REGISTRATION DOCUMENT

"The date of this Registration document is 28 September 2021.

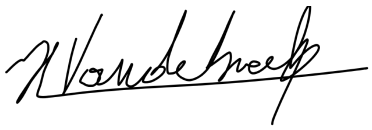
This Registration Document is valid for a period of twelve months from its date of approval (until 28 September 2022). The obligation to supplement this Registration Document in the event of significant new factors, material mistakes or material inaccuracies does not apply when this Registration Document is no longer valid.

This Registration Document has been approved as a registration document by the Belgian Financial Services and Markets Authority (the "FSMA"), as competent authority under Regulation (EU) 2017/1129 (the "Prospectus Regulation"). The FSMA only approves this Registration Document as meeting the standards of completeness, comprehensibility and consistency imposed by the Prospectus Regulation and such approval by the FSMA should not be considered as an endorsement of the issuer."

The Board of Directors of Bone Therapeutics assumes responsibility for the content of the Registration Document. The Board of Directors declares that, having taken all reasonable care to ensure that such is the case, the information contained in this Listing Prospectus, is to the best of its knowledge, in accordance with the facts and contains no omission likely to affect its contents.

On behalf of the Board of Directors

mC4Tx SRL,
represented by Miguel Forte



Finsys Management SRL,
represented by Jean-Luc Vandebroek

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1 RISK FACTORS

The risks and uncertainties that the Company believes to be material are described below. The occurrence of one or more of these risks may have a material adverse effect on the Company's cash flows, results of operations, financial condition and/or prospects and may even endanger the Company's ability to continue as a going concern. Moreover, the Company's share price could fall significantly if any of these risks were to materialise. However, these risks and uncertainties may not be the only ones faced by Bone Therapeutics. Additional risks, including those currently unknown or deemed immaterial, may also impair the Company's business operations.

The risk factors are presented in seven categories, depending on their nature. In each category, the risk factor which in the assessment of the Company is the most material, considering the negative impact on the Company (including any relevant mitigation measures) and the probability of its occurrence, is mentioned first. The remaining risk factors within each category are not ranked in order to their materiality.

Prospective investors should also carefully read the detailed information set out elsewhere in this Registration Document (including any documents incorporated in it by reference) and reach their own view prior to making any investment decision.

1.1 Risk factors related to Company's financial position and capital requirement

a. *Bone Therapeutics is a clinical-stage biotechnology company and has not yet commercialised any of its products. It has therefore incurred net losses since its inception and expects to continue to incur net losses in the foreseeable future. As a result, the Company might never achieve sustained profitability.*

The Company is a biotechnology company active in the orthopaedic space. It has completed a Phase I/IIa clinical trial for the treatment of delayed-union (2018) and a Phase IIa study for lumbar spinal fusion (2019) with ALLOB, and a Phase IIb study for the treatment of knee osteoarthritis (2018) with JTA-004. As the Company is still developing its product candidates in clinical settings and has not completed the development of any product, it does not anticipate generating revenue from sales for the foreseeable future and has incurred significant losses since its incorporation in 2006. Under IFRS, the negative retained earnings on 30 June2021 was € 74.60 million. This amount can be found into the Interim Consolidated statement of changes in equity in the Interim Report as of 30 June 2021 (on page 7). These losses resulted principally from costs incurred in research and development, preclinical testing, clinical development of its product candidates as well as costs incurred for research programmes and from general and administrative expenses. In the future, the Company intend to continue its efforts to conduct preclinical testing, product development, clinical trials and regulatory compliance activities and improve manufacturing capabilities. These activities together with anticipated general and administrative expenses will result in incurring further significant losses for several years. For next several years, the Company anticipates that its expenses and accumulated consolidated losses will increase substantially mainly due to:

- conducting the Phase IIb clinical trial with its allogeneic bone cell therapy product, ALLOB, in patients with difficult-to-heal tibial fractures, using its optimized production process, and
- the expansion of the pre-clinical and clinical pipeline with new indications through new technologies.

The size of Company's future net losses will depend, in part, on the rate of future growth of its expenses and its ability to generate revenue. It may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may have a material adverse effect on its business and financial situation. In addition, these losses, among other elements, will continue to cause the Company's working capital and the shareholders' equity to decrease. Therefore, the Company cannot assure that it will generate positive clinical data, receive regulatory approval, earn revenues or achieve profitability, which could impair the Company's

ability to sustain operations, obtain any required additional funding or continue as a going concern. Even if the Company achieves profitability in the future, it may not be able to sustain profitability in subsequent periods.

b. As the Company has limited cash flow generating commercial activities, it is largely dependent on external funding which may not be available on acceptable terms when needed, if at all.

On 30 June 2021, Company's cash position amounted to € 6.01 million. For more information about the Company's current cash situation, please see Section 3.6 of this Registration Document. The Company will require additional funding in the future to sufficiently finance its operations and to take advantage of new business opportunities.

The Company's future financing needs will depend on many factors, including the progress, costs and timing of its research and development activities, the clinical trials, the costs and timing of obtaining regulatory approval, the costs of obtaining, maintaining and enforcing its patents and other intellectual property rights, the costs and timing of maintaining or obtaining manufacturing for its products and product candidates, the costs and timing of establishing sales and marketing capabilities and the terms and timing of establishing additional collaborations, licence agreements and other partnerships. Company's existing capital resources are not sufficient to fund the completion of all its current clinical trials through commercialisation. Accordingly, the Company will need to raise additional funds. Currently, the Company mainly relies on equity and bond financing and the issuance of convertible bonds for additional funding.

The Company also receives non-dilutive financing and grants from the Walloon Region (the "**Region**"). More information about the Company's non-dilutive financing and grants, please refer to Section 4.15 of this Registration Document. However, changes in regional financing and grant policies, a shift in regional investment priorities or challenges by the European instances may reduce or jeopardise the Company's ability to obtain or retain non-dilutive financing, grants and/or other benefits. In addition, future growth of the Company, whether or not including geographical expansion, could limit the Company's eligibility to obtain similar non-dilutive financing or grants.

Furthermore, the Company's ability to raise additional funds will depend on financial, economic and market conditions and other factors, over which it may have no or limited control, and the Company cannot guarantee that additional funds will be available to it, when necessary, on commercially acceptable terms, if at all. If the necessary funds are not available, the Company may need to seek funds through forced collaborations and licensing arrangements, which may require it to reduce or relinquish significant rights to its research programmes and product candidates, to grant licences on its technologies to partners or third parties or enter into new collaboration agreements, the terms could be less favourable to the Company than those it might have obtained in a different context. If adequate funds are not available on commercially acceptable terms when needed, this could have a material adverse effect on the Company as it may be forced to delay, reduce or terminate the development or commercialisation of all or part of its product candidates or it may be unable to take advantage of future business opportunities.

1.2 Risk factors related to Company's business activities and industry

a. The absence of similar cell therapy products on the market generates a number of unknown factors which may have an adverse effect on the business, the results, the financial situation and the development of the Company.

The existing treatments (for which the Company aims to develop an alternative through cell technology-based product(s) candidates) are often old techniques, which are painful and invasive. Cell therapy however, is an emerging medical technology, in which few products have yet been proven beneficial, safe and efficient and

have obtained marketing authorisation. In general, the early stage of the technology, and consequently the lack of established practices and benchmarks, create uncertainty about prospects and come with inherent risk of unanticipated problems in every stage of the product life, including development, regulations, approvals, reimbursement, market acceptance and operations.

Especially in the orthopaedic field, Company's innovative cell product, ALLOB, would, if and when authorised for marketing, constitute a novel treatment paradigm. To its knowledge, the Company is the only clinical stage company that develops cell products using differentiated bone-forming cells derived from human bone marrow for the treatment of orthopaedic conditions. However other companies are developing similar innovative solutions with the use of (undifferentiated) mesenchymal stem cells often in combination with supportive matrices composed of human cadaver bone or other materials. To date, there are no similar products authorised for commercialisation. The lack of similar products causes uncertainty about the registration, the reimbursement and revenues of the product candidates related to the ALLOB platform and its acceptance by the regulators, third party payers, doctors and patients. The Company cannot give any assurance that it will be able to deal with these unknown factors which may have an adverse effect on the business, the results, the financial situation and the development of the Company.

More information about the principal markets and competitors is set out in Section 4.7 of this Registration Document.

b. The Company's business environment is characterised by rapid technological change and complexity which could limit or eliminate the market opportunity for its product candidates.

The changing competitive landscape is a main issue facing the healthcare industry. The Company competes with other companies based on technology, product offering, therapeutic area, intellectual property, geographic area and time to market or other factors. The Company's success depends on, *inter alia*, the ability to establish a competitive position with respect to all these factors. For more information about the principal markets for the Company, please see Section 4.7 of this Registration Document. The Company believes that its main competitive advantages are its expertise and know-how in skeletal biology and physiology, in cell therapy in general and in cell therapy for bone diseases in particular, the quality (*i.e.*, efficacy and safety) of its product candidates, its know-how in respect to efficient and robust manufacturing processes, the minimal invasive technique through which its products are administrated and the choice of the indications (*i.e.*, unmet medical needs in the fields of bone diseases and orthopaedics). However, the Company's competitors may have greater financial, human and other resources than the Company does.

Markets medical for treatments are in general highly competitive and the fields in which the Company operates are characterised by an increase in innovation. No assurance can be given that competitors of the Company are not currently developing, or will not in the future, develop technologies and products that are equally or more effective, safe and/or economical as the current or future offering of the Company and may therefore have a negative impact on the success of the Company in the fields in which it operates.

c. Risk factor related to the ongoing COVID-19 pandemic

The spread of COVID-19 and the resulting government-imposed containment measures could have a significant adverse effect on Bone Therapeutics' business activities and financial condition and lead to potential delay in its clinical trial activities.

On 11 March 2020 the World Health Organization declared the novel strain of coronavirus (COVID-19) a global pandemic and recommended containment and mitigation measures worldwide.

In Belgium, the pandemic has resulted in government-imposed containment measures intended to stop the spread of the virus which could temporarily require again most or all employees of the Company to work remotely, suspend all non-essential travel worldwide for its employees and discourage/forbid employee attendance at industry events and in-person work-related meetings. Such measures could have a significant negative impact on the Company's business activities, financial condition and process of its clinical trial activities.

Given the continuing COVID-19 pandemic, the Company believes that there is a substantial risk that its business operations and financial condition may be significantly adversely affected.

The impacts of COVID-19 on the Company's business activities and financial condition include, but are not limited to, the following:

- The Phase IIb ALLOB clinical study in high-risk tibial fractures is currently experiencing a delay in patient recruitment due to the COVID-19 pandemic and the associated containment measures which have resulted in fewer accidents and reduced availability of health care facilities in the first half of 2021. Bone Therapeutics has instituted corrective measures to mitigate the impact of the pandemic on recruitment for the trial, in collaboration with its clinical research organization. At this point, Bone Therapeutics does not expect the pandemic delay in recruitment rate to have a material effect on the anticipated completion of recruitment in H1 2022 and still currently expects to deliver top line results in H2 2022 as planned. Should the pandemic continue, Bone Therapeutics may have to re-evaluate these timelines.
- Although the Company's laboratory facilities remain operational, the Company had and may have to temporarily implement again staggered laboratory shifts and work-from-home policies for non-essential staff members which may lead to a potential delay.

The extent to which COVID-19 affects the Company's business activities and financial condition in the longer term will ultimately depend on future developments, which are highly uncertain and cannot be predicted at present, including the duration of the pandemic, additional information that may emerge concerning the severity of COVID-19 and ongoing actions to contain COVID-19. However, potential prolonged closures or other business disruptions may negatively affect its operations and the operations of its agents, contractors, consultants or collaborators, which could have a material adverse impact its business activities and financial condition.

1.3 Risk factors related to clinical development

a. *Company's research programmes and product candidates, ALLOB and JTA-004, must undergo rigorous pre-clinical tests and clinical trials, of which the start, timing of completion, number and results are uncertain and could substantially delay or prevent the products from reaching the market. If the Company experiences significant delays or is unable to obtain marketing authorisation, this would have a material adverse effect on its business.*

The research programmes and product candidates of the Company must undergo rigorous pre-clinical and clinical trials, of which the start, the timing of completion, the number and the results are uncertain. Such trials could delay or prevent the product candidates from reaching the market. ALLOB and JTA-004 clinical trials may be delayed for a variety of reasons, including, but not limited to, delays in obtaining regulatory approval from Competent Authorities to commence a trial, in reaching agreement on acceptable terms with prospective research organisations, manufacturing organisations and clinical trial sites, in recruiting sufficient number of suitable patients to participate in a trial, in having patients complete a trial or return for follow-up, in obtaining sufficient supplies of clinical trial materials, clinical sites dropping out of a trial and in the availability to the Company of appropriate clinical trial insurances. In particular, the clinical trials related to orthopaedics require longer follow-up periods of up to 24 months. Although the Company is developing products for conditions with large patient populations, many factors other than patient population size affect patient enrolment and could lead to a slower than expected patient recruitment rate. Factors that could affect patient enrolment include, but are not limited to, the proximity of patients to clinical sites, the eligibility criteria for the trial, competing clinical trials, clinicians' and patients' perceptions as to the potential advantages of the product being studied in relation to other available therapies, including any new products that may be approved for the indications that the Company is investigating and whether the clinical trial design involves comparison to placebo or standard of care. If the Company experiences lower than expected enrolment in the trials, the trials may not be completed as envisaged or may become more expensive to complete, which may have an adverse effect on the Company's business, prospects, financial condition and results of operations.

b. *Results of preclinical studies and early-stage clinical trials of Company's product candidates may not be predictive of the results of later-stage clinical trials.*

The Company's cell products are highly innovative and are based on the *ex vivo* differentiation of human bone marrow cells with a view to producing bone-forming cells. Although the Phase II clinical results for the use of these differentiated cells in the treatment of delayed-union fractures and in lumbar spinal procedures showed statistically and clinically relevant benefits and demonstrated satisfying safety and efficacy, success in subsequent studies cannot be guaranteed as demonstrated by the osteonecrosis Phase III study with Company's first generation of autologous cell therapy product, PREOB, in which superiority over standard of care could not statistically demonstrated and may not lead to successful therapy products. A similar statement can be made for the off-the-shelf protein solution in development, JTA-004, as the promising results of the Phase IIB study for knee osteoarthritis do not warrant a positive outcome for the follow up Phase III study.

c. *Company's product candidates may have serious adverse, undesirable or unacceptable side effects which may delay or prevent marketing approval.*

If serious adverse side effects are identified for any product candidate, the Company may need to abandon or limit its development of that product candidate, which may delay, limit or prevent marketing approval, or, if approval is received for the product candidate, require it to be taken off the market, require it to include safety warnings or otherwise limit its sales.

Although the safety of Company's product candidates has already been evaluated in clinical programmes, not all adverse side effects of the product candidates are known or can be foreseen. Important unpredicted side effects from any of the Company's product candidates could arise either during further clinical development or, if approved by the Competent Authorities, after the approved product has been commercialised. While the Company's clinical studies for its product candidates to date have demonstrated an acceptable safety profile, the results from future trials may not support this conclusion. Adverse side effects could prevent the Company or any potential future partner from achieving or maintaining market access and market acceptance of the affected product or could substantially increase commercialisation costs and expenses, which would have an adverse effect on the Company's business, prospects, financial condition and results of operations.

d. *Failure to successfully identify, develop and commercialise additional products or product candidates could impair the Company's ability to grow.*

The Company's main focus is to continue its clinical trials and ultimately to obtain approval of its product candidate for the treatment of delayed-union fractures, lumbar fusion for degenerative disease of the spine (ALLOB) and knee osteoarthritis (JTA-004). The Company plans to initiate a Phase IIb clinical trial with ALLOB, in patients with difficult-to-heal fractures, and a Phase III study with JTA-004, for the treatment of pain in patients with knee osteoarthritis early 2020. For more information about the Company's clinical pipeline, please see Section 4.6 of this Registration Document.

The Company also runs preclinical research programmes and develops new product candidates. The Company intends to leverage its preclinical research, clinical expertise and manufacturing ability to expand its pipeline to indications for which it believes its products have therapeutic potential. The accumulated data is expected to reduce the time and costs associated with early-stage clinical trials for additional diseases and disorders. However, the identification, selection and development of additional promising products or product candidates require additional resources, whether or not any product or product candidate is ultimately identified. Furthermore, the lack of existing benchmarks in the field of regenerative medicines in general and cellular therapy in particular prevents the Company from relying on existing precedents with respect to such identification, selection and development. The success of the Company's strategy depends partly on the Company's ability to identify, select and develop such products.

1.4 Risk factors related to post-authorization risks

a. ***Failure to obtain marketing authorisation, additional post-authorisation studies, restricted use, withdrawal or limited market acceptance of the Company's products among third party payers, doctors, patients and the medical community in general would affect the Company's ability to generate revenues from such products or become profitable.***

To date, the Company has no product authorised for commercialisation, and has not undertaken any steps for registration and/or authorisation. The Company's current product candidates are in different phases of clinical trials and the Company may never have a product that is commercially successful. Even the product candidates in Phase III clinical programmes require further clinical trials, regulatory review, marketing authorisations, significant marketing efforts and substantial investment before they may provide revenue to the Company.

Clinical data are often susceptible to varying interpretations and analyses, so that a product that performed to satisfaction during clinical trials may nonetheless fail to obtain regulatory approval for marketing. Due to the inherent risk in the development of biopharmaceutical products, there is a risk that not all or none of the product candidates of the Company will be successfully developed and commercialised.

Once commercialised, products may be subject to post-authorisation like safety studies or other pharmacovigilance or biovigilance activities, may be subject to limitations on their uses or may be withdrawn from the market for various reasons, including if they are shown to be unsafe or ineffective, or when used in a larger population that may be different from the trial population studied prior to introducing the product on the market. Regulatory approval guidelines may change during the course of the product development and review process, making the chosen development strategy suboptimal. This is even more the case in view of the early stage nature and the absence of benchmarks in the area in which the Company conducts its activities, which may still undergo important regulatory changes. These factors may result in significant delays, increased trial costs, significant changes to commercial assumptions or failure of the products to obtain marketing authorisation. In addition, the Competent Authority may impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, once introduced to the market, the Company's products may not achieve the desired level of acceptance of the products and perception of the advantages of the products by third-party payers, doctors and patients and the medical community in general.

The limited number of scientific publications regarding cell-based technology used to develop the Company's products could adversely affect the benefits, efficacy or safety perception of the Company's products. Efforts to educate the medical community and third-party payers on the benefits of the Company's products may require significant resources and may never be successful, which would prevent the Company from generating significant revenues, or becoming profitable.

In particular with respect to allogeneic cells, the safety concerns associated with human materials may affect the ability to generate revenues from the Company's products. Future medical events or studies that would raise or substantiate concerns about the safety of the raw materials used by the Company or other similar raw materials could negatively impact public perception of all human products and of their procurement process. Further, any failure in screening, whether by the Company or by other manufacturers of these human materials, could adversely affect its reputation, the support it receives from the medical community and overall demand for the Company's products.

b. The price setting, the availability and level of adequate reimbursement by third parties, such as insurance companies, governmental and other healthcare payers is uncertain and may

impede the Company's ability to generate sufficient operating margins to offset operating expenses.

The commercial success of the Company's products depends in part on the conditions for setting the sales price of its products and the conditions of their reimbursement by the health agencies, insurance companies or other healthcare payers in the countries where the Company intends to commercialise its products. Considering the innovative nature of the Company's product candidates and the lack of similar products, the possible reimbursement levels are difficult to predict. The Company's ability to adapt an adequate pricing strategy is uncertain. Moreover, there is pressure on healthcare spending, on reimbursement and price levels in most countries, due to *inter alia* the current context of healthcare cost control, the economic and financial crisis and the increase in healthcare budgets caused by an aging population.

Moreover, the Company's products may not fit within the existing health technology assessment and reimbursement processes applied throughout the different jurisdictions in which the Company envisages to operate, and may be subject to different reimbursement facilities depending on the jurisdiction in which the Company's products are being offered.

Failure to obtain favourable price settings and/or adequate reimbursement by third parties, such as insurance companies, governmental and other healthcare payers may impede the Company's ability to generate sufficient operating margins to offset operating expenses.

c. The Company has no experience in sales, marketing and distribution.

The Company will have to hire, train, incentivise and retain a techno-commercial sales force or enter into a partnership with an industrial partner, gain the support of key opinion leaders, establish referral networks and introduce a new standard of care in orthopaedic treatment, to successfully commercialise its products once they have been approved for commercialisation. The Company has no experience in sales, marketing and distribution. The Company may be or perceived to be EU centred and may encounter difficulties gaining access to the USA or other markets. There is a risk that the Company will not be able to successfully manage its sales, marketing and distribution when its products come on the market, which will have an adverse effect on the Company's business, prospects, financial condition and results of operations.

Furthermore, market conditions may change resulting in the emergence of new competitors or new treatment guidelines, which may require alterations in the marketing and sales strategy or even of its development strategy.

1.5 Risk factors related to legal and regulatory risks

a. ***Nearly all aspects of the Company's activities are subject to substantial regulation, which may have a significant adverse effect on the Company's business, prospects, financial condition and results of operations if not complied with.***

The international biopharmaceutical industry is highly regulated by governmental bodies ("**Competent Authorities**") imposing substantial requirements on almost all aspects of the Company's activities, notably on research and development, manufacturing, preclinical trials, clinical trials, labelling, marketing, sales, handling, transport and storage of human material, record keeping, promotion and pricing of its research programmes and product candidates. In each country where the Company, or any of its partners or licensees, operates, it has to comply with the standards and regulations imposed by the local Competent Authorities.

The Company has to constantly comply with the standards imposed by the Competent Authorities, which are subject to regular reviews and may possibly result in changes in the applicable regulations. The standards imposed by a Competent Authority and the approval procedure for clinical trials and/or marketing authorisation

may vary from country to country (except for the approval procedure of Company's cell therapy products in Europe where the marketing authorisation is mandatory through a centralized procedure while for its non-cellular off-the-shelf protein solution, JTA-004, a decentralized procedure may need to be followed if the eligibility for centralised is not granted), *inter alia* in timing, detailed costs and efforts necessary to complete those procedures *e.g.*, different reporting procedures. For the decentralized procedure which is a mutual recognition procedure, the sponsor may select the country which will be the Reference Member State (main reviewer of the Marketing Authorization Application (MAA)). The list of countries (Concerned Member States) to include in the MAA is also defined by the sponsor depending on market objectives. An identical application for marketing authorisation is submitted simultaneously to the competent authorities of the Reference Member State and of the Concerned Member States. Moreover, the various reasons for which the Competent Authority's approval of clinical trials may be refused, delayed, suspended or withdrawn are not predictable by the Company. If the Company does not comply with one or more of the standards of the Competent Authorities, in a timely manner or at all, it could experience significant delays in development or commercialisation, additional costs, refusals, suspension, withdrawals of approvals resulting in a significant adverse effect on the Company's business, prospects, financial condition and results of operations. Please also see Section 4.10 of this Registration Document for more information of the regulatory framework that applies to the Company.

b. *If any product liability claims are successfully brought against the Company or its collaborators, the Company may incur substantial liabilities and may be required to limit the commercialisation of its product candidates.*

Product liability claims due to (unpredicted) adverse side effects of the product candidates may be brought against the Company or its collaborators by participants enrolled in clinical trials, practitioners, researchers, other health/research professionals or others using, administering or selling any of the Company's future approved products. The Company is currently insured for risks related to clinical studies. The Company may incur substantial liabilities if it cannot successfully defend itself against such claims. From the adverse events reported with the Company's products in clinical trials to date, none have been qualified as severe. To date, no such claims or legal actions have been filed against the Company.

c. *Failure to comply with Good Manufacturing Practices and other manufacturing regulations may impede the Company's ability to develop and commercialise its product and scale-up of manufacturing.*

Until November 2020, the Company had its own Good Manufacturing Practices license, for its facility located at the BioPark of Gosselies (south of Brussels) and owned by its affiliate SCTS. In addition, the Company had obtained three manufacturing and intra-EU distribution authorisations from the Competent Authorities in Belgium. All the material (IMP) required for the ongoing clinical trials have been produced and released on the behalf of these authorisations.

In November 2020, the Company has sold to Catalent its affiliate SCTS including its facilities located at the BioPark of Gosselies (south of Brussels). The Company entered then in a Master Service Agreement with Catalent to ensure its production capability of its cellular product ALLOB in the future. The production of JTA-004 is subcontracted to Baccinex in Switzerland since the manufacturing of the first clinical batches. For JTA-004, Catalent is not involved at any time during the manufacturing or release of JTA-004.

However, the Company is not relieved from continuously complying with the relevant standards. The Company, and key third party subcontractors and suppliers on which it relies currently or in the future, must continuously comply with Good Manufacturing Practices and the corresponding manufacturing regulations of the Competent Authorities. In complying with these regulations, the Company and its third-party subcontractors and suppliers must expend significant time, money and effort in the areas of design and development, testing, production, record-keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could have significant adverse results for the Company such as an enforcement action against the Company, including the seizure of products and shutting down of production. Any of the third-party subcontractors and suppliers and the Company also may

be subject to inspections by the Competent Authorities. If any of the Company's third-party suppliers or the Company itself fails to comply with Good Manufacturing Practices or other applicable manufacturing regulations, the Company's ability to develop and commercialise the products could suffer significant interruptions.

The Company's manufacturing process involves the handling, transport and storage of human materials and the transformation of human body tissue into a treatment product. The Company has obtained a license as a tissue bank for handling autologous human biological materials and a license as a tissue bank for handling allogeneic human biological materials in collaboration with hospital tissue banks. In order to maintain such license, the Company needs to comply with applicable regulations in this respect. Furthermore, the applicable legislation with respect to the handling and transport of human body tissue varies amongst the different jurisdictions in which the Company could envisage operations, potentially impairing relocation and export opportunities. This human biological license has not been impacted by the selling of the affiliate SCTS.

The Company may have difficulties in finding suitable Contract Manufacturing Organization or commercially acceptable terms for subcontracting manufacturing activities. Finally, the Company may have difficulties to ensure sufficient supply of human biological materials. These uncertainties and risks relating to the development, manufacturing, handling, quality assurance may have a materially adverse effect on the business and financial position of the Company.

1.6 Risk factors linked to intellectual property

a. ***The Company's patents and other intellectual property rights portfolio may not adequately protect its research programmes and other product candidates, or the Company may not be able to protect and/or enforce its intellectual property rights in all key countries or territories, which may impede the Company's ability to compete effectively.***

The Company's success will depend in part on the ability of the Company to obtain, maintain and enforce its patents and other intellectual property rights. The Company's research programmes and product candidates are covered by several patent application families, which are either licensed to the Company or owned by the Company. For more information about the Company's patents and patent applications, please see Section 4.16 of this Registration Document. Currently, the company manages 8 patent families related to the ALLOB technology and 4 patent families related to the JTA technology. The Company cannot guarantee that it will be able to obtain or maintain these patent rights against patent offices and other third-party challenges to their validity, scope and or enforceability. The Company cannot guarantee that it is or has been the first to conceive an invention and to file a patent or a patent application. Because patent law in the biopharmaceutical industry is highly uncertain, there can be no assurance that the technologies used in the Company's research programmes and product candidates are patentable, that patents will be granted to the Company or its licensors under pending or future applications, or that patents will be of sufficient breadth to provide adequate and commercially meaningful protection against competitors with similar technologies or products, or that patents granted to the Company or its licensors will not be successfully challenged, circumvented, invalidated or rendered unenforceable by third parties, hence enabling competitors to circumvent or use them and depriving the Company of the protection it may expect against competitors. Moreover, it cannot be excluded that the debate on the patentability of elements of the human body could lead to a situation whereby the technology developed by or licensed to the Company can no longer be protected by patents or that such patents cannot be enforced against third parties. A third party's ability to use unpatented technologies is enhanced by the fact that the published patent application contains a detailed description of the relevant technology. The Company cannot guarantee that third parties will not claim ownership rights over the patents or other intellectual property rights owned or held by the Company. To date, no invalidation or opposition process has been made against the Company patent portfolio.

Several of Company's patents are already granted in Europe, US, Japan, Australia, Canada, China, Hong Kong, Israel, India, South Korea and Singapore. However, the Company cannot guarantee that the current prosecution of its or its licensors' patent applications will result in granted patents in each of the territories. Filing, prosecuting and defending their patents throughout the world would be prohibitively expensive for the Company and its licensors. Competitors may use the Company's technologies in jurisdictions where the Company or its licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where the Company has patent protection but where enforcement is not as well developed as in the United States or the European Union. These products may compete with the Company's products in jurisdictions where the Company or its licensors do not have any issued patents and the Company's patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favour the enforcement of patents and other intellectual property rights, particularly those relating to biopharmaceuticals, which could make it difficult for the Company to stop the infringement of its patents or marketing of competing products in contravention of its proprietary rights generally. The inability of the Company to protect and/or enforce its intellectual property rights in the selected territories in which the Company seeks IP protection could have a severe adverse effect on its business, prospects, financial condition and results of operations.

b. If the Company is not able to prevent disclosure of its trade secrets, know-how, or other proprietary information, the value of its technology and product candidates could be significantly diminished.

The Company relies on trade secret protection to protect its interests in its know-how or other proprietary information and processes for which patents are difficult to obtain or enforce, all of which constitute confidential information. The Company may not be able to protect its confidential information adequately. The Company has a policy of requiring its consultants, contract personnel, advisers and third-party partners to enter into confidentiality agreements. However, there is no assurance that such agreements will provide for the meaningful protection of confidential information in the event of any unauthorised use or disclosure of information. Furthermore, the Company cannot provide any assurance that any of its employees, consultants, contract personnel or third-party partners, either accidentally or through wilful misconduct, will not cause serious damage to its programmes and/or its strategy, by, for example, disclosing confidential information to its competitors. It is also possible that confidential information could be obtained by third parties as a result of breaches of physical or electronic security systems of the Company, its consultants, advisers, third-party partners or other parties that have had access to its confidential information. Any disclosure of confidential data into the public domain or to third parties could allow the Company's competitors to learn confidential information and use it in competition against the Company. In addition, others may independently discover the Company's confidential information. Any action to enforce the Company's rights against any misappropriation or unauthorised use and/or disclosure of confidential information is likely to be time-consuming and expensive, and may ultimately be unsuccessful, or may result in a remedy that is not commercially valuable.

c. If the Company fails to comply with its obligations under the agreement pursuant to which it licenses intellectual property rights from third parties, or otherwise experiences disruptions to its business relationships with its licensors, the Company could lose the rights to intellectual property that is important to its business.

The Company's activities are dependent - at least in part - on the use of intellectual property rights which are for some projects not owned by it, but have been granted to it pursuant to license agreements and which are important to the business.

In particular, for its clinical programmes, the Company has entered into license agreements with third parties regarding the ULB-028 patent family. Also, the Company has been granted exclusive worldwide rights from

Glob-Co SRL to develop, manufacture, sublicense and sell any products of the JTA technology for human application.

The conditions under which Company may maintain the rights granted to it include, but are not limited to, the payment of (i) fees upon achievement of certain milestones, (ii) royalties on the (net) sales of relevant licensed products, (iii) a percentage of revenues incurred from sub-licensees, as well as the performance of other obligations, such as compliance with research and development obligations and with marketing and distribution arrangements. Furthermore, delays or interruptions in the development or exploitation of the relevant technology may be sanctioned under the terms and conditions of the license agreements. If the Company fails to comply with its obligations under the respective license agreements, licensors may reduce the scope of the license or terminate the license, resulting in the loss of the use of the related intellectual property rights. Should the Company lose any of its licenses, or if it would be unable to obtain new rights on reasonable terms similar to those which it holds under such license, it might be unable to develop, manufacture or sell its products. This could have an adverse effect on the Company's business, prospects, financial condition and operational results. The termination of certain license agreements could substantially impair the Company's ability to generate revenues.

d. The Company may infringe on the patents or intellectual property rights of others and may face patent litigation, which may be costly and time consuming and could result in the Company having to pay substantial damages or limit the Company's ability to commercialise its product candidates.

The Company's success will depend in part on its ability to operate without infringing on or misappropriating the intellectual property rights of others. The Company cannot guarantee that its activities, or those of its licensors, will not infringe on the patents or other intellectual property rights owned by others. The Company may expend significant time and efforts and may incur substantial costs in litigation if it is required to defend patent or other intellectual property right claims brought against the Company or its licensors regardless of whether the claims have any merit. Additionally, the Company cannot predict whether it or its licensors will be successful in any litigation. If the Company or its licensors are found to have infringed the patents or other intellectual property rights of others, it may be subject to substantial claims for damages, which could materially impact the Company's cash flow and financial position. The Company may also be required to cease development, use or sale of the relevant research programme, product candidate or process or it may be required to obtain a license for the disputed rights, which may not be available on commercially reasonable terms, if at all. The Company may be unable to develop or commercialise a product, product candidate or research programme, or may cease some of its operations, which may have an adverse effect on the Company's business, prospects, financial condition and results of operations. To date, no patent infringement claim has been made against the Company.

e. Obtaining and maintaining patent protection depends on compliance with various procedural, documentary, fee payment and other similar requirements imposed by governmental patent agencies, and the Company's or its licensor's patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid by the Company and/or its licensors to the relevant patent agencies in several stages over the lifetime of the licensed patents and/or applications. The relevant patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse may be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance may result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, the Company's competitors might be able to use its technologies and those technologies licensed to the Company and this circumstance would have an adverse effect on the Company's business, prospects, financial condition and results of operations.

1.7 Risk factors linked to the Company's dependence on third parties and on key personnel

a. The Company has obtained significant grants and subsidies. The terms of certain of these agreements may significantly hamper the Company in its flexibility to choose a convenient location for its activities.

The Company has entered into several funding agreements with the Region and to a lesser extent with the European Commission, to partially finance its research and development programmes (the "**Research Grants**" and "**Research Subsidies**") and its patent applications (the "**Patent Subsidies**"). Please refer to Section 4.15 of this Registration Document for an overview of the grants and subsidies.

Most of the Patent Subsidies provide that the Company must ensure a valorisation of the relevant patent or patent application in a certain area (in most cases in the Region), unless the prior written consent of the Region is obtained. Although the Region may not refuse such consent if the Company proves that its valorising activities outside of the Region's territory are carried out in the framework of a cooperation with an overall positive effect (in terms of technological or economic development) on the Region's territory, this provision restricts the Company in its choice of geographical location to carry out or further develop its activities. Also, if the Region would refuse to provide its consent, the Company may only valorise the relevant patent (application) outside the Region's territory provided that it informs the Region thereof in writing and refunds the entire subsidy related to the relevant patent (application) to the Region.

