REGISTRATION DOCUMENT

The date of this Registration Document is 26 March 2024.

This Registration Document is valid for a period of twelve months from its date of approval (until 25 March 2025), provided that it is completed by any supplement required pursuant to article 23 of the Prospectus Regulation 2017/1129. 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significant new factors, material mistakes or material inaccuracies does not apply when this Registration Document is no longer valid.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.

In the context of a concrete transaction requiring a prospectus, this Registration Document should be read in conjunction together with the relevant securities note (the "**Securities Note**") and summary (the "**Summary**"). The Securities Note and the Summary, together with this Registration Document, are available on BioSenic's website (https://biosenic.com/investors).

The Board of Directors of BioSenic SA assumes responsibility for the content of the 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 makes no omission likely to affect its import.

On behalf of the Board of Directors

Prof. François Rieger
President of the Board

Véronique Pomi-Schneiter
Director

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1 RISK FACTORS

The risks and uncertainties that BioSenic believes to be material are described below. The occurrence of one or more of these risks may have a material adverse effect on BioSenic's cash flows, results of operations, financial condition and/or prospects and may even endanger BioSenic's ability to continue as a going concern. Moreover, BioSenic'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 BioSenic. Additional risks, including those currently unknown or deemed immaterial, may also impair BioSenic's business operations.

The risk factors are presented in eight categories, depending on their nature. In each category, the risk factors which in the assessment of BioSenic are the most material, considering the negative impact on BioSenic (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.

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

a. *BioSenic and its subsidiary Medsenic are clinical-stage biotechnology companies and have not yet commercialised any of their products. They have therefore incurred net losses since their inception and expect to continue to incur net losses in the foreseeable future. As a result, BioSenic Group might never achieve sustained profitability.*

BioSenic is a biotechnology company exploiting the possibilities offered by the therapeutic use of arsenic salts for patients with autoimmune diseases. Currently, BioSenic Group is concentrating specifically on the development of its most advanced clinical assets, targeting markets with large unmet medical needs and limited innovation. BioSenic Group is currently involved in setting up a Phase III study for the treatment of Chronic Graft versus Host Disease (cGvHD) with a patented oral formulation of arsenic trioxide, ArsciCor, while preparing two Phase IIb studies for the treatment of moderate to severe Systemic Lupus erythematosus (SLE) and Systemic Sclerosis (SSc). As BioSenic Group is still developing its product candidates in clinical settings and has not completed the full development of any product, it does not anticipate generating revenue from sales for the foreseeable future and has incurred significant losses since the incorporation of BioSenic and Medsenic. The consolidated statement of financial position for the financial year ended 31 December 2022 of the BioSenic Group shows negative retained earnings of € 5.72 million. Under IFRS, BioSenic's negative retained earnings on 30 June 2023 were € 26.65 million. 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, BioSenic Group intends to continue its efforts to conduct preclinical testing, product development, clinical trials and regulatory compliance activities and improve product formulations and clinical delivery techniques. These activities together with anticipated general and administrative expenses will result in incurring further significant losses for several years. For next several years, BioSenic Group anticipates that its expenses and accumulated consolidated losses will increase substantially mainly due to:

1) Conducting the Phase III clinical trial with arsenic trioxide in the first-line treatment of cGvHD; and

2) Preparing and partnering/conducting the Phase IIb clinical trials for SLE and SSc.

3) Expanding its pre-clinical and clinical pipeline with new indications through new technologies (definition of the molecular targets of the arsenic active ingredient (API), combination of matter formulations, nanoparticles for delivery, development of exosomes from bone marrow mesenchymal cells (ALLOB cells), in the context of new autoimmune/inflammatory pathologies or organ repair clinical opportunities).

The size of BioSenic Group's future net losses will depend, in part, on the rate of future growth of its expenses and its ability to generate revenue, mainly through out-licencing. Given that the patient recruitment for the Phase III clinical trial with arsenic trioxide in the first-line treatment of cGvHD, the Group's most advanced

clinical asset, still has to start, BioSenic Group expects that it will take at least five years before market authorisation could potentially be obtained for this asset and commercialisation could start. BioSenic Group may encounter unforeseen expenses, difficulties, complications, delays and other presently unknown factors that may have a material adverse effect on its business and financial situation. BioSenic Group does not have a commercial organisation in place to launch its product candidates on its own. BioSenic Group does currently not intend to develop itself a sales and distribution organisation anywhere in the world and will rely for the distribution of its products on license and supply deals with commercial partners. Such arrangements may require BioSenic Group to incur additional expenses, increase its capital expenditures, issue securities that dilute its shareholders or disrupt its management and business. Furthermore, BioSenic Group cannot assure that it will generate positive clinical data, find licensees, receive regulatory approval, get into commercialization and earn revenues or achieve profitability, which could impair its ability to sustain operations, obtain any required additional funding or continue as a going concern. Even if BioSenic Group achieves profitability in the future, it may not be able to sustain profitability in subsequent periods.

b. *As BioSenic Group does not have 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 31 December 2023, BioSenic's Group cash position amounted to € 150,000. The BioSenic Group does currently not have sufficient working capital to meet its present requirements and cover the working capital needs for a period of at least 12 months as of the date of this Prospectus. For more information about current cash situation of BioSenic and Medsenic, please see Section 3 of this Registration Document and the Securities Note. BioSenic Group will require additional funding in the future to sufficiently finance its core operations and to take advantage of new business opportunities.

The BioSenic Group's future financing needs will depend on many factors, including the progress, costs and timing of its research and development activities, the sustained performance (recruiting patients and generating positive results) of its 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, license agreements and other partnerships. The existing capital resources of BioSenic Group are not sufficient to fund the completion of its planned Phase III clinical trial with arsenic trioxide in the first-line treatment of cGvHD or any of its other envisaged clinical trials. Accordingly, BioSenic will need to raise significant additional funds. Currently, BioSenic Group mainly relies on equity and bond financing and intends to pursue additional funding opportunities in the future, including potentially the issuance of convertible bonds.

Please refer to Section 4.13 of this Registration Document for more information about BioSenic Group's non-dilutive financing and grants. It should in this respect be noted that changes in regional financing and grant policies, a shift in regional investment priorities or challenges by the European instances may reduce or jeopardise the Group's ability to obtain or retain non-dilutive financing, grants and/or other benefits. In addition, future growth of the BioSenic Group, whether or not including geographical expansion, could limit the Group's eligibility to obtain similar non-dilutive financing or grants.

Furthermore, BioSenic Group'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, additional funds may not be available to it, when necessary, on commercially acceptable terms, if at all. If the necessary funds are not available, BioSenic Group 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 licenses on its technologies to partners or third parties or enter into new collaboration agreements, the terms could be less favourable to BioSenic Group 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 BioSenic Group 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. For more information on BioSenic Group's working capital, please see the Securities Note.

The BioSenic Group has a considerable position of outstanding debts that needs to be paid back or refinanced. As of 30 November 2023, total financial liabilities amounted to € 29.20 million of which € 5.50 million (relating to the (non-convertible) bonds (€ 3.5 million) issued in June 2019 and the (remaining convertible) bonds (€ 2 million) issued in May 2020) had to be repaid in June 2023 (see Section 4.12 (*Financing Agreements*) for more information in this respect). In September 2023, BioSenic reached an agreement with the relevant holders of the aforementioned bonds, Patronale and Monument, to replace the bonds as well as a €2 million outstanding loan by convertible bonds to be issued. The new convertible bonds would be unsecured and have a maturity date of 31 December 2030, which can be further extended by BioSenic for up to 24 months depending on its cash balance. The outstanding loan from the European Investment Bank ("EIB") for a principal outstanding amount of € 8 million would also be extended to 2030, with the same 24-month extension possibility as for the new convertible bonds. Completion of the refinancing of the loans granted by Patronale, Monument and the EIB is subject to BioSenic raising sufficient new equity so that it can continue its operations including the Phase 3 clinical trial of its lead Oral ATO therapeutic candidate targeting cGvHD. Parties envisaged completing the refinancing in 2023, but until the date of this Registration document it was not possible to do so because BioSenic was unable to raise sufficient new equity. If BioSenic does not manage to raise sufficient new equity in the short term, the risk exists that Patronale, Monument or EIB would terminate the refinancing agreement with BioSenic and would claim the immediate repayment of all outstanding principal amounts and accrued interests, which would likely lead to the liquidation or bankruptcy of the Company and which would have a material adverse impact on the BioSenic Group, and its shareholders leading to the potential total loss of their entire investment.

In addition to the above-mentioned financial liabilities to Patronale, Monument and EIB, BioSenic is also preparing the restructuring of other financial liabilities linked to the historical clinical development of ALLOB and JTA. It is uncertain whether the relevant creditors or, as the case may be, the court would approve any restructuring proposal for such financial liabilities, which could have a material adverse impact on the BioSenic Group, and its shareholders leading to the potential total loss of their entire investment.

The volatility on the financial markets caused by the increased global geopolitical tension may hinder raising necessary funding on the financial markets. As the BioSenic Group does currently not have sufficient working capital to meet its present requirements and cover the working capital needs for a period of at least 12 months, it depends on the financial markets to organise its future funding operations (in the form of placements of shares or (convertible) bonds). Volatile financial markets might make such funding operations more difficult or impossible, or might force BioSenic Group to complete the operations on less advantageous terms (for instance triggering additional dilution for the shareholders).

1.2 Risk factors related to BioSenic Group's business activities and industry

a. *BioSenic Group'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. BioSenic Group competes with other companies based on technology, product offering, therapeutic area, intellectual property, geographic area and time to market or other factors. The success of BioSenic Group 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 BioSenic Group, please see Sections 4.6 and 4.7 of this Registration Document.

Through its subsidiary Medsenic, BioSenic Group believes that it benefits from its expertise and international recognition in the application of the beneficial effects of arsenic trioxide in the field of innate immunity and auto-immune diseases, which was built on the basis of original results and patents granted to the *Centre National de la Recherche Scientifique* (CNRS) in France. Medsenic has been granted all worldwide rights from the French FIST / CNRS Innovation to develop the use of arsenic trioxide for all autoimmune diseases and

cGvHD, in Europe and Canada and is limited to Lupus and cGvHD in the USA. The patents from CNRS cover the use of arsenic trioxide, whichever the formulations, but they end April 2023 in Europe and Canada and in 2029 in the US. However, BioSenic Group does not believe that this will have a material impact as the Group is developing its pipeline of indications in such a way that they are covered by new formulation patents, as is provided by the exclusive licence for oral ATO obtained from Phebra in 2021 (on the basis of patents that are valid up until 2036).

However, the competitors of BioSenic Group may have greater financial, human and other resources than BioSenic Group does.

Medical markets for treatments are in general highly competitive and the fields in which BioSenic Group operates are characterised by a sharp increase in innovation. If competitors of BioSenic Group are currently developing, or would in the future, develop technologies and products that are equally or more effective, safe and/or economical as the current or future offering of BioSenic Group, this may have a negative impact on the success of the Group in the fields in which it operates.

1.3 Risk factors related to clinical development

a. ***Biosenic Group's research programmes and product candidates must undergo rigorous pre-clinical tests and regulatory reviews before, during and after each phase of the 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. As most autoimmune diseases are rare diseases, a smaller patient population is available which needs to be recruited over multiple clinical sites. Moreover, many factors other than patient population size affect patient enrolment and could lead to a slower than expected patient recruitment rate. If BioSenic Group experiences significant delays or is unable to obtain marketing authorisation, this would prevent the product candidates from reaching the market and could have adverse effects on BioSenic Group's activities, costs and valuation, as well as on the shareholders' investment.***

The research programmes and product candidates of BioSenic Group must undergo rigorous pre-clinical and clinical trials, of which the start, the timing of completion, the number and the results are uncertain. The conditions or results of such trials could delay or prevent the product candidates from reaching the market. The clinical trials with arsenic trioxide to treat cGvHD, severe Systemic Lupus erythematosus (SLE) or Systemic Sclerosis (SSc) 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 BioSenic Group of appropriate clinical trial insurances. In particular, the clinical trials related to chronic diseases such as autoimmune pathologies require long follow-up periods of up to 12 if not 24 months. Delays in clinical trials due to the above-mentioned reasons may be expected, but if it becomes significant, this would be likely to have a material adverse impact on BioSenic's activities, costs, and ultimately on its valuation, which would adversely impact shareholders, and eventually could threaten BioSenic's ability to raise future funding and continue as a going concern, which could lead to its liquidation or bankruptcy and which could result in shareholders losing the total value of their investment.

Although some of the products that the BioSenic Group is developing are for conditions with rather 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, other competing clinical trials on the same pathology, 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 BioSenic Group is investigating and whether the clinical trial design involves

comparison to placebo or standard of care. Most of the autoimmune diseases that BioSenic Group is targeting for its treatment with ATO are rare diseases that affect a smaller patient population. This makes patient recruitment for clinical trials more challenging and competitive and requires more participating clinical centres, which may not be willing to participate if they are not convinced by the preclinical studies, animal models or early clinical proof of concept.

If BioSenic Group 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 BioSenic Group's business, prospects, financial condition and results of operations.

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

BioSenic Group's small molecule products based on the arsenic trioxide active ingredient benefit from a favourable status in terms of established safety of use in humans, since they are of a privileged class of repositioned molecules that are already used in a different field of pathologies (cancer). Although the possible long-term adverse effects of arsenic trioxide, and the way to protect patients from such adverse effects, are reasonably well documented, unexpected new safety issues might still arise and the successful outcome of the Group's ongoing and planned clinical trials with arsenic trioxide cannot be guaranteed.

c. ***Unanticipated safety issues or side effects with BioSenic Group's product candidates due to the reaction of arsenic trioxide with biological materials cannot be fully excluded and if such issues would arise these might have a material impact on the success of the clinical trial or on the development of the relevant clinical asset or BioSenic Group. Serious adverse, undesirable or unacceptable side effects may delay or prevent marketing approval. The risk also exists that the side effects appear after the commercialisation and would require to take a product off the market or limit its sales.***

Arsenic salts - and specifically arsenic trioxide, have benefited from reports over centuries of its beneficial effects in a number of conditions, among which its use as an active antimicrobial (such as in syphilis) before the advent of antibiotics. More recently, the discovery in the late decade of 1990 of its successful use to decisively treat a deadly cancer - acute promyelocytic leukaemia - has generated a wealth of scientific and medical observations on the conditions of its safe use and safety data all applicable to the pathologies of the immune system, for which Medsenic possesses both applications and formulations patents. These available data have the benefit of allowing Medsenic to enter into clinical trials at the level of Phase II for all autoimmune and inflammatory indications it wishes to further develop using the IV or oral formulations of arsenic trioxide, since all preclinical and safety data publicly are available from the initial studies in human cancer patients, gathered over two decades, in all main hospital settings dealing with leukemic patients. Main regulatory bodies such as the FDA and EMA have now recognised the favourable safety profile of arsenic trioxide for the treatment of acute promyelocytic leukaemia, with good pharmacovigilance since its market authorizations in the year 2002, rendering it much easier to satisfy regulatory requirements dealing with new formulations including the basic API, arsenic trioxide. However, any formulation of arsenic trioxide involving a combination of matter will in principle require a Phase I clinical trial to establish the safety and bioavalability and bioequivalence. Notwithstanding the documented positive safety profile of arsenic trioxide, unanticipated safety issues or side effects due to the reaction of arsenic trioxide with biological materials cannot be fully excluded and if such issues would arise these might have a material impact on the success of the clinical trial or on the development of the relevant clinical asset or BioSenic Group in general as it future success largely depends on the successful outcome of its ongoing and planned clinical trials with arsenic trioxide.

If any new or additional serious adverse side effects are identified for any product candidate, BioSenic Group 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 BioSenic Group'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 BioSenic Group'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 Group'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 BioSenic Group or any potential future partner from achieving or maintaining market access and market acceptance of the affected product or could justify further studies for adequate conditioning or formulations of the products, which would substantially increase development and commercialisation costs and expenses, which would have an adverse effect on BioSenic Group's business, prospects, financial condition and results of operations.

d. ***Failure to successfully identify, develop and commercialise competitive additional products or product candidates could impair BioSenic Group's ability to grow in the immediate and longer term.***

The main focus of BioSenic Group is to continue its clinical trials and ultimately to obtain approval of its product candidates for the treatment of autoimmune diseases such as cGvHD, SLE and SLE, subject in each case to BioSenic being able to raise sufficient additional funding for the necessary clinical trials. For more information about BioSenic Group's current clinical pipeline, please see Section 4.5 of this Registration Document.

BioSenic Group also runs preclinical research programmes and aims at developing new product candidates, although such efforts are currently being reduced given the focus on the ongoing and envisaged clinical trials with existing product candidates. BioSenic Group intends to leverage its preclinical research, clinical expertise and new formulations for the set-up of manufacturing processes, to expand its pipeline to indications for which it believes its products have therapeutic potential. The accumulated preclinical data are 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 and duly protected by international patent submissions. The BioSenic Group intends to devote a specific effort to expand its line of products in two directions: new formulations for new ways to administer the arsenic salts; and a combination of MSCs/exosomes produced from MSCs with arsenic, through cell/nanoparticle efficient loading. The success of BioSenic Group's strategy depends partly on its 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 BioSenic's products among third party payers, doctors, patients and the medical community in general would affect BioSenic's ability to generate revenues from such products or become profitable.***

To date, BioSenic Group has no product authorised for commercialisation, and has not undertaken any steps for registration and/or authorisation for Market Access (MA). BioSenic Group's current product candidates are in different phases of preclinical and particularly clinical trials and it may never have a product that is commercially successful. Even the product candidates in Phase III clinical programmes may require further clinical trials, accompanied by regulatory reviews, specific marketing authorisations, very significant marketing efforts and substantial investments before they may provide revenue to BioSenic Group.

Clinical data are often susceptible to varying interpretations and analyses when submitted for patient care or therapies, so that a product that performed to statistical 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 BioSenic Group 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. Altogether, 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, BioSenic Group'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. Efforts to educate the medical community and third-party payers on the benefits of BioSenic Group's products may also require significant resources and may never be successful, which would prevent BioSenic Group from generating significant revenues, or becoming profitable in this area of development.

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 BioSenic Group's ability to generate sufficient operating margins to offset operating expenses.*

The commercial success of BioSenic Group'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 BioSenic Group intends to commercialise its products. Considering the innovative nature of BioSenic Group's product candidates, the possible reimbursement levels are difficult to predict. BioSenic Group'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, part or all of BioSenic Group's products may be found to not have a sufficient benefit/risk profile within the existing health technology assessment and reimbursement processes applied throughout the different jurisdictions in which BioSenic Group envisages to operate, and may be subject to different reimbursement facilities depending on the jurisdiction in which its 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 BioSenic Group's ability to generate sufficient operating margins to offset operating expenses.

c. *BioSenic Group has no experience in sales, marketing and distribution, which may have an adverse effect on its ability to successfully manage its sales, marketing and distribution when its products come on the market.*

BioSenic Group 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 potentially introduce new standards of care in inflammatory/autoimmune diseases, orthopaedic or other indications, to successfully commercialise its products once they have been approved for commercialisation. BioSenic Group has no experience in sales, marketing and distribution. There is a risk that BioSenic Group 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 its 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 BioSenic Group's activities are subject to substantial regulation and if BioSenic Group does not comply with one or more of the standards of the Competent Authorities, it could experience significant delays in development or commercialisation, additional costs, refusals, suspension, withdrawals of approvals.***

The international biopharmaceutical industry is highly regulated by governmental bodies ("**Competent Authorities**") imposing substantial requirements on almost all aspects of BioSenic Group'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 BioSenic Group, or any of its partners or licensees, operates, it has to comply with the standards and regulations imposed by the local Competent Authorities.

BioSenic Group has to constantly comply with the standards imposed by the Competent Authorities, which are subject to regular reviews and may possibly impose new 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 BioSenic Group's cell therapy and ATO-based products in Europe where the marketing authorisation is mandatory through a centralized procedure, whereas for its noncellular off-the-shelf protein solution, JTA-004, a decentralised procedure could be followed), *inter alia* in timing, detailed costs and efforts necessary to complete those procedures e.g., different reporting procedures. 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 BioSenic Group. If BioSenic Group 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 BioSenic Group's business, prospects, financial condition and results of operations.

b. ***If any product liability claims are successfully brought against BioSenic Group or its collaborators, BioSenic Group 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 BioSenic Group or its collaborators by participants enrolled in clinical trials, practitioners, researchers, other health/research professionals or others using, administering or selling any of BioSenic Group's future approved products. BioSenic Group is currently insured for risks related to clinical studies. BioSenic Group may incur substantial liabilities if it cannot successfully defend itself against such claims. From the adverse events reported with BioSenic Group'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 BioSenic Group.

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

For arsenic trioxide, BioSenic's subsidiary Medsenic has had a manufacturing contract with Pierre Fabre CDMO in Pau (France) for its IV (intravenous) formulation of arsenic trioxide (called Arscimed). This formulation has been accepted for clinical use in Medsenic's Phase II trial in cGvHD. The oral formulation of arsenic trioxide is under the control of Medsenic's partner and shareholder Phebra, a biopharma with manufacturing facilities in Australia and UK. Medsenic has entered into a marketing and supply agreement with Phebra for the supply the necessary capsules for oral administration in Medsenic's indications for inflammatory/autoimmune diseases clinical trials. Please revert to Section 6.4.4.2 for more information.

However, BioSenic Group is not relieved from continuously complying with the relevant standards. BioSenic Group, and key third party subcontractors and suppliers on which it relies currently or in the future, must continuously comply with Good Manufacturing Practices on its own or partner sites and the corresponding manufacturing regulations of the Competent Authorities. In complying with these regulations, BioSenic Group 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 BioSenic Group such as an enforcement action against BioSenic Group, including the seizure of products and shutting down of production. Any of the third-party subcontractors and suppliers and BioSenic Group also may be subject to inspections by the Competent Authorities. If any of BioSenic Group's third-party suppliers or BioSenic Group itself fails to comply with Good Manufacturing Practices or other applicable manufacturing regulations, the Group's ability to develop and commercialise the products could suffer significant interruptions.

Given that BioSenic Group relies on external Contract Manufacturing Organizations for the materials required for its ongoing and envisaged clinical trials, a third-party manufacturer may not comply with the required quality standards or devote sufficient resources to the manufacturing of the products or may otherwise fail in the manufacturing of such compound, in which event the development and commercialization of BioSenic Group's product candidates could be delayed (for example because of product reruns) or even terminated. Were concerns to arise with the manufacturing of its product, BioSenic Group's business could be substantially harmed. 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 BioSenic Group.

1.6 Risk factors linked to intellectual property

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

BioSenic Group's success will depend in part on its ability to obtain, maintain and enforce its patents and other intellectual property rights. BioSenic Group's research programmes and product candidates are covered by several patent application families, which are either licensed to BioSenic Group or owned by the Group. For more information about BioSenic Group's patents and patent applications (please see Section 4.14 of this Registration Document for further details). Currently, BioSenic Group manages:

- 8 patent families related to the ALLOB technology (including one patent family owned and exclusively licensed by the ULB) with expiry dates comprised between 2027 and 2039;

- 5 patent families related to the JTA technology (including three patent family co-owned with Enrico Bastianelli) with expiry dates comprised between 2029 and 2043;

- 4 patent families related to the medical use of arsenic salts alone or in combination with metal ions (Arscicop and Arscimed) with expiry dates comprised between 2038 and 2043;

- two patent families licensed to Medenic by Phebra related to oral formulations of arsenic trioxide (Arscicor / OATO), their preparation, and their use for treating various immunopathologies when commercially exploited in specified territories, with expiry dates comprised between 2036 and 2037;

- one patent family covering the use of the IV formulation ATO for treating specific autoimmune and inflammatory diseases (licensed from CNRS) with expiry dates comprised between 2030 and 2031 (in USA only; already expired in other jurisdictions).

Although BioSenic Group can still benefit from its developed know-how, once patent protection is lost this could force BioSenic Group to license or develop new formulations of ATO. The advantage of BioSenic Group's changed focus on OATO (instead of IV formulation) – in additional to the treatment advantages of OATO as further described in this Registration Document – allows it to benefit from the additional patent protection on OATO and to minimise the impact of the recent expiry in 2023 of CNRS' European patent relating to the IV formulation. In addition, the loss of patent protection could negatively affect the revenues of BioSenic Group from the relevant products as competitors might want to take advantage of the expiration of patent protection.

BioSenic Group may not be able to obtain or maintain these patent rights against patent offices and other third-party challenges to their validity, scope and or enforceability. BioSenic Group may not be (or have 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 BioSenic Group's research programmes and product candidates are patentable, that patents will be granted to BioSenic Group 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 BioSenic Group 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 BioSenic Group of the protection it may expect against competitors. Moreover, it cannot be excluded for the ALLOB product 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 BioSenic Group 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. Third parties might claim ownership rights over the patents or other intellectual property rights owned or held by BioSenic Group. To date, no invalidation or opposition process has been made against the patent portfolio of BioSenic Group.

Several of BioSenic Group's patents are already granted in Europe, US, Japan, Australia, Canada, China, Hong Kong, Israel, India, South Korea and Singapore, depending on the patent family considered. The current prosecution of its or its licensors' patent applications may not result in granted patents in each of the territories. Filing, prosecuting and defending their patents throughout the world would be prohibitively expensive for BioSenic Group and its licensors. Competitors may use BioSenic Group's technologies in jurisdictions where BioSenic Group or its licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where BioSenic Group 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 BioSenic Group's products in jurisdictions where BioSenic Group or its licensors do not have any issued patents and BioSenic Group'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 BioSenic Group to stop the infringement of its patents or marketing of competing products in contravention of its proprietary rights generally. The inability of BioSenic Group to protect and/or enforce some of its intellectual property rights in the selected territories in which it seeks patent protection could have a material adverse effect on the Group's ability to maximise the market potential of its product candidates, which would result in severe adverse effect on its business, prospects, financial conditions, and results of operations.

Moreover, periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid by BioSenic Group 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, BioSenic Group 's competitors might be able to use its technologies and those technologies licensed to BioSenic Group and this circumstance would have an adverse effect on its business, prospects, financial conditions, and results of operations.

b. ***Should BioSenic Group be unable to obtain new license rights on reasonable terms, or if it would lose any of its licenses or otherwise experiences disruptions to its business relationship with its licensors, BioSenic Group might be unable to develop, manufacture or sell its products.***

BioSenic Group'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 given exclusive access pursuant to license agreements and which are important to the business.

BioSenic Group is currently renegotiating the scope and commercial terms of (i) the license agreement and (ii) the marketing and supply agreement entered into between Medsenic and Phebra respectively on 21 and 31 May 2021. Under these agreements, Phebra has granted an exclusive license to Medsenic to use the oral formulation of arsenic trioxide for its research and clinical development in various immunopathologies and to market and distribute the product in such field in the European Union, Switzerland, and in other non-European countries (defined as "**Medsenic Territories**" in the agreement). Phebra agreed to provide a free clinical supply (either directly or via a contract manufacturer) of up to an equivalent of EUR 200,000 of the oral formulation of arsenic trioxide for Medsenic's indication at the start of the Phase III clinical trial, which should allow BioSenic Group to cover approximately the first 12 months of the trial. In consideration for the license granted for the Medsenic Territories, Phebra received 3,151 shares (4.3% of the shares currently outstanding) in Medsenic. Phebra retains the right to commercialise the product in all countries outside the Medsenic Territories against payment to Medsenic of a royalty of 55% of the net sales profits. BioSenic Group and Phebra are now currently analysing the possibility to extend the Medsenic Territories and the commercial terms thereof, which is expected to require lengthy and complex discussions and agreements based on partially unknown commercial and competitive factors. A letter of intent and non-binding term sheet are being prepared. As a result, there is a clear risk that BioSenic Group might not obtain the right to commercialise the oral formulation of arsenic trioxide in key jurisdictions (including the USA, Japan and UK) or acquire such rights on commercially unfavourable terms, specifically in relation to the definition of milestones and corresponding payments to be made by BioSenic Group to Phebra. This could substantially impair BioSenic Group's ability to generate sufficient future revenues from its existing clinical programmes, which would have an adverse impact on its valuation and possibility its ability to raise additional funding thereby threatening BioSenic Group's ability to continue as a going concern. Under the current license agreement with Phebra, Medsenic had agreed to commence a clinical study using Phebra OATO before 31 May 2023. If such study would not start before 31 May 2023, Phebra could terminate the license agreement unless the parties agree to postpone such date. On 29 May 2023, BioSenic announced the amendment of the license agreement with Phebra. The license agreement grant is now subject to Medsenic’s ability to secure sufficient funding before 31 May 2024 to commence a clinical study using OATO. Although BioSenic Group is confident that the deadline could be further extended if necessary, this means that BioSenic Group needs to secure sufficient funding before such deadline to be able to start the Phase III clinical study with OATO in cGvHD (i.e., allowing completion of the IND application with the FDA, and starting CRO preparation, sites selection and data collection for the clinical study).

On 15 January 2024, BioSenic announced the signature of a binding term sheet with Phebra related to the adaptation of the License Agreement and the MDA signed in May 2021. The initial License Agreement provided a commercialization agreement of 100% net profits for Medsenic mainly in Europe and 55 % net sales profit for Phebra in the rest of the world (including major markets such as the US, Canada, South America, Japan, South East Asia, China and Australia). In particular, the binding term sheet for the indication chronic Graft versus Host Disease (cGvHD) license now provides for a royalty payment of 2% on worldwide sales, which simplifies the conditions for offering sublicenses to new external partners. In addition, under the license agreement, Phebra agrees that Medsenic will have exclusive worldwide territorial rights for the use of OATO in GvHD. Regarding the MDA, Phebra agrees that the net profit allocation as stated in the initial MDA will be deleted for the sales revenues and profits generated from the sale of product, restricted to the indication cGvHD. Phebra also agrees to cover the costs of maintaining and updating the drug substance file to comply with the rules of all active territories; of controlling the compliance with various regulators on ongoing supplier approval and compliance to Good Manufacturing Practices (GMP) requirements; of updating the drug master file of OATO; of managing the Contract Manufacturing Organization (CMO) and supply chain from the active pharmaceutical ingredient to the clinical release of the product and of covering the regulatory and quality and GMP expenses. To take into account these costs for Phebra, the cost-of-goods for the Medsenic final clinical OATO product will be increased by a mark-up of 20%. In addition, Medsenic will have the right to establish an Australian entity to use the OATO patents for cGvHD indication. The Australian entity will not commercially compete with Phebra, particularly in the field of APL (acute promyelocytic leukemia) cancer treatment, by having Medsenic's GvHD treatment produced in product-specific packaging.

BioSenic Group has also a dependence on the license agreement entered into by Medsenic with CNRS regarding the patent family owned by the CNRS that claims the use of arsenic salts for autoimmune indications patent. We refer to Section 4.10.2.1 (License agreement with the Centre National de la Recherche Scientifique (CNRS) in France) for further information in that regard. The patents licensed from the CNRS relate to the use of arsenic salts generally to treat autoimmune diseases. As the patents of the CNRS covering the European Union and the U.S. expire(d), respectively, in 2023 and 2029, BioSenic Group is dependent on the development of new formulations of ATO (such OATO as licensed from Phebra or a combination of matter such as ArsciCop) to be able to obtain additional patent protection for its clinical assets. As BioSenic Group is indeed focussing its clinical development on the oral formulation of ATO (for which patent protection is available until 2036) and given that it has received orphan drug designation for the treatment of GvHD with ATO from EMA and FDA (which gives market exclusivity of, respectively, 7 and 10 years in the US and Europe once the medicine is approved for commercialisation), the risk related to the expiry of the aforementioned CNRS patent in the European Union is considered to be low.

For its clinical programmes BioSenic Group has also entered into license agreements with third parties regarding the ULB-028 patent family. Also, BioSenic Group had previously been granted exclusive worldwide rights from Enrico Bastianelli SRL to develop, manufacture, sublicense and sell any products of the JTA technology for human application, but such license and co-ownership agreement ended in 2022 when BioSenic decided to stop the development of the JTA technology before any exploitation of the JTA technology (see section 4.10.1.2 for more information). Although BioSenic has been discussing for quite some time the opportunity with Enrico Bastianelli SRL to enter into a co-ownership agreement for the old JTA-Gen1 patent families (i.e. the patent families BPBONE-001, BONE-002, BONE-011), such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement creates exploitation problems with third parties and possible licensees for the use of the JTA technology. This has therefore a negative impact on BioSenic's possibilities to collaborate with external partners for the future development and valorisation of the JTA technology as it exists.

The conditions under which BioSenic Group may acquire future rights or 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 BioSenic Group 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 BioSenic Group be unable to obtain new rights on reasonable terms similar to those which it holds under such license, or if it would lose any of its licenses, BioSenic Group might be unable to develop, manufacture or sell its products or should be obliged to develop new innovative products, with important delayed access to the desired market. This could have adverse effects on BioSenic Group's business, prospects, financial conditions, and operational results for a longer period.

c. ***If BioSenic Group is not able to prevent disclosure of its trade secrets, know-how, (non)biological materials, or other proprietary information, the value of its technology and product candidates could be significantly diminished.***

BioSenic Group relies on trade secret protection to protect its interests in its know-how, (non-)biological materials, or other proprietary information and processes for which patents are difficult to obtain or enforce, all of which constitute confidential information. BioSenic Group may not be able to protect its confidential information adequately. BioSenic Group 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 and that any of BioSenic Group 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 BioSenic Group, 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 BioSenic Group's competitors to learn confidential information and use it in competition against BioSenic Group. In addition, others may independently discover BioSenic Group's confidential information. Any action to enforce BioSenic Group'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.

d. ***BioSenic Group 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 BioSenic Group having to pay substantial damages or limit BioSenic Group's ability to commercialise its product candidates.***

BioSenic Group's success will depend in part on its ability to operate without infringing on or misappropriating the intellectual property rights of others. BioSenic Group's activities, or those of its licensors, might infringe on the patents or other intellectual property rights owned by others. BioSenic Group 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 BioSenic Group or its licensors regardless of whether the claims have any merit. Additionally, BioSenic Group cannot predict whether it or its licensors will be successful in any litigation. If BioSenic Group 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 BioSenic Group 's cash flow and financial position. BioSenic Group 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. BioSenic Group 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 BioSenic's business, prospects, financial conditions, and results of operations.

To date, no patent infringement claim has been made against the BioSenic Group but, in such a situation, BioSenic Group will evaluate legal opportunities and provisions that may allow limiting or invalidating the claims

in patents owned by others being allegedly infringed by BioSenic Group in a given country and/or for any specific commercial, development, research, or manufacturing activity.

e. *BioSenic co-owns the JTA patent families together with Enrico Bastianelli SRL and has been discussing the opportunity to enter into new co-ownership rules for the JTA patent families. Such discussions, however, did not result in the conclusion of a new co-ownership agreement, the absence of which could give rise to co-ownership and exploitation problems for the use of the JTA technology and could therefore have a negative impact on BioSenic's possibilities to collaborate with external partners for the future development of the JTA technology.*

BioSenic co-owns the JTA patent families – being BPBONE-001, BPBONE-002 and BONE-011 patent families – alongside Enrico Bastianelli SRL (previously Glob-Co SRL). Enrico Bastianelli SRL, with registered office is in Jumet, Belgium, is controlled by Mr Enrico Bastianelli.

In 2020, BioSenic entered into a license and co-ownership agreement with Enrico Bastianelli SRL regarding the JTA patent families BPBONE-001, BONE-002, BONE-011 and any future patents related to the JTA technology. This agreement provided to BioSenic an exclusive, worldwide and sublicensable right to use the co-owned patent families for all human applications. This agreement further provided to Enrico Bastianelli SRL an exclusive, worldwide and sublicensable right to use the same co-owned patent families for all veterinary applications.

Following disappointing Phase III clinical results, Biosenic transferred its rights to the JTA technology to the Walloon Region and consequently terminated the license agreement with Enrico Bastianelli SRL in 2022. In March 2023, however, BioSenic obtained new statistical analysis results from the JTA-004 Phase III clinical trial data. This new post-hoc analysis changes the therapeutic profile of the molecule and potentially allows for the possibility of stratifying patients for a new, optimized Phase III clinical study. The agreement with respect to the JTA technology (including intellectual property rights forming the JTA-Gen1 patent families) has been since reacquired from the Walloon Region, as the Walloon Region accepted to retrocede its rights to the JTA technology to BioSenic Group in 2023. Although BioSenic has been discussing the opportunity with Enrico Bastianelli SRL to enter into a new co-ownership agreement for the JTA-Gen1 patent families, such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement for the JTA-Gen1 patent families creates exploitation problems with third parties for the use of the JTA technology and has therefore a negative impact on BioSenic's possibilities to collaborate with external partners and possible licensees for the future development and valorisation of the JTA technology as it currently exists.

