OF THE ALLOGENEIC PLATFORM ALLOB®



## DELAYED UNION FRACTURES

**Promising results for ALLOB® Phase IIA**



## SPINAL FUSION

**Promising results for ALLOB® Phase IIA**



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# DELAYED UNION FRACTURES

## Promising results for ALLOB® Phase IIA

**15 May 2016:** **Bone Therapeutics announces further positive efficacy in ALLOB® Phase I/IIA delayed-union fracture trial**

Seven out of eight patients met primary endpoints

Overall 77% radiological and 68% clinical improvement demonstrated

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**9 March 2017:** **Bone Therapeutics completes recruitment of 16 patients in ALLOB® Phase I/IIA delayed-union study**

Last patient for interim analysis treated end of February

Results interim data analysis expected in September 2017



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# DELAYED UNION – SUCCESS IN 7 OUT OF 8 PATIENTS

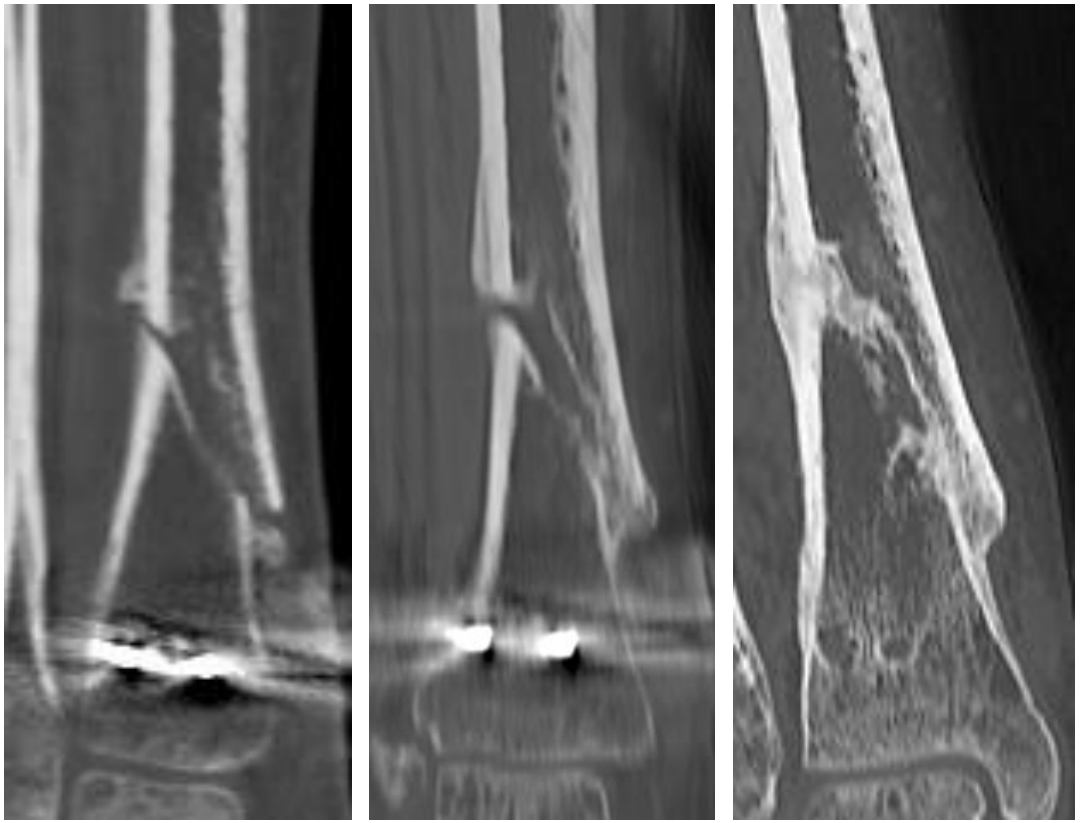
**Phase I/IIA proof-of-concept delayed-union open study**

No safety issues on 8 first patients

Positive results at 6 months:

- 7 out of 8 patients met primary endpoints
- 77% radiological improvement
- 68% improvement in pain

| Baseline | Month 3 | Month 6 |
|---|---|---|





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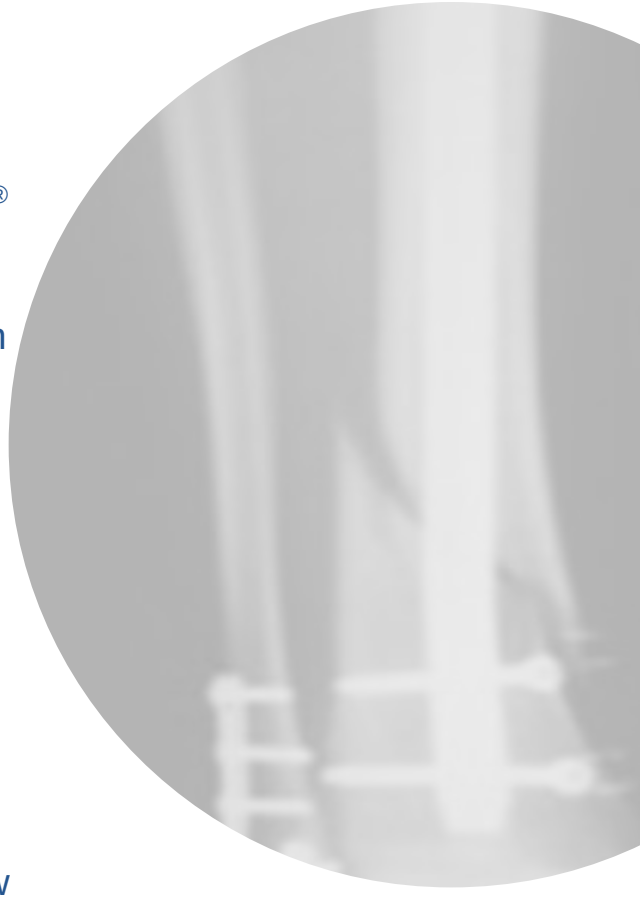
# DELAYED UNION – PROMISING RESULTS FOR ALLOB® PHASE IIA

**STATUS**

- Phase I/IIA trial ongoing – Continuous follow-up of safety and efficacy
- All patients received one single injection of ALLOB® at bone defect site
- 7 out of 8 first patients met primary endpoints within 6 months
- Recruitment 16 patients for interim analysis completed (9 March 2017)
- Safety Monitoring Committee confirms safety of treatment for the 16 patients (14 March 2017)