In addition, the Research Grants provide that the Company must carry out its exploitation activities (the production and commercialisation of products and the realisation of certain services) in relation to the research domain funded in accordance with the relevant Research Grants on the Member States' territory until the end of the exploitation phase as defined in the respective Research Grants. Some of the Research Subsidies also provide that the experimental development activities carried out by the Company in the framework of the exploitation of the research results obtained in the framework of the relevant Research Subsidy must be carried out on the Member States' territory. These provisions affect the Company's ability to relocate its activities. Furthermore, the Company's ability to relocate its activities is limited by the provisions of the SME Agreement, pursuant to which the Company, in order to keep the funding granted to it, must employ a specific number of employees at its site in Wallonia.

b. Manufacturing of the Company's products requires human or derived raw materials to be obtained from third parties and may be more costly than expected.

For the development of its research and the conduct of pre-clinical and clinical trials, the Company needs, in particular, human biological materials from diseased or healthy donors. The sourcing of these materials is regulated extensively by the Competent Authorities. The failure to comply with these regulations could cause the Company to be liable or could adversely affect its ability to source these materials. The public perception about the safety of human-derived materials, including bone cells, could adversely affect the market. The inability of the Company to ensure adequate supply and quality of human or derived raw materials may have a materially adverse effect on the business, the results, the financial situation and the development of the Company.

The Company will have to establish a scalable process platform with third parties in the relevant regions to manufacture its products. To be able to supply the products at acceptable prices, the Company will have to control the costs and work continuously on the optimization of the manufacturing processes to prolong shelf-life, increase product stability and reduce processing time. The inability of the Company to produce the products at reasonable costs could prevent it from achieving its overall objectives and could thus have an adverse effect on its business, prospects, financial condition and results of operations.

c. *The Company relies, and expects to continue to rely, on third parties, including independent clinical investigators, and CROs, and CDMOs to conduct its preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, the Company may not be able to obtain regulatory approval for or commercialize its product candidates and its business could be substantially harmed.*

The Company has relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct its preclinical studies and clinical trials and to monitor and manage data for its ongoing preclinical and clinical programs. The Company relies on these parties for execution of its preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, its reliance on these third parties does not relieve the Company of its regulatory responsibilities and it is responsible for ensuring that each of its studies and trials is conducted in accordance with the applicable protocol, scientific standards and legal and regulatory requirements such as Good Clinical Practice (GCP) and cGMP regulations. If the Company, the participating investigators or any of its CROs fail to comply with applicable GCPs or the tested products do not meet cGMP regulations, the clinical data generated in its clinical trials may be deemed unreliable and the regulatory authorities may require the Company to perform additional clinical trials before approving the marketing applications of its product candidates.

Further, the investigators and CROs are not employees of the Company and the Company will not be able to control, other than by contract, the amount of resources, including time, which they devote to its product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of its product candidates, if they do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to Company's clinical protocols, regulatory requirements or for other reasons, clinical trials may be extended, delayed or terminated and the Company may not be able to obtain regulatory approval for or successfully commercialize its product candidates. As a result, results of operations and the commercial prospects for Company's product candidates would be harmed, Company's costs could increase and its ability to generate revenues could be delayed.

Since the sale of Bone Therapeutics' subsidiary SCTS and the associated GMP accredited cell production facility and the subsequent signing of supply agreement for the further development of ALLOB, the Company has a strong collaborative relationship with Catalent. Catalent is a leading global service provider for cell product manufacturing, in particular in the bone repair field, and who will collaborate with the Company on production, quality control and assurance and storage and distribution of cell products. Although Bone Therapeutics has already produced all required clinical and quality control batches for the ongoing Phase IIb clinical trial with ALLOB, the Company relies on Catalent's services, in particular for the manufacturing of its cell therapy products for future clinical trials and potential commercialisation. Failure in timely production and delivery of ALLOB can substantially delay the clinical development of ALLOB, its marketing approval and potential commercialisation.

There is a limited number of third-party service providers that specialize or have the expertise required to achieve Company's business objectives. If any of the relationships with these third-party CROs, CDMOs or clinical investigators terminate, the Company may not be able to enter into arrangements with alternative CROs, CDMOs or investigators or to do so on commercially reasonable terms. Switching or adding additional CROs, CDMOs (or investigators) involves additional cost and requires management time and focus. In addition, the use of third-party service providers requires the Company to disclose its proprietary information to these parties, which could increase the risk that this information will be misappropriated.

d. *The Company is subject to competition for its skilled personnel and challenges in identifying and retaining key personnel could impair the Company's ability to conduct and grow its operations effectively.*

The services of the Company's Executive Committee are critical to the successful implementation of its business, research, product development and regulatory strategies. Members of the Company's Executive Committee may terminate their employment or services with the Company at any time with relatively short notice. In general, conflicts between key managers may result in the Company losing the services of a manager or otherwise affect the cohesion within the Executive Committee. Upon the departure of certain clinical and scientific personnel or members of its Executive Committee, the Company's research and development efforts may be seriously and adversely affected.

The Company's ability to compete in the highly competitive health care sector depends on its ability to attract and retain highly qualified management, scientific and medical personnel. Many of the other biotechnology and pharmaceutical companies and academic institutions that it competes against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than the Company does. Therefore, the Company might not be able to attract or retain these key persons on conditions that are economically acceptable. Furthermore, the Company will need to recruit new managers and qualified scientific personnel to develop its business if the Company expands into fields that will require additional skills. The inability of the Company to attract and retain these key persons could prevent it from achieving its overall objectives and could thus have an adverse effect on its business, prospects, financial condition and results of operations.

e. The Company might not find suitable industrial partners to pursue the development, the commercialisation or the distribution of its products candidates.

Depending on the region and depending on the product candidate, the Company's strategy may include out-licensing and co-developing its products candidates or partnering for the distribution of products developed and/or commercialised on a stand-alone basis. However, in order to conduct this strategy, the Company may need to find a partner, which has sufficient capacity for conducting research, on an international level or which is capable of distributing and commercialising the products. Therefore, the future international success of the Company may depend on its ability to conclude partnerships and on the ability of its partner(s) to meet the aforementioned characteristics.

2 GENERAL INFORMATION

This document is a registration document within the meaning of the Article 6 and Article 10 of the Prospectus Regulation 2017/1129.

On 28 September 2021, the Financial Services and Markets Authority approved the English version of this registration document in accordance with article 20 of the Prospectus Regulation 2017/1129. The approval of the registration document by the FSMA doesn't constitute an appreciation of the situation of the Company.

a. the registration document has been approved by the FSMA, as competent authority under Regulation (EU) 2017/1129;

b. the FSMA only approves this registration document as meeting the standards of completeness, comprehensibility and consistency imposed by Regulation (EU) 2017/1129;

c. such approval shall not be considered as an endorsement of the issuer that it the subject of this registration document.

d. that the registration document has been drawn up as part of a simplified prospectus in accordance with Article 14 of Regulation (EU) 2017/1129.

2.1 Legal Information

The legal and commercial name of the Company is Bone Therapeutics SA. Bone Therapeutics is registered with the legal entities register (Charleroi) under number 0882.015.654 and was incorporated in Belgium on 16 June 2006, for an indefinite period of time. The Company is a limited liability company incorporated in the form of a 'société anonyme' under the laws of Belgium. The Company's registered office is currently located at Rue Auguste Piccard 37, 6041 Gosselies (Belgium) (phone: +32 71 12 10 00 and fax: +32 71 12 10 01). The Legal Entity Identifier (LEI) code of the Company is 549300HFIIMTOP1DFR76.

2.2 Language of this Registration Document

The Company published its Registration Document in English. The Company has also prepared a French translation of this Registration Document and is responsible for the consistency between the French and English version of this Registration Document.

2.3 Persons responsible for the contents of the Registration Document

The Board of Directors (see Chapter 5), assumes responsibility for the content of this Registration Document. The Board of Directors declares that the information contained in this Registration Document is, to the best of its knowledge, in accordance with the facts and contains no omission likely to affect its content.

We undersigned, mC4Tx SRL, with as permanent representative Miguel Forte, CEO, and Finsys Management SRL, with as permanent representative Jean-Luc Vandebroek, CFO, on behalf of the Board of Directors of the Company, declare that to the best of our knowledge:

- the annual accounts, are established in accordance with the applicable standards for the preparation of the financial accounts, and do represent a fair and true view of the assets, the financial position and the results of the issuer and the entities which were included in the consolidation;

- the Registration Document provides a fair and true view of the developments and the results of the Company and of the position of the issuer and of the entities included in the consolidation, as well as a description of the most important risks and uncertainties faced by them.

2.4 Statutory auditor

Deloitte Réviseurs d'Entreprises SCCRL, a civil company having the form of a co-operative company with limited liability organised and existing under the laws of Belgium, with registered office at Gateway building, Luchthaven Nationaal 1, boite J, 1930 Zaventem, Belgium, represented by Mr Pieter-Jan Van Durme, member of the Belgian *Institut des Réviseurs d'Entreprises/Instituut voor Bedrijfsrevisoren*, replacing Julie Delforge from 9 June 2021 – date of the General Assembly Meeting – is appointed statutory auditor of the Company, for a term of three years ending immediately following the adjournment of the annual general shareholders' meeting of the Company to be held in 2022, resolving upon the financial statements for the fiscal year ended on 31 December 2021.

2.5 Forward-looking statements

Certain statements in this Registration Document are not historical facts and are forward-looking statements. Forward-looking statements include statements concerning the Company's plans, objectives, goals, strategies, future events, future revenues or performance, capital expenditure, research and development, financing needs, plans or intentions relating to partnership or acquisitions, competitive strengths and weaknesses, business strategy and the trends which the Company anticipates in the industries and the political, economic, financial, social and legal environment in which it operates and other information that is not historical information.

Words such as "believe", "anticipate", "estimate", "expect", "intend", "predict", "project", "could", "may", "will", "plan" and similar expressions are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements.

By their very nature, forward-looking statements involve inherent risks and uncertainties, both general and specific, and risks exist that the predictions, forecasts, projections and other forward-looking statements will not be achieved. These risks, uncertainties and other factors include, amongst other things, those listed in the Section "Risk Factors".

2.6 Market and industry information

Information relating to markets and other industry data pertaining to the Company's business included in this Registration Document has been obtained from internal surveys, scientific publications, section association studies and government statistics. The Company accepts responsibility for having correctly reproduced information obtained from publications or public sources, and, in so far as the Company is aware and has been able to ascertain from information published by those industry publications or public sources, no facts have been omitted which would render the reproduced information inaccurate or misleading. However, the Company has not independently verified information obtained from industry and public sources. Certain other information in this Registration Document regarding the industry reflects the Company's best estimates based on information obtained from industry and public sources. Information from the Company's internal estimates and surveys has not been verified by any independent sources.

2.7 Other available information

The Company has filed its deed of incorporation and must file its restated articles of association and all other deeds and resolutions that are to be published in the Belgian Official Gazette (*Moniteur belge*) with the clerk's office of the commercial court of Charleroi (Belgium), where such documents are available to the public. The Company is registered with the register of legal entities of Charleroi under company number 0882.015.654. A copy of the most recent restated articles of association, the reports of the Board of Directors and the minutes of the shareholders' meeting are also available on the Company's website (www.bonetherapeutics.com) or can be provided upon request to Bone Therapeutics SA, Investor Relations, 37, rue Auguste Piccard, B-6041 Gosselies, Belgium (Tel: +32 71 12 10 00, Fax: +32 71 12 10 01 and e-mail: investorrelations@bonetherapeutics.com).

The Company prepares annual audited and consolidated financial statements. All financial statements, together with the reports of the Board of Directors and the statutory auditor are filed with the National Bank of Belgium, where they are available to the public. Furthermore, as a Company with shares listed and admitted to trading on Euronext Brussels and Paris, the Company publishes an annual financial report (included its financial statements and the reports of the Board of Directors and the statutory auditor) and an annual announcement prior to the publication of the annual financial report, as well as a half-yearly financial report on the first six months of its financial year. Copies of these documents will be made available on the Company's website (www.bonetherapeutics.com) and STORI, the Belgian central storage platform which is operated by the FSMA and can be accessed via its website (www.fsma.be).

The Company must also disclose price sensitive information and certain other information relating to the public. In accordance with the Belgian Royal Decree of 14 November 2007 relating to the obligations of issuers of financial instruments admitted to trading on a Belgian regulated market (*Arrêté royal relative aux obligations des émetteurs d'instruments financiers admis à la négociation sur un marché reglementé*), such information and documentation will be made available through the Company's website (www.bonetherapeutics.com), press releases and the communication channels of Euronext Brussels.

2.8 Availability of the Registration Document

The Registration Document is available in English and in French. The Registration Document will be made available, free of charge, for the public upon request to:

Bone Therapeutics SA
To the attention of Investor Relations
Rue Auguste Piccard 37
B-6041 Gosselies
Belgium
Tel: +32 71 12 10 00
Fax: +32 71 12 10 01
E-mail: investorrelations@bonetherapeutics.com

An electronic version of the Registration Document is also available on Bone Therapeutics' website (www.bonetherapeutics.com). The posting of this Registration Document on the internet does not constitute an offer to sell or a solicitation of an offer to buy any of the shares to any person in any jurisdiction in which it is unlawful to make such offer or solicitation to such person. The electronic version may not be copied, made available or printed for distribution. Other information on the website of the Company or on another website does not form part of the Registration Document.

3 FINANCIAL INFORMATION CONCERNING THE COMPANY'S ASSETS AND LIABILITIES, FINANCIAL POSITION AND PROFITS, AND LOSSES

3.1 Information incorporated by reference

This Registration Document shall be read and construed in conjunction with the following documents:

(i) the annual report and audited consolidated financial statements of the Company prepared in accordance with IFRS for the financial year ended **31 December 2020** (in English and French), together with the related audit report thereon; and

(ii) the condensed consolidated unaudited interim financial statements of the Company prepared in accordance with IFRS for the financial period ended **30 June 2021** (in English and French), together with the related audit report thereon.

Copies of documents incorporated by reference in this Registration Document may be obtained (without charge) from the registered offices of the Company and the website of the Company (http://www.bonetherapeutics.com/en/financial-reports). The Company confirms that it has obtained the approval from its auditors to incorporate the audited consolidated financial statements and the auditors' reports thereon for the financial years ended 31 December 2020 and 30 June 2021 in this Registration Document.

The tables below include references to the relevant pages of the audited consolidated financial statements of the Company for the financial years ended 31 December 2020 and 30 June 2021, as set out in the annual reports of the Company (in English and French). Information contained in the documents incorporated by reference other than information listed in the tables below is either not relevant for the investor or covered elsewhere in the prospectus.

Audited consolidated financial statements of the Company prepared in accordance with IFRS for the financial period ended 31 December 2020, as set out in the annual report (in English and French).

Consolidated statement of financial position	p. 80
Consolidated statement of comprehensive income	p. 81
Consolidated statement of cash flows	p. 82
Consolidated statement of changes in equity	p. 83
Notes to the consolidated financial statements	p. 84-123
Auditor' s report	p. 73-79

Condensed consolidated unaudited interim financial statements of the Company prepared in accordance with IFRS for the financial period ended 30 June 2021, as set out in the interim report (in English and French).

Consolidated statement of financial position	p. 7
Consolidated statement of comprehensive income	p. 8
Consolidated statement of cash flows	p. 10
Consolidated statement of changes in equity	p. 9
Notes to the consolidated financial statements	p. 11-26
Auditor' s report	p. 28-30

3.2 Securities issued by the Company

At the date of this document, the Company's capital amounts to € 3,812,557.67, represented by 16,478,168 ordinary shares without nominal value.

The total of exercisable warrants is 225,554 warrants for the Executive committee members, consultants and Board members, 800,000 warrants for EIB and 200,000 warrants for Patronale Life, which give right to subscribe to an equal number of shares. This represents a total of 1,225,554 warrants.

3.3 Overview funding

Up to the date of this document, the Company has been able to fund its operations with a long-term perspective through the following funding instruments:

- € 100.96 million in net proceeds from private equity placements in the Company;
- € 2.51 million in invested cash through the non-controlling interest held by third parties in its affiliate SCTS SA;
- € 35.81 million of non-dilutive funding, mainly through recoverable cash advances, subsidies and patents provided by the Region and to lesser extent through regular grants.
- € 3.25 million as a long-term investment credit provided by BNP Paribas Fortis SA/NV and ING Belgique SA/NV (each for half of the amount) for the construction of the SCTS building at the Biopark of Gosselies (South of Brussels);
- € 7.50 million via the Bond Issuance;
- € 3.97 million in loans, provided by related parties (regional investment vehicles) which have been recorded as current and non-current financial liabilities and
- € 2.53 million through an investment grant provided by the Region on the SCTS building.

3.4 Legal proceedings

The Company is not, nor has been, involved in any governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which the Company is aware) during the 12 months preceding the date of this Registration Document which may have or has had in the recent past significant effects on the financial position or profitability.

3.5 Significant change in the financial position of Bone Therapeutics since 31 December 2020

Financing from the European Investment Bank

On 1 July 2021, the Company announced that it has signed a loan agreement of up to €16 million with the European Investment Bank (EIB).

The EIB financing will support and prepare Bone Therapeutics' lead asset, the enhanced viscosupplement JTA-004 for future regulatory approval and commercialization. JTA-004, is being evaluated in a registrational phase III clinical trial for the treatment of osteoarthritic pain in the knee. This is the most prevalent knee condition affecting an estimated 250 million patients world-wide.

The EIB financing will also be used to accelerate the clinical development of ALLOB, Bone Therapeutics' scalable allogeneic cell therapy platform. ALLOB is currently being tested in a phase IIb study in patients with

difficult-to-heal tibial fractures. Patient recruitment of this study is currently anticipated to be completed in H1 2022 and the planned top line results are expected in H2 2022.

The EIB loan financing will be disbursed in two tranches of €8 million each, subject to conditions precedent. The first tranche of €8 million was reived on 6 September 2021 (upon approval of the issuance of associated warrants by Bone Therapeutics' General Meetings on 23 August 2021). The second €8 million tranche will be released when specific clinical and commercial milestones have been achieved.

The loan facility will be in the form of a senior loan, repayable to the EIB in a single payment five years following the disbursement of each of the two tranches. The loan carries a fixed interest of 2% per year paid annually and a 3% capitalized interest.

The loan financing is further supplemented by an agreement to issue warrants to the EIB: 800,000 warrants will be issued with the disbursement of the first tranche and 500,000 warrants with the disbursement of the second tranche. Each warrant will give the holder the right to subscribe to one ordinary share of Bone Therapeutics at the subscription price of €0.01 and with an exercise price which will be equal to the minimum of the 30 day volume-weighted average price and the last closing price of Bone Therapeutics' shares at the date of the pricing. The warrants have a maturity of 10 years and become exercisable from the repayment date of the relevant tranche, subject to certain customary exceptions. The warrant agreement further includes an anti-dilution provision which could apply in case of change in Bone Therapeutics' share capital, including capital increases if they exceed €15 million in aggregate starting from the disbursement of the first tranche.

3.6 Current cash situation

- Net cash at the end of June 2021 amounted to € 6.01 million.
- The Company reiterates its previous guidance of a net cash use of € 16-18 million for the full year 2021.
- The Company received the first tranche of € 8.00 million from the EIB loan agreement on 6 September 2021.
- With the received disbursement of the first tranche of the EIB financing, the Company anticipates having sufficient cash to carry out its business objectives into Q2 2022.

3.7 Dividends and dividend policy

3.7.1 *Entitlement to dividends*

Dividends can only be distributed if, following the declaration and payment of the dividends, the amount of the Company's net assets on the date of the closing of the last financial year as follows from the statutory financial statements prepared in accordance with Belgian GAAP (*i.e.*, the amount of the assets as shown in the balance sheet, decreased with provisions and liabilities), decreased with the non-amortised activated costs of incorporation and extension and the non-amortised activated costs for research and development, does not fall below the amount of the paid-up capital (or, if higher, the called capital), increased with the amount of non-distributable reserves. In addition, pursuant to the Belgian Code of Companies and Associations and the articles of association, the Company must allocate at least 5% of its annual net profits under its statutory non-consolidated accounts to a legal reserve until the reserve equals 10% of the Company's share capital.

In accordance with Belgian law, the right to collect dividends declared on ordinary shares expires five years after the date the Board of Directors has declared the dividend payable, whereupon the Company is no longer under an obligation to pay such dividends.

3.7.2 *Dividend policy*

The Company has never declared or paid any dividends on its shares.

The Company's dividend policy will be determined by, and may change from time to time by determination of, the Company's Board of Directors. Any declaration of dividends will be based upon the Company's earnings, financial condition, capital requirements and other factors considered important by the Board of Directors. The calculation of amounts available to be distributed as dividends or otherwise distributed to shareholders must be made on the basis of the Belgian statutory financial statements, taking into account the limits set out in the Belgian Code of Companies and Associations.

Belgian law and the Company's articles of association do not require the Company to declare dividends. The Board of Directors expects to retain all earnings, if any, generated by the Company's operations for the development and growth of its business and does not anticipate paying any dividends to the shareholders in the near future.

4 BUSINESS OVERVIEW

4.1 Important recent events in the development of the Company's business

Year	Key Milestones		
Year	**Corporate**	**ALLOB**	**JTA**
2021	• Bone Therapeutics and Rigenerand sign partnership for cell therapy process development • Appointment of Anthony Ting, PhD as Chief Scientific Officer • Appointment of Anne Leselbaum, MD as Chief Medical Officer • Bone Therapeutics secures up to €16M loan financing from the EIB to accelerate clinical and commercial development of innovative orthopaedic treatments • Bone Therapeutics agrees final settlement with the FSMA regarding clinical studies communication issues in 2016 and 2017	• Treatment of the first patient in ALLOB Phase IIb tibial fracture study • Bone Therapeutics publishes results of ALLOB Phase I/IIa study for the treatment of delayed-union fractures in Stem Cell Research & Therapy	• Strong clinical progress in JTA-004 Phase III study thanks to high patient compliance and retention • Topline results from Phase III knee osteoarthritis study with its enhanced viscosupplement JTA-004

4.2 Investments

In October 2020, the Company signed a manufacturing collaboration with Catalent, Inc. to streamline the production of ALLOB. Under the terms of the share purchase agreement, Catalent acquired Bone Therapeutics' cell therapy manufacturing subsidiary, Skeletal Cell Therapy Support SA (SCTS), for gross proceeds of €12 million. The equity purchase price, net of SCTS's debt (€3 million), cash adjustments, and taking into account the restructuring of some Bone Therapeutics' existing liabilities (€3 million), generated net proceeds of approximately €6 million.

From this date, the Company is renting the offices and labs to Catalent SA at the Biopark of Gosselies (rue Auguste Piccard 37, 6041 Gosselies) and is not anymore, the owner of the building constructed by SCTS SA.

4.3 Activities of the Company

The Company is a biotechnology company with an advanced clinical pipeline of innovative products for orthopaedic conditions and bone diseases (one Phase IIb clinical studies and one Phase III study). The Company targets medical areas with high unmet medical needs characterized by the lack of efficacious and safe, non-invasive, treatments. Indeed, most current standard-of-care treatments involve heavy surgery and long recovery periods.

The Company's core technology is based on its allogeneic cell therapy platform, ALLOB, which uses a unique, proprietary approach to bone regeneration, which turns undifferentiated stem cells from healthy donors into bone-forming cells. These cells can be administered via a minimally invasive percutaneous procedure or added

through a simple addition/injection to the current standard-of-care, expected to offer significant benefits over or enhancing the current standard-of-care.

The Company is also developing an off-the-shelf protein solution, JTA-004, for the treatment of pain in knee osteoarthritis. This product is developed as a single intra-articular injection treatment, expected to offer superior benefits to existing intra-articular injections of hyaluronic acid. Based on the recently announced topline results of the Phase III knee osteoarthritis study with JTA-004, the Company, in collaboration with existing and potential partners, will consider the options for the future of JTA-004 development.

Solid preclinical foundations and clinical results support the Company's research and development programs. The Company has extensive knowledge of bone physiology and pathophysiology and collaborates closely with prestigious academic and medical institutions. The Company has worldwide rights for a series of patents and technologies related to its products, their production methods and their applications.

4.4 Company mission and strategy

The Company aims to be a leading regenerative company providing innovative cell therapy products for high unmet medical needs (defined as a medical need that is not addressed adequately by an existing therapy[1]) in the fields of orthopaedics and bone diseases. To achieve this objective, the Company is pursuing the following strategies:

- Enhance the development of its commercially oriented, off-the-shelf, allogeneic platform, to maximize benefits for patients and value creation for investors
- Progress and complete the ALLOB Phase IIb controlled trial for difficult-to-heal tibial fractures, building on encouraging Phase IIa clinical data
- Advance and expand the (pre)clinical pipeline with additional indications by enhancing and specializing the therapeutic capacity of its cell and gene therapy platform.
- Build development and commercial partnerships

4.5 Technology

The Company's technology platform is based on a unique approach in which mesenchymal stem cells (MSC), derived from bone marrow of healthy donors, are stimulated to differentiate into bone-forming cells. These bone-forming cells are involved in bone homeostasis and regulate the dynamic and constant remodelling of the skeleton. They are responsible for bone matrix synthesis and subsequent mineralization, thus the generation of new bone tissues.

Local implantation of biologically active bone-forming cells at the bone defect site is intended to mimic the natural process of bone formation and repair.

More specifically, the mode-of-action is dual.

- On the one hand, the bone-forming cells will replace the defective or missing bone-forming cells and will form new bone and repair the defective bone.
- On the other hand, the presence of bone-forming cells will create a healthy bone environment by recruiting haematopoietic and osteoprogenitor cells and secreting matrix proteins.

[1] FDA Guidance for Industry – Available Therapy, July 2004.

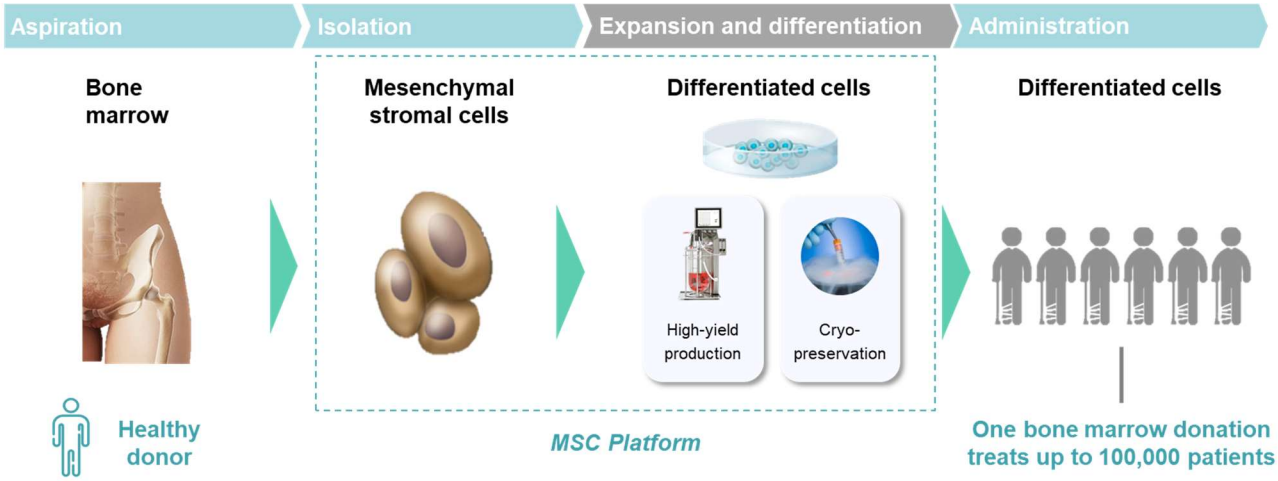
The implanted cells are expected to adhere onto the existing tissue and matrix, where they will produce new bone matrix that will be calcified. Finally, the cells will differentiate into osteocytes and become imbedded into the calcified new bone matrix.

The Company aims to improve:

- Efficacy: by developing innovative cell products composed of differentiated bone-forming cells.
- Safety: by offering a minimally invasive approach involving implanting the cells with a needle or trephine directly at the bone defect site through the skin, replacing the need for invasive surgery.

The unique use of differentiated bone-forming cells offers potential advantages compared to other types of cells (including undifferentiated stem cells):

- In terms of efficacy, the Company's differentiated cells have already acquired the capacity to form bone and are therefore more likely to have beneficial effects in bone diseases.
- Increased safety is also expected by this differentiation. Acquired function is expected to minimise the toxicity risk due to unwanted biological activities as well as uncontrolled proliferation.



The above figure shows the manufacturing process of the Company's allogeneic cell therapy platform (ALLOB) starting with bone marrow harvesting from healthy donors to obtain the mesenchymal stem cells that are expanded and differentiated into bone-forming cells and implanted at the bone defect site. The finished product is delivered in an off-the-shelf cryopreserved formulation. One bone marrow donation allows the production of 100,000 doses.

4.5.1 *ALLOB: allogeneic cell product*

ALLOB is the Company's allogeneic cryopreserved product that consists of human allogeneic bone-forming cells derived from cultured bone marrow MSC of healthy adult volunteer donors. A bone marrow aspirate is performed from the iliac crest of the donor under local anaesthesia, after which MSC are isolated, expanded and differentiated. The active part of the product thus comprises human allogeneic bone-forming cells. ALLOB has been classified as Tissue Engineered Product (non-combined) by the EMA under the ATMP classification 1394/2007. The manufacturing process is performed in strict GMP compliance and follows procedures that ensure aseptic manufacturing, full traceability, and quality control.

ALLOB cells express master osteoblast genes, mesenchymal and bone matrix adhesion markers and display bone-forming properties. High throughput genomic study (RNAseq) revealed a clear distinct and reproducible genomic profile for ALLOB compared to MSC which is a key result demonstrating the differentiation of ALLOB cells compared to the former cells.

In vitro, ALLOB cells are able to adhere, synthesize and mineralize new bone matrix. *In vivo*, bone forming properties have been demonstrated in relevant mouse models such as bone formation and bone non-union (NU) models. Importantly the osteogenic activity of ALLOB signed by the presence of bone of human origin has been clearly demonstrated while with MSC this property has not been evidenced. Engraftment of the ALLOB cells as well as bone-forming and bone repair capacities were demonstrated in mouse models by local administration at the defect site in a bone NU model. The presence of ALLOB cells at administration site has been evidenced by qPCR in mice at week 1, week 10 and 6 months. Importantly these biodistribution studies revealed that majority of administration sites are positive until 6 months and that ALLOB cells have low dissemination potential.

In vivo safety studies did not show changes in clinical signs or in laboratory parameters and no anomalies in microscopic or macroscopic observations. Additionally, no ectopic (meaning in an abnormal location) bone formation could be detected when ALLOB cells were injected in muscles. Safety was further investigated by intravenous administration of ALLOB cells at high doses to immunodeficient mice. These high doses did not cause any excess morbidity or mortality during a 24-week observation period and no evidence for ectopic bone formation or other abnormalities was detected. A long-term safety study in a bone NU model demonstrated that ALLOB did not induce any findings regarding weight, clinical signs, macroscopical, anatomopathological, haematological, biochemical and ophthalmological changes during a 6-month observation period.

Additional preclinical experiments were performed to investigate the use of ALLOB in combination with bioceramic granules or collagen-sponge scaffold for spinal fusion procedures. The bioceramic or collagen scaffolds are bone substitutes designed, optimized, and indicated for bone void filling, in particular in spinal fusion procedure. ALLOB cells were shown to adhere and spread within the pores of the granules or survive in a collagen sponge. Importantly, ALLOB cells were shown to migrate out of the scaffolds, adhere and grow in culture. The efficacy of the ALLOB alone and combined with a scaffold were assessed *in vivo* in a bone NU model and compared to the administration of the scaffold or excipient alone as controls. After several weeks, all animals treated with ALLOB alone or combined with a scaffold showed healing superior to controls.

4.5.2 *Administration via a minimally invasive approach*

In the treatment of fractures, administration of ALLOB cells is achieved via a minimally invasive technique. The cells are administered directly into the fracture site through a small skin incision using a small-diameter trephine (similar to a large needle – diameter is 5 mm). During the implantation, the position of the trephine into the fracture site is visualized by fluoroscopy (a standard radiography used by orthopaedic surgeons). The simple procedure is performed under anaesthesia in an operating room, taking 20 to 40 minutes in total.

In case of lumbar spinal fusion, ALLOB is combined with a scaffold and administered locally at the spine surgery site. The procedure includes placement of an interbody (*i.e.*, between the vertebrae) cage and is performed under general anaesthesia in accordance with the standard-of-care procedure of the investigating site.

4.5.3 *Optimizing the allogeneic manufacturing process*

With its main focus on its off-the-shelf, allogeneic cell therapy platform, Bone Therapeutics has been optimizing its ALLOB manufacturing process in order to improve consistency, scalability, cost effectiveness and ease of use, which are critical for development and commercialisation in cell therapy.

The Company is continuing to develop an optimized commercial manufacturing process that it believes will satisfy these objectives. The optimized production process significantly increases the production yield, generating up to one hundred thousand doses of ALLOB per single bone marrow donation. Additionally, the final ALLOB product is cryopreserved, enabling easy shipment and the capability to be stored in a frozen form at the hospital level, making it readily available for patients in need. The process will therefore substantially reduce overall production costs, simplify supply chain logistics, improve patient accessibility and facilitate global commercialisation to large patient populations more affordably.

Bone Therapeutics believes the optimized manufacturing process is vital to the future commercial success of ALLOB. In order to avoid process changes in later phases of development, improve cost effectiveness and

streamline ALLOB's route to market, the Company will implement the optimized scaled-up production process for all future clinical trials with ALLOB.

4.5.4 *JTA-004: off-the-shelf protein solution*

In parallel with its core cell therapy pipeline and in line with its mission of creating innovative solutions for orthopaedic conditions, Bone Therapeutics is also developing an off-the-shelf protein solution for the symptomatic treatment of knee osteoarthritis, JTA-004. JTA-004 is developed as a single intra-articular injection solution composed of 3 active substances: (1) human plasma supplemented with (2) hyaluronic acid (HA) and (3) an analgesic agent.

Once injected in the joint cavity, JTA-004 increases the viscosity of the synovial fluid, leading to joint lubrication, mechanical support and cartilage protection of the arthritic joint.

Due to its unique composition, JTA-004 has shown distinct advantages in preclinical studies over intra-articular injections of hyaluronic acid, including anti-inflammatory activity in an *in vitro* monocyte cell assay and statistically significant reduction of cartilage degradation in a non-human primate model.

