Press Release
Media Contacts:
IB Communications
Tel +44 (0)20 89434685
biosenic@ibcomms.agency

BioSenic publishes new evidence of beneficial effects of arsenic trioxide treatment supporting clinical trial for systemic sclerosis

Arsenic trioxide (ATO) therapeutic potential to treat systemic sclerosis (SSc) is now confirmed in a new preclinical model - Fra2- characterized by severe pulmonary lesions

Mont-Saint-Guibert, Belgium, September 19, 2023 – BIOSENIC (Euronext Brussels and Paris: BIOS), the clinical-stage company specializing in serious autoimmune and inflammatory diseases and cell therapy, today announces 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.

The data are published in an article entitled 'Arsenic trioxide demonstrates efficacy in a mouse model of preclinical systemic sclerosis' in the international journal Arthritis Research & Therapy. This work studies the effects of ATO on a preclinical auto-immune disease model, that develops severe abnormal vascular remodelilng of pulmonary arterioles and nonspecific interstitial pneumonia-like lung disease, closely resembling human systemic sclerosis (SSc)-associated pulmonary hypertension.

Marked beneficial effects of ATO on skin and lung fibrosis, vascular damage and scleroderma-like lesions have been previously described by Kavian et al. (J Immunol 2012 May; Arthritis Rheum 2012 Oct) *in vitro* and in SSc preclinical models, at the Cochin Institute's facilities in Paris, France. The new data, in a third valuable preclinical model, show a significant reduction in inflammatory infiltration and a strong improvement in vascular remodelling, mediated by an immune status improvement, particularly involving T-cells. These findings represent a substantial advancement in understanding of the complex interplay between inflammation-driven fibrosis and the pathophysiology of SSc. These results give ground to the proposed clinical relevance of ATO treatment in SSc, and more generally in autoimmune pathologies, where lung is often impacted by fibrosis and vascular remodelling.

In oncology, ATO is now recognized as a first-line treatment for acute promyelocytic leukaemia, with demonstrated safety and long-term remission. BioSenic had recently further demonstrated the safety and efficacy of ATO treatment in successful clinical programs targeting chronic Graft-versus-Host Disease, in a phase 2 and Systemic Lupus Erythematosus (SLE), in a phase 2a trial. BioSenic believes that the clinical data it has helped to generate over the past decade, together with its ongoing efforts to understand the cellular pathways that are controlled by ATO administration at the right dose and time, now allow for further expansion of clinical trials targets. This applies to new indications in autoimmunity and inflammatory diseases. This is a reason why BioSenic specifically selected SSc for a systematic clinical approach to testing ATO as a novel first-in-class therapy.

François Rieger, PhD, Chairman and CEO, BioSenic said: *"BioSenic is now focusing on the final preparations for its phase 3 trial with ATO targeting chronic Graft-versus-Host Disease, one of the most common complications affecting survival of allogeneic hematopoietic stem cell transplantation patients. It is also essential that BioSenic continues to pave the way for clinical progression of its ATO programs to treat Systemic Lupus Erythematosus and systemic sclerosis. These new pre-clinical data add to the raft of in vitro and in vivo experimental data generated by BioSenic, by the scientific community and across the industry, supporting the potential of arsenic salt medication in correcting the pathophysiological parameters of the immune system gone awry in a number of autoimmune diseases. These results demonstrate the potential of ATO on the cellular characteristics of damaged organs, with chronic and aggravating functional abnormalities. This will provide invaluable knowledge for BioSenic's ATO application and formulation for the ongoing clinical development, and further contribute towards the future success of ATO's late-stage clinical development. Compounded observations, both widely published and collected in various international studies, fully justify the initiation of trials on SSc patients, in need of new and decisive medications, other than existing palliative ones. The hope for success is high and BioSenic is working hard in translating the present fundamental results into real therapeutic advances with the necessary help of available international funding."*

About BioSenic
BioSenic is a leading biotech company specializing in the development of clinical assets issued from: (i) the arsenic trioxide (ATO) platform (with key target indications including Graft-versus-Host Disease (GvHD), systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) and (ii), the development of innovative products to meet unmet needs in orthopedics.
Following a reverse merger in October 2022, BioSenic combined a strategic positionings and strengths to use, separately and combined, an entirely new arsenal of various anti-inflammatory and anti-autoimmune formulations using the immunomodulatory properties of ATO/oral ATO (OATO) with its innovative cell therapy platform and strong IP for tissue repair protection.
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 ATO platform, which has been successfully developed, has immunomodulatory properties with fundamental effects on the activated cells of the immune system. The first effect is the increase of the cell oxidative stress in activated B, T and 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 cytokines involved in inflammatory or autoimmune cell pathways, with return to homeostasis. One direct application is its use in onco-immunology to treat GvHD (Graft-versus-Host Disease) in its chronic, established stage. cGvHD is one of the most common and clinically significant complications affecting long-term survival of allogeneic hematopoietic stem cell transplantation (allo-HSCT). cGvHD is primarily mediated by the transplanted immune cells that can lead to severe multiorgan damage. BioSenic has been successful in a Phase 2 trial with its intravenous formulation, which has orphan drug designation status by FDA and EMA. The Company is heading towards an international Phase 3 confirmatory study, with its new, IP-protected, OATO formulation. Another selected target is moderate-to-severe forms of systemic lupus erythematosus (SLE), using the same oral formulation. ATO has shown good safety and significant clinical efficacy on several affected organs (skin, mucosae and the gastrointestinal tract) in an early Phase 2a study. Systemic sclerosis is also part of the clinical pipeline of BioSenic. This serious chronic disease badly affects skin, lungs or vascularization, and has no actual current effective treatment. Preclinical studies on pertinent animal models are positive, giving good grounds to launch a Phase 2 clinical protocol.
2) The allogeneic cell and gene therapy platform developed by BioSenic, with differentiated bone marrow sourced Mesenchymal Stromal Cells (MSCs), which can be stored at the point of use in hospitals. ALLOB represents a unique and 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. ALLOB has recently been evaluated in a randomized, double-blind, placebo-controlled Phase 2b 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. However, in June 2023, BioSenic decided to suspend its interventional trial on fracture healing using ALLOB, following negative results obtained for the primary endpoint in this exploratory Phase 2b clinical trial, interpreted as a failure of a too early cell injection, just after fracture. BioSenic is now focusing on determining the best time to optimise the efficacy of ALLOB (choice between early or late treatment).
Note: Biosenic has reevaluated a previous important and years-long clinical development program. In March 2023, after the clinical identification of distinct OA subtypes, BioSenic delivered a new post-hoc analysis of its Phase 3 JTA-004 trial on knee OA, demonstrating positive action on the most severely affected patient subpopulation. This new post-hoc analysis drastically changes the therapeutic profile of the combined components and allows for better patient targeting in future clinical developments. This leads to a next generation of JTA, off-the-shelf enhanced viscosupplement to treat knee osteoarthritis (OA), made of a unique combination of mammalian plasma proteins, derivatives of hyaluronic acid (a natural component of synovial fluid in the knee) and a third active component. JTA or some derivatives are intended to provide effective lubrication and protection to the cartilage of the arthritic joint and to alleviate osteoarthritic (OA) pain and inflammation.
The company, will nevertheless focus its present R&D and clinical activities on a selective, accelerated development of its autoimmune (ATO/OATO) platform.

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