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ICHNOS SCIENCES INC.



















NOVEMBER 2022 UPDATE

ABOUT ICHNOS

Ichnos Sciences aims to shift the way the world thinks about innovation in medicine by developing potentially transformative biologic treatments in immuno-oncology. The company, currently a subsidiary of Glenmark Holding, SA, plans to pursue external financing following achievement of clinical proof of concept for its lead assets.

Headquartered in New York City, Ichnos has discovery and manufacturing operations at two sites in Switzerland. As a fully integrated biotechnology company with approximately 225 employees, Ichnos has strong capabilities in research, antibody engineering, CMC, and clinical development of biotechnologies.

Ichnos is guided by an accomplished management team with experience developing immune cell engagers within the biopharmaceuticals industry, and is led by Cyril Konto, M.D., President and Chief Executive Officer.

<p>CYRIL KONTO, M.D. President and Chief Executive Officer</p> <p>  </p>	<p>ERIC J. FELDMAN, M.D. Chief Medical Officer</p> <p> </p>	<p>ROBERTO GIOVANNINI, Ph.D. Chief Process and Manufacturing Officer</p> <p> </p>
<p>PATRICIA JAQUET Global Head of Human Resources</p> <p></p>	<p>GRACE MAGUIRE Head of Communications and Corporate Affairs</p> <p> </p>	<p>ASHOK MARÍN General Counsel</p> <p> </p>
<p>MICHAEL D. PRICE Chief Financial Officer</p> <p> </p>	<p>EUGENE ZHUKOVSKY, Ph.D. Chief Scientific Officer</p> <p>   </p>	

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The proprietary BEAT® technology platform¹ is the basis for Ichnos' clinical-stage oncology pipeline. Using this technology, coupled with the proprietary common light chain library, the company is developing novel multispecific immune cell engagers and modulators, with the goal of realizing its mission to provide breakthrough, potentially curative therapies that may extend and improve lives, writing a new chapter in healthcare.

ONCOLOGY PIPELINE

The first wave of Ichnos' multispecific antibody pipeline consists of five programs targeting a range of hematologic malignancies and solid tumor indications through engagement of a broad spectrum of immune cells. The most advanced programs are ISB 1342, a clinical-stage, potentially first-in-class bispecific antibody targeting CD38 and CD3, which is in Phase 1 for the treatment of relapsed/refractory multiple myeloma, and ISB 1442, a biparatopic bispecific antibody targeting CD38 and CD47, currently in a Phase 1/2 dose escalation/expansion study for the same indication. The first patient in the study for ISB 1442 was dosed this past quarter, in September 2022.

Ichnos is looking for asset-level and platform-level collaboration partners in development and research. For more information, email us at Partnership@IchnosSciences.com.

MOLECULE MECHANISM/CLASS	PHASE/STATUS	LEAD INDICATION
ISB 1342 CD38 x CD3 BEAT® 1.0 bispecific antibody	Phase 1	Relapsed/Refractory Multiple Myeloma; T-ALL is also under consideration
ISB 1442 CD38 x CD47 BEAT® 2.0 bispecific antibody	Phase 1	Relapsed/Refractory Multiple Myeloma; AML is also under consideration
ISB 2001 BCMA x CD38 x CD3 TREAT™ trispecific antibody ²	IND-Enabling Studies	Relapsed/Refractory Multiple Myeloma
ISB 2004 BEAT® 2.0 bispecific antibody	Discovery	Hematologic Malignancies/ Solid Tumors
NK-cell engaging multispecific platform (formerly ISB 2005)	Discovery	Solid Tumors

¹ Bispecific Engagement by Antibodies based on the TCR

² Trispecific Engagement by Antibodies based on the TCR



OVERVIEW OF SELECT ONCOLOGY DRUG PRODUCT CANDIDATES

ISB 1342 (CD38 X CD3 BISPECIFIC ANTIBODY)

- A Phase 1, open-label, dose-escalation, first-in-human study of ISB 1342 in patients with relapsed/refractory multiple myeloma is ongoing.
 - + Enrollment of patients receiving a weekly dosing regimen is ongoing.
 - + Number of sites participating in the study was expanded at the end of calendar year 2021 to enhance enrollment. New locations in the U.S. were added and 11 sites were opened for enrollment in France and are now recruiting subjects.
 - + Clinical proof of concept in the ongoing study is anticipated towards the end of calendar year 2022, or in early 2023.
- The primary objectives of the study are to:
 - + Determine maximum tolerated dose and/or recommended Phase 2 dose of ISB 1342 (Part 1 dose escalation).
 - + Assess anti-myeloma activity of ISB 1342 according to the International Myeloma Working Group response criteria (Part 2 dose expansion).
- Clinical data on this ongoing Phase 1 study will be presented at the American Society of Hematology (ASH) Annual Meeting in December 2022:
 - + Initial Results of Dose Escalation of ISB 1342, a Novel CD3 x CD38 Bispecific Antibody, in Patients with Relapsed / Refractory Multiple Myeloma (RRMM); Poster presentation on Sunday, December 11 from 6:00PM – 8:00PM CST
- ISB 1342 was granted Orphan Drug Designation for multiple myeloma by the FDA.
- The bulk drug substance is manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland.