Furthermore, JTA-004 has demonstrated improved efficacy in osteoarthritic pain reduction in a Phase 2b clinical trial compared with Hylan G-F 20, a market leading viscosupplement.

4.6 Current clinical pipeline and outlook

Bone Therapeutics' allogeneic cell therapy product, ALLOB, and its off-the-shelf protein solution, JTA-004, are currently under clinical development for three indications in the field of orthopaedics and bone diseases.

ALLOB was evaluated in two Phase II studies:

- Delayed-union fractures: Based on strong efficacy data from the interim analysis for the first 16 patients after a six-month follow-up, the Data and Safety Monitoring Board (DSMB) recommended stopping the trial early in September2017. In September 2018, the Company reported positive final results for its Phase I/IIA study in 21 patients, confirming previous interim data and supporting the future clinical development of ALLOB in fracture healing.

- Lumbar spinal fusion: In June 2019, Bone Therapeutics announced that its allogeneic cell therapy product, ALLOB, met the primary endpoints in the Phase IIa study in 30 patients undergoing a lumbar spinal fusion procedure. In October 2020, the Company reported positive 24-month follow-up results for the Phase IIa study, showing a high percentage of successful lumbar vertebrae fusion of 90%. Patients also continued to experience important clinical improvements in function and pain, from as early as six months after treatment, up to the 24-month follow-up period. The next development steps for ALLOB in this indication are planned to be considered after the results of the ongoing ALLOB clinical study in tibial fractures.

ALLOB is currently being evaluated in an ongoing randomized, double-blind, placebo-controlled Phase IIb study with high-risk tibial fractures. This study will assess and compare against placebo, in association with standard of care stabilization surgery, the potential of 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 24-96 hours post-definitive reduction surgery in patients with fresh tibial fractures at risk for delayed or non-union. The study has been approved in 7 European countries (Belgium, Czech Republic, France, Germany, Hungary, Poland and Spain) and is currently enrolling patients. The first patient was enrolled in January 2021 and 178 patients are expected to be enrolled in over 40 sites. Bone Therapeutics anticipates finalizing patient recruitment in H1 2022. Topline results are expected in second half of 2022. Both dates are subject to the evolution of the ongoing COVID-19 pandemic.

JTA-004 has been evaluated in a Phase IIb and Phase III study in symptomatic knee osteoarthritis (KOA):

- In October 2018, the Company reported positive final results for its Phase IIb study in 164 patients. The results indicated that a single intra-articular injection of JTA-004 delivered higher pain reduction than the reference product, the global market leader in intra-articular injection of hyaluronic acid.

- In August 2021, Bone Therapeutics announced the topline results from the multicenter, randomized, double-blind, placebo- and active-controlled Phase III study. The study was conducted in 7 European countries and Hong Kong and included a total of 743 patients. Despite JTA-004's favourable safety profile, the study did not achieve its main objectives as no statistically significant difference in pain reduction could be observed between any of the treatment, placebo and comparator groups, with all treatment arms showing similar efficacy. A statistically significant difference in favour of JTA-004 and the active comparator versus placebo was seen in a post-hoc analysis in a subset of patients with higher pain scores at entry. The Company, in collaboration with existing and potential partners, will consider the options for the future of JTA-004 development.

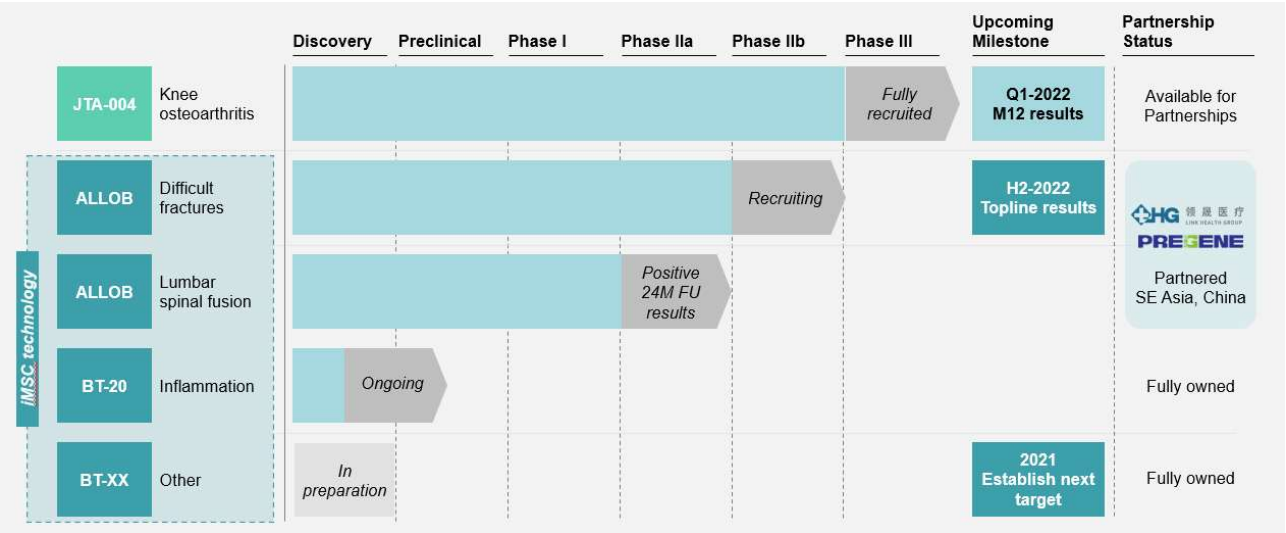


Figure: Clinical pipeline with ALLOB (allogeneic cell therapy approach) and JTA-004 (off-the-shelf protein solution)

Future Pipeline Development

The Company continues to advance development of its cell therapy platform with a view to creating innovative products based on professional MSCs for orthopaedic applications and beyond, at the cutting-edge of innovation in cell therapies, including inflammatory disease and other disease areas of high unmet medical need. As such, novel enabling technologies are currently being evaluated, including technologies for genetic engineering and the use of induced pluripotent stem cells (iPSCs) and partnerships with companies with expertise and intellectual property rights in these areas are being sought.

Outlook

For the ongoing Phase IIb ALLOB clinical study in difficult tibial fractures, Bone Therapeutics expects patient recruitment to be completed by the end of first half of 2022 and topline results by the end of 2022. Although early recruitment rates were very promising, as across the industry, the rate of recruitment has temporarily slowed in recent months due to short term pandemic-related factors, such as reduced site activities due to staff availability, and number of available patients due to less accidents. Bone Therapeutics' clinical team, in

partnership with the clinical research organization, has instituted corrective measures to mitigate the impact of the pandemic. Given the early stage of the study conduct and recruitment and further mitigation actions, the Company believes it could maintain the aforementioned timelines. Should the pandemic continue, Bone Therapeutics may have to re-evaluate these timelines and, in that eventuality, will communicate again to the market.

Bone Therapeutics will continue to expand its allogeneic differentiated MSC based cell therapy platform, beyond ALLOB, into other therapeutic indications. Bone Therapeutics is also intensifying its efforts to expand its preclinical and clinical pipeline with additional indications by enhancing and "professionalizing" the therapeutic capacity of its cell and gene therapy platform. This activity includes the development of a next generation of genetically engineered mesenchymal stromal cells (MSC) and the use of highly scalable and versatile cell sources such as induced pluripotent stem cells (iPSC).

Bone Therapeutics will continue to hold discussions with potential partners to explore business opportunities while ALLOB is being evaluated in a double-blind, placebo-controlled, proof-of-concept Phase IIb study.

Bone Therapeutics will continue its discussions with the US FDA (Food and Drug Administration) in preparation for the next steps in the clinical development of ALLOB in the US.

LinkHealth and Pregene, Bone Therapeutics' partners in Asia continue to drive the development of ALLOB towards the submission of Investigational New Drug Application (IND) with the Chinese National Medical Products Administration (NMPA). A successful IND application could result in new milestone payments to Bone Therapeutics.

4.7 Principal bone disorder markets

The bone-related disorder industry, in which the Company operates, encompasses various pathologies, from orthopaedic conditions such as severe fractures and treatments of degenerating disc disease. Depending on the indication, competition could come from pharmaceutical, biopharmaceutical (including regenerative and cell therapy companies) and/or medical devices companies, as well as new discoveries from academic research institutions.

The market space in which the Company operates covers fracture repair, spinal implants, bone growth stimuli and orthobiologics (excluding the osteoporosis market) and represents an estimated global market of around $ 22 billion (2019) for the treatment of more than 250 million patients, which can be broken down in the following segments[2] [3]:

Segment	Number of patients	Product sales in million USD	% Change YOY
Fracture repair	8,000,000	7,449.3	3.4%
Spinal implants / instrumentation	3,000,000	9,654.1	3.5%
Bone growth stimulation	Included above	670	
Orthobiologics	250,000,000	5,291.1	4.0%
Total	**261,000,000**	**23,064.5**	

[2] Orthoworld, The Orthopaedic Industry Annual Report, 2020 (relating to fracture repair, spine and orthobiologics) – Global Data - Medipoint, Bone Growth Stimulators Analysis and Market Forecast, 2017 (relating to bone growth stimulation).
[3] Vos et al., *A systematic analysis for the Global Burden of Disease Study 2010*. Lancet 2012; 380:2163-96

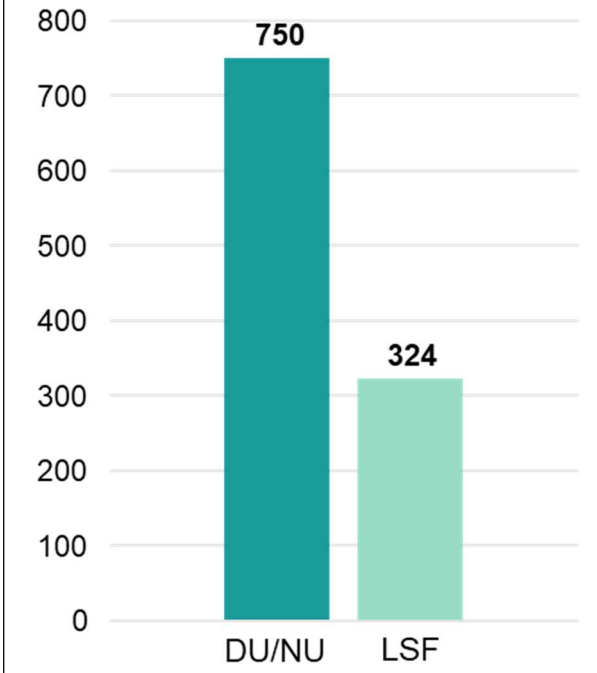
- Fracture repairs covers all the materials used today for repairing fractures both internally and externally such as plates, screws, intramedullary nails, pins, wires, staples and external fixators.

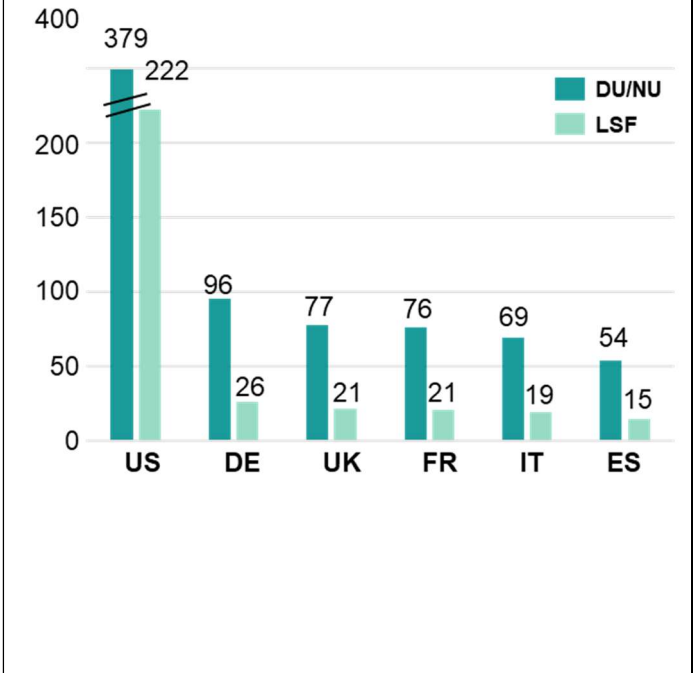
- Spinal implants/instrumentation are all the materials used to treat degenerative disc disease, herniated discs, scoliosis, vertebral fractures and others such as pedicle screws, plates, rods, hooks, screws, artificial discs, motion preserving devices, discectomy tools and vertebroplasty/kyphoplasty products.

- Bone growth stimulation refers to equipment that is used for treating fractures and in support of spinal fusion to stimulate bone growth through ultrasound, pulsed electromagnetic fields and extracorporeal shock wave therapy.

- Orthobiologics are biologic and biochemical products with application across orthopaedics such as allograft and xenograft, synthetic bone graft substitutes, hyaluronic acid viscosupplements, autologous platelet/plasma systems, cell-based products for tissue repair, growth factors and bone proteins, soft tissue repair, replacement and reinforcement products and anti-adhesion technologies.

Target Patient Numbers EU5 and US (thousands)





Sources: IQVIA Primary Market Research, n=32; [1] Mills et al., 2017; [2] Wennergren et al., 2015; [3] Papin et al., 2017; [4] Coles et al., 2000; [5] Robinson et al, 2003; [6] Audigé et al., 2005; [7] Phieffer et al., 2006; [8]Rajaee, S. et al., 2012 [9] GlobalData. Spinal Fusion ;[10] Lieberman et al., 2003;[11] Vail & Convington, 1997;[12] Makin, 1992; EMA 2015, Public summary of opinion on orphan designation for ALLOB in ON; [13] United Nations World Prospects Population 2017

In this space, the Company currently focuses on three main orthopaedic conditions: difficult-to-heal fractures, lumbar spinal fusion and osteoarthritis of the knee (addressed below). The market addressed by the Company is characterized by high unmet medical needs (defined as a medical need that is not addressed adequately by an existing therapy[4]). Indeed, most current treatments have either shown limited efficacy or require invasive surgery at significant risk of major complications and often limited long-term benefit. In addition, most treatments are associated with long hospitalization and recovery time after surgery with a persisting risk for re-intervention. Despite this, the fields targeted by the Company have so far remained relatively clear of new

[4] FDA Guidance for Industry – Available Therapy, July 2004.

treatments and there are very few reported clinical trials. In bone cell therapy, clinical development programmes are still limited to a small number of indications and companies, although there is a growing interest at the level of academic research.

4.7.1 *Difficult-to-heal fractures*

Description

Bone is a naturally regenerative organ, and fractures are currently well-managed in a majority of patients. However, there are traumatic situations in which bone fails to regenerate, leading either to a slowed-down regeneration process (delayed-union) or even a totally interrupted regeneration process (non-union). Inadequate reduction of a fracture leading to instability or poor immobilization may be a reason for delay in fracture union. Clinical studies have shown that several factors can impair one or more stages of the natural fracture healing process causing delayed-union or non-union that may require further pharmacological or surgical interventions. Factors which may influence fracture healing and increase the risk of a delayed-union or a non-union fracture can be patient-independent such as the type and degree of injury or the localization and the type of the fracture (e.g. high-energy and/or open fractures) and the quality of the initial surgery, or patient-related, such as age, smoking, alcohol consumption or a medical condition.

Typically, delayed-union suggest that the union is slow, but will eventually occur without additional surgical or non-surgical interventions. Currently, there is no universally validated approach to quantitatively evaluate the progression of fracture healing at various time points from fracture onset to complete recovery. Fracture leads to acute pain and functional impairment that gradually resolve over time if bone fracture healing progresses to a point allowing full functional recovery. The definitions of delayed-union are still subject of interpretations, and the diagnosis of delayed-union is mainly based on time. Commonly, a delayed-union fracture is defined as a fracture that has not united within a period of time (3-7 months) that would be considered adequate for bone healing[5].

Because the lack of commonly accepted criteria for diagnosis, combined with heterogeneity in need for intervention, there are, for now, no standard approaches to assess the risk for and treatment of delayed-unions. Consequently, diagnosis and therapeutic decisions are made on a case by case basis. Once the risk of delayed-union is established, surgeons re-assess the assumption of fracture stability and evaluate the need or feasibility for an immediate revision surgery affecting the fracture site. Commonly, the severity of the patient's condition does not require or allow an immediate revision, and a "wait and see" attitude is mostly adopted until the diagnosis of delayed-union is confirmed or the situation improves. This "wait and see" approach may last several months, which delays the patient's return to a normal life and places a significant financial burden on society.

Market Size

In the US, long bone fractures account for approximately 10% of all non-fatal injuries[6]. Close to 10 million fractures occur every year and over 3 million fracture repair surgeries are performed in Europe, the US and Japan. This led to revenues of almost $7.5 billion in the global fracture repair market in 2019, an increase of 3.4% compared to the year before. This market is expected to continue to grow steadily over the coming years[7]. Major driving factors for the fracture repair devices market are population growth, the increase in the elderly population, growing healthcare costs, and the increase in prevention measures for various orthopaedic-related problems. The leading causes of orthopaedic fracture cases are the ageing population, increasing participation in sports and rising number of road accidents.

Tibia fractures are common. In the USA there are 492,000 tibia, fibula and ankle fractures, leading to 77,000 hospitalizations p.a. In the UK, the incidence is 55/100,000 (18-49 yrs old) and 65/100,000 (<50 yrs old) p.a.

[5] Liebergall et al., Stem cell-based therapy for prevention of delayed fracture union. Molecular Therapy 2013 (8), 1631-1638
[6] Kanakaris et al., The health economics of the treatment of long-bone non-unions. *Injury* 2007(38S)S77-S84.
[7] Orthoworld. The orthopaedic industry annual report for year ending December 31, 2017.

In tibial shaft fracture, non-union was reported in up to 10–20% of patients; in an analysis on 853 US patients, 12% had NU[8]. The target population (high risk patients) is therefore estimated around 750,000. Recombinant human Bone Metalloproteinase 2 (rhBMP-2) has been popular in the USA (Infuse® from Medtronic), but has been plagued by safety concerns and is currently only used off-label for the most severe cases.

Competition

The Company is developing cell products using allogeneic optimally differentiated bone-forming cells for the treatment of delayed-union fractures that retain the bone-inducing (osteoinductive) properties of the MSCs they are derived from. To its knowledge, it is the only company that develops products that combine the osteoinductive properties of MSC, with the bone-forming (osteogenic) capabilities of osteoblasts, thereby demonstrating much greater regenerative potential. Bone Therapeutics' allogeneic bone cell products, ALLOB, is now a Phase IIb clinical trial for the treatment of difficult-to-heal fractures, i.e. fractures considered at risk of delayed-union or non-union. Delayed-union or non-union fractures are rarely treated by physicians which is reflected in the very limited number of ongoing clinical trials reported on *ClinicalTrials.gov* for these conditions.[9,10] The Company believes that it can play a significant role in leading this market, as an early actor in the field evolving the paradigm for the treatment of high-risk fractures. Instead of waiting (for the confirmation of a delayed-union or non-union diagnosis), surgeons will be provided with ALLOB as an early non-invasive therapeutic option, offering reduced healing time and yielding substantial cost savings[11].

Established non-unions are generally treated with bone autograft, harvested from the patient's ileac crest with or without intramedullary nailing, plating, and external fixation devices. Besides the fact that this treatment presents a success rate 1-year post-surgery of about 75-85%, it is still associated with considerable side-effects, with complications, such as the need for a secondary invasive surgery at the harvest site and pain at harvest site that can persist for several years, and infection reported in 20% of patients (for iliac crest harvest procedures in particular)[12].

In the early phase of delayed-union fractures, several non-invasive techniques have been developed to stimulate a biological healing response of the fracture, such as ultrasound stimulation (Exogen® from Bioventus). In the rare cases that delayed-union fractures are surgically treated, the use of osteosynthesis material and bone grafts is a well-established practice for the repair of fractures. There are numerous choices for bone graft matrices ranging from (i) bone autograft to (ii) multitude allografts, mostly cadaver bone, demineralized bone matrix (DBM), and cellular bone matrix (CBM) (from Nuvasive, Zimmer Biomet, Orthofix, Allosource, etc.), or (iii) synthetic bone substitutes (from Stryker, Zimmer Biomet, Kuros Bioscience, DePuy Synthes, etc.). Next to bone void filler products in support of bone graft surgeries, some medical devices company have also developed "injectable" bone void filler products for unhealed fractures of non-weight-bearing bones. These products are all registered as Devices, not Drugs.

Apart from bone grafting, Infuse®/InductOs® (the ortho-biological product (*i.e.*, protein) rhBMP-2; Medtronic) is, to the Company's knowledge, the only pharmaceutical therapy approved in Europe and in the US in a restricted indication (treatment of acute, open tibial shaft fractures that have been stabilized with intramedullary nail fixation after appropriate wound management). Studies have revealed unsatisfactory results for other "orthobiologics" in fracture healing (rhBMP-7 from Olympus Biotech, rhPDGF from Wright Medical Group, PTH from Lilly and *Romosozumab* from Amgen/UCB), forcing them to withdraw the products from the market or discontinue their clinical development. Kuros Biosciences completed in 2011 a Phase IIb

[8] Antonova E, et al. Tibia shaft fractures: costly burden of non-unions, *BMC Musculoskeletal Disorders*, 2013, 14, 42; Curtis E, et al, Epidemiology of Fractures in the United Kingdom 1988-2012: Variation with age, sex, geography, ethnicity and socioeconomic status, *Bone*. 2016 Jun; 87: 19–26; Hernandez RK, et al, Patient-related risk factors for fracture-healing complications in the United Kingdom General Practice Research Database, *Acta Orthop*. 2012 Dec; 83(6): 653–660

[9] From www.clinicaltrials.gov, Indication "Delayed Union of Fracture", Status "Not yet recruiting", "Recruiting", "Active, non-recruiting" and recently "Completed", last consulted on October 25, 2019.

[10] From www.clinicaltrials.gov, Indication "Non-Union of Fracture", Status "Not yet recruiting", "Recruiting", "Active, non-recruiting" and recently "Completed", last consulted on October 25, 2019.

[11] Heckman et al. The economics of treating tibia fractures. The cost of delayed unions. Bull Hosp Jt Dis. 1997(56)63-72.

[12] Friedlaender G, et al. Osteogenic protein-1 (BMP-7) in the treatment of tibial non-unions: a prospective, randomised clinical trial comparing Rhop-1 with fresh autograft. *J Bone Joint Surg Am.* 2001(83)151-158.

trial with vPTH (variant of the parathyroid hormone) in combination with a matrix for treating fresh tibia fractures however since then no further news has been announced.

The majority of the identified companies work on non-union fractures. To Company's knowledge, Bone Therapeutics is the only cell therapy company focusing on providing an early, allogeneic (off-the-shelf and ready to use immediately), minimally-invasive therapeutic option for difficult-to-heal fractures.

Overview of cell therapy companies active in unhealed fractures and spinal fusion[13].

Marketed Products				
Company	**Indications**	**Type of product**	**Route of Administration**	**Regulatory Path***
Medtronic	• Spinal fusion • Tibial fractures	Orthobiologic (rhBMP-2) with scaffold	Local Injection	BLA
DePuy Synthes *(supplied by LifeNet Health)*	• Spinal fusion	Bone Fillers	Surgery	Device / Procedure
Nuvasive *(supplied by AlloSource)*	• Spinal fusion	Bone allograft with cells	Surgery	Device / Procedure
Stryker	• Spinal fusion • Trauma	Bone Fillers	Surgery	Device / Procedure
Zimmer Biomet	• Musculoskeletal defects	Bone allograft Bone Marrow Aspirate	Surgery	Device / Procedure
Orthofix *(supplied by MTF Biologics)*	• Spinal fusion • Orthopedic reconstruction	Bone allograft with cells	Surgery	Device / Procedure
AlloSource	• Spinal fusion • Trauma	Bone allograft With/without cells Bone Fillers	Surgery	Device / Procedure
Smith and Nephew (Bioventus)	• Osseous defects (incl. fresh fractures, delayed unions, non-unions)	Low frequency ultra-sound device	Procedure	Procedure

Products in Development					
Company	**Indications**	**Type of product**	**Route of Administration**	**Regulatory Path***	**Phase of Development**
Bone Therapeutics	• **Delayed union fractures** • **Spinal fusion**	**Off-the-shelf differentiated osteoprogenitor cells**	**Local Injection**	**ATMP**	**Phase 2b**
Kuros	• Spinal fusion • Tibial fractures	Orthobiologic (PTH) + scaffold	Local Injection	BLA	Phase 2
Novadip	• Spinal fusion • Other bone defects	Autologous, adipose-derived MSC (3D structure)	Surgery	ATMP	Phase 1/2 (Enrolled)

[13] Company websites and clinicaltrials.gov.

Epibone	Bone defects	Adipose-derived MSC + scaffold	Surgery	ATMP	Phase 1/2
Mesoblast	Chronic low back pain	Bone marrow-derived MPC + scaffold	Local injection	ATMP	Phase 3
Shanghai iCELL Biotechnology Co.	Non-union fractures	Human amniotic epithelial cells (hAECs)	Local injection	ATMP?	Preclinical
DiscGenics	Disc degenerative disease	allogeneic (off-the-shelf), injectable discogenic cells	Local Injection	ATMP	Phase 1/2
EntaraBio	Non-union fractures	Orthobiologic (PTH)	Local injection	BLA	Preclinical
Stryker (Olympus Biotech)	Tibial fractures	Orthobiologic (BMP-7) + scaffold	Local injection	BLA	Discontinued in US & EU since 2014
Biostar	Osteonecrosis	Autologous adipose-derived MSC	Local injection	ATMP	Clinical (status unclear)

* Products approved as devices/procedures are not required to demonstrate efficacy to the same standards

ALLOB has multiple advantages over these products. It is composed of MSCs that have been differentiated into bone progenitor cells, which therefore demonstrate osteoinductive (induce bone formation) and osteogenic (form bone themselves) properties. This is clearly advantageous compared with other products that only have undifferentiated cells that only demonstrate osteoinductive properties, or only have a small number of cells remaining in the bone graft. Furthermore, ALLOB is off-the-shelf and therefore available immediately, as no manufacture of patient (autologous) cells is needed. As such, the patient can be treated early, where they are most likely to benefit from the treatment and higher numbers of cells are available to be used, further enhancing ALLOB's efficacy.

4.7.2 *Spinal fusion*

Description

Spinal fusion is considered as the gold standard surgery for treating a broad spectrum of degenerative spine disorders, including degenerative disc disease, spondylolisthesis, scoliosis and stenosis, to relieve pain and improve function. Spinal fusion consists of bridging two or more vertebrae with the use of a cage and graft material, traditionally autologous bone graft or bone substitutes such as bioceramics (β-tricalcium phosphate or β-TCP) and cadaver bone – placed into the intervertebral space – for fusing an unstable portion of the spine or immobilizing a painful vertebral motion segment.

Despite the fact that spinal fusion surgery is routine, complications such as non-union and failure to relieve lower back pain are unfortunately still frequent. One of the most common complications encountered in spinal fusion surgery is failed fusion (complete or partial), reported in approximately 5% to 35% of procedures, which could lead to debilitating pain, deformities, and often require subsequent revision surgery. Its management is one of the most challenging problems in this field. Procedures to salvage failed lumbar fusions focus on achieving a solid fusion, and consequently relieving and controlling pain and symptoms, minimizing disability, and improving the quality of life. However, revision surgeries are associated with higher procedure-related complication rates, technical difficulties, and longer operative times. Moreover, success rates are poor and often unreliable for both fusion and clinical results. Furthermore, bone autograft is a very painful

procedure, though efficacious, that surgeons want to move away from. Orthobiologics such as Infuse®/InductOs® have shown efficacy but also significant safety concerns.

Market Size

Over 1.5 million spinal fusions are performed each year in Europe and the US, the majority of which are to address degenerative disc diseases[14]. The Company's estimates regarding market size are based on hospital discharge data and market reports. Using these data, the Company estimates that each year 686,000 patients in EU5[15], the US and Japan undergo lumbar spinal fusion surgery.

In recent years, the spinal fusion market in the US has grown considerably, from 260,000 procedures in 2002[16] to 797,604 in 2019[15]. According to a recent GlobalData report, this growth is largely due to the increase in indications for which spinal surgery can be performed[17]. GlobalData estimated that the market will continue to grow, albeit at a smaller annual rate of 3.5-4.5%. On the one hand, the ageing population and sedentary lifestyle result further expansion in the number of procedures, but on the other hand, changing reimbursement policies may start putting pressure on the market.

Competition

The spinal fusion market (see table in previous section) is segmented into two product classes, namely, (i) hardware devices (plates, screws and cages) and (ii) bone grafts. These two classes are inter-related as the hardware is needed to stabilise the vertebrae and the grafts are needed to promote fusion. Bone autograft is still perceived as the gold-standard for spinal fusion procedures, despite safety concerns (in particular donor site pain)[18]. As a wide array of alternatives is now on the market, a gradual shift is observed from bone autograft towards bone substitutes. This overcrowded product class - with over 200 different products available for the surgeons - is currently dominated by the major medical device manufacturers. The bone substitutes on the market are (i) allografts (mostly cadaver bone) demineralized bone matrix (DBM), and cellular bone matrix (CBM) (from Zimmer Biomet, Orthofix, etc.) and (ii) ceramics and other fillers (from DePuy Synthes, Stryker, Zimmer Biomet, Kuros Bioscience, etc.). The market for bone substitutes is characterized by rapid technological change, frequent introduction of new products and evolving surgical practices toward minimally invasive procedures. Experts estimate that this market will be driven mostly by innovation and by the companies' novel positioning as part of a broad therapy system. In such a therapeutic setting, the synergic combination of hardware devices, bone substitutes and adapted surgeries would ensure better therapeutic outcomes.

By contrast, the regenerative segment of the spinal fusion market has little or no competition with only one approved orthobiologic therapy available in Europe and in the US, Infuse®/InductOs® (the recombinant growth factor rhBMP-2 from Medtronic). The negative media coverage surrounding Medtronic's Infuse® (along with FDA and US Senate investigations and lawsuits, and decreased sales) has opened the market to alternative therapies[19]. For orthobiologics, the vPTH biomaterial (KUR-113) from Kuros is currently evaluated in a Phase IIa trial in the US in spinal fusion[20]. However, in this changing landscape, the Company believes that its allogeneic cell products, used as an add-on therapy to synthetic bone substitutes in standard fusion procedures, could offer a better treatment option and be cost-effective by achieving a faster and more solid fusion.

Multiple companies are addressing spinal fusion, or other spinal applications through cell therapy[21]:

[14] Spinal Fusion – Global Market 2015-2028, Global Data, 2019.
[15] France, Germany, Italy, Spain and United Kingdom
[16] North Maerica Spinal Surgery Market Outlook to 2025. GlobalData, August 2018.
[17] Spinal Fusion – Global Analysis and Market Forecast. GlobalData, Linda Tian, December 2016.
[18] Myeroff C and Archdeacon M. Autogenous Bone Graft: Donor sites and Techniques. The Journal of Bone and Joint Surgery. 2011; 93A (23): 2227-36.
[19] http://www.drugwatch.com/infuse/ and "Medtronic must face revived U.S. lawsuit over Infuse" (Reuters, 28 Dec. 2016)
[20] Press Releases from Kuros Bioscience, dated 3 September 2019.
[21] From www.clinicaltrials.gov, Indication "Spinal Fusion" + "Cell", Status "Not yet recruiting", "Recruiting", "Active, non-recruiting" and recently "Completed", last consulted on October 28, 2019.

Novadip Biosciences (BEL) has initiated a Phase I/II trial in 2017 with expected completion in beginning 2021 using their autologous adipose derived MSC's incorporated in an allogeneic DBM (product candidate NVD-001) for the treatment of low grade degenerative lumbar spondylolisthesis by interbody fusion. As mentioned previously, Novadip is now focusing its development with its second-generation therapy (NVD-003) for critical size bone reconstruction. Unlike Novadip Biosciences, the Company's ALLOB is allogeneic and off-the-shelf and readily available for patients in the first instance and at greater numbers of cells. Secondly, ALLOB retains the osteoinductive properties of MSCs, while also able to form bone itself (osteogenic properties), unlike un-differentiated MSCs.

Other companies are addressing chronic low back pain through cell therapy[22], such as Mesoblast (AUS) and its product candidate Rexlemestrocel-L currently in phase III study with completion expected in 2021, or DiscGenics (USA) and its product candidate IDCT in phase I/II study in the US. These cell therapies are developed to address the underlying degenerative disc disease and could become an additional treatment option to patients with degenerative disc disease before going for a surgical intervention. However, these products do not target the other degenerative spine disorders, such as spondylolisthesis, scoliosis and stenosis, which will ultimately require a spinal fusion. These products are not developed to promote spinal fusion.

Please refer to the table in the previous section for a comprehensive list of companies and competing products.

4.8 Osteoarthritis of the knee

Description and Market Size

Osteoarthritis ("**OA**"), also known as degenerative joint disease, is the most common chronic joint condition in which the protective cartilage in the joints progressively breaks down resulting in joint pain, swelling, stiffness and limited range of motion. The knee is one of the joints that are mostly affected by osteoarthritis, with an estimated 250M cases worldwide[23]. Based on studies analysing the prevalence of symptomatic knee osteoarthritis, the Company estimated that there are about 27 million patients suffering from this common orthopaedic condition in the US, Europe and Japan or about 3% of the total population of 838 million people in these countries.

The prevalence of knee osteoarthritis ("**KOA**") is expected to increase in the coming years due to an increasingly aging and obese population. Annual growth is currently estimated at 5-6% according to a recent Global Data report[24]. Currently, there is no cure for KOA and treatments focus on relieving and controlling pain and symptoms, (inadequately) preventing disease progression, minimizing disability, and improving quality of life. Most drugs prescribed to KOA patients are topical or oral analgesics and anti-inflammatory drugs. Ultimately, severe KOA leads to highly invasive surgical interventions such as revision, or total knee replacement.

Intra-articular injections are the most commonly used treatments for moderate KOA. Intra-articular injection of corticosteroids is used to relieve pain, but the treatment effect only lasts several weeks following an injection and could be associated with adverse effects on cartilage (increased cartilage volume loss) in patients receiving prolonged treatment. Intra-articular injection of hyaluronic acid ("**HA**"), also know as viscosupplementation, is also widely used for treating symptomatic KOA, despite controversies around its potential efficacy. The worldwide sales of viscosupplements had an estimated value of $2.1B in 2016[25].

JTA-004 is developed as a single intra-articular injection composed of 3 active substances: human plasma supplemented with HA and an analgesic agent. Once injected in the joint cavity, JTA-004 aims to increase the viscosity of the synovial fluid, leading to joint lubrication, mechanical support and cartilage protection of the arthritic joint.