**NEXT STEPS**

- Interim data analysis planned for September 2017
- Positive efficacy data at interim analysis could allow to accelerate into next stage of clinical development



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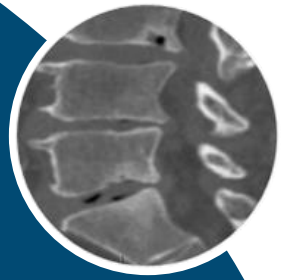

# SPINAL FUSION

## Promising results for ALLOB® Phase IIA

**17 February 2016:** Bone Therapeutics treats 12 patients without safety concerns in ALLOB® Phase IIA spinal fusion trial

Recruitment almost complete with four patients left to treat

**24 February 2016:** Bone Therapeutics presents ALLOB® 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

**3 May 2016:** Bone Therapeutics completes recruitment of its ALLOB® Phase IIA spinal fusion study

Trial extended to assess early onset and dynamics of fusion process

**5 October 2016:** Bone Therapeutics reports positive efficacy data for the ALLOB® Phase IIA spinal fusion trial

Study follow-up completed for 50% of patients

All primary and secondary radiological and clinical endpoints met



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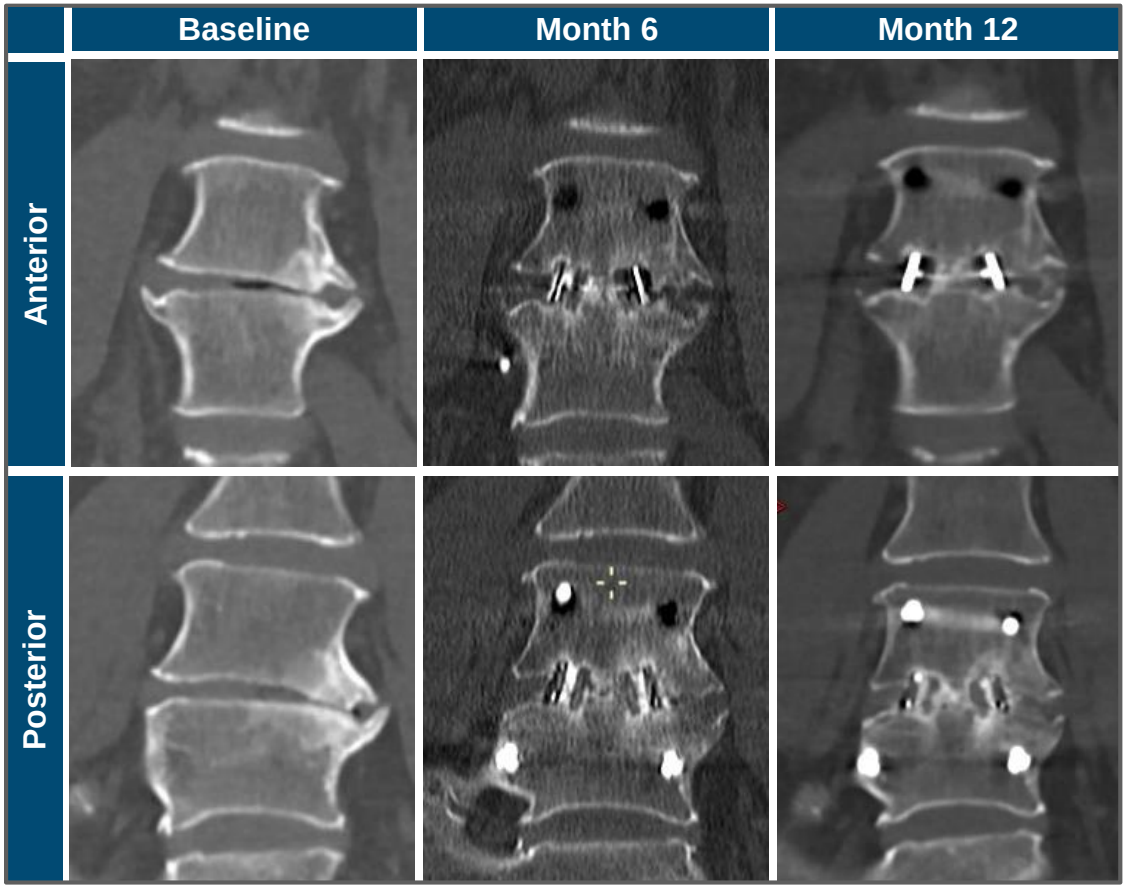
# SPINAL FUSION - POSITIVE PRELIMINARY PHASE IIA RESULTS

**Phase IIA proof-of-concept and recruitment completed without safety issues**

**Positive efficacy results of first 8 patients** (as from month 6):

- 33% improvement in functional disability score at 6 months and 40% at 12 months
- Back (50%) and leg (80%) pain improved dramatically as from month 6
- General health status improved 50% at 6 months and was maintained
- No vertebral motion on dynamic x-rays & radiological signs of fusion on CT scan