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

a. *Manufacturing of BioSenic Group's products requires chemicals, human or derived raw materials to be obtained from third parties and may be more costly than expected.*

BioSenic Group will have to establish a scalable process platform with third parties in the relevant regions to manufacture its products. BioSenic Group has a particular dependence on Phebra for providing the oral formulation of ATO. Phebra will supply OATO through a contract manufacturer based in the United Kingdom, which is chosen and selected by Phebra. Phebra itself purchases the active pharmaceutical ingredient arsenic trioxide from the Umicore group. Given that arsenic trioxide is currently manufactured by a number of suppliers, BioSenic Group does not expect any supply problems of arsenic trioxide.

BioSenic Group is currently preparing the regulatory file, which includes guarantees on clinical batches supplies, to submit an IND application for the use of OATO in Medsenic's indications with the FDA by end-Q2 2024. BioSenic Group expects to receive a positive answer from the FDA in an IND meeting end-Q3 2024. The failure to manufacture oral ATO in compliance with the regulatory framework of the FDA and other Competent Authorities could adversely affect BioSenic Group's ability to start its Phase III cGvHD clinical trial,

which might lead to delays in the development of its drug candidates and higher than anticipated development costs.

To be able to supply the products at acceptable prices, BioSenic Group 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 BioSenic Group to purchase or 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.

b. *BioSenic Group 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, BioSenic Group may not be able to obtain regulatory approval for or commercialize its product candidates and its business could be substantially harmed.*

BioSenic Group has relied upon and plans 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. BioSenic Group relies on these parties for execution of its preclinical studies and clinical trials, and controls only certain aspects of their activities. Nevertheless, its reliance on these third parties does not relieve BioSenic Group 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 GMP regulations. If BioSenic Group, the participating investigators or any of its CROs fail to comply with applicable GCPs or the tested products do not meet GMP regulations, the clinical data generated in its clinical trials may be deemed unreliable and the regulatory authorities may require BioSenic Group to perform additional clinical trials before approving the marketing applications of its product candidates.

Further, the investigators and CROs are not employees of BioSenic Group and BioSenic Group will not be able to control, other than by contract, the number 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 BioSenic Group's clinical protocols, regulatory requirements or for other reasons, clinical trials may be extended, delayed or terminated and BioSenic Group 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 BioSenic Group's product candidates would be harmed, BioSenic Group's costs could increase and its ability to generate revenues could be delayed.

There is a limited number of third-party service providers that specialize or have the expertise required to achieve BioSenic Group's business objectives. If any of the relationships with these third-party CROs, CDMOs or clinical investigators terminate, BioSenic Group 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 BioSenic Group to disclose its proprietary information to these parties, which could increase the risk that this information could be misappropriated.

c. *BioSenic Group is subject to competition for its skilled personnel and challenges in identifying and retaining key personnel could impair BioSenic Group's ability to conduct and grow its operations effectively.*

The services of the BioSenic's Executive Committee are critical to the successful implementation of its business, research, product development and regulatory strategies. Members of the Executive Committee may terminate their employment or services with BioSenic at any time with relatively short notice. In general,

conflicts between key managers may result in BioSenic 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, BioSenic's research and development efforts may be seriously and adversely affected.

BioSenic Group heavily depends on the skills, experience and relationships of its major shareholder and CEO and director, Dr François Rieger for the clinical development of it product candidates based on ATO. Although the appointment of Dr Carole Nicco as COO and CSO, and the continued support of Medsenic's scientific committee (chaired by Prof. Jules Hoffmann and consisting of specialists in the field of immunology) intends to mitigates the risk, the departure of Dr François Rieger could have a material adverse effect on BioSenic Group's clinical and research and development efforts (including the ongoing preparations of the Phase III clinical trial in cGvHD) and its ability to obtain future funding.

BioSenic Group'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. As of 31 December 2023, BioSenic employed 2 persons and it subsidiary Medsenic employed 3 persons. These numbers do not take into account the temporary workers, consultants and the members of management. 60% of employees have obtained a doctorate and 40% a master's degree. Scientific specialization domains include cellular and molecular biology, pharmaceutical sciences, veterinary medicine, physiology and life sciences. BioSenic has not yet hired a new CFO as the Company's managers and consultants can currently adequately assume such work. BioSenic does, however, intend to hire a CFO once the Phase III clinical trial in cGvHD has further advanced, as it is expected that at that point in time more financial management resources will be required.

Many of the other biotechnology and pharmaceutical companies and academic institutions that BioSenic Group competes against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than BioSenic Group does. Therefore, BioSenic Group might not be able to attract or retain these key persons on conditions that are economically acceptable. Furthermore, BioSenic Group will need to recruit new managers and qualified scientific personnel to develop its business if BioSenic Group expands into fields that will require additional skills. The inability of BioSenic Group to retain these key persons or attract new specialists 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.

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

BioSenic, 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 4.13 of this Registration Document for an overview of the grants and subsidies.

Most of the Patent Subsidies provide that BioSenic 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 BioSenic 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 BioSenic in its choice of geographical location to carry out or further develop its activities. Also, if the Region would refuse to provide its consent, BioSenic 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 BioSenic 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 BioSenic 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 BioSenic's ability to relocate its activities. Furthermore, BioSenic's ability to relocate its activities is limited by the provisions of the SME Agreement, pursuant to which BioSenic, in order to keep the funding granted to it, must employ a specific number of employees at its site in Wallonia.

e. *BioSenic Group 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, BioSenic Group'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, BioSenic Group 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. BioSenic Group currently expects that proceeds of future fundraisings over the next 12 months will in priority be used to finance the start of the Phase III clinical trial with cGvHD, as well as for general working capital requirements. As a result, it will only be possible to start the SLE and SSc Phase 2b clinical trials if the BioSenic Group succeeds in concluding a strong partnership with a biopharmaceutical company or if it manages to successfully out-license some of its technology. As BioSenic currently does not intend to allocate further R&D resources for the clinical development of JTA-004 and ALLOB, it is seeking to collaborate with existing and potential partners to explore options for the future develop of these product candidates. Therefore, the future international success of BioSenic Group may depend on its ability to conclude partnerships and on the ability of its partner(s) to meet the aforementioned characteristics. The risk furthermore exists that any such partnerships are terminated early as was recently the case for the partnership agreement between BioSenic and Pregene.

1.8 Risks relating to the Contribution

a. *BioSenic Group inability to successfully integrate Medsenic or any other companies acquired in the future and to retain its current and prospective employees, could have a material adverse effect on its business.*

BioSenic has recently acquired 51.81% of the shares of Medsenic SAS and is expected to acquire the remaining 48.19% as described hereinafter. BioSenic Group may in the future acquire other businesses, companies with complementary technologies or products to expand its activities. As a consequence, intangible assets, including goodwill, may account for a larger part of the balance sheet total than is currently the case. The business combination brings opportunities for renewed financing, but also for the future to offer new ways to correct the cell or organ damages observed in autoimmune diseases with active inflammation and immune damage. Despite the fact that BioSenic will carefully investigate every acquisition, the risk remains, amongst others, that corporate cultures may not match, expected synergies may not be fully realized, restructurings may prove to be more costly than initially anticipated and that acquired companies may prove to be more difficult to integrate than foreseen. BioSenic may therefore not be able to successfully integrate Medsenic or any other acquired companies on the long term.

BioSenic Group 's ability to manage its growth effectively will require BioSenic Group to continue to improve its operations, financial and management controls, reporting systems and procedures, and to train, motivate and manage its employees and, as required, to install new management information and control systems. BioSenic Group may not be able to implement improvements to its management information and control systems in an efficient and timely manner or such improvements, if implemented, may not be adequate to support its operations.

The acquisition (via the Contribution in 2022 and the conversion of convertible bonds issued by Medsenic to BioSenic in 2023) of 51.81% of the shares of Medsenic (and the contractual commitment to acquire the

remaining 48.19%) is the largest acquisition that BioSenic has ever undertaken. BioSenic has made certain assumptions relating to the forecast level of future earnings, cost savings, synergies and associated costs of the Medsenic acquisition (such total aggregate transaction-related fees and expenses estimated at approximately EUR 781,000 for BioSenic and Medsenic). The acquisition also represented the entry by BioSenic Group into a new area of therapy based on the use of arsenic trioxide, although the safety risks related to the development of a small active molecule, with safety data already available in human subjects, are more limited as compared to those of a therapy using live cells, with unknown factors of expansion, proliferation or dedifferentiation in live subjects. BioSenic Group 's assumptions relating to the forecast level of future earnings, cost savings, synergies and associated costs of the acquisition may be inaccurate, including as a result of the failure to realize the expected benefits of the acquisition, higher than expected transaction and integration costs and unknown liabilities as well as general economic and business conditions that adversely affect the combined company following the completion of the acquisition.

BioSenic intends, to the extent possible, to integrate its operations with those of Medsenic, into the BioSenic Group. BioSenic's goal in integrating these operations is to increase future revenues by expanding its pipeline into the treatment of diseases (such as cGvHD, SLE or SSc) with arsenic trioxide and achieve cost savings by taking advantage of the significant anticipated synergies of consolidation. To achieve this goal, BioSenic Group has incurred significant legal, accounting and transaction fees and other costs related to the Medsenic Contribution. In addition, BioSenic Group expects to incur a number of non-recurring costs associated with combining the operations of the two companies. Some of these may be higher than anticipated.

b. ***The contribution of the remaining 48.19% of the shares of Medsenic will result in additional dilution for existing shareholders of BioSenic.***

Pursuant to a shareholders' agreement dated 24 October 2022 between BioSenic and the shareholders of Medsenic holding the remaining 48.19% of the shares of Medsenic (the "**Minority Shareholders**"), the Minority Shareholders agreed to contribute all of their remaining Medsenic shares into BioSenic in two instalments, each time for half of their remaining shareholding. For more information, please revert to Sections 4.10.1.5 and 6.4.4.1.

Based on the valuations and price per share used for the Contribution, the contribution of the additional 48.19% of shares of Medsenic will result in a dilution of BioSenic's existing shareholders of around 34.80%. The actual dilution for BioSenic's shareholders might be higher or lower depending on the price per share used for the equity raises and on the aforementioned potential revaluation of Medsenic (see Section 4.10.1.5b for more information) and, eventually, of BioSenic in the case of a material change in the BioSenic's assets, liabilities or clinical trials.

The table below provides an overview of the maximum dilution for the existing shareholders, based on all existing warrants and convertible bonds at 31 January 2024 and taking into account the contribution of the remaining 48.19% of Medsenic shares.

	Full exercise of the Outstanding Warrants (a)[1]	Full conversion of the convertible bonds (b)[2]	Full conversion of envisaged new Patronale and Monument convertible bonds (c)[3]	Full contribution of the remaining 48.19% shares of Medsenic (d)	Combined operations of (a), (b), (c) and (d) = (e)
Current total number of	163,181,474	163,181,474	163,181,474	163,181,474	163,181,474

shares (31/01/2024)					
Number of New Shares after respectively (a), (b), (c), (d) or (e)	1,197,554	56,277,520	134.971.467	87,109,184	279.555.725
Total number of shares after (a), (b), (c), (d) or (e)	164,379,028	219,458,994	298,152,941	250,290,658	442,737,199
Dilution	0.73%	25.64%	45.27%	34.80%	63.14%

Note 1: Number of Outstanding Warrants as of 31 January 2024.

Note 2: 56,277,520 shares could be issued in case all 137 convertible bonds effectively subscribed for by GTO 15 were exercised and converted into shares based on the conversion price of EUR 0,0494869 (95% of 1-day VWAP on 30 January 2024; rounded).

Note 3: Patronale and Monument agreed to replace their outstanding loans granted to BioSenic by an aggregate outstanding principal amount of EUR 7.5 million plus accrued interests, by new convertible bonds to be issued by BioSenic later in 2023. The conversion price will be equal to 95% of the 30-calendar day VWAP immediately preceding the date of the conversion notice. The Outstanding Warrants of Patronale will be cancelled. In light of the foregoing, 134.971.467 shares could be issued in case all of the EUR 7.5 million worth of convertible bonds are exercised and converted into shares based on the conversion price of EUR 0,0555673 (95% of the 30-calendar day VWAP preceding 30 January 2024; rounded).

2 GENERAL INFORMATION

This document is a registration document within the meaning of the Articles 6 (paragraph 3) and 10 of the Prospectus Regulation 2017/1129. This Registration Document has been drawn up as part of a simplified prospectus in accordance with Article 14 of Regulation (EU) 2017/1129.

On 26 March 2024, the Financial Services and Markets Authority (FSMA) approved the English version of this Registration Document as competent authority 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 BioSenic. The FSMA only approves this Registration Document as meeting the standards of completeness, comprehensibility and consistency imposed by Regulation (EU) 2017/1129 and such approval shall not be considered as an endorsement of the issuer that is the subject of this Registration Document.

2.1 Legal Information

The legal and commercial name of BioSenic is BioSenic SA. BioSenic is registered with the legal entities register (Walloon-Brabant) under number 0882.015.654 and was incorporated in Belgium on 16 June 2006 (under the name Bone Therapeutics), for an indefinite period of time. BioSenic is a limited liability company incorporated in the form of a "*société anonyme*" under the laws of Belgium. BioSenic's registered office is currently located at Granbonpré 11, Building H, 1435 Mont-Saint-Guibert (Belgium) (phone: +32 71 12 10 00 and fax: +32 71 12 10 01). The Legal Entity Identifier (LEI) code of BioSenic is 549300HFIIMTOP1DFR76.

2.2 Language of this Registration Document

BioSenic published its Registration Document in English. BioSenic 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 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, Prof. François Rieger, CEO / President of the Board and Véronique Pomi-Schneiter COO, Member of the Board, on behalf of the Board of Directors of the BioSenic, 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 BioSenic 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.

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

2.4 Statutory auditor

BioSenic's statutory auditor is BDO Bedrijfsrevisoren – Réviseurs d'entreprises BV/SRL, a company having the form of a private limited liability company organised and existing under the laws of Belgium, with registered office at Elsinore Building - Corporate Village, Da Vincilaan 9/E6, 1930 Zaventem, Belgium, represented by Mr Rodrigo Abels, member of the Belgian *Institut des Réviseurs d'Entreprises/Instituut voor Bedrijfsrevisoren*, for a term of three years ending immediately following the adjournment of the annual general shareholders' meeting of BioSenic to be held in 2025, resolving upon the financial statements for the fiscal year ended on 31 December 2024. BDO Bedrijfsrevisoren – Réviseurs d'entreprises BV/SRL reviewed financial statements for the fiscal year ended on 31 December 2022.

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 BioSenic'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 BioSenic 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 BioSenic Group's business included in this Registration Document has been obtained from internal surveys, scientific publications, section association studies and government statistics. Where information has been sourced from third parties, this information has been accurately reproduced. As far as BioSenic is aware and is able to ascertain from information published by those third parties, no facts have been omitted which would render the reproduced information inaccurate or misleading. The market, economic and industry data have primarily been derived and extrapolated from reports, datasets and articles provided by third parties such as GlobalData, IQVIA, BiotechFinances, Les Echos and The Lancet.

The third-party sources BioSenic has used generally state that the information they contain has been obtained from sources believed to be reliable. Some of these third-party sources also state, however, that the accuracy and completeness of such information is not guaranteed and that the projections they contain are based on significant assumptions. As BioSenic does not have access to the facts and assumptions underlying such market data, or statistical information and economic indicators contained in these third-party sources, BioSenic is unable to verify such information. Hence, while the information has been accurately reproduced, and as far as BioSenic is aware and is able to ascertain from information published by that third-party, no facts have been omitted which would render the reproduced information inaccurate or misleading, and BioSenic believes it to be reliable, BioSenic cannot guarantee its accuracy or completeness. The inclusion of this third party industry, market and other information should not be considered as the opinion of such third parties as to the value of the BioSenic shares or the advisability of investing in the shares of BioSenic.

In addition, certain information in this Prospectus is not based on published data obtained from independent third parties or extrapolations therefrom, but rather is based upon BioSenic's best estimates, which are in turn based upon information obtained from trade and business organizations and associations, consultants and other contacts within the industries in which BioSenic operates, information published by BioSenic's competitors and BioSenic's own experience and knowledge of conditions and trends in the markets in which it operates.

BioSenic cannot assure that any of the assumptions it has made while compiling this data from third party sources are accurate or correctly reflect BioSenic's position in the industry and none of BioSenic's internal estimates have been verified by any independent sources. BioSenic does not make any representation or warranty as to the accuracy or completeness of this information. BioSenic has not independently verified this information and, while BioSenic believes it to be reliable, BioSenic cannot guarantee its accuracy.

2.7 Other available information

BioSenic 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 enterprise court of the Walloon Brabant (Belgium), where such documents are available to the public. BioSenic is registered with the register of legal entities of Walloon Brabant (Belgium) 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, as well as other documents, valuations and statements prepared by any expert at BioSenic's request any part of which is included or referred to in the Registration Document, are also available on BioSenic's website (https://biosenic.com/investors) or can be provided upon request to BioSenic SA, Investor Relations, rue Granbonpré 11, Building H, 1435 Mont-Saint-Guibert, Belgium (Tel: +32 71 12 10 00, Fax: +32 71 12 10 01 and e-mail: investorrelations@biosenic.com).

BioSenic 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, BioSenic 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 BioSenic's website (https://biosenic.com/investors) and STORI, the Belgian central storage platform which is operated by the FSMA and can be accessed via its website (www.fsma.be).

BioSenic 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 BioSenic's website (https://biosenic.com/investors), 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:

BioSenic SA
To the attention of Investor Relations
Rue Granbonpré 11, Building H
1435 Mont-Saint-Guibert
Belgium
Tel: +32 71 12 10 00

Fax: +32 71 12 10 01
E-mail: investorrelations@biosenic.com

An electronic version of the Registration Document is also available on BioSenic's website (https://biosenic.com/investors). 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. The information on the website does not form part of the Prospectus unless that information is incorporated by reference into the Prospectus.

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

3.1 Information incorporated by reference

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

(i) the annual report and audited consolidated financial statements of BioSenic prepared in accordance with IFRS for the financial year ended 31 December 2022 (in English and French), together with the related audit report thereon (available on the Company's website); and

(ii) the condensed consolidated unaudited interim financial statements of BioSenic prepared in accordance with IFRS for the financial period ended 30 June 2023 (in English and French) (available on the Company's website).

Copies of documents partly incorporated by reference in this Registration Document may be obtained (without charge) from the registered offices of BioSenic and the website of BioSenic (http://www.biosenic.com/investors). BioSenic confirms that it has obtained the approval from its auditor to incorporate in the Prospectus the audited consolidated financial statements and the auditor's report thereon for the financial year ended 31 December 2022.

The tables below include references to the relevant pages of the audited consolidated financial statements of BioSenic for the financial year ended 31 December 2022, as set out in the annual report of BioSenic (in English and French), as well as of the unaudited condensed consolidated interim financial statements for the financial period ended 30 June 2023. 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 BioSenic prepared in accordance with IFRS for the financial year ended 31 December 2022, as set out in the annual report (in English and French).	
Business overview	p. 10-19
Financial review of the year ending 31 December 2022	p. 20-25
Board of Directors	p. 33-42
Executive Committee	p. 42-45
Remuneration report	p.50-59
Consolidated statement of financial position	p. 87
Consolidated statement of comprehensive income	p. 88
Consolidated statement of cash flows	p.89
Consolidated statement of changes in equity	p. 90
Notes to the consolidated financial statements	p. 91-135
Auditor's report	p. 80-86

Condensed consolidated unaudited interim financial statements of BioSenic prepared in accordance with IFRS for the financial period ended 30 June 2023, as set out in the interim report (in English and French).	
Condensed consolidated statement of financial position	p. 6
Condensed consolidated statement of comprehensive income	p. 7
Condensed consolidated statement of changes in equity	p. 8
Condensed consolidated statement of cash flows	p. 9
Notes to the interim condensed consolidated financial statements	p. 10-20

3.2 Securities issued by BioSenic

As per 31 December 2023, BioSenic's capital amounts to € 35,100,668.71, represented by 163,181,474 ordinary shares without nominal value.

The total of exercisable warrants within BioSenic is 197,554 warrants for the (former) 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 1,197,554 warrants. Subject to completion of the debt restructuring, it is envisaged to cancel the 1,000,000 outstanding warrants issued to Patronale and EIB.

3.3 Overview of funding

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

- € 112.55 million in net proceeds from private equity placements in BioSenic;
    - These proceeds include amongst other convertible bonds issued in 2018, 2019, 2020 and converted into shares;
    - These proceeds include amongst other € 3.1 million from 62 convertible bonds converted into shares by GTO 15;
- € 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);
- €8 million under a loan agreement of up to €16 million with the European Investment Bank (EIB);
- € 7.50 million via the issuance of bonds towards Patronale Life and Integrale (now Monument Assurance Belgium Services);
- € 5.6 million via the issuance of convertible bonds towards ABO;
- € 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

There are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which the BioSenic Group is aware), during the previous 12 months which may have, or have had in the recent past, significant effects on the BioSenic Group and/or its financial position or profitability.

3.5 Significant change in the financial position of the BioSenic Group since 31 December 2022

On 21 February 2023, BioSenic announced it received EUR 1 million (minus 6% taxes) from Pregene in accordance with the terminated license agreement.

From 1 January 2023 until 31 December 2023, a total of EUR 1.5 million of convertible bonds previously subscribed for by GTO 15 was converted into shares for a total of 41,283,728 shares. Following the conversions, the total of shares as of 31 December 2023 amounted to 163,181,474 shares.

In June 2023, BioSenic entered into an agreement with the ABO Securities' subsidiary, Global Tech Opportunities 15, to secure short term financing based on the existing convertible bond program. Subject to the terms and conditions of the agreement, BioSenic shall be entitled to draw down three tranches of each EUR 0.3 million in June, July, and August under the existing convertible bond program, for an aggregate principal amount of EUR 0.9 million. On 18 October 2023, BioSenic announced that it has reached a definitive agreement with GTO 15 with respect to the finalization of the existing convertible bonds program. GTO 15 will fund two tranches of EUR 300,000 each of the existing convertible bonds program. The two final tranches of 6 convertible bonds each were subscribed and fully paid-up by GTO 15 according to the subscription agreement of 30 May 2022 (as amended), respectively on 6 November 2023 and 20 November 2023 for a total amount of EUR 600,000.

In the first half of 2023, total operating income amounted to EUR 0.37 million, compared to EUR 0.13 million in 2022. Operating loss for the period amounted to EUR 3.90 million, compared to EUR 0.48 million in 2022. BioSenic ended June 2023 with EUR 0.52 million in cash and cash equivalents. Net cash used for the period amounted to EUR 1.33 million, compared to EUR 0.39 million in 2022.

On 14 September 2023, BioSenic announced that it had reached an agreement with Patronale, Monument and the European Investment Bank for the restructuring of its key financial debts for an aggregate outstanding principal amount of EUR 15.5 million plus accrued interests. Under the terms of the agreed binding term sheet, Patronale and Monument agreed to replace their outstanding loans granted to BioSenic for an aggregate outstanding principal amount of EUR 7.5 million plus accrued interests, by new convertible bonds to be issued by BioSenic. The convertible bonds will not be secured and will have a maturity date of 31 December 2030, which can be further extended by BioSenic for up to 24 months depending on its cash balance, end of 2032. BioSenic has also negotiated a lower interest rate of 5% per year, payable annually, with an additional non-compounding interest of 3% per year that will be added to the principal amount upon conversion or (p)repayment of a convertible bond. The convertible bonds will only become convertible as from 10 trading days after the announcement of the official remittance to the Regulatory Agency of the Final Clinical Report following the final results of BioSenic's phase 3 clinical trial of its lead Oral ATO therapeutic candidate targeting chronic graft versus host disease (cGVHD). The conversion price will be equal to 95% of the 30-calendar day VWAP immediately preceding the date of the conversion notice. The outstanding warrants of Patronale are being cancelled. The outstanding loan from the European Investment Bank ("EIB") for a principal outstanding amount of EUR 8 million should as well be extended to 2030, with the same 24-month extension possibility as for the new convertible bonds. The interest rate will also be aligned with the new convertible bonds. The outstanding warrants of the EIB should also be cancelled, and EIB should receive a similar return as Monument and Patronale if the new convertible bonds are effectively converted into shares. The key refinancing principles discussed with EIB remain subject to formal EIB approval. Completion of the refinancing of the loans granted by Patronale, Monument and the EIB will be subject to BioSenic raising sufficient new equity for BioSenic to continue its operations including the initiation of the patient treatment in Q1 2025 of a Phase 3 clinical trial of its lead Oral ATO therapeutic candidate targeting cGvHD.

End December 2023, the Company decided to convert the EUR 1,000,000 convertible bonds previously issued by Medsenic SAS to the Company, in accordance with the terms agreed upon on 8 September 2022. As a result of the conversion, the Company has increased its participation in its subsidiary Medsenic SAS by 0.81%, bringing its total participation in Medsenic SAS to 51.81%.

On 8 January 2024, BioSenic announced that it has signed a new subscription agreement for a maximum EUR 1.2 million convertible bonds facility, arranged by ABO Securities through its affiliated entity GTO 15.

On 2 February 2024, BioSenic announced that it raised €500,000 in gross proceeds through a private placement of 12,195,120 new shares at an issue price of €0,041 per share with institutional investors.

3.6 Current cash situation

BioSenic Group does currently not have sufficient working capital to meet its present requirements and cover the working capital needs for a period of at least 12 months as of the date of this Registration Document.

As of 31 December 2023, BioSenic had EUR 0.15 million in cash and cash equivalent. The Company is in the process of closing the ALLOB Phase 2b clinical trial, with many actions to be carried out to follow up the last patients recruited at the end of last year and the beginning of 2023, as well as the regulatory closure of the 24 European centers involved. BioSenic anticipates having sufficient cash to launch the Phase 3 clinical trials in cGvHD, considering the following relevant assumptions:

- Finalisation and implementation of the key terms that were agreed with certain key historical creditors of the Company to postpone the maturity date and interest payments of the ongoing loans for an aggregate principal amount of EUR 15.5 million.
- A full use of the new convertible bonds funding program with GTO 15 in Q1 2024. There are no liquidity conditions under the new funding program with GTO 15, other than that for the fourth tranche, the 20-day average daily value traded – trimmed for 10% of the outliers (meaning the data points from the top and bottom tails) – must be greater than EUR 15,000 prior to the disbursement of the tranche. GTO 15 can also terminate the funding program if a material adverse effect has occurred.
- BioSenic signed a term sheet in December 2023 with TrialCap Pte. Ltd. for a proposed debt and equity financing. In accordance with the term sheet, two term loan facilities of each up to USD 4,000,000 will be provided to BioSenic, as well as an equity investment of USD 800,000 in new shares of BioSenic. BioSenic is seeking the funds to continue its clinical development. Completion of the transactions set out in the term sheet is subject to the following conditions: (i) the satisfactory completion of due diligence by the lender, (ii) the signing of the definitive agreements for the debt and equity financing, (iii) the signing with a Clinical Research Organization and (iv) an equity raise by BioSenic of an amount to be further determined.
- A successful fundraising or the negotiation of a renewed convertible bond program.
- A reinforced strict policy of cost management.

The assumptions made above comprise various risks and uncertainties.

As the cash runway of the Company is currently expected into Q2 2024 (assuming the full use of the new convertible bonds program with GTO 15), BioSenic Group will continue to require additional financing to continue its operations in the longer turn. BioSenic Group therefore continues to evaluate other options with a potential positive impact on going concern, including as follows:

- *Fundraising*. BioSenic is currently preparing a fundraising to be organized in Q1 2024. Securing this fundraising will be a condition to a successful deal with the main creditors. BioSenic Group expects to use the proceeds of anticipated future fundraisings in priority for progressing the Phase 3 clinical trial in cGvHD. As a result, it will only be possible to start the SLE and SSc Phase 2b clinical trials if the BioSenic Group succeeds in concluding a strong partnership with a biopharmaceutical company or if it manages to successfully out-license some of its technology.
- *Potential partnership to develop and commercialize of JTA*. BioSenic, which does not intend to allocate R&D resources to support the clinical development of JTA-004, is seeking to collaborate with existing and potential partners to explore options for the future development of JTA-004 based on this new post-hoc analysis. Following disappointing Phase 3 clinical results, Biosenic transferred its rights to the JTA technology to the Walloon Region and consequently terminated the license and co-ownership agreement with Enrico Bastianelli SRL in 2022. In March 2023, however, BioSenic obtained new statistical analysis results from the JTA-004 Phase 3 clinical trial data. This new post-hoc analysis

changes the therapeutic profile of the molecule and potentially allows for the possibility of stratifying patients for a new, optimized Phase 3 clinical study. The agreement with respect to JTA technology (including Intellectual Property Rights forming the JTA-Gen1 patent families) has been since reacquired from the Walloon Region, as the Walloon Region accepted to retrocede its rights to the JTA technology to BioSenic Group in 2023. Although BioSenic has been discussing for quite some time the opportunity with Enrico Bastianelli SRL to enter into a co-ownership agreement for the old JTA-Gen1 patent families (i.e. the patent families BPBONE-001, BONE-002, BONE-011), such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement creates exploitation problems with third parties and possible licensees for the use of the JTA technology. This has therefore a negative impact on BioSenic's possibilities to collaborate with external partners for the future development and valorisation of the JTA technology as it exists.

- *Potential partnership to develop and commercialize of ALLOB*. In October 2022, BioSenic regained worldwide rights to develop, manufacture and commercialised ALLOB following the termination by Shenzhen Pregene Biopharma Co., Ltd ("**Pregene**") of the exclusive license agreement entered into between BioSenic, Pregene and Link Health Pharma Co., Ltd ("**LinkHealth**") in October 2020. Following the recovery of the worldwide rights to ALLOB, BioSenic received a final payment of € 1.00 million from Pregene linked to the achievement of a development milestone. Although regulatory changes in China have halted establishment of ALLOB in the Chinese market, BioSenic continues preliminary discussions with Pregene, LinkHealth and other potential partners to reach an agreement for the development and commercialization of ALLOB in other geographies, including in the U.S., based on the information collected by BioSenic's past preclinical research as well as the present review and work on the clinical trials performed.

All of the above circumstances and events are however subject to material uncertainties, which may cast significant doubt about the Company's ability to continue as a going concern.

If all convertible bonds have been subscribed for the aggregate amount of € 1.2 million and if BioSenic is not in breach of the subscription agreement of 8 January 2024 with Global Tech Opportunities 15 in any material respect, BioSenic has the option to renew the € 1.2 million program prior to 8 July 2024.

- BioSenic Group's net cash at the end of November 2023 amounted to € 377,000.
- The total use of funds by BioSenic Group in 2024 is expected to be € 9.2 million.
- Taking into account the net proceeds of the private placement announced on 2 February 2024 and assuming the full drawdown of the convertible bonds program, BioSenic Group currently expects its cash runway to extend into Q2 2024. The remaining net requirement in cash is expected to amount to approximately € 6.8 million in 2024. BioSenic Group has in its projections not taken into consideration yet any income from partnering activities which could positively impact the cash burn in the future.

The assumptions made above comprise various risks and uncertainties, mainly but not limited to the uncertainty to satisfy the conditions under the convertible bonds funding program with GTO 15 and the uncertainty related to the equity.

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 BioSenic'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 on Companies and Associations and the

articles of association, BioSenic 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 BioSenic'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 BioSenic is no longer under an obligation to pay such dividends.

3.7.2 *Dividend policy*

BioSenic has never declared or paid any dividends on its shares.

BioSenic's dividend policy will be determined by, and may change from time to time by determination of, BioSenic's Board of Directors. Any declaration of dividends will be based upon BioSenic'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 on Companies and Associations.

Belgian law and BioSenic's articles of association do not require BioSenic to declare dividends. The Board of Directors expects to retain all earnings, if any, generated by BioSenic's operations for the development and growth of its business. Also following the Contribution, the Board of Directors 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 BioSenic Group's business

Key Milestones of BioSenic	
YEAR 2023	
Corporate	• Appointment of Dr Carole Nicco as Chief Scientific Officer. • Appointment of Mr Yves Sagot as Independent Director. • BioSenic received EUR 1 million (minus 6% taxes) Pregene as a settlement following the termination by Pregene of the exclusive license agreement entered into between BioSenic, Pregene and Link Health Pharma. • Appointment of Lieven Huysse, MD as Chief Medical Officer. • Agreement with Patronale, Monument and the European Investment Bank for the restructuring of BioSenic's key financial debts.
ALLOB	• Optimization of ongoing Phase IIb clinical trial ALLOB and completion of patient recruitment. • BioSenic and Pluristyx sign term sheet for market availability of ALLOB mesenchymal cells. • BioSenic puts Phase IIb ALLOB trial on hold following negative results obtained for the primary endpoint (mid-June).
JTA	• Post-hoc analysis of the results of its Phase III trial of JTA-004 targeting knee osteoarthritis in the subset of patients with the most painful and inflammatory form of knee osteoarthritis shows a pain-relieving effect of JTA-004 not only superior to placebo but also to the active comparator. • BioSenic reacquired intellectual property rights to JTA-004 from the Walloon region.
Immune diseases	• Publication of data providing additional details about the mechanism of action of its lead API arsenic trioxide (ATO) to prevent autoimmune diseases published in the peer-reviewed paper *Frontiers in Immunology*[1]. • BioSenic received a key European patent from EPO, for further therapeutic development in cancer, infectious and immune disease covering the therapeutic use of a new composite formulation of anti-inflammatory compounds with unique advantages. • BioSenic identifies key biomarkers for cGvHD and submits patent to EPO. • Amendment of the license agreement between Medsenic SAS and Phebra Pty Ltd to extend the deadline for securing the necessary funding to commence the phase 3 clinical trial of OATO for the treatment of cGvHD from 31 May 2023 to 31 May 2024. • BioSenic received a Chinese patent protecting the combined use of metal ions and arsenic salts to treat a wide range of serious diseases. • Publication of data providing additional key indications of arsenic trioxide (ATO) to treat systemic sclerosis (SSc) in a peer-reviewed international journal[2]. • BioSenic completed a post-hoc analysis of its phase 2 clinical trial of ATO, finding the best scheme for administration of oral arsenic trioxide for an efficient treatment of cGvHD.

[1] Charlotte Chêne, Dominique Rongvaux-Gaïda, Marine Thomas, François Rieger, Carole Nicco, Frédéric Batteux "Optimal combination of arsenic trioxide and copper ions to prevent autoimmunity in a murine HOCl-induced model of systemic sclerosis", in *Front. Immunol.*, 30 March 2023, Volume 14. Link: https://www.frontiersin.org/articles/10.3389/fimmu.2023.1149869/full.

[2] Anne Cauvet, Arthur Decellas, Christophe Guignabert, Dominique Rongvaux-Gaïda, Raphaël Thuillet, Mina Ottaviani, Ly Tu, François Rieger, Jérôme Avouac and Yannick Allanore, "Arsenic trioxide demonstrates efficacy in a mouse model of preclinical systemic sclerosis". *Arthritis Res Ther* 25, 167 (2023). https://doi.org/10.1186/s13075-023-03143-2.

	• BioSenic signed (end of H2) a term sheet with Singapore based TrialCap Pte. Ltd. and/or other lenders for a proposed debt and equity financing. BioSenic is seeking the funds to continue its clinical development, backed by previous encouraging Phase 2 and pre-clinical results of arsenic trioxide (ATO).
YEAR 2024	
Corporate	• BioSenic signed a new subscription agreement for a maximum EUR 1.2 million convertible bonds facility, arranged by ABO Securities through its affiliated entity GTO 15. • Promotion of Dr Carole Nicco to Chief Operating Officer (COO) in addition to her position as Chief Scientific Officer (CSO). • BioSenic raises €500,000 in private placement of new shares with established new investors.
JTA	• BioSenic filed a U.S. patent for JTA-004, a viscosupplement in late-stage clinical development, following new evidence of its efficacy in a recently defined subtype of osteoarthritis (OA).
Immune diseases	• BioSenic signed a binding term sheet with Phebra Pty Ltd. related to the adaptation of the License Agreement and the MDA signed in May 2021. • BioSenic received a patent by the Canadian Intellectual Property Office to expand protection of the arsenic trioxide (ATO) platform.

4.2 Activities of the BioSenic Group

The BioSenic Group is a biotech company with operations in Belgium and in France focused on the development of new treatments for autoimmune diseases using arsenic trioxide (As(2)O(3)).

Through its subsidiary Medsenic, the BioSenic Group focuses on clinical trials in two selected autoimmune diseases. Two successful clinical trials were Phase II trials, which provided encouraging results for both safety of use and efficacy in moderate to severe SLE, first, and chronic GvHD second. These trials were allowed by the regulatory body in France (the *Agence Nationale de Sécurité du Médical et des produits de santé*) in multiple clinical sites, specialized in each given disease. Medsenic continues to gather scientific and medical data to enable the future launching of a new Phase II clinical trial on Systemic sclerosis on the basis of the latest research data and scientific findings for this indication.