[22] From www.clinicaltrials.gov, Indication "Spinal Fusion" or "Symptomatic Lumbar Disc Degeneration" + "Cell", Status "Not yet recruiting", "Recruiting", "Active, non-recruiting" and recently "Completed", last consulted on October 28, 2019.
[23] Vos et al., *A systematic analysis for the Global Burden of Disease Study 2010*. Lancet 2012; 380:2163-96
[24] Viscosupplementation: Global Analysis and Market Forecasts, April 2017, Global Data
[25] Viscosupplementation: Global Analysis and Market Forecasts, April 2017, Global Data

Competition

There is currently no cure for OA. Treatments for OA focus on relieving and controlling pain and symptoms, preventing disease progression, minimizing disability, and improving quality of life. Management of OA includes varied techniques and principles, both non-pharmacological and pharmacological in nature.

Most treatments consist of a combination of the following methods: education, weight loss, exercise, joint protection, physical and occupational therapy. A large number of drugs are also prescribed for patients with OA, typically used to reduce the inflammation, which in turn decreases pain and stiffness. These drugs include paracetamol and non-steroidal anti-inflammatory drugs ("**NSAIDs**"), COX-2 inhibitors, topical analgesics, narcotic analgesics, glucosamine and chondroitin, tramadol and intra-articular (IA) corticosteroids (Manek and Lane, 2000). Although effective in reducing symptoms, NSAIDs are often associated with side effects sometimes described as costly for society. The primary safety concern with NSAIDs is the increase in gastrointestinal problems, including ulceration, haemorrhage, and perforation (Roth, 2011). Compared to traditional NSAIDs, COX-2 inhibitors claim to be more selective in their mode of action, with reduced gastrointestinal complications. However, an increased risk of cardiovascular complications has been attributed to various NSAIDs including COX-2 inhibitors (McGettigan and Henry, 2006). IA steroids are effective but usually have quite short duration of effect (Godwin and Dawes, 2004).

In severe cases, when the therapies above cease to provide benefit or pain relief, surgery may be considered as a last-resort effort to manage OA symptoms. Surgical interventions include total joint arthroplasty and joint lavage and debridement. There is no evidence demonstrating that lavage or debridement is more effective in relieving pain or improving function than non-surgical treatment (Moseley et al., 2002). Arthroplasty has, however, demonstrated significantly reduced knee pain and increased functionality in patients who were severely incapacitated before surgery (Pendleton et al., 2000). Prosthesis loosening and infection are among the complications that can occur. Moreover, such surgical procedures are highly invasive taking months of revalidation to gain recovery.

Although there are several non-surgical treatments available for the treatment of knee OA, their long-term use and their safety have not been systematically monitored. Intra-articular injection of HA has been used in the treatment of symptoms associated with KOA with a favourable safety profile (Pagnano and Westrich, 2005). This therapeutic technique for the treatment of KOA is based on the physiologic importance of HA in synovial joints. Its therapeutic goal is to address the cause of pain by improving mobility of the joint and protection of the cartilage by replacing the low elastoviscous osteoarthritic synovial fluid with high elastoviscous solutions of HA or its derivatives.

HA-based treatments dominate the sales in the KOA space, with sales of $1.3bn in 2016 in the seven major markets. There are several different formulations of intra-articular injection of HA with widely different molecular weights. This difference of molecular weight ("MW") is thought to be of importance with respect to the volume/amount and number of injections, the residence time in the joint and biological effects (Huang et al., 2010).

Today, the US market is dominated by Sanofi, whose products (namely, Synvisc® and Synvisc-One®) have an estimated market share of about 40-50%. Other players on the US market are Anika Therapeutics, Ferring and Fidia Pharma each of which has an estimated market share of 12-13%. The European market is much more fragmented, and each local market has its leading brands[26].

In Europe, HA-based products are not reimbursed in most major countries (in the UK they are reimbursed on a local hospital level) due to their questionable efficacy and long-term benefit. HA-based products are, however, reimbursed in the US.

Competing Products for KOA:

[26] Viscosupplementation: Global Analysis and Market Forecasts, April 2017, Global Data

Company	Product	Technology	Indication	Status	Trials
INTRA-ARTICURAL INJECTIONS					
Sanofi (FR)	Synvisc Synvisc One	HA Three injections One injection	Knee osteoarthritis	Market (2009)	NCT04333160 – Ph III completed 2020 NCT00131352 – Ph III completed 2009 Sales $432.7m (2018)
Anika (US)	Cyngal (Medical Device)	HA (Crosslinked, HMW) + Corticosteroid	Pain in osteoarthritis	Market EU (2016) Canada	NCT01891396 – Ph III Completed 2014 NCT02381652 – Open Completed 2015 NCT03191903 – Ph III Completed 2018
Flexion (US)	Zilretta (Drug)	Corticosteroid	Pain in knee osteoarthritis	Market USA (2017)	NCT02357459 – Ph III Completed 2016 NCT03046446 – Open Completed 2016 Oct 31, 2019 : FDA Clearance of the IND for FX201, a Gene Therapy Candidate for the Treatment of OA Sales ~$20m (2018)
Ferring	Euflexxa (Medical Device)	HA	Pain in knee osteoarthritis	Market (2011)	NCT00423371 – Phase II/III Completed 2007
Fidia	Hymovis (Medical Device)	HA	Pain in knee osteoarthritis	Market (2015)	NCT01372475 – Phase III Completed 2013
IN DEVELOPMENT FOR PAIN					
Centrexion (US)	CNTX-4975	Trans-capsein TRPV1 agonsit	Pain in knee osteoarthritis	Phase III (FDA Fast Track)	NCT03429049 – Ph III NCT03660943 – Open NCT03661996 – Different Treatment Regimen
Mestex (CH)	Lopain (MTX-071)	Resiniferatoxin TRPV1 agonist	Pain in knee osteoarthritis	Phase IIb	NCT02566564
IN DEVELOPMENT AS Disease Modifying Osteoarthritis Drug (DMOAD)					
Samumed (US)	Lorecivivint (SM04690)	Wnt pathway inhibitor (DYRK1A and CLK2 inhibitor)	Pain DMOAD	Phase III	NCT03928184 – Ph III
Galapagos (BE)	GLPG1972	ADAMTS-5 inhibitor	Pain DMOAD	Phase II	NCT03595618 – Ph II – Completed **Failed to meet primary endpoints**
Unity Biotechnology (US)	UBX0101	MDM2/p53 protein interaction	Pain DMOAD	Phase II	NCT04129944 – Phase II – Completed **Failed to meet primary endpoint**
Symic Bio (US)	SB-061	Extracellular matrix targeting drug	Pain DMOAD	Phase IIA	NCT03231280 – Phase IIA

HMW: High Molecular Weight; DMOAD: Disease-modifying Osteoarthritis Drug

Due to the difference in HA preparations (linear or reticulated, varying MW and/or concentration), assessment criteria, statistical methodologies, injection schedules (1, 2, 3 or 5 injections per cycle for 1 to 3 cycles per year), the quality and injection techniques among other causes, outcome of clinical trials with intra-articular injection of HA had been contradictory, which has led to a critical view by certain medical associations with regards to this symptomatic treatment. However, during the last few years, multiple large scale meta-analyses on the efficacy of intra-articular injection of HA have been conducted (Maheu et al., 2018; Johansen et al., 2016; Strand V. et al., 2015; Campbell et al., 2015;) and several independent experts groups from US (Bannuru et al., 2015; Bhadra et al., 2017; Trojian et al., 2015), EU (Henrotin et al. 2015; Bruyère et al., 2016; Cooper et al., 2016) and Canada (Bhandari et al., 2017) have reviewed these and previous findings to address the controversies surrounding HA. As the meta-analyses have demonstrated the efficacy and safety of intra-articular injection of HA showing that 60-70% of patients were responders, the experts groups recommended the use of HA as a treatment option for early to moderate knee osteoarthritis. These recommendations are also supported by the wide use of intra-articular injection of HA in practice (representing a $2 bn global market), which shows that patients find the benefit of it in real life.

JTA-004 has the opportunity to provide a novel treatment option to the currently underserved KOA patient population that, albeit not a DMOAD, will offer better long-term benefit compared to existing HA-based treatments on the market, by providing better symptom relief and maintaining cartilage integrity for longer, thereby delaying the need for surgery. The non-clinical and clinical data that has been collected so far (please refer to the following sections) have provided strong support for this hypothesis.

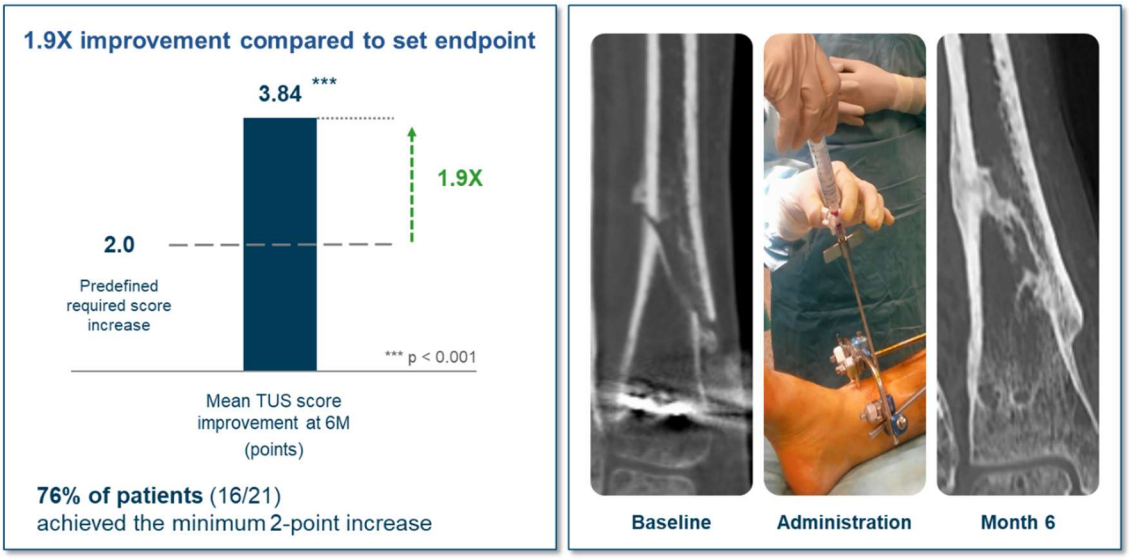
4.9 Results clinical studies

4.9.1 *Delayed-union fractures*

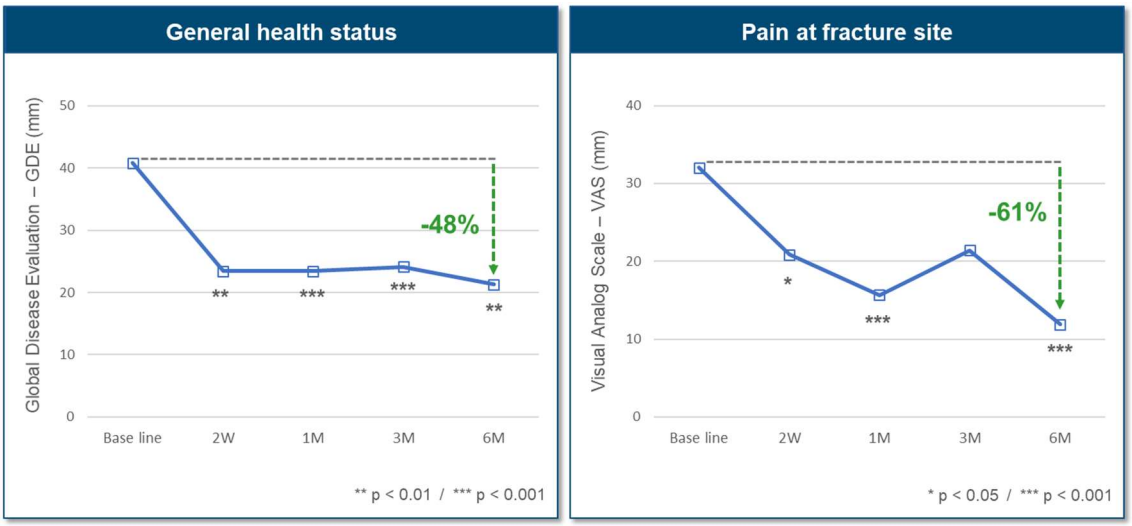
The Phase I/IIa study was a six-month open-label trial to evaluate the safety and efficacy of ALLOB in the treatment of delayed-union fractures of long bones. The study evaluated 21 patients, who each had a fracture that had failed to consolidate after a minimum of three and a maximum of seven months. Each patient received a single percutaneous administration of ALLOB directly into the fracture site and completed a six-month follow-up. Fracture healing of ALLOB-treated patients was assessed using both radiological evaluation (based on CT-scan) and clinical evaluation (e.g. health status and pain).

At six months post administration, 100% of the patients met the primary endpoint, defined as an increase of at least two points on the radiological Tomographic Union Score (TUS) or an improvement of at least 25% of the clinical Global Disease Evaluation (GDE) score vs. baseline.

From a radiological perspective, the patients improved by on average 3.84 points on the TUS score (statistically significant) almost twice the required increase of two points. This minimum two-point increase was achieved by 16 out of 21 patients (76%).



From a clinical perspective, the health status of patients, as measured by the GDE score, improved statistically significantly by on average 48%. The minimum 25% improvement was achieved by 16 out of 21 patients (76%). Pain at the fracture site, an important secondary endpoint, was statistically significantly reduced by on average 61%.



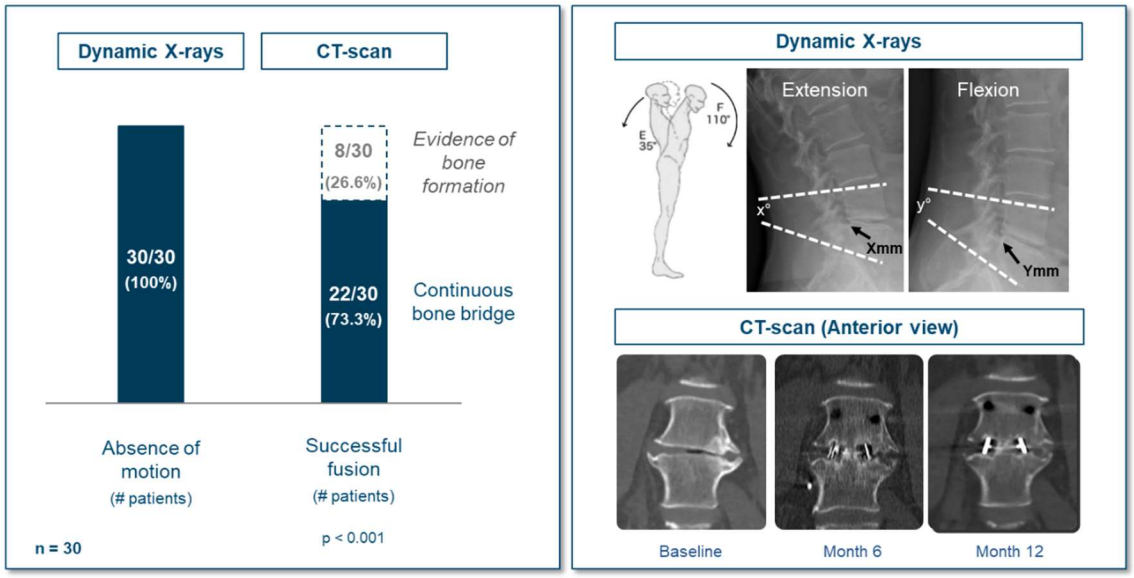
Overall, ALLOB was shown to be well-tolerated and the safety profile was consistent with the interim analysis reported on 20 September 2017. As previously described in the literature covering clinical studies with allogeneic mesenchymal stem cells or their derivatives, it was observed that blood samples of about half of the patients contained donor-specific antibodies, either pre-existing or developed after administration, without clinical consequences.

ALLOB is currently being evaluated in a randomized, double-blind, placebo-controlled Phase IIb study in patients with high-risk tibial fractures. The study is in the process of recruiting the planned 178 patients. Bone Therapeutics anticipates completing the recruitment in H1 2022 and expects to deliver top line results in H2 2022. Both dates are subject to the evolution of the COVID-19 pandemic.

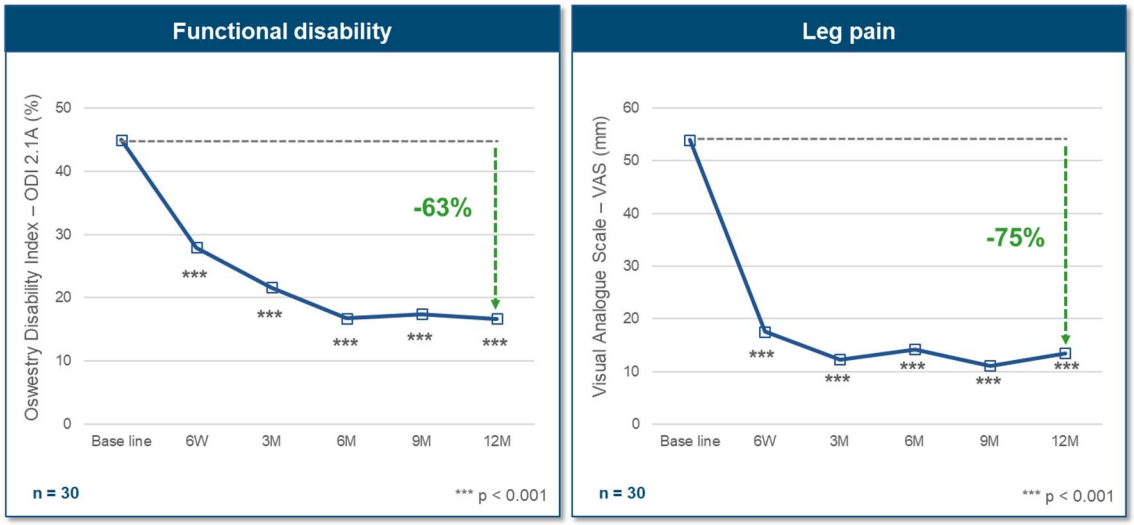
4.9.2 *Lumbar spinal fusion*

The Phase IIa trial in lumbar spinal fusion was designed to evaluate the safety and efficacy of the addition of ALLOB to the standard of care procedure in which an interbody cage with bioceramic granules is implanted to achieve fusion of the lumbar vertebrae. The primary endpoints of the study assessed at 12-month included radiological assessments to evaluate fusion (continuous bone bridges) and clinical assessments to evaluate improvement in patients' functional disability. The secondary endpoints included the assessment of intervertebral mobility (absence of motion at the treated lumbar level), back and leg pain reduction, as well as safety and tolerability. The study evaluated 30 patients treated with ALLOB in combination with standard of care procedure.

From a radiological perspective, data collected from CT-scans over a 12-month period showed successful fusion ($p < 0.001$) of the lumbar vertebrae in 22 out of 30 patients (73.3%), while the remaining 8 patients showed evidence of bone formation. For the first 15 patients who already reached the 24-month follow-up time point, 13 out of 15 patients (86.7%) showed successful fusion. In addition, radiological data collected from dynamic X-rays at 12 months demonstrated that treatment with ALLOB resulted in the immobilisation of the treated intervertebral segment in all patients.



From a clinical perspective, treatment with ALLOB resulted in a clear and statistically significant clinical improvement from the pre-treatment baseline in functional disability, with a mean score improvement of 63.0% ($p < 0.001$) on the Oswestry Disability Index. Furthermore, treatment with ALLOB resulted in a strong reduction in back and leg pain of 67.0% and 75.0% respectively.



From a safety perspective, treatment with ALLOB was well tolerated in all patients. As previously described in the literature covering clinical studies with allogeneic mesenchymal stem cells or their derivatives, it was observed that blood samples of 65% of the patients contained donor-specific antibodies, either pre-existing or developed after administration, however no clinical consequences were observed.

These strong results showed an improvement (60.0% to 73.3%) compared to 12-month interim analysis reported in September 2017 for the first cohort of 15 patients.

In October 2020, Bone Therapeutics announced positive 24-month follow-up results for the Phase IIa lumbar spinal fusion study. Radiological data collected from CT-scans at 24 months showed a successful fusion of the lumbar vertebrae in 27 out of 30 patients (90%). In addition, the remaining 3 patients showed radiological evidence of bone formation. Treatment with ALLOB also resulted in a clear and statistically significant clinical improvement in function and reduction in pain over the 24-month follow-up period. Functional disability improved from the pre-treatment baseline to 24-month by a mean score of 60% ($p<0.001$) on the Oswestry Disability Index. Back and leg pain were strongly reduced by 57 to 62% ($p<0.001$) and 68 to 70% ($p<0.001$) respectively compared to pre-treatment baseline. Treatment with ALLOB was generally well-tolerated by the patients, consistent with previous reported results.

4.9.3 *Osteoarthritis of the knee*

Bone Therapeutics is developing JTA-004, an off-the-shelf protein solution supplemented with hyaluronic acid and an analgesic agent, with the objective to provide substantial, long-term pain relief to patients.

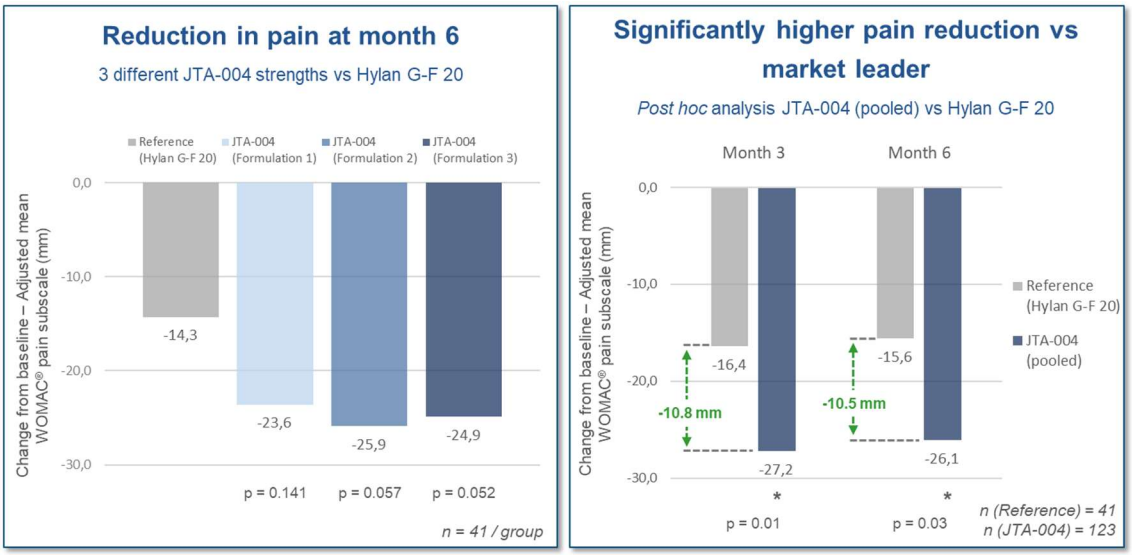
JTA-004 was evaluated in a prospective, multicentre, randomised, double-blind, controlled Phase IIb study including three JTA-004 strengths and one reference product, Hylan G-F 20 (Synvisc-One®), the global market leader in intra-articular injection of hyaluronic acid. The main objective of the study was to demonstrate the superiority of a single intra-articular JTA-004 injection to the reference product in patients suffering from symptomatic osteoarthritis of the knee.

164 patients were randomly assigned to the reference group or one of the three JTA-004 groups. The primary endpoint of the study was the mean change in WOMAC® VA 3.1 pain subscale score (ranging between 0 and 100 mm) between baseline and 6 months after treatment.

The single intra-articular injection of JTA-004 was generally well tolerated. At six months, patients in the three JTA-004 groups showed an improvement in pain vs. baseline ranging from 23.6 mm to 25.9 mm, while patients in the reference group only showed a 14.3 mm[27] improvement. Due to high variability in primary endpoint at

six months, statistically significant differences between the individual JTA-004 groups and the reference group were not achieved.

Analysis of the results revealed that the three JTA-004 strengths had a similar efficacy. Therefore, a post hoc exploratory analysis was subsequently performed between the reference group and all pooled JTA-004 treated patients. The exploratory analysis showed a 26.1 mm improvement for the pooled JTA-004 group vs. 15.6 mm[27] for the reference group at month 6, demonstrating a statistically significant superiority of the pooled JTA-004 group compared to the global market leader in intra-articular injection of hyaluronic acid. A 10 mm difference on the WOMAC® Index pain subscale is considered to be a beneficial improvement for the patient (Ehrich et al., 2000; Bellamy et al, 2005).



JTA-004 has subsequently been assessed in a controlled, randomized, double-blind, placebo- and active-controlled Phase III clinical study in symptomatic knee osteoarthritis. In this study, the potential of JTA-004 to leads to a reduction in knee pain intensity, and to improve knee physical function, subject global health and well-being in subjects suffering from symptomatic knee OA has been evaluated and compared to placebo and/or active comparator 3 and 6 months after a single JTA-004 knee intra-articular administration. The study was approved in 7 countries and included a total of 743 patients.

In August 2021, Bone Therapeutics announced the topline results from the Phase III study. Despite JTA-004's favourable safety profile, the study did not achieve its main objectives as no statistically significant difference in pain reduction could be observed between any of the treatment, placebo and comparator groups, with all treatment arms showing similar efficacy. A statistically significant difference in favour of JTA-004 and the active comparator versus placebo was seen in a post-hoc analysis in a subset of patients with higher pain scores at entry.

4.10 Regulatory framework

In each country where it conducts its research and intends to market its products and product candidates, the Company has to comply with regulatory laws and regulations (hereinafter, collectively the "**Regulatory Regulations**"), including regulations laid down by regulatory agencies and by other national or supra-national regulatory authorities (hereinafter, collectively the Competent Authorities). The Competent Authorities include the European Medicines Agency ("**EMA**") in the European Union and the national Competent Authorities, and Food and Drug Administration ("**FDA**") in the United States. The Company also has to comply with industry standards incorporated by such Regulatory Regulations, that regulate nearly all aspects of the Company's activities.

[27] The difference in the mean improvement of the reference group at Month 6 between the two analyses was a consequence of the statistical adjustments for both sample size and sample variation in the covariance analysis that was used in both studies.

The Company's pharmaceutical product candidates are subject to substantial requirements that govern among other things their testing, manufacturing, quality control, safety, efficacy, labelling, storage, record keeping, marketing approval, advertising, promotion, pricing, and reimbursement. The process of maintaining continued compliance with the regulatory requirements requires the expenditure of substantial amounts of time and money.

4.10.1 *Medicinal product regulations*

ALLOB

ALLOB is an advanced therapy medicinal product (ATMPs – as defined in regulation 1394/2007) which has been developed in compliance with the European legislation. ALLOB has been classified as tissue engineered products by EMA on 19 July 2011 based on Regulation 726/2004. Under Regulation 1394/2007, a "tissue engineered product" means a product that contains or consists of engineered cells (cells that have been subject to substantial manipulation or are not intended to be used for the same function in the recipient as in the donor) or tissues, and is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue. In the US, ALLOB is a cellular therapy as defined in the CFR - Code of Federal Regulations Title 21, part 1271 "Human Cells, Tissues, and Cellular and Tissue-based products" and regulated as biological products under section 351 of the PHS Act (42 U.S.C. 262) and the Federal Food, Drug, and Cosmetic Act (the act) and will fall under the Biological Licence Application regulation. In Japan, ALLOB will fall under the legislation for regenerative medicine which allows for conditional marketing approval after Phase II clinical trials.

The Company received orphan drug status for ALLOB (EMA: 2013; FDA: 2014) for the treatment of (non-traumatic) osteonecrosis (EMA: 2013; FDA: 2014) as well as for the osteogenesis imperfecta treatment for ALLOB product (EMA: 2015; USFDA: 2015). When obtaining orphan designation, the Company benefits from a number of incentives, including protocol assistance, a type of scientific advice specific for designated orphan medicines, and market exclusivity (10 years in Europe and 7 years in the US) once the medicine is on the market. Fee reductions are also available depending on the status of the sponsor and the type of service required

JTA-004

JTA-004 is combination product which is comprised of a protein solution supplemented with hyaluronic acid (HA) and an analgesic agent. The product has been developed in compliance with the European legislation. The current published scientific literature supports that hyaluronic acid achieves its primary intended purpose of treatment of pain in OA of the knee through chemical action within the body (reference made to the FDA's announcement in the Federal Register in December 2018 (83 FR 64844). In addition, JTA-004 utilizes a biologic (human plasma) to entrap the HA fibres. Therefore, JTA-004 is classified in Europe as a medicinal product (as defined in Directive 2001/83/EC as amended, Article 1) and in US as a Drug (as defined in Section 201(g) of the FD&C Act (21 USC 321(g)) unlike most products containing hyaluronic acid which are registered as devices.

4.10.2 *Manufacturing site regulations*

The testing, storage, and distribution of human tissues and cells (intended for human use) and of manufactured products derived from human tissues and cells (intended for human use) is specifically regulated (in Europe by Directive 2004/23/EC, which e.g., requires the licensing of tissue establishments).

The Company is registered as a "Tissue Establishment" (according to the Belgian RD2 of 28 September 2009 and the Belgian Law of 19 December 2008 to transposing the Directive 2004/23/EC).

The Company's manufacturing site[28] has been inspected by the Belgian national competent authorities (Federal Agency for Medicines and Health Products, Belgium) and is registered as a "Pharmaceutical Establishment" and accredited as a "GMP" facility by the Belgian Competent Authorities (Federal Agency for Medicines and Health Products), as requested by the Directive 2001/83/EC, 2009/120/EC and regulation EC 1394/2007. Manufacturing authorization and intra-EU distribution for ALLOB and JTA-004 Human Investigational Medicinal Products has been granted by the Belgian National Competent Authority under the number 1698 IMP.

[28] In November 2020, the Company sold its manufacturing site but kept GMP certification to cover packaging, storage, distribution and QC activities

Overview of manufacturing authorizations

Agreement / license	Competent Authority*	Date of approval
Manufacturing authorization and intra-EU distribution authorization for JTA & ALLOB	Federal Agency for Medicines and Health Products	Authorization since February 2011 updated on 8 Jan 2013. Last update (JTA-004) on January 2017 Scope reviewed to cover packaging, storage, importation, distribution and QC activities since March 2021
GMP agreement	Federal Agency for Medicines and Health Products	Authorization since 23 Jan 2012 (Addition of production site-Gosselies- on 19 December 2017) Authorization for JTA since 29 Sept 2014 Scope reviewed to cover packaging, storage, importation, distribution and QC activities since March 2021 (after on-site inspection)
Tissue Bank / Intermediary Structure (ALLOB)	Federal Agency for Medicines and Health Products	Authorization since 1 March 2013 Not impacted by the deal with Catalent
Tissue Importer Establishment	Federal Agency for Medicines and Health Products	Authorization since 1 March 2020 Not impacted by the deal with Catalent

** In the EU, the national Competent Authority is entitled to grant accreditation to the whole of the EU.*

4.10.3 *Clinical study regulation*

The preclinical and clinical development paths are broadly similar in Europe (governed by Directive 2001/20) and in the US. Initially, non-clinical studies are conducted to evaluate the mode of action and safety through *in vitro* and *in vivo* studies. Upon successful completion of preclinical studies, a request for a Clinical Trial Authorisation (CTA, in the EU) or an Investigational New Drug application (IND, in the US), needs to be approved by the relevant Competent Authorities to be allowed to start. In addition to obtaining Competent Authority approval, clinical trials must receive Ethics Committee (in the EU) or Institutional Review Board, "IRB" (in the US) approval for every research site (e.g., hospital) where the clinical trials are conducted. Clinical trials are typically conducted in sequential phases, Phases I, II, III and IV. Phase IV trials are conducted as post-marketing pharmacovigilance studies to identify and evaluate the causality of any long-term effects during a lengthy period treatment for a greater number of patients. These phases may be compressed, may overlap or may be omitted in some circumstances.

The rate of completion of the Company's clinical trials may be delayed by many factors, including slower than anticipated patient enrolment or adverse events occurring during clinical trials.

Competent Authorities are aware of the specificities of cell-based product candidates, and pay more attention to their upfront characterisation and to the development of assays to measure their biological activity. For clinical studies with ATMPs, Competent Authorities typically have between two and six months from the date of receipt of the CTA application to raise any objections to the proposed trial. USFDA shall provide a written determination 30 days after FDA receives the IND application. Competent Authorities may also require additional data before allowing studies to commence and could demand that studies be discontinued, for example if there are significant safety issues.

For most of its studies, the Company sought National Scientific advice and EMA scientific advice before designing its clinical trials in order to incorporate the requirements of the EMA.

The Company has received approval from Regulatory Agencies and Ethic Committees of several European countries for its clinical trials concerning ALLOB and JTA-004.

ALLOB

ALLOB Phase I/IIa studies were approved in Belgium and Germany. ALLOB Phase IIb study (ALLOB-TF2) was approved in Belgium, Czech Republic, Germany, France, Hungary, Poland and Spain. The study is in the recruitment phase (first patient treated in January 2021) and the end of recruitment is planned for the first half of 2022. Topline results are expected by the second half of 2022.

JTA-004

JTA-004 phase II/III study (JTA-KOA1) was approved in Belgium and is finalized. A phase III study (JTA-KOA2) was approved in Belgium, Czech Republic, Denmark, Moldavia, Poland, United Kingdom and Hong-Kong. The recruitment has ended in December 2020 (last patient first visit) and topline results were reported on 21 August 2021.

4.10.4 *Marketing approval*

Although different terminology is used, the data requirements, overall compliance to GMP, GCP and other regulatory requirements and the assessment as well as decision making process for marketing approval are similar in the EU and in the US. Upon availability of initial efficacy data from Phase II clinical trials *and* confirmatory/pivotal Phase III clinical trial data, the Company may submit a request for marketing authorization:

- ALLOB: to EMA in the EU (a Marketing Authorization Application ("**MAA**")) or a Biologics License Application ("**BLA**") to FDA in the US.
- JTA-004: to national Competent Authorities ("CA") through a Decentralized Procedure ("DCP") in the EU (MAA) or a New Drug Application ("NDA") to FDA in the US.

Authorities (FDA and/or EMA and/or CA may grant approval if the quality, safety *and* efficacy of the medicinal product/drug are proven, deny the approval or request additional studies or data. Following favourable assessment and decision, the products may be commercially launched in the relevant territory. There can be no guarantee that such approval will be obtained or maintained. In practice, effective market launch is often further conditioned upon completion of pricing and reimbursement negotiations with Competent Authorities involved in healthcare and pharmaceutical expenditure at the national or regional level.