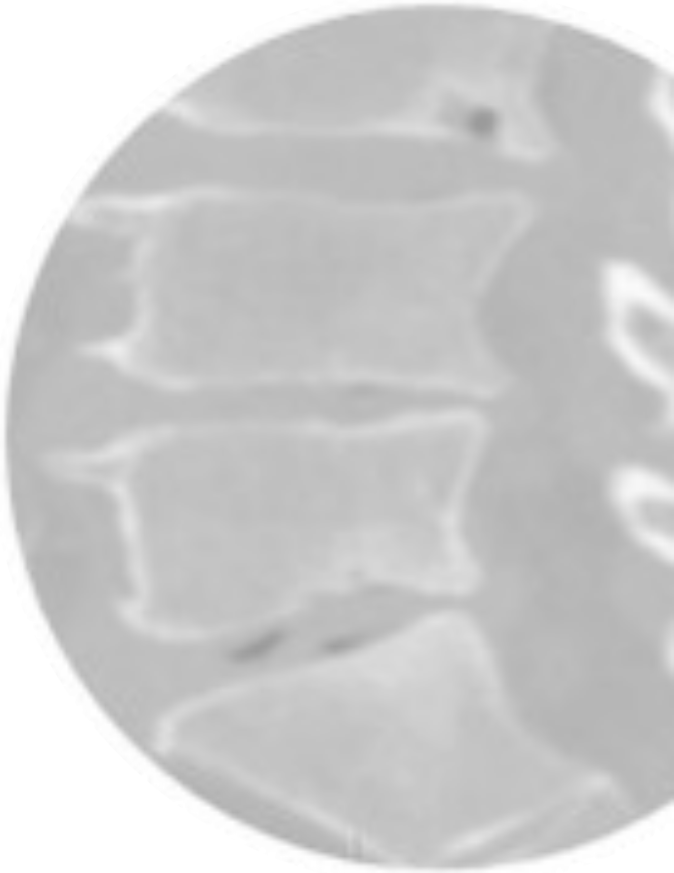
# SPINAL FUSION - PROMISING RESULTS FOR ALLOB® PHASE IIA

**STATUS**

- Phase IIA (non-controlled) ongoing
- 16 patients treated – results from full set of 8 first patients communicated Oct. 2016
- No treatment-related safety concerns
- Trial extended to 32 patients

**NEXT STEPS**

- Results from 16 patients expected summer 2017
- Development in US under evaluation subject to positive Phase IIA results





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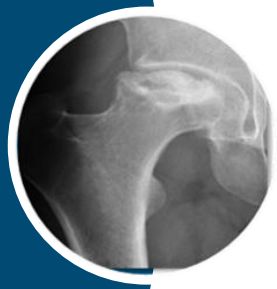
# FURTHER DEMONSTRATION OF CLINICAL POTENTIAL OF BONE THERAPEUTICS' BONE CELL THERAPY PRODUCTS IN PREOB® OSTEONECROSIS PROGRAMME



## OSTEONECROSIS

**Validating Bone Therapeutics' bone-forming cell therapy**



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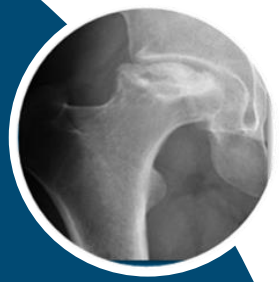

# OSTEONECROSIS

## Validating Bone Therapeutics' bone-forming cell therapy

**8 June 2016:** **Bone Therapeutics demonstrates superiority of PREOB® in Phase IIB osteonecrosis study presented at EULAR**

**Statistically significant superiority of PREOB® over standard of care in osteonecrosis treatment**

**50% reduction in hip fracture risk**

**Significant reduction in hip pain (50%) and significant improvement of hip function (45%)**



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# OSTEONECROSIS – PROMISING PHASE IIB (FINAL RESULTS)

**Reference-controlled Phase IIB trial with PREOB®** in early-stage osteonecrosis of the femoral head

**Method:** Core decompression and PREOB®/bone marrow concentrate (BMC)

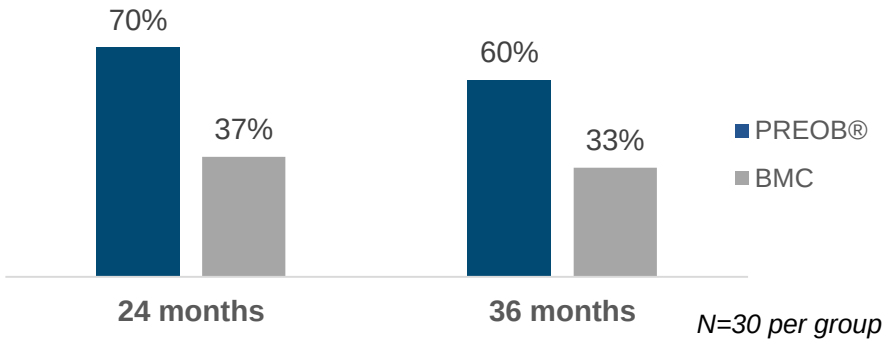
**Number of patients:** 63 hips treated, of which 60 were assessable* and included in the analyses (PREOB® n=30, BMC n=30)

**Primary endpoints:** proportion of responders at 24 months, defined as

- Absence of progression to fractural stage
- And clinically significant (>10mm) pain improvement

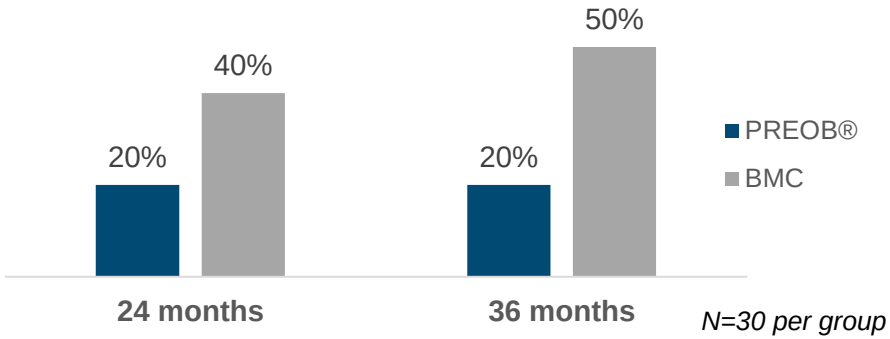
Ref: Gangji et al., Poster presented at EULAR, 2016

## Responders

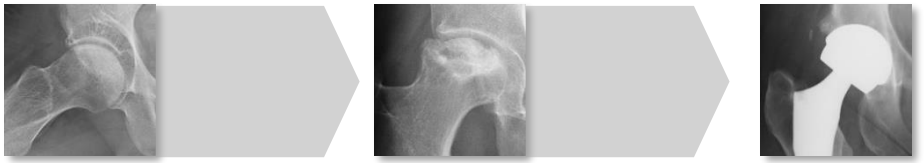



*N=30 per group*

## Progression to fracture




*N=30 per group*



**Prefractural stage** | **Fracture & collapse** | **Prosthesis**

** 3 hips were not included in the analysis as, upon treatment, it was discovered that these hips had already evolved to stage III osteonecrosis*