Medsenic did not need to invest in lengthy preclinical and clinical (Phase I) studies since the arsenic trioxide used as the investigational drug was an intravenous formulation already used in cancer treatment (acute promyelocytic leukaemia (APL)) and was accepted by FDA and EMA not only for research purposes but also for human use in this particular oncologic indication, with good pharmacovigilance since its market authorizations in the year 2002. BioSenic Group foresees that the clinical data this has created during the last two decades will be acceptable for its trial submissions of new indications in the field of autoimmunity and inflammatory diseases and of new formulations of ATO, including OATO (with proven bioavalability and bioequivalence with IV formulation). However, any formulation of arsenic trioxide involving a combination of matter with another element, will in principle require a Phase I clinical trial to establish the safety and bioavalability and bioequivalence.

Medsenic devoted its efforts to preclinical studies on cells in vitro and animal models of diseases of the immune system, targets of its clinical development, with the particular objective to understand its mechanisms of action, in order to better define the dosage necessary for positive therapeutic action and the best route of administration given the sites of the lesions of each disease considered. Over ten years, the clinical development has been accompanied by the successive completion of animal studies on SLE (with three different animal models, including studies developed with the University of Louvain. Profs Houssiau and Lauwerys; internal Medicine), Crohn's disease, Multiple sclerosis with a recognized Experimental Allergic Encephalomyelitis, chronic GvHD, an animal model quasi identical to the human disease, and a model for

Systemic Sclerosis (Fra 2 and HOCI mice models, in Hospital Cochin; Prof Y. Allanore, 3 articles published in 2022 abd 2023). All these studies provide encouraging results regarding the treatment of these autoimmune diseases by arsenic trioxide and justify Medsenic's efforts to set up the conditions for using oral arsenic trioxide for patients' and clinicians' benefit (lower dosage and lower reversible adverse effects, at our chosen levels of medication).

BioSenic also proceeded to past clinical development in the field of orthopaedics through its JTA-004 and ALLOB assets. At the date of this Registration Document, the trials are ended, the data is further analysed, and partnerships are being searched in this respect.

4.3 BioSenic Group's mission and strategy

BioSenic Group (through its subsidiary Medsenic) aims to exploit the new possibilities offered by the therapeutic use of arsenic trioxide (As(2)O(3)) and thereby provide treatment for patients with autoimmune diseases. To achieve this objective, Medsenic is pursuing the following strategies:

- Find funding in order to recruit patients and perform the Phase III randomized, on top of standard care, against placebo clinical trial for the use of oral arsenic trioxide for cGvHD, its lead project, over the next four years.

- Search for solid partnerships with interested biopharmaceutical companies for performing the clinical trials ready to start for two Phase II randomized, on top of standard care, against placebo for SLE and SSc.

- Get deeper into the mechanisms of action of arsenic trioxide to prove to the medical community at large (KOLs and leading clinicians in the field of inflammation/autoimmunity) its quality of first-in-class medication of a series of closely related autoimmune diseases.

- Focus on the US market as BioSenic Group believes that US patients and clinicians will more readily accept the premises of arsenic trioxide in its applicability to cGvHD. Moreover, BioSenic believes that the FDA is quick to appreciate new ways to treat a disease with unmet medical needs in the field of immuno-oncology. Finally, approval of a new drug application by the FDA will ensure central market access throughout the U.S.

- BioSenic is also looking for partnership opportunities allowing the further development of its existing assets JTA-004 and ALLOB, for which BioSenic no longer envisages conducting the clinical development itself.

BioSenic Group also applies for the following European Innovation Council fundings:

- In 2024: EIC Accelerator Grant funding which is in two periods. First a non-dilutive, up to € 2.5 million, for innovation activities only (TRL 5-8), to be completed within 24 months (2025-2027) to develop an improved arsenic trioxide oral formulation. Second a dilutive, up to € 15 million, for market deployment (TRL 9), «patient capital» principle with a 7-10 years perspective, to finance a clinical trial with the new formulation for systemic sclerosis patients.

- In 2025: EIC Pathfinder Open provides funding for projects, based on high-risk/high-gain science-towards-technology breakthrough interdisciplinary research. BioSenic will apply for up 3.5 million euro to support early stage development of future technologies to treat severe inflammatory osteoarthritis.

4.4 Technology

BioSenic's cell repair technology is based on its cutting-edge allogeneic cell and gene therapy platform with differentiated bone marrow sourced Mesenchymal Stromal Cells (MSCs) which can be stored at the point of use in the hospital. Its leading investigational medicinal product, ALLOB, represents a unique, proprietary approach to bone regeneration, which turns undifferentiated stromal cells from healthy donors into bone-

forming cells. These cells are produced via BioSenic's scalable manufacturing process and should lead to interesting development, allowed by both genetic engineering to confer them with new therapeutic properties and the development of new techniques to obtain nucleus free nanoparticles, carrying analogous properties than the intact cells, which could additionally loaded with small molecules with therapeutic properties, like arsenic salts. ALLOB has been evaluated in a randomized, double-blind, placebo-controlled Phase IIb study in patients with high-risk tibial fractures, using its optimized production process. ALLOB has been evaluated for other orthopaedic indications including spinal fusion, with interesting potentialities to be further developed.

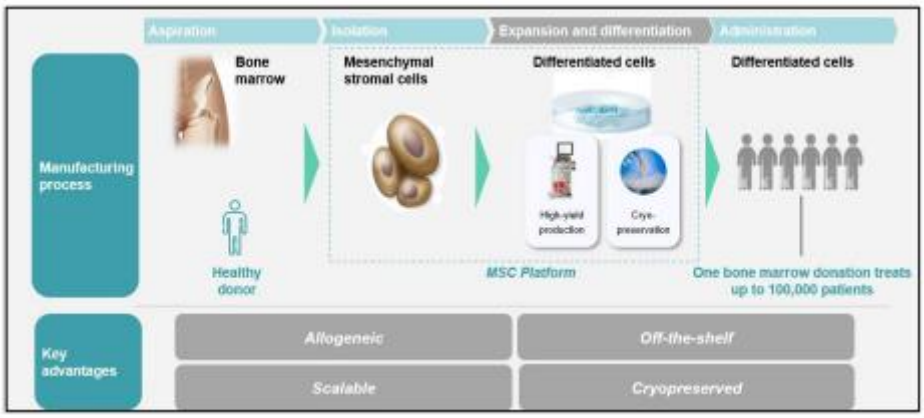
The inflammation/immunopathology technology brought by BioSenic's subsidiary Medsenic, consists essentially in various formulations of arsenic trioxide existing or to be further developed depending on the indication. Medsenic masters the liquid IV mode of administration and now a patented oral type of formulation for easiness of use and decreased adverse effects.

BioSenic Group believes that it will be interesting to examine the anti-inflammatory properties of arsenic trioxide in combination with the anti-inflammatory properties of the MSCs (ALLOB) cells, which could potentially have a complementary effect. The activities to be developed on the basis of MSCs (ALLOB) cells are not only restricted to bone repair but could potentially also be applied to tissue repair. As tissue damage is observed in autoimmune diseases, BioSenic Group would like to examine if innovative techniques from the use of MSCs (ALLOB) cells can be applied to the autoimmune diseases treatable by arsenic trioxide.

4.4.1 *ALLOB: allogeneic cell product (clinical trial activities discontinued; search for partnership opportunities)*

ALLOB is BioSenic's off-the-shelf, allogeneic cell therapy platform consisting of human allogeneic bone-forming cells derived from *ex-vivo* cultured bone marrow mesenchymal stromal cells (MSC) from healthy adult donors, offering numerous advantages in product quality, injectable quantity, production, logistics and cost as compared to an autologous approach.

To address critical factors for the development and commercialization of its cell therapy products, BioSenic has established a proprietary, optimized cell production process that improves consistency, scalability, cost effectiveness and ease of use of the product ALLOB or its possible innovative derivatives, whenever they will be deemed necessary in the course of BioSenic's business development. This optimized cell production process has significantly increased the production yield, generating 100,000 of doses of ALLOB per bone marrow donation. Additionally, the final ALLOB product will be cryopreserved, enabling easy shipment and the capability to be stored in a frozen form at the hospital level. The process will therefore substantially reduce overall production costs, simplify supply chain logistics, improve patient accessibility, and facilitate global commercialization.



The above scheme shows the manufacturing process of BioSenic'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.

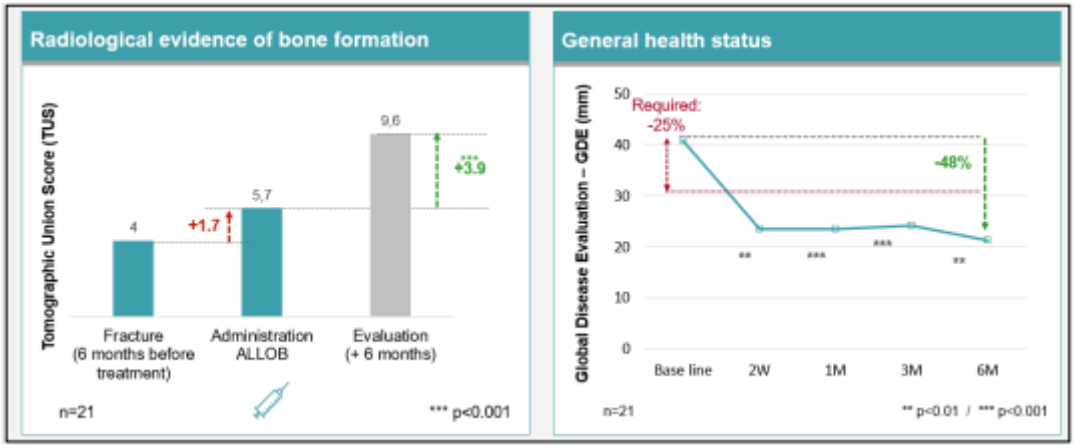
ALLOB targets one indication: difficult tibial fractures and could be further developed for lumbar spinal fusion.

a. ALLOB – Difficult fractures

Although most fractures heal normally, some fractures may not heal within the usual time frame and is known as delayed bone healing within 4 to 6 months and absence of bone healing within 9 to 12 months in the most severe cases. Several factors can increase the risks of delayed healing complications like, for example, smoking, violent shocks (for example, due to a road accident) or even the type of fracture (an open fracture). The location of the fracture is also an important factor: among the bones of the arms and legs, the tibia is known for being the most at risk for complications. Tibial fractures with several risk factors could lead to complications such as delayed union and greatly reduce the quality of life. To date, there is no treatment for fractures considered at risk of delayed complications. The current practice on diagnosis of complications is to wait at least 6-12 months before considering alternative interventions to promote fracture healing.

Constituted of bone cells produced from the bone marrow of healthy adult donors, ALLOB cells have shown to be capable of forming bone and repairing fractures after injection in preclinical studies. When directly injected into a fracture, ALLOB cells should therefore promote the healing of the fracture by re-establishing a healthy environment, stimulating bone healing, reducing healing time, reducing repair complications, and thus to lead to improvement of the quality of life for the patient.

ALLOB has shown preliminary evidence of effectiveness in the treatment of delayed bone healing fractures in a Phase I/IIa study involving 21 patients. The study demonstrated efficacy in bone formation and improvement of general health status, when injected three months after the fracture. 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. Radiological evaluation of fracture healing showed an improvement of 3.9 points on average on the TUS scale, nearly twice the required minimum of 2.0 points. This minimum two-point increase was achieved by 16 out of 21 patients (76%). The Global Disease Evaluation (GDE) score to assess the general health condition of the patient, improved 48% on average. The minimum 25% improvement was achieved by 16 out of 21 patients (76%).



ALLOB has been evaluated in a Phase IIb study in patients with expected difficult-to-heal tibial fracture. The Phase IIb study was a randomized, double-blind, placebo-controlled study. In this study, the potential of ALLOB to accelerate fracture healing and prevent late-stage complications in patients with difficult fractures in the shinbone (tibia), was tested and compared to placebo, on top of standard of care after a follow-up period of 6 months. ALLOB was applied – at variance to the first study – by a single percutaneous injection 24-96 hours post reduction surgery in patients with fresh tibial fractures, thought to be 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). The study had been expected to enrol 178 patients in over 40 sites. However, BioSenic managed to improve the statistical analysis of the study via an optimal radiological assessment of the acceleration of bone formation at 3 months following an intra-fracture administration of ALLOB, compared to standard practice alone. This allowed BioSenic to reduce the number of required patients to 132 evaluable patients while maintaining the same statistical power. In addition, BioSenic also introduced an interim analysis based on the assessment of radiological data from approximately 66 evaluable patients at 3 months post-

administration. Following the CTA approval by regulatory authorities in Europe, BioSenic had initiated patient recruitment in January 2021 and reached the inclusion of 56 patients, in January 2023. In June 2023, BioSenic announced that it decided to suspend the Phase IIB study in light of the negative results obtained for the study's primary endpoint. BioSenic is currently looking for partnership opportunities allowing the further development of ALLOB, for which BioSenic no longer envisages conducting the clinical development itself. If no concrete licensing options would materialise in the near future, BioSenic does not exclude that it might stop its efforts to seek collaborations with external partners for the future development of ALLOB.

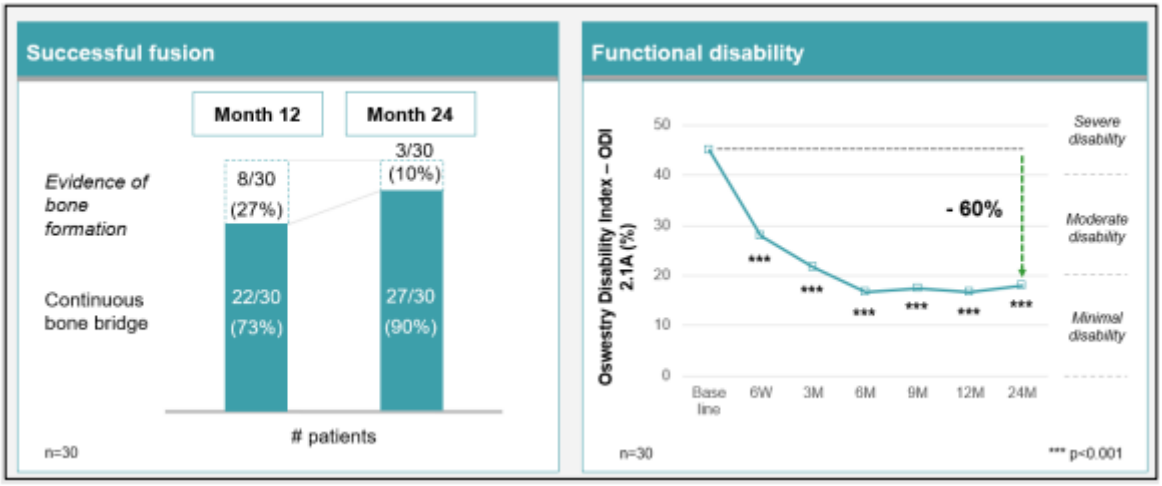
b. ALLOB – Lumbar spinal fusion

Due to ageing populations and sedentary lifestyles, the number of people suffering from degenerative spine disorders continues to increase. Today, spinal fusion procedures are performed to relieve pain and improve patient daily functioning in a broad spectrum of degenerative spine disorders. Spinal fusion consists of bridging two or more vertebrae with the use of a cage and graft material, traditionally autologous bone graft or demineralized bone matrix – placed into the intervertebral space – for fusing an unstable portion of the spine and immobilizing a painful intervertebral motion segment.

Over 1,000,000 spinal fusion procedures are performed annually in the US and EU, of which half at lumbar level and the market is growing at a rate of 5% per year. Although spinal fusion surgery is routine, non-fusion, slow progression to fusion and failure to eliminate pain are still frequent with up to 35% of patients not being satisfied with their surgery.

A multi-center, open-label proof-of-concept Phase IIa study was designed to evaluate the safety and efficacy of ALLOB administered in addition to the standard of care procedure in which an interbody cage with bioceramic granules is implanted into the spine to achieve fusion of the lumbar vertebrae. The main endpoints of the 24-month follow-up analysis included safety and radiological assessments to evaluate vertebrae fusion (continuous bone bridges) and clinical assessments to evaluate improvement in patients' functional disability as well as reduction in back and leg pain. The study evaluated 30 patients treated with ALLOB, 29 patients attended the 24-month visit.

In the Phase IIa study, ALLOB Lumbar Spinal Fusion showed promising 24-month results in bone formation and disability reduction. The 24-month data showed 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.

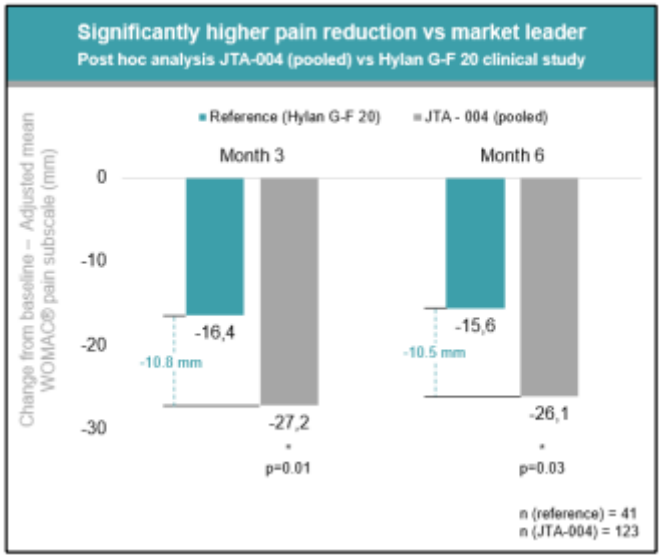


4.4.2 *JTA-004: off-the-shelf three components solution (clinical trial activities discontinued; search for partnership opportunities)*

JTA-004 is a next generation of intra-articular injectable for the treatment of osteoarthritic pain in the knee. Consisting of a unique patented mix of plasma proteins, hyaluronic acid a natural component of knee synovial fluid, and a fast-acting analgesic, JTA-004 intends to provide added lubrication and protection to the cartilage of the arthritic joint and to alleviate osteoarthritic pain.

Osteoarthritis (OA), also known as degenerative joint disease, is the most common chronic joint condition in which the protective cartilage in the joints progressively break 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 250 million cases worldwide. The prevalence of knee osteoarthritis (KOA) is expected to increase in the coming years due to increasingly aging and obese population. Currently, there is no cure for KOA and treatments focus on relieving and controlling pain and symptoms, while 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 led to highly invasive surgical interventions such as total knee replacement.

In a completed Phase IIb study involving 164 patients, JTA-004 showed an improved pain relief at 3 and 6 months compared to Hylan G-F 20, the global market leader in osteoarthritis treatment.



In August 2021, BioSenic announced the topline results from the multicentre, 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. This is still under investigation and may justify further work on a particular subtype of patients with very active knee osteoarthritis.

In March 2022, BioSenic announced it was redefining its strategic priorities and all activities related to the development of the pre-clinical iMSCg platform as well as all other non ALLOB related activities, including the further development or reshaping of JTA-004, were put, transiently at least, on hold. Although the primary and consequently key secondary endpoints of the Phase III trial with JTA-004 were not reached, BioSenic announced in March 2023 that a post-hoc analysis indicated that a statistically significant difference in favour of JTA-004 and the active comparator versus placebo was seen in a subset of patients with higher pain scores

at entry. BioSenic is therefore seeking to collaborate with existing and potential partners to explore options for the future development of JTA-004 based on this new post-hoc analysis.

4.4.3 *Arsenic trioxide (ATO)*

ATO is currently classified as an antineoplastic agent (ATC code L01XX27: Anti immunomodulating agents – other antineoplastic agents). The classification as chemotherapy results from its first established properties as an anti-cancer agent. In the case of a successful outcome of the envisaged clinical trials of the BioSenic Group based on ATO, it can be expected that ATO will also become classified as anti-inflammatory or immunomodulatory agent.

ATO in Oncology

Arsenic derivatives have been identified as compounds with therapeutic potential for over 2000 years in Greek and Chinese medicine. Orally administered arsenic, in the form of Fowler's Solution was first discovered to have leuco-reductive properties and used in the treatment of leukaemia in 1878. Since then, ATO (Trisenox®) has been investigated and used in the treatment of various types of leukaemia including chronic myeloid leukaemia (CML) and acute promyelocytic leukaemia (APL).

ATO in autoimmune and inflammatory indications

Pre-clinical studies

Although ATO can potentially be widely used in many auto-immune diseases that benefit from its dual mechanism of action (induction of apoptosis in activated, pathogenic cells and regulatory action on pro-inflammatory cytokine levels), Medsenic focus on Chronic Graft versus Host Disease (cGvHD), moderate to severe Systemic Lupus erythematosus (SLE) and Systemic Sclerosis (SSc) is based on preclinical studies which provided good preliminary data for the ensuing clinical studies in human patients.

The role of ATO has also been explored in murine models of autoimmune and inflammatory diseases (Bobe et al., 2006)[3].

Intraperitoneal administration of ATO was able to achieve quasi total regression of antibody and cell mediated manifestations in MRL lymphoproliferative strain (MRL/*lpr*) mice. ATO was also shown to eliminate, through activation of caspases, activated autoreactive T lymphocytes responsible for lymphoproliferation and skin, lung and kidney lesions, leading to significant prolonged survival rates. ATO markedly reduced anti-DNA autoantibodies, rheumatoid factor, Interleukin 18 (IL-18), interferon gamma (IFN-γ), nitric oxide metabolite, Tumor necrosis factor alpha (TNF-α), Fas ligand, and Interleukin – 10 (IL-10) levels. Furthermore, ATO restored cellular reduced glutathione levels, thereby limiting the toxic effect of nitric oxide overproduced in MPR/*lpr* mice. Overall, ATO protected young mice from developing the syndrome and induced almost total disease disappearance in older affected mice (Bobe et al., 2006).

In a Trinitrobenzene sulfonic acid (TNBS) induced colitis model of inflammatory bowel disease, ATO used either in a preventive or curative mode markedly reduced the induced colitis, leading to prolonged mice survival. In addition, intraperitoneal ATO was able to inhibit NF-κB expression and DNA-binding in colon extracts, leading to decreased cytokine gene expression (i.e., TNFα, IL-1β, IL-12, IL-17, IL-18 and IL-23). Furthermore, ATO reduced nitric oxide synthase and highly enhanced procaspase-3 and activated caspase-3, leading to neutrophil elimination by probably inducing apoptosis (Singer et al., 2011)[4].

[3] Bobé P, Bonardelle D, Benihoud K, Opolon P, Chelbi-Alix MK. Arsenic trioxide: A promising novel therapeutic agent for lymphoproliferative and autoimmune syndromes in MRL/lpr mice. Blood. 2006 Dec 15;108(13):3967–75.

[4] Singer M, Trugnan G and Chelbi-Alix M.K. Arsenic trioxide reduces 2,4,6-trinitrobenzene sulfonic acid-induced murine colitis via nuclear factor- κB down-regulation and caspase-3 activation, in *Innate Immunity*, 2011 Aug;17(4):365-74. doi: 10.1177/1753425910371668. Epub 2010 Aug 6. Abstract.

In a murine model of scleroderma (hypochlorite induced), (Kavian et al., 2012)[5], intraperitoneal ATO inhibited the production of autoantibodies and was associated with a clinical benefit, as shown by the reduced skin and lung fibrosis. These beneficial effects were mediated through reactive oxygen species (ROS) generation that selectively killed activated pathogenic fibroblast containing low levels of glutathione.

In the direct murine model of sclerodermatous cGvHD (Kavian et al., 2012), the ATO effect was reportedly mediated through the depletion of glutathione and the overproduction of Hhat killed activated CD4 T cells, in particular Th17 cells, and plasmacytoid dendritic cells, two key cell types in cGvHD pathophysiology initiation.

The above studies show arsenic trioxide is an active medication for a series of autoimmune disorders and may be used in clinical trials since it gives positive data at the preclinical level to substantiate promising expectations for clinical studies at the proof of concept or observatory levels (Phase II type studies).

Clinical studies

Medsenic is first developing the use of arsenic trioxide (ATO) for the treatment of Chronic Graft versus Host Disease (cGvHD), moderate to severe Systemic Lupus erythematosus (SLE) and Systemic Sclerosis (SSc). The initial clinical work of Medsenic with ATO was based on the development of an IV formulation, ArsciMed. Given the challenges with the IV administration for both patients and hospitals, Medsenic is now focussing on the use of a patented oral formulation of ATO. The bioequivalence of oral ATO with IV ATO has been shown by Medsenic in a bioavailability study APML5. Please see Section 4.9 for more details.

a. cGvHD

Graft versus Host Disease is one of the most common and clinically significant complications affecting long-term survivors of allogeneic hematopoietic stem cell transplantation. GvHD is divided into two main categories: acute and chronic. GvHD is primarily mediated by the transplanted immune system that can lead to severe multiorgan damage and represents one of the major limitations of allogeneic hematopoietic cell transplantation, with substantial morbidity and mortality. It is estimated that 30% to 70% of patients surviving more than 100 days will develop chronic GvHD (cGvHD)[6]. GvHD is the cause of death in up to one third of all long-term survivors after transplantation for leukaemia. Furthermore, cGvHD is consistently associated with decreased quality of life, impaired functional status, ongoing need for immunosuppressive medications and infectious complications. The cGvHD condition is a challenge clinically because it is a systemic disease, affecting several organs and functions and corticosteroids remain the primary therapy available at present.

Medsenic already completed two Phase II clinical trials with ATO in relation to cGvHD. The first clinical trial (Study GMED16-001) investigated the overall response rate to treatment with ATO in combination with prednisone with or without cyclosporine. As this trial was conducted with an IV formulation of ATO developed by Medsenic and given that the envisaged Phase III trial will be using an oral formulation of ATO rather than IV ATO, a bioavailability study (Study APML5) was also carried out, which successfully confirmed the bioequivalence of the two formulations. The clinical protocol of phase II is now easily extrapolated to a planned Phase III clinical trial for a confirmatory treatment of cGvHD and essentially involves a limited course of daily administration of arsenic trioxide in an oral form, executed over a limited period of time, i.e. three to four weeks, with a possible additional course of equivalent time of administration (that is possibly two cycles of treatment) in the case of a positive, long term result, justified by the mode of action of arsenic trioxide, which has been found to change the pathological immune system, giving some type of immune tolerance to the treated organism and thus return to homeostasis and normal functioning. Please revert to Section 4.9.4 for more information about the clinical trials.

b. SLE

Systemic lupus erythematosus (SLE) is the most common type of lupus. SLE is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. The seriousness of SLE

[5] Kavian N, Marut W, Servettaz A, et al. Reactive oxygen species-mediated killing of activated fibroblasts by arsenic trioxide ameliorates fibrosis in a murine model of systemic sclerosis. Arthritis Rheum. 2012 Oct;64(10):3430–3440. Abstract.
[6] Cooke et al., The Biology of Chronic Graft-versus-Host Disease: A Task Force Report from the National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease, Biol Blood Marrow Transplant 23 (2017) 211–234.

can range from mild to life-threatening. SLE can limit a person's physical, mental, and social functioning. These limitations experienced by people with SLE can impact their quality of life, especially if they experience fatigue. Fatigue is the most common symptom negatively affecting the quality of life of people with SLE. Based on available data on incidence, it is estimated that each year 16,000 to 17,000 persons are newly diagnosed with lupus in the United States, of which approximately 70% suffer from SLE. An estimated number of 1.5 million Americans, and at least 5 million people worldwide have a form of lupus[7]. There is currently no cure for lupus, in spite of many clinical trials, some reaching some positive results in delaying the disease or decreasing symptoms.

The same scheme of treatment as for cGvHD will be applied to SLE patients. A Phase IIa clinical trial for SLE conducted by Medsenic on a limited cohort of SLE patients has previously established proof of concept of safety for the patient and efficacy on the course of the autoimmune disease, published in 2021.[8]

c. SSc

Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterised by excessive production and accumulation of collagen, called fibrosis, in the skin and internal organs and by injuries to small arteries. SSc is often categorised as "limited" or "diffuse" referring to the degree of skin involvement. The limited form affects areas below, but not above, the elbows and knees with or without involvement of the face. The diffuse form also affects the skin above the elbows and knees and can also spread to the torso. Visceral organs, including the kidneys, heart, lungs, and gastrointestinal tract can also be affected by the fibrotic process. Prognosis is determined by the form of the disease and the extent of visceral involvement. Patients with limited systemic sclerosis have a better prognosis than those with the diffuse form. Death is most often caused by lung, heart, and kidney involvement. Overall 10-year survival is 90% for limited systemic sclerosis and is 70% for diffuse systemic sclerosis.[9] Predictors of early mortality include male sex, late onset, diffuse disease, pulmonary arterial hypertension, and renal crisis. There is currently no cure for SSc.

Also for systemic sclerosis patients BioSenic Group intends to apply the same scheme of treatment as described in paragraph a. above, with the limitation that only preclinical data are available on two different models of SSc in the mouse. These preclinical data are positive and highly encouraging to proceed towards human clinical trials.

Given that the safety of ATO has been well established in the framework of human cancer patients studies and recognised by the FDA and EMA, this will allow the BioSenic Group to enter into clinical trials for SSc at the level of Phase II. The protocol for the Phase II trial is largely finalised, before an IND meeting can be submitted and the trial can start.

d. Septic shock and other indications

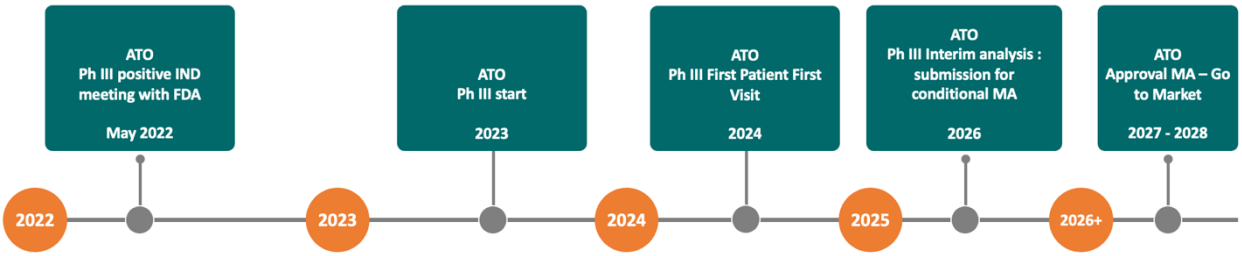
Preclinical data validating the positive action of ATO on animal models show that septic shock is potentially also amenable to treatment with ATO. The same could apply for other diseases such as Crohn's disease, rheumatoid arthritis, multiple sclerosis and COVID 19 (Long COVID). However, given the current phase of development of the BioSenic Group and the funding available, the Group is currently concentrating on cGvHD, SLE and SSc. Although direct preclinical work for septic shock (on the bacteria most commonly found in sepsis in humans) still needs to be carried out by the BioSenic Group in complex and potentially dangerous experiments in a high safety L4 laboratory, the consequences of a septic shock are however known, with specific cytokines released in excessive quantities. These cytokines are indeed established targets of arsenic in the recent preclinical experiments of BioSenic Group. Sepsis is thus the most likely next candidate for the further expansion of the clinical pipeline of BioSenic Group (funding permitting).

[7] Best estimates of the Lupus Foundation of America, https://www.lupus.org/resources/lupus-facts-and-statistics.
[8] Mohamed Hamidou, Antoine Néel, Joel Poupon, Zahir Amoura, Mikael Ebbo, Jean Sibilia, Jean-Francois Viallard, Benjamin Gaborit, Christelle Volteau, Jean Benoit Hardouin, Eric Hachulla and François Rieger, Safety and efficacy of low-dose intravenous arsenic trioxide in systemic lupus erythematosus: an open-label phase IIa trial (Lupsenic), Arthritis Res Ther. 2021, Mar 3, 23(&):70. Doi: 10.1186/s13075-021-02454-6. Abstract.
[9] BioSenic's estimation.

4.5 Current clinical pipeline and outlook

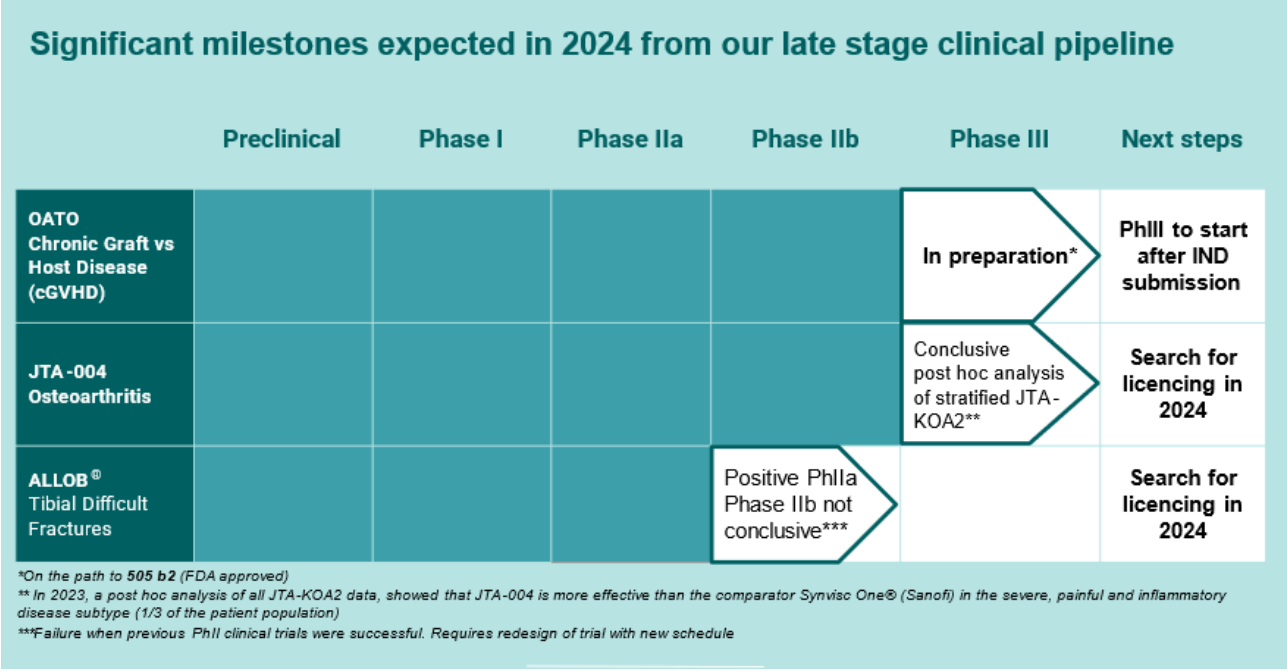
Currently BioSenic Group is concentrating specifically on the preparation of a Phase III clinical trial for the use of oral arsenic trioxide for the treatment of cGvHD, which is expected to take approximately 4 years to complete the last patient visit.

See the summary timeline below for more details on these two clinical assets.



BioSenic's subsidiary Medsenic has completed the set-up of the technical conditions (regulatory, CRO designation and clinical centers identification) for the Phase III clinical trial for the use of oral arsenic trioxide to treat cGvHD. BioSenic started the process to formally engage the CRO and is currently expecting to treat the first recruited patient in Q1 2025, subject to BioSenic finding additional equity or debt financing for the start of the CRO preparation, sites selection and data collection for this clinical trial.

Future Pipeline Development



BioSenic Group will continue to prepare for the start of its Phase III for the use of oral arsenic trioxide for cGvHD and, in parallel, BioSenic Group will search for partnerships with interested biopharmaceutical companies for performing the two Phase II clinical trials, randomized, on top of standard care, against placebo for SLE and SSc. BioSenic Group expects to use the existing cash and the proceeds of anticipated future fundraisings (via shares or (convertible) bonds) in priority for progressing the Phase III clinical trial in cGvHD. As a result, it will only be possible to start the SLE and SSc Phase II clinical trials if the BioSenic Group succeeds in concluding a strong partnership with a biopharmaceutical company or if it manages to successfully out-

license some of its technology. The start of SLE and SSc Phase II clinical trials is therefore not envisioned before end of 2024.

Outlook

In October 2022, BioSenic regained worldwide rights to develop, manufacture and commercialised ALLOB following the termination by Shenzhen Pregene Biopharma Co., Ltd ("**Pregene**") of the exclusive license agreement entered into between BioSenic, Pregene and Link Health Pharma Co., Ltd ("**LinkHealth**") in October 2020. Although regulatory changes in China have halted establishment of ALLOB in the Chinese market, BioSenic has started preliminary discussions with Pregene, LinkHealth and other potential partners to reach an agreement for the development and commercialization of ALLOB in other geographies, including in the U.S., based on the information collected by BioSenic's past preclinical research as well as the present review and work on the clinical trials performed.