When granting marketing authorization, Competent Authorities may impose upon the Company an obligation to conduct additional clinical testing or other post-approval commitments in addition to mandatory pharmacovigilance requirements (referred to as Phase IV clinical trials) (Regulation 1394/2007). Additionally, marketing authorization may be subjected to limitations on the indicated uses for the product. Also, after marketing authorization has been obtained, the marketed product and its manufacturer and marketing authorization holder will continue to be subject to Regulatory Regulations and monitoring by Competent Authorities. The conditions for marketing authorization include requirements that the manufacturer of the product complies with applicable legislation including GMP, related implementing measures and applicable guidelines that involve, amongst others, ongoing inspections of manufacturing and storage facilities.

The Company has not received approvals for commercialisation yet.

4.10.5 *Pricing and reimbursement*

In Europe, pricing and reimbursement for pharmaceuticals are not harmonized and fall within the exclusive competence of the national authorities, provided that basic transparency requirements defined at the European level are met as set forth in the EU Transparency Directive 89/105/EEC. Consequently, reimbursement mechanisms by private and public health insurers vary from country to country. In public health insurance systems, reimbursement is determined by guidelines established by the legislator or a competent national authority. In general, inclusion of a product in reimbursement schemes is dependent upon proof of the product efficacy, medical need, and economic benefits of the product to patients and the healthcare system in general. Acceptance for reimbursement comes with cost, use and often volume restrictions, which again vary from country to country.

The pricing and reimbursement level for the Company's products will depend on the strength of the clinical data set and, as for most novel therapies, restrictions may apply. In most countries, national Competent Authorities ensure that the prices of registered medicinal products sold in their territory are not excessive. In making this judgment, they usually compare the proposed national price either to prices of existing treatments and/or prices in other countries also taking into account the type of treatment (preventive, curative or symptomatic), the degree of innovation, the therapeutic breakthrough, volume of sales, sales forecast, size of the target population and/or the improvement (including cost savings) over comparable treatments. Given the growing burden of medical treatments on national health budgets, reimbursement and insurance coverage is an important determinant of the accessibility of medicines. The various public and private plans, formulary restrictions, reimbursement policies, patient advocacy groups, and cost-sharing requirements may play a role in determining access to products marketed by the Group. The national Competent Authorities may also use a range of policies and other initiatives intended to influence pharmaceutical consumption. To address the above, the Company integrates as part of its clinical development programs the collection of data aimed at facilitating the evaluation of therapeutic benefit, in terms of efficacy and/or reduction in side effect profile, and of its cost. Concomitantly with marketing authorization applications, the Company will engage in a dialogue with key decision makers at different payers in order to identify unique preferences and concerns by payer type and to obtain insight in the perceived value drivers, reimbursement barriers and price elasticity for its products.

4.11 Material agreements

The Company has entered into the following material agreements:

4.11.1 *License agreement between Université libre de Bruxelles (ULB) and the Company regarding ULB-028 patent family*

The Company entered into a license agreement with the ULB regarding the ULB-028 patent family which is owned by the ULB. This agreement provides the Company and its affiliates with an exclusive and worldwide license over the technology claimed by the ULB-028 patent family for all human applications and in the field of skeletal (bone, joint, any orthopaedic) and dental applications for veterinary applications. The ULB retains the right to operate this technology for research and educational purposes only. The Company may grant sublicenses, the identity of such sub-licensee(s) being subjected to prior approval by the ULB. In consideration of the rights granted to the Company, the Company must make payments to the ULB upon achievement of certain development and patent related milestones. In addition, the Company must pay to the ULB royalties based on the net sales of the Company and on the revenues received from sublicensees.

The royalty duty on net sales and revenues received from sublicensees shall exist as long as valid claims exist. The royalties are 2% as long as said licensee improvement (i.e. ALLOB product), if unlicensed, would infringe a ULB-028 patent valid claim in that given territory and 1% instead of 2% in territories where no ULB-028 patent valid claim is covering the Licensee Improvement (i.e. ALLOB product) if a valid claim is covering said

Licensee Improvement in the territory where the product is manufactured. Otherwise, if there is no valid patent claim where the ALLOB product is distributed and manufactured, there is no royalty.

The royalty should stop on the date of expiry of the patent.

This license agreement will expire on the date of expiry of the last to expire patents in the licensed patent family or ten years after the first commercialization date, whichever is latest. Either party may terminate the agreement if the other party (i) is in breach of its terms and fails or has not taken reasonable steps to remedy the breach within 60 days of receiving written notice to do so, (ii) is declared bankrupt, is the subject of any proceeding related to its liquidation or insolvency, has its assets placed in the hands of a receiver or makes accommodation for the benefits of creditors or (iii) ceases to do business. The Company shall have the right, but shall be under no obligation, to terminate the agreement, within six months prior written notice to ULB. If the company (i) commits an act of dishonesty or fraud with respect to ULB or the bone cell therapy technology or (ii) challenges (or assists others to challenge) ULB's ownership of, or the validity of the ULB-028 patent, ULB shall have the right to terminate the agreement immediately upon written notice to the Company, without court intervention and without having to respect any notice period.

4.11.2 *License agreement between Glob-Co and the Company regarding the BPBONE-001, BPBONE-002 and BONE-011 patent families (JTA patent families)*

The previous agreements between the Company and Enrico Bastianelli regarding the BPBONE-001, BPBONE-002 and BONE-011 (dated 2007, 2014 and 2016) were replaced in 2020 by an agreement between the Company and Glob-Co SRL. Glob-Co SRL is owned by more than 25% by Enrico Bastianelli and its registered office is in Jumet, Belgium.

In 2020, the Company entered into a license agreement with Glob-Co SRL regarding the JTA patent families BPBONE-001, BONE-002, BONE-011 and any future patents related to the JTA technology. This agreement provides to the Company an exclusive, worldwide and sublicensable license over the technology claimed by the BPBONE-001, BPBONE-002 and BONE-001 patent families for all human indications. This agreement further provides to Glob-Co SRL an exclusive, worldwide and sublicensable license over the same technology for all veterinary applications.

In consideration of the rights granted to the Company, the Company pays to Glob-Co SRL an annual fee of 48.000 EUR until the first commercialization of a product from the JTA technology.

Royalties agreed on net sales from product of the JTA technology are 6%, until 300.000 EUR payment and then 3%. Royalties for indirect revenues (i.e., sub-license revenues) are 8.75%.

The Company recognizes that it must diligently perform research and development obligations and objectives and must use its best efforts to promote, market and distribute the above technology. In the case of failure to do so, Glob-Co SRL may terminate the agreement. If the exploitation of the technology by the Company would be delayed for a period of 15 months in comparison to the objectives except in case of *force majeure*, Glob-Co SRL may also terminate the license agreement.

The license agreement will expire on the date of expiry of the patents in the licensed patent family or ten years after the first commercialization date. Either party may terminate the agreement if the other party (i) is in breach of its terms and fails or has not taken reasonable steps to remedy the breach within 60 days of receiving written notice to do so, (ii) is declared bankrupt, has its assets placed in the hands of a receiver or makes accommodation for the benefits of creditors or (iii) ceases to do business. If the development of the technology is not sufficiently supported by public research grants, the Company has also the right to terminate the agreement.

4.11.3 *Sublicense agreement between Enrico Bastianelli SPRL and the Company regarding the BONE-001, BONE-002, BONE-013, BONE-017, BONE-018 and BONE-019 ALLOB patent families*

The previous agreement between the Company and Enrico Bastianelli regarding BONE-001, BONE-002, BONE-013 and BONE-017 ALLOB patent families (dated 2016) was replaced in 2020 by an agreement between the Company and Glob-Co SRL. Glob-Co SRL is owned by more than 25% by Enrico Bastianelli and its registered office is in Jumet, Belgium.

Under this agreement, Glob-Co is granted an exclusive, royalty-free, sublicensable, and worldwide license over the technology claimed by the BONE-001, BONE-002, BONE-013, BONE-017, BONE-018 and BONE-019 ALLOB patent families (patent rights, data and know how related to the said patent rights) for veterinary applications.

Bone will further pay Glob-Co a royalty of 1% of the net revenues from any Commercial Exploitation or License of any ALLOB Technology product or program used for the treatment of severe acute respiratory syndrome (SARS).

4.12 Partnerships

The Company is conducting several partnerships in product licensing, manufacturing, process development and research. These transactions reposition Bone Therapeutics around its focus on product and platform development.

	LICENSING	MANUFACTURING	PROCESS DEVELOPMENT	RESEARCH
Partner	HG 领晟医疗 LINK HEALTH GROUP PREGENE	Catalent	RIGENERAND Steps Ahead In Cell Technology	3D-SIDE, BioWin, CERHUM, IREC, mSkill, LIÉGE
Deal	• **Exclusive license** to ALLOB and related IP and knowhow • **China**, Hong Kong, Macau, Taiwan, Singapore, **Thailand, South Korea**	• Catalent acquired Bone Therapeutics' cell therapy **manufacturing facilities** • Catalent will manufacture and supply **ALLOB**	• Collaboration focusing on **product and process development** for Bone Therapeutics' cell therapy products as they advance towards patients	• **Research Collaboration** for the development of patient-specific **scaffolds for use in combination with ALLOB**
Financials	• **€55 million in total** upfront and milestone payments plus tiered **double-digit royalties** on net sales	• **€12 million** in total payments to Bone Therapeutics		• **€3 million** in total grant funding from BioWin, the health cluster of the Wallonia Region (Belgium)
Notes	• **Link Health** and **Pregene** will conduct and finance development in Asia	• **Catalent** is a leading global CDMO for drugs, biologics, **gene therapies**, and consumer health products	• Potential for Bone Therapeutics to broaden its therapeutic targets and **explore new mechanisms of action with potential gene modifications** for its therapeutic portfolio	• The new **biocompatible scaffolds** will be modelled with state-of-the-art software and **3D printed**

a) Licensing agreement with Link Health and Pregene

In October 2020, Bone Therapeutics, Link Health and Pregene signed an exclusive license agreement for the manufacturing, clinical development and commercialization of Bone Therapeutics' allogeneic, off-the-shelf, bone cell therapy platform ALLOB in China (including Hong Kong and Macau), Taiwan, Singapore, South Korea, and Thailand.

Under the agreement, Bone Therapeutics is eligible to receive up to €55 million in development, regulatory and commercial milestone payments. Bone Therapeutics is also entitled to receive tiered double-digit royalties on annual net sales of ALLOB. Bone Therapeutics retains development and commercialization rights to ALLOB in all other geographies outside of those covered by this agreement. Until the date of the Document, the Company already received €1 million as upfront payment.

b) Manufacturing collaboration with Catalent

In October 2020, Bone Therapeutics signed share purchase and supply agreements with Catalent Pharma Solutions, Inc., the leading global provider of advanced delivery technologies, development, and manufacturing solutions for drugs, biologics, cell and gene therapies, and consumer health products The agreements streamline and economize the manufacturing operations of ALLOB, Bone Therapeutics' allogeneic cell therapy product.

Under the terms of the transaction, Catalent acquires Bone Therapeutics' cell therapy manufacturing subsidiary, SCTS, for gross proceeds of €12 million. Following completion of the transaction, the SCTS manufacturing infrastructure and production operating teams became part of Catalent's Cell & Gene Therapy division.

Concurrently, Bone Therapeutics and Catalent entered into associated supply agreements. This grants Bone Therapeutics access to Catalent's global network of clinical and commercial manufacturing facilities, and ensures ongoing optimization, sustainability and a global reach for the production of ALLOB as the product heads through clinical development and anticipated commercialization.

c) Cell therapy process development with Rigenerand

In January 2021, Bone Therapeutics and Rigenerand SRL, the biotech company that both develops and manufactures medicinal products for cell therapy applications, primarily for regenerative medicine and oncology, signed a first agreement for a process development partnership.

The scope of collaborations between Bone Therapeutics and Rigenerand aims to focus on different aspects of product and process development for Bone Therapeutics' expanding therapeutic portfolio. Rigenerand will contribute to improving the processes involved in the development and manufacture of Bone Therapeutics' MSC based allogeneic differentiated cell therapy products as they advance towards patients. The first collaboration between the two organizations will initially focus on augmented professional bone-forming cells – cells that are differentiated and programmed for a specific task. There is also potential for Bone Therapeutics to broaden its therapeutic targets and explore new mechanisms of action with potential gene modifications for its therapeutic portfolio.

d) BioWin research consortium, Bonerec

In November 2020, Bone Therapeutics joined a research collaboration with expert industry and academic partners, Cerhum, 3D-Side, mSKIL and IREC, to develop biologically active, patient-tailored, 3D printed, bioresorbable implants enriched with Bone Therapeutics' allogeneic bone forming cells, ALLOB. The consortium, named Bonerec, was established under the "Competitiveness Clusters" framework of the Belgian Walloon Health Association, BioWin, and received €3 million non-dilutive funding from the Walloon Government.

This 28-months collaboration aims to develop biologically active, custom-made tissue engineered bone implants that could replace bone transplants harvested from patient's own bones (autografts). By combining the tailored scaffold with Bone Therapeutics' differentiated bone forming cells, ALLOB, the enhanced tissue engineered product is expected to exhibit strong bone-forming activities and stimulate bone regeneration. The aim of the resultant cell-enriched implant is to form a safe and structurally superior alternative to bone autografts.

4.13 Collaborations

4.13.1 *Industrial collaborations*

The Company has entered into industrial collaborations with CER Groupe (Belgium), to study the immune response of human cells xenografts in a non-animal heterologous model, to study the effect of ALLOB product on osteomyelitis and to study the efficacy and biodistribution of allogenic products in an ARDS model. Both

two first projects are CWALity[29] projects founded by the Region, while the third project is a "Technical support" project founded by the Region. The first project (XENOMOD) ended in April 2017, the second project (ALLGEL) ended in May 2019, and the third project (2020131) is still ongoing. CER Groupe is the merger of various non-profit associations, has forged a solid expertise in the field of biomedical research, and is currently recognized by the Region as a certified Research Centre.

4.13.2 *Academic / Clinical collaborations*

4.13.2.1 Collaboration with the Université libre de Bruxelles

The Company has a core academic, research and license collaboration with the Université libre de Bruxelles and Erasme University Hospital (Brussels). The Université libre de Bruxelles, owner of the ULB-028 patent family entitled "Osteogenic differentiation of bone marrow stem cells, and osteoprogenitor or osteoblastic cells and populations" (see Section 4.11.1 "License agreement between Université libre de Bruxelles (ULB) and the Company regarding ULB-028 patent family") concerning the cell therapy, has granted the Company a worldwide and exclusive license to use, modify, perform research, develop, manufacture and commercialize the licensed product for all human applications and in the field of skeletal (bone, joint, any orthopaedic) and dental applications for veterinary indications.

4.13.2.2 Collaboration with CHU of Liège (Sart-Tilman)

According to Belgian Law, when human biological material is used for the manufacturing of allogeneic advanced therapy medicinal products, the reception and processing of the human biological material and its distribution to a Pharmaceutical Establishment can be done via an accredited "Intermediary Structure" tissue establishment if the latter has an agreement with an accredited Tissue Bank which remains responsible for the donation, testing, procurement and release of the human biological material. The Company works in collaboration with the LTCG, the accredited Tissue Bank from the CHU based in Liège Sart-Tilman.

4.13.2.3 Collaboration with the Centre for Microscopy and Molecular Imaging (CMMI)

The Company is cooperating for several of its research projects with the Centre for Microscopy and Molecular Imaging (CMMI) that was created in a joint venture between the Université de Mons and Université libre de Bruxelles. The CMMI has created a profound expertise in imaging and cellular labelling that gives the Company access to essential information for preclinical characterization and validation of products and allows better evaluation of safety and efficacy of clinical products in development. Currently, one project, funded by the Region, is ongoing in cooperation with the CMMI: the "BIOPOTAN" project study the short-term and mid-term biodistribution and functional evaluation of human osteoblastic cells in a delayed union murine fracture model.

4.14 Financing Agreements

The Company has entered into a number of agreements with its bankers ING Belgique SA/NV and BNP Paribas Fortis SA/NV which cover short (<1 year) term financing requirements. In addition, the Company has obtained a number of loan facilities through regional investment offices (considered as related parties) such as Novallia SA and Sofipôle SA.

Bone Therapeutics SA has the following financing agreements in place:

- Under the framework of the European Regional Development Fund 2007-2013 (ERDF/FEDER) the Company has been granted, through a selection progress organized by the Region through Novallia SA, a long-term subordinated loan for an amount of € 500,000 for a period of 10 years (with a 2 years moratorium in respect of capital reimbursements). The loan served to finance the development of PREOB for the treatment of non-union fractures. The loan carries a market-based interest rate and as of the third-year fixed quarterly

[29] CWALity, Collaboration in Wallonia ability, a platform from the Region to promote collaboration between PMEs and local research organisms.

instalments are due to reimburse the capital. There are no securities provided by the Company in respect of this loan agreement. The loan was granted on 25 May 2012, the loan was received on 21 June 2016 and the final repayment is foreseen on 30 June 2022. The outstanding balance on 30 June 2021 amounts to € 0.06 million.

- Under the framework of the European Regional Development Fund 2007-2013 (ERDF/FEDER) the Company has been granted, through a selection progress organized by the Region through Novallia SA, a long-term subordinated loan for an amount of € 300,000 for a period of 7 years (with a 1-year moratorium in respect of capital reimbursements). The loan served to finance A Phase IIA, multicentre, open study on the safety and efficacy of allogeneic bone-forming cells (ALLOB) implantation in multiple non-infected delayed-union (DU) fractures. The loan carries a market-based interest rate and as of the second-year fixed quarterly instalments are due to reimburse the capital. There are no securities provided by the Company in respect of this loan agreement. The loan was granted on 2 May 2016, received on 11 May 2016 and the final repayment is foreseen on 30 June 2023. The outstanding balance on 30 June 2021 amounts to € 0.10 million.

- In June 2019, the Company obtained non-dilutive subordinated bonds for an amount of € 3.5 million. The non-dilutive subordinated bonds were issued in registered form, redeemable at 100% of their principal amount with a maturity of 48 months and a coupon of 8% per annum. The coupon will be payable annually.

- In May 2020, the Company obtained non-dilutive subordinated bonds (1,600 bonds) for an amount of € 4.0 million with the option to convert. This enables Bone Therapeutics' bond investors to be repaid in the company's shares, with a conversion price of EUR 7.0 per share. The unsecured convertible bonds will be issued in registered form, redeemable at 100% of their principal amount with a maturity of 38 months and a coupon of 8% per annum. The coupon will be payable annually. The conversion price of EUR 7.0 per share mitigates the dilution of existing shareholders in the event that the bonds would be redeemed in ordinary shares of Bone Therapeutics. The Company renegotiated 800 convertible bonds issued on 7 May 2020 (for an amount of EUR 2 million) to Patronale Life into a loan subject to the same repayment terms as the agreement with the EIB, with the issuance of 200,000 additional warrants approved by the Extraordinary General Meeting.

- In May 2020, the Company obtained 4.75 million bridge loans provided by commercial banks (ING Belgique SA/NV, BNP Paribas Fortis SA/NV and Belfius Banque SA) and Sambrinvest. The bridge loans have been fully repaid in the course of 2021.

- In July 2021, the Company secured a loan agreement of up to EUR 16.0 million with the European Investment Bank (EIB). The EIB loan financing will be disbursed in two tranches of EUR 8.0 million each, subject to conditions precedent. Following the approval of the issuance of associated warrants by Bone Therapeutics' General Meetings at the end of August 2021, Bone Therapeutics received a payment from the EIB for the first tranche of EUR 8.0 million and the EIB was granted 800,000 warrants approved by the Extraordinary General Meeting.

4.15 Grants and subsidies

From incorporation until 30 June 2021, the Company has been awarded non-dilutive financial support from the Region and by the European Commission totalling € 35.81 million. This financial support has been granted in the form of recoverable cash advances ("RCAs") for an amount of € 30.66 million of which € 28.99 million has been paid out to the Company as of 30 June 2021, and in the form of (non-refundable) subsidies for an amount of € 5.15 million of which € 4.48 million has been paid out to the Company as of 30 June 2021. The Company intends to continue to apply for RCAs and subsidies to fund its development and research programs.

Each subsidy is defined by a contract number and a name (subsidy name).

4.15.1.1 Recoverable cash advances

RCAs are dedicated to support specific research and development programs. After approval/grant, RCA contracts consist of three steps, i.e., the "research phase", the "decision phase" and the "exploitation phase". During the research phase, the Company receives funds from the Region based on statements of expenses. At the end of the research phase, the Company should within a period of six months decide whether or not to exploit the results of the research program (decision phase). The exploitation phase has a duration of in nearly all cases of 25 years. In the event the Company decides to exploit the results under an RCA, the relevant RCA becomes refundable. The reimbursements of the RCAs to the Region consist of two elements, i.e., turnover-dependent reimbursements (a percentage of turnover) and turnover-independent reimbursements (an annual lump-sum independent of the Company's turnover).

The Company owns the results of the subsidized research. Subject to certain exceptions, the Company cannot grant to third parties, by way of license or otherwise, any right to use the results of the subsidized research without the prior consent of the Region. A similar prior consent by the Region is needed in case of a transfer by the Company of an intellectual property right resulting from the subsidized research or a transfer or license of a prototype or installation. Obtaining such consent from the Region could give rise to a review of the applicable financial terms.

Contracts granted contain the following specific conditions:

- Funding by the Region covers **45%** of the budgeted costs (contracts 7539, 7646, 7720, 7763, 7813, 7845, 7852 and 1510583), covered **55%** of the budgeted costs (contracts 7280, 7405, 7406, 7433 and 7620), covered **60%** of the budgeted costs (contracts 6064, 6187, 6700, 6446, 6337, 6539, 6804, 6805, 6834, 6855, 7029, 7028, 7187, 7217 and 7253), covered **70%** of the budgeted costs (contracts 5369 and 5827) **or** covered **75%** of the budgeted project costs if there is a collaboration with a Company established in Region (contracts 5993, 6081 and 7186);
- Certain activities have to be performed within the European Union;
- Turnover-independent reimbursements represent in the aggregate 30% of the principal amount;
- The exploitation phase has a duration of **25 years** (except 15 years for contract 7720);
- Turnover-dependent reimbursements are detailed in the table below and depends on the actual outcome of the project compared to the outcome projected at the time of grant of the RCA (below or above projections);
- Interests (at Euribor 1 year or at IBOR 1 year if higher and as applicable on the first day of the month in which the decision to grant the relevant RCA was made + 100 basis points) accrue as of the 1st day of the exploitation phase;

- Turnover-independent reimbursements and turnover-dependent reimbursements are, in the aggregate (including the accrued interests), capped at **200%** of the principal amount paid out by the Region;
- In case of bankruptcy, the research results obtained by the Company under the Contracts granted are expressed to be assumed by the Region by operation of law.

The Company has contracted the following RCAs with the Region:

Contract N°	Name	Budget (k€)	Exploitation phase	Turnover-independent reimbursement (k€)	Total reimbursed 06/2021 (k€)	Turnover-dependent reimbursement
5369	HOMING*	648	2012-2041	648	605	5%
5827	MATOB*	744	2012-2041	744	670	5%
6064	PREOB*	998	2013-2041	240	240	0.2%
6446	METHODES*	660	2014-2041	198	164	0.073%
5993	JOINTAIC*	432	2014-2042	130	104	0.085%
6804	PROFAB*	734	2015-2042	110	110	1.28%
6834	STABCELL*	394	2015-2041	118	59	0.04%
6805	ALLOB NU*	600	2015-2042	180	74	0.2%
6337	PREOB NU*	2,960	2015-2041	444	444	0.59%
6187-6700	ALLOB*	1,306	2015-2042	392	104	1.2%
6081	GXP*	1,519	2015-2041	167	167	0.007%
6539	MAXBONE*	676	2015-2042	203	66	0.08%
6855	JTA*	600	2016-2042	180	70	0.042%
7029	CRYO*	550	2016-2042	165	55	0.37%
7028	PREOB ON3*	815	2016-2041	81	81	0.05%
7187	BANK*	258	2016-2042	78	8	0.175%
7253	JTA PROD*	742	2017-2041	223	37	0.1%
7186	ALLOB IF*	620	2017-2042	186	37	1.28%
7217	MXB BIOPRINTING*	995	2017-2042	294	30	0.1093%
7405	MECA OB*	1,815	2018-2043	545	9	0.847%
7539	LIPO*	519	2018-2043	156	0	0.23%
7280	MO SELECT*	353	2018-2043	106	9	0.082%
7406	CRYOFIN*	1,185	2018-2043	355	24	0.553%
7433	ALLOB SEQ*	1,892	2019-2043	568	19	0.90%
7620	EXCIP*	1,576	2019-2044	0	0	0.08%
1510583	ALLGEL	155	2019-2043	47	0	0.04%
7720	RUSTUS	454	2019-2033	136	0	0.25%
7763	PROSTERIL	719	2020-2045	219	0	0.04%
7852	ALLOPROD	913	2021-2046	274	0	0.05%
7646	JTA-NEXT	2,156	2020-2044	648	0	0.20%
7813	CELLSORT	613	2020-2045	184	0	0.05%

7845	BIOPOTAN	1,057	2021-2046	317	0	0.05%
8251	JTA KOA2	1,000	2022-2047	300	0	0.25%
TOTAL		**30,658**		**8,636**	**3,186**	

**Exploitation already signified to the Region*

A brief description of the Company's subsidies is given in the table below.

Subsidy Names	Related Company's Projects & Activities	Description
HOMING	Cell therapy product	Study of homing properties of the cell therapy product
MATOB	Cell therapy product	Study of secretion of extracellular matrix proteins of the cell therapy product
PREOB	PREOB	Phase IIB clinical study in osteonecrosis with PREOB
METHODES	PREOB & ALLOB	Optimisation of QC analytical methods
JOINTAIC	JTA	Pharmaceutical development of JTA
STABCELL	PREOB & ALLOB	Optimisation of PREOB and ALLOB stability
ALLOB NU	ALLOB	Preclinical and clinical development of ALLOB
PREOB NU	PREOB	Non-union clinical study with PREOB
ALLOB	ALLOB	Preclinical and clinical development of ALLOB
GXP	Quality system	Set-up of preclinical, clinical and quality control quality systems
MAXBONE	MXB	Pharmaceutical development of MXB
JTA	JTA	Pharmaceutical development of JTA
CRYO	ALLOB	Development of cryopreservation of ALLOB
PREOB ON3	PREOB	Phase III clinical study in osteonecrosis with PREOB
BANK	ALLOB	Optimization of human biological material supply
ALLOB IF	ALLOB	Preclinical and clinical development of ALLOB in spine fusion
MXB BIOPRINTING	MXB	Preclinical development of 3D MXB cell-matrix products
MECA OB	ALLOB	Study of cell mechanisms implicated in chemotaxis and migration of osteoblastic cells
ALLOB SEQ	ALLOB	Study of the ALLOB cells secretome and its impact on the serum profile of key proteins implicated in bone reconstruction in delayed-union fractures phase II study.
LIPO	ALLOB	Influence of obesity and diabetes on osteogenic potential of ALLOB
ALLGEL	ALLOB	Preclinical study of ALLOB for bone repair in osteitis in small animals
JTA-NEXT	JTA	Increased stability of JTA-004 and product development of JTA-NEXT
RUSTUS	ALLOB	Radiographic and tomographic scores during fracture healing
CELLSORT	ALLOB	Characterization of allogenic product by Cell sorting
BIOPOTAN	ALLOB	Short and middle term biodistribution and functional evaluation of allogeneic products in DU murine model

Subsidy Names	Related Company's Projects & Activities	Description
PROFAB	PREOB	Optimisation of PREOB production
JTA PROD	JTA	Optimisation of JTA production
MO SELECT	ALLOB	Optimisation of bone marrow selection
CRYOFIN	ALLOB	Optimisation of ALLOB cryopreservation
EXCIP	PREOB	Development of a new excipient to increase the stability of PREOB
PROSTERIL	ALLOB	Manufacturing of cell therapy products: aseptic risk assessment, detection methods and product protection techniques
ALLOPROD	ALLOB	Increasing the production capacity of allogenic product and optimization of the production process

4.15.1.2 Subsidies

Subsidies granted by the Region are dedicated to funded research programs and patent applications.

Subsidies granted by the Region and amounting to € 5,151,000 are related to patent applications (contracts 820020, 920572, 820018, 920571, 820060, 820126, 920569, 820127, 820125, 920570, 1120242, 1320011, 1320145, 1320190, 820019, 820046, 820047, 1120198, 1220075, 1320146, 1120197, 1220076, 1320144, 1220028, and 1220029) together the "**Patent Subsidies**") and research programs (contracts n° 1017112, 6559, 607051, 1217891, 1318272, 1318269 and 1318215).

As of 30 June 2021, the Company has been granted subsidies related to patent applications totalling € 1,621,000 of which € 1,278,000 has been received. The balance will be granted based on statements of expenses to be submitted to the Region.

The Company has also been granted subsidies for a total amount of € 3,530,000 of which € 3,199,000 by the Region to fund:

- 45% of costs of research programs under the contracts with the number 8346, 8353, 8325 and 2020131 for an amount of € 948,000
- 70% of costs of research programs under the contracts with the number 1017112, 6559, 1217891, 1318272 and 1318269 for an amount of € 1,653,000
- 80% of costs of research programs under contract n°1318215 for an amount of € 224,000
- 90% of costs of research program under contract n°7120 for an amount of € 395,000.

and by the European Commission to fund 100% of costs of a research program for an amount of € 309,000 (contract n° 607051).

These Region and European Commission subsidies for research are not refundable. Out of the abovementioned subsidies € 2,185,000 has been effectively paid out on 31 December 2018.

In addition, the Company had received non-refundable subsidies from different programs (AWEX, Horizon…) for a total amount of € 274,000.

The Company owns the intellectual property rights which would result from the research programs or with regard to a patent covered by a subsidy. Subject to certain exceptions, the Company cannot grant to third parties, by way of license, transfer or otherwise, any right to use the patents (with regard to the Patent Subsidies) or the results (with regard to Research Subsidies) without the prior consent of the Region. In addition, certain subsidies contain an obligation for the Company to exploit the patent in the countries where the protection was granted and to make an industrial use of the underlying invention.

In case of bankruptcy, liquidation or dissolution, the rights to the patents covered by the Patent Subsidies relating thereto will be assumed by the Region by operation of law unless the subsidy is reimbursed, in case of liquidation or dissolution. If the Company would lose its qualification of "small or medium-sized enterprise", the subsidies under the Patent Subsidies will terminate and no additional expenses will be covered by such Patent Subsidies.

4.16 Intellectual property

4.16.1 *Patents and patent applications owned or licensed by the Company*

The Company's research programmes and product candidates are covered by several patent families (patents and patents applications), which are either owned by the Company or licensed to the Company. There are three key ALLOB product patents: (i) ULB-028 granted in Europe, Japan, Singapore, Hong-Kong, the US and Canada, (ii) BONE-001 granted in Europe, Japan, Canada, India, Hong Kong, Singapore, South Korea and Australia, and (iii) BONE-017 granted in Australia, Belgium, South Korea and Israel and in pending application in Europe, the US, Japan, China, Canada, India, South Korea, Hong Kong, Singapore, Macau, Thailand, Brazil and Russia. Further JTA-004 is covered by two key patents: (i) BPBONE-0001 is granted in Europe, US, Japan, Australia, Canada, China, Hong Kong, Israel, India, South Korea, Brazil and Singapore, and (ii) BONE-011 is granted in Europe, Australia, Hong Kong, Israel, South Korea, China, Canada and Singapore.

In total, the Company's intellectual property portfolio comprises 13 patent families:

- ULB-028 (WO 2007/093431): Cell populations comprising osteoblastic cells characterised by the expression of certain cell markers, and further comprising the method for obtaining such cell populations.

- BONE-001 (WO 2009/087213): Cell populations comprising osteoblastic cells characterised by the expression of certain cell markers, and further comprising the method for obtaining such cell populations.

- BONE-002 (WO 2009/080749): Therapeutic use of isolated bone-forming cells in the treatment of the inflammatory component of inflammatory rheumatic diseases (IRD).

- BONE-004 (WO 2009/135905): Isolated mesenchymal stem cells (MSC) derived from bone marrow and expressing certain cell-surface markers and methods for obtaining such MSC.

- BONE-006 (WO 2009/135914): Therapeutic use of isolated bone-forming cells in the treatment of bone diseases or conditions associated with immunodeficiency or immunosuppression.

- BONE-011 (WO 2014/049063): Discovery of advantageous properties of solvent/detergent-treated plasma in pharmaceutical formulations, which render the formulations particularly suitable for administration to bone or joints, such as to treat musculoskeletal diseases.

- BPBONE-001 (WO 2009/101194): Intra-articular pharmaceutical composition for use in the treatment and/or the prevention of acute or chronic osteoarticular diseases, such as osteoarthritis, and acute or chronic osteoarticular symptoms (*i.e.*, pain, loss of mobility and/or function).

- BPBONE-002 (WO 2009/101210): Pharmaceutical composition for use in the treatment and/or the prevention of acute or chronic osteoarticular diseases and acute or chronic osteoarticular symptoms, especially osteoarthritis.

- BONE-013 (WO 2016/170112): Method for *in vitro* preservation of cells comprising maintaining adherent mesenchymal stem cells (MSC) or adherent MSC-derived cells in suspension in a composition comprising at least 20% v/v human plasma or human serum or a mixture thereof.

- BONE-017 (WO 2019/076591): Cell populations comprising osteoblastic cells characterised by the expression of certain cell markers, and further comprising the method for obtaining such a cell population.

- BONE-018 (WO 2020/064791): Cell populations comprising osteoblastic cells characterised by the expression of certain cell markers, and further comprising the method for obtaining such a cell population.

- BONE-019 (WO 2020/064793): Methods and uses for determining osteogenic potential of *in vitro* differentiated cells.

- BONE-020 (WO 2020/229526): Improved lyophilized formulations involving hyaluronic acid and plasmatic proteins, and uses thereof.

The Company owns the exclusive worldwide license on ULB-028.

Overview of patents and patent applications.