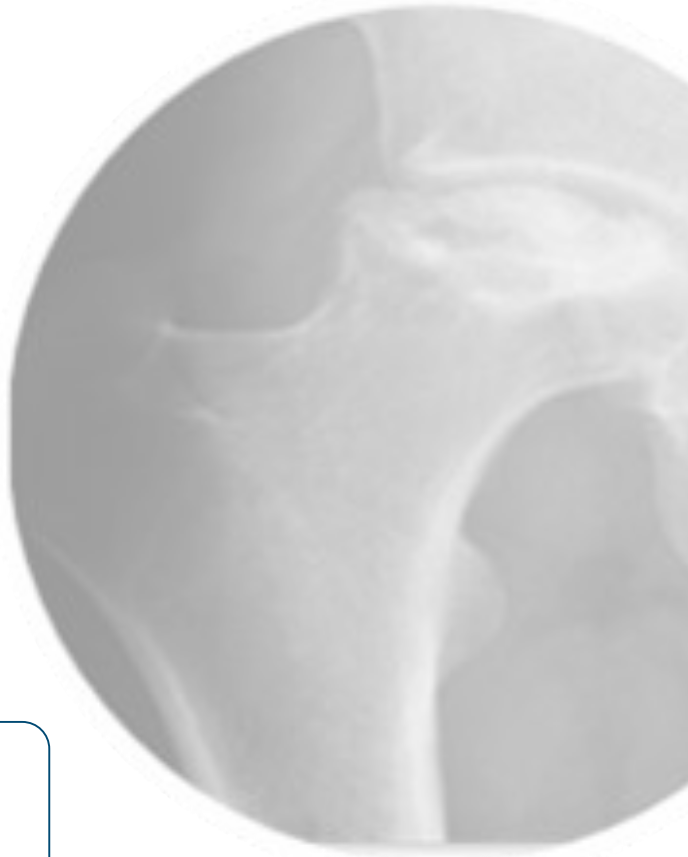
# OSTEONECROSIS – BONE-FORMING CELL THERAPY PRODUCT VALIDATION

**STATUS**

- Most advanced clinical program (Phase III)
- Currently recruiting patients: 130 patients in 1-to-1 vs placebo
- Primary endpoints: absence of progression to fractural stage & clinically significant pain improvement

**NEXT STEPS**

- Recruitment update
- DSMB report (1 year following completion 1st cohort)



***On completion Phase III:***

- ***External validation of Bone Therapeutics' bone forming cell therapy products***
- ***1st potential product to market***



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# STRATEGY & OUTLOOK 2017

# STRATEGY TO MAXIMISE VALUE CREATION

## Focus on:

The **allogeneic platform ALLOB®:**

- A therapeutically attractive bone regenerative solution:
  - ✓ Industrial: scalable, cost-effective, off-the-shelf cell therapy product solution
  - ✓ Commercial: suited for larger markets
  - ✓ Business development: more attractive to partners
- Europe: maintain high-level investments in ALLOB® clinical programs
- US: prioritising clinical development of ALLOB®

Delivering **Phase III clinical trial data in osteonecrosis with PREOB®** to bring **1st potential commercial product** to market

- Demonstrating and confirming high added value of Bone Therapeutics' bone-forming cell therapy products
- Propelling the company into commercialisation stage



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# BUSINESS DEVELOPMENT & PARTNERING STRATEGY

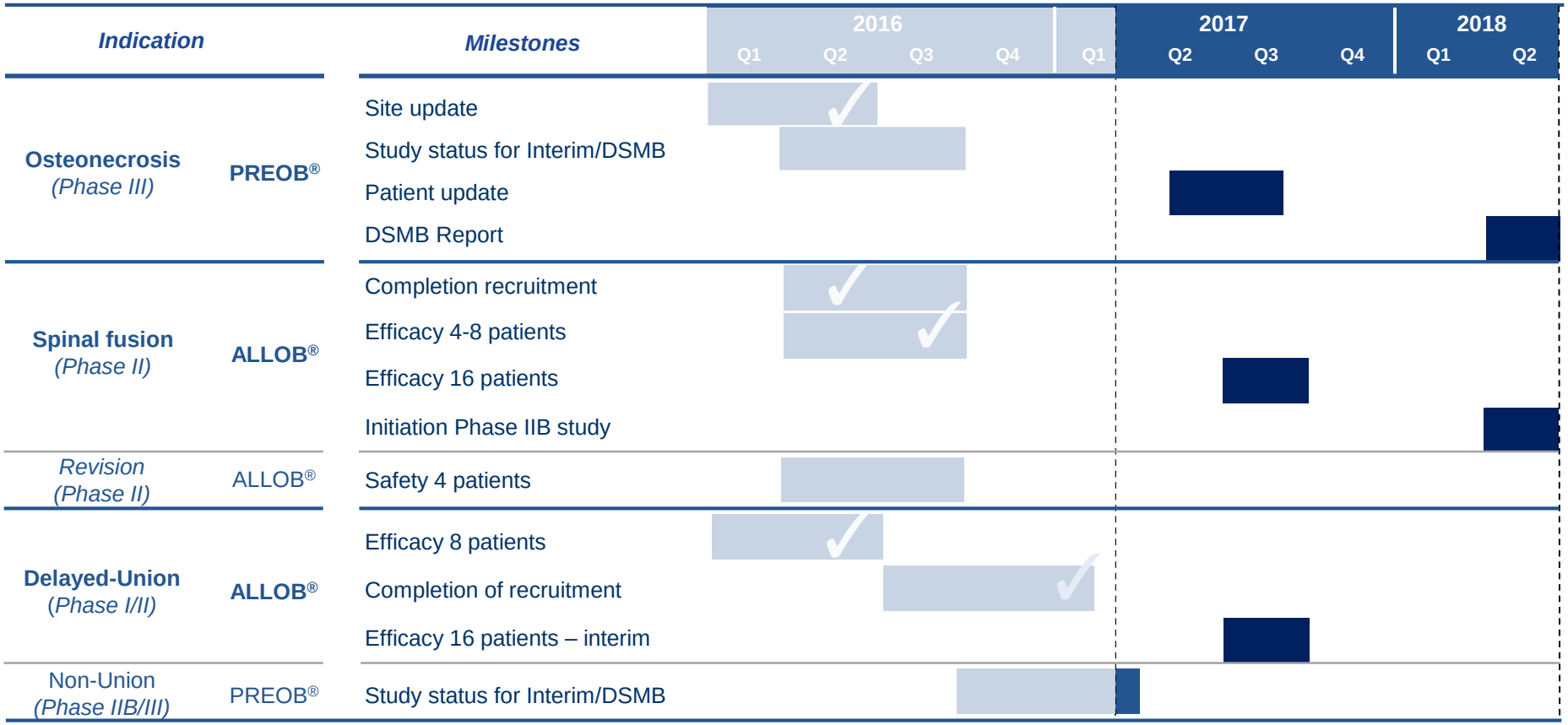
- Stand-alone development in EU – commercial partnership for going to market
- Partnership in the US for co-development and commercialisation
- Licensing of portfolio in Japan and SE Asia

