Press Release
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BioSenic and Pluristyx sign term sheet for market availability of ALLOB mesenchymal cells

Potential license agreement to produce and commercialize original and transformed ALLOB cells BioSenic to potentially receive royalty rates on net sales up to 25 percent

Mont-Saint-Guibert, Belgium, May 24, 2023 – BioSenic (Euronext Brussels and Paris: BIOS), the clinical stage company specializing in serious autoimmune and inflammatory diseases and cell repair, today announces 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.

This term sheet will be used as basis for the preparation of a potential wider licensing and collaboration agreement to make BioSenic's well characterized cells with various original properties available to the market. These cells include immune privilege, anti-inflammatory properties et tissue repair established capacities, both in vitro and in vivo. BioSenic has derived these GMP-manufactured cells from Mesenchymal Stem Cells (MSCs), bone marrow cells from healthy donors. The cells have then been prepared for a number of preclinical and clinical studies. These cells constitute BioSenic's investigational medicinal product, ALLOB, which is currently being evaluated in a randomized, double-blind, placebo-controlled Phase IIb study in patients with high-risk tibial fractures. Subject to the fulfillment of customary condition precedents, BioSenic and Pluristyx aim to further negotiate the terms and conditions with a view on completing a final agreement and to fully execute it by Q3 2023. Depending on the outcome of the negotiations, a final license and collaboration agreement might, however, never be entered into.

In 2021, BioSenic (at the time Bone Therapeutics, prior to its merger to create BioSenic) and Pluristyx (previously Implant Therapeutics) entered into its original research evaluation agreement. The agreement enabled BioSenic to access, evaluate and materially transfer Implant Therapeutics' Induced Pluripotent Stem Cell (iPSC) lines, media, differentiation protocols and expertise. These specific single-source MSCs are highly standardized, are expandable and scalable. They are also more flexible with regards to modification methodologies, including gene editing and transduction, than existing autologous and allogeneic approaches. Pluristyx has developed technologies to conditionally transform dividing cell populations, including cells such as ALLOB.

The potential BioSenic / Pluristyx licensing and collaboration agreement, if entered into, would enable BioSenic to prepare these cells for market availability for preclinical research and possible clinical applications. Pluristyx specializes in partnerships with companies and research institutions to create and commercialize new therapies and offer services to clients who need support with their own cell therapy development, manufacturing, and/or regulatory compliance.

"BioSenic's pre-merged Bone Therapeutics has spent over 10 years establishing the scientific and technical foundations for the safe use of manufactured mesenchymal stem cells originating from the bone marrow of healthy human donors. This has involved pre-clinical and clinical studies demonstrating cartilage and bone formation or repair. Phase 2 clinical studies have also demonstrated spinal fusion and bone fractures enhanced repair," **said Prof. François Rieger, PhD, Chairman and Chief Executive Officer of BioSenic.** *"BioSenic has therefore extensively demonstrated that bone marrow cells that originate from stem cells are able to differentiate in a variety of tissue types in addition to bone. They are of a very low immunogenic type with a so-called immune privilege, and they can be prepared as partially differentiated cells along their cell differentiation multiple pathways. As a result, these cells can be further transformed in vitro with specific genes adding to their initial properties with new anti-inflammatory properties or cell division regulatory mechanisms able to control excessive division or abnormal migration or misdirected organ implantation. This partnership between BioSenic and Pluristyx will enable the wider sector to expand the use of the ALLOB and related cells and deliver new ways to treat numerous human pathologies still with unsatisfactory or unmet medical needs. The availability of the ALLOB cell clones and lines will generate a very significant income. BioSenic will be able to utilize this income to financially support its own projects based on its present two main technical Arsenic and ALLOB platforms, targeting autoimmune and cancer conditions and bone and cartilage repair."*

"Pluristyx will be able to apply using its conditional immortalizing and transforming strategies in partnership with BioSenic to generate transformed versions of the ALLOB line. We believe this will generate clonal cell lines resources that will be invaluable to a number of companies and laboratories internationally," **said Dr Mahendra Rao, Vice President of Pluristyx**. *"Using Pluristyx's base immortalized line to add to our platform technologies, such as Failsafe and Hypoimmune, will enable the development of safe cellular therapy for use by Biosenic and its licensed partners."*

Subject to the terms and conditions of the definitive license and collaboration agreement, BioSenic will grant to Pluristyx conditional non-exclusive, non-transferable, sublicensable (on a case-by-case basis) and royalty-bearing license on the BioSenic technology to exploit ALLOB. The main responsibilities of Pluristyx shall include the production and sale of immortalized ALLOB cells, the exploitation of licensed products and the generation of a Cell Bank.