Reference	Publication No	Title (product)	Priority date	Territory	End of term
ULB-028	WO 2007/093431	Osteogenic differentiation of bone marrow stem cells, and osteoprogenitor or osteoblastic cells and populations (ALLOB)	16 Feb 2006	JP SG US CA EP HK	16 Feb 2027 16 Feb 2027 30 Aug 2028 16 Feb 2027 16 Feb 2027 16 Feb 2027
BONE-001	WO 2009/087213	Osteogenic differentiation of bone marrow stem cells and mesenchymal stem cells using a combination of growth factors (ALLOB)	11 Jan 2008	JP SG AU AU-DIV EP CA IN HK KR-DIV (US)	9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 9 Jan 2029 under examination
BONE-002	WO 2009/080749	Human bone-forming cells in the treatment of inflammatory rheumatic diseases (ALLOB)	21 Dec 2007	AU EP HK JP SG CA KR (US)	19 Dec 2028 19 Dec 2028 19 Dec 2028 19 Dec 2028 19 Dec 2028 19 Dec 2028 19 Dec 2028 under examination
BONE-004	WO 2009/135905	Mesenchymal stem cells and bone-forming cells (ALLOB)	7 May 2008	EP SG AU US JP	7 May 2029 7 May 2029 7 May 2029 13 Feb 2030 7 May 2029
BONE-006	WO 2009/135914	Human bone-forming cells in the treatment of conditions and bone diseases associated with immunodeficiency or immunosuppression (cell technology)	7 May 2008	JP-DIV2 HK	7 May 2029 7 May 2029

Reference	Publication No	Title (product)	Priority date	Territory	End of term
BONE-011	WO 2014/049063	Formulations involving solvent/detergent-treated plasma (S/D plasma) and uses thereof (JTA-004)	26 Sep 2013	EP	26 Sep 2033
				SG	26 Sep 2033
				KR	26 Sep 2033
				AU	26 Sep 2033
				HK	26 Sep 2033
				IL	26 Sep 2033
				CA	26 Sep 2033
				CN	26 Sep 2033
				(CN-DIV, IN, JP-DIV, US)	under examination
BPBONE-001	WO 2009/101194	Pharmaceutical composition for use in the treatment and/or the prevention of osteoarticular diseases (JTA-004)	13 Feb 2009	EP	13 Feb 2029
				JP-DIV	13 Feb 2029
				CN	13 Feb 2029
				HK	13 Feb 2029
				SG	13 Feb 2029
				AU	13 Feb 2029
				KR	13 Feb 2030
				KR-DIV	13 Feb 2029
				CA	13 Feb 2029
				US	13 Feb 2029
				US-DIV	13 Feb 2029
				IN	13 Feb 2029
				IL	13 Feb 2029
				BZ	13 Feb 2029
BPBONE-002	WO 2009/101210	Pharmaceutical composition for use in the treatment and/or prevention of osteoarticular diseases (JTA cell technology)	16 Feb 2009	EP	16 Feb 2029
				SG	16 Feb 2029
				AU	16 Feb 2029
				JP	16 Feb 2029
				US	16 Feb 2029
				IL	16 Feb 2029
				IN	16 Feb 2029
				CA	16 Feb 2029
BONE-013	WO 2016/170112	*In vitro* preservation of therapeutic cells (cell technology)	23 Apr 2015	AU	23 April 2036
				CA	23 April 2036
				KR	23 April 2036
				EP	23 April 2036
				JP	23 April 2036
				HK	23 April 2036
				SG	23 April 2036
				(CN)	under examination
BONE-017	WO 2019/076591	Method for differentiating mesenchymal stem cells (ALLOB)	20 Oct 2017	AU	25 Sept 2038
				BE	25 Sept 2038
				KR	25 Sept 2038
				IL	25 Sept 2038
				(EP, US, CN, JP, BR, RU, HK, MA, IN, SG, TH, CA)	under examination
BONE-018	WO 2020/064791	Method for differentiating mesenchymal stem cells (ALLOB)		Belgium	25 Sep 2039
				(Australia, Brazil, China, Europe, India, Indonesia, Israel, Japan, Korea, Malaysia, Mexico, Russia, Singapore, Taiwan, Thailand, US)	under examination
BONE-019	WO 2020/064793	Method for assessing the osteogenic properties of a cell product (ALLOB)		Belgium	25 Sep 2039
				(Australia, China, Europe, Korea,	under examination

Reference	Publication No	Title (product)	Priority date	Territory	End of term
				Japan, Singapore, Thailand, US)	
BONE-020	WO 2020/229526	Freeze-dried cake suitable for rapid resuspension (JTA-004)		Belgium (other national entries planned by the end of 2021)	13 May 2040 under examination

Overview of patent ownership and related contracts.

Reference	Product (Clinical stage)	Owner(s)	Contract(s)
ULB-028	ALLOB (Phase IIb)	Université libre de Bruxelles (ULB)	Exclusive, sublicensable, worldwide license to the Company
BONE-001	ALLOB (Phase IIb)	Bone Therapeutics SA	The Company grants an exclusive right to Glob-Co SPRL for veterinary applications
BONE-002	ALLOB (Phase IIb)	Bone Therapeutics SA	The Company grants an exclusive right to Glob-Co SPRL for veterinary applications
BONE-004	ALLOB (Phase IIb)	Bone Therapeutics SA	
BONE-006	Cell technology	Bone Therapeutics SA	
BONE-011	JTA-004 (Phase III)	Bone Therapeutics SA (50%) Glob-Co SRL (50%)	A worldwide exclusive license has been granted to Glob-Co SRL on veterinary applications
BPBONE-001	JTA-004 (Phase III)	Bone Therapeutics SA (50%) Glob-Co SRL (50%)	A worldwide exclusive license has been granted to Glob-Co SRL on veterinary applications
BPBONE-002	JTA cell technology	Bone Therapeutics SA (50%) Glob-Co SRL (50%)	A worldwide exclusive license has been granted to Glob-Co SRL on veterinary applications
BONE-013	Excipient for cell products	Bone Therapeutics SA	The Company grants a worldwide and exclusive right to Glob-Co SRL for veterinary applications
BONE-017	ALLOB (Phase IIb)	Bone Therapeutics SA	The Company grants a worldwide and exclusive right to Glob-Co SRL for veterinary applications
BONE-018	ALLOB (Phase IIb)	Bone Therapeutics SA	The Company grants a worldwide and exclusive right to Glob-Co SRL for veterinary applications
BONE-019	ALLOB (Phase IIb)	Bone Therapeutics SA	The Company grants a worldwide and exclusive right to Glob-Co SRL for veterinary applications
BONE-020	JTA-004 (Phase III)	Bone Therapeutics SA	The Company grants a worldwide and exclusive right to Glob-Co SRL for veterinary applications

4.16.2 *Trademarks and designs*

On the date of this Registration Document, the Company obtained trademarks for ALLOB, MXB and JTA products. ALLOB was internationally registered under class 5 and/or class 42 in the Benelux, the EU, the US, Canada, Japan, Taiwan, Hong Kong and South Korea. International registration of MXB under class 5 and class 42 was obtained in September 2015 in EU, US, Japan, Korea, Australia, Canada, Israel and Hong Kong.

International registration of JTA under class 5 and/or class 42 was obtained in September 2015 in the EU, the US, Japan, Korea, China, Australia, Canada Israel and Hong Kong.

4.16.3 *Orphan Drug Designation*

Orphan Drug Designation ("**ODD**") provides a special status to a drug developed for the treatment of rare diseases or rare medical conditions. When obtaining orphan designation, the Company benefits from a number of incentives, including regulatory assistance and market exclusivity (10 years in Europe and 7 years in the US) once the medicine is approved for commercialisation. Through the ODD scheme, the Company benefits from significant fee reductions (90% or more) in respect of the protocol development and scientific advice and product registration procedure in Europe as well as in the US. The Company received ODD for PREOB and ALLOB for the treatment of (non-traumatic) osteonecrosis. ALLOB received ODD for osteonecrosis from the EMA in July 2013 and from the FDA in January 2014. In addition, the Company announced that it received ODD for ALLOB for osteogenesis imperfecta from the EMA and FDA.

4.17 Manufacturing

The Company aims to achieve the following objectives through its manufacturing process:

- Provide adequate production capacity at all stages of the development of the Company;
- Continuous optimization of processes to reduce costs and increase capacity of the available infrastructure;
- Protection of knowhow through in-house production and strictly manage relations with contract manufacturing organisation.

The cellular based product manufactured has been manufactured by the Company until November 2020. Sufficient number of doses have been produced and release to support the current clinical trial ALLOB-TF2 with a comfortable overage. These batches have the following product specifications:

- ALLOB is a cellular-based product consisting in viable human allogeneic bone-forming cells derived from *ex vivo* cultured bone marrow mesenchymal stromal cells. They are not genetically modified and not combined.
- The product is a medicinal product which has been developed in compliance with the European legislation and has been classified as a tissue engineered product within the European regulatory framework governing the advanced therapy in Europe (Regulation 1394/2007). Under Regulation 1394/2007, a tissue engineered product means a product that contains or consists of engineered cells (cells that have been subject to substantial manipulation or are not intended to be used for the same function in the recipient as in the donor), administered to human beings with a view to regenerating, repairing or replacing a human tissue.
- In the US, ALLOB is a cellular therapy as defined in the CFR - Code of Federal Regulations Title 21, part 1271 "Human Cells, Tissues, and Cellular and Tissue-based products" and regulated as biological products under section 351 of the PHS Act (42 U.S.C. 262) and the Federal Food, Drug, and Cosmetic Act (the act) and will fall under the Biological Licence Application regulation.
- Today based on one Bone Marrow collection from a healthy donor, up to 100.000 doses of ALLOB drug product can be produced. The drug product is cryo-preserved allowing easy shipment to the patient and ready to be used injectable medicinal product.

The protein-based products manufactured by the third-party (since the first clinical batches) have the following specifications:

- JTA-004 is an off-the-shelf protein solution containing three active pharmaceutical ingredients (API): the virus-inactivated pooled fresh frozen human plasma, the sodium hyaluronate (HA) and the α2-adrernergic receptor agonist 2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride (clonidine HCl), developed for the treatment of patients suffering from osteoarthritis (OA).

- The product is a medicinal product which has been developed in compliance with the European legislation. The product is lyophilized and should be resuspended just before intra-articular injection into the patient knee.

The manufacturing process of the Company's products is as follows:

- ALLOB, for current clinical trials, was manufactured in the Company certified facilities[30] until November 2020.

- The ALLOB manufacturing process consists in the *ex vivo* culture of human bone marrow-derived mesenchymal stromal cells in order to generate human bone-forming cells. ALLOB manufacturing processes have been developed to minimize the number of cell manipulations and to limit the number of reagents entering in contact with the cells. ALLOB is manufactured following standardized and validated manufacturing process by trained operators. Manufacturing process includes several key steps. At the end of manufacturing, ALLOB cells are collected, formulated in excipient, aseptically filled and then cryopreserved. Each ALLOB batch is controlled for safety, identity and potency prior release.

- Future ALLOB production campaigns will be done in collaboration with a Contract Manufacturing Organisation.

- The manufacturing process of JTA is based on a mixing of the different APIs followed by a lyophilisation cycle.

- The production of JTA is done in collaboration with a Contract Manufacturing Organisation.

Facilities and capacity:

The Company has been producing at its facility based at the Biopark in Gosselies which is GMP approved. The available capacity met the requirements for the current pre-clinical, clinical developments and the first commercialization steps.

- The Company's production activities were transferred to the new facilities at the BioPark of Gosselies (south of Brussels) in the course of 2018. The new facility has been inspected by the inspectorate of the Belgian Federal Agency for Medicines and Health Products (FAMHP). The GMP certificate has been issued by the FAMHP on 19 December 2017 and the authorization to manufacture the ALLOB investigational medical products according to GMP on 19 January 2018.

- The registration of the Gosselies site as "Structure Intermediaire" for human body material, according the Belgian Royal Decree of 28 September 2009 has been introduced with the Blood and Human Body Material division of the FAMHP. The site has been inspected successfully on 22 March 2018.

- The Company is also registered as Tissue Importer Establishment according to the Belgian Royal Decree of 28 September 2009 since March 2020 after being successfully inspected by the Blood and Human Body Material division of the FAMHP.

[30] The Company received a GMP agreement for its facilities at the Plateforme Wallonne de Therapie Cellulaire (PWTC) building in Gosselies from the FAMPH on 21 November 2017. A renewal of the authorization was received following an inspection on 24 December 2019.
In March 2021, the Company renewed its GMP agreement to cover Quality Control and Supply Activities (Manufacturing Activities have been removed from the agreement). The Company received authorization under number 1698 IMP for the manufacturing, quality control, importation and intra-EU distribution for ALLOB and JTA.

5 CORPORATE GOVERNANCE

5.1 General

This section summarizes the rules and principles on the basis of which the corporate governance of the Company has been organized pursuant to Belgian Code of Companies and Associations, and the Company's corporate governance charter (the "**Corporate Governance Charter**") adopted by the Board of Directors on 25 August 2020 in accordance with the new Belgian Corporate Governance Code 2020 (the "**Corporate Governance Code**" or "**CGC**") by the Royal Decree of 12 May 2019 designating the corporate governance code to be complied with by listed companies published on 17 May 2019 in the Belgian Official Gazette (*Moniteur belge*). The Corporate Governance Charter is available on the Company's website (www.bonetherapeutics.com, under the section Investors / Governance). A copy of the Corporate Governance Charter can be obtained free of charge at the registered office of the Company.

The text of the Corporate Governance Code is available on the website of the Corporate Governance Committee at https://www.corporategovernancecommittee.be/en/over-de-code-2020/2020-belgian-code-corporate-governance.

5.2 Compliance with the Corporate Governance Code

The Board of Directors intends to comply with the provisions of the Corporate Governance Code but believes that the size and the current state of development of the Company justifies certain deviations. These deviations are further detailed in 5.3 Section hereinafter.

The Corporate Governance Charter includes the following main chapters:

- Definitions;
- Structure and organisation;
- Shareholders;
- Transactions between the Company and its Board Members or the Members of the Management Team;
- Transactions involving Shares of the Company;
- Application of the CGC; and
- Miscellaneous.

The Appendices to the Corporate Governance Charter include the following:

- Terms of Reference of the Board;
- Policy for Transactions and other Contractual Relationships between the Company and its Board Members or Members of the Management Team;
- Rules for the Prevention of Market Abuse;
- Terms of Reference of the Audit Committee;
- Terms of Reference of the Nomination and Remuneration Committee; and
- Terms of Reference of the Management Team.

5.3 Deviations from the Corporate Governance Code

The Board of Directors of the Company complies with the Corporate Governance Code. However, the Company deviates from the following principles:

- *Remuneration of non-executive directors in company's shares (principle 7.6):* given the legal constraints of Belgian laws, the non-executive directors of the Company do not receive a portion of their remuneration in Company's shares.

- *No grant of stock options to non-executive directors (principle 7.6):* given the technical impossibility to grant Company's shares to non-executive directors, those directors can receive subscription rights (warrants) under the template 2020 Subscription Rights Plan. This plan provides that the subscription rights (warrants) shall vest and be exercisable at any time and without restriction unless the Company decides that these subscription rights (warrants) may not be exercised before the end of the third calendar year following the calendar year during which the subscription rights (warrants) were offered and indicates this in the offer thereof. Those grants can attract profiles with high potential, incentivize the beneficiaries in the development of the Company, and play a role as retention tool of the teams.

- *Minimum threshold of shares to be held by the executives (principle 7.9):* at the date hereof, the Company has not fixed any minimum threshold for the detention of shares by the Executive Directors. However, subscription rights (warrants) on the Company's shares were granted to the two Executive Directors (i.e. the CEO and the CFO) on 28 May 2020. These subscription rights (warrants) shall vest and be exercisable at any time and without restriction unless the Company decides that these subscription rights (warrants) may not be exercised before the end of the third calendar year following the calendar year during which the subscription rights (warrants) were offered and indicates this in the offer thereof.

- *Appointment of a company secretary (principle 3.19):* At the date hereof, no Company secretary has been appointed by the Board. Since the IPO (6 February 2015), the Board of Directors has assigned the law firms Allen & Overy (Belgium) LLP (until March 2019) and Osborne Clarke SCRL / CVBA (since March 2019) to provide services in this respect, including the drafting of minutes of Board meetings. Given the limited size of the Company, the Board of Directors is of the opinion that there is no need to appoint a full time Company secretary.

- *The audit committee, the remuneration committee and the nomination committee should be composed of at least three board members (principle 4.3):* At the date hereof, the Audit Committee and the Nomination and Remuneration Committee of the Company are only composed of 2 members. The Board of Directors is of the opinion that the current members of these two committees have the necessary independence, skills, knowledge, experience and capacity to execute their duties effectively.

- *Promotion of diversity (principle 4.23)*: The Company has not adopted a diversity policy yet. However, the Company ensures that it meets the minimum gender diversity requirement at the level of the Board of Directors of the Company.

  Article 7:86 of the Belgian Code of Companies and Associations imposes that at least one third of the board members are of a different gender than the other board members. The minimum is rounded to the closest unit and if the director is a legal person, his or her gender shall be determined by that of its permanent representative. The Board of Directors of the Company complies with Belgian laws on gender as it is currently composed of 7 Directors, out of which two are of a different gender.

  In addition, except for the Remuneration and Nomination Committee, one third of the members of the Executive Committee are of a different gender and half of the members of the Audit Committee are of a different gender.

  As regards the employees not included above, the Company records 69% female employees and 31% male employees.

In accordance with the Corporate Governance Code, the Board of Directors will review the Corporate Governance Charter from time to time and adopt such amendments thereto as it deems necessary and appropriate. The Corporate Governance Charter and the Company's articles of association are available at the Company's website and at its registered office and can be obtained free of charge.

5.4 Board of Directors

5.4.1 *Composition of the Board of Directors*

The Board of Directors is the main decision-making body of the Company and has full power to perform all acts that are necessary or useful to accomplish the Company's corporate purpose, save for those acts for which only the shareholders' meeting of the Company has the required powers in accordance with applicable laws or the Company's articles of association. The responsibility for the management of the Company is entrusted to the Board of Directors as a collegial body.

The Board of Directors pursues the long-term success of the Company by providing entrepreneurial leadership, while assessing and managing the risks of the Company.

The Board of Directors is composed of at least three members as set out in the articles of association and the Corporate Governance Charter.

At least half of the members of the Board of Directors are Non-Executive Directors, and at least three members of the Board of Directors are Independent Directors, within the meaning of inter alia Article 7:87, §1 of the Belgian Code of Companies and Associations.

The members of the Board of Directors are appointed by the shareholders' meeting of the Company for a renewable term of maximum four years. If a director mandate becomes vacant, the remaining members of the Board of Directors will have the right to temporarily appoint a new director to fill the vacancy. The shareholders' meeting can revoke the mandate of any director at any time.

In principle the Board of Directors meets at least four times a year, and also whenever a meeting is deemed necessary or advisable for its proper functioning. A meeting of the Board of Directors is validly constituted if there is a quorum, which requires that at least half of the members of the Board of Directors or present or represented during the board meeting. In any event, the Board of Directors can only validly deliberate if at least two Directors are present in person.

The table below provides an overview of the current mandates at the date of this Document:

Name	Position	Start or renewal of mandate	End of mandate	Nature of mandate	Professional address
Jean Stéphenne, permanent representative of Innoste SA	Chairman	2018	2025	Independent	Avenue Alexandre 8, 1330 Rixensart, Belgium
Miguel Forte, permanent representative of mC4Tx SRL	Managing Director	2020	2022	Executive	Rue du Moulin 12, 1330 Rixensart, Belgium
Claudia D'Augusta	Director	2018	2023	Independent	Calle Estrelas 5, 28224 Pozuelo De Alarcon - Madrid – Spain
Damian Marron, permanent representative of Castanea Management SARL	Director	2020	2023	Independent	401 Chemin du Val Martin, 06560 Valbonne, France
Gloria Matthews, permanent representative of ClearSteer Consulting LLC	Director	2020	2023	Independent	880 Roswell Rd, Suite 430, Roswell, GA, United States
Jean-Paul Prieels	Director	2017	2025	Independent	Avenue Louise 32-46, 1050 Brussels, Belgium

Name	Position	Start or renewal of mandate	End of mandate	Nature of mandate	Professional address
Jean-Luc Vandebroek, permanent representative of Finsys Management SRL	Managing Director	2018	2022	Non-Executive[31]	Rue Charles Plisnier 25, 1420 Braine l'Alleud, Belgium

A brief overview of the relevant experience of the Independent Directors in place is set out below.

- **Mr. Jean Stéphenne (permanent representative of Innoste SA)** is a highly experienced life sciences executive, who has served in senior leadership roles at a large number of biotechnology and pharmaceutical companies, most recently as Chairman of TiGenix. Together with the Board of TiGenix, he oversaw the clinical development and European marketing authorization of its most advanced allogeneic cell therapy product for the treatment of complex perianal fistulas in Crohn's disease. Jean Stéphenne was also previously a Member of the Corporate Executive Team of GlaxoSmithKline (GSK) and Chief Executive of GSK Biologicals (now GSK Vaccines). During his 40-year tenure, he grew a company of 50 people into a fully integrated worldwide leader in vaccine development, with 12,000 employees. Jean Stéphenne currently serves on the Board of various life sciences companies including OncoDNA, CureVac, Vaxxilon and Bepharbel. Previous board positions include Besix Group, BNP Paribas Fortis, GBL and IBA. For his contribution to the Belgian economy and global public health, he has received diverse business recognitions and was honored with various titles by the Belgian and British governments.

- **Dr. Claudia D'Augusta** has over 20 years of experience in the field of corporate finance, capital markets and M&A. She was most recently Chief Financial Officer of Therachon, prior to its acquisition by Pfizer in early 2019. Previously she served as General Manager at TiGenix after its acquisition by Takeda. Prior to this appointment, Claudia was Chief Financial Officer of TiGenix, where she led the company's IPO on Nasdaq in 2016, served as a member of the Executive Committee and held responsibility for the Finance, Legal and Investor Relations areas. She also served as the Chief Financial Officer of Cellerix and led its merger with TiGenix, a company listed on Euronext. Before joining Cellerix in 2004, Claudia was Finance Director of Aquanima (Santander Group). Previous experiences include Deloitte & Touche in Milan and Apax Partners in Madrid.

- **Damian Marron (permanent representative of Castanea Management SARL)** is an experienced life sciences executive with a successful track record of value creation through public and venture capital financing, portfolio planning and turnaround, M&A, licensing agreements and research and marketing collaborations. He has particular competencies in cell therapy, immuno-oncology and orphan diseases. Damian currently serves on a number of Boards of biotech companies and advise biotech companies on strategy and financing. Previously he was Chief Executive Officer of Agalimmune and has also served as Chief Executive Officer of TxCell, a France-based specialist in personalised T-cell immunotherapies, where he led the Company's IPO on Euronext Paris. As Chief Executive Officer of Trophos, France, he helped raise EUR 34 million in financing and positioned the company for a subsequent acquisition by Roche for EUR 700 million. Damian Marron also served as Executive Vice President, Corporate Development, for NiCox, where he supported the CEO in financing rounds raising over EUR 175 million.

- **Dr. Gloria Matthews (permanent representative of ClearSteer Consulting LLC)** has more than 20 years of research and clinical experience in orthopaedics, osteoarthritis, rheumatology and cartilage repair with extensive expertise in medical devices, biologicals, and regenerative medicine. She has a strong track record of supporting life sciences companies to grow and evolve from start-up stage to fully integrated biopharma companies and has built an impressive business and medical network over the years. She was Senior Vice President of MiMedx, a biopharma company focused

[31] Non-Executive position as of 20 September 2021

on the development and commercialisation of regenerative and therapeutic biologicals in wound care, and spine and sports medicine. Prior to that, she was Chief Medical Officer of the restorative cell therapy company Histogenics and Senior Director of Orthopaedics at Genzyme, a Sanofi company.

- **Dr. Jean-Paul Prieels, PhD** holds a PhD in Biochemistry from Université libre de Bruxelles in Belgium. He started his industrial career at Petrofina in 1983 as Biotechnology Manager and joined GlaxoSmithKline Biologicals in 1987. His responsibilities gradually expanded to lead the vaccine preclinical R&D development activities as Senior Vice President of Research & Development at GlaxoSmithKline Biologicals in Rixensart, Belgium, in 2011. His career spans from basic research to applied research and product development. He was instrumental in the development of several commercially available vaccines, such as Rotarix, Cervarix and Synflorix. Today he is Director and member of scientific advisory board at a number of biotechnology companies.

At the date of this Document, none of the Directors and the members of the Executive Committee have at any time within at least the past five years:

- had any conviction in relation to fraudulent offences; or
- been adjudged bankrupt or entered into an individual voluntary arrangement; or
- been a director of any company at any time of, or within 12 months preceding, any receivership, compulsory liquidation, administration or partnership voluntary arrangement of such partnership; or
- had his assets from the subject of any receivership or has been a partner of a partnership at the time of, or within 12 months preceding, any assets thereof being the subject of a receivership; or
- been subject to any official public incrimination and/or sanctions by any statutory or regulatory authority; or
- ever been disqualified by a court from acting as a director of a company or from acting in the management or conduct of the affairs of any company.

5.4.2 Other mandates

Other than set out in the table below, no member of the Board of Directors or member of the Executive Committee has, at any time in the previous five years, been a member of the administrative, management or supervisory bodies or partner of any companies or partnerships. Over the five years preceding the date of this Registration Document, the members of the Board of Directors and the members of the Executive Committee hold or have held in addition to their function with the Company, the following main directorships of administrative, management or supervisory bodies and partnerships:

Board of Directors and/or Executive Committee Members	Current Mandates	Past Mandates
Jean Stéphenne (permanent representative of Innosté SA)	Chairman at Vesalius Biocapital Chairman at Nanocyl Chairman at Bepharbel Chairman at OncoDNA Director at NSide Chairman at Curevac Director at Belgian Foundation against Cancer	Director at Ronveaux Chairman at Tigenix Chairman of BioWin Director at Merieux Development Chairman at Vaxxilon Chairman at BESIX

Board of Directors and/or Executive Committee Members	Current Mandates	Past Mandates
	President of Welbio and Foundation University Louvain	
Claudia D'Augusta	Chief Financial Officer at VectivBio Holding AG	General Manager and CFO at Tigenix SAU and NV Director at TiGenix NV Director at TiGenix SAU Director at TiGenix Inc Director at TiGenix US, Inc Director at ReNeuron Group plc Venture Partner at Ysios Capital
Damian Marron (permanent representative of Castanea Management SARL)	Chair of Board at Targovax ASA Chair of Board at Imophoron Ltd Chair of Board at CytoSeek Ltd Director at Cantargia AS Director at Resolys Bio Director at Raodrunner Representative Ltd	Chair of Board at PepGen CEO and director at Agalimmune
Gloria Matthews (permanent representative of ClearSteer Consulting LLC)	Chief Medical Officer at Ankasa Regenerative Therapeutics President and Managing Member at ClearSteer Consulting, LLC	Senior Vice President at Mimedx Corporation Chief Medical Officer at Histogenics Corporation ORS Presidential Line Members at AAOS Board of Specialities Committee member of Musculoskeletal Gene and Cell Therapy at American Society Gene & Cell Therapy
Jean-Paul Prieels	Director of NCardia Director of Leukocare Director of Nouscom Director of PDC*line Pharma Director of Paracrine Biologicals Director of Quantoom Biosciences	Director of Abivax SA Director of Promethera Biosciences Director of Ogeda Director of Vaximm AG Board Member of DNAlytics Director of Themis Director of Masthercell Director of Asit Biotech Director of Keires
Miguel Forte (permanent representative of mC4Tx SRL)	Board Member of the Alliance of Regenerative Medicine Board Member of Escencia-Wallonie	CEO of Zelluna Immunotherapy CMO of Bone Therapeutics SA Board Member of ISCT
Jean-Luc Vandebroek (permanent representative of Finsys Management SRL)	N/A	Director of Bihr Europe SA Director of Moteo Two Wheels Europe NV Director at SISE SA
Lieve Creten (permanent representative of Lieve Creten NV)	Board Member Barco Board Member Elia Board Member Médecins Sans Frontières	Director Deloitte Consulting & Advisory
Stefanos Theoharis	N/A	N/A

Board of Directors and/or Executive Committee Members	Current Mandates	Past Mandates
(permanent representative of Venture Advanced Therapies Limited)		
Anthony Ting	Board Member of Board for the International Society for Cell and Gene Therapy	N/A
Anne Leselbaum	N/A	N/A
Anne-Sophie Lebrun	N/A	N/A

5.4.3 *Activity report*

In 2020, the Board of Directors met 16 times discuss and decide on specific matters. Below is the detail of the attendance:

BOARD OF DIRECTORS	Number of attendances[32]
Innoste SA, represented by M. Jean Stéphenne	16/16
mC4Tx SRL, represented by Miguel Forte	16/16
Claudia D'Augusta	16/16
Castanea Management SARL, represented by M. Damian Marron	16/16
ClearSteer Consulting LLC, represented by Mrs Gloria Matthews	14/16
M. Jean-Paul Prieels	16/16
Finsys Management SRL, represented by Jean-Luc Vandebroek	16/16

5.4.4 *Committees within the Board of Directors*

5.4.4.1 General

The Board of Directors has established a nomination and remuneration committee (the "**Nomination and Remuneration Committee**") and an Audit Committee (the "**Audit Committee**"). These committees (the "**Committees**") have a mere advisory role.

The Board of Directors has determined the terms of reference of each Committee with respect to its respective organisation, procedures, policies and activities.

5.4.4.2 Audit Committee

5.4.4.2.1 Role

The Audit Committee supports the Board of Directors in fulfilling its monitoring responsibilities in respect of control in the broadest sense.

[32] Number of attendances compared to the maximum number of attendances considering time of appointment and conflicts of interest. All Directors who were not present, were excused.

5.4.4.2.2 Composition

The Corporate Governance Charter of the Company states that the Audit Committee is composed out of at least two members, all its members being Non-Executive Directors. At least one of the members of the Audit Committee is an independent Director, who has accounting and auditing expertise. This expertise in accounting and auditing implies a degree of higher studies in economics or finance or relevant professional experience in those matters.

The Audit Committee is chaired by one of its members, who may not be the chairman of the Board of Directors.

The duration of the mandate of a member of the Audit Committee will not exceed the duration of his/her mandate as director of the Company.

The composition of the Audit Committee is as follows:

Name	Position	Professional address
Claudia D'Augusta	President—Independent Director	Calle Estrelas 5, 28224 Pozuelo De Alarcon, Madrid, Spain
Jean-Paul Prieels	Member—Independent Director	Chemin du Gros Tienne 61, 1380 Lasne, Belgium

Currently the Audit Committee is counting 2 members. Claudia D'Augusta and Jean-Paul Prieels qualify both in respect of having the necessary competences and qualifications in respect of accounting and audit matters as well as both of the members having an extensive experience in the management of biotech companies.

5.4.4.2.3 Operation

The Audit Committee will meet at least four times a year and whenever a meeting is deemed necessary or advisable for its proper functioning. Decisions are taken by a majority vote. The Chairman of the Board of Directors has a permanent invitation to attend the meetings of the Audit Committee. The Audit Committee may also invite other persons to attend its meetings.

The Audit Committee meets with the external auditor and the internal auditor (if any) at least twice a year, to discuss matters relating to its terms of reference, issues falling within the powers of the Audit Committee and any issues arising from the audit process and, in particular, any material weaknesses in the internal audit.

During 2020, the Audit Committee met seven times.

5.4.4.3 Nomination and Remuneration Committee

5.4.4.3.1 Role

The Nomination and Remuneration Committee makes recommendations to the Board of Directors with respect to the appointment of Directors, the Executive Directors and other members of the Executive Committee. In addition, the Nomination and Remuneration Committee makes recommendations to the Board of Directors on the Company's remuneration policy, on any remuneration whatsoever granted to the Directors and members of the Executive Committee and on any agreements or provisions relating to the early termination of employment or collaboration with the Directors and members of the Executive Committee.

5.4.4.3.2 Composition

The Nomination and Remuneration Committee is composed of at least three Directors. All members of the Nomination and Remuneration Committee are Non-Executive Directors, with a majority being independent Directors. The majority of the members has the necessary expertise with regard to remuneration policies, *i.e.* has a degree in higher education and has at least three years' experience in personnel management matters or matters related to the remuneration of Directors and managers of companies. The Board of Directors considers that all members of the Nomination and Remuneration Committee have sufficient experience in personnel management and matters related to remuneration.

The Nomination and Remuneration Committee is chaired by the chairman of the Board of Directors or by another non-executive member of the Nomination and Remuneration Committee. The chairman of the Board of Directors has a permanent invitation to attend the meetings of the Nomination and Remuneration Committee, except for meetings at which his own appointment, removal or remuneration is discussed. The chairman of the Board of Directors does not chair the Nomination and Remuneration Committee when dealing with the designation of his or her successor.

The duration of the term of a member of the Nomination and Remuneration Committee will not exceed the duration of his mandate as director of the Company.

The following Directors are members of the Nomination and Remuneration Committee:

Name	Position	Professional address
Jean Stéphenne, permanent representative of Innoste SA	Chairman—Independent Director	Avenue Alexandre 8, 1330 Rixensart, Belgium
Damian Marron, permanent representative of Castanea Management SARL	Member—Independent Director	401 Chemin du Val Martin, 06560 Valbonne, France

5.4.4.3.3 Operation

The Nomination and Remuneration Committee meets at least twice a year, and whenever a meeting is deemed necessary and advisable for its proper functioning. Decisions are taken by a majority vote. The chairman of the Board of Directors has a permanent invitation to attend the meetings of the Nomination and Remuneration Committee, except for meetings at which his own appointment, removal or remuneration is discussed. The Nomination and Remuneration Committee may invite other persons to attend its meetings (it being understood that a member of the Board of Directors may not attend the meeting of the Nomination and Remuneration Committee which handles his remuneration).

During 2020, the Nomination and Remuneration Committee met five times with particular emphasis on the:

- performance evaluation 2019 of the Executive Directors including bonus determination;
- definition of the objectives 2020 of the Executive Directors;
- discussion about a new stock option plan for Board members and employees;
- discussion about nomination of Stefanos Theoharis (CBO) and of a new CSO.

5.5 Executive Committee

5.5.1 *General*

The Board of Directors has established an Executive Committee (the "**Executive Committee**"), which advises the Board of Directors, and which therefore does not constitute a management committee (*comité de direction*) under article 7:104 of the Belgian Code of Companies and Associations. The terms of reference of the Executive Committee have been determined by the Board of Directors.

5.5.2 *Executive Committee*

5.5.2.1 Role

The Executive Committee assists the Executive Directors in the management of the Company. The Executive Committee reports to and is accountable to the Board of Directors for the discharge of its responsibilities.

5.5.2.2 Composition

The Executive Directors (CEO and CFO) together with the senior managers (CMO, CBO, CSO and COO) are members of the Executive Committee. The Executive Committee is chaired by the CEO of the Company and in his absence by the CFO. The members of the Executive Committee are appointed and may be dismissed by the Board of Directors at any time. The Board of Directors appoints them on the basis of the recommendations of the Nomination and Remuneration Committee, which also assists the Board of Directors on the remuneration policy for the members of the Executive Committee, as well as their individual remunerations

The remuneration, duration and the conditions of the resignation of the members of the Executive Committee are governed by the agreements entered into between the Company and each member of the Executive Committee in respect of their function within the Company.

