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ICHNOS SCIENCES INC.

MAY 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. This past quarter, Ichnos expanded the executive team with the additions of Ashok Marín, Esq., as General Counsel and Eugene Zhukovsky, Ph.D., as Chief Scientific Officer. Both Ashok and Eugene have significant industry leadership experience and strong track records of success at biotechnology companies.

CYRIL KONTO, M.D. President and Chief Executive Officer Allogene, Pfizer, Bristol Myers Squibb	**ERIC J. FELDMAN, M.D.** Chief Medical Officer GlycoMimetics, Inc., AMPHIVENA	**ROBERTO GIOVANNINI, Ph.D.** Chief Process and Manufacturing Officer Boehringer Ingelheim, glenmark
PATRICIA JAQUET Global Head of Human Resources COVANCE	**GRACE MAGUIRE** Head of Communications and Corporate Affairs Forest Laboratories, Inc., Wyeth	**ASHOK MARÍN, Esq.** General Counsel sanofi, GILEAD
MICHAEL D. PRICE Chief Financial Officer AKCEA, novelion	**EUGENE ZHUKOVSKY, Ph.D.** Chief Scientific Officer AFFIMED, BIOMUNEX	

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The proprietary BEAT® technology platform[1] 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 program is 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.

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 under consideration
ISB 1442 CD38 x CD47 BEAT® 2.0 bispecific antibody	IND Cleared	Relapsed/Refractory Multiple Myeloma; AML and T-ALL are under consideration
ISB 2001 BCMA x CD38 x CD3 TREAT™ trispecific antibody	IND-Enabling Studies	Relapsed/Refractory Multiple Myeloma
ISB 2004 BEAT® 2.0 bispecific antibody	Discovery	Hematologic Malignancies/ Solid Tumors
ISB 2005 TREAT™ trispecific antibody	Discovery	Solid Tumors

[1] Bispecific 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 in the middle of calendar year 2022.
- 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).
- Preclinical data on ISB 1342 were presented at the 2021 ASCO Annual Meeting and EHA 2021 Virtual Congress.
- 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 2+1 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-SIRPα axis to increase antibody-dependent cellular phagocytosis (ADCP) and enhance antibody-dependent cellular cytotoxicity through complement dependent cytotoxicity (CDC) and antibody-dependent cell cytotoxicity (ADCC), enabled by the architecture and engineered Fc of the molecules.
- An IND was filed with the US Food and Drug Administration earlier this calendar year and was recently cleared. A Phase 1/2 first-in-human dose-finding study of ISB 1442 in relapsed/refractory multiple myeloma is currently planned to start in the summer of 2022. Ichnos plans to develop ISB 1442 in other hematologic malignancies, including acute myeloid leukemia (AML) and T-cell acute lymphoblastic leukemia (T-ALL).

- Preclinical data on ISB 1442 were shared in an oral presentation at the 2021 American Society of Hematology Meeting on December 11, 2021. These data, which may be viewed at this link, show:
    + 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 preclinical data on ISB 1442 were presented at the 2022 American Association for Cancer Research (AACR) Annual Meeting in April.
- The first bulk drug substance batches to support IND filing and early clinical studies 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 BEAT® 2.0 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 fragment crystallizable (Fc) domain was fully silenced to suppress Fc effector functions.
    - In vitro studies showed that ISB 2001 exhibited increased killing potency of tumor cells compared to all tested antibodies that are either currently approved therapeutics for 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.

- Currently in IND-enabling studies, Ichnos intends to file a US IND for ISB 2001 in Q4 FY23.
- Process development is ongoing at the Ichnos site in La Chaux-de-Fonds, Switzerland.

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, ISB 880, an anti-IL-1RAP antagonist, was licensed to Almirall, S.A. in December 2021, and the second, ISB 830 (telazorlimab), an OX40 antagonist that completed a Phase 2b study in moderate to severe atopic dermatitis in calendar year 2021, is in out-licensing discussions. Both compounds have potential across a range of autoimmune diseases.

ASSETS IN AUTOIMMUNE DISEASE

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS
ISB 880 IL-1RAP Antagonist Monoclonal Antibody	Autoimmune Diseases	IND-enabling studies completed	Licensed to Almirall S.A. in December 2021. Almirall's start of a Phase 1 study is planned for first half of calendar year 2022.
ISB 830 Telazorlimab OX40 Antagonist Antibody	Atopic Dermatitis	Phase 2b	Successfully completed a Phase 2b study in atopic dermatitis. Out-licensing discussions ongoing.
	Other autoimmune diseases, including Rheumatoid Arthritis	U.S. IND for RA 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 will assume full cost and responsibility for the global development and commercialization of the compound. Ichnos received an upfront payment of €20.8 million and the deal also includes development and commercial milestone payments and tiered royalties based upon future global sales.

- 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 will enable U.S. IND filing by Almirall and start of a Phase 1 study in the first half of calendar year 2022.

- 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 will retain 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. 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 telazorlimab versus placebo in adults with moderate-to-severe atopic dermatitis (AD).
- Results from the double-blind portion of the study are summarized below.
    + **Efficacy:** The primary endpoint of EASI score, % change from baseline to Week 16, was achieved for the two highest doses of telazorlimab tested (300 mg and 600 mg q 2 weeks) versus placebo. Numerical improvements were also seen for the two higher dose arms of telazorlimab compared to placebo in the secondary endpoints of EASI-75 and Investigator Global Assessment, but most of the differences were not statistically significant.

	Part 1				Part 2	
	TELAZORLIMAB 300 MG Q2W (n=76*)	**TELAZORLIMAB 300 MG Q4W (n=78*)**	**TELAZORLIMAB 75 MG Q4W (n=77*)**	**PLACEBO (n=80*)**	**TELAZORLIMAB 600 MG Q2W (n=75*)**	**PLACEBO (n=74*)**
EASI Score % Change from Baseline to Week 16 Mean (SD)	-57.59 (36.20)	-56.73 (32.54)	-38.10 (39.69)	-42.14 (38.19)	-59.74 (27.12)	-43.25 (41.24)
P-value	0.008	0.061	0.691	n/a	0.008	n/a

Q2W, every 2 weeks; Q4W, every 4 weeks; n/a, not applicable

*Includes subjects who were randomized and dosed. Subjects who received rescue medication for atopic dermatitis during the study are considered non-responders in the efficacy analyses.

    + **Safety:** Telazorlimab 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 telazorlimab group died due to a presumed cardiovascular event during the treatment period. The investigator considered the death to be unrelated to the study drug.

- In addition to data from the 16-week primary analysis period, preliminary results from the open-label extension and follow-up period of this study, which was ongoing at the time, were presented at the 2021 Society for Investigative Dermatology Virtual Meeting and are accessible here. Of note:
  - Clinical efficacy continued to improve after Week 16, with maximal impact achieved several weeks later.
  - Reduction in AD disease activity was maintained after discontinuation of telazorlimab, through three months of follow-up.
- A U.S. IND to conduct studies of telazorlimab in autoimmune diseases, including Rheumatoid Arthritis (RA), is active.
- Licensing discussions are ongoing.