Bone Therapeutics optimizes statistical analysis and introduces interim analysis in the ongoing ALLOB Phase IIb study for high-risk tibial fractures.

Recent medical publications provide new insights in timing and dynamics of fracture healing using early radiological assessment

With the improved statistical analysis, the number of required patients could be reduced by 20%

An interim analysis will be added to the study providing an early assessment of ALLOB's efficacy based on radiological data of the first 66 evaluable patients and more stringent efficacy end point criteria

Mont-Saint-Guibert, Belgium, 15 July 2022, 7am CEST – BONE THERAPEUTICS (Euronext Brussels and Paris: BOTHE), the cell therapy company addressing unmet medical needs in orthopedics and other diseases, today announces an optimized statistical analysis and the implementation of an interim analysis for the ongoing Phase IIb clinical trial with its allogeneic bone cell therapy product, ALLOB. Subsequent to the consultation just completed with our existing and potential partners, Bone Therapeutics will proceed in the near term with the submission of the amendments to the study protocol for approval to the regulatory authorities.

Serious and difficult fractures, including tibial fractures, are a leading cause of delayed and non-union fractures and continue to be a high unmet medical need with frequent complications. This poses a serious burden to patients, their family and society. As a result, there is a pressing demand to develop accelerated bone regeneration in these patients. Bone Therapeutics has administered ALLOB in approximately 60 patients in several Phase I and I/IIa clinical trials. The clinical results so far have demonstrated both good tolerability, evidence of increased bone formation and other clinical benefits. Based on these promising initial results, Bone Therapeutics is conducting an additional controlled Phase IIb study in tibial fractures at risk for delayed or non-union.

Recent published medical data has provided new information on timing and dynamics of radiological evidence of fracture resolution. Based on this new evidence, Bone Therapeutics has improved the statistical analysis of the ALLOB Phase IIb study. The updated analysis will provide an optimal radiological assessment of the acceleration of bone formation at 3 months following an intra-fracture administration of ALLOB, compared to standard practice alone. The updated statistical analysis converts one of the current secondary endpoints to a primary endpoint and will therefore have limited impact on the study conduct. The amendment also enables a reduction of approximately 20% of the required patient numbers from 178 patients to 132 evaluable patients while maintaining the same statistical power. Additionally, this updated analysis is expected to facilitate the definition of clinical trial objectives and endpoints in the measurement of fracture healing in subsequent studies, namely the expected confirmatory Phase III study in fractures as well as in studies for bone regeneration in other clinical indications.

In addition, Bone Therapeutics will also introduce an interim analysis based on the assessment of radiological data from approximately 66 evaluable patients at 3 months post-administration. The interim analysis will provide an opportunity to document the efficacy of ALLOB and to achieve a relevant clinical milestone at an earlier time point. An independent Data and Safety Monitoring Board (DSMB) will evaluate the interim analysis and could recommend completing the study early for efficacy if the targeted, more stringent interim efficacy level in bone healing has been achieved. Similarly, the study will operationally remain unchanged.

"*Bone Therapeutics' ALLOB represents a significant opportunity for clinical unmet medical needs in bone regeneration namely difficult tibial fractures. These affect more than 300.000 patients per year in US and EU alone and can have a significant impact to the lives of those affected,*" **said Anne Leselbaum, MD, Chief Medical Officer of Bone Therapeutics**. "*The improved statistical analysis derived from emerging clinical data, will more precisely document the potential benefit of ALLOB over standard practice alone in difficult tibial fractures and could become a reference for future clinical trial objectives and endpoints. The current operational focus of Bone Therapeutics on the conduct of the study aims at ensuring the delivery of top line data as scheduled by of the first half of 2023. With the inclusion of the*

interim analysis, we gain an opportunity to evaluate the efficacy of ALLOB at a slightly earlier time in 2023 and to potentially advance its development to the next stage."

ALLOB Phase IIb clinical trial is a randomized, double-blind, placebo-controlled study in patients with high-risk tibial fractures. This study will assess and compare against placebo, in association with standard of care stabilization surgery, the potential for ALLOB to accelerate fracture healing after 3-months follow-up and prevent late-stage complications in these patients, after a follow-up period of 6 months. ALLOB will be applied by a single percutaneous injection within 24-96 hours post-definitive reduction surgery in patients with fresh tibial fractures at risk of delayed or non-union. Following the approval in seven European countries, the study is currently enrolling patients in over 40 sites.

The proposed amendments to the statistical analysis and the introduction of the interim analysis will be submitted to the relevant regulatory authorities for approval. It is expected that, even if the amended study protocol is approved, this will not have a significant impact on the overall timing of the ALLOB Phase IIb study as previously communicated. Bone Therapeutics expects to announce the recommendation of the DSMB for the interim analysis and to report topline results as scheduled by the first half of 2023. Should the pandemic continue to have impact on patient availability, Bone Therapeutics may have to re-evaluate this timeline and, in that eventuality, will communicate again to the market.

About ALLOB

ALLOB is Bone Therapeutics' off-the-shelf allogeneic cell therapy platform consisting of human allogeneic bone-forming cells derived from cultured bone marrow mesenchymal stromal cells (MSC) from healthy adult donors. To address critical factors for the development and commercialization of cell therapy products, Bone Therapeutics has established a proprietary, optimized production process that improves consistency, scalability, cost effectiveness and ease of use of ALLOB. This optimized production process significantly increases the production yield, generating thousands of doses per bone marrow donation. Additionally, the final ALLOB product is cryopreserved, enabling easy shipment and the capability to be stored at the point of care for easy clinical use. The process will therefore substantially improve product quality, reduce overall production costs, simplify supply chain logistics, increase patient accessibility and facilitate global commercialization. The Company has implemented the optimized production process to produce clinical batches for the ongoing Phase IIb clinical trial in patients with difficult-to-heal tibial fractures.

About Bone Therapeutics

Bone Therapeutics is a leading biotech company focused on the development of innovative products to address high unmet needs in orthopedics and other diseases. Currently Bone Therapeutics is concentrating specifically on the development of its most advanced clinical asset, the allogeneic cell therapy platform, ALLOB.

Bone Therapeutics' core technology is based on its cutting-edge allogeneic cell and gene therapy platform with differentiated bone marrow sourced Mesenchymal Stromal Cells (MSCs) which can be stored at the point of use in the hospital. Its leading investigational medicinal product, ALLOB, represents a unique, proprietary approach to bone regeneration, which turns undifferentiated stromal cells from healthy donors into bone-forming cells. These cells are produced via the Bone Therapeutics' scalable manufacturing process. Following the CTA approval by regulatory authorities in Europe, the Company has initiated patient recruitment for the Phase IIb clinical trial with ALLOB in patients with difficult tibial fractures, using its optimized production process. ALLOB continues to be evaluated for other orthopedic indications including spinal fusion, osteotomy, maxillofacial and dental.

Bone Therapeutics' cell therapy products are manufactured to the highest GMP (Good Manufacturing Practices) standards and are protected by a broad IP (Intellectual Property) portfolio covering ten patent families as well as knowhow. The Company is based in the Louvain-la-Neuve Science Park in Mont-Saint-Guibert, Belgium. Further information is available at www.bonetherapeutics.com.

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