The current members of the Executive Committee are listed in the table below:

Name	Title
Miguel Forte, permanent representative of mC4Tx SRL	Chief Executive Officer and Executive Director
Jean-Luc Vandebroek, permanent representative of Finsys Management SRL	Chief Financial Officer and Executive Director until 20 September 2021
Lieve Creten, permanent representative of Lieve Creten NV	Interim Chief Financial Officer from 20 September 2021
Stefanos Theoharis, permanent representative of Venture Advanced Therapies Limited	Chief Business Officer
Anthony Ting	Chief Scientific Officer from 1 April 2021
Anne Leselbaum, permanent representative of Clinical Drug Development, S.L.	Chief Medical Officer from 23 August 2021
Anne-Sophie Lebrun	Chief Operations Officer

A brief overview of the relevant experience of the Executive Committee members in place is set out below.

- **Mr. Miguel Forte (permanent representative of mC4Tx SRL)**, (61) (**CEO**). Dr. Forte has significant experience in regenerative medicine and in the cell therapy industry, most recently as Chief Executive Officer of Zelluna Immunotherapy, a biopharma company focusing on developing transformative T cell receptors (TCR) based cellular immunotherapies for the treatment of cancers.

  Dr. Forte held in the past a senior position at the European Medicines Agency (EMA), was Vice-President Global Medical Affairs Inflammation at UCB, Chief Medical Officer (CMO) at TxCell, a cellular therapy company, where he played a key role in TxCell's 2014 IPO, and served as Chief Medical Officer

of Bone Therapeutics in 2017. In this last position, Dr. Forte was responsible for the Company's clinical development strategy and advancing its products towards the market. He played a key role in increasing the visibility of the Company throughout the medical community.

With over 20 years professional activity in Clinical, Academic and Pharmaceutical Industry environments with deep experience in the management of operational and strategic functions across Research & Development, Manufacturing, Medical and General Management, Dr. Forte is a recognized leader in the regenerative medicine field who has gained broad expertise in medical and regulatory affairs and commercialization, leading early and late stage clinical trials to market authorization and the launch of new biologic products for various indications.

Dr. Forte graduated in Medicine from the University of Lisbon, specializing in infectious diseases. He then obtained a PhD in Immunology at the University of Birmingham. He is a Fellow of the Faculty of Pharmaceutical Medicine of the Royal College of Physicians, UK and Associate Professor in Health Sciences and Pharmacy at the University of Lisbon.

- **Jean-Luc Vandebroek (permanent representative of Finsys Management SRL**, (50) (**CFO**). Jean-Luc Vandebroek is a seasoned finance executive with extensive international finance experience at major public and privately-owned companies. Jean-Luc has built a successful career spanning 15 years at the Belgian-US retailer, Delhaize Group (now Ahold Delhaize). During this period, he held various senior financial positions with increasing responsibility, including roles as Corporate Director Finance Europe and US and Vice President Finance BeLux. He later became Group Chief Financial Officer at Fluxys, a listed, pan-European gas infrastructure group, where he was responsible for the financing of large infrastructure investments using diverse forms of funding on capital markets. Prior to joining Bone Therapeutics, Jean-Luc served as Director and Chief Financial Officer of Moteo Two Wheels and Bihr Europe, the motorcycle division of Alcopa Group, a Belgian family holding with an annual revenue of around EUR 1.7 billion.

- **Lieve Creten (permanent representative of Lieve Creten NV**, (56) (ad-interim **CFO**). Lieve Creten has a large experience in management, finance reporting and business deals including acquisitions or mergers for both public and private companies. Lieve's extensive financial experience gained as a partner with Deloitte Financial Advisory in Belgium and being a certified public accountant from origin will ensure optimal financial control, oversight and compliance during Bone Therapeutics strategic refocus on the iMSC platform, which includes its product ALLOB.

- **Stefanos Theoharis (permanent representative of Venture Advanced Therapies Limited)**, (46) (**CBO**). Stefanos contributes more than 15 years of business development experience in the pharma and biotech industry to Bone Therapeutics, specifically in the cell and gene therapy space. This includes his achievements as Senior Vice-President at Cell Medica, a clinical-stage biotech company, where he expanded the company's allogeneic T-cell immunotherapy platform through strategic partnerships with leading research institutions and targeted acquisitions. Prior to Cell Medica, Stefanos was Chief Business Officer at apceth GmbH, a company developing genetically-engineered mesenchymal stromal (MSC) cell products and also acting as a contract manufacturer in the ATMP space. He led all apceth's business development activities, including in- and out-licensing and service contracts negotiations. He also held positions as Head of Business Development at the antisense RNA drug specialist Antisense Pharma (now Isarna), and Director Business Development at Roche, focused on partnering activities in emerging science and technologies. Stefanos also worked at Lazard, the global investment bank, advising to a variety of life sciences firms on M&As and financing transactions. Stefanos achieved an MSc. in Molecular Medicine and a PhD in Pathology and Immunology from Imperial College London.

- **Anthony Ting**, (58) (**CSO**). Dr. Ting brings to Bone Therapeutics over 30 years of academic and industry experience in translational science and global regulatory filing, and 20 years specifically in stromal cell-based therapeutics. He is currently the Chief Commercialization Officer on the board of

directors for the International Society for Cell and Gene Therapy (ISCT) and is serving on committees for the Alliance for Regenerative Medicine (ARM) and the Health and Environmental Sciences Institute (HESI). Most recently, Dr. Ting served in the senior management team of Athersys, a Nasdaq-listed clinical-stage cell therapy company. As Vice President of Regenerative Medicine and Head of Cardiopulmonary Programs, he was responsible for all stages of development, from the bench to the bedside for the cardiovascular and pulmonary programs with Athersys' most advanced cell therapy product MultiStem®, an allogeneic adult bone marrow-derived stem cell product. Prior to joining Athersys, Dr. Ting was a Principal Investigator and Head of the Novel Inhibitors Screening Group at the Institute of Molecular and Cell Biology (IMCB) at the National University of Singapore, which identified new therapeutic targets through high-throughput screening. Dr. Ting received his PhD in Cell Biology from Johns Hopkins University and his B.A. in Biology from Amherst College.

- **Anne Leselbaum, MD (permanent representative of Clinical Drug Development S.L.)** (55) **(CMO).** Dr. Leselbaum brings three decades of experience in strategic international clinical development, clinical operations and medical affairs. She has directly managed more than 10 clinical studies (from phase I to III) involving more than 3,500 patients and 350 sites in Europe, Americas and Asia-Oceania regions. She has also led clinical and regulatory interactions with both the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA). This includes for a number of products including vaccines and cell therapies, from pre-Investigational New Drug (IND) activity up to the filing of Marketing Authorization Applications (MAA).

  Dr. Leselbaum was most recently Vice President Clinical Development at Aelix Therapeutics. leading the clinical development of novel HIV vaccines. Prior to this, Dr. Leselbaum was Director Clinical Development at Tigenix. She was responsible for the development and implementation of clinical development of Tigenix' allogeneic cell therapy product, Alofisel, for the treatment of complex perianal fistulas in Crohn's disease. She has also held leadership positions at the international pharmaceutical companies Almirall and Ipsen. Dr. Leselbaum received her Medical Degree from Paris Rene Descartes (Paris V), France.

- **Anne-Sophie Lebrun,** (38) **(COO).** Dr. Lebrun joined Bone Therapeutics in 2010 and has subsequently held several roles of increasing responsibilities. She currently serves as Head of Operations and Associate Director of Production and oversees all manufacturing and logistic activities of company's cell therapy pipeline. She plays an instrumental role in the optimization of Bone Therapeutics allogenic platform ALLOB into a scalable, off-the-shelf cell therapy product. Previously, as a technology consult at Amaris Consulting, Dr. Lebrun advised a global vaccine manufacturer in quality assurance of its complex biomanufacturing processes. Dr. Lebrun obtained a bioengineering degree in chemistry and bio-industry and a PhD in agronomic sciences, both at the Catholic University of Louvain (UCL).

5.5.3 *Operation*

The Executive Committee meets regularly whenever it is required for its proper functioning.

The CEO and the CFO have been appointed as Executive Directors of the Company and can be removed by the Board of Directors of the Company. The CEO and the CFO are entrusted by the Board of Directors with the day-to-day management of the Company.

5.6 Internal control and risk management systems

5.6.1 *Internal mechanism*

The role of the Executive Directors & Executive Committee is to develop and maintain adequate control system to assure:

- the realization of company objectives;
- the reliability of financial information;
- the adherence to applicable laws and regulations;
- monitor the internal and external impact of the risks identified by its Committees, and the management of the risks identified.

The Audit Committee has guiding, supervisory and monitoring role with respect to the Executive Directors & Executive Committee, as regards the development, maintenance and execution of internal controls and:

- assists the Board of Directors in respect of control issues in general;
- acts as the interface between the Board of Directors and the external auditors of the Company.

No internal audit role has been assigned at this point in time as the size of the business does not justify a permanent role in this respect - typical internal audit activities will be outsourced from time to time whereby the Audit Committee will determine frequency of these audits and select topics to be addressed

In 2015, the Company took measures to improve the controls and the efficiency of the payment process and implemented tools to allow for a more detailed budget follow-up.

Based on observations made by the external auditors in respect of payroll process, the recoverable cash advances process, the expenditure process and the process for capitalisation of the R&D costs, an action plan was established for implementation in the course of 2016.

A new budgeting process was implemented. Each department was asked to provide a separate budget which were subsequently integrated into a global company budget. The new budgeting procedure was designed to provide a stronger involvement to the departments of the Company providing a more accurate forecast of the spending on a more granular level. A monthly reporting of the actual spending was also installed such that each department could follow their spending compared to their budgets creating an additional level of cost-awareness.

The Company improved its ERP with the integration of the new ERP system for the formalization of the purchase orders and the approval of the orders and the invoices.

5.6.2 *Financial risk management*

5.6.2.1 Liquidity risk management

The Company manages liquidity risk by continuously monitoring forecast and actual cash flows, and by matching the maturity profiles of financial assets and liabilities.

The Company's main sources of cash inflows at current are obtained through capital increases, subsidies, government loans and where appropriate loans from commercial banks to finance long-term requirements (investment in infrastructure). A key objective of the Board together with the Executive Directors is to ensure that the Company remains adequately financed to meet its immediate and medium-term needs.

If necessary and appropriate the Company assures itself of short-term borrowing facilities to cover short-term cash requirements.

5.6.2.2 Interest rate risk management

The Company has limited interest rate risk on long term investments loans granted by regional investment bodies but also including the turnover independent reimbursements (30%) related to RCA's concluded as of 2009 are carrying fixed interest rates. The group at current does not undertake any hedging.

5.6.2.3 Credit risk

The Company believes that its credit risk, relating to receivables, is limited because currently almost all of its receivables are with public institutions. Cash and cash equivalent and short-term deposits are invested with highly reputable banks and financial institutions.

The maximum credit risk, to which the Group is theoretically exposed as at the balance sheet date, is the carrying amount of the financial assets. At the end of the reporting period no financial assets were past due, consequently no financial assets were subject to impairment.

5.6.2.4 Foreign exchange risk

The Company is currently not exposed to any significant foreign currency risk.

However, should the Company enter into long term collaboration agreements with third parties for which revenues would be expressed in a foreign currency, the Company might in such case consider to enter into a hedging arrangement to cover such currency exposure (in case the related expenditure is planned in local currency). The Company will also monitor exposure in this respect following the establishment of its US subsidiary. At current, there is no significant exposure in USD.

5.6.3 *Controls, supervision and correctives actions*

Within the Board of Directors, an annual strategy meeting is organised:

- The management presents strategic plans for the different aspects of the business;
- The Board of Directors reviews these plans and selects between strategic options when necessary;
- The Board reviews on a regular basis the validity of the strategic options chosen and redirect where necessary.

The Executive Directors develop a long term financial plan (minimum 3 years looking forward) incorporating the strategy decided upon – this plan is updated on a regular basis to keep it in line with the strategy plans.

The Executive Directors develop an annual budget which is approved by the board and which is closely monitored during the year. Deviations are reported to the board and corrective action is taken when necessary.

The Company has implemented an ERP system in support of its financial and logistics management. This system will be evaluated at regular intervals in how far it meets the needs of the organization. Where and when necessary, the system will be further upgraded to address new needs or to strengthen controls.

In general supervision and monitoring of the operations of the Company is done on a permanent/daily basis at all levels within the Company. As a general policy deviations are reported at all times to the supervisory level.

5.7 Market abuse regulations

In its Governance Charter, the Company established several rules to prevent illegal use of inside information by Directors, shareholders, management members and employees, or the appearance of such use.

These prohibitive provisions and the monitoring of compliance with them are primarily intended to protect the market. Insider dealing attacks the very essence of the market. If insiders are given the opportunity to make profits on the basis of inside information (or even if the mere impression thereof is created), investors will turn their back on the market. A decreased interest may affect the liquidity of listed shares and prevents optimal company financing.

An insider can be given access to inside information within the scope of the normal performance of his duties. The insider has the strict obligation to treat this information confidentially and is not allowed to trade financial instruments of the Company to which this inside information relates.

The Company keeps a list of all persons (employees or persons otherwise working for the Company) having (had) access, on a regular or occasional basis, to inside information. The Company will regularly update this list and transmit it to the FSMA whenever the FSMA requests the Company to do so.

5.8 Remuneration report

The Company complies with the new law of 28 April 2020. This new law combines new rules that have been introduced in Belgian company law, implementing the EU Directive 2017/828 as regards the encouragement of long-term shareholder engagement.

5.8.1 *Procedure*

The Nomination and Remuneration Committee (or Remco), set up by the Board, is responsible for outlining a remuneration policy for the executive and non-executive directors.

5.8.1.1 Directors

Board members are remunerated based on a benchmarking exercise done on a regular basis by the Remco with other peer companies to ensure that this remuneration is fair, reasonable and competitive and is sufficient to attract, retain and motivate the Directors of the Company. In this respect the Remco and the Board shared the view that all board members independent and non-independent, should be compensated equally with a fixed compensation. For the Chairman and the chairs of the committees the board proposed a supplementary compensation.

Without prejudice to the powers granted by law to the shareholders meeting, the Board of Directors may set and revise at regular intervals the rules and the level of compensation for its Directors.

5.8.1.2 Executive Directors and the Executive Committee

The remuneration of the Executive Directors and the remuneration of the members of the Executive Committee are determined by the Board of Directors on recommendations made by the Nomination and Remuneration Committee, further to recommendations made by the Executive Directors (except where their own remuneration is concerned). The Company strives to offer a competitive remuneration within the sector.

5.8.2 *Remuneration policy*

5.8.2.1 Director's remuneration

The remuneration of the Directors is determined by the shareholders' meeting upon proposal of the Board of Directors on the basis of the recommendations made by the Nomination and Remuneration Committee. The following remuneration policy is in place for the Non-Executive Directors' remuneration.

The Non-Executive Directors received a fixed remuneration in consideration for their membership of the Board of Directors and their membership of the Committees.

The Nomination and Remuneration Committee recommends the level of remuneration for Non-Executive Directors, subject to approval by the Board of Directors and, subsequently, by the shareholders' meeting. The Nomination and Remuneration Committee benchmarks Directors' compensation against peer companies to ensure that it is competitive. Remuneration is linked to the time committed to the Board of Directors and its various committees.

The shareholders' meeting decides to maintain the resolution approved in 2016 concerning the remuneration of the non-executive Directors, as follows: a fixed annual remuneration for the members of the Board of Directors of €20,000; an additional annual remuneration for the Chairman of the Board of Directors of €20,000; and an additional annual remuneration for membership of each committee of the Board of Directors of €5,000 for committee members and €10,000 for the chairman of the committee.

The shareholders' meeting also decides to approve the proposal of the Company's Nomination and Remuneration Committee to grant each year: 6,666 subscription rights to the Chairman of the Board of Directors; 1,000 subscription rights to each non-executive Director of the Company; 500 subscription rights to each committee or sub-committee Chairman; as well as 500 additional subscription rights to any Director in charge of a special mandate within the Board of Directors. The shareholders' meeting confirms that the granting of subscription rights cannot be considered as variable remuneration. Any changes to these fees will be submitted to the shareholders' meeting for approval. The Executive Directors will not receive any specific remuneration in consideration for their membership of the Board of Directors.

The total remuneration for the Non-Executive Directors for 2020 amounts to €150,000. The table below provides an overview of the remuneration per Independent Directors.

	Fixed Remuneration (€)			Variable Remuneration (€)						
Name, Position	Base compensation	Attendance fees	Other benefits	One-year variable	Multi-year variable	Extra-ordinary items (€)	Pension expense (€)	Total remu-neration (€)	Fixed	Variable
Innoste S.A., with as permanent representative Jean Stéphenne	50,000	/	/	/	/	/	/	50,000	100%	0%
Claudia D'Augusta	30,000	/	/	/	/	/	/	30,000	100%	0%
Castanea Management SARL with as permanent representative Damian Marron	25,000	/	/	/	/	/	/	25,000	100%	0%
Jean-Paul Prieels	25,000	/	/	/	/	/	/	25,000	100%	0%
ClearSteer Consulting LLC with permanent representative Gloria Matthews	20,000	/	/	/	/	/	/	20,000	100%	0%

Total	**150,000**	**/**	**/**	**/**	**/**	**/**	**/**	**150,000**	**100%**	**0%**

All Directors will be entitled to a reimbursement of out-of-pocket expenses actually incurred as a result of participation in meetings of the Board of Directors.

There are no loans outstanding from the Company to the members of the Board of Directors. There are no employment or service agreements that provide for notice periods or indemnities between the Company and Non-Executive Directors.

Also, any agreement, entered or extended on or after 3 May 2010, between the Company and a Non-Executive Director, which would provide for a variable remuneration, must be submitted for approval to the next annual shareholders' meeting.

The table below provides an overview of significant positions of shares held directly or indirectly on 31 December 2020 by the Non-Executive Members of the Board of Directors. The overview must be read together with the notes referred to below.

	Shares	
Non-Executive Directors	**Number**	**%***
Innoste S.A., with as permanent representative Jean Stéphenne	47,038	0.27%
** calculated as the percentage of all outstanding shares and warrants (17,703,722 which is 16,478,168 shares and 1,225,554 warrants) at the date of the Document*		

The table below provides an overview of the main condition of the warrant plans as well as information related to the financial year 2020 regarding Non-Executive Members of the Board of Directors:

	Main condition of the warrant plans					**Information related to the financial year 2020**		
Name Position[33]	**Plan ID**	**Grant date**	**Vesting Date**	**Retention period**	**Exercise period**	**A) Number of options vested; B) Value at exercise price (€)**	**A) Number of options exercised ; B) Date of exercise**	**Number of options expired**
Jean Stéphenne, Chairman	Plan A	28-02-19	1/3 at 28-02-2020 2/3 at 28-02-2021 3/3 at 28-02-2022	-	28-02-2019 - 28/02/2029	A) 6,666 B) 4.11	-	-
Jean Stéphenne, Chairman	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 14,332 B) 2.74	-	-
Claudia D'Augusta, Director	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 3,000 B) 2.74	-	-
Jean-Paul Prieels, Director	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 3,000[34] B) 2.74	-	-
Damian Marron, Director	Plan A	28-02-19	1/3 at 28-02-2020 2/3 at 28-02-2021 3/3 at 28-02-2022	-	28-02-2019 - 28/02/2029	A) 666 B) 4.11	-	-
Damian Marron, Director	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 2,000 B) 2.74	-	-

[33] Please note that the warrants have been offered to the Company of the representative named in the table, which is the case for Jean Stéphenne, Damian Marron and Gloria Matthews

[34] Jean-Paul Prieels refused the warrants in February 2021

Gloria Matthews, Director	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 2,000 B) 2.74	-	-

5.8.2.2 Remuneration of the CEO and the other Executive Directors and the Executive Committee

5.8.2.2.1 Remuneration policy

The remuneration package applicable in 2020 for the Executive Directors and the members of the Executive Committee is in line with the remuneration levels in comparable companies for these functions.

The key components of this policy can be summarized as follows:

- The Company wants to offer a market competitive compensation to allow the recruitment, retention and motivation of expert and qualified professionals and considering the scope of their responsibilities.

- The remuneration will be structured to allow linking an appropriate part of the remuneration to individual performance and the performance of the Company and to align the interest of the individual as much as possible with the interest of the Company and its shareholders.

- For this purpose, key performance indicators (corporate and individual) are agreed upon in advance. These indicators can be operational or financial in nature (progress in clinical and preclinical programs, financial management of key financial parameters, realization of collaborations or concluding new grants, investor relation activities, compliance matters and regulatory approvals and successful completion of audits). The valuation period is aligned with the fiscal year. The weights of each performance factors applied in 2020 can be found in the table below.

Performance factor	Weight
Financial (cash position end of year, budget management, funding strategy development)	35%
Business development & Commercialization strategy development (commercial deal, scientific partnership)	30%
Clinical trials progress (recruitment timelines, sites initiations and activations)	25%
Regulatory Strategy development	10%

- The variable remuneration will be partly in cash and partly in shares, warrants or other instruments allowing acquiring shares through schemes to be approved by the annual shareholder meeting. For the year 2020, 100% of the variable remuneration of the CEO and of other executive committee members has been paid in cash.

- The variable remuneration will only be paid when the key performance indicators agreed upon in advance are effectively met. The remuneration committee will evaluate the realization of the performance criteria and will make a proposal in respect of the variable remuneration to the Board.

- The maximum variable remuneration is set at [50% * base salary] for the CEO. For the other Executive Directors, the maximum variable remuneration is set between [20% and 30% * base salary] depending on the positions.

- The Company's articles of association explicitly allow to deviate from what has been defined under Article 7:91 of the Belgian Code of Companies and Associations (by decision of the General meeting date: 5 February 2015). Article 7:91 stipulates that: "Unless otherwise provided for in the articles of association or expressly approved by the general meeting, at least one quarter of the variable remuneration of an Executive Director in a listed company must be based on predetermined and objectively measurable performance criteria over a period of at least two years, and another quarter must be based on predetermined and objectively measurable criteria over a period of at least three years.

- In accordance with Article 7:149 of the Belgian Code of Companies and Associations, which applies to agreements with leaders entered into or extended after 3 May 2010, any such agreement which includes a provision providing for a severance package exceeding 12 months' remuneration, or, on motivated advice of the Nomination and Remuneration Committee, exceeding 18 months, must be submitted for prior approval to the next annual shareholders' meeting. Any proposal to grant a higher severance package must be communicated to the works council (or to other designated bodies or persons representing the employees, if this council does not exist; i.e., the employee representatives in the committee for the prevention and protection in the workplace or, in the absence of this committee, to the trade union delegation) at least thirty days prior to the publication of the convening notice of the next annual general shareholders meeting, which may then give its advice to the annual general shareholders meeting, at the latest on the day of publication of the convening notice of the annual general shareholders' meeting. This advice is published on the website of the Company.

- In accordance with Article 7:90 of the Belgian Code of Companies and Associations, the criteria for granting variable remuneration to leaders must, as of 1 January 2011, be included in the contractual or other provisions governing the relevant legal relationship. The variable remuneration can only be paid out if the milestones for the reference period have been met. If the aforementioned obligations are not complied with, the variable remuneration may not be taken into account for calculating the severance pay.

- The Company currently does not foresee in a specific pension plan neither for the CEO nor for the other members of the Executive Committee, except for the members on payroll such as Anne-Sophie Lebrun and Anthony Ting.

In accordance with Article 3:6 of the Belgian Code of Companies and Associations, this remuneration report includes the amount of the remuneration of, and any other benefits granted to, the Company's CEO, on a broken-down basis.

	Fixed Remuneration (€)			Variable Remuneration (€)		Extra-ordinary items (€)	Pension expense (€)	Total remu-neration (€)	Fixed	Variable
Name, Position	Base compensation	Administrator compensation	Other benefits	One-year variable	Multi-year variable					
Miguel Forte, CEO	300,000	/	19,900	112,500	/	/	/	432,400	74%	26%

Other benefits include transportation repayments and phone bills repayments.

The one-year variable is a bonus based on key performance indicators stated above. The maximum variable remuneration is set at [50% * base salary] for the CEO. For the year 2020, the CEO performance was set at 75%.

Following his resignation as CEO it was agreed that Thomas Lienard will continue to provide support to the company until 17 June 2020. For these services, a total amount of €134,610 has been paid of the period 1 January 2020 until 17 June 2020.

In accordance with Article 3:6 of the Belgian Code of Companies and Associations, this remuneration report also includes the amount of the remuneration of, and any other benefits granted to, the Company's other Members of the Executive Committee, on a broken-down basis.

The Executive Committee (excluding the CEO) in place during 2020 was as follows:

- Finsys Management SRL, represented by Jean-Luc Vandebroek, CFO;
- Venture Advanced Therapies Limited, represented by Stefanos Theoharis, CBO, from 26 March 2020;
- Benoit Moreaux SRL, represented by Benoit Moreaux, COO until 13 November 2020;
- Zam Consulting SRL, represented by Olivier Godeaux, CMO;
- Lebon Regulatory Science Strategy, represented by Linda Lebon, CRO, until 30 September 2020;
- Anne-Sophie Lebrun, COO, from 1 August 2020.

Currently, all members of the Executive Committee (excluding Anne-Sophie Lebrun and Anthony Ting) are engaged on the basis of a service agreement. The contracts with all members of the Executive Committee can be terminated at any time, subject to certain pre-agreed notice periods not exceeding 12 months, which may, at the discretion of the Company, be replaced by a corresponding compensatory payment.

Please find the amount of remuneration on a broken-down basis for the other Members of the Executive Committee:

	Fixed Remuneration (€)			Variable Remuneration (€)		Extra-ordinary items (€)	Pension expense (€)	Total remunera-tion (€)		
Name, Position	Base compensation	Administrator compensation	Other benefits	One-year variable	Multi-year variable				Fixed	Variable
Other Members of the Executive Committee	861,000	/	46,000	153,000	/	/	/	1,060,000	86%	14%

The one-year variable is a bonus based on key performance indicators stated above. The maximum variable remuneration is set between [20% and 30% * base salary] depending on the positions. For the year 2020, the average performance of the Executive Committee (excluding the CEO) was set at 89%.

The table below provides an overview of the main condition of the warrant plans as well as information related to the financial year 2020 regarding members of the Executive Committee:

	Main condition of the warrant plans					Information related to the financial year 2020		
Name Position	Plan ID	Grant date	Vesting Date	Retention period	Exercise period	A) Number of options vested; B) Value at exercise price (€)	A) Number of options exercised; B) Date of exercise	Number of options expired
Miguel Forte, CEO	Plan 2020	29-05-20	29-05-20	-	30/05/2023 - 29/05/2027	A) 51,724 B) 2.74	-	-
Miguel Forte, CEO	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 58,000 B) 2.55	-	-
Jean-Luc Vandebroek, CFO	Plan A	28-02-19	1/3 at 28-02-2020 2/3 at 28-02-2021 3/3 at 28-02-2022	-	28-02-2019 - 28/02/2029	A) 24,000 B) 4.11	-	-
Jean-Luc Vandebroek, CFO	Plan 2020	29-05-20	29-05-20	-	30/05/2023 - 29/05/2027	A) 12,000 B) 2.74	-	-
Jean-Luc Vandebroek, CFO	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 7,500 B) 2.55	-	-
Olivier Godeaux, CMO	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 5,000 B) 2.55	-	-
Stefanos Theoharis, CBO	Plan 2020	23-12-20	23-12-20	-	24/12/2023 - 23/12/2027	A) 5,000 B) 2.55	-	-

The table below provides an overview of significant positions of shares held directly or indirectly on 31 December 2020 by the other Members of the Executive Committee. The overview must be read together with the notes referred to below.

Executive Committee Member	Shares	
	Number	%*

Finsys Management SRL	2,880	0.02%

** calculated as the percentage of all outstanding shares and warrants (17,703,722 which is 16,478,168 shares and 1,225,554 warrants) at the date of the Document*

6 RELATED PARTY TRANSACTIONS

6.1 General

Each member of the Executive Committee and each Director needs to focus to arrange his or her personal business to avoid direct and indirect conflicts of interest with the Company. The Company's corporate governance charter contains specific procedures when potential conflicts could appear.

6.2 Conflicts of interest of Directors

There is a conflict of interest when the administrator has a direct or indirect financial interest adverse to that of the Company. In accordance with Article 7:96 of the Belgian Code of Companies and Associations, a director of a limited company which "*has, directly or indirectly, an interest of an economic nature in a decision or an operation under the Board of Directors*" is held to follow a particular procedure. If members of the Board, or of the Executive Committee or their permanent representatives are confronted with possible conflicting interests arising from a decision or transaction of the Company, they must inform the Chairman of the Board thereof as soon as possible. Conflicting interests include conflicting proprietary interests, functional or political interests or interests involving family members (up to the second degree).

If Article 7:96 of the Belgian Code of Companies and Associations is applicable, the Board member involved must abstain from participating in the deliberations and in the voting regarding the agenda items affected by such conflict of interest. Below is an overview of the meetings of the Board of Directors in which the conflict of interest procedure has been applied.

6.2.1 *Board of Directors of 11 February 2020*

Prior to discussing the items on the agenda, the Board acknowledged that, in accordance with Article 7:96 of the Belgian Code of Companies and Associations:

- mC4Tx SPRL, represented by Mr Miguel Forte and Finsys Management SPRL, represented by Mr Jean-Luc Vandebroek, directors of the Company, declares having a direct or indirect financial interest, conflicting with certain decisions that fall within the scope of the powers of the board of directors, in particular with respect to item 8 of the agenda as it concerns the discussions relating to the HR structure of the Company and the approval of the recommendations of the Nomination and Remuneration Committee (NRC) regarding the bonus plan for 2019 and the objectives for 2020.

These board members were present at the meeting but did not take part in any deliberation and resolutions where they had a conflict of interest.

The other directors of the Company present as aforementioned, each declared not to have any direct or indirect financial interest conflicting with the decisions to be taken.

Justification of the Decision to be Taken:

The Board believes that the discussions regarding the evaluation of the performance in 2019 and the determination of the objectives for 2020 are in line with the strategic orientation of the Company and are in the interest of the Company.

Financial Consequences for the Corporation:

The exact financial impact of the decision on the Company are summarized in the financial package of the directors.

Deliberations and Decisions:

Assessment of 2019 objectives and 2020 objectives:

The Nomination and Remuneration Committee ("NRC") presents the objectives 2020 for the CEO. The Board shall review and approve the finalised version once circulated by the CEO.

Regarding the 2019 objectives, and based on the recommendations of the NRC, the Board decides that:

- CFO achieved 75% of his objectives.
- CTMO achieved 80% of his objectives.
- CMO achieved 80% of his objectives.

Regarding the stock option plan, the Board decides to approve the preparation of a plan to be attributed to the CEO and the CFO in accordance with and under the proportions set out in the previous commitments of the Company in that regard.

6.2.2 *Board of Directors of 5 May 2020*

Prior to discussing the items on the agenda, the board of directors acknowledged that, in accordance with Article 7:96 of the Belgian Code of Companies and Associations:

- Finsys Management SRL, represented by Mr Jean-Luc Vandebroek, director of the Company, declares having a direct or indirect financial interest, conflicting with certain decisions that fall within the scope of the powers of the board of directors, in particular with respect to item 4 of the agenda as it concerns the approval of the grant of SOP to Finsys Management SRL, represented by Mr Jean-Luc Vandebroek and being the CFO of the Company, in the framework of the authorised capital on the basis of the authorisation of 0.6% approved in the 2019 General Assembly.
- mC4Tx SRL, represented by Mr Miguel Forte, director of the Company, declares that he might have a direct or indirect financial interest, conflicting with certain decisions that fall within the scope of the powers of the board of directors, in particular with respect to item 4 of the agenda as it concerns the approval of the grant of SOP to mC4Tx SRL, represented by Mr Miguel Forte and being the CEO of the Company, in the framework of the authorised capital on the basis of the authorisation of 0.6% approved in the 2019 General Assembly.

Justification of the Decision to be Taken:

The Board believes that the grant of SOP incentivises the CEO and CFO and is therefore in the interest of the Company.

In accordance with Article 7:96 of the Belgian Code of Companies and Associations, the auditor of the Company, Deloitte Réviseurs d'Entreprises SC SRL, represented by Julie Delforge, shall receive a copy of the Board minutes and the extract of these minutes relating to the conflict of interests will be added in the annual report of the directors in relation to the financial year ending 31 December 2020 of the Company.

These board members are present at the meeting, but do not take part in the deliberation or resolutions in respect of which they have a conflict of interest.

The other directors of the Company, present as aforementioned, each declare not to have any direct or indirect financial interest conflicting with the decisions to be taken.

Deliberations and Decisions:

The Board noted the terms and conditions of the SOP Plan 2020, a copy of which was circulated to the Board prior to the meeting, and APPROVED the SOP Plan 2020, subject to the finalisation thereof.

Upon recommendation of the Nomination and Remuneration Committee and as suggested on 18 December 2019, the Board RESOLVED to grant subscription rights ("SOP") subject to the terms and conditions of the SOP Plan 2020 to the following persons and in the following proportions:

Beneficiary	**Number of SOP to be granted**	**Date of offer**
mC4Tx SRL, represented by Mr Miguel Forte (CEO)	51,724	May 2020
Finsys Management SRL, represented by Mr Jean-Luc Vandebroek (CFO)	12,000	May 2020
TOTAL	**63,724**	

This grant of SOP shall be done in the framework of the authorised capital of the Company on the basis of the authorisation of 0.6% (+/- 65,000 SOP) approved in the 2019 General Assembly and shall be considered as fixed compensation.

Notwithstanding Article 5.6 of the SOP Plan 2020, the Board RESOLVED that the SOP granted to mC4Tx SRL and Finsys Management SRL may be transferred to the directors of these companies representing them in the execution of the services provided by these companies to Bone Therapeutics. Any other *inter vivos* transfer of SOP covered by Article 5.6 of the SOP Plan 2020, including the transfer from a natural person to another beneficiary remains excluded.

The decision of the Board to (i) grant the SOP to mCT4x SRL and Finsys Management SRL under the proportions and conditions set out above and (ii) allow the transfer of the SOP granted to mC4Tx SRL and Finsys Management SRL to the directors of these companies representing them in the execution of the services provided by these companies to the Company is subject to the effective issuance of the SOP.