ISB 1442 (CD38 X CD47 BISPECIFIC ANTIBODY)

- This first-in-class biparatopic bispecific antibody targeting CD38 x CD47 was generated using the BEAT[®] 2.0 technology developed by scientists in Ichnos' laboratories in Lausanne at the Biopole life sciences campus.
- ISB 1442 is designed to kill CD38-expressing tumor cells through inhibition of the CD47-SIRP α axis to increase antibody-dependent cellular phagocytosis (ADCP) and enhance antibody-dependent cellular cytotoxicity (ADCC) as well as complement-dependent cytotoxicity (CDC).
- An IND was filed with the US Food and Drug Administration earlier this calendar year and a Phase 1/2 first-in-human dose-finding study of ISB 1442 in relapsed/refractory multiple

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myeloma began dosing patients in September 2022. Ichnos also plans to develop ISB 1442 in other hematologic malignancies such as acute myeloid leukemia (AML).

- The preclinical data package for ISB 1442, which may be viewed at this [link](#), shows:
 - + Higher potency in vitro for ISB 1442 relative to daratumumab in CD38 high/low tumor models as measured by a multiple antibody-dependent mechanisms of action killing assay
 - + Higher tumor growth inhibition for ISB 1442 than daratumumab in CD38 high preclinical in vivo xenograft models
 - + Low on-target off-tumor binding with ISB 1442 compared to anti-CD47 mAb (5F9), is anticipated to result in lower red blood cell depletion in clinic, and potentially a better therapeutic index than anti-CD47 bivalent monoclonal antibodies
- Additional information on the ongoing Phase 1 study and on preclinical models in other hematologic malignancies will be presented at the ASH Annual Meeting in December 2022:
 - + [A Phase 1/2, First-in-Human, Multicenter, Open-Label, Dose Escalation and Dose-Expansion Study of Single-Agent ISB 1442 in Patients with Relapsed/Refractory Multiple Myeloma; Poster presentation on Monday, December 12 from 6:00PM – 8:00PM CST](#)
 - + [Preclinical Evaluation of ISB 1442, a First-in-Class CD38 and CD47 Bispecific Antibody Innate Cell Modulator for the Treatment of AML and T-ALL; Poster presentation on Sunday, December 11 from 6:00PM – 8:00PM CST](#)
- The first bulk drug substance batches to support IND filing and the ongoing Phase 1/2 dose escalation and expansion study were manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland in 2021.

ISB 2001 TREAT™ TRISPECIFIC ANTIBODY

- ISB 2001 is the first T cell-engaging antibody that targets BCMA and CD38 on multiple myeloma cells. It is a trispecific antibody based on TREAT™ technology, a proprietary platform allowing maximal flexibility and manufacturability of full-length multispecific antibodies. Additional ISB 2001 details include:
 - + ISB 2001 combines three proprietary fragment antigen-binding arms, each targeting a different antigen, with one arm binding to the epsilon chain of CD3 on T cells, and the other two binding BCMA and CD38 on myeloma cells. Its Fc domain was fully silenced to suppress Fc effector functions.
 - + In vitro studies showed that ISB 2001 exhibited increased killing potency of tumor

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cells compared to all tested antibodies that are either currently approved for the treatment of multiple myeloma or are being tested in ongoing clinical studies. In vivo studies in the multiple myeloma models also demonstrated superior potency of ISB 2001 relative to approved antibody treatments of multiple myeloma.

- + ISB 2001 redirects CD3+ T lymphocytes to kill tumor cells expressing low to high levels of both BCMA and CD38. With two different tumor-associated antigens instead of one, ISB 2001 has increased binding specificity to multiple myeloma cells due to enhanced avidity-based binding and is also expected to be more resistant to antigen escape associated with treatment of multiple myeloma patients.
- The preclinical data package for ISB 2001 was selected for oral presentation at the ASH Annual Meeting on Saturday, December 10 at 5:00PM CST:
 - + ISB 2001, a First-in-Class Trispecific BCMA and CD38 T Cell Engager Designed to Overcome Mechanisms of Escape from Treatments for Multiple Myeloma by Targeting Two Antigens
- Currently in IND-enabling studies, Ichnos intends to file an Australian CTN and US IND for ISB 2001 in the first quarter of calendar year 2023 and is considering expansion of clinical studies to additional countries in parallel.
- The first bulk drug substance batches to support IND filing and the Phase 1 dose escalation and expansion study were manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland in 2022.