In March 2023, BioSenic has obtained new statistical analysis results from the JTA-004 Phase III clinical trial data. This new post-hoc analysis changes the therapeutic profile of the molecule and potentially allows for the possibility of stratifying patients for a new, optimized Phase III clinical study. BioSenic, which does not intend to allocate R&D resources to support the clinical development of JTA-004, is seeking to collaborate with existing and potential partners to explore options for the future development of JTA-004 based on this new post-hoc analysis. However, following disappointing Phase III clinical results, Biosenic terminated the license and co-ownership agreement and transferred its rights to the JTA-004 technology to the Walloon Region in 2022. The agreement with respect to the JTA-004 patent and technology has been since reacquired from the Walloon Region, as the Walloon Region accepted to retrocede its rights to the JTA-004 technology to BioSenic in 2023. Although BioSenic has been discussing for quite some time the opportunity with Enrico Bastianelli SRL to enter into a co-ownership agreement for the old JTA-Gen1 patent families (i.e. the patent families BPBONE-001, BONE-002, BONE-011), such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement creates exploitation problems with third parties and possible licensees for the use of the JTA technology. This has therefore a negative impact on BioSenic's possibilities to collaborate with external partners for the future development and valorisation of the JTA technology as it exists. On 23 January 2024, BioSenic announced the filing of a U.S. patent for a specific indication (a subtype of inflammatory OA) of JTA-004, making obsolete the previous global patented claims of treating "Osteoarthritis" as a wholly characterized disease.

The Medsenic Phase II clinical study with arsenic trioxide in the first-line treatment of cGvHD is complete and provided positive results. A Phase III study with oral arsenic trioxide in the first-line treatment of cGvHD, for which Medsenic received positive pre-IND response from the FDA, is currently anticipated to start in 2024. A phase IIa clinical trial for systemic lupus erythematosus ("**SLE**") had previously established safety for the patient and efficacy on the course of the autoimmune disease. Positive preclinical work gives good grounds for a Phase II clinical trial on systemic sclerosis ("**SSc**"). Phase IIb clinical trials for SLE and SSc are in the planning stage with the protocols for both studies being ready.

BioSenic Group expects for 2024 to use the proceeds of anticipated fundraisings in priority for progressing the Phase III clinical trial with arsenic trioxide (ATO) to treat chronic graft versus host disease (cGvHD), for which patient treatment is currently scheduled to start in Q1 2025. As a result, it will only be possible to start the SLE and SSc Phase IIb clinical trials if the BioSenic Group succeeds in concluding a strong partnership with a biopharmaceutical company or if it manages to successfully out-license some of its technology. The start of SLE and SSc Phase II clinical trials is therefore not envisioned before the end of 2024.

BioSenic Group also expects to materialise the binding term-sheet signed with Phebra Pty Ltd. related to the adaptation of the License Agreement and the MDA signed in May 2021. Please revert to Section 6.4.4.2 of this Registration Document for more information.

Disciplined cost and cash management will remain a key priority. The situation will be actively and closely monitored.

4.6 Principal autoimmune markets

The below table summarises the market size, opportunities and competition for the treatments of cGvHD, SLE and SSc:

	ATO	ATO	ATO
	Chronic Graft vs Host Disease (cGVHD)	**Systemic Lupus Erythematosus (SLE)**	**Systemic Sclerosis (SSc)**
Addressable Population	Pool/Incidence USA : 32'462/4'061 Europe : 28'276/3'342	Pool/Incidence USA : 201'297/16'960 Europe : 179'588/9'469	Pool/Incidence USA : 79'656/ 6'207 Europe : 50'284/3'918
Market Size (patients)	15'184/1'851	125'692/8'722	42'880/3'341
Peak Sales (Forecast)	400-500m€	3-4b€	1-1,5b€
Competition	• **No real treatment** on the market. Other actual tested medications are second or third line therapies.	• **No real treatment** on the market. Other actual tested medications are second or third line therapies.	• **No real treatment** on the market. Other actual tested medications are second or third line therapies.
Unmet Medical Need	• **First line treatment** to replace the only existing treatment is ciclosporin and corticosteroids	• **First line treatment** to replace the only existing treatment is ciclosporin and corticosteroids	• **First line treatment** to replace the only existing treatment is mycophenolate mofetil (MMF) and small doses of corticosteroids

Source: Non-public info provided by Phebra to Medsenic in 2022; Market Analysis NextStep 2019; Nature 2022; IPSOR Survey with data from EMBT; ASTCT; NIH; SNFMI Top 7: EU5, US, JP & CN (2020)

4.6.1 *Chronic Graft versus Host Disease*

Graft versus Host Disease (GvHD) is one of the most common and clinically significant complications affecting long-term survivors of allogeneic hematopoietic stem cell transplantation (allo-SCT). GvHD is primarily mediated by the transplanted immune system that can lead to severe multiorgan damage and represents one of the major limitations of allogeneic hematopoietic cell transplantation (HSCT), with substantial morbidity and mortality. It is estimated that 30% to 70% of patients surviving more than 100 days will develop chronic GvHD (cGvHD). GvHD is the cause of death in up to one third of all long-term survivors after transplantation for leukaemia. Furthermore, cGvHD is consistently associated with decreased quality of life, impaired functional status, ongoing need for immunosuppressive medications and infectious complications. The cGvHD condition is a challenge clinically and corticosteroids remain the primary therapy available at present. (Socié and Ritz, 2014)[10].

GvHD is divided into two main categories: acute and chronic. While these categories were historically defined as clinical manifestations before and after day 100 post-transplant, respectively, the National Institute of Health (NIH) Consensus Development Projects on Criteria for Clinical Trials in Chronic GvHD abolished the day 100 as the time limit in 2005 (refined in 2014). Characteristics of each category are detailed in Table 1.

[10] Gérard Socié and Jerome Ritz. Current issues in chronic graft-versus-host disease. Blood. 2014 Jul 17;124(3):374-384. doi: 10.1182/blood-2014-01-514752. Epub 2014 Jun 9. Article.

Table 1: Comparison of the 2 categories of GvHD

	Acute GvHD (aGvHD)	**Chronic GvHD (cGvHD)**
Timing of Onset	Usually manifests within 100 days (most typically within 20-40 days) after HSCT; Can also present as persistent, recurrent (relapse of an earlier episode), or late- onset acute GvHD occurring more than 100 days after transplantation	Generally manifests more than 100 days after HSCT
Clinical Manifestation Locations	Skin, liver, gastrointestinal tract	Skin, mouth, eyes, liver, lung, vagina, esophagus, nails, hair, musculoskeletal, kidney, other
Pathological Manifestation	Selective epithelial damage of target organs	May involve inflammation, cell-mediated immunity, humoral immunity, and fibrosis
Cause	Caused by response of mature donor T cells to mismatched host polymorphic histocompatibility	Not fully understood, however, involves a complex immune reaction with both T and B cells

*Sources: Socié and Ritz, 2014[11]

Chronic GvHD – Manifestation and Pathophysiology:

Chronic GvHD is a multiorgan disease associated with significant immunodeficiency which makes treatment with immunosuppressive medications challenging due to the increased risk of severe, life-threatening infections[12]. This form is a serious and common complication of allogeneic HSCT, which incidence varies widely (35–70%) among studies of allogeneic recipients, based upon the time period specified, source of hematopoietic stem cells, type of donor, and post- transplant immunosuppression. It can develop after or extend from aGvHD or develop de novo.

Transplant recipients with cGvHD have a reduced quality of life and increased risks of long-term morbidity and mortality, as compared with transplant recipients who do not have cGvHD. cGvHD is the main cause of late non-relapse mortality and morbidity after allo-SCT.

Signs and symptoms of cGvHD vary between individuals and in the same individual over time, making determination of GvHD severity challenging; cGvHD commonly affects the skin, eyes, mouth, liver, gastrointestinal tract, lungs and genitalia. Main histopathologic and clinical manifestations of cGvHD include lichen-type skin involvement, dryness, and sclerosis of a number of organs (including skin, mouth, vagina, eyes, liver, and lung), serositis, and fasciitis. It is often characterized by fibrosis of the organ affected.

Although the pathophysiology of chronic GvHD remains poorly understood when compared with acute GvHD, some of the most severe organ manifestations are linked to end organ fibrosis. In particular, fibrotic cutaneous and bronchiolar changes, resulting in scleroderma-like changes and bronchiolitis obliterans syndrome (BOS), respectively, are two of the most devastating outcomes for these patients. Clinical manifestations of chronic GvHD nearly always present during the first year after transplantation[13].

Chronic GvHD – Diagnosis and Scoring:

Historically, diagnosis and scoring for chronic GvHD have been difficult because of pleiotropic organ manifestations and heterogeneous diagnostic criteria; however, a major advancement in the field was the development of NIH consensus criteria to define a clinical disease model and framework that could be

[11] Gérard Socié and Jerome Ritz. Current issues in chronic graft-versus-host disease. Blood. 2014 Jul 17;124(3):374-384. doi: 10.1182/blood-2014-01-514752. Epub 2014 Jun 9. Article.
[12] Bruce R. Blazar, Kelli P. A. MacDonald, Geoffrey R. Hill; Immune regulatory cell infusion for graft-versus-host disease prevention and therapy. Blood 2018; 131 (24): 2651–2660. doi: https://doi.org/10.1182/blood-2017-11-785865
[13] Madan Jagasia, Robert Zeiser, Michael Arbushites, Patricia Delaite, Brian Gadbaw, Nikolas von Bubnoff, Ruxolitinib for the treatment of patients with steroid-refractory GVHD: an introduction to the REACH trials, Immunotherapy (2018) 10(5), 391–402. Abstract.

rigorously applied to clinical studies. The revised 2014 NIH criteria have brought much-needed consistency to terminology and methods for disease diagnosis and staging.

The NIH Staging and Working Group established a scoring system on a 0–3 scale that described the extent and severity of cGvHD for each organ or site based on consensus criteria for organ scoring. cGvHD is classified as mild, moderate or severe, based on the number and severity of involved organs.

Mild chronic GvHD involves 2 or fewer organs with no more than score 1 and no lung involvement. Mild cGvHD is associated with a good prognosis and is generally treated with topical or local therapies, although systemic therapy may sometimes be required for patients presenting high risk features such as thrombocytopenia and hyperbilirubinemia. Patients with mild or asymptomatic manifestations limited to a single organ or site can often be managed with close observation or topical treatment or by slowing the taper of prophylactic immunosuppressive treatment (Jagasia et al., 2015)[14].

Moderate disease is 3 or more organs involved with score 1, any organ with score 2, or lung with score 1. Severe disease is any organ with a score of 3 or lung with a score of 2, and means that substantial organ damage already exists. Moderate to severe cGvHD usually requires systemic immunosuppressive treatment, with the most severe cases being associated with higher treatment-related mortality and lower survival.

Please see table below for more details on scoring.

Table 2: Chronic GvHD Classification

Classification	**Criteria**
Mild Chronic GvHD	1 or 2 organs involved with no more than score 1 *And* Lung score 0
Moderate Chronic GvHD	3 or more organs involved with no more than score 1 OR At least 1 organ (not lung) with a score of 2 OR Lung score 1
Severe Chronic GvHD	At least 1 organ with a score of 3 OR Lung score of 2 or 3

Key Points:
1. In skin: higher of the two scores to be used for calculating global severity.
2. In lung: FEV1 (forced expiratory volume in 1 second) is used instead of clinical score for calculating global severity.
3. If the entire abnormality in an organ is noted to be unequivocally explained by a non-GVHD documented cause, that organ is not included for calculation of the global severity.
4. If the abnormality in an organ is attributed to multifactorial causes (GVHD plus other causes) the scored organ will be used for calculation of the global severity regardless of the contributing causes (no downgrading of organ severity score).

Chronic GvHD is clearly a debilitating and life-threatening disease in its moderate to severe forms. cGvHD continues to account for significant morbidity and mortality in the outcome of patients undergoing allo-SCT. Although improvements have been made in the prevention of acute GvHD through better genetic choices in donors, these advances have not resulted in a concomitant decrease in the incidence of cGvHD (Lee et al., 2015). On the contrary, the prevalence of cGvHD keeps increasing over the past 20 years (Socié and Ritz, 2014)[15]. Though improvements in supportive care have been made, most of cGvHD patients continue to have

[14] Madan H. Jagasia, Hildegard T. Greinix, Mukta Arora, Kirsten M. Williams, Daniel Wolff, EdwardW. Cowen, Jeanne Palmer, DanielWeisdorf, Nathaniel S. Treister, Guang-Shing Cheng, Holly Kerr, Pamela Stratton, Rafael F. Duarte, George B. McDonald, Yoshihiro Inamoto, Afonso Vigorito, Sally Arai, Manuel B. Datiles, David Jacobsohn, Theo Heller, Carrie L. Kitko, Sandra A. Mitchell, Paul J. Martin, Howard Shulman, Roy S. Wu, Corey S. Cutler, Georgia B. Vogelsang, Stephanie J. Lee, Steven Z. Pavletic, Mary E.D. Flowers, National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group Report, in Biol Blood Marrow Transplan 21 (2015) 389 – 401. Link to publication.

[15] Gérard Socié and Jerome Ritz. Current issues in chronic graft-versus-host disease. Blood. 2014 Jul 17;124(3):374-384. doi: 10.1182/blood-2014-01-514752. Epub 2014 Jun 9. Article.

poor clinical function and altered quality of life. Thus, there is currently an unmet medical need for successful cGvHD therapies.

Market size[16]

The total patient population in the U.S. suffering from cGvHD (prevalence) early 2023 is estimated at 32,462 patients. This estimate is based on the prevalence as observed in the U.S. in 2016[17], an annual growth rate of 2% and the observation that for severe cases the average mortality rate within 2 to 10 years is approximately 50%. The number of new patients suffering from cGvHD (incidence) in the U.S. is estimated at 4,061 in 2022.

The incidence of cGvHD in the European Union is estimated at 3,342 patients in 2022. The total patient population in the European Union is estimated at 28,276.

Taking into account the expected competitive landscape and the fact that BioSenic Group targets moderate to severe cases of cGvHD (approx. 75% of all cases), BioSenic Group believes to be able to cover 25% of the total addressable patient population with is treatment, leading to an estimated total number of patients treated with ATO (market size) of 15,184 for the incidence and 1,851 new patients per year.

Overview of current treatments

Standard of care for the treatment of cGvHD is dependent upon the organ or site affected and can be topical or systemic. The National Comprehensive Cancer Network (NCCN) guidelines and the European Society for Blood and marrow Transplantation (EBMT) consensus both agree that steroids should be the first line treatment and advocate the use of ibrutinib, approved in the U.S. and the EU for second or further line treatment. However, both also state that there are no standard therapies for steroid resistant patients. About half of the patients become resistant to increasing daily doses of corticosteroids.

Treatment of cGvHD would be aimed at improving quality of life by reducing symptoms, preventing immune mediated damage and disability whilst avoiding the toxicities associated with treatment. There are three treatment goals: 1) to reduce the activated status of B and T cells, 2) to have an anti-inflammatory effect and 3) to slow down the development of fibrosis. The current available treatments for cGvHD include corticosteroids, which has been the mainstay of first line treatment for the last three decades, administered along or in combination with other immunosuppressants such as calcineurin inhibitors. Systemic treatment typically begins with prednisone at 0.5 to 1 mg/kg per day, followed by a taper to reach an alternate-day regimen, with or without cyclosporine or tacrolimus[18]. However, treatment with corticosteroids is problematic and often inadequate or toxic. Side effects include myopathy, infections, hyperglycaemia, avascular necrosis, cataracts and decline in bone mass. Appropriate management of cGvHD requires a continuous recalibration of immunosuppressive treatment, and as a general principle the minimum dose sufficient to control GvHD manifestations should be used. Manifestations of chronic GvHD can reappear or worsen when the intensity of immunosuppressive treatment is closely calibrated to the minimum dose needed to control GvHD. Treatment with corticosteroids is associated with suboptimal results in the management of chronic GvHD.[19]

Duration of immunosuppressive therapy is determined largely by clinical response but is often prolonged. Approximately 50% of patients are cured within 7 years after starting systemic treatment, as indicated by resolution of disease manifestations and permanent withdrawal of systemic treatment. Approximately 10% require continued systemic treatment of an indefinite period beyond 7 years, and the remaining 40% have recurrent malignancy or die within 7 years during treatment of chronic GvHD. It is therefore necessary to

[16] Study from ISPOR (the Professional Society for Health Economics and Outcomes Research) with respect to the European market and ASTCT (American Society for Transplantation and Cellular Therapy) for the U.S. market.
[17] Prevalence of cGvHD in the U.S. based on the Medicare FFS and PharMetrics commercial databases.
[18] Cyclosporin or tacrolimus are T-cells immunosuppressants specifically aimed at treating acute GvHD, an early pathological stage after grafting which is different from a chronic (later) disease, which is autoimmune and distinct (and sometimes overlapping). BioSenic Group excludes these patients from our clinical trials. Cyclosporine and tacrolimus are still in various types of trials to test for their benefits, usually as second line treatments after the first line of corticosteroids has failed.
[19] Dominique Rongvaux-Gaïda, Maëva Dupuis, Joël Poupon, Nouzha Djebrani-Oussedik, Catherine Lemonnier, François Rieger. High Response Rate and Corticosteroid Sparing with Arsenic Trioxide-Based First-Line Therapy in Chronic Graft-versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation, in Transplantation and Cellular Therapy, Volume 28, Issue 10, October 2022, Pages 679.e1-679.e11. Abstract.

develop alternative treatments of cGvHD as first-line therapy that would allow reducing the dose and the time of corticosteroids administration, and that would allow for good efficacy, tolerability and safety.

Additionally, corticosteroids are only effective in approximately 40-50% of cases meaning that 50-60% of patients experience a reoccurrence of cGvHD and require a second line treatment within 2 years after initial systemic treatment. Indications for secondary treatment include worsening manifestations of chronic GvHD in a previously affected organ, development of signs and symptoms of cGvHD in a previously unaffected organ, absence of improvement after 1 month of standard primary treatment, inability to decrease prednisone below 1 mg/kg per day within 2 months, or significant treatment-related toxicity.[20]

After four decades of evaluating different therapeutic approaches including antibodies, cellular therapies, small molecule inhibitors and cytokines, three drugs were approved by the FDA in the last five years for second line treatment and beyond: ibrutinib, belumosudil and ruxolitinib:

- Ibrutinib, a Bruton Tyrosine Kinase (BTK) inhibitor, was approved by the FDA in August 2017 for cGvHD after failure of one or more lines of systemic therapy (IMBRUVICA PI 2020)
- Belumosudil, a ROCK2 inhibitor, was approved in July 2021, for adult and paediatric patients 12 years and older with cGVHD after failure of at least two prior lines of systemic therapy (REZUROCK PI 2021)
- Ruxolitinib, a JAK 1 and 2 inhibitors, was approved in September 2021 for cGvHD after failure of one or two lines of systemic therapy in adult and paediatric patients 12 years and older (JAKAFI)

	Ibrutinib (Imbruvica®) JANSSEN	Ruxolitinib (Jakafi®) INCYTE (listed on Nasdaq) NOVARTIS (license for outside US)	Belumosudil (REZUROC®) ROCKstar (KD025) KADMON (Sanofi group, listed on Euronext Paris)	Arscimed (GMED16-001) Phase II Arsicor (GMED23-002) Phase III MEDSENIC
Phase completed	III	III	III	II
Adverse effects	+++	++	++	+
Administration	Oral; chronic	Oral; chronic	Oral; chronic	Oral; two 3-week cycles
Orphan designation	YES	YES	YES	YES
Indications	cGvHD 2nd line – repositioning	cGvHD 2nd line – repositioning	cGvHD 3nd line – repositioning	cGvHD 1rd line – repositioning
Characteristics	Janus kinase ½ inhibitor ; cancer Study PCYC-1129-CA (NCT02195869), an open-label, multi-center, single-arm clinical trial enrolling 42 patients with cGVHD after failure of first-line corticosteroid therapy and requiring additional therapy	Janus kinase ½ inhibitor; cancer A Randomized, open-label, multicenter trial – REACH-3 (NCT03112603) – of ruxolitinib compared to best available therapy (BAT) for corticosteroid-refractory cGvHD after allogeneic stem cell transplantation	A ROCK2 inhibitor In a pivotal clinical trial in the United States for the treatment of chronic graft-versus-host-disease (cGvHD). In Oct 2018, the U.S. Food and Drug Administration granted Breakthrough Therapy Designation to KD025 for the treatment of cGvHD) after two or more lines of systemic therapy	- A ROS activator - An inflammatory cytokine inhibitor Non chronic delivery (Few weeks) A Phase II IV trial with demonstrated safety and efficacy on moderate to severe cGvHD; Primary endpoint met at 6 months; Rapid decrease of initial prednisone. Adequate as a first line therapy IV drug (Arscimed) with Generics, however

[20] Dominique Rongvaux-Gaïda, Maëva Dupuis, Joël Poupon, Nouzha Djebrani-Oussedik, Catherine Lemonnier, François Rieger. High Response Rate and Corticosteroid Sparing with Arsenic Trioxide-Based First-Line Therapy in Chronic Graft-versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation, in Transplantation and Cellular Therapy, Volume 28, Issue 10, October 2022, Pages 679.e1-679.e11. Abstract.

				with cancer authorization only. Our oral drug formulation is under IP protection (priority date: 2015). Its equivalent bioavailability to the IV drug is now proven.
Marketing Authorisation **Approval date:** - **Europe (EMA)** - **USA (FDA)**	EMA: NO for cGvHD (only for types of blood cancers) (Oct 21, 2014) FDA: YES (Aug 2, 2017)	EMA: YES (May 2022) FDA: YES (Sept 22, 2021)	EMA: NO FDA: YES (July 19, 2021)	NO – dependent on Phase III success (2023 – 2027)

However, apart from arsenic trioxide based treatments, the above-mentioned drugs are long-term immunosuppressive treatments and come with a risk of serious side effects (including serious infections; haemorrhage; increase in the risk of atrial fibrillation and heart failure; increased risk of certain types of cancer) [21,22]. Compared to corticosteroids, which are non-specific potent immunosuppressors, ATO is a specific immunomodulator, which has the advantage to significantly lower possible adverse effects.

Therefore, BioSenic Group believes that there continues to be a high unmet medical need for a first line therapy for alternative treatments and/or in combination with corticosteroids having a higher risk-benefit ratio. The proposed treatment with (O)ATO only includes 3 to 4 weeks for two cycles and the clinical studies with arsenic trioxide in acute promyelocytic leukaemia have shown side effects of low intensity and all reversible. BioSenic Group therefore believes that arsenic trioxide, as a specific immunomodulator (not an immunosuppressant) and anti-fibrotic, for the first-line treatment of cGvHD, could offer significant benefits over the other available treatment options.

ATO in GvHD – Rationale for Development

As all the manifestations described above are closely related to those observed in humans with cGvHD, Medsenic decided to develop ATO in combination with corticosteroids as first line therapy for patients with newly diagnosed cGvHD after allo-SCT. The addition of ATO to prednisone should increase the Overall Response Rate (ORR) and enable a more rapid and effective corticosteroid taper.

In regard to the nonclinical proof-of-concept for GvHD, recent ATO data is publicly available. Briefly, (Hu et al., 2019)[23] demonstrated that intraperitoneal ATO could improve the clinical symptoms and prolonged the survival of aGvHD mice through upregulating the expression of Nrf2 and HO-1 proteins to reduce the CD4+ T/CD8+ T ratio and decrease the concentration of TNF-α and IFN-γ. Moreover, (Liu et al., 2020)[24] aimed to explore macrophage polarization in acute graft- versus-host disease after hematopoietic stem cell transplantation. They investigated if intraperitoneal ATO could correct this imbalance. The data suggest that

[21] Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ Grade 3, serious, or any central nervous system events) occurred in 4.2% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA® in 27 clinical trials. Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients who received IMBRUVICA® in clinical trials. Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials. Link to source.

[22] Jakafi can cause serious side effects including low blood counts and infection. Some people who take Jakafi have developed certain types of non-melanoma skin cancers. Increases in blood cholesterol levels can also occur. In patients who took another JAK inhibitor to treat rheumatoid arthritis, there was an increased risk of potentially fatal cardiovascular events like heart attack or stroke in patients with risk factors for these events who smoke now or smoked in the past, as well as an increased risk of blood clots in legs or lungs and new (secondary) cancers like lymphoma, especially in patients who smoke now or smoked in the past. Link to source.

[23] Xiaoli Hu, Liwei Li, Sai Yan, Zhiqiang Li. Arsenic trioxide suppresses acute graft-versus-host disease byactivating the Nrf2/HO-1 pathway in mice. British Journal of Haematology, 2019,186,e117–e162. Link to article.

[24] Xiao Liu, Yan Su, Xueyan Sun, Haixia Fu, Qiusha Huang, Qi Chen, Xiaodong Mo, Meng Lv, Yuan Kong, Lanping Xu, Xiaojun Huang, Xiaohui Zhang.Arsenic trioxide alleviates acute graft-versus-host disease by modulating macrophage polarization. Sci China Life Sci. 2020 Nov;63(11):1744-1754. Abstract.

macrophage polarization is involved in the pathogenesis of aGvHD and that ATO treatment modulates macrophage polarization toward an M2 phenotype.

ATO's mechanism of action

As3+ from ATO exerts its biochemical effects intracellularly (Leung et al., 2007). Interaction with the thiol (or sulfhydryl) groups (–SH) of proteins with a high cysteine content constitutes the basic biochemical reaction of As3+ (Emadi et al., 2010), which alters protein conformation, resulting in loss of their function, and affects their recruitment and interaction with other proteins and DNA (Shen et al., 2013). The thiol group is ubiquitous in our body and mostly found in its oxidized form as disulfide linkages. The disulfide linkages are generally key to the tertiary and quaternary structures of proteins. As2O3 has high affinity for sulfhydryl groups and can react with reduced cysteines in peptides and proteins. Thus, arsenic binding to a specific protein can alter the conformation of the protein, resulting in loss or gain of function, and affect its recruitment of and interaction with other proteins and DNA.

Apart from the direct arsenic-protein binding, recent studies revealed that many key proteins are modulated through more complicated post-translational stepwise regulations (De Thé, 2018). The mechanisms of action of As2O3 are different at low doses and short times of exposure. Arsenic is clearly involved in:

- Pro-apoptotic mechanisms, mainly due to the generation of oxidative stress;
- Metabolic modulations;
- Redox regulations.

In vivo, arsenic chemical activity can influence many different biological pathways among which:

- Proteins and enzymes implicated in the metabolism (Pyruvate Dehydrogenase, glucose oxidase…);
- Enzymes implicated in redox status, mitochondrial functions and oxidative stress modulation;
- DNA Repair Enzymes;
- Post-translational modification that facilitates the SUMOylation and subsequent degradation of target proteins;
- Direct binding of Arsenic to cysteine residues in zinc fingers;
- Tissue dependent bidirectional regulation on inflammasomes;
- Epigenetic DNA methylation and Histone acetylation.

As mentioned above, multiple molecular targets have been reported in the literature for arsenic trioxide. Arsenic trioxide does affect several intracellular signal transduction pathways and leads to important modifications in the cell function. As reported years ago, arsenic trioxide actions may result in apoptosis (i.e., induced cell death) induction for overactive immune cells, inhibition of growth, inhibition of inflammatory signal transduction and promotion of cell differentiation (Miller et al., 2002)[25].

Arsenic trioxide can disturb natural oxidation and reduction equilibria in activated cells through various mechanisms involved in complex redox reactions with endogenous oxidants and cellular antioxidant systems. Reactive oxygen species generated in response to arsenic exposure lead to accumulation of intracellular hydrogen peroxide, and trigger apoptosis through Cytochrome C release and subsequent activation of the caspase pathway (Miller et al., 2002).

ATO has been shown to induce apoptosis in human CD4+ and CD8+ T cells via the mitochondrial pathway by inducing oxidative stress and by regulating Bcl-2 family protein expression (Gupta et al., 2003)[26]. ATO may induce apoptosis via changes in the mitochondrial membrane potential (Miller et al., 2002). It has been established (Maier et al., 2014)[27] that ATO inhibits NLRP1 inflammasome activation, and also the NAIP5/NLRC4 and NLRP3 inflammasome responses to their effectors leading to inflammation inhibition.

[25] Wilson H. Miller, Hyman M. Schipper, Janet S. Lee, Jack Singer, and Samuel Waxman, Mechanisms of Action of Arsenic Trioxide, CANCER RESEARCH 62, 3893–3903,2002. Abstract.
[26] Gupta S, Yel L, Kim D, Kim C, Chiplunkar S, Gollapudi S. Arsenic trioxide induces apoptosis in peripheral blood T lymphocyte subsets by inducing oxidative stress: a role of bcl-2. Mol Cancer Ther (2003) 2(8):711–9. Abstract.
[27] Nolan K. Maier, Devorah Crown, Jie Liu, Stephen H. Leppla and Mahtab Moayeri. Arsenic trioxidesand other arsenical compounds inhibit the NLRP1, NLRP3, and NAIP5/NLRC4 inflammasomes, J Immunol. 2014 Jan 15; 192(2): 10.4049/jimmunol.1301434. Abstract.

Arsenic has a selective effect from metabolism to the epigenetic status of the cells, with redox as a key reaction. Arsenic is found to generally have a beneficial action on many different types of immune cells in both the innate and the adaptive response. It potentiates a return to homeostasis, alternatively to apoptosis when this is no longer possible. The cytokines secreted by arsenic-targeted immune cells can modulate the differentiation of other cell types, such as fibroblasts into myofibroblasts (Luo et al. 2014). All these mechanisms of action can happen in various types of cells. Arsenic action will also depend on the pathways by which it enters the cells before triggering the above mechanisms. The expression of certain pores on the surface of the cells will determine its rapid action on the cell under consideration. Once in the cells, depending on the intracellular activity and the redox status, arsenic may act with greater or lesser efficacy on different activated signalling or regulatory pathways involved in cell differentiation and/or activation.

As2O3 has been evaluated by Medsenic/BioSenic in mouse models of autoimmune and pro-fibrotic diseases such as Graft-versus-Host Disease (GvHD) and Systemic Scleroderma (SSc) for its anti-fibrotic properties. The results are clear: low-dose ATO has been shown to have a clear anti-fibrotic action in these diseases murine preclinical models. In cGvHD and SSc mouse models, the combination affects both macrophages and fibroblasts, reducing inflammation and fibrosis (Chêne et al. 2022; Chêne et al. 2023).

Pharmaceutical Development of Oral ATO Formulation

An intravenous formulation of ATO (Trisenox®) has been marketed in the United States since September 2000 for the treatment of APL. However, the IV administration of ATO is a challenge for both patients and hospitals due to the frequency of vascular administration required. In order to improve the convenience of administration and tolerance for patients, an oral formulation of ATO has been developed by Phebra, an Australian-owned manufacturer that developed and holds the license to Phenasen® Concentrated Injection (ATO) which is virtually identical to Trisenox and is approved for patient with APL in Australia, New Zealand, United Kingdom, and Canada. Oral ATO (OATO) contains the same active ingredient as Trisenox®. The bioequivalence of OATO with IV ATO has been researched by Medsenic in a bioavailability study APML5.

Chemistry, Manufacturing and Controls

For its envisaged clinical trials, Medsenic intends to use the arsenic element as the starting material for the manufacturing of Arsenic (III) oxide (As) drug substance in accordance with the Guidance for Industry ICH Q11 Guidance for Industry ICH Q11 "Development and manufacture of drug substances (November 2012) and ICH Q11 Q&As (August 2017)".

More information about the arsenic trioxide element that Medsenic intends to use as starting material are as follows:

- Molecular Formula: As
  CAS RN#: 7740-38-2;
  Molecular weight: 74.92 g/mol
- As is manufactured by PPM PURE METALS starting from As.

Arsenic Powder is justified as a regulatory starting material on the basis of the following considerations in ICH Q11:

- Arsenic Powder is a substance of defined chemical properties and structure.
- Arsenic Powder is incorporated as a significant fragment into the structure of the drug substance.
- Arsenic Powder is a commercially available chemical sold as a commodity in a preexisting, non-pharmaceutical market: high purity Arsenic has numerous applications as a semiconductor and other electronic applications.
- Arsenic Powder can be sourced from several suppliers.
- Arsenic Powder is controlled by appropriate specifications to ensure adequate control of impurities in the final drug substance.

4.6.2 *Systemic lupus erythematosus*

4.6.2.1 Description

Systemic lupus erythematosus (SLE) is the most common type of lupus. SLE is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. The seriousness of SLE can range from mild to life-threatening. SLE can limit a person's physical, mental, and social functioning. These limitations experienced by people with SLE can impact their quality of life, especially if they experience fatigue. Fatigue is the most common symptom negatively affecting the quality of life of people with SLE.

4.6.2.2 Market size

Based on a recent review published in Nature Reviews in 2022[28], the incidence in the European Union is 2.9/100,000 per year. Taking into account a population in top 5 countries of 326.5 million, this leads to nearly 9,500 new cases per year. The prevalence is estimated at 55/100,000, which leads to an addressable population in Europe of nearly 180,000 patients.

In the U.S. the incidence is 5.11/100,000, leading to approximately 17,000 new cases each year, of which 1,300 are serious cases of lupus. The prevalence in the U.S. is estimated at 60.65/100,000. Mortality is estimated at 1.72/100,000.

The above-mentioned incidence rates have remained stable, but overall patient population has grown due to a general population increase.

Taking into account the expected competitive landscape, BioSenic Group believes to be able to cover 33% of the total addressable patient population with is treatment, leading to an estimated total number of patients treated with ATO (market size) of 125,692 and 8,722 new patients per year.

4.6.2.3 Competition

There is no real treatment for SLE on the market. Standard of care is treatment with hydrochloroquine and corticosteroids. Given the specific immunomodulatory effects of ATO, which have a direct effect on specific aspects of the response of the immune system (rather than suppressing the entire immune system), BioSenic Group intends to position ATO as a potential first line treatment for SLE.

To BioSenic's knowledge, the two main competitors having an FDA approved treatment for SLE are:

(i) Aurinia and its product Voclosporine®, which received FDA approval in January 2021 for use in combination with a background immunosuppressive therapy regimen for one subtype of SLE (lupus nephritis which affects the kidneys); and

(ii) GlaxoSmithKline and its product Benlysta®, which received its first FDA approval in March 2011, for which however efficacy results are not high[29] and which does not treat the same diseases as the ones targeted by Medsenic.

BioSenic Group believes that notwithstanding the above-mentioned available treatments, there is still a high unmet medical need for further treatment options for SLE. Especially for treatments, like with ATO, that could

[28] Barber, M.R.W., Drenkard, C., Falasinnu, T. et al. Global epidemiology of systemic lupus erythematosus. Nat Rev Rheumatol 17, 515–532 (2021). https://doi.org/10.1038/s41584-021-00668-1.

[29] See for example: "What are the benefits and risks of belimumab for treating systemic lupus erythematosus (an autoimmune disease that affects the whole body)?", link: When compared against placebo: (i) belimumab is more likely to reduce SLE disease activity, and to reduce the amount of glucocorticoids needed;(ii) belimumab probably makes little to no difference to health-related quality of life improvement; numbers of serious adverse events; and deaths.

potentially target a wider spectrum of actions because it affects all types of SLE or that could evidence a higher efficacy result than current treatment options.

Although BioSenic Group is not aware of any significant results, other future competitors of the BioSenic Group might be the companies as set out in Section 4.6.1 (Overview of the current treatments) that are currently commercialising a therapy for cGvHD and that might decide to conduct further research to reposition their drug for the treatment of SLE.

4.6.3 *Systemic sclerosis*

4.6.3.1 Description

Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterised by excessive production and accumulation of collagen, called fibrosis, in the skin and internal organs and by injuries to small arteries. SSc is often categorised as "limited" or "diffuse" referring to the degree of skin involvement. The limited form affects areas below, but not above, the elbows and knees with or without involvement of the face. The diffuse form also affects the skin above the elbows and knees and can also spread to the torso. Visceral organs, including the kidneys, heart, lungs, and gastrointestinal tract can also be affected by the fibrotic process. Prognosis is determined by the form of the disease and the extent of visceral involvement. Patients with limited systemic sclerosis have a better prognosis than those with the diffuse form. Death is most often caused by lung, heart, and kidney involvement. Overall 10-year survival is estimated at 90% for limited systemic sclerosis and 70% for diffuse systemic sclerosis[30]. Predictors of early mortality include male sex, late onset, diffuse disease, pulmonary arterial hypertension, and renal crisis.

4.6.3.2 Market size[31]

The incidence in the European Union is estimated between 4.5 and 18.7/1,000,000. Based on an average incidence of 12/1,000,000, this leads to 3,918 patients per year. The total patient population suffering from SSC in the European Union is estimated at 50,284, with a prevalence of 154/1,000,000.