# OUTLOOK 2017

- **Clinical results**
  - Results interim data analysis for the first 16 patients in the Phase I/IIA ALLOB® **delayed-union** trial
  - Results interim data analysis for the first 16 patients in the Phase IIA **spinal fusion** trial with ALLOB®
  - Recruitment update for Phase III **osteonecrosis** trial, now ongoing in five European countries

- **Finance**
  - Good cash management remains a key priority
  - Strong focus on net cash burn (expected to be in the range of EUR 15 million for 2017)
  - Sufficient cash to carry out its strategic objectives into Q2 2018 in line with earlier guidance

# UPCOMING CLINICAL NEWS



# SUMMARY

**Unique** bone cell **Technologies** targeting unmet needs in orthopaedics and bone diseases

**Minimally Invasive** approach with significant benefits over current standard of care

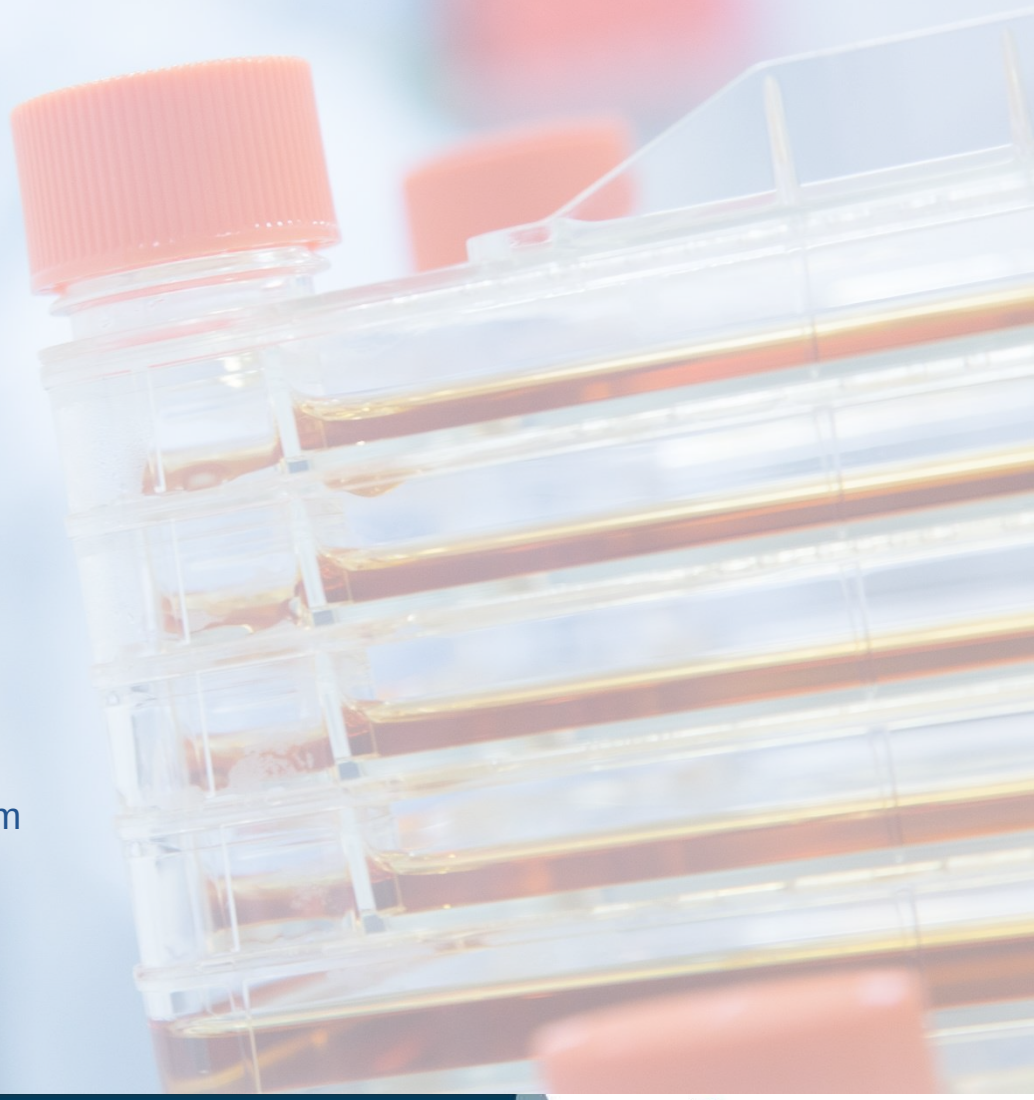
Lead products in **Advanced Clinical Trials** with potential in multiple indications

Multiple **Near-term Data Catalysts** including spinal fusion and delayed union fracture

**Experienced Management Team** focused on clinical development

Headquarters in Belgium, listing on **Euronext Paris & Brussels**

# Questions




**Contact:** **Thomas LIENARD**
Chief Executive Officer

**Wim GOEMAERE**
Chief Financial Officer

Phone: +32 (0)2 529 59 90

Fax: +32 (0)2 529 59 93

E-mail: info@bonetherapeutics.com

Website: www.bonetherapeutics.com


Wallonie



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# OVERVIEW OF THE TECHNOLOGY



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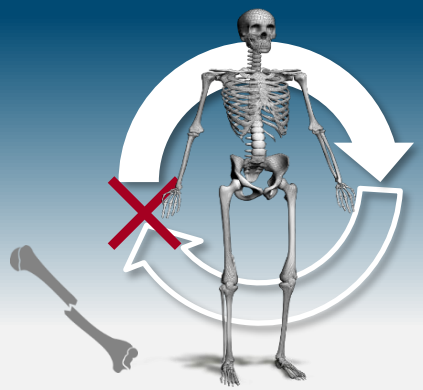
# BONE THERAPEUTICS: A GAME CHANGER IN ORTHOPAEDICS