About Pluristyx
Pluristyx with panCELLa offers an enlarged portfolio of unique and effective non-modified and genetically engineered iPSC-based technologies and related services to provide end-to-end client support throughout the product lifecycle. Pluristyx is fast becoming the leading provider of gene-edited iPSC and cell therapy solutions, accelerating the path to clinic and providing the best route to commercialization.

About BioSenic
BioSenic is a leading biotech company specializing in the development of clinical assets issued from: (i), the allogeneic cell therapy platform ALLOB and (ii) the Arsenic TriOxide (ATO) platform. Key target indications for the platforms include Graft versus Host Disease (GvHD), Systemic lupus erythematosus (SLE), Systemic Sclerosis (SSc) and high-risk tibial fractures.
Following the merger in October 2022, BioSenic combines the strategic positionings and strengths of Medsenic and Bone Therapeutics. The merger also enables Biosenic to add to its innovative cell therapy platform and strong IP for tissue repair protection with an entirely new arsenal of various anti-inflammatory and anti-autoimmune formulations using the immunomodulatory properties of ATO/OATO.
BioSenic is based in the Louvain-la-Neuve Science Park in Mont-Saint-Guibert, Belgium. Further information is available at http://www.biosenic.com.

About BioSenic technology platforms
BioSenic's technology is based on two main platforms:

1) The allogeneic cell and gene therapy platform, developed by BioSenic with differentiated bone marrow sourced Mesenchymal Stromal Cells (MSCs) that can be stored at the point of use in hospitals. Its current investigational medicinal product, ALLOB, represents a unique, proprietary approach to organ repair and specifically to bone regeneration, by turning undifferentiated stromal cells from healthy donors into bone-forming cells on the site of injury after a single local injection. These cells are produced via a BioSenic's scalable manufacturing process. Following the CTA approval by regulatory authorities in Europe, BioSenic has initiated patient recruitment for the Phase IIb clinical trial with ALLOB in patients with difficult tibial fractures, using its optimized production process. ALLOB is currently being evaluated in a randomized, double-blind, placebo-controlled Phase IIb study in patients with high-risk tibial fractures, using its optimized production process, after a successful first safety and efficacy study (Phase 1/2a) on fractured long bones, with late delayed union. The patient recruitment has been halted late February 2023 with 57 patients and the new rules permitted for statistical analysis should allow BioSenic to get the main results of this trial much earlier than anticipated in the original protocol, since they are expected by mid-2023.
2) The Arsenic TriOxide (ATO) platform developed by Medsenic. The immunomodulatory properties of ATO have demonstrated a double basic effect on cells of the immune system. The first effect is the increase of the cell oxidative stress in activated B, T or other cells of the innate/ adaptative immune system to the point they will enter a cell death program (apoptosis) and be eliminated. The second effect is potent immunomodulatory properties on several pro-inflammatory cytokines involved in inflammatory or autoimmune cell pathways. One direct application is its use in onco-immunology to treat GvHD (Graft-versus-Host Disease) in its chronic, established stage. GvHD is one of the most common and clinically significant complications affecting long-term survival of allogeneic hematopoietic stem cell transplantation (allo-SCT). GvHD is primarily mediated by the transplanted immune system that can lead to severe multiorgan damage. Medsenic had been successful in a Phase II trial with its intravenous formulation, allowing arsenic trioxide to be granted an orphan drug designation status by FDA and EMA and is heading towards an international Phase III confirmatory study, with a new, IP protected, oral (OATO) formulation. Moderate to Severe forms of Systemic Lupus erythematosus (SLE) is another selected target, using the same oral formulation. ATO has shown good safety and significant clinical efficacy on several affected organs (skin, mucosae and the gastro-intestinal tract) in a Phase IIa study.

Systemic Sclerosis is, in addition, part of the clinical pipeline of BioSenic. Preclinical studies on pertinent animal models are positive. This gives good grounds to launch a Phase II clinical protocol for this serious disease that badly affects skin, lungs or vascularization, and with no actual current effective treatment.

In addition, BioSenic is developing an off-the-shelf next-generation improved viscosupplement, JTA-004, consisting of a unique combination 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 (OA) and inflammation. In March 2023, after the identification of new OA subtypes, BioSenic delivered a new post-hoc analysis of its Phase III JTA-004 trial on knee OA with positive action on the most severely affected patient population. 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) and cell therapy (ALLOB) platforms, is now 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.