In the U.S. the incidence is 18.7/1,000,000, leading to approximately 6,207 new patients each year. The prevalence in the U.S. is estimated at 240/1,000,000 which leads to a total patient population of nearly 80,000.

Taking into account the expected competitive landscape, BioSenic Group believes to be able to cover 33% of the total addressable patient population with is treatment, leading to an estimated total number of patients treated with ATO (market size) of 42,880 and 3,341 new patients per year.

4.6.3.3 Competition

There are no real treatments on the market. Standard of care is low doses of corticosteroids (as high doses could worsen the disease). Medsenic envisages to develop a first line treatment based on ATO given the specific immunomodulatory effects of ATO, which have a direct effect on specific aspects of the response of the immune system rather than suppressing the entire immune system such as corticosteroids.

In this field, repositioned drugs are under development but BioSenic is not aware any successful medication to date. BioSenic is aware that the following companies are working on the repositioning of drugs for treatment of SSc: Bristol-Myers Squibb Company (abatacept); Boehringer Ingelheim International GmbH; AbbVie; Johnson & Johnson (Guselkumab (phase II)); GlaxoSmithKline plc; and Biogen.

Other future competitors of the BioSenic Group might be the companies as set out in Section 4.6.1 (Overview of the current treatments) that are currently commercialising a therapy for cGvHD and that might decide to

[30] Company estimates.
[31] SNFMI, Orphanet maladies rares, NIH.

conduct further research to reposition their drug for the treatment of SSc (as is currently the case for Belumosudil (REZUROCK™)).

4.7 Principal Bone disorder markets (*clinical trial activities discontinued; search for partnership opportunities*)

The bone-related disorder industry, in which BioSenic 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.

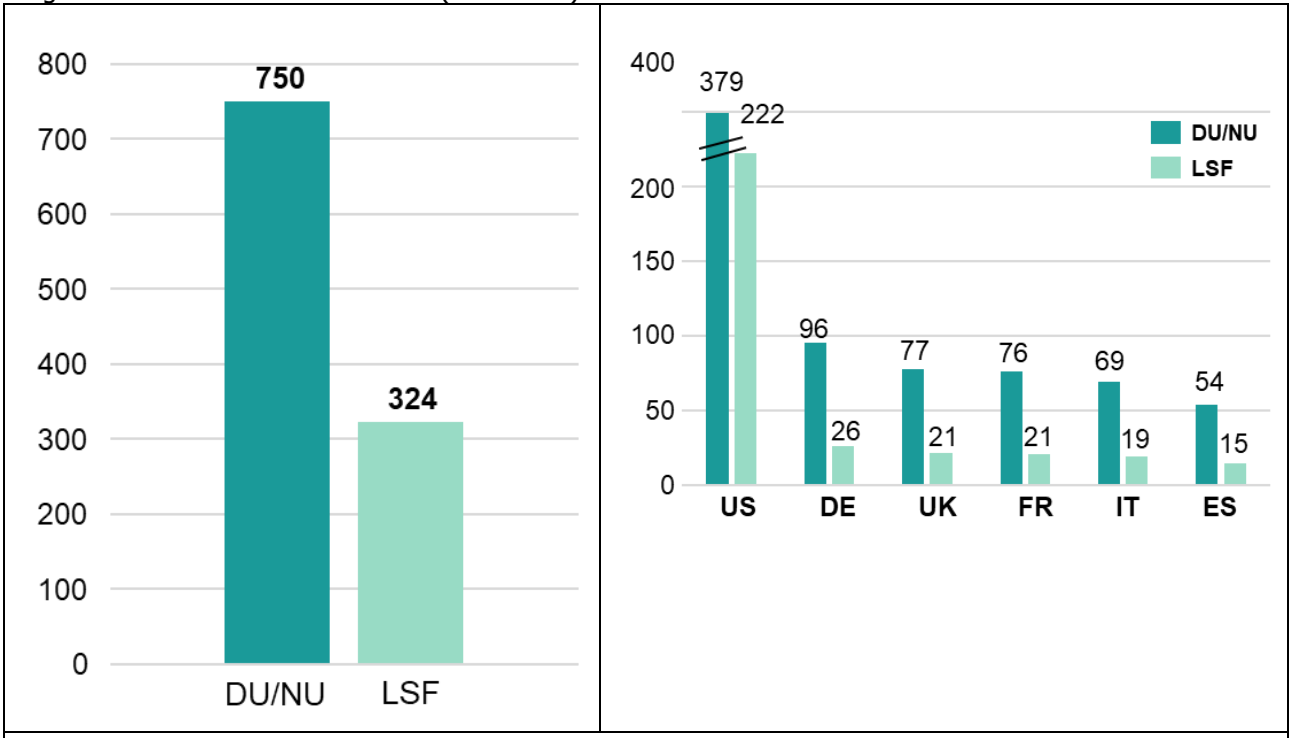
The market space in which BioSenic operates covers fracture repair, spinal implants, bone growth stimuli and orthobiologics (excluding the osteoporosis market) and represents an estimated global market of around $ 22 billion (2019) for the treatment of more than 250 million patients, which can be broken down in the following segments[32] [33]:

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**	

- 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.

[32] 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).
[33] Vos et al., *A systematic analysis for the Global Burden of Disease Study 2010*. Lancet 2012; 380:2163-96

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, BioSenic 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 BioSenic is characterized by high unmet medical needs (defined as a medical need that is not addressed adequately by an existing therapy[34]). 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 BioSenic have so far remained relatively clear of new 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 naturally 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

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

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[35].

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[36]. 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[37]. 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. 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[38]. 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

BioSenic 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. BioSenic's 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-

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

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.[39] BioSenic 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[40].

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)[41].

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 companies 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-the recombinant bone morphogenetic factor) is, to BioSenic'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 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 BioSenic's knowledge, BioSenic is the only cell therapy company focusing on providing an early (first three months for the phase IIa and a few days for ALLOb IIb), 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[42].

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

[39] 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.
[40] Heckman et al. The economics of treating tibia fractures. The cost of delayed unions. Bull Hosp Jt Dis. 1997(56)63-72.
[41] 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.
[42] Company websites and clinicaltrials.gov.

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**
BioSenic	• Delayed union fractures • Spinal fusion	Off-the-shelf differentiated osteoprogenitor cells	Local Injection	ATMP	Phase II2b
Kuros	• Spinal fusion • Tibial fractures	Orthobiologic (PTH) + scaffold	Local Injection	BLA	Phase II (recruiting)
Novadip	• Spinal fusion • Other bone defects	Autologous, adipose-derived MSC (3D structure)	Surgery	ATMP	Phase I/II (completed)
Epibone	Bone defects	Adipose-derived MSC + scaffold	Surgery	ATMP	Phase I/II
Mesoblast	Chronic low back pain	Bone marrow-derived MPC + scaffold	Local injection	ATMP	Phase III (completed)
Shanghai iCELL Biotechnology Co.	Non-union fractures	Human amniotic epithelial cells (hAECs)	Local injection	ATMP?	Phase I/II (status unknown)
DiscGenics	Disc degenerative disease	allogeneic (off-the-shelf), injectable discogenic cells	Local Injection	ATMP	Phase I/II (completed)
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 local bone cell differentiation) 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[43]. BioSenic's estimates regarding market size are based on hospital discharge data and market reports. Using these data, BioSenic estimates that each year 686,000 patients in EU5[44], 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[45] 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[46]. GlobalData estimated that the market will continue

[43] Spinal Fusion – Global Market 2015-2028, Global Data, 2019.
[44] France, Germany, Italy, Spain and United Kingdom
[45] North Maerica Spinal Surgery Market Outlook to 2025. GlobalData, August 2018.
[46] Spinal Fusion – Global Analysis and Market Forecast. GlobalData, Linda Tian, December 2016.

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)[47]. 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 orthobiologics 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[48]. For orthobiologics, the vPTH biomaterial (KUR-113) from Kuros is currently evaluated in a Phase IIa trial in the US in spinal fusion[49]. However, in this changing landscape, BioSenic 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[50]:

Novadip Biosciences (BEL) has initiated a Phase I/II trial in 2017 which completed end 2020 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[51]. As mentioned previously, Novadip is now focusing its development with its second-generation therapy (NVD-003) for critical size bone reconstruction. Unlike Novadip Biosciences, BioSenic'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[52], such as Mesoblast (AUS) and its product candidate Rexlemestrocel-L currently in phase III study[53], 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

[47] Myeroff C and Archdeacon M. Autogenous Bone Graft: Donor sites and Techniques. The Journal of Bone and Joint Surgery. 2011; 93A (23): 2227-36.
[48] http://www.drugwatch.com/infuse/ and "Medtronic must face revived U.S. lawsuit over Infuse" (Reuters, 28 Dec. 2016)
[49] Press Releases from Kuros Bioscience, dated 3 September 2019.
[50] 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.
[51] https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-002642-23/results#endPointsSection
[52] 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.
[53] End of recruiting – www.clinicaltrials.gov

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 (*clinical trial activities discontinued; search for partnership opportunities*)

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[54]. Based on studies analysing the prevalence of symptomatic knee osteoarthritis, BioSenic 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[55]. 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 known 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[56].

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.

Such a composition with viscoelastic properties and analgesics may be modified depending the subtype of KOA considered. Although the further clinical development of JTA-004 itself is currently on hold given the negative outcome of the Phase III trial (see Section 4.9.3 for more information), BioSenic Group will be undertaking preclinical work involving the scientific and physiological aspects of the co-use of arsenic trioxide as an anti-inflammatory component.

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.

[54] Vos et al., *A systematic analysis for the Global Burden of Disease Study 2010*. Lancet 2012; 380:2163-96
[55] Viscosupplementation: Global Analysis and Market Forecasts, April 2017, Global Data
[56] Viscosupplementation: Global Analysis and Market Forecasts, April 2017, Global Data

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[57].

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:

Company	Product	Technology	Indication	Status	Trials
INTRA-ARTICURAL INJECTIONS					

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

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 (completed with results) NCT03660943 – Ph III (completed with results) NCT03661996 – Ph III Different Treatment Regimen (completed with results)
Mestex (CH)	Lopain (MTX-071)	Resiniferatoxin TRPV1 agonist	Pain in knee osteoarthritis	Phase IIb	NCT02566564 (completed)
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 (completed)
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 - Completed

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. Although the primary and consequently key secondary endpoints of the Phase III trial with JTA-004 were not reached (please refer to Section 4.9.3 below) a post-hoc analysis indicated that a statistically significant difference in favour of JTA-004 and the active comparator versus placebo was seen in a subset of patients with higher pain scores at entry. BioSenic therefore plans to re-evaluate the data of JTA-004 in the light of new ideas, involving the fact that KOA may have several clinical subtypes and one subtype could be more amenable to the treatment.

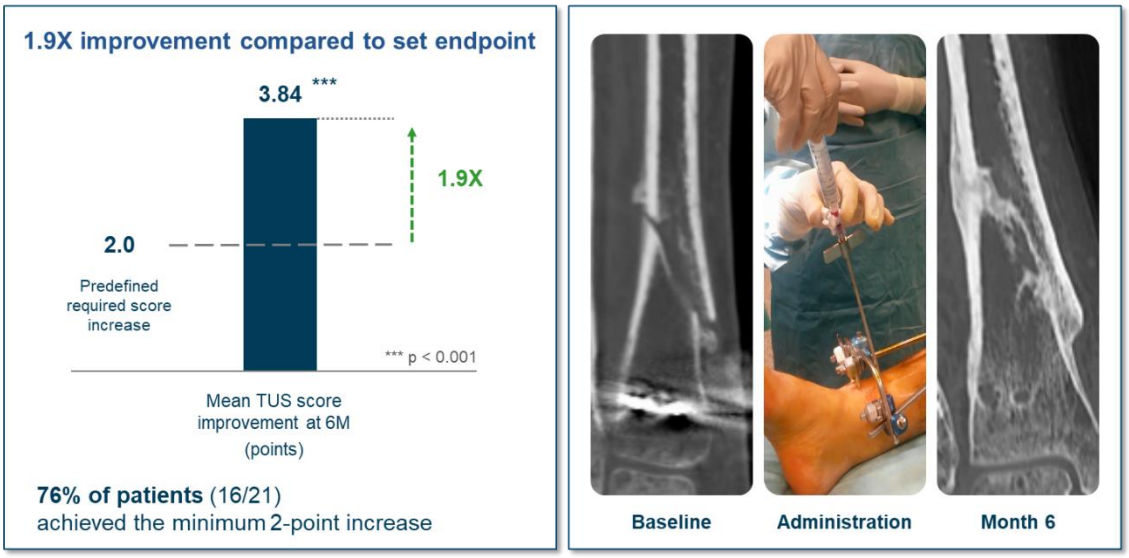
4.9 Results of clinical studies

4.9.1 *Delayed-union fractures (clinical trial activities discontinued; search for partnership opportunities)*

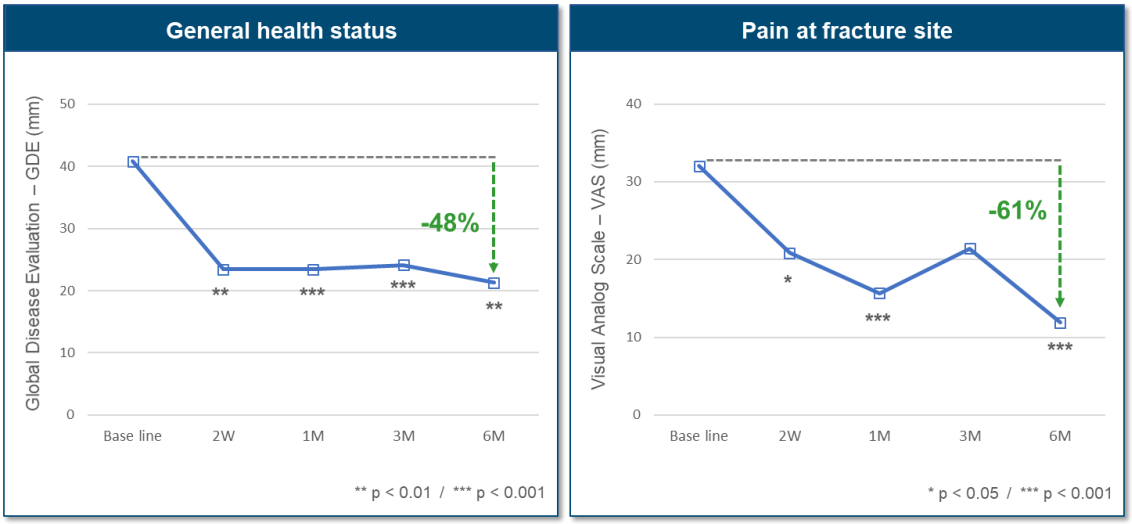
The Phase I/IIa study was a six-month open-label trial to evaluate the safety and efficacy of ALLOB in the treatment of delayed-union fractures of long bones. The study evaluated 21 patients, who each had a fracture that had failed to consolidate after a minimum of three and a maximum of seven months. 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 scale (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 Global Disease Evaluation (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 has been evaluated in a randomized, double-blind, placebo-controlled Phase IIb study in patients with high-risk tibial fractures. The study is over and initially planned a recruitment of 132 patients.

Recent published medical data has provided new information on timing and dynamics of radiological evidence of fracture resolution. Based on this new evidence, BioSenic has improved the statistical analysis of the ALLOB Phase IIb study. The updated analysis will provide an optimal radiological assessment of the acceleration of bone formation at 3 months following an intra-fracture administration of ALLOB, compared to standard practice alone. The updated statistical analysis converts one of the current secondary endpoints to a primary endpoint

and will therefore have limited impact on the study conduct. The amendment also enables a reduction of approximately 20% of the required patient numbers from 178 patients to 132 evaluable patients while maintaining the same statistical power. Additionally, this updated analysis could facilitate the definition of clinical trial objectives and endpoints in the measurement of fracture healing in subsequent studies.

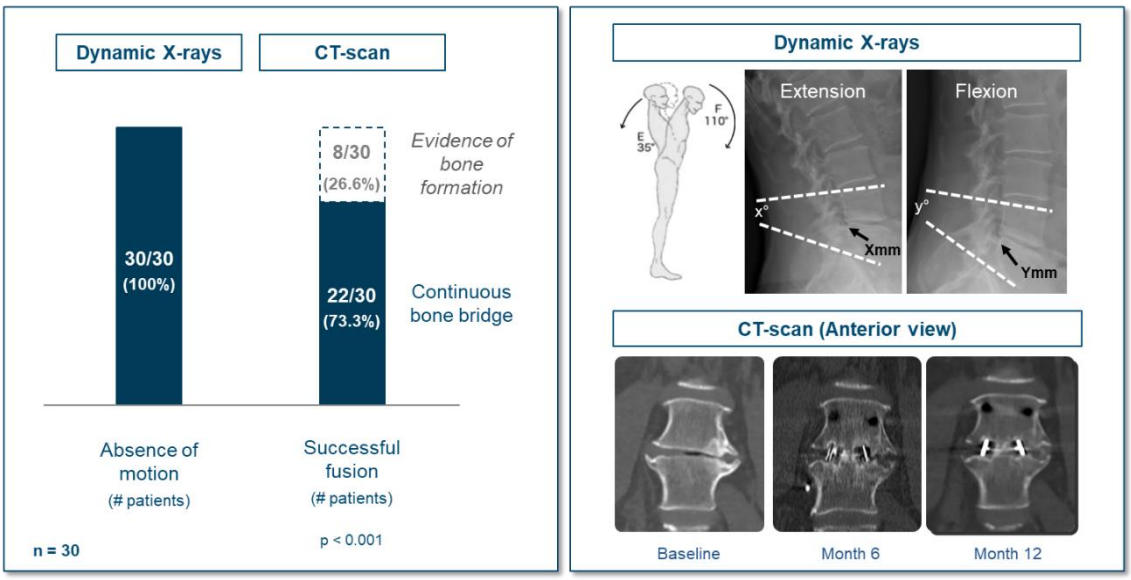
In February 2023, BioSenic announced an optimization of the study and patient recruitment completion. BioSenic has utilized scientific advances and market knowledge in feature healing and scientific advances in radiology to initiate positive modifications to its trial. As a result, the study has advanced from seeking pure basic clinical assessments to involving more quantitative data. This has allowed for a superior significance analysis. This advance in the trial results assessment has been achieved through advances in radiographic procedures enabling increased clarity in statistical interpretation. As a result, BioSenic has decided, based on consultation with its external biostatistical advisors, that clinical investigators may stop the recruitment of patients. The cohort of treated patients, amounting to 57 patients, was found to be sufficient for a sufficient level of significance.

On 19 June 2023, BioSenic announced putting the Phase IIb ALLOB trial on hold following negative results obtained for the primary endpoint. The Company is therefore closing the ALLOB Phase IIb clinical trial. As the combination of the Phase IIa and Phase IIb clinical trial with ALLOB, as well as preclinical data, suggest that the administration of ALLOB should be carried out outside the acute -early- post traumatic inflammatory period in order to potentially promote a complex bone repair process, BioSenic believes that ALLOB treatment remains potentially useful to complement standard care, when administered at the right time, to improve recovery after extreme bone injury. BioSenic is therefore currently looking for partnership opportunities for ALLOB. If no concrete partnership options would materialise in the near future, BioSenic does however not exclude that it might stop its efforts to seek collaborations with external partners for the future development of ALLOB.

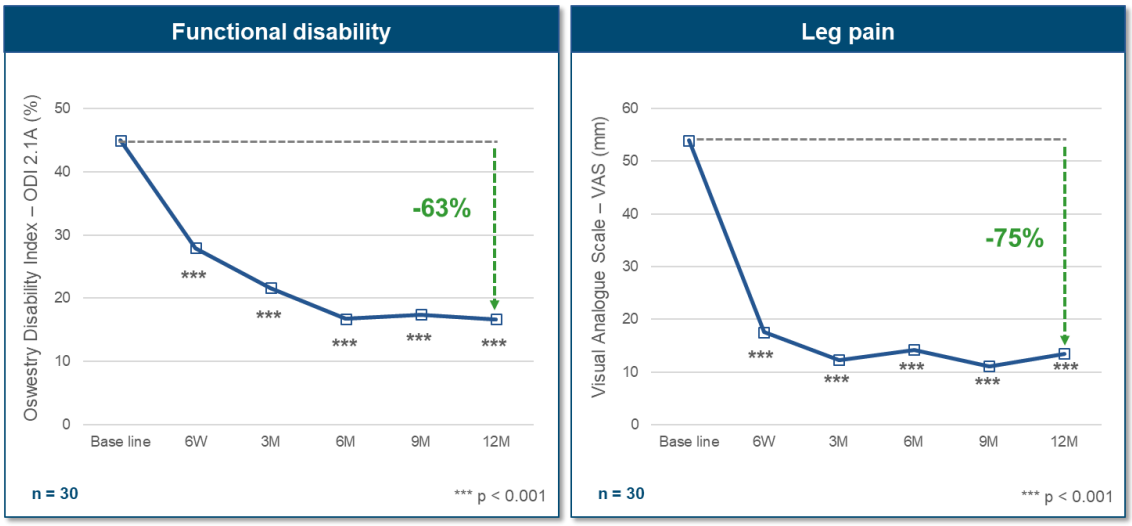
4.9.2 *Lumbar spinal fusion (clinical trial activities discontinued; search for partnership opportunities)*

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 some evidence of bone formation without fusion. 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, BioSenic 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 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

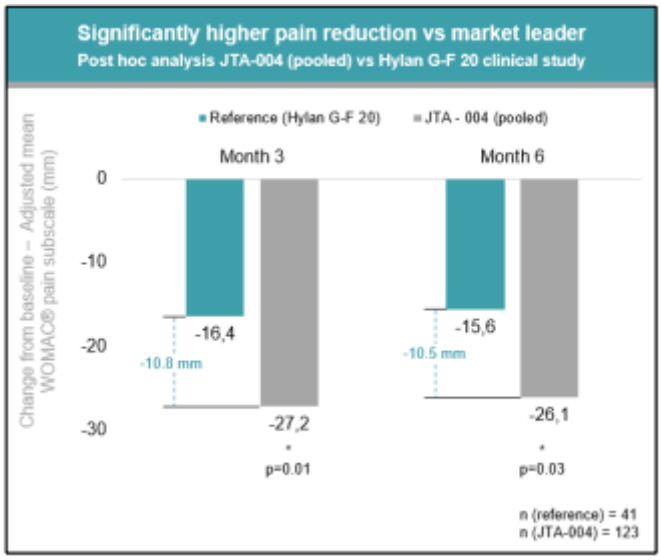
compared to pre-treatment baseline. Treatment with ALLOB was generally well-tolerated by the patients, consistent with previous reported results.

4.9.3 *JTA-004 (clinical trial activities discontinued; search for partnership opportunities)*

JTA-004 is a next generation of intra-articular injectable for the treatment of osteoarthritic pain in the knee. Consisting of a unique patented mix of plasma proteins, hyaluronic acid - a natural component of knee synovial fluid, and a fast-acting analgesic, JTA-004 intends to provide added lubrication and protection to the cartilage of the arthritic joint and to alleviate osteoarthritic pain.

Osteoarthritis (OA), also known as degenerative joint disease, is the most common chronic joint condition in which the protective cartilage in the joints progressively break 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 250 million cases worldwide[58]. The prevalence of knee osteoarthritis (KOA) is expected to increase in the coming years due to increasingly aging and obese population. Currently, there is no cure for KOA and treatments focus on relieving and controlling pain and symptoms, 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 led to highly invasive surgical interventions such as total knee replacement.

In a completed Phase IIb study involving 164 patients, JTA-004 showed an improved pain relief at 3 and 6 months compared to Hylan G-F 20, the global market leader in osteoarthritis treatment.



In August 2021, BioSenic announced the primary results of its Phase III study evaluating the potential of a single intra-articular injection of JTA-004 for the reduction of osteoarthritis pain in the knee for up to 12 months, compared to placebo or Hylan G-F 20, the current market-leading osteoarthritis treatment. The Phase III study was a randomized, double-blind, controlled trial conducted at 22 centers in six European countries and in the Hong Kong SAR. Over 700 patients were treated. JTA-004 had an excellent safety profile. However, the study did not meet its primary or secondary endpoints. No statistically significant difference in pain reduction between the treatment, placebo or comparative groups could be observed, with all treatment arms showing similar efficacy.

In March 2023, BioSenic announced that it has used the statistical analysis capabilities of Artialis to re-evaluate the results of the Phase III JTA-004 trial in the subset of patients with the most painful and inflammatory form of knee osteoarthritis (OA). This allowed BioSenic to distinguish a group of patients, representing about one third of the total patients, who show a pain-relieving effect of JTA-004 not only superior to placebo but also to the active comparator. By identifying three subtypes of OA, amongst which a subtype of OA patients with

[58] Vos et al., A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380:2163-96

more severe symptoms and inflammation, this new post-hoc analysis gives a better appreciation for the therapeutic profile of the molecule and potentially allows for the possibility of precisely stratifying patients for a new, optimized Phase III clinical study. BioSenic, which does not intend to allocate R&D resources to support the clinical development of JTA-004 and will continue to focus its R&D activities on the development of its autoimmune (ATO) platform, is seeking to collaborate with existing and potential partners to explore options for the future commercial development of the JTA technology based on this new post-hoc analysis and corresponding new intellectual property rights.

Following the disappointing Phase III clinical results, Biosenic transferred its rights to the JTA technology to the Walloon Region and consequently terminated the license and co-ownership agreement with Enrico Bastianelli SRL in 2022. Given the new statistical analysis results from the JTA-004 Phase III clinical trial data obtained in March 2023, the agreement with respect to the JTA technology (including intellectual property rights forming the JTA-Gen1 patent families) has been since reacquired from the Walloon Region, as the Walloon Region accepted to retrocede its rights to the JTA technology to BioSenic Group in 2023. Although BioSenic has been discussing for quite some time the opportunity with Enrico Bastianelli SRL to enter into a co-ownership agreement for the old JTA-Gen1 patent families (i.e. the patent families BPBONE-001, BONE-002, BONE-011), such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement creates exploitation problems with third parties and possible licensees for the use of the JTA technology. This has therefore a negative impact on BioSenic's possibilities to collaborate with external partners for the future development and valorisation of the JTA technology as it exists.

4.9.4 *Chronic Graft vs Host Disease*

4.9.4.1 General – ATO – Drug product specifications

Most of the nonclinical data is derived from the published literature, from U.S. Trisenox® Approval Package (NDA_21-248) and from the supportive European Public Assessment Report of Trisenox® (Trisenox® EPAR, 2016).

In line with the 3Rs principles (reduce, replace, refine), Medsenic considers that clinical data should prevail on nonclinical investigations and that existing nonclinical data adequately characterize the safety profile in animals; additional nonclinical studies would not add value and are therefore deemed unnecessary to support the proposed clinical development program, and thereafter in anticipation of an Market Approval in the target indication. This position was endorsed for arsenic trioxide (IV formulation) by the FDA in 2019 (PIND 145160 meeting minutes).

To support the development of oral ATO and to allow reliance on the nonclinical data already available for the IV formulation of ATO and the currently marketed product Phenasen®, equivalent to Trisenox® marketed in Australia, New Zealand and Canada a bioavailability (BA) study (Study APML5) was conducted in APL patients and confirmed the bioequivalence (BE) between the IV and oral formulations. Therefore, Medsenic considers that no additional nonclinical investigations are necessary for oral ATO.

As ATO is not described in any pharmacopeia, its specifications have been defined in-house based on current available data and in line with ICH guidance (ICH guidelines Q6A *Specifications: Tests Procedures and Acceptance Criteria for New Drug substances and New Drug Products*, Q3A (R2) *Impurities in New Drug Substances*, Q3C (R8) *Guideline for Residual Solvents* and Q3D *Guideline on Elemental Impurities*).
The drug substance specifications of oral ATO developed by Medsenic are presented in Table 1 below.

Medsenic considers that the specifications comply with current compendial standards and provide a good characterization of the drug substance in terms of identity, purity and content, and are adequate for control of the quality of ATO. These specifications are fully supported by batch data and stability data.

Further detailed justifications are provided below for tests for the control of impurities:

- Metallic Arsenic test: As (0) may remain in suspension due to incomplete oxidation. Despite it is removed by filtering, its level is controlled in the drug substance to ensure complete removal.

- Arsenic pentoxide content: Arsenic could potentially be oxidized to As (V) which in consequence may form Arsenic (V) oxide. Therefore, the level of arsenic pentoxide is controlled in the drug substance.
- Loss on drying test: water content and acetone are controlled by this test. The limit of 0.5% is in keeping with batch data and provides sufficient control of the Class 3 solvent acetone at the maximum daily dose in accordance with ICH guideline Q3C (R8).
- The levels of potential metal residues different from Arsenic (which is a microelement of Arsenic Trioxide molecule) are routinely controlled in the drug substance. Acceptance criteria have been established in accordance with ICH guideline Q3D (R1) for elemental impurities in drug substance with daily dose of not more than 1 g per day. It should also be noted that that the parenteral route of administration was considered for setting the specifications for elemental impurities in the drug substance, which leads to the establishment of more stringent acceptance limits compared to the oral route of administration intended for oral ATO capsules.

Table 1: Specifications for ATO Drug Substance

Test	Acceptance Criteria		Method
Appearance	White to off white powder.		Visual
Identification	A. The resulting yellow precipitate dissolves when adding NH3 solution.		Chemical test
	B. HPLC: The retention time of the major peak in the Sample solution corresponds to that in the Standard solution, as obtained in the As 2O5 test.		HPLC
	C. IR: The spectrum of the sample matches the I.R. spectrum of Arsenic Trioxide reference standard.		IR spectroscopy
Solubility	Practically insoluble to sparingly soluble in water. Practically insoluble in ethanol, chloroform and ethyl ether. It dissolves in solutions of alkali hydroxides (1M NaOH).		Dissolution test
Appearance of solution	Clear and colourless.		Turbidity and colour tests
pH of solution	4.0 – 7.0		Potentiometry
Sulphides	≤ 10 ppm		Colour test
Nitrate	≤ 100 ppm		IC
Nitrite	≤ 100 ppm		IC
Chloride	≤ 50 ppm		IC
Assay	99.5 – 101.5% (on dried basis)		Titration
Metallic Arsenic content	≤ 0.10%		Gravimetry
As 2O5 content	≤ 0.05%		HPLC
Loss on drying	≤ 0.5%		Gravimetry
Metallic Impurities	Cd	≤ 2 ppm	ICP-OES
	Pb	≤ 5 ppm	
	Hg	≤ 3 ppm	
	Co	≤ 5 ppm	
	V	≤ 10 ppm	
	Ni	≤ 20 ppm	
	Li	≤ 250 ppm	
	Sb	≤ 90 ppm	
	Cu	≤ 300 ppm	
Iron content	≤ 5 ppm		ICP-OES

Test	Acceptance Criteria		Method
Bacterial endotoxins	≤ 1.0 EU/mg		LAL test
Microbiological analysis	TAMC	≤ 100 CFU/g	USP <61>

	TYMC	≤ 10 CFU/g	USP <61>
	Escherichia coli	Absence	USP <62>
	Salmonella	Absence	USP <62>
	Pseudomonas aeruginosa	Absence	USP <62>
	Staphylococcus aureus	Absence	USP <62>

The drug product specifications have been developed in line with ICH guidance for an oral solid dosage form (ICH guidelines Q6A *Specifications: Tests Procedures and Acceptance Criteria for New Drug substances and New Drug Products* and Q3B (R2) *Impurities in New Drug Products* and USP General Chapter <2> *Oral Drug Products – Products Quality Tests*).

The drug product specifications for the oral ATO capsules developed by Medsenic are presented in Table 2 below. These specifications are fully supported by batch data and stability data.

Table 2: Specifications for Oral ATO Capsules, 1mg, 5 mg and 10 mg

Appearance
1 mg: Orange coloured size 3 capsule white to off white powder fill
5 mg: White coloured size 3 capsule with white to off white powder fill
10 mg: Orange and white coloured size 3 capsule with white to off white powder fill
Visual
All strengths:
Release: Retention time of the
sample is ± 2% of that of the reference standard.
Shelf-life: N/A

Test	**Acceptance Criteria at Release and Shelf-life (Unless Specified Otherwise)**	**Method**
Assay	**1 mg:** **Release**: 93.0 - 105.0% of Label Claim **5 mg and 10 mg:** **Release**: 95.0 - 105.0% of Label Claim **All strengths:** **Shelf-life:** 90.0 - 105.0% of Label Claim	HPLC-UV
Uniformity of Dosage Units	**All strengths:** **Release:** Complies USP <905> **Shelf-life:** N/A	USP <905>
Limit test for Related Substances	**All strengths:** NMT 0.5% Arsenic Pentoxide (As 2O5, Arsenic (V) oxide)	HPLC-UV
Dissolution	Q ≥ 80% at 30 minutes	USP II (Paddles), HPLC-UV
Water Content	Report Result	USP <921> (Karl Fischer)
Microbiological Content		
TAMC	≤ 10^3 CFU/g	USP <61>
TYMC	≤ 10^2 CFU/g	USP <62>
Specified Microorganisms: Escherichia coli	Absent in 1 g	USP <62>

4.9.4.2 Phase II IV ATO Study

Design and Objective:

Study GMED16-001 was a single-arm, prospective, national, multicentre, (non-randomized), open-label phase II trial to investigate the overall response rate (complete response and partial response) to treatment with ATO in combination with prednisone with or without cyclosporine, at 6 months after diagnosis of moderate to severe cGvHD conducted in France[59].

Secondary Endpoints:

Secondary endpoints included Failure-free survival (FFS), Non-relapse mortality (NRM) of infectious and non-infectious origin, Overall survival (OS), Progression-free survival (PFS), Sparing of long-term use of corticosteroids, quality of life self-reported by patient (Lee Symptom Scale (LSS) and FACT-BMT), tolerability and safety of ATO + prednisone, with or without cyclosporine.

Patient Enrolment and Demographics:

The study was planned to enrol 24 patients. A total of 22 (21 + 1 not treated P01-01) patients were enrolled in the study with recruitment starting in December 2016 and ending on 30 June 2019.

- One patient did not receive ATO because of relapse of leukaemia before treatment was initiated (Patient N ° P01-01). This patient is not considered in the full analysis set nor in the safety set and is not part of the final analysis.
- One patient was withdrawn per patient wishes and with physician approval following hepatic toxicity after receiving 2 ATO infusions. Withdrawal occurred once the toxicity resolved (Patient N° P01-05). This patient is not considered in the full analysis set population.
- Seventeen patients (81%) were counted in the Per Protocol (PP) population (3 were excluded with protocol deviations: 2 patients with late M6 visit + 21 and 26 days from planned date) and 1 patient with a half-dose in part of the 1st treatment cycle.

Table 3: Chronic GvHD at Baseline (Safety Population)

Overall severity according to physicians, n (%)	**Safety Population (n=21)**
Mild	1 (4.8)
Moderate	6 (28.6)
Severe	14 (66.7)
Number of organs involved according to Chronic Form A, n (%)	**Safety Population (n=21)**
1	2 (9.5)
2	2 (9.5)
3	4 (19.0)
4	3 (14.3)
5	8 (38.1)
6	2 (9.5)

Methodology:

In this study, the ATO was administered during a cycle of 4 weeks including 11 infusions of 0.15 mg/kg/day, while the administration of prednisone was maintained at 1 mg/kg/day every day during the first 2 weeks, before eventually tapering down (as per investigator's choice) until the response assessment at 6 weeks.

The first 11 patients of the study received ATO as the solution for injection Trisenox®, while all subsequent patients recruited in this study were given Arscimed®, the IV formulation developed by Medsenic. Each patient

[59] See for further details: https://clinicaltrials.gov/ct2/show/NCT02966301?term=gmed16&draw=2&rank=1

was administered the same product throughout the treatment cycles, therefore the same patient always received the same formulation.

The response rate was defined according to the NIH consensus response criteria (Jagasia et al., 2019; Lee et al., 2015):

- Complete remission (CR): the complete disappearance of any sign of chronic GvHD.
- Partial remission (PR): improvement of 1 or more point on a 4 to 7-point scale or an improvement of 2 or more points on a 10 to 12-point scale in at least 1 organ or site without progression in any other organ or site.

If the response assessment at 6 weeks (and later) indicated Complete or Partial Response, prednisone administration was to be tapered down.

A threshold of 60% overall response rate for treatment with corticosteroids with or without cyclosporin in study GMED16-001 was chosen as a realistic estimate. According to modern diagnostic and response assessment criteria, an improvement of the overall response rate by 15% to 75% is considered to be clinically meaningful for the treatment of moderate to severe cGvHD.