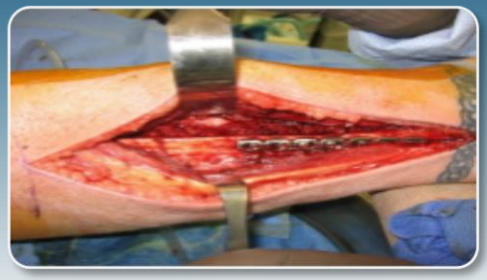
**SKELETON**

A naturally regenerative system



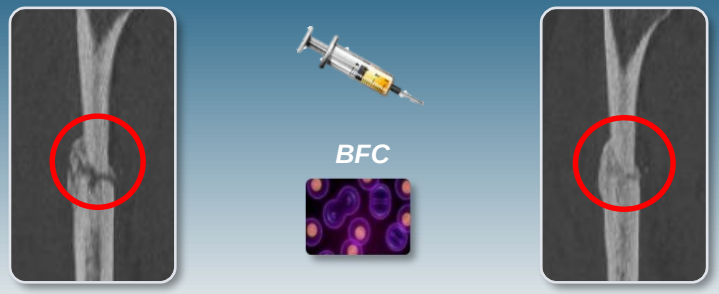
Impaired in orthopaedic conditions and bone diseases

## STANDARD ORTHOPAEDIC APPROACHES



- Highly invasive
- Long Recovery
- Limited efficacy

## CELL THERAPY




- **Bone-forming cells** (BFC)
- **Minimally invasive**
- **Potential in multiple indications**



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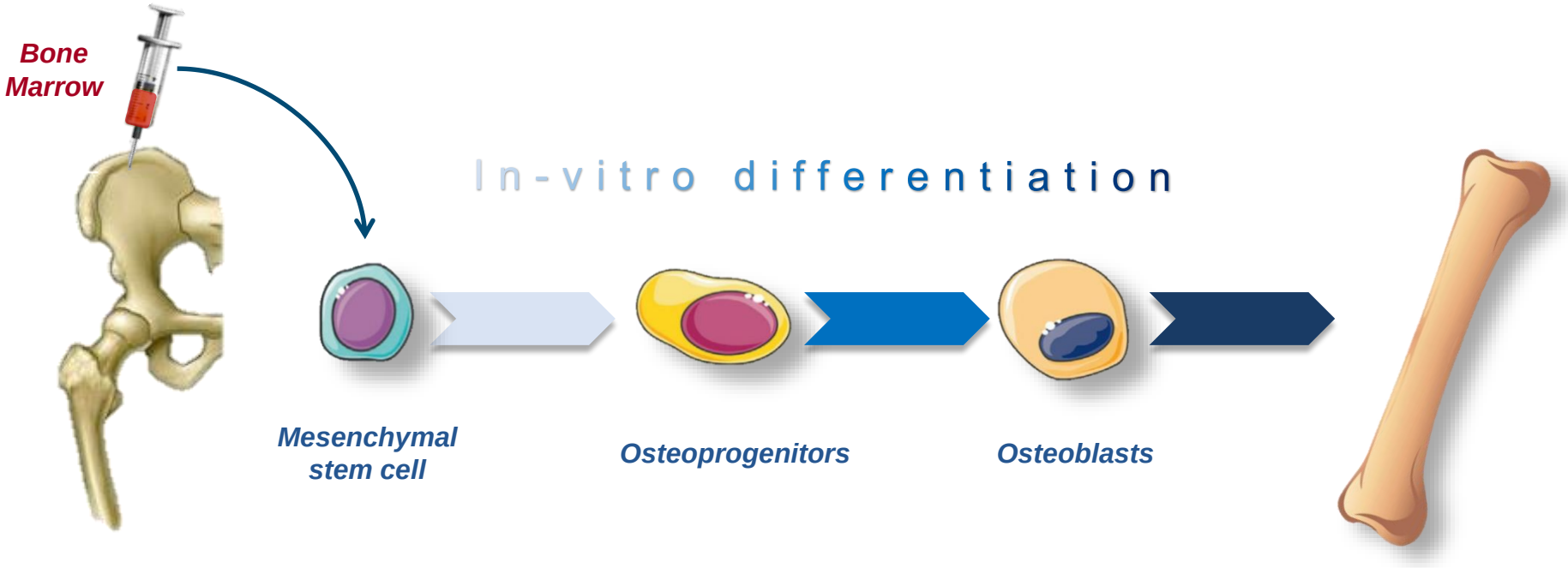
# BY THE UNIQUE USE OF DIFFERENTIATED BONE-FORMING CELLS




**Advantages:**

- *MORE POTENT* - Faster and better bone-forming capacity
- *SAFER* - No unwanted cell types or no unwanted activity