AUTOIMMUNE DISEASES

Ichnos has two monoclonal antibody drug product candidates addressing autoimmune diseases in the pipeline. In order to enhance the company's focus on oncology, future development of both assets will be overseen by out-licensing partners.

The first asset, ISB 880, an anti-IL-1RAP antagonist, was licensed to Almirall, S.A. in December 2021. Initiation of dosing in a Phase 1 study of ISB 880 was announced by Almirall in September 2022. The second antibody, ISB 830 (telazorlimab), an OX40 antagonist that completed a Phase 2b study in moderate to severe atopic dermatitis in calendar year 2021, is in partnering discussions. Both compounds have potential across a range of autoimmune diseases.

ASSETS IN AUTOIMMUNE DISEASE

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS
ISB 880 (ALM 27134) IL-1RAP Antagonist Monoclonal Antibody	Autoimmune Diseases	Phase 1	Licensed to Almirall S.A. in December 2021. Dosing of participants in the Phase 1 study was announced by Almirall in September 2022 .
ISB 830 Telazorlimab OX40 Antagonist Antibody	Atopic Dermatitis	Phase 2b	Successfully completed a Phase 2b study in Atopic Dermatitis. Exploring partnership(s).
	Other autoimmune diseases, including Rheumatoid Arthritis	U.S. IND for Rheumatoid Arthritis and other autoimmune indications is active.	

ISB 880 (IL-1RAP ANTAGONIST)



- Ichnos entered an exclusive global licensing agreement for ISB 880 in autoimmune diseases with Almirall in December 2021. Within the terms of the agreement, Almirall assumed full cost and responsibility for the global development and commercialization of the compound. Ichnos received an upfront payment of €20.8 million. The deal includes development and commercial milestone payments and tiered royalties based upon future global sales. As part of the agreement, Ichnos is also being paid to manufacture batches of ISB 880 to support early clinical studies to be sponsored by Almirall and realized revenue this year for drug supplies for the ongoing Phase 1 study.

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- ISB 880, a fully-human, high-affinity, monoclonal antibody blocking IL-1RAP signaling, has completed IND-enabling studies for patients with autoimmune diseases. The optimal antibody profile, the strong *in vitro* and *in vivo* data package, as well as toxicology, CMC, and clinical pharmacology plans enabled U.S. IND filing by Almirall, and a Phase 1 study is under way.
- Blockade of IL-1RAP simultaneously abrogates multiple disease drivers among the IL-1 family of proinflammatory cytokine receptors, including IL-1R, IL-33R, and IL-36R, differentiating ISB 880 from single cytokine blockade therapies. These cytokines have been implicated in numerous autoimmune conditions, opening opportunities for ISB 880 to be positioned across broad disease indications.
- To date, there is no IL-1RAP antagonist approved or under clinical development for autoimmune disease, positioning ISB 880 as a potential first-in-class therapeutic.
- Ichnos retains rights for antibodies acting on the IL-1RAP pathway for oncology indications.

ISB 830 (TELAZORLIMAB, OX40 ANTAGONIST)

- The database for the ISB 830-204 Phase 2b clinical study in atopic dermatitis was locked in October 2021, and the final results were posted on [ClinicalTrials.gov](https://clinicaltrials.gov). This study, which was conducted in the U.S., Canada, Germany, Czech Republic, and Poland, had a randomized, controlled, multicenter design and assessed three doses and two dosing schedules of telazollimab versus placebo in adults with moderate-to-severe atopic dermatitis.
- Results from the double-blind portion of the study are summarized below:
 - + **Efficacy:** The primary endpoint of the EASI score, % change from baseline to Week 16, was achieved for the two highest doses of telazollimab tested (300 mg and 600 mg q 2 weeks) versus placebo.
 - + **Safety:** Telazollimab was well tolerated. The most commonly reported adverse events (>5%) were atopic dermatitis, nasopharyngitis, upper respiratory tract infection, and headache. One patient with pre-existing hypertension in the telazollimab group died due to a presumed cardiovascular event during the treatment period. The investigator considered the death to be unrelated to the study drug.
- Ichnos has clearance from the FDA to study telazollimab in seropositive autoimmune diseases (Rheumatoid Arthritis, Systemic Lupus Erythematosus, Sjogren's Syndrome, Multiple Sclerosis, Type I Diabetes Mellitus, Myasthenia Gravis), and is actively seeking a partner to further develop the drug in atopic dermatitis and other indications. For more information, email us at Partnership@IchnosSciences.com.