Twelve patients (57.1%) had 1 cycle of treatment with ATO and 9 (42.9%) had two cycles of treatment with ATO. 10 Patients had a concomitant treatment with ciclosporin at one point during the study. At entry, all patient received corticosteroids at a mean dose of 0.93 ± 0.21 mg/kg/day.

Results:

Primary endpoint

In the FAS (Full Analysis Set) population, 75% of patients achieved complete (35%) or partial (40%) clinical response at 6 months per investigator evaluation (main endpoint). In the PP (Per Protocol) population, 82.4% of patients achieved complete (41.2%) or partial (41.2%) remission.

Secondary endpoints

Table 4: Survival Secondary Endpoints

	Timepoint	**Percentage of FAS Population**	**Additional Notes**
Estimated failure-free survival rate	**Month 6**	90%	Two patients received additional systemic treatment for cGvHD before M6. Between M6 and M12, 4 patients received additional systemic treatment for cGvHD and 1 patient died. No patient experienced early failure (before week 6).
	Month 12	65%	
Progression-free Survival	**Month 6**	95%	cGvHD progression was diagnosed in one (5%) patient within 6 months after first ATO infusion and in 2 patients (15%) between M6 and M12.
	Month 12	83.8%	
Overall survival rate	**Month 6**	100%	One patient died after 6.4 months from a septic shock not related to ATO. One patient died after the planned M12 date, but before the M12 visit could take place.
	Month 12	95%	
Estimated non-relapse mortality rate	**Month 6**	0%	As mentioned above, one patient died after 6.4 months.
	Month 12	5%	

As regards sparing corticosteroids, the mean daily dose of prednisone was 0.92 ± 0.21 mg/Kg at baseline, and decreased quickly after first ATO infusion. Six out of 20 patients (30.0%) at M6 and 9 out of 19 patients (47.4%) at M12 were definitively weaned from prednisone[60].

For quality-of-life secondary endpoints:
- According to the Lee Symptom Scale, there was a significant decrease from baseline: -8.5 ± 20.14 (median: -10.2) points at M6 (p=0.030) which was not significant anymore at M12: -5.2 ± 20.6 (median -1.0; p=0.189) with high between-individual heterogeneity.
- The FACT-BMT was only partially responded in most patients, limiting the interpretation of the results.
- The Chronic Form B (a self-evaluation of severity) was assessed at baseline by 13 patients. Between baseline and M6, 4/10 patients (40%) estimated that their cGvHD improved, 4/10 (40%) considered that there was neither improvement nor worsening and 2/10 (20%) considered their condition to be worsened. From baseline to M12, 1/8 patients (12.5%) considered their disease worse and 5/8 (62.5%) that it did not vary and 2/8 (25%) that it improved.

Conclusion

Though this is a non-comparative study, these results can be contrasted with the average overall response rate observed with the standard of care of corticosteroids averaging at 40-60%.[61] Additionally, in this study the mean daily dose of Prednisone decreasing quickly after first ATO shows the potential of ATO to reduce patient exposure to corticosteroids. As regards the tolerability and safety results, two types of adverse effects linked to ATO (hepatic toxicity and cardiac QT lengthening (rare)) were observed, but these effects were reversible once the treatment with ATO was transiently stopped. (Hamidou et al 2021[62]).

This study demonstrates that the response rate with ATO is far larger than that observed in corticosteroids alone therefore this Phase II study can be considered as a proof of concept to support the initiation of the Phase III trial. Of note, the study was conducted in accordance to Good Clinical Practice, as required per FDA Acceptance of Foreign Clinical Studies Not Conducted Under an IND.

4.9.4.3 APML5 Bioavailability Study

As the envisaged Phase III study for cGvHD will be using an oral formulation of ATO rather than IV ATO, which has been more thoroughly researched, a bioavailability study (Study APML5) to confirm the bioequivalence of the two formulations was also carried out.

Design and Objectives:

The APML5 trial (ACTRN12616001022459) was a phase 1, 2-part 2- sequence, 4-period bioavailability study in 31 patients with previously untreated acute promyelocytic leukaemia (APL), embedded with a standard-of-care consolidation regimen (ATRA + IV ATO). The study aim was to characterise the bioavailability of encapsulated oral ATO (licensed from Phebra) in patients with APL by comparing the total arsenic AUC whole blood (WB) and plasma (PL) after oral and IV ATO administration.

Patient Enrolment and Demographics:

Initial pharmacokinetic data from the APML5 part 1 pilot (n=9) indicated oral and IV ATO provide comparable arsenic exposure over repeated cycles of consolidation.

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[60] Dominique Rongvaux-Gaïda, Maëva Dupuis, Joël Poupon, Nouzha Djebrani-Oussedik, Catherine Lemonnier, François Rieger. High Response Rate and Corticosteroid Sparing with Arsenic Trioxide-Based First-Line Therapy in Chronic Graft-versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation, in Transplantation and Cellular Therapy, Volume 28, Issue 10, October 2022, Pages 679.e1-679.e11. Abstract.

[61] Bruce R. Blazar, Kelli P. A. MacDonald, Geoffrey R. Hill; Immune regulatory cell infusion for graft-versus-host disease prevention and therapy. Blood 2018; 131 (24): 2651–2660. doi: https://doi.org/10.1182/blood-2017-11-785865

[62] Mohamed Hamidou, Antoine Néel, Joel Poupon, Zahir Amoura, Mikael Ebbo, Jean Sibilia, Jean-Francois Viallard, Benjamin Gaborit, Christelle Volteau, Jean Benoit Hardouin, Eric Hachulla and François Rieger, Safety and efficacy of low-dose intravenous arsenic trioxide in systemic lupus erythematosus: an open-label phase IIa trial (Lupsenic), Arthritis Res Ther. 2021, Mar 3, 23(&):70. Doi: 10.1186/s13075-021-02454-6. Abstract.

To conclusively establish bioequivalence, 22 patients at 12 sites were randomized in APML5 part 2 (Jan 2019-June 2020) to IV or oral ATO 0.15 mg/kg/d. The target accrual of 20 evaluable patients was reached after 2 replacements (replaced patients had insufficient PK data). Median age was 45.9 years (range 23.4-75.2), 10 male, 10 female, 14 standard-risk, and 6 high-risk.

Methodology:

PK sampling was conducted in week 1 of cycles 1 and 3, and the alternate route in week 1 of cycles 2 & 4. Total arsenic was quantitated by inductively coupled plasma mass spectrometry. Point estimates of mean oral/IV arsenic ratios +/- 90% confidence intervals (CI) for AUC (µmol/l.h) and C (µmol/l) in WB and PL were calculated by linear mixed model analysis incorporating fixed and random effects.

Results:

Both ATO formulations were associated with significant increases in AUCain WB and PL from day 1 to day 4 of each cycle ($p<0.001$), indicative of short-term arsenic accumulation, but no accumulation occurred between sequential cycles. Estimates of the geometric mean of the oral/IV ratio for each PK parameter closely approximate unity and the 90% CI fall with the conventional bioequivalence limits (0.80, 1.25). Distinguishing adverse events (AEs) specifically related to oral ATO from those related to IV ATO is problematic, since IV ATO was also administered for 3 weeks in cycles that commenced with 1 week of oral ATO. Nevertheless, no excess of grade 3-4 AEs (including gastrointestinal toxicity) was noted in cycles that contained oral ATO, and no instances of oral or IV ATO-associated QTc prolongation were observed during part 2 of APML5, despite monitoring with twice weekly electrocardiograms in each cycle. One patient with high-risk disease relapsed after consolidation.

These results confirmed the bioequivalence of oral and IV formulations of ATO when administered in the context of standard-of-care. Unexpected toxicity signals were also not evident. This study provides rationale for the use of oral ATO in the place of IV ATO.

Geometric Mean of Oral/IV Ratio

The data demonstrated low inter and intra patient variability and indicate that oral ATO (OATO) and IV ATO provide comparable arsenic exposure over repeated cycles of consolidation. The study APML5 provides clear evidence supporting the use of efficacy and safety data from studies with IV formulation, in clinical development of the oral ATO formulation.

APML 5 Study Safety Data

In addition to the safety data regarding IV ATO specifically, study APML5, a randomized crossover bioavailability study supported the bioequivalence of the OATO and IV ATO when administered in the context of SOC consolidation, and unexpected toxicity signals were not seen.

A review of AEs (adverse events) from the study shows a safety profile similar to that previously reported for ATO. 12 on treatment SAEs (serious adverse events) were reported in 10 patients on the study. The SAEs were typical of those expected to be observed in APL patients undergoing ATO treatment (infection, hip deformity, febrile neutropenia, peripheral neuropathy, laryngeal mucositis, pain in extremity, upper respiratory tract infection, headache, thromboembolic event, worsening diverticulitis, and vascular access complication).

The most common AEs were headache, nausea, peripheral sensory neuropathy, constipation, fatigue, vomiting, infection, decreased neutrophil count, and pain. When comparing AEs that occurred in cycles where oral ATO was administered with AEs that occurred in cycles without oral ATO, both vomiting (5 out of 6 patients experiencing the AE) and nausea (10 of the 17 patients experiencing the AE) were more common with oral ATO. Peripheral sensory neuropathy was less commonly observed in cycles with oral ATO (2 of 9 patients with AEs). Elevation in serum enzymes (alanine amino transferase, aspartate aminotransferase, GGT, or alkaline phosphatase) were more common with oral ATO cycles (11 events in 4 patients) when compared to cycles without oral ATO (3 events in 2 patients). Serum enzyme elevations in cycles with oral ATO did lead to the withdrawal of 1 patient after their 3rd cycle.

Conclusion

BioSenic believes that the totality of safety data available at the time of filing will be sufficient for the regulator to make an informed decision about safety of OATO in forthcoming clinical trials.

4.9.4.4 Phase III study for cGvHD (Study GMED23-002)

The proposed Phase III study (Study GMED23-002) that BioSenic Group envisages to start in 2023 is a multicentre, international, randomized, double- blind placebo-controlled Phase 3 study to assess the efficacy and safety of OATO as add on therapy to corticosteroids as first line treatment of in cGvHD.

One hundred and eighty-two (182) total patients with newly diagnosed moderate or severe cGvHD as defined by the NIH Consensus Development Project Criteria are planned to be enrolled and will be randomized in a 1:1 ratio (91 patients in each group) receiving either 0.15 mg/kg/day OATO (Arm A) or matching placebo (Arm B) both arms in combination with prednisone (starting at 1 mg/kg/day). Treatment with OATO/placebo will be administered continuously during a cycle of three weeks (21 days of administration) started within 7 days after cGvHD established diagnosis. Systemic corticosteroids are currently the standard-of-care (SOC) for cGvHD. Corticosteroid therapy will be tapered as per a standard taper regimen with the goal of reducing exposure to high- moderate dose corticosteroids as quickly as possible according to clinical severity of cGvHD. A standard steroid taper schedule is provided in table below. The randomization between arms will be stratified according to NIH Global Severity grade (moderate vs. severe), immunosuppressive treatment at inclusion (yes or no), and region of participant's study site. An interim analysis will be performed when 50% of patients have completed their M6 visit. Based on the statistical date of the interim analysis, BioSenic will consider applying for conditional market approval by the FDA in the U.S. or the like in selected countries (e.g. compassionate use in France).

The design of Study GMED23-002 as a controlled study avoids the difficult interpretability of single arm trials. The controlled add-on design proposed is in line with the NIH consensus development project on criteria for clinical trials in first line treatment of chronic GvHD. The study is proposed to be a randomized trial in order to reduce bias in the conduct and interpretation of the results in line with the recommendation of *ICH Topic E9 Statistical Principles for Clinical Trials* (ICH-E9_ Guideline, 1998). A double-blind design was chosen for this study in accordance with the ICH Guideline as preferable for the main endpoints and the Patient Reported Outcome (PRO) measures.

The chosen study design will allow for interpretation of treatment effect in terms of efficacy and safety. The safety of this study will be monitored by an independent data monitoring committee (IDMC) as outlined in the DMC charter and in accordance with Medsenic's Pharmacovigilance procedures.

Approximately 70 centres in various countries including the U.S. will participate and are expected to enrol 3 to 4 patients each. The overall duration of the study is expected to be 48 months (study duration for a considered patient: 6 months).

The planned study timelines are as follows:

- First patient first visit: early-2025
- Last patient last visit: end-2028

Prednisone Taper Schedule

Week	Dose (mg/kg actual body weight/day)
0	1.00 qod
2	0.85 qod
4	0.75 qod
6	0.65 qod
8	0.55 qod
10	0.45 qod

12	0.35 qod
14	0.25 qod
16	0.20 qod
18	0.15 qod
20	0.10 qod
22	0.05 qod
24	0.0

Medsenic aims to achieve that this randomized, double- blind, placebo-controlled Phase III study will provide sufficient evidence of safety and efficacy of OATO in combination with corticosteroids as first line treatment of cGvHD.

4.9.5 *Phase IIa study to evaluate ATO in Systemic Lupus (SLE)*

Background

Lupus animal model has shown that arsenic trioxide (ATO), a treatment of acute promyelocytic leukaemia, could be effective in SLE. The clinical trial was conducted with 11 SLE patients (LUPSENIC study; NCT01738360)[63] to evaluate the safety and efficacy of a short course of intravenous ATO in patients with active SLE (Hamidou et al., 2021)[64].

Methods

This phase IIa, open-label, dose-escalating study enrolled 11 adult SLE patients with a non-organ threatening disease, clinically active despite conventional therapy. Patients received 10 IV infusions of ATO within 24 days. The first group received 0.10 mg/kg per injection, with dose-escalating to 0.15 mg/kg in a second group, and to 0.20 mg/kg in a third group. The primary endpoint was the occurrence of adverse events (AEs) and secondary endpoints were the number of SLE Responder Index 4 (SRI-4) responders at week 24 and reduction of corticosteroid dosage. In an exploratory analysis, we collected long-term data for safety and attainment of lupus low disease activity state (LLDAS).

Results

The study results demonstrated an acceptable safety and tolerability of the doses between 0.10 and 0.20 mg/kg used repeatedly during less than one month. Twelve SAEs related to six patients were observed. Four SAEs were related to the treatment (grade 3 neutropenia, osteitis, neuropathy), two of which were attributable to ATO (neutropenia in the two patients treated with mycophenolate). Two patients suffered a severe flare during the last 4 weeks of the trial. The other SAEs were attributed to the SLE condition itself and to concomitant immunosuppressive treatments. A total of 119 adverse events were observed and defined as non-serious. Causality to ATO was not fully determined in 45% of the non-serious AEs, however a toxicity of ATO was excluded and the observed symptoms were not unusual.

At W24, five patients among 10 were SRI-4 responders. Overall, mean corticosteroid dosage decreased from 11.25 mg/day at baseline to 6 mg/day at W24 ($P < 0.01$). In the long term, 6 patients attained LLDAS at W52, which continued at last follow-up (median LLDAS duration 3 years, range 2-4).

Conclusions

A short course of ATO has an acceptable safety profile in SLE patients and encouraging efficacy.

[63] https://clinicaltrials.gov/ct2/show/study/NCT01738360?term=NCT01738360&draw=2&rank=1

[64] Mohamed Hamidou, Antoine Néel, Joel Poupon, Zahir Amoura, Mikael Ebbo, Jean Sibilia, Jean-Francois Viallard, Benjamin Gaborit, Christelle Volteau, Jean Benoit Hardouin, Eric Hachulla and François Rieger, Safety and efficacy of low-dose intravenous arsenic trioxide in systemic lupus erythematosus: an open-label phase IIa trial (Lupsenic), Arthritis Res Ther. 2021, Mar 3, 23(&):70. Doi: 10.1186/s13075-021-02454-6. Abstract.

4.10 Material agreements of BioSenic Group

4.10.1 *Material agreements of BioSenic*

BioSenic has entered into the following material agreements:

4.10.1.1 License agreement between Université libre de Bruxelles (ULB) and BioSenic regarding ULB-028 patent family

BioSenic entered into a license agreement with the ULB regarding the ULB-028 patent family which is owned by the ULB. This agreement provides BioSenic 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. BioSenic 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 BioSenic, BioSenic must make payments to the ULB upon achievement of certain development and patent related milestones. In addition, BioSenic must pay to the ULB royalties based on the net sales of BioSenic 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. BioSenic shall have the right, but shall be under no obligation, to terminate the agreement, within six months prior written notice to ULB. If BioSenic (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 BioSenic, without court intervention and without having to respect any notice period.

4.10.1.2 License and co-ownership agreement between Enrico Bastianelli and BioSenic regarding the BPBONE-001, BPBONE-002 and BONE-011 patent families (JTA patent families)

The previous agreements between BioSenic 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 BioSenic and Enrico Bastianelli SRL. Enrico Bastianelli SRL is owned by more than 25% by Enrico Bastianelli and its registered office is in Jumet, Belgium.

In 2020, BioSenic entered into a co-ownership and license agreement with Enrico Bastianelli SRL regarding the JTA patent families BPBONE-001, BONE-002, BONE-011 and any future patents related to the JTA technology. This agreement provided to BioSenic 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 provided to Enrico Bastianelli SRL an exclusive, worldwide and sublicensable license over the same technology for all veterinary applications.

This co-ownership and license agreement was terminated when BioSenic decided to stop the development of the JTA technology before any exploitation of the JTA technology. This decision triggered the transfer of the rights of Bone Therapeutics in the JTA patent families BPBONE-001, BONE-002, BONE-011 to the Walloon Region.

In March 2023, BioSenic announced that it had used the statistical analysis capabilities of Artialis to re-evaluate the results of the Phase III JTA-004 trial in the subset of patients with the most painful and inflammatory form of knee osteoarthritis (OA). This allowed BioSenic to distinguish a group of patients, representing about one third of the total patients, who show a pain-relieving effect of JTA-004 not only superior to placebo but also to the active comparator. By identifying three subtypes of OA, amongst which a subtype of OA patients with more severe symptoms and inflammation, this new post-hoc analysis changes the therapeutic profile of the molecule and potentially allows for the possibility of stratifying patients for a new, optimized Phase III clinical study. BioSenic, which does not intend to allocate R&D resources to support the clinical development of JTA-004 and will continue to focus its R&D activities on the development of its autoimmune (ATO) platform, is seeking to collaborate with existing and potential partners to explore options for the future development of JTA-004 based on this new post-hoc analysis. If no concrete licensing options would materialise in the near future, also because such licensing option may trigger the need for a new Phase III clinical trial with a different patient recruitment (which BioSenic does not intend to conduct), BioSenic will likely stop its efforts to seek collaborations with external partners for the future development of JTA-004.

Given BioSenic's statistical analysis results from the JTA-004 Phase III clinical trial data obtained in March 2023, BioSenic decided to reacquire the intellectual property rights in the JTA technology owned by the Walloon Region, including the rights in the JTA patent families BPBONE-001, BONE-002, BONE-011 and the Walloon Region accepted to retrocede its rights to the JTA technology to BioSenic Group in 2023. Although BioSenic has been discussing for quite some time the opportunity with Enrico Bastianelli SRL to enter into a co-ownership agreement for the old JTA-Gen1 patent families (i.e. the patent families BPBONE-001, BONE-002, BONE-011), such discussions did not result in the conclusion of a new co-ownership agreement. The absence of such co-ownership agreement creates exploitation problems with third parties and possible licensees for the use of the JTA technology. This has therefore a negative impact on BioSenic's possibilities to collaborate with external partners for the future development and valorisation of the JTA technology as it exists.

4.10.1.3 Sublicense agreement between Enrico Bastianelli SRL and BioSenic regarding the BONE-001, BONE-002, BONE-013, BONE-017, BONE-018 and BONE-019 ALLOB patent families

The previous agreement between BioSenic 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 BioSenic and Enrico Bastianelli SRL. Enrico Bastianelli SRL is owned by more than 25% by Enrico Bastianelli and its registered office is in Jumet, Belgium.

Under this agreement, Enrico Bastianelli SRL 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.

BioSenic will further pay Enrico Bastianelli 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).

4.10.1.4 Loan agreement with the European Investment Bank

On 1 July 2021, BioSenic announced that it had signed a loan agreement of up to €16 million with the European Investment Bank (EIB). The EIB financing would support and prepare Bone Therapeutics' lead asset, the enhanced viscosupplement JTA-004 for future regulatory approval and commercialization. JTA-004, was being evaluated in a registrational phase III clinical trial for the treatment of osteoarthritic pain in the knee. Due to

the fact that the primary endpoints and accompanying objectives of the Phase III results were not met as anticipated, further investments are currently put on hold.

The EIB financing would primarily be used to accelerate the clinical development of ALLOB, BioSenic's scalable allogeneic cell therapy platform. ALLOB has been tested in a phase IIb study in patients with difficult-to-heal tibial fractures.

The loan financing has been 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 BioSenic 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 BioSenic's 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 BioSenic's share capital, including capital increases if they exceed €15 million in aggregate starting from the disbursement of the first tranche.

The first tranche of €8 million was received on 6 September 2021 (upon approval of the issuance of associated warrants by BioSenic's General Meetings on 23 August 2021).

Given the disappointing results of JTA Phase III published in 2021, the second €8 million tranche has accordingly been excluded in the forward-looking cash projections of BioSenic and new negotiations with the European Investment Bank will need to be scheduled first.

Pursuant to the loan facility, BioSenic is not allowed to incur financial indebtedness towards third parties exceeding €2 million. As of 30 September 2023, such permitted financial indebtedness amounted to €1.4 million.

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.

As of 30 June 2023, the total amount is equal to €8.10 million.

On 14 September 2023, BioSenic announced that it has reached a non-binding agreement with the EIB for the restructuring of the loan agreement. The outstanding loan for a principal outstanding amount of €8 million will be extended to 2030 and can be further extended by BioSenic for up to 24 months depending on its cash balance, end of 2032. The interest rate will become 5% per year, payable annually, with an additional non-compounding interest of 3% per year that will be added to the principal amount upon (p)repayment of the loan. The outstanding warrants of the EIB would be cancelled, and EIB should receive a similar return as Monument and Patronale if the latter's new convertible bonds are effectively converted into shares. Completion of the restructuring is still subject to (i) formal EIB approval and (ii) BioSenic raising sufficient new equity for BioSenic to continue its operations including the Phase 3 clinical trial of its lead Oral ATO therapeutic candidate targeting cGvHD.

4.10.1.5 Agreements between BioSenic and Medsenic's shareholders

BioSenic entered into two agreements in relation to Medsenic.

a. Subscription agreement between a large majority of the shareholders of Medsenic, as subscribers, and BioSenic

Upon the terms and subject to the conditions set forth in a subscription agreement dated 9 August 2022, the subscribers transferred to BioSenic 37,649 shares in Medsenic, representing 51% of the fully diluted share

capital of Medsenic, on 24 October 2022 (the "**Completion Date**"). In exchange for the subscription, the subscribers received 90,668,594 new ordinary shares of BioSenic on the Completion Date.

b. Shareholders' agreement relating to Medsenic between BioSenic, as majority shareholder, and Medsenic's minority shareholders

Pursuant to a shareholders' agreement dated 24 October 2022 between BioSenic and the shareholders of Medsenic holding the remaining 48.19% of the shares of Medsenic (the "**Minority Shareholders**"), the Minority Shareholders agree to contribute all of their remaining Medsenic shares into BioSenic in two instalments, each time for half of their remaining shareholding. These additional contributions shall in principle take place at the same time as the first two equity raises of BioSenic (except for capital increases relating to the exercise of warrants and conversions of convertible bonds, if the conditions for execution are met) to be carried out in order to finance the continuation of BioSenic's activities. It is however not contemplated to proceed with these additional contributions together with the placement of new securities that is currently envisaged by BioSenic in 2024.

Except in case of material adverse change in BioSenic's assets, liabilities or clinical trials, these contributions will be made on the basis of Medsenic's valuation as used for the Contribution and by using the same price per share of BioSenic as used for the simultaneous equity raise (which shall not be lower than the valuation of BioSenic used for the Contribution). However, if Medsenic obtains extended development and commercialisation rights from Phebra (including for the US, UK and Japan) under economically favourable terms for Medsenic, the valuation of any shares not yet contributed to BioSenic will be revaluated by an independent expert if the value of Medsenic would exceed the range set out in the external valuation report prepared for the Contribution. For more information on the license agreement and the marketing and supply agreements with Phebra, please revert to Section 6.4.4.2. Positive events can also be expected to lead to a higher share price and could therefore also result in a positive revaluation of BioSenic.

The contribution of the remaining 48.19% should occur within two years following the Completion Date (i.e., by 24 October 2024) and if BioSenic has not completed a capital increase within these 2 years , the contribution of their remaining Medsenic shares will be made in one instalment based on the same valuations as used for the Contribution. BioSenic also benefits from a call option right over the remaining 48.19% of Medsenic's shares to enforce such contributions. BioSenic may exercise the call option, at its sole discretion, for all (and not part) of the shares until the 24 October 2025.

4.10.2 *Material agreements of Medsenic*

BioSenic's subsidiary Medsenic has entered into the following material agreements:

4.10.2.1 License agreement with the *Centre national de la recherche scientifique* (CNRS) in France

Medsenic entered into a license agreement with CNRS regarding the arsenic salts for autoimmune indications as claimed in the patent family the CNRS has filed in 2002 and still owns. This agreement provides Medsenic and its affiliates with an exclusive and worldwide license over the technology claimed by the CNRS patent family for all human and veterinary autoimmune applications. CNRS retains the right to operate this technology for research and educational purposes only. BioSenic may grant sublicenses, the identity of such sub-licensee(s) being subjected to prior approval by CNRS. In consideration of the rights granted to Medsenic, Medsenic must make payments to the CNRS upon achievement of certain development and patent related milestones. This part has been amended by an agreement with CNRS through 3% Medsenic shares granted against the suppression of the milestones and royalty payments. It is worth mentioning that any new intellectual property on the use of arsenic salts will be 100% property of Medsenic.

4.10.2.2 License agreement and marketing and supply agreement with Phebra

Medsenic and Phebra entered into (i) a license agreement on 21 May 2021 and (ii) a marketing and supply agreement on 31 May 2021 for the oral formulation of arsenic trioxide in the following indications: Graft Versus Host Disease, Systemic Sclerosis, Systemic Lupus Erythematosus, infectious diseases related to COVID-19 and CNS inflammatory diseases related to Multiple Sclerosis. In consideration for the license, Phebra received 3,151 shares (4.3% of the shares currently outstanding) in Medsenic. In addition, under the license agreement, Phebra agrees that Medsenic will have exclusive worldwide territorial rights for the use of OATO in GvHD. On 15 January 2024, the signature of a binding term sheet between BioSenic and Phebra has been announced modifying the agreements signed in May 2021. Notably, the initial license agreement of 2021 provides for a commercialization agreement of 100% net profits for Medsenic mainly in Europe and 55 % net sales profit for Phebra in the rest of the world (including major markets such as the US, Canada, South America, Japan, South East Asia, China and Australia), while the binding term sheet for the indication chronic Graft versus Host Disease (cGvHD) license now provides for a royalty payment of 2% on worldwide sales, which simplifies the conditions for offering sublicenses to new external partners. Please revert to Section 6.4.4.2 of this Registration Document for more information about the agreements with Phebra.

4.11 Partnerships

Medsenic and Phebra entered into (i) a license agreement on 21 May 2021 and (ii) a marketing and supply agreement on 31 May 2021 for the oral formulation of arsenic trioxide in the following indications: Graft Versus Host Disease, Systemic Sclerosis, Systemic Lupus Erythematosus, infectious diseases related to COVID-19 and CNS inflammatory diseases related to Multiple Sclerosis. In addition, under the license agreement, Phebra agrees that Medsenic will have exclusive worldwide territorial rights for the use of OATO in GvHD. On 15 January 2024, the signature of a binding term sheet between BioSenic and Phebra was announced modifying the agreements signed in May 2021. Notably, the initial license agreement provides for a commercialization agreement of 100% net profits for Medsenic mainly in Europe and 55 % net sales profit for Phebra in the rest of the world (including major markets such as the US, Canada, South America, Japan, South East Asia, China and Australia), while the binding term sheet for the indication chronic Graft versus Host Disease (cGvHD) license now provides for a royalty payment of 2% on worldwide sales, which simplifies the conditions for offering sublicenses to new external partners. Please revert to Section 6.4.4.2 of this Registration Document for more information.

4.12 Financing Agreements

BioSenic Group has entered into a number of agreements which cover long and short (<1 year) term financing requirements. In addition, BioSenic has obtained a number of loan facilities through regional investment offices (considered as related parties) such as Novallia SA.

BioSenic has the following financing agreements in place:

- Under the framework of the European Regional Development Fund 2007-2013 (ERDF/FEDER) BioSenic 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 BioSenic in respect of this loan agreement. The loan was granted on 2 May 2016, received on 11 May 2016 and was fully repaid in June 2023.

- In June 2019, BioSenic issued non-dilutive subordinated bonds to Patronale Life and Monument for an aggregate 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 (in June 2023) and a coupon of 8% per annum. The coupon will be payable annually. The maturity date of the debt has been reached but not repaid by BioSenic following the agreement reached with Patronale Life and Monument in September 2023. Indeed, under the terms of the agreed binding term sheet, Patronale and Monument agreed to replace their outstanding loans granted to BioSenic by new convertible bonds to be issued by BioSenic (please refer to the Section 3.5 for more information in this respect). In the meantime – awaiting completion of the refinancing – no interests are been paid by BioSenic.

- In May 2020, BioSenic issued non-dilutive subordinated bonds (1,600 bonds) to Patronale Life and Monument for an aggregate amount of € 4.0 million with the option to convert. This enables BioSenic's bond investors to be repaid in BioSenic's shares, with a conversion price of € 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 € 7.0 per share mitigates the dilution of existing shareholders in the event that the bonds would be redeemed in ordinary shares of BioSenic. BioSenic renegotiated 800 convertible bonds issued on 7 May 2020 (for an amount of € 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. The maturity date of the debt has been reached but not repaid by BioSenic as, in September 2023, new binding term sheets were signed for the replacement of the Monument and Patronale bonds and loans by new unsecured convertible bonds. Please refer to the Section 3.5 for more information in this respect. In the meantime – awaiting completion of the refinancing – no interests are being paid by BioSenic.

- In July 2021, BioSenic secured a loan agreement of up to € 16.0 million with the European Investment Bank (EIB). The EIB loan financing will be disbursed in two tranches of € 8.0 million each, subject to conditions precedent. Following the approval of the issuance of associated warrants by BioSenic's General Meetings at the end of August 2021, BioSenic's received a payment from the EIB for the first tranche of € 8.0 million and the EIB was granted 800,000 warrants. Each of the two tranches is repayable to the EIB in a single payment five years following the disbursement of each respective tranche. The loan carries a fixed interest of 2% per year paid annually and a 3% capitalized interest. The maturity date has been reached but not repaid by BioSenic following the agreement reached with the EIB in September 2023 in order to, notably, replace the outstanding loan granted to BioSenic by new convertible bonds to be issued by BioSenic (please refer to the Section 3.5 for more information in this respect). The key refinancing principles discussed with EIB remain subject to formal EIB approval. In the meantime – awaiting completion of the refinancing – no interests are being paid by BioSenic.

- In May 2022, BioSenic signed a subscription agreement for a maximum € 5 million convertible bonds ("**CBs**") facility arranged by ABO Securities, through its affiliated entity Global Tech Opportunities 15 ("**GTO 15**"). All twelve tranches (seven tranches of 10 convertible bonds and five tranches of 6 convertible bonds) of convertible bonds have been subscribed for by GTO 15 in accordance with the subscription agreement entered into on 30 May 2022 for a total aggregate nominal value of € 5 million. All 100 convertible bonds have therefore been subscribed.

- In January 2024, BioSenic signed a new subscription agreement for a maximum € 1.2 million CBs facility, arranged by ABO Securities, through its affiliated entity GTO 15. The proceeds of the financing will essentially contribute to continuing to advance the clinical development of BioSenic's lead asset, its ATO product, in the treatment of chronic graft versus host disease (cGvHD). GTO 15 has committed to subscribe for up to € 1.2 million in CBs (subject to certain conditions precedent set forth in the CB facility). The CBs will be issued and subscribed for in a maximum of four tranches. The three first tranches of 30 CBs each with an aggregate principal amount of € 300,000 have been subscribed for and paid by GTO 15. The issue and subscription of the final tranche, with a principal amount of € 300,000, can be requested at BioSenic's sole discretion over a six-month period beginning on the signing date of the subscription agreement, subject to customary conditions to be met (including (i) the possibility to immediately list any new shares resulting from the conversion of the CBs and (ii) with respect only to the fourth and final tranche, that the average

daily value of the company's shares over the trailing 20 trading days – trimmed for 10% of the outliers – being higher than € 15,000).

BioSenic's subsidiary Medsenic has the following financing agreements in place:

Repayable advances:

- Medsenic has been granted a repayable advance from ADI – BPI France (conditional advances at zero interest) for an amount of € 900,000 for a period of 9 years. The loan served to finance the validation of the efficacy of an arsenical compound for the treatment of the chronic and autoimmune component of graft versus host disease. The loan does not carry any interest rate. Fixed quarterly instalments of € 37,500 are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. The loan was granted in 2016 and the final repayment is foreseen on 30 June 2025.

- Medsenic has been granted a repayable advance from ADI – BPI France for a total amount of € 700,000 (€ 210,000 of which will be paid in 2024) for a period of 11 years. The loan served to finance the testing on efficacy and tolerance of arsenic trioxide in first-line treatment of systemic sclerosis. The loan does not carry any interest rate. Variable instalments based on a depreciation table are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. The loan was granted in 2018 and the final repayment is foreseen on 30 September 2029.

Loans from BPI

- Medsenic has been granted a long-term subordinated loan from BPI ("*Prêt Amorçage Investissement FEI*") for an amount of € 375,000 for a period of 8 years. The loan served to finance the validation of the efficacy of an arsenical compound for the treatment of the chronic and autoimmune component of graft versus host disease. The loan carries an annual market-based interest rate of 4.68% and fixed quarterly instalments of € 18,750 are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. This financing benefits from a 40.00% guarantee from the Fonds National de Garantie "Prêt d'Amorçage Investissement" and a 40.00% guarantee from the European Investment Fund (EIF). The loan was granted on 5 July 2017 and the final repayment is foreseen on 31 March 2026.

- Medsenic has been granted a long-term subordinated loan of from BPI ("*Prêt Amorçage Investissement FEI*") for an amount of € 125,000 for a period of 8 years. The loan served to finance the studies on efficacy and tolerance of arsenic trioxide in first-line treatment of systemic sclerosis. The loan carries an annual market-based interest rate of 4.09% and fixed quarterly instalments of € 6,250 are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. This financing benefits from a 30.00% guarantee from Bpifrance Financement under the national guarantee fund "Prêt d'Amorçage Investissement" as well as a 50.00% guarantee from the InnovFin scheme of the European Investment Fund (EIF). The loan was granted on 29/06/2018 and the final repayment is foreseen on 31 March 2027.

- Medsenic has been granted a long-term subordinated loan from BPI (*prêt garanti par l'état* or "State Guaranteed Loan") for an amount of € 300,000 for a period of 6 years. The loan is a Covid support financing. The loan carries an annual market-based interest rate of 2.25% and fixed monthly instalments of € 6,445 are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. This financing benefits from a 90% State guarantee under the "FDG Etat Coronavirus" guarantee fund. The loan was granted on 21 April 2020 and the final repayment is foreseen on 25 April 2026.

- Medsenic has been granted a long-term subordinated loan of from BPI ("*Prêt Innovation R&D*") for an amount of € 500,000 for a period of 6 years. The loan served to finance the R&D innovation project - 3 generation drug project. The loan carries an annual market-based interest rate of 0.79% and fixed annually

instalments of € 100,000 are due to reimburse the principal amount. There are no security interests provided by Medsenic in respect of this loan agreement. The loan was granted on 06/08/2021 and the final repayment is foreseen on 31 December 2028.

Other loans

- Medsenic has been granted a State-guaranteed loan (*prêt garanti par l'état*) of € 300,000 with the CIC Ouest bank on 20 April 2020 for an initial term of one year, then amended to 21 January 2021, and on 12 March 2021 for 5 years, at 0.70% per year. This loan has a deferred principal repayment from the initial maturity of the State Guaranteed Loan (SGP) on 25 April 2021 to 24 May 2022. This financing is accompanied by a State guarantee provided for by the Amending Finance Act No. 2020-289 of 23 March 2020 and the specifications defined by the Order of 23 March 2020 granting a 90% State guarantee to credit institutions and financial companies pursuant to the aforementioned Act.

4.13 Grants and subsidies

From incorporation until 30 June 2023, BioSenic has been awarded non-dilutive financial support from the Region and by the European Commission totalling € 35.22 million. This financial support has been granted in the form of recoverable cash advances ("**RCAs**") for an amount of € 30.19 million of which € 30.139 million has been paid out to BioSenic as of 30 June 2023, and in the form of (non-refundable) subsidies for an amount of € 5.03 million of which € 4.80 million has been paid out to BioSenic as of 30 June 2023. BioSenic 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).