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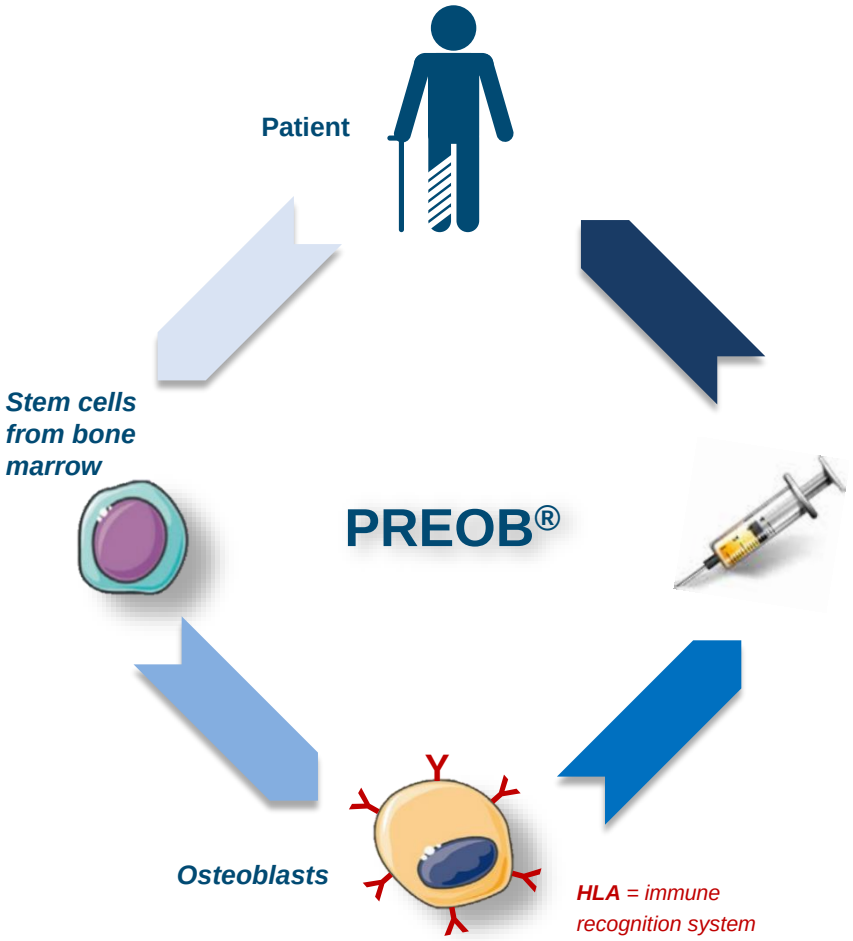
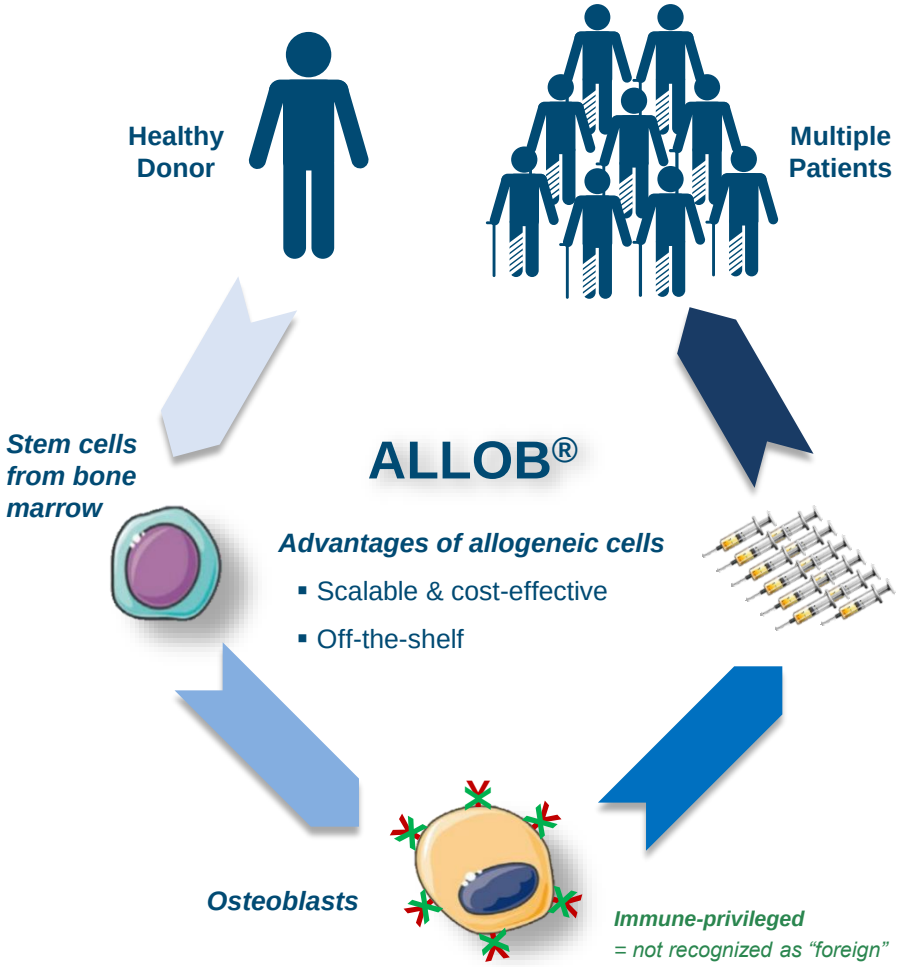
# UNMATCHED EXPERTISE IN MANUFACTURING OSTEOBLASTS