The Board APPROVED the execution of the SOP Plan 2020, subject to the finalisation of the documentation, including:

- the SOP Plan 2020; and
- the Special Report prepared by the Board in accordance with Article 7:180 *juncto*, 7:191 of the Belgian Code of Companies and Associations;
- the draft Deloitte report.

Subject to the recommendation of the Nomination and Remuneration Committee, the Board granted power to Mr Miguel Forte and Mr Jean-Luc Vandebroek to finalise, amend and sign the documentation of the Board in the name and on behalf of the Board including the signature of the deed at the notary.

6.2.3 *Board of Directors of 29 October 2020*

The directors of the Company, present as aforementioned, each declared not to have any direct or indirect financial interests conflicting with the decisions to be taken. Except for Finsys Management represented by Jean-Luc Vandebroek.

Finsys Management SRL, represented by Mr Jean-Luc Vandebroek, director of the Company, declares having a direct or indirect financial interest, conflicting with certain decisions that fall within the scope of the powers of the board of directors, in particular with respect to item 3 of the agenda as it concerns the approval of the grant of SOP to Finsys Management SRL, represented by Mr Jean-Luc Vandebroek and being the CFO of the Company, in the framework of the authorised capital on the basis of the authorisation of 0.6% approved in the 2020 General Assembly.

Justification of the Decision to be Taken:

The Board believes that the grant of SOP incentivises the CFO and is therefore in the interest of the Company.

Deliberations and Decisions:

The Board discussed the proposal of the RemCo of 25 August 2020 for allocating warrants under the SOP plan as approved by the shareholders' meeting on 10 June 2020. It was proposed to issue and allocate 99,832 warrants as follows:

- Board: (23,332)
    - 2019-2020: 11,666 (Chairman 6,666 – Director: 1,000 – Chairman Remco/Audit: 500)
    - 2020-2021: 11,666 (Chairman 6,666 – Director: 1,000 – Chairman Remco/Audit: 500)
- Management + advisor: (76,500)
    - CEO: 58,000
    - CFO: 7,500
    - CMO: 5,000
    - CBO: 5,000
    - External advisor: 1,000

The Board decided unanimously to grant and allocate the warrants as recommended by RemCo, which is in line with the authorisation given by the shareholders' meeting on 10 June 2020.

The Board furthermore decided unanimously that the offer date of the warrants will be the 10th day after completion of the equity raise. The warrants will be issued in the framework of the authorised capital of the Company, as authorised by the shareholders' meeting in 2020. The board therefore decided to request mC4Tx SRL, represented by Mr Miguel Forte and Finsys Management SRL, represented by Mr Jean-Luc Vandebroek to finalise the draft board reports relating to the issuance of the warrants and the cancellation of the preferential subscription right and to take any other actions that are required or useful for the issuance and offer of the new warrants.

The Board furthermore decided to grant a special power of attorney to Mr Miguel Forte and Finsys Management SRL, represented by Mr Jean-Luc Vandebroek to sign all necessary reports, deeds, agreements and other documents (including the draft board reports and the notarial deed) to complete the allocation and issue of the warrants, and the effective offer thereof to the beneficiaries.

6.3 Existing conflicts of interest of members of the Board of Directors and of the Executive Committee and related party transactions

Currently, as far as the Company is aware, none of the other members of the Board of Directors have a conflict of interest within the meaning of Article 7:96 of the Belgian Code of Companies and Associations that has not been disclosed to the Board of Directors. Other than potential conflicts arising in respect of compensation-related matters, the Company does not foresee any other potential conflicts of interest in the near future.

6.4 Related Party Transactions

At the date of this Registration Document, the Company has the following affiliates:

6.4.1 *Transactions with Bone Therapeutics USA Inc.*

In course of 2020 and 2021, expenses related to all activities executed through Bone Therapeutics USA Inc. have been re-invoiced to the Company on 30 June 2021.

6.4.2 *Transactions with the Walloon Region*

As a result of the relationship of the government (i.e. Walloon Region) with some shareholders of the Group and the extent of financing received, the Group judges that the government is a related party. In total till date, an amount of € 35.81 million was granted by the Walloon Region in recoverable cash advances ("avances récupérables"), patent subsidies and other operational subsidies (2020: €35.54 million). Next to the government grants, government agencies granted loans to the Group for a total amount of € 3.97 million (€ 3.97 million in 2020).

6.4.3 *Transactions with the Executive Committee*

There are no transactions with the Executive Committee.

For information on the Executive Committee remuneration, see Section 5.7.2.2 "Remuneration of the CEO and the other Executive Directors and the Executive Committee".

6.5 Transactions with affiliates

Article 7:97 of the Belgian Code of Companies and Associations provides for a special procedure which must be followed for transactions with Bone Therapeutics' affiliated companies or subsidiaries. Such a procedure does not apply to decisions or transactions that are entered into the ordinary course of business at usual market conditions or for decisions and transactions whose value does not exceed one percent of the Companies' consolidated net assets.

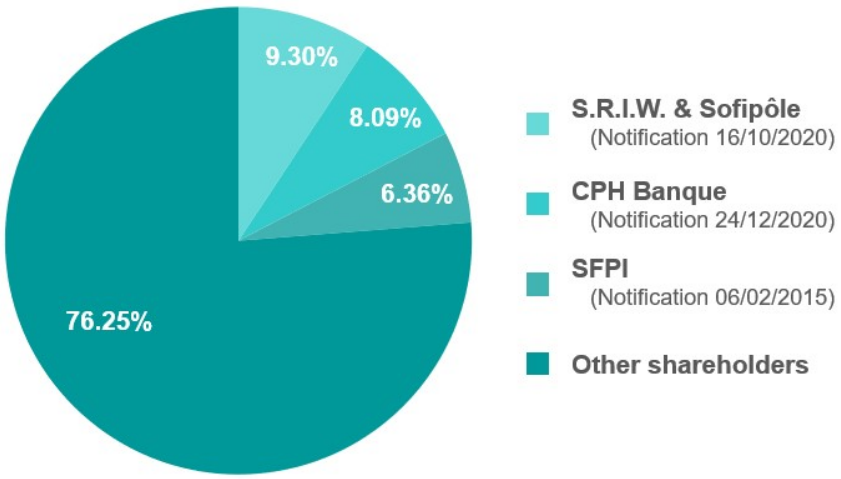
7 SHARES AND SHAREHOLDERS

7.1 Shareholders

At the date of this Document, there are 16,478,168 shares representing a total share capital of the Company of € 3,812,557.67. There are only ordinary shares, and there are no special rights attached to any of the ordinary shares, nor special shareholder rights for any of the shareholders of the Company.

The total of exercisable warrants is 225,554 warrants for the Executive committee members, consultants and Board members, 800,000 warrants for EIB and 200,000 warrants for Patronale Life, which give right to subscribe to an equal number of shares. This represents a total of 1,225,554 warrants.

The graph[35] below provides an overview of the shareholders that have notified the Company of their ownership of securities of the Company. This overview is based on the most recent transparency declaration submitted to the Company.



7.2 History of capital since IPO - Capital increase and issuance of shares

On 5 February 2015, the share capital was increased by a contribution in cash further to the completion of the initial public offering of the Company, in the amount of € 6,077,750 with issuance of 2,012,500 shares. The new shares were issued at a price of € 16 per share (of which 3.02 in share capital and 12.98 in issuance premium). The aggregate issuance premium amounted to € 26,122,250.00. Following the capital increase, the share capital of the Company amounted to € 16,544,052.63 and was represented by 5,470,740 shares.

On 5 February 2015, the share capital was increased by a contribution in cash further to the conversion of the convertible bonds, in the amount of € 3,252,657.78 with issuance of 1,077,039 shares. The new shares were issued at a price of € 9.61 per share (of which 3.02 in share capital and 6.59 issuance premium). The aggregate issuance premium amounted to € 7,097,342.22. Following the capital increase, the share capital of the Company amounted to € 19,796,710.41 and was represented by 6,547,779 shares.

[35] Denominator for S.R.I.W. & Sofipole = 12,069,287, denominator for CPH Banque = 16,478,168 and denominator for SFPI = 6,549,779.
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On 10 February 2015, the share capital was increased by contribution in cash further to the exercise of the over-allotment subscription right, in the amount of € 911,662.50 with issuance of 301,875 shares. The new shares were issued at a price of € 16 per share (of which 3.02 in share capital and 12.98 in issuance premium). The aggregate issuance premium amounted to € 3,918,337.50. Following the capital increase, the share capital of the Company amounted to € 20,708,372.90, represented by 6,849,654 shares.

On 30 October 2017, the share capital was decreased by an incorporation of losses of an amount of € 6,045,571.41 without any reduction of shares.

On 7 March 2018, a total amount of € 19.45 million in committed capital has been subscribed.

On 9 March 2018, as a result of the exercise of bond warrants and the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by € 1,210,754 with issuance of 565,773 shares. The aggregate share premium for this transaction amounts to € 4,791,588.

From April 2018 to June 2018, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by € 464,215 with issuance of 216,923 shares. The aggregate share premium for this transaction amounts to € 1,413,251.

On 9 July 2018, the share capital was decreased by an incorporation of losses of an amount of € 4,830,335.13 without any reduction of shares.

From July 2018 to December 2018, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by € 1,051,076 with issuance of 678,196 shares. The aggregate share premium for this transaction amounts to € 4,608,258.

From January 2019 to June 2019, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by € 968,552 with issuance of 641,425 shares. The aggregate share premium for this transaction amounts to € 1,313,907.

Via the Private Placement on 27 June 2019, the Company has raised EUR 5.0 million and placed 1,351,352 new shares with current and new institutional investors in Belgium. The share capital was increased by € 2,040,542. The aggregate share premium for this transaction amounts to € 2,959,458. Following the capital increase, the share capital of the Company amounted to € 15,540,605 and was represented by 10,303,323 shares.

From July 2019 till 12 December 2019, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by €479,218 with issuance of 317,363 shares and amounts to €16,019,823.16 and is represented by 10,620,686 shares. The aggregate share premium for this transaction amounts to €595,732.

On 12 December 2019, the Company decided to reduce its share capital by the incorporation of the losses. After the operation the share capital amounts to €5,427,597.19.

On 18 December 2019, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by €26,116.08 with issuance of 51,208 shares. The aggregate share premium for this transaction amounts to €136,378.31.

On 29 January 2020, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by €80,699.85 with issuance of 158,235 shares. The aggregate share premium for this transaction amounts to €451,774.60.

On 26 February 2020, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by €61,311.18 with issuance of 120,218 shares. The aggregate share premium for this transaction amounts to €393,671.85.

On 25 March 2020, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by €79,592.64 with issuance of 156,064 shares. The aggregate share premium for this transaction amounts to €320,397.19.

On 30 April 2020, as a result of the immediate conversion of the convertible bonds placed via a private placement announced on 29 April 2020, the share capital was increased by € 203,302.32 with issuance of 398,632 shares. The aggregate share premium for this transaction amounts to € 796,697.15.

On 7 May 2020, as a result of the conversion of the convertible bonds placed via a private placement on 7 March 2018, the share capital was increased by € 80,629.47 with issuance of 158,097 shares. The aggregate share premium for this transaction amounts to € 306,864.56.

On 21 August 2020, as a result of the conversion of the convertible bonds placed via a private placement announced on 29 April 2020, the share capital was increased by € 100,332.81 with issuance of 196,731 shares. The aggregate share premium for this transaction amounts to € 312,154.16.

On 8 October 2020, as a result of the conversion of the convertible bonds placed via a private placement announced on 29 April 2020, the share capital was increased by € 106,802.16 with issuance of 209,416 shares. The aggregate share premium for this transaction amounts to € 280,691.85.

Via the Private Placement on 15 December 2020, the Company has raised EUR 9.92 million and placed 4,408,881 new shares with current and new institutional investors in Belgium. The share capital was increased by €2,248,529. The aggregate share premium for this transaction amounts to €7,671,471. Following the capital increase, the share capital of the Company amounted to €8,414,913 and was represented by 16,478,168 shares.

On 26 February 2021, the Company decided to reduce its share capital by the incorporation of the losses. After the operation the share capital amounts to €3,812,557.67.

Date	Transaction	Number and class of shares issued	Issue price per share (€) including issuance premium	Capital increase/decrease (€)	Share capital after transaction (€)	Aggregate number of shares after capital increase
05/02/2015	Capital increase	2,012,500	16	6,077,750	16,544,052.63	5,470,740
05/02/2015	Capital increase	1,077,039	9.61	3,252,657.78	19,796,710.41	6,547,779
10/02/2015	Capital increase	301,875	16	911,662.50	20,708,372.90	6,849,654
30/10/2017	Incorporation of losses	None	Not applicable	-6,045,571.41	14,662,801.49	6,849,654
09/03/2018	Capital increase / conversion convertible bonds	565,773	10.61	1,210,754.22	15,873,555.71	7,415,427
04/2018 – 06/2018	Capital increase / conversion convertible bonds	216,923	8.66 (average issue price)	94,872.62	16,337,770.93	7,632,350
09/07/2018	Incorporation of losses	None	Not applicable	-4,830,335.13	11,507,435.80	7,632,350
07/2018 – 12/2018	Capital increase / conversion convertible bonds	678,196	8.30 (average issue price)	1,024,076	12,531,511.76	8,310,546
01/2019 – 06/2019	Capital increase / conversion convertible bonds	641,425	3.56 (average issue price)	968,552	13,500,063.51	8,951,971
01/07/2019	Capital increase	1,351,352	3.70	2,040,542	15,540,605.03	10,303,323
10/07/2019	Capital increase / conversion	49,522	3.79 (average issue price)	74,778	15,615,383.25	10,352,845

	convertible bonds					
21/08/2019	Capital increase / conversion convertible bonds	93,952	3.51 (average issue price)	141,868	15,757,250.77	10,446,797
11/09/2019	Capital increase / conversion convertible bonds	33,200	3.54 (average issue price)	50,132	15,807,382.77	10,479,997
14/11/2019	Capital increase / conversion convertible bonds	140,689	3.13 (average issue price)	212,440	16,019,823.16	10,620,686
12/12/2019	Incorporation of losses	None	Not applicable	-10,592,225.97	5,427,597.19	10,620,686
18/12/2019	Capital increase/conversion convertible bonds	51,208	3.17 (average issue price)	26,116	5,453,713,27	10,671,894
29/01/2020	Capital increase/conversion convertible bonds	158,235	3.37 (average issue price)	80,700	5,534,413.12	10,830,129
26/02/2020	Capital increase/conversion convertible bonds	120,218	3.78 (average issue price)	61,311	5,595,724.30	10,950,347
25/03/2020	Capital increase/conversion convertible bonds	156,064	2.79 (average issue price)	79,593	5,675,316.94	11,106,411
30/04/2020	Capital increase / conversion convertible bonds	398.632	2.51 (average issue price)	203,302.32	5,878,619.26	11.505.043
07/05/2020	Capital increase / conversion convertible bonds	158.097	2.45 (average issue price)	80,629.47	5.959.248.73	11.663.140
21/08/2020	Capital increase / conversion convertible bonds	196,731	2.10 (average issue price)	100,332.81	6,059,581.54	11,859,871
08/10/2020	Capital increase / conversion convertible bonds	209,416	1.85 (average issue price)	106,802.16	6,166,383.70	12,069,287
15/12/2020	Capital increase	4,408,881	2.25	2,248,529	8,414,913.01	16,478,168
26/02/2021	Incorporation of losses	None	Not applicable	-4,602,355.34	3,812,557.67	16,478,168

7.3 Warrant plans

7.3.1 *Warrant plans issued*

The Company currently has 3 subscription rights plans outstanding for its employees (Board members, Executive committee members and consultants):

On 24 February 2014, the extraordinary general shareholders' meeting of the Company created and approved a plan which consisted in the issue of 113,760 subscription rights for employees, consultants and Directors (plan A). At the date of the Document, 87,998 subscription rights have been granted and accepted. The Ordinary General Meeting of 10 June 2020 took note of the number of Plan A subscription rights still available for granting, i.e. 25,761 subscription rights and decided to cancel the said residual subscription rights.

On 28 May 2020, the Board of directors of the Company created and approved a plan which consisted in the issue of 69,978 subscription rights for employees, management members and Directors (plan 2020/05).

On 23 December 2020, the Board of directors of the Company created and approved a plan which consisted in the issue of 99,832 subscription rights for employees, management members and Directors (plan 2020/12).

On the date of this Document, the following subscription rights are outstanding in accordance with the above-mentioned plan:

Plan	Total
CEO	109,724
CFO	43,500
CBO	5,000
Consultant	5,000
Board members	29,330
Former CMO	5,000
Former CEO	28,000
Total	**225,554**

On 23 August 2021, the Extraordinary General Meeting of the Company issued warrants to the EIB and to Patronale Life.

Plan	Total
European Investment Bank	800,000
Patronale Life NV	200,000
Total	**1,000,000**

7.3.2 *Summary of the outstanding warrant plans*

The relevant terms and conditions of the Company's existing **warrant plan A** are set out below:

- **Vesting**: 1/3 on the first anniversary of the grant of the warrants, 1/3 on the second anniversary of the grant and 1/3 on the third anniversary of the grant, under the conditions that the beneficiary is working for the Company. Warrants will vest immediately in case of a change of control, an initial public offering or a public takeover bid.

- **Exercise period**: when vested, the warrants are exercisable at any time outside the closed period (as determined in Company's Dealing Code), but not later than 10 years following the creation of these warrants.

- **Exercise price**: the exercise price will be determined by the Board of Directors of the Company, in accordance with the rules applicable to listed companies.

    - at the closing price of the share of the day preceding the day of the offer; or

    - the 30-day average price of the share of the 30 calendar days preceding the date of the offer.

- **Term**: ten years. All warrants that have not been exercised within the ten-year period as of their creation become null and void.

The relevant terms and conditions of the Company's existing **warrant plan 2020 of May and December** are set out below:

- **Vesting:** The Warrants will become vested to the Grantee upon acceptance by the Grantee (without any further conditions), i.e. upon receipt by the Company of the duly completed acceptance form within the time limit.

- **Exercise period:** the Warrants shall not become exercisable before the first day of the fourth calendar year following the Offer and after the last day of the tenth year following the date of issuance (the "Exercise Period").

- **Exercise price**: the exercise price will be determined by the Board of Directors of the Company, in accordance with the rules applicable to listed companies.

    - at the closing price of the share of the day preceding the day of the offer; or

    - the 30-day average price of the share of the 30 calendar days preceding the date of the offer.

- **Term**: seven years. All warrants that have not been exercised within the seven-year period as of their creation become null and void.

The relevant terms and conditions of the Company's existing **warrant plan for the EIB Subscription Right** are set out below:

- **Subscription Price**: The subscription price is equal to €0.01 per EIB Subscription Right (and offset by an arrangement fee of the same amount paid by Bone Therapeutics to the EIB).

- **Maturity Date**: The EIB Subscription Rights have a defined life of five (5) years. However, Bone Therapeutics undertakes to issue identical subscription rights with a life of five (5) years after the Expiry Date.

- **Exercise price**: The exercise price of each EIB Subscription Right will be equal to the lower of (i) the average of the closing prices of the Company's shares during the thirty (30) days preceding the notarisation of the unconditional subscription of the EIB Subscription Rights and (ii) the closing price of the Bone Therapeutics share on the day preceding the notarisation of the unconditional subscription of the EIB Subscription Rights.

- **Exercise Period**: The EIB Subscription Rights may be exercised from the earlier of (i) the occurrence of a Voluntary or Mandatory Early Redemption Event and (ii) six months prior to the maturity of a Tranche, until maturity.

- **Other**: In cases where the Beneficiary has the right to transfer the EIB Subscription Rights, the Company, its agent or its shareholders (in that order), has a right of first refusal to redeem the EIB Subscription Rights on the same terms and conditions.

The relevant terms and conditions of the Company's existing **warrant plan for the Patronale Life Subscription Right** are set out below:

- **Subscription Price**: The subscription price is equal to €0.01 per Patronale Life Subscription Right.

- **Maturity Date**: The Patronale Life Subscription Rights have a defined life of five (5) years.

- **Exercise price**: The exercise price of each Patronale Life Subscription Right will be equal to the lower of (i) the average of the closing prices of the Company's shares during the thirty (30) days preceding the notarisation of the unconditional subscription of the Patronale Life Subscription Rights and (ii) the closing price of the Bone Therapeutics share on the day preceding the notarisation of the unconditional subscription of the Patronale Life Subscription Rights.

- **Exercise Period**: The Patronale Life Subscription Rights may be exercised from the earlier of (i) the occurrence of a Voluntary or Mandatory Early Redemption Event and (ii) six months prior to the maturity of a Tranche, until maturity.

- **Other**: In cases where the Beneficiary has the right to transfer the Patronale Life Subscription Rights, the Company, its agent or its shareholders (in that order), has a right of first refusal to redeem the Patronale Life Subscription Rights on the same terms and conditions.

8 SUMMARY OF INFORMATION DISCLOSED UNDER REGULATION (EU) NO 596/2014

The following information is a summary of the inside information that has been disclosed under the Market Abuse Regulation over the last 12 months and is relevant as at the date of the Document of the Company:

Clinical results:

On 14 October 2020, Bone Therapeutics' allogeneic cell therapy product, ALLOB, shows 90% fusion rate at 24 months in Phase IIa study in lumbar spinal fusion.

On 20 October 2020, Bone Therapeutics reached 50% treated patients in ongoing JTA-004 Phase III pivotal knee osteoarthritis study.

On 22 December 2020, Bone Therapeutics completed recruitment and patient treatment in JTA-004 pivotal Phase III knee osteoarthritis study.

On 12 January 2021, Bone Therapeutics announced that the Company treated first patient in ALLOB Phase IIb tibial fracture study.

On 19 July 2021, Bone Therapeutics provided updates on the progress of clinical studies.

On 30 August 2021, Bone Therapeutics announces topline results from Phase III knee osteoarthritis study with its enhanced viscosupplement JTA-004.

Cash position:

On 30 October 2020, Bone Therapeutics provided Third Quarter 2020 Business Update.

On 16 December 2020, Bone Therapeutics announced closing of the private placement.

On 20 January 2021, Bone Therapeutics provided fourth quarter 2020 business update and 2021 outlook.

On 29 April 2021, Bone Therapeutics announced 2020 full year results.

On 26 May 2021, Bone therapeutics provided First Quarter 2021 Business Update.

On 1 July 2021, Bone Therapeutics announced that the Company secured up to €16M loan financing from the EIB to accelerate clinical and commercial development of innovative orthopedic treatments.

On 27 July 2021, Bone Therapeutics announced that the Company agreed final settlement with the FSMA regarding clinical studies communication issues in 2016 and 2017.

On 27 August 2021, Bone Therapeutics strengthens its financial structure with the implementation of its financing agreement with the European Investment Bank.

On 8 September 2021, Bone Therapeutics reports half year 2021 results.

Corporate:

On 5 October 2020, Bone Therapeutics, Link Health and Pregene to develop and commercialize the ALLON allogeneic bone cell therapy platform in China and Southeast Asia.

On 29 October 2020, Bone Therapeutics and Catalent signed agreements to streamline production of the allogeneic cell therapy product, ALLOB.

On 16 November 2020, Bone Therapeutics announced completion of the acquisition of its cell therapy manufacturing subsidiary SCTS by Catalent.

On 14 January 2021, Bone Therapeutics and Rigenerand signed partnership for cell therapy process development.

On 27 July 2021, Bone Therapeutics agrees final settlement with the FSMA regrading clinical studies communication issues in 2016 and 2017.

On 21 September 2021, Bone Therapeutics appoints Lieve Creten as interim Chief Financial Officer.

9 APPENDIX A – ABBREVIATIONS AND DEFINITIONS

Abbreviations

ATMP	Advanced Therapy Medicinal Product
BLA	Biologics Licence Application
β-TCP	β-tricalcium phosphate
BMP	Bone Morphogenetic Protein
CCRO	Chief Clinical and Regulatory Officer
CDMO	Contract Development and Manufacturing Organizations
CEO	Chief Executive Officer
CFO	Chief Financial Officer
CHU	*Centre Hospitalier Universitaire*
CMO	Chief Medical Officer
CTA	Clinical trial application
DBM	Demineralized Bone Matrix
DU	Delayed Union (fracture)
EFDR/FEDER	European Regional Development Fund (*Fonds Européen de Développement Régional*)
EMA	European Medicines Agency
EU	European Union
FAMHP	(Belgian) Federal Agency for Medicines and Health
FDA	Food and Drug Administration (in the US)
FSMA	Financial Services and Markets Authority in Belgium (*Autorité des services et marchés financiers*)
GAAP	(Belgian) Generally Accepted Accounting Principles
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
GIE	*Groupement d'Intérêt Economique* (Economic Interest Grouping)
HA	Hyaluronic acid
hAEC	human Amniotic Epithelial Cell
IA	Intra-articular
IFRS	International Financial Reporting Standards
IND	Investigational New Drug application (in the US)
IRD	Inflammatory Rheumatic Disease
KOA	Knee Osteoarthrisis
MMA	Marketing authorization application
MSC	Mesenchymal Stem Cells
MW	Molecular weight
NSAIDs	Non-steroidal anti-inflammatory drugs
NU	Non-Union (fracture)

OA	Osteoarthrisis
ODD	Orphan Drug Designation
ON	Osteonecrosis
PDGF	Platelet-Derived Growth Factor
PTH	ParaThyroid Hormone
PWTC	*Plateforme Wallonne de la Thérapie Cellulaire* (Walloon Platform for cell therapy)
RCA(s)	Recoverable Cash Advance(s)
RA	Rheumatoid Arthritis
rh	recombinant human
SCTS	Skeletal Cell Therapy Support SA
SISE	*Société d'Infrastructures, de Services et d'Energies SA*
SME	Small and Medium Enterprise
SF	Spinal Fusion
THA	Total Hip Arthroplasty
ULB	*Université libre de Bruxelles*
ULg	*Université de Liège*

Definitions

Advanced therapy medicinal product	Medicine for human use that are based on gene therapy, somatic cell therapy or tissue engineering (EMA classification 1394/2007).
Allogeneic	Said for tissues or cells when the donor is different from the recipient (i.e., the patient)
Audit Committee	The audit committee installed by the Board of Directors.
Autologous	Said for tissues or cells when the donor is the same as the recipient (i.e., the patient).
Belgian Code of Companies and Associations	*Code des sociétés et des associations* enacted by the Belgian Law of 23 March 2019 regarding the implementation of the Belgian code of companies and associations, as applicable to the Company as of 24 June 2019 following the publication in the Belgian Official Gazette (*Moniteur belge*) of the approval by the extraordinary shareholders' meeting dd. 12 June 2019 to opt-in under the Belgian Code on Companies and Associations.
Biovigilance (MCH)	The process of monitoring, reporting and preventing all risks associated with the therapeutic use of products derived from human biological materials, in accordance with the Belgium law (as issued on 12 December 2003 and as amended on 17 July 2017).
Board of Directors	The board of directors of the Company.
Chairman	The chairman of the Board of Directors
CHU	Centre Hospitalier Universitaire de Liège
Competent Authority (Regulatory Agency)	National organization that regulates medicinal products for human use in accordance with the European directives and national law.

	Clinical trials of medicinal products in human subjects require authorisation by the competent authority.
Corporate Governance Code (or CGC)	The new Belgian Corporate Governance Code 2020 introduced by the Royal Decree of 12 May 2019 designating the corporate governance code to be complied with by listed companies published on 17 May 2019 in the Belgian Official Gazette (*Moniteur belge*). The third Belgian Code on Corporate Governance, which replaces the versions previously published in 2004 and 2009.
Company	Bone Therapeutics SA.
Corporate Governance Charter	The corporate governance charter of the Company.
Delayed-union fracture	A medical condition defined as a fracture that has not united within a period of time that would be considered adequate for bone healing.
Directive 2004/23/EC	European Law on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.
Director	A member of the Board of Directors
Ethics Committee	Established committee that ensures that research conducted within a hospital complies with moral and ethical principles. Clinical trials of medicinal products in human subjects require positive opinion by the ethic committee.
Euronext Brussels	The regulated market operated by Euronext Brussels SA/NV.
Euronext Paris	The regulated market operated by Euronext Paris SA.
Ex vivo	Taking place outside the organism.
Executive Committee	The team consisting of the CEO, CFO, CCRO, CMO and Director of Clinical Operations.
Executive Directors	Directors entrusted with the day-to-day management of the Company.
GMP (Good manufacturing practise)	Tart of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use.
Group	The Company and SCTS.
Homeostasis	Self-regulating process by which biological systems tend to maintain internal stability.
Hospital Exemption	Allows hospitals and medical practitioners to provide ATMP-classified products to patients, e.g., in case of high unmet medical need because there is no authorized ATMP alternative available. Said products are custom-made for an individual patient, prepared on a non-routine basis, and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner.
Inflammatory Rheumatic Diseases	Autoimmune diseases characterized by inflammation and loss of function of muscles, joints, bones and other tissues producing symptoms such as pain, swelling and stiffness (e.g., osteoarthritis, rheumatoid arthritis, ankylosing spondylitis…)
JTA Technology	Enhanced hyaluronan-based bone void fillers, and viscosupplements for osteoarthritis (including JTA-004 and JTA NEXT)

Mesenchymal stem cells	Multipotent stem cells that can convert into cell types such as bone cells, cartilage cells, fat cells, etc.
MXB	A combined cell-matrix product of Bone Therapeutics for large bone defects and maxillofacial applications.
New Shares	The new shares initially offered in the Offering, including the new shares offered as a result of the possible exercise of the Increase Option.
Nomination and Remuneration Committee	The nomination and remuneration committee of the Company installed by the Board of Directors.
Non-Executive Directors	Directors who are not entrusted with the daily management of the Company.
Non-union fracture	A medical condition characterised by a failure to achieve bone union within 6-9 months as, all reparative processes have ceased, hence requiring additional surgical intervention.
Orphan Drug Designation	A special status to a drug developed for the treatment of a rare disease or medical condition. This enables the product to gain exclusivity when reaching market and creates additional value (e.g., easier marketing approval, extended exclusivity periods, fee reduction etc.) This status was received for PREOB and ALLOB in osteonecrosis of the femoral head by the EMA and the FDA.
Offering	A public offering in Belgium and France to Retail Investor and a private placement to certain Institutional Investors in certain jurisdictions outside the United States in accordance with Regulation S under the Securities Act.
Osteoarthritis	A degenerative joint disease.
Osteoblast	Bone-forming cell.
Osteocyte	A terminal bone forming cell embedded in mineralized bone matrix.
Osteogenesis	The capacity to produce new bone
Osteonecrosis (of the hip)	A medical condition characterized by the death of bone cells and loss of the associated marrow elements. It is a painful condition in which the joint degenerates progressively, ultimately leading to collapse of the femoral head.
Osteosynthesis	A surgical procedure performed to stabilize a fracture by mechanical devices such as metal plates, pins, rods, wires or screws.
Orthobiologics	Substances (e.g., growth factors) naturally found in human body, which are used as a drug (in higher concentrations) to improve bone healing.
Patent Subsidies	The subsidies granted by the Region and, to a lesser extent, the European Commission, to partially finance the Company's patents applications.
Phase I/IIa	A first-in-man proof-of-concept pilot study in which the product will be administered to humans for the first time and in which efficacy parameters will be assessed.
Phase IIa	A proof-of-concept pilot study in which the product has already been administered to human – in general in another indication - and in which efficacy parameters will be assessed.
Phase IIb	A proof-of-concept pilot study in which the product has already been administered to human – in general in another indication - and in which efficacy parameters will be assessed.

Phase III	A pivotal study in which the product has already been shown to be safe and efficacious in the indication, and in which the safety and efficacy will be further confirmed in a larger group of patients.
Phase IV	Studies done after the product has been marketed to gather information on the drug's effect in various populations and any side effects associated with long-term use.
Pharmacovigilance	The process of collecting, monitoring and evaluating adverse events in clinical trials for safety purpose.
Region	The Walloon Region
Registration Document	This registration document, as well as any supplement thereto.
Regulation S	Regulation S under the Securities Act.
Regulatory regulations	Applicable regulatory laws and regulations.
Research Grants and Research Subsidies	The grants and subsidies granted by the Region, and to a lesser extent the European Commission, to partially finance the Company's research and development programmes.
Rheumatoid arthritis	A chronic systemic inflammatory disease affecting the joints.
Scaffold	Scaffolds in orthopaedics are surgical implants that replace and/or strengthen injured musculoskeletal tissues. Besides providing structural integrity, scaffolds form a substrate for cells to growth. Scaffolds are composed of natural material derived from autograft, allograft, xenografts or plants, synthesized from synthetic polymers, ceramics or metals, or are a composite of the aforementioned materials.
Scoliosis	A medical condition that causes abnormal curvature of the spine.
Securities Act	The United States Securities Act of 1933, as amended.
Significant shareholder	A shareholder holding at least 5% of the share capital.
Skeletal Cell Therapy Support SA	A limited liability company incorporated under the laws of Belgium with registered office at avenue Georges Lemaitre 62, 6041 Gosselies and registered with the register of legal entities under number 0841.570.812.
SME Agreement	The agreement dated 24 April 2014 between the Walloon Region and Groupement d'Intérêt Economique BOCEGO (consisting of the Company and SCTS) (BOCEGO).
Société d'Infrastructures, de Services et d'Energies SA	A limited liability company incorporated under the laws of Belgium with registered office at avenue Georges Lemaitre 62, 6041 Gosselies and registered with the register of legal entities under number 0841.727.101.
Spinal fusion	A surgical procedure that consists of bridging two or more vertebrae to obtain fusion of an unstable portion of the spine or to immobilize a painful vertebral motion segment.
Spondylolisthesis	A condition in which one or more vertebrae slips out of place onto the vertebra above and below it/them
Stenosis	A narrowing of a channel or a vessel… In this document, spinal stenosis is the narrowing of spaces in the spine (backbone) which causes pressure on the spinal cord and nerves.
Third party payer	An institution or company that provides reimbursement to health care providers for services rendered to a third party (i.e., the patient).

Tissue Bank	An entity that is licensed, accredited or regulated under federal or state law to engage in the recovery, screening, testing, processing, storage or distribution of human biological materials. The Company has obtained a license as a tissue bank for handling autologous human biological materials and a license as a tissue bank for handling in collaboration with hospital tissue banks allogeneic human biological materials.
ULB-028 Licence	The licence agreement pursuant to which the Company (and its affiliates) has been granted an exclusive and worldwide licence in the field of skeletal and dental applications over the technology claimed by the ULB-028 patent family.
Viscosupplementation	A treatment using intra-articular injection of hyaluronan-based preparations which absorb shocks and provide lubrication in order to decrease pain and improve mobility.
Warrants	Warrants issued by the Company.