4.13.1.1 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, BioSenic receives funds from the Region based on statements of expenses. At the end of the research phase, BioSenic 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 BioSenic 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 BioSenic's turnover).

BioSenic owns the results of the subsidized research. Subject to certain exceptions, BioSenic 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 BioSenic 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 BioSenic under the Contracts granted are expressed to be assumed by the Region by operation of law.

BioSenic has contracted the following RCAs with the Region:

Contract N°	Name	Budget (k€)	Exploitation phase	Turnover-independent reimbursement (k€)	Total reimbursed 06/2023 (k€)	Turnover-dependent reimbursement
5369	HOMING*	648	2012-2041	648	648	5%
5827	MATOB*	744	2012-2041	744	744	5%
6064	PREOB*	998	2013-2041	240	240	0.2%
6446	METHODES*	660	2014-2041	198	184	0.073%
5993	JOINTAIC*	432	2014-2042	130	117	0.085%
6804	PROFAB*	734	2015-2042	110	110	1.28%
6834	STABCELL*	394	2015-2041	59	59	0.04%
6805	ALLOB NU*	600	2015-2042	180	112	0.2%
6337	PREOB NU*	2,960	2015-2041	444	444	0.59%
6187-6700	ALLOB*	1,306	2015-2042	392	176	1.2%
6081	GXP*	1,519	2015-2041	167	167	0.007%
6539	MAXBONE*	676	2015-2042	203	101	0.08%
6855	JTA*	600	2016-2042	180	130	0.042%
7029	CRYO*	550	2016-2042	165	110	0.37%
7028	PREOB ON3*	815	2016-2041	81	81	0.05%
7187	BANK*	258	2016-2042	78	26	0.175%
7253	JTA PROD*	742	2017-2041	223	52	0.1%
7186	ALLOB IF*	620	2017-2042	186	93	1.28%
7217	MXB BIOPRINTING*	995	2017-2042	299	99	0.1093%
7405	MECA OB*	1,815	2018-2043	545	27	0.847%
7539	LIPO*	519	2018-2043	156	10	0.23%
7280	MO SELECT*	353	2018-2043	106	9	0.082%
7406	CRYOFIN*	1,185	2018-2043	355	36	0.553%

7433	ALLOB SEQ*	1,892	2019-2043	568	57	0.90%
7620	EXCIP*	1,576	2019-2044	0	0	0.08%
1510583	ALLGEL*	155	2019-2043	47	1	0.04%
7720	RUSTUS*	454	2019-2033	136	9	0.25%
7763	PROSTERIL*	719	2020-2045	216	7	0.04%
7852	ALLOPROD*	913	2021-2046	274	9	0.05%
7646	JTA-NEXT*	2,156	2020-2044	647	43	0.20%
7813	CELLSORT*	613	2020-2045	184	0	0.05%
7845	BIOPOTAN	658	2021-2046	197	0	0.05%
8251	JTA KOA2*	926	2022-2047	278	0	0.25%
TOTAL		**30,185**		**8,436**	**3,902**	

**Exploitation already signified to the Region*

A brief description of BioSenic'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

Subsidy Names	Related Company's Projects & Activities	Description
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
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

4.13.1.2 Subsidies

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

Subsidies granted by the Region and amounting to € 5.09 million 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 2023, BioSenic has been granted subsidies related to patent applications totalling € 1.55 million of which € 1.34 million has been received. The balance will be granted based on statements of expenses to be submitted to the Region.

BioSenic has also been granted subsidies for a total amount of € 3.21 million of which € 2.90 million 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 € 629,000;
- 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;100% of costs of a research program funded by the European Commission for an amount of € 0.31 million (contract n° 607051).

These Region and European Commission subsidies for research are not refundable. Out of the abovementioned subsidies € 3.19 million has been effectively paid out on 30 June 2022.

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

BioSenic 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, BioSenic 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 BioSenic 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 BioSenic 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.

4.14 Intellectual property

4.14.1 *Patents and patent applications owned or licensed by BioSenic*

A first panel of BioSenic Group's research programmes and product candidates are covered by patent families (including patents and patent applications still pending and under examination), which were initially either

- filed in the name of Bone Therapeutics and presently owned by BioSenic; or
- licensed by Bone Therapeutics and presently licensed by BioSenic.

The management and maintenance of these patent families are under the responsibility of BioSenic Group. Further details for each program are provided below.

4.14.1.1 ALLOB

The eight patent families related to this program can be associated in two groups:

- Those having an earlier filing date defining the most general features and uses of the cell-based products (**ALLOB-Gen1**), including one patent family owned and exclusively licensed by the ULB to BioSenic Group;
- Those having a later filing date covering features and related to cell manufacturing and medical uses of ALLOB products in cell-based therapies (**ALLOB-Gen2**).

The details of the PCT international patent applications from which the ALLOB patent families are originated, and the main objects of these patent families are summarized below.

Publication No (BioSenic ref. no.)		**Main subject-matter (based on EP pending or granted claims)**
ALLOB-Gen1	WO2007/093431 (ULB-028)	• Methods for obtaining osteoprogenitors or osteoblasts from adult human bone marrow stem cells (BMSC) or adult human mesenchymal stem cells (MSC) in vitro or ex vivo, comprising culturing said BMSC or MSC in a medium including human plasma and/or specific growth factors • Cell populations comprising human osteoprogenitors or osteoblasts that are obtained using such methods and defined by the expression of CD surface markers, cytokines, biological activities and/or differentiation properties • Related pharmaceutical uses and compositions based on such cells
	WO2009/087213 (Bone-001)	
	WO2009/135905 (Bone-002)	
	WO2009/080749 (Bone-004)	Human osteoblasts that are derived by differentiation from BMSC or MSC for autologous or allogeneic administration to human subjects for treating inflammatory rheumatic diseases (IRD, such as systemic lupus erythematosus or rheumatoid arthritis), alone or in combination with anti-inflammatory drugs
AL	WO2016/170112 (Bone-013)	In vitro, non-cryogenic preservation from BMSC or MSC for autologous or allogeneic administration to human subjects that apply specific cell culture conditions

	WO2019/076591 (Bone-017) WO2020/064791 (Bone-018) WO2020/064793 (Bone-019)	• Specific methods for obtaining osteoprogenitors or osteoblasts from adult human bone marrow stem cells (BMSC) or adult human mesenchymal stem cells (MSC) in vitro or ex vivo, comprising culturing said BMSC or MSC in a medium including human plasma and/or specific growth factors, in particular for improved cryopreservation • Cell populations comprising human osteoprogenitors or osteoblasts that are obtained using such methods • Related pharmaceutical uses and compositions based upon such cells

The details of the status of the national or regional patent applications that have been filed and prosecuted on the basis of PCT international patent applications for ALLOB-Gen1 patent families are summarized below.

BioSenic ref.	**ULB-028**	**Bone-001**	**Bone-002**	**Bone-004**
PCT no.	WO2007/093431	WO2009/087213	WO2009/135905	WO2009/080749
Priority date	Feb. 2006	Jan. 2008	Jan. 2008	Dec. 2007
Expiry date	Feb. 2027	Jan. 2029	Jan. 2029	Dec. 2028
Europe	Granted (validated in 18 jurisdictions)	Granted (validated in 19 jurisdictions)	Granted (validated in 19 jurisdictions)	Granted (validated in 6 jurisdictions)
USA	Granted	Pending		Granted
Canada	Granted	Granted	Granted	
Australia		Granted	Granted	Granted
Japan	Granted	Granted	Granted	Granted
Singapore	Granted	Granted	Granted	
South Korea		Granted	Granted	Granted
India		Granted		

The details of the status of the national or regional patent applications that have been filed and prosecuted on the basis of PCT international patent applications for ALLOB-Gen2 patent families are summarized below.

BioSenic ref.	**Bone-013**	**Bone-017**	**Bone-018**	**Bone-019**
PCT no.	WO2016/170112	WO2019/076591	WO2020/064791	WO2020/064793
Priority date	Apr. 2015	Oct. 2017	Sep. 2018	Sep. 2018
Expiry date	Apr. 2036	Sep. 2038	Sep. 2039	Sep. 2039
Europe	Granted (validated in 7 jurisdictions)	Pending (near to be granted)	Granted (validated in 20 jurisdictions)	Pending (near to be granted)
Belgium	Granted	Granted	Granted	Granted
USA		Granted (divisional appl. still pending)	Pending	Pending
Canada	Granted	Granted	Pending	
Australia	Granted	Granted	Pending	Pending
China		Pending	Pending	Pending
Japan	Granted	Granted	Pending	Pending
Taiwan			Pending	
Singapore	Granted	Granted	Pending	Pending
South Korea	Granted	Granted	Pending	Pending
India		Pending	Pending	
Thailand		Pending	Pending	Pending
Mexico			Pending	
Brazil		Pending	Pending	
Russia		Pending (allowed)	Pending (allowed)	
Israel		Granted	Pending	

4.14.1.2 JTA

The five patent families related to this program can be associated in two groups:

- Those having an earlier filing date defining the most general features and uses of JTA technology (**JTA-Gen1**) and co-owned with Glob-Co SRL;

- Those having a later filing date covering more recent development in manufacturing and uses of JTA technology in clinical settings (**ALLOB-Gen2**).

The details of the PCT international patent applications and EP priority patent applications from which the ALLOB patent families are originated, and the object of these patent families are summarized below.

Publication No (Int. code)		Main subject-matter (based on EP pending or granted claims)
JTA-Gen1 (co-owned with Glob-Co)	WO2009/101194 (BPBone-01)	• Preparation and use of pharmaceutical formulations comprising hyaluronic acid, and one or more other anti-inflammatory drugs, such as clonidine, for treating musculoskeletal diseases (with or without adding cells) • These pharmaceutical formulations specific methods of administration of these pharmaceutical formulations
	WO2009/101210 (BPBone-02)	
	WO2014/049063 (Bone-011)	• Preparation of pharmaceutical formulations comprising pre-treated preparations of plasmatic proteins, hyaluronic acid, and optionally one or more other products, such as clonidine, cells, growth factors • The resulting pharmaceutical formulations and their use for treating musculoskeletal diseases such as bone or joint disease
JTA-Gen2	WO2020/229526 (Bone-020)	• Preparation of lyophilized pharmaceutical formulations comprising pre-treated preparations of plasmatic proteins, hyaluronic acid, and optionally one or more other products, such as clonidine, cells, growth factors • The resulting lyophilized pharmaceutical formulations and their use for treating musculoskeletal diseases such as bone or joint disease
	EP24nnnnnnn (ClinJTA)	• Use of products based on JTA technology such as JTA-004 in specific patients' group affected by knee osteoarthritis • Methods to define most effective products based upon JTA technology that are suitable for treating subjects affected by osteoarthritis

The details of the status of the national or regional patent applications that have been filed and prosecuted on the basis of PCT international patent applications for JTA-Gen1 and JTA-Gen2 patent families are summarized below. ClinJTA patent family is presently pending only as EP priority patent application and the decision about filing the corresponding PCT international patent application will be taken in 2024.

BioSenic ref. no.	**JTA-Gen1**			**JTA-Gen2**
	BPBone-01	**BPBone-02**	**Bone-011**	**Bone-020**
PCT no.	WO2009/101194	WO2009/101210	WO2014/049063	WO2020/229526
Priority date	Feb. 2008	Feb. 2008	Sep. 2012	May 2019
Expiry date	Feb. 2029	Feb. 2029	Sep. 2033	May 2040
Europe	Granted (validated in 18 jurisdictions)	Granted (validated in 5 jurisdictions)	Granted (validated in 18 jurisdictions)	Pending
Belgium	Granted		Granted	Granted
USA	Granted	Granted (2 patents)	Granted	Pending
Canada	Granted	Granted	Granted	Pending
Australia	Granted	Granted	Granted	
China	Granted		Granted (a divisional appl. still pending)	Pending
Japan	Granted	Granted	Pending	Pending
Taiwan				Pending
Singapore	Granted	Granted	Granted	
South Korea	Granted		Granted	Pending
India	Granted	Granted		
Brazil	Granted			
Israel	Granted	Granted	Granted	Pending

4.14.2 *Overview of intellectual property owned or licensed by Medsenic*

A second panel of BioSenic Group's research programmes and product candidates are covered by patent families (including patents and patent applications still pending and under examination), which were either:

- filed in the name of Medsenic; or
- licensed by Medsenic.

Unless indicated otherwise, the management and maintenance of these patent families are under the responsibility of Medsenic. Further details for each program are provided below.

4.14.2.1 Patent families filed by Medsenic

The details of the PCT international patent applications and of the EP priority patent application, and the main objects of these patent families are summarized below.

Publication No (BioSenic ref. no.)	Main subject-matter (based on EP pending or granted claims)
WO2018/206465 (MEDS-01)	Methods for preventing, delaying, or treating multiple sclerosis, in particular relapsing-remitting multiple sclerosis and Graft-vs-Host-Disease, using arsenic trioxide
WO2020/234414 (MEDS-02)	Combination of an arsenic compound and a metal (in particular copper) for increasing the effects of arsenic for treating cancers, autoimmune or inflammatory diseases
WO2021/198535 (MEDS-03)	Use of an arsenic compound, alone or combined with a metal (in particular copper), for treating a cytokine storm (as after SARS-CoV-2 infection)
EP23nnnnnn (MEDS-04)	In vitro methods for the diagnosis, prognosis, stratification and/or monitoring of chronic graft-versus-host disease in an individual who has received an allogeneic hematopoietic stem cell transplantation alone or in combination with other drugs (such as an arsenic compound)

The details of the status of the national or regional patent applications that have been filed and prosecuted on the basis of PCT international patent applications for MEDS-01, MEDS-02, and MEDS-03 patent families are summarized below. MEDS-04 patent family is presently pending only as EP priority patent application and the decision about filing the corresponding PCT international patent application will be taken in 2024.

BioSenic ref. no.	MEDS-01	MEDS-02	MEDS -03
PCT no.	WO2018/206465	WO2020/234414	WO2021/198535
Priority date	May 2017	May 2018	Apr. 2020
Expiry date	May 2038	May 2039	Apr. 2041
Europe	Pending	Granted (validated in 8 jurisdictions)	Pending
USA	Granted	Pending	Pending
Canada		Pending (allowed)	Pending
Australia		Granted	Pending
China	Pending	Granted (a divisional appl. Is pending)	
Japan		Pending	
Russia		Pending	

4.14.2.2 Patent families licensed by Medsenic

The details of the PCT international patent applications and of the EP priority patent application, and the main objects of these patent families are summarized below. Related cost and management are under the responsibility of filing entities (Phebra, Australia; CNRS, France).

Publication No (Int. code)		Main subject-matter (based on EP pending or granted claims)
Licensed from Phebra	WO2016/119019 (PHEB-01)	Highly soluble arsenic carbonate and/or bicarbonate compound for preparing pharmaceutical combination (in particular using a process starting from arsenic trioxide) as a solid, orally deliverable, bioequivalent form of arsenic trioxide solution, in particular to be used in the treatment of cancers
	WO2018/098519 (PHEB-02)	Solid, orally deliverable, pharmaceutical composition comprising a diarsenic tetraoxide, in particular to be used in the treatment of cancers

Licensed from CNRS	WO2003/090766 (CNRS-01)	Use of an arsenic compound (such an arsenic oxide and related salts) for treating autoimmune or inflammatory diseases, such as Graft-versus-host disease, rheumatoid arthritis, or Sjogren's Syndrom

The details of the status of the national or regional patent applications that have been filed and prosecuted on the basis of PCT international patent applications for PHEB-01, PHEB-02, and CNRS-01 patent families are summarized below.

BioSenic ref. no.	**PHEB-01**	**PHEB-02**	**CNRS -01**
PCT no.	WO2016/119019	WO2018/098519	WO2003/090766
Priority date	Jan. 2015	Dec. 2016	Apr. 2002
Expiry date	Jan. 2036	Aug. 2037	Apr. 2023
Europe	Granted (validated in 17 jurisdictions)	Granted (validation still ongoing; 11 jurisdictions until today)	Expired
USA	Granted	Granted	Granted (2 patents extended until 2031 for Graft-versus-host disease and 2030 for lupus erythematosus)
Canada	Granted	Pending	Expired
Australia	Granted	Granted	
China	Granted		
Japan	Granted	Granted (a divisional appl. Is pending)	
New Zealand	Granted	Granted	
Singapore	Granted	Granted	
Taiwan		Granted	
South Korea	Granted	Granted	
India	Granted		
Mexico	Granted	Granted	
Peru		Pending	
Chile		Granted	
Brazil	Granted	Pending	
Israel	Granted	Granted	
Saudi Arabia		Allowed	
UAE		Pending	
South Africa	Granted	Granted	

4.14.3 *Trademarks and designs of BioSenic*

BioSenic Group obtained the trademark registration for Biosenic, under class 5 in the Benelux, the EU, France, Great Britain, USA, Japan, China, Australia, and Canada.

BioSenic Group obtained the trademark registration for the following trademarks:

- ALLOB was internationally registered under class 5 and/or class 42 in the Benelux, the EU, USA, Australia, Canada, Israel, Japan, Taiwan, Hong Kong, Singapore, Thailand, and South Korea;
- JOINTAIC was internationally registered under class 5 and/or class 42 in the Benelux, the EU, Great Britain, Hong-Kong, Japan, China, Australia, and South Korea;
- MaxBone was internationally registered under class 5 and/or class 42 in the Benelux, the EU, Great Britain, Canada, Japan, China, Hong-Kong, and Australia;
- MXB was internationally registered under class 5 and/or class 42 was obtained in September 2015 in EU, US, Japan, Korea, Australia, Canada, Israel and Hong Kong;

- JTA was internationally registered under class 5 and/or class 42 was obtained in September 2015 in the Benelux, the EU, Japan, Korea, China, Australia, Canada, Israel and Hong Kong.
- Arscimed is registered under class 5 was obtained in October 2015 in France.

With regard to the designs, the following names and logos are respectively protected for BioSenic and Medsenic:

4.15 Manufacturing

BioSenic Group aims to achieve the following objectives:

- Provide adequate production capacity of any galenic form of arsenic trioxide at all stages of the development of BioSenic;
- Continuous optimization of processes to reduce costs and increase capacity of the available external or internal manufacturing infrastructures;
- Protection of know-how through in-house production and strictly manage relations with contract manufacturing organisations.

The production of arsenic trioxide is a complex process, but handled by several chemical companies (ChemCon, Umicore, etc.) and no specific difficulties are envisioned concerning the supply of raw material (As).

The IV formulation ("**Arscimed**") is protected by Medsenic's know-how and allows its manufacturing by any contracting CDMO.

The oral formulation of arsenic trioxide ("**ArsciCor**" / "**OATO**") is under exclusive licencing from Phebra and supply is subject to the terms of a marketing and supply agreement signed in 2021 with Phebra. The manufacturing facilities were in Australia but are being established in the United Kingdom. Phebra will supply OATO through a contract manufacturer based in the United Kingdom, which is chosen and selected by Phebra.

BioSenic Group intends to develop an new oral formulation arsenic trioxide / copper combination ("**ArsciCop**"), granting BioSenic Group the exclusive right to use such OATO/copper formulation. Pre-clinical studies on animals have indicated a potential for allowing decreased amounts of administered arsenic for equivalent therapeutic effects and less reversible adverse effects. The further development of ArsciCop will in principle require a Phase I clinical trial to establish the safety and bioavalability and bioequivalence.

5 CORPORATE GOVERNANCE

5.1 General

This Section summarizes the rules and principles on the basis of which the corporate governance of BioSenic has been organized pursuant to Belgian Code on Companies and Associations, and BioSenic'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 BioSenic's website (https://biosenic.com/investors). A copy of the Corporate Governance Charter can be obtained free of charge at the registered office of BioSenic.

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 BioSenic justifies certain deviations. These deviations are further detailed in Section 5.3 hereinafter.

The Corporate Governance Charter includes the following main chapters:

- Definitions;
- Structure and organisation;
- Shareholders;
- Transactions between BioSenic and its Board Members or the Members of the Management Team;
- Transactions involving Shares of BioSenic;
- 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 BioSenic 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 BioSenic complies with the Corporate Governance Code. However, BioSenic deviates from the following principles:

- *Remuneration of non-executive directors in BioSenic's shares (principle 7.6):* given the legal constraints under Belgian law to purchase own shares in order to grant these to relevant beneficiaries, the non-executive directors of BioSenic do not receive a portion of their remuneration in BioSenic's shares.

- *No grant of stock options to non-executive directors (principle 7.6):* given the technical impossibility for BioSenic to purchase its own shares and grant such existing shares of BioSenic to non-executive directors, those directors can receive warrants (subscription rights) to subscribe for new shares under the template 2020 Warrants Plan. This plan provides that the warrants shall vest and be exercisable at any time and without restriction unless BioSenic decides that these warrants may not be exercised before the end of

the third calendar year following the calendar year during which the 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 BioSenic, 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, BioSenic has not fixed any minimum threshold for the detention of shares by the Executive Directors. However, warrants on BioSenic's shares were granted to the ex-CEO and ex-CFO on 28 May 2020. These warrants shall vest and be exercisable at any time and without restriction unless BioSenic decides that these warrants may not be exercised before the end of the third calendar year following the calendar year during which the warrants were offered and indicates this in the offer thereof (which was not done for the warrants granted on 28 May 2020).

- *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 SRL / BV (since March 2019) to provide services in this respect, including the drafting of minutes of Board meetings. Given the limited size of BioSenic, 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 BioSenic 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)*: BioSenic has not adopted a diversity policy yet. However, BioSenic ensures that it meets the minimum gender diversity requirement at the level of the Board of Directors of BioSenic.

  Article 7:86 of the Belgian Code on 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 BioSenic 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 Audit Committee, one third of the members of the Executive Committee are of a different gender and half of the members of the Remuneration and Nomination Committee are of a different gender.

  As regards the employees not included above, BioSenic records 86% female employees and 14% 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 BioSenic's articles of association are available at BioSenic'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*

5.4.1.1 Composition of the Board of Directors of BioSenic SA

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

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

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 on Companies and Associations.

The members of the Board of Directors are appointed by the shareholders' meeting of BioSenic 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
François Rieger	Chairman	2022	2026	Executive	27, rue des Délices, 1203 Geneva, Switzerland
Véronique Pomi-Schneiter	Executive Director	2022	2026	Executive	26, route de la Robardière, 44120 Vertou, France
Finsys Management SRL, represented by Jean-Luc Vandebroek	Director	2022	2026	Non-Executive	Rue Charles Plisnier 25, 1420 Braine l'Alleud, Belgium
Capital Grand Est, represented by Jean-François Rax	Director	2022	2026	Non-Executive	Avenue de l'Europe 16, Immeuble Sxb1, 67300 Schiltigheim, France
Innoste SA, represented by Jean Stéphenne	Director	2018	2025	Independent	Avenue Alexandre 8, 1330 Rixensart, Belgium
Revital Rattenbach	Director	2022	2026	Independent	Rue des Ecouffes 1, 75004 Paris, France

Name	Position	Start or renewal of mandate	End of mandate	Nature of mandate	Professional address
Yves Sagot	Director	2023	2026	Independent	Chemin de la Combe, 73100 Tresserve, France

A brief overview of the relevant experience of the members of the Board of Directors is set out below.

- **Mr François Rieger** holds a PhD in Neurobiology, which he completed in 1973 at the Ecole Normale Supérieure de Paris, rue d'Ulm. His work allowed him to purify and characterize the structure of acetylcholinesterase, the main current target of Alzheimer's disease treatments. He then went on to study the cholinergic synapse and neuromuscular pathologies related to deficient functioning of nerve impulse transmission. He was appointed Visiting Assistant Professor of Neuropathology at Harvard University from 1975 to 1978, and upon his return to France, he developed a research team in a joint INSERM/CNRS unit at the Pitié-Salpêtrière Hospital on the role of ion channels in the function and morphogenesis of mammalian nerve and muscle. A stay from 1985 to 1988, at the Rockfeller University in New-York, in the laboratory of Professor Gerald Edelman, Nobel Prize, as Senior Associate Researcher, allowed him to extend his field of investigation to the field of Cellular Adhesion Proteins and to demonstrate the implication of N-CAM and cytotactin/tenascin in synaptic morphogenesis and innervation-reinnervation phenomena. In 1990, he established in his laboratory a new line of research on the primary factors of Multiple Sclerosis, an autoimmune demyelinating disease in humans, which led his laboratory to characterize a gliotoxic protein factor in MS patients and, later, in 1998, to discover in humans a fossil retrovirus still active through its envelope protein, and involved in the triggering of the autoimmune cascade in the disease. In 2007, F. Rieger created in Geneva a Binational Scientific Interest Group on the Broader Theme of Aging and Longevity, with the participation of several Franco-Swiss scientific leaders, intended to take into account both the molecular and societal aspects of this largely unexplored field. F. Rieger is Director of Research at the CNRS and author or co-author of more than 175 international publications in the field of Life Sciences and Neurosciences. F. Rieger is currently leading an Innovative Project concerning the therapeutics of Autoimmune Diseases and a co-Founder of the biotech Medsenic. He has led two successful Phase II clinical trials on Systemic Lupus erythematosus and Graft-versus Host Disease, opening a solid path towards the use of several formulations of active arsenic for the treatment of chronic, autoimmune diseases.

- **Ms Véronique Pomi-Schneiter** has 30 years of experience in operational leadership, human resource management, resource utilisation and organisational development in highly decentralised organisations. Graduated of the IFG Lorraine Business School, she has been a consultant, manager and director of companies in the consulting and human resources sector. In 2010, Véronique decided to found Medsenic with Prof François Rieger, to bring her expertise in business development and fundraising. Her experience includes streamlining operations, developing, and implementing organisational solutions and applying global HR expertise to influence the achievement of strategic objectives.

- **Mr Jean-Luc Vandebroek (permanent representative of Finsys Management SRL)** 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 BioSenic, 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. Until 2021 Jean-Luc was active within BioSenic as CFO. Today he is Chief Financial Officer at Hyloris Pharmaceuticals.

- **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 BioSenic. Together with the Board of BioSenic, 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.

- **Mr Jean-François Rax** graduated as a Biochemistry and Biotechnology engineer from INSA Lyon and joined Capital Grand Est in 2014, an independent regional private equity firm approved by the AMF with more than €180M of assets under management and which has been supporting more than 60 SMEs and start-ups in the French Grand Est Region since 2012. With 12 years of experience in venture capital & seed financing and before that 4 years in consulting and technology transfer (Inserm Transfert Initiative, Alcimed, Inra Transfert, Inserm Transfert), Jean-François is now a member of the Executive Board / Director of Investments at Capital Grand Est.

- **Ms Revital Rattenbach** is a seasoned entrepreneur in biotech with 15+ years of experience, Revital Rattenbach is the founding CEO of 4P pharma, a clinical stage biotech specialized in drug regeneration for treating severe diseases including osteoarthritis and acute and chronic pulmonary complications of viral infections (for more information, see https://4p-pharma.com/). Under her CEOship, 4P Pharma assembled a unique circular drug development platform which delivered 2 programs in clinical stage while nurturing a furnished preclinical pipeline. She signed multiple academic and pharma collaborations worldwide and closed series of fundraising since 4P incorporation 8 years ago. Prior to her role at 4P, Revital was the founding CEO of PharmaSeed Europe (2013-2014) a research organization specialized in early development where she supervised all BD activities, finance and operations. Prior to PharmaSeed, Revital started her entrepreneurship path by co-founding Astem, a spin-off of Sorbonne University to activate endogenous adult stem cells. She holds a PhD in Biology from University of Paris VI and an MBA from Sorbonne University.

- **Mr Yves Sagot** co-founded Relief Therapeutics in 2013 to develop a clinical asset acquired from Merck Serono. In 2016, Relief Therapeutics went public on the Swiss stock exchange (SIX) after a reverse merger with THERAMetrics. Whilst maintaining his activities as Chief Scientific Officer at Relief Therapeutics, Yves Sagot created MBS Sagot Consulting in 2018 to provide to the life science market senior expertise covering research and early clinical development. Subsequently, after leaving Relief Therapeutics, he is a private investor in biotechnology via MBS Invest & Consult Sàrl. He is also one of the ambassadors of the Léon Bérard Cancer Center, an internationally recognized research center in Lyon, France. He has authored 25 papers that have been published in international peer-reviewed journals, holds three granted patents and received the Serono CEO Award in 2001 and the Merck Serono Reward and Recognition Award in 2008. Yves received a Certificate of Advanced Studies in Management of Medtech, Biotech & Pharma Ventures from the Management of Technology EPFL in Lausanne, Switzerland., holds a Ph.D in Neurobiology and a Masters in Pharmacology and Fundamental Toxicology from the Université Paul Sabatier (UPS), Toulouse, France.

5.4.1.2 Litigations statement

At the date of this Document, none of the members of the Board of Directors and the Executive Committee of BioSenic, 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 agreement with creditors to pay all or part of its debts; or
- been a director, member of the administrative, management or supervisory bodies and/or senior manager of any company at any time of, or within 12 months preceding, any bankruptcy, receivership, liquidation or administration; or
- had his assets be 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 by designated professional bodies; or
- ever been disqualified by a court from acting as a director member of the administrative, management or supervisory bodies and/or senior manager 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 of BioSenic 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 BioSenic, the following main directorships of administrative, management or supervisory bodies and partnerships:

Board of Directors and/or Executive Committee Members	Current Mandates	Past Mandates
François Rieger	Chairman of Medsenic Member and Chairman of the CS	None
Véronique Pomi-Schneiter	Executive Director Medsenic	None
Jean-Luc Vandebroek (permanent representative of Finsys Management SRL)	CFO Hyloris	Director of Bihr Europe SA Director of Moteo Two Wheels Europe NV Director at SISE SA
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 Ronveaux Chairman at BioSenic Chairman of BioWin Director at Merieux Development Chairman at Vaxxilon Chairman at BESIX Director at Belgian Foundation against Cancer

Board of Directors and/or Executive Committee Members	Current Mandates	Past Mandates
		President of Welbio and Foundation University Louvain
Jean-François Rax (permanent representative of Capital Grand Est)	Director of the following companies: Anagenesis Biotechnologies Defymed Emosis Diagnostics Exeliom Biosciences Fibermetrix Fizimed Peptimimesis Pims Technology Syndivia Urania Therapeutics VistaCare Medical Wizzvet	None
Revital Rattenbach	President of the following companies: 4P-Pharma 4moving Biotech 4Living biotech	None
Yves Sagot	Manager of MBS Sagot Consulting	Managing Partner of Relief Therapeutics S.A.

5.4.3 *Activity report*

In 2023, the Board of Directors met 11 times discuss and decide on specific matters. Below is the detail of the attendance:

BOARD OF DIRECTORS	Number of attendances[65]
François Rieger	11/11
Véronique Pomi-Schneiter	11/11
Finsys Management SRL, represented by Jean-Luc Vandebroek	11/11
Innoste SA, represented by Jean Stéphenne	7/11
Capital Grand Est, represented by Jean-François Rax	10/11
Revital Rattenbach	10/11
Yves Sagot	8/11

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.

[65] 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 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.

5.4.4.2.2 Composition

The Corporate Governance Charter of BioSenic 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 BioSenic.

Following completion of the Contribution, the composition of the Audit Committee shall be as follows:

Name	Position	Professional address
Finsys Management SRL, represented by Jean-Luc Vandebroek	President—Non-executive Director	Rue Charles Plisnier 25, 1420 Braine l'Alleud, Belgium
Revital Rattenbach	Member—Independent Director	Rue des Ecouffes 1, 75004 Paris

Currently the Audit Committee is counting 2 members. Jean-Luc Vandebroek (as permanent representative of Finsys Management SRL) and Revital Rattenbach 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 2023, the Audit Committee met 3 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

BioSenic'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 two 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 BioSenic.

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

Name	Position	Professional address
François Rieger	Chairman – Executive Director	Rue des Délices 27, 1203 Geneva, Switzerland
Innoste SA, represented by Jean Stéphenne	Member – Independent Director	Avenue Alexandre 8, 1330 Rixensart, Belgium
Revital Rattenbach	Member – Independent Director	Rue des Ecouffes 1, 75004 Paris

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 2023, the Nomination and Remuneration Committee met with particular emphasis on the (i) performance evaluation 2023 of the Executive Directors and (ii) definition of the objectives 2024 of the Executive Directors.

No variable remuneration was granted for the year 2023 to any member of the Board of Directors or Executive Committee.

5.5 Executive Committee

5.5.1 *General*

The Board of Directors of BioSenic 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 on 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 BioSenic. 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 Deputy-CEO) together with the CSO/COO, the Chief Investor Relation Officer and the CMO are members of the Executive Committee. The Executive Committee is chaired by the CEO of BioSenic and in his absence by the Deputy-CEO. 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.

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

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

Name	Title
François Rieger	Chief Executive Officer and Executive Director
Véronique Pomi-Schneiter	Deputy Chief Executive Officer and Executive Director
Carole Nicco	Chief Scientific Officer and Chief Operating Officer
Alexia Rieger	Chief Investor Relation Officer
Lieven Huysse	Chief Medical Office

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

- **Mr François Rieger** (80), **(CEO)** holds a PhD in Neurobiology, which he completed in 1973 at the *Ecole Normale Supérieure de Paris, rue d'Ulm*. His work allowed him to purify and characterize the structure of acetylcholinesterase, the main current target of Alzheimer's disease treatments. He then went on to study the cholinergic synapse and neuromuscular pathologies related to deficient functioning of nerve impulse transmission. He was appointed Visiting Assistant Professor of Neuropathology at Harvard University from 1975 to 1978, and upon his return to France, he developed a research team in a joint INSERM/CNRS unit at the Pitié-Salpêtrière Hospital on the role of ion channels in the function and morphogenesis of mammalian nerve and muscle. A stay from 1985 to 1988, at the Rockfeller University in New-York, in the laboratory of Professor Gerald Edelman, Nobel Prize, as Senior Associate Researcher, allowed him to extend his field of investigation to the field of Cellular Adhesion Proteins and to demonstrate the implication of N-CAM and cytotactin/tenascin in

synaptic morphogenesis and innervation-reinnervation phenomena. In 1990, he established in his laboratory a new line of research on the primary factors of Multiple Sclerosis, an autoimmune demyelinating disease in humans, which led his laboratory to characterize a gliotoxic protein factor in MS patients and, later, in 1998, to discover in humans a fossil retrovirus still active through its envelope protein, and involved in the triggering of the autoimmune cascade in the disease. In 2007, F. Rieger created in Geneva a Binational Scientific Interest Group on the Broader Theme of Aging and Longevity, with the participation of several Franco-Swiss scientific leaders, intended to take into account both the molecular and societal aspects of this largely unexplored field. F. Rieger is Director of Research at the CNRS and author or co-author of more than 175 international publications in the field of Life Sciences and Neurosciences. F. Rieger is currently leading an Innovative Project concerning the therapeutics of Autoimmune Diseases and a co-Founder of the biotech Medsenic. He has led two successful Phase II clinical trials on Systemic Lupus erythematosus and Graft-versus Host Disease, opening a solid path towards the use of several formulations of active arsenic for the treatment of chronic, autoimmune diseases.

- **Ms Véronique Pomi-Schneiter** (59), **(Deputy-CEO)** has 30 years of experience in operational leadership, human resource management, resource utilisation and organisational development in highly decentralised organisations. Graduated of the IFG Lorraine Business School, she has been a consultant, manager and director of companies in the consulting and human resources sector. In 2010, Véronique decided to found Medsenic with Prof François Rieger, to bring her expertise in business development and fundraising. Her experience includes streamlining operations, developing, and implementing organisational solutions and applying global HR expertise to influence the achievement of strategic objectives.

- **Dr Carole Nicco** (51), **(CSO and COO)** obtained a Ph.D. in human physiology and physiopathology from Denis Diderot University of Paris in 2000. After two years working for the startup Protexel, she obtained a full-time position as a research engineer at Paris Cité University. From 2005 to 2023 she was one of the PI's and the lab manager of the research team now called "Pathogeny and innovative treatments for chronic fibro-inflammatory diseases'' at Cochin Institute, a biomedical research center affiliated with INSERM (Unit 1016), CNRS (UMR 8104) and the Paris Cité University. She was head of the conventional pré-clinical facility of the Cochin Institute for 10 years. Dr. Nicco brings research experience in cancer biology, inflammation, immunity, new target identification, and drug discovery. she has directed dozens of preclinical studies for pathologies ranging from cancer to endometriosis, as well as in autoimmune diseases (systemic lupus erythematous, systemic sclerosis, chronic graft versus host disease) or pathologies implicating the immune system, including wound healing, uveitis, sepsis, hepatitis, and endometriosis. Additionally, she has led numerous therapeutic projects from initial inception to preclinical development in cancer, gynecologic and autoimmune diseases for academic projects but also in collaboration with Vertex, Boiron, IPRAD, GYNOV and Medsenic. She has more than 110 articles published in international referenced journals. Dr. Nicco was vice-president of the international non-profit International Society of Antioxidants in Nutrition and Health for 2 years and becomes president of Redox Medicine Society in 2023. Since 2016, she has been a member of the scientific committees and advisory board of four international congresses: Paris Redox, Targeting Mitochondria, Targeting Microbiota, Skin challenges.