## PREOB®
*Autologous bone cell therapy*




## ALLOB®
*A scalable allogeneic solution*



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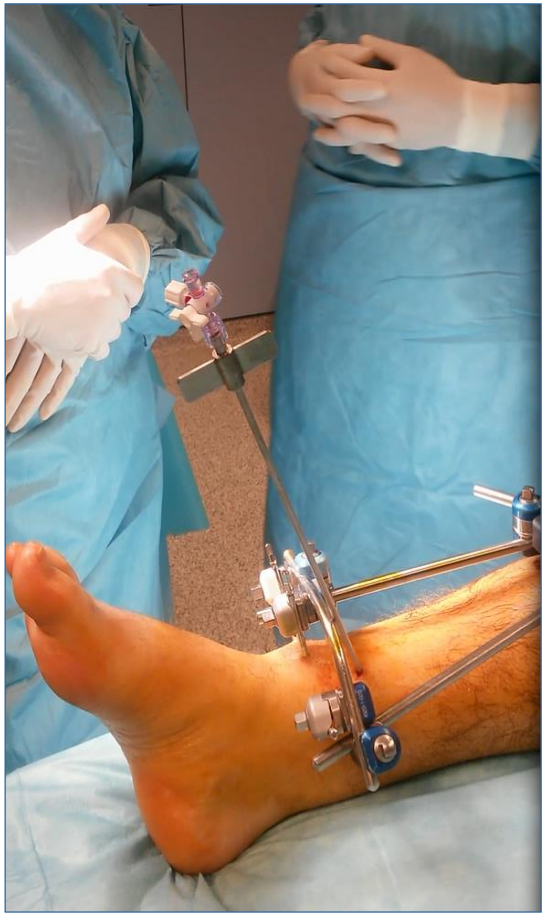
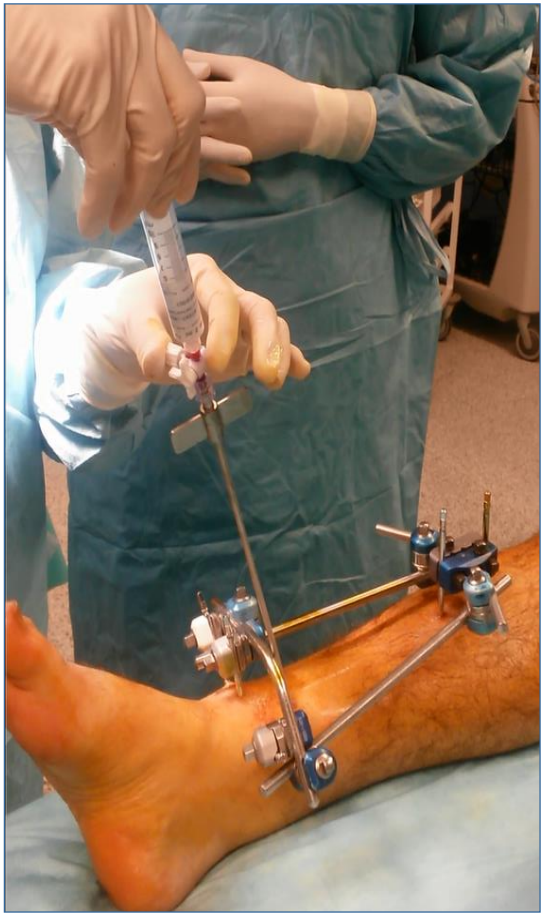
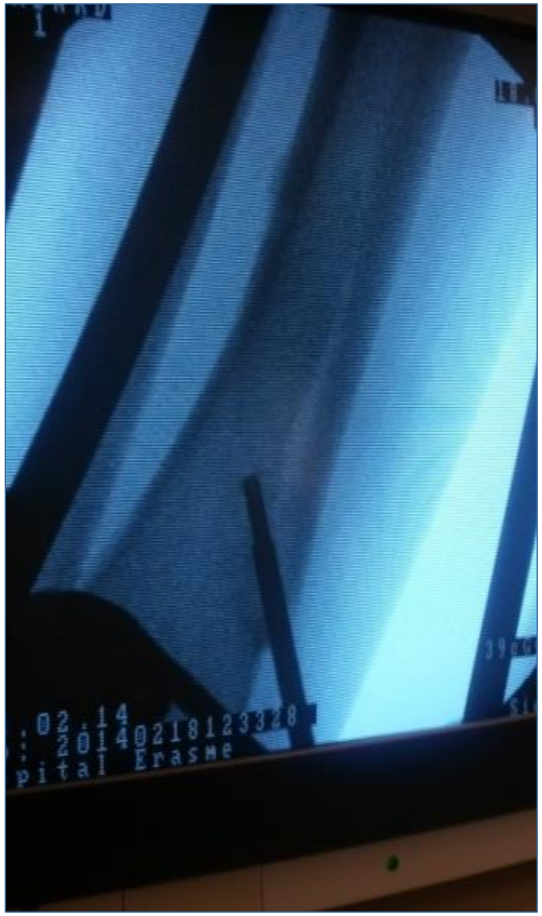
# MINIMALLY INVASIVE ADMINISTRATION

*Single percutaneous implantation into fracture site: simple & fast procedure*
*one-day clinic - no open surgery*









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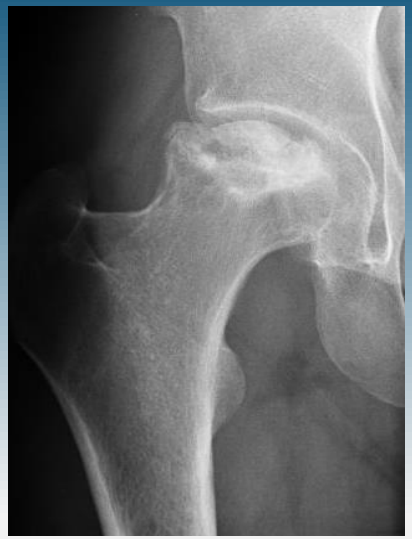
# OUR PORTFOLIO

# BONE CONDITIONS WITH HIGH UNMET MEDICAL NEEDS

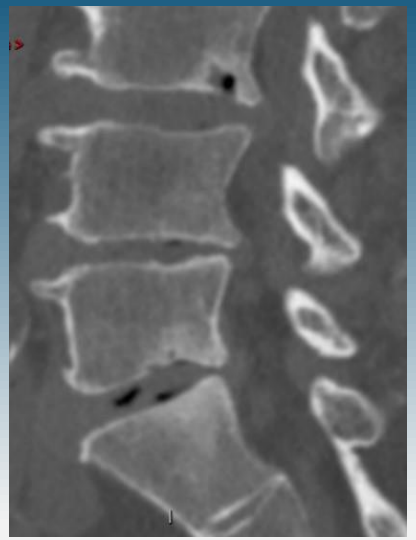
## DEGENERATIVE HIP DISORDERS



**Osteonecrosis**

**~0.15M patients p.a.**

## DEGENERATIVE SPINE DISEASES

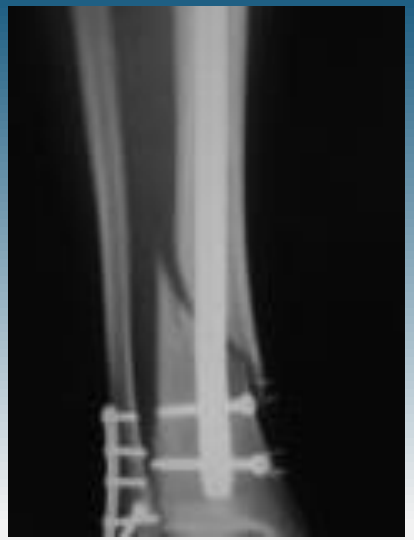


**Spinal fusion ***

***Revision***

**~0.5M (0.12M) procedures p.a.**

## SEVERE UNHEALED FRACTURES



**Delayed-union**

***Non-union***

**~1M (0.3M) patients p.a.**

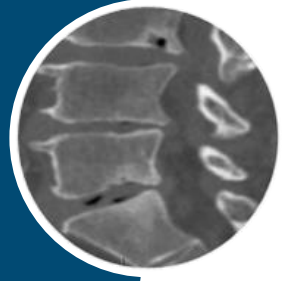


** Only lumbar spine fusion procedures*

# CLINICAL TRIALS IN PROGRESS

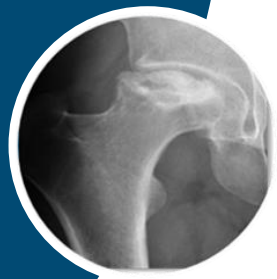
## DELAYED UNION FRACTURES

**Promising results for ALLOB® Phase IIA**



## SPINAL FUSION

**Promising results for ALLOB® Phase IIA**



## OSTEONECROSIS

**Validating Bone Therapeutics' bone-forming cell therapy**



Bone Therapeutics