- **Alexia Rieger** (28), **(Chief Investor Relation Officer)** Alexia Rieger graduated from the Ecole Hotelière of Lausanne and pursued her studies in the field of the finance by getting a Master degree in Financial Markets and Investments at Skema Business School. She cumulated professional experiences in different financial fields such as in portfolio management for Architas (AXA subsidiary) and in an M&A boutique focused on helping startups to raise funds (VC: Seed to Serie B), based in Geneva. More recently, Alexia joined Medsenic SAS as Business and Financial Officer. She works on the strategy and the finances of BioSenic to develop the entity in the future, in addition to working, since the beginning, on the reverse merger between BioSenic and Medsenic. Alexia is the daughter of Executive Director and CEO François Rieger.

- **Lieven Huysse** (54), **(CMO)** Lieven Huysse obtained his medical degree from the University in Gent, graduating in 1995. After an internship of 2.5 years, part of a training plan in orthopaedic surgery, he switched to the healthcare industry. Lieven gained sound experience both in the medical device (17 years- endovascular catheters, trauma products, hip, knee, spine) and in the pharma industry (8 years, psychiatry, cardiovascular, allergy/immunology, diabetes). In 2003 he finished an executive MBA at the Swiss Business school. Lieven has held different positions in senior leadership in both national and mainly international positions, including eleven years working abroad (Switzerland, Spain and the Netherlands). His expertise includes managing multi-center international clinical studies, including pre-market approval studies for submission to the U.S. Food and Drug Administration, working with reimbursement authorities and Key Opinion Leader management. He previously served as CMO for Anaconda Biomed S.L., senior director of medical affairs at Intrinsic Therapeutics, Inc., director of clinical and regulatory affairs at Wright Medical EMEA (now Microport®), medical director for Menarini Group, global brand medical manager for Switzerland-based UCB Farchim, manager clinical Affairs EMEA at Stryker Corp. and Medical Advisor EMEA at Janssen. Lieven is a Belgian national with mother tongue Dutch and is also fluent in English, French and German.

5.5.3 *Operation*

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

The CEO and the Deputy-CEO have been appointed as Executive Directors of BioSenic and can be removed by the Board of Directors of BioSenic. The CEO is entrusted with the day-to-day management of BioSenic.

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 BioSenic.

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.

5.6.2 *Financial risk management*

5.6.2.1 Liquidity risk management

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

BioSenic'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 BioSenic remains adequately financed to meet its immediate and medium-term needs.

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

5.6.2.2 Interest rate risk management

BioSenic and Medsenic have long term investments loans granted by third parties (including the European Investment Bank and investors in (convertible) bonds issued by BioSenic)) and by regional investment bodies (for the fixed part, but also including the turnover independent reimbursements (30%) related to RCA's concluded as of 2009). The group at current does not undertake any hedging.

All the negotiated interest rates are fixed and no loans are exposed to variable rates.

5.6.2.3 Credit risk

BioSenic 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

BioSenic is currently not exposed to any significant foreign currency risk.

However, should BioSenic enter into long term collaboration agreements with third parties for which revenues would be expressed in a foreign currency, BioSenic 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). BioSenic 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 of Directors and corrective action is taken when necessary.

BioSenic 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 BioSenic is done on a permanent/daily basis at all levels within BioSenic. As a general policy deviations are reported at all times to the supervisory level.

5.7 Market abuse regulations

In its Corporate Governance Charter, BioSenic 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 BioSenic to which this inside information relates.

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

With a view to preventing market abuse (insider dealing and market manipulation), the Board of Directors has established a dealing code. The dealing code describes the declaration and conduct obligations of Directors, executives and staff members of the Company with respect to transactions in shares and other financial instruments of the Company. The dealing code sets limits on carrying out transactions in shares and other financial instruments of the Company and allows dealing by the above-mentioned persons only during certain windows.

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 BioSenic. BioSenic'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 director has a direct or indirect financial interest adverse to that of BioSenic. In accordance with Article 7:96 of the Belgian Code on 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. In accordance with BioSenic's Corporate Governance Charter, 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 BioSenic, 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 on 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.

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

Mr François Rieger (CEO and Executive Director) and Ms Véronique Pomi-Schneiter (Deputy-CEO and Executive Director) are both party to a shareholders agreement with BioSenic dated 24 October 2022 in relation to the shares they hold in Medsenic. Mr François Rieger currently holds 14,88% of the shares in Medsenic and Ms Véronique Pomi-Schneiter currently holds 7,44% of the shares in Medsenic. Under that shareholders' agreement they have both committed to contribute their remaining shares in Medsenic to BioSenic in exchange for newly issued shares, based on a price per share of BioSenic equal to the price as used for the envisaged future equity raise. However, if Medsenic obtains extended development and commercialisation rights from Phebra (including for the US, UK and Japan) under economically favourable terms for Medsenic, the valuation of any shares not yet contributed to BioSenic will be need to be revaluated which could potentially lead to a conflict of interests. See Section 6.4.4.1 below for more information.

In addition, a potential conflict might arise in the future for any Executive Directors to whom a variable remuneration would be granted (if any) or in relation to any other compensation-related matters.

On the basis of information provided by the relevant members of the Board of Directors and of the Executive Committee of BioSenic, and except as disclosed above, there are, on the date of this Prospectus, no potential conflicts of interest between any duties of the members of the Board of Directors and members of the Executive Committee of BioSenic, and their private interest and/or other duties.

6.4 Related Party Transactions

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

- BioSenic USA Inc., with registered office at School Street 44, Suite 505, Boston, MA 02108, 100% owned; and
- Medsenic SAS, owned at 51.81%.

6.4.1 *Transactions with BioSenic USA Inc.*

In course of 2023, expenses related to all activities executed through BioSenic USA Inc. have been re-invoiced to BioSenic on 31 December 2023.

6.4.2 *Transactions with the Executive Committee*

There are no transactions with the Executive Committee.

6.4.3 *Transactions with Medsenic*

End December 2023, the Company decided to convert the EUR 1,000,000 convertible bonds previously issued by Medsenic SAS to the Company, in accordance with the terms agreed upon on 8 September 2022. As a result of the conversion, the Company has increased its participation in its subsidiary Medsenic SAS by 0.81%, bringing its total participation in Medsenic SAS to 51.81%.

6.4.4 *Transactions with the shareholders of Medsenic*

6.4.4.1 BioSenic's transaction with the shareholders of Medsenic

BioSenic entered into two agreements relating to Medsenic.

a. Subscription agreement between a large majority of the shareholders of Medsenic, as subscribers, and BioSenic

Upon the terms and subject to the conditions set forth in this subscription agreement, the subscribers transferred to BioSenic 37,649 shares in Medsenic, representing 51% of the fully diluted share capital of Medsenic. In exchange to the subscription, the subscribers received 90,668,594 new ordinary shares of BioSenic.

b. Shareholders' agreement relating to Medsenic between BioSenic, as majority shareholder, and Medsenic's minority shareholders

Pursuant to a shareholders' agreement dated 24 October 2022 between BioSenic and the shareholders of Medsenic holding the remaining 48.19% of the shares of Medsenic (the "**Minority Shareholders**"), the Minority Shareholders agree to contribute all of their remaining Medsenic shares into BioSenic in two instalments, each time for half of their remaining shareholding. For more information, please revert to Section 4.10.1.5. These additional contributions shall in principle take place at the same time as the first two equity raises of BioSenic (except for capital increases relating to the exercise of warrants and conversions of convertible bonds, if the conditions for execution are met) to be carried out in order to finance the continuation of BioSenic's activities. It is however not contemplated to proceed with these additional contributions together with the placement of new securities that is currently envisaged by BioSenic in 2024.

6.4.4.2 Medsenic's transaction with the shareholders of Medsenic

a. Medsenic’s transaction with Phebra PTY Ltd.

Medsenic and Phebra entered into (i) a license agreement on 21 May 2021 (the "**License Agreement**") and (ii) a marketing and supply agreement on 31 May 2021 (the "**MDA**") for the oral formulation of arsenic trioxide ("**OATO**") in the following indications (the "**Field**"): Graft Versus Host Disease ("**GvHD**"), Systemic Sclerosis ("**SSc**"), Systemic Lupus Erythematosus ("**SLE**"), infectious diseases related to COVID-19 and CNS inflammatory diseases related to Multiple Sclerosis (referred to as Multiple Sclerosis) (the "**Phebra Agreements**").

Under the agreements, Phebra has granted an exclusive license to Medsenic to use the oral formulation of arsenic trioxide for its research and clinical development in the above-mentioned immunopathologies and to market, sell and distribute OATO in such field in the European Union and in French speaking territories ("**Medsenic Territories**"). Under the license agreement, Medsenic agreed to secure the necessary funding before 31 May 2024 to commence a clinical study using Phebra OATO. Although BioSenic Group is confident that the deadline can be further extended if necessary, this means that BioSenic Group needs to secure sufficient funding before such deadline to be able start the Phase III clinical study with OATO in cGvHD (i.e., allowing completion of the IND application with the FDA, and starting CRO preparation, sites selection and data collection for the clinical study). If such funding would not be secured by 31 May 2024, Phebra could terminate the license agreement unless the parties agree to postpone such date (which cannot be guaranteed). All costs relating to the research and clinical development will be borne by Medsenic. Phebra will supply (either directly or via a contract manufacturer) the OATO for Medsenic and Phebra will be responsible and retain full liability for the manufacture, packaging, testing and batch release of OATO in the Field, regardless of whether it carries out such responsibilities itself or uses one or more subcontractors to do so.

In consideration for the license granted for the Medsenic Territories, Phebra received 3,151 shares (4.3% of the shares currently outstanding) in Medsenic. Phebra has the right to commercialise OATO in the Field in all countries outside the Medsenic Territories against payment to Medsenic of a royalty of 55% of the net sales profits. BioSenic Group and Phebra are currently analysing the possibility to extend the Medsenic Territories and the commercial terms thereof, which is expected to require lengthy and complex discussions and agreements based on partially unknown commercial and competitive factors.

On 15 January 2024, BioSenic announced the signature of a binding term sheet with Phebra related to the adaptation of the License Agreement and the MDA signed in May 2021. The initial License Agreement provided a commercialization agreement of 100% net profits for Medsenic mainly in Europe and 55 % net sales profit for Phebra in the rest of the world (including major markets such as the US, Canada, South America, Japan, South East Asia, China and Australia). In particular, the binding term sheet for the indication chronic Graft versus Host Disease (cGvHD) license now provides for a royalty payment of 2% on worldwide sales, which simplifies the conditions for offering sublicenses to new external partners. In addition, under the license agreement, Phebra agrees that Medsenic will have exclusive worldwide territorial rights for the use of OATO in GvHD. Regarding the MDA, Phebra agrees that the net profit allocation as stated in the initial MDA will be deleted for the sales revenues and profits generated from the sale of product, restricted to the indication cGvHD. Phebra also agrees to cover the costs of maintaining and updating the drug substance file to comply with the rules of all active territories; of controlling the compliance with various regulators on ongoing supplier approval and compliance to Good Manufacturing Practices (GMP) requirements; of updating the drug master file of OATO; of managing the Contract Manufacturing Organization (CMO) and supply chain from the active pharmaceutical ingredient to the clinical release of the product and of covering the regulatory and quality and GMP expenses. To take into account these costs for Phebra, the cost-of-goods for the Medsenic final clinical OATO product will be increased by a mark-up of 20%. In addition, Medsenic will have the right to establish an Australian entity to use the OATO patents for cGvHD indication. The Australian entity will not commercially compete with Phebra, particularly in the field of APL (acute promyelocytic leukemia) cancer treatment, by having Medsenic's GvHD treatment produced in product-specific packaging.

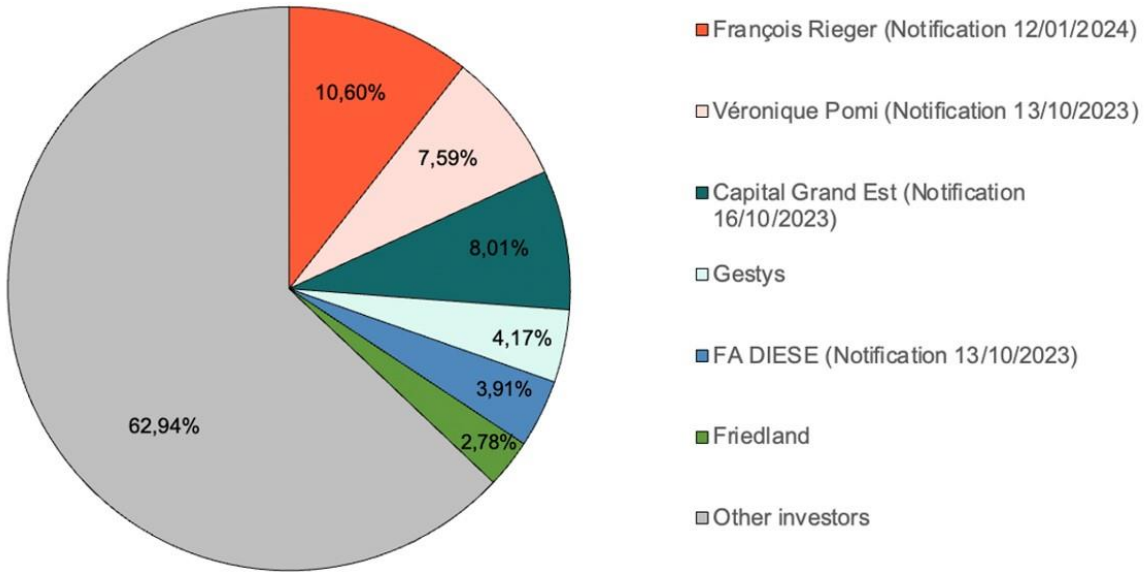
7 SHARES AND SHAREHOLDERS

7.1 Shareholders

As per 19 March 2024, there are 187,873,548 shares representing a total share capital of BioSenic of € 35,950,668.63. There are only ordinary shares without nominal value, and there are no special rights attached to any of the ordinary shares, nor special shareholder rights for any of the shareholders of BioSenic. Each shareholder of BioSenic is entitled to one vote per share. The share capital is entirely and unconditionally subscribed and fully paid up.

As per 19 March 2024, the total of exercisable warrants is 161,556 warrants for the former 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 1,161,556 warrants. See Section 7.2 for more information about the outstanding warrants.

The graph below provides an overview of the shareholders that have notified BioSenic of their ownership of shares of BioSenic. This overview is based on the most recent transparency declaration submitted to BioSenic. All transparency notifications are available under the 'Investors' section of https://www.biosenic.com/investors.



** Note: on 10 January 2024, the shareholding of Mr François Rieger decreased from 16.29% to 11.39% as the result of a loan of 8 million shares granted by Mr François Rieger to GTO 15, as a condition to the new Convertible Bonds programme dated 8 January 2024. Upon termination of the Convertible Bonds programme, and provided that BioSenic respects its obligations thereunder, the 8 million shares will be returned by GTO 15 to Mr François Rieger.*

BioSenic has a relatively widely held shareholder base, and no single shareholder controls BioSenic. To the best knowledge of BioSenic, there are no arrangements in place which may, at a subsequent date, result in a change in control of BioSenic.

7.2 Warrant plans of BioSenic

7.2.1 *Warrant plans issued*

BioSenic currently has 2 outstanding warrant plans outstanding for its employees, Board members, Executive committee members and consultants:

On 28 May 2020, the Board of Directors of BioSenic created and approved a plan which consisted in the issue of 69,978 warrants for employees, management members and Directors (plan 2020/05). All warrants have been granted and accepted.

On 23 December 2020, the Board of Directors of BioSenic created and approved a plan which consisted in the issue of 99,832 warrants for employees, management members and Directors (plan 2020/12). All warrants have been granted and accepted except for Jean-Paul Prieels that refused 2,000 warrants.

On the date of this Prospectus, the following warrants are outstanding in accordance with the above-mentioned plans:

Plan	Total
Former CEO	109,724
Former CFO	19,500
Former CBO	5,000
Consultant	1,000
Board members	21,332
Former CMO	5,000
Total	**161,556**

On 23 August 2021, the extraordinary shareholders' meeting of BioSenic issued warrants to the European Investment Bank and to Patronale Life. On the date of this prospectus, the following warrants are outstanding:

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

The total of exercisable warrants within BioSenic is therefore of 161,556 warrants for the (former) 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 1,161,556 warrants. Subject to completion of the debt restructuring, it is envisaged to cancel the 1,000,000 Outstanding Warrants issued to Patronale and EIB.

7.2.2 *Summary of the outstanding warrant plans*

The relevant terms and conditions of BioSenic'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 BioSenic 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 BioSenic, 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 BioSenic's existing **warrant plan for the EIB Warrant** are set out below:

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

- **Maturity Date**: The EIB Warrants have a defined life of five (5) years. However, BioSenic undertakes to issue identical warrants with a life of five (5) years after the Expiry Date.

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

- **Exercise Period**: The EIB Warrants 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 Warrants, BioSenic, its agent or its shareholders (in that order), has a right of first refusal to redeem the EIB Warrants on the same terms and conditions.

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

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

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

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

- **Exercise Period**: The Patronale Life Warrants 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 Warrants, BioSenic, its agent or its shareholders (in that order), has a right of first refusal to redeem the Patronale Life Warrants on the same terms and conditions.

7.3 Warrant plans of Medsenic

Medsenic has granted warrants (*bons de souscription de parts de créateur d'entreprise* – "BSPCE") to the following persons and in the following proportions:

- 1,513 BSPCE-2016 and 218 BSPCE-2017 to Mrs. Véronique Pomi, employee and founder of Medsenic;
- 1,512 BSPCE-2016 and 217 BSPCE-2017 to Mr. François Rieger, President and founder of Medsenic.

All 3,025 BSPCE-2016 and 435 BSPCE-2017 remain outstanding.

The relevant terms and conditions of the Medsenic's existing **BSPCE-2016** are set out below:

- **Exercise period**: from May 26, 2017 to May 25, 2027.
- **Exercise price**: € 162 per ordinary share.
- **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 Medsenic's existing **BSPCE 2017** are set out below:

- **Exercise period:** from December 20, 2017 to December 19, 2027.
- **Exercise price**: € 217 per ordinary share.
- **Term**: seven years. All warrants that have not been exercised within the ten-year period as of their creation become null and void.

According to provision 3.2.3 (vi) of the Subscription Agreement both of the BSPCE 2016 and BSPCE 2017 will become null and void if they are not exercised before the last contribution of the remaining 49% of Medsenic's shares, which is expected to occur by no later than 24 October 2024.

In the context of the contribution of the 51% of shares of Medsenic into BioSenic's capital on 24 October 2022, the value per Medsenic share was set at € 1,083.

No new warrant plan has been issued since 2017.

7.4 Convertible bonds of BioSenic

7.4.1 *Convertible bonds issued on 7 May 2020*

In May 2020, BioSenic obtained non-dilutive subordinated bonds (1,600 bonds) for an amount of € 4.0 million with the option to convert. This enables BioSenic's bond investors to be repaid in BioSenic's shares, with a conversion price of € 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 € 7.0 per share mitigates the dilution of existing shareholders in the event that the bonds would be redeemed in ordinary shares of BioSenic.

BioSenic renegotiated 800 convertible bonds issued on 7 May 2020 (for an amount of € 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.

The maturity date of the remaining 800 convertible bonds has been reached on 6 July 2023 and the conversion possibility has therefore expired. Subject to completion of the debt restructuring, which is subject to a new equity raising (see Section 3.5 for more information), it is envisaged to replace the 800 convertible bonds by new convertible bonds that will have be convertible into shares at a price equal to 95% of the 30-calendar day VWAP immediately preceding the date of the conversion notice.

7.4.2 *Convertible bonds issued to GTO 15*

On 30 May 2022, the Company entered into an agreement for the issuance and irrevocable subscription of convertible bonds (the "**First Subscription Agreement**") with Global Tech Opportunities 15, having its registered office at PO Box 2775, 67 Fort Street, Artemis House, Grand Cayman KY1-1111, Cayman Islands ("**GTO 15**"). Under the terms of the First Subscription Agreement, GTO 15 agreed to make available to the Company a convertible bond facility for a total amount of up to € 5 million to be drawn down for the full amount by the way of the issuance of a maximum of 100 convertible bonds at an issue price of €50,000 each (to be fully paid up in cash at the time of subscription). The convertible bonds are non-interest bearing, unsecured and subordinated to the existing loan granted to the Company by the European Investment Bank (the "**EIB**") pursuant to the loan agreement dated 30 June 2021.

On 22 December 2022, the First Subscription Agreement was amended in order to, among others, amend the cooldown period of the fifth tranche, amend the payment method for the commitment fees payable to GTO 15 and to agree upon trading limitations for BioSenic's shares issued to GTO 15 upon conversion of the convertible bonds. On 29 June 2023, GTO 15 and BioSenic agreed, among others, to further deviate from the First Subscription Agreement with respect to the eighth tranche, the ninth tranche and the tenth tranche, in order to reduce the nominal amount of such tranches from €500,000 to €300,000 and to waive for such tranches the conditions regarding a minimum €4 million market capitalisation and a minimum daily trading value of BioSenic's shares.

On 18 Octobre 2023, BioSenic announced that it had reached an agreement with GTO 15 with respect to the finalisation of the first convertible bonds program. GTO 15 agreed to fund two final tranches of €300,000 each of the first convertible bonds program. BioSenic agreed to pay a waiver fee to GTO 15 in the aggregate principal amount of €60,000 (payable in new convertible bonds with terms comparable to the already existing convertible bonds). This put an end to the funding commitments of GTO 15 under the first convertible bonds program.

Also, under the terms of the First Subscription Agreement, GTO 15 agreed to voluntarily withdraw its latest conversion notice for €1,400,000, that would have led to an issuance of 58 million of shares. In exchange for this withdrawal, GTO 15 received from BioSenic a compensation of €125,000 in convertible bonds with terms comparable to the existing convertible bonds under the First Subscription Agreement. These new convertible bonds have been issued by Company within the framework of the authorized capital.

On 8 January 2024, the Company entered into a second agreement for the issuance and irrevocable subscription of convertible bonds (the "**Second Subscription Agreement**") with GTO 15. Under the terms of the Second Subscription Agreement, GTO 15 agreed to make available to the Company a new convertible bond funding program for a total amount of up to € 1.2 million to be drawn down for the full amount by the way of the issuance of a maximum of 120 convertible bonds with a nominal value of € 10,000 each (to be fully paid up in cash at the time of subscription). The convertible bonds will be subscribed for by GTO 15 in four tranches of € 300,000 each (each such tranche including 30 convertible bonds). Between each tranche, from the second tranche onwards, there will be a cool down period of 20 trading days with respect to each remaining tranche. The Company agreed to drawdown up to one (1) tranche on the demand of GTO 15. There are no liquidity conditions, other than that for the fourth tranche, the 20-day average daily value traded – trimmed

for 10% of the outliers (meaning the data points from the top and bottom tails) – must be greater than € 15,000 prior to the disbursement of the tranche. The convertible bonds are non-interest bearing, unsecured and subordinated to the existing loan granted to the Company by the European Investment Bank pursuant to the loan agreement dated 30 June 2021. On the date of this Registration Document, three of the four tranches of convertible bonds have been fully subscribed by GTO 15 for an aggregate amount of € 900,000.

The convertible bonds subscribed for by GTO 15 constitute convertible bonds within the meaning of articles 7:65 and following of the Belgian Code on Companies and Associations and are convertible into new shares. The maturity date of the Convertible Bonds will be 5 years following the issue date of the relevant convertible bond (the "**Maturity Date**"). The convertible bonds may be converted into ordinary shares at a conversion price (the "**Conversion Price**") which shall be equal to the lowest 1-day volume-weighted average price (the "1-day VWAP") at which the Company's existing shares are tradable on the Euronext Brussels and Euronext Paris markets during a period of 10 consecutive trading days immediately preceding the date of the conversion notice with the application of a discount of 5%.

The convertible bonds may be converted at the holder's request at any time from the issue date until the close of business on the date expected to be 10 trading days prior to the final Maturity Date of such convertible bond, or in the event of early redemption 10 trading days prior to the relevant early redemption date, at the Conversion Price (as defined above) upon delivery of a conversion notice. The Company is required to issue the relevant new shares fully paid and listed no later than the opening of business on the third trading day (or if the Company's shares are suspended from trading upon the end of the suspension) following receipt by the Company of the conversion notice from GTO 15. The number of new shares to be issued upon conversion of a convertible bond shall be determined by dividing the principal amount of the convertible bond to be converted (i.e., the issue price) by the Conversion Price.

8 SUMMARY OF MATERIAL INFORMATION DISCLOSED SINCE MARCH 2023

The following information is a summary of the inside information that has been disclosed under the Market Abuse Regulation (Regulation 5EU) No. 596/2014) and other relevant information disclosed over the last 12 months and that is relevant as at the date of the Document of BioSenic:

Clinical results:

On 16 March 2023, BioSenic delivered a new post-hoc analysis of its Phase III JTA-004 trial on knee osteo-arthritis with positive action on the most severely affected patient population.

On 30 March 2023, BioSenic published new data on the mechanism of action of arsenic trioxide.

On 4 May 2023, BioSenic announced the identification of key biomarkers for cGvHD.

On 19 June 2023, BioSenic announced the decision to suspend its interventional trial on ALLOB.

On 19 September 2023, BioSenic announced the publication of data providing additional key indications of its lead API (Active Pharmaceutical Ingredient) arsenic trioxide (ATO) to treat systemic sclerosis (SSc) in a peer-reviewed international journal.

On 27 September 2023, BioSenic announced the completion of a post-hoc analysis of its phase 2 clinical trial of ATO, finding the best scheme for administration of an efficient treatment of cGvHD.

On 12 March 2024, BioSenic announced the publication of an open-access article describing an optimized schedule for administration of oral arsenic trioxide (OATO) treatment for chronic graft-versus-host disease (cGvHD), based on an earlier post-hoc analysis of Phase 2 data.

Financing and cash position:

On 31 March 2023, BioSenic provided Financial Update and Financial Calendar 2023.

On 27 April 2023, BioSenic announced 2022 full year results.

On 22 May 2023, Biosenic announced its business update for the first quarter, ended 31 March 2023.

On 30 June 2023, BioSenic provided a financial update.

On 10 July 2023, BioSenic announced a further update on its financial arrangements with its main historical creditors, Patronale, Monument and the European Investment Bank.

On 7 September 2023, BioSenic published its business update for the first half, ended 30 June 2023, prepared in accordance with IFRS as adopted by the European Union, and the outlook for the remainder of the year.

On 14 September 2023, BioSenic announced that it has reached an agreement with Patronale, Monument and the European Investment Bank for the restructuring of its key financial debts.

On 18 October 2023, BioSenic announced that it has reached a definitive agreement with GTO 15 with respect to the finalization of the existing convertible bonds program.

On 8 December 2023, BioSenic announced that it has signed a term sheet with Singapore based TrialCap Pte. Ltd. and/or other lenders for a proposed debt and equity financing. BioSenic is seeking the funds to continue its clinical development, backed by previous encouraging Phase 2 and pre-clinical results of arsenic trioxide (ATO).

On 8 January 2024, BioSenic announced that it has signed a new subscription agreement for a maximum € 1.2 million convertible bonds facility, arranged by ABO Securities through its affiliated entity GTO 15.

On 2 February 2024, BioSenic announced that it raised €500,000 in gross proceeds through a private placement of 12,195,120 new shares at an issue price of €0,041 per share with institutional investors.

Corporate:

On 18 April 2023, BioSenic received key European patent from EPO, for further therapeutic development in cancer, infectious and immune diseases.

On 24 May 2023, BioSenic announced the signing of a term sheet with Pluristyx, a leading provider of gene-edited iPSC and cell therapy solutions, with a view to further negotiate the terms and conditions of a potential license and collaboration agreement.

On 29 May 2023, BioSenic announced the amendment of the license agreement between its affiliate Medsenic SAS and Phebra Pty Ltd, the leading Australian developer, manufacturer and supplier of high quality and innovative pharmaceuticals.

On 24 August 2023, BioSenic announced the issuance of a key new patent entitled 'Use of metal ions to potentiate the therapeutic effects of arsenic' to its subsidiary company Medsenic by the China National Intellectual Property Administration (CNIPA).

On 10 January 2024, BioSenic announced the promotion of Dr Carole Nicco to Chief Operating Officer (COO) in addition to her position as Chief Scientific Officer (CSO).

On 15 January 2024, BioSenic announced the signature of a binding term sheet with Phebra Pty Ltd. related to the adaptation of the License Agreement and the MDA signed in May 2021.

On 23 January 2024, BioSenic announced the filing of a U.S. patent for JTA-004, a viscosupplement in late-stage clinical development, following new evidence of its efficacy in a recently defined subtype of osteoarthritis (OA).

On 30 January 2024, BioSenic announced the granting of a key patent by the Canadian Intellectual Property Office to expand protection of the arsenic trioxide (ATO) platform.

9 APPENDIX – ABBREVIATIONS AND DEFINITIONS

Abbreviations

AE	Adverse Event
Allo-SCT	Allogeneic hematopoietic stem cell transplantation
API	Active Pharmaceutical Ingredient
APL	Acute promyelocytic leukaemia
ATMP	Advanced Therapy Medicinal Product
ATO	Arsenic trioxide
BLA	Biologics License Application
β-TCP	β-tricalcium phosphate
BMP	Bone Morphogenetic Protein
CDMO	Contract Development and Manufacturing Organizations
CEO	Chief Executive Officer
CFO	Chief Financial Officer
CHU	*Centre Hospitalier Universitaire*
CMO	Chief Medical Officer
CMC	Chemistry, Manufacturing and Controls
CNRS	*Centre National de la Recherche Scientifique*
COO	Chief Operational Officer
CSO	Chief Scientific Officer
CTA	Clinical trial application
DBM	Demineralized Bone Matrix
DU	Delayed Union (fracture)
DSMB	Data Safety Monitoring Board
ERDF/FEDER	European Regional Development Fund (*Fonds Européen de Développement Régional*)
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration (in the US)
FSMA	Financial Services and Markets Authority in Belgium
GAAP	(Belgian) Generally Accepted Accounting Principles
GCP	Good Clinical Practice
GDE	Global Disease Evaluation
GMP	Good Manufacturing Practice
HA	Hyaluronic acid
hAEC	human Amniotic Epithelial Cell
HSCT	Allogeneic hematopoietic cell transplantation
IA	Intra-articular
ICH	International Council for Harmonisation
IFRS	International Financial Reporting Standards
IND	Investigational New Drug application (in the US)

IRD	Inflammatory Rheumatic Disease
IV	Intravenous
KOA	Knee Osteoarthrisis
KOL	Key opinion leader
MAA	Marketing authorization application
MSC	Mesenchymal Stem Cells
MW	Molecular weight
NCE	A New Chemical Entity is an active ingredient that contains no active moiety that has been previously approved by the Agency in an application submitted under section 505 of the Federal Food, Drug, and Cosmetic Act or has been previously marketed as a drug in the US
NIH	National Institute of Health
NSAIDs	Non-steroidal anti-inflammatory drugs
NU	Non-Union (fracture)
OA	Osteoarthrisis
OATO	Oral formulation of arsenic trioxide
ODD	Orphan Drug Designation
PDGF	Platelet-Derived Growth Factor
PTH	ParaThyroid Hormone
Pre-IND	Pre-investigational new drug application, which allows the sponsor-investigator the opportunity to discuss the proposed project and receive guidance directly from the FDA prior to submitting an IND
RCA(s)	Recoverable Cash Advance(s)
rh	Recombinant human
SAE	Serious Adverse Events
SCTS	Skeletal Cell Therapy Support SA
SISE	*Société d'Infrastructures, de Services et d'Energies SA*
SME	Small and Medium Enterprise
SLE	Systemic Lupus erythematosus, which is the most common type of lupus, is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs.
SOC	Standard of care
SSc	Systemic Sclerosis is an autoimmune rheumatic disease characterised by excessive production and accumulation of collagen, called fibrosis, in the skin and internal organs and by injuries to small arteries
TUS	Tomographic Union Score
ULB	*Université libre de Bruxelles*

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)
aGvHD	Acute Graft versus Host Disease
cGvHD	Chronic Graft versus Host Disease
ArsciCop	The oral formulation of arsenic trioxide combined with metal ions to potentiate the therapeutic effects of arsenic
ArsciCor	The oral formulation of arsenic trioxide
Arscimed	IV (intravenous) formulation of arsenic trioxide
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 on 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 on companies and associations, as applicable to BioSenic 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
BioSenic	BioSenic SA, a limited liability company incorporated in the form of a 'société anonyme' under the laws of Belgium, with registered office at Granbonpré 11, Building H, 1435 Mont-Saint-Guibert (Belgium) and registered with the legal entities register (Charleroi) under number 0882.015.654
BioSenic Group or Group	The consolidated group of BioSenic, Medsenic SAS and BioSenic USA Inc.
Board of Directors	The board of directors of BioSenic
cGvHD	Chronic Graft versus Host Disease
Chairman	The chairman of the Board of Directors
CHU	Centre Hospitalier Universitaire de Liège
CNRS	The *Centre National de la Recherche Scientifique* located in France
Company	BioSenic SA
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
Contribution	The contribution of 51% of the shares in Medsenic SAS into BioSenic as approved by the extraordinary shareholders' meeting on 24 October 2022.
Corporate Governance Charter	The corporate governance charter of BioSenic
Corporate Governance Code (or CGC)	The new and third 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), which replaces the versions previously published in 2004 and 2009
Completion Date	The date of approval of the contribution of the 51% stake in Medsenic into BioSenic by the extraordinary shareholders' meeting of BioSenic, being 24 October 2022
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, Deputy-CEO, COO, CSO, Chief Investor Relation Officer, and CMO
Executive Directors	Directors entrusted with the day-to-day management of BioSenic
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
GTO 15 or Global Tech Opportunities	Global Tech Opportunities 15, a Cayman Islands company with its registered office situated at 71 Fort Street, George Town, Grand Cayman KY1-1111
GvHD	Graft versus Host Disease
FAS population	The full analysis set population, meaning that the targets of the analysis are only the treated patients
Homeostasis	Self-regulating process by which biological systems tend to maintain internal stability
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)
Medsenic	Medsenic SAS, a company incorporated and existing under the laws of France, having its registered office at No 204 Avenue de Colmar, F-67100 Strasbourg (France), 527 761 530 R.C.S. Strasbourg
Mesenchymal stem cells	Multipotent stem cells that can convert into cell types such as bone cells, cartilage cells, fat cells, etc.
Minority Shareholders	The minority shareholders of Medsenic currently holding the remaining 48.9% of the shares of Medsenic
MXB	A combined cell-matrix product of BioSenic for large bone defects and maxillofacial applications
Nomination and Remuneration Committee	The nomination and remuneration committee of BioSenic installed by the Board of Directors

Non-Executive Directors	Directors who are not entrusted with the daily management of BioSenic
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
Osteoarthritis	A degenerative joint disease
Osteoblast	Bone-forming cell
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 BioSenic'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
Phebra	Phebra PTY Limited, (ABN 99 059 357 890) having its principal place of business at 19 Orion Road, Lane Cove West, NSW 2066, Australia
PP population	Per protocol population, meaning that the targeted population is the one that is treated with no protocol deviation
Region	The Walloon Region

Registration Document	This registration document, as well as any supplement thereto
Regulatory regulations	Applicable regulatory laws and regulations.
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
Shareholders' Agreement	The shareholders' agreement relating to Medsenic dated 24 October 2022 between BioSenic and the shareholders of Medsenic holding the remaining shares of Medsenic
Skeletal Cell Therapy Support SA	An absorbed limited liability company incorporated under the laws of Belgium with registered office at rue Auguste Piccard 37, 6041 Charleroi 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 BioSenic 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
SLE	Systemic Lupus erythematosus, which is the most common type of lupus, is an autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs
SSc	Systemic Sclerosis is an autoimmune rheumatic disease characterised by excessive production and accumulation of collagen, called fibrosis, in the skin and internal organs and by injuries to small arteries
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
Subscription Agreement	The contribution agreement entered between all existing shareholders of Medsenic and BioSenic, with respect to the contribution in kind of 51% of the shares of Medsenic into BioSenic's capital
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. BioSenic 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	The license agreement pursuant to which BioSenic (and its affiliates) has been granted an exclusive and worldwide license 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