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ICHNOS SCIENCES INC.

NOVEMBER 2021 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 and autoimmune diseases. The company, headquartered in New York City, with discovery and manufacturing at two sites in Switzerland, has approximately 225 employees and strong capabilities in the research and development of new biological entities (NBEs).

The first wave of Ichnos' multispecific antibody oncology pipeline consists of five programs, including a clinical-stage, potentially first-in-class T-cell engager, ISB 1342 (CD38 x CD3), which is in Phase 1 for the treatment of relapsed/refractory multiple myeloma.

Ichnos' proprietary BEAT® technology platform[1] enables the company to develop novel immune cell engagers and modulators in oncology, with the goal of realizing its mission to provide breakthrough, potentially curative therapies that will hopefully extend and improve lives, writing a new chapter in healthcare.

Beyond oncology, Ichnos has a pipeline of two first-in-class therapeutics addressing autoimmune diseases. ISB 830 (telazorlimab, OX40 antagonist) successfully completed a Phase 2b study in moderate to severe atopic dermatitis, and ISB 880 (anti-IL-1RAP antagonist) has completed IND-enabling studies. Both compounds have potential across a range of autoimmune diseases and are in the process of being out-licensed, enabling Ichnos to focus on oncology moving forward.

Officially launched on October 15, 2019, Ichnos has an experienced executive leadership team and board of directors. The company is a subsidiary of Glenmark Holding SA, which is currently funding operating expenses until additional investors come on board.

[1] Bispecific Engagement by Antibodies based on the T-cell receptor

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QUARTERLY HIGHLIGHTS

BUSINESS UPDATES

Ichnos' pipeline continues to grow. Enrollment in a Phase 1 study for ISB 1342 is ongoing, and six investigative sites in France were added this past quarter. Additionally, preclinical-stage assets focused on CD38 x T-cell engagers and macrophage modulators are advancing.

Ichnos has entered into advanced out-licensing discussions with potential partners for the autoimmune disease portfolio, which includes the Phase 2b OX40 antagonist telazorlimab (ISB 830) and the IL-1RAP antagonist ISB 880, which recently completed IND-enabling studies.

With the continued progress in resolving the COVID-19 pandemic, Ichnos opened its global headquarters at One World Trade Center in New York City this past quarter.

Eric Feldman, M.D., an accomplished oncology drug developer with significant industry experience, joined Ichnos as Chief Medical Officer in early November.

FISCAL YEAR 2022 OBJECTIVES

- Establish clinical proof of concept for ISB 1342 and the BEAT® platform
- File an IND for ISB 1442
- Finalize out-licensing of ISB 830 and ISB 880
- Continue to prepare for equity capital raise

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UPDATE ON ICHNOS ONCOLOGY BIOLOGICS PIPELINE

MOLECULE MECHANISM/CLASS	PHASE/STATUS	LEAD INDICATION
ISB 1342 CD38 x CD3 BEAT® 1.0 bispecific antibody	Phase 1	Relapsed/Refractory Multiple Myeloma
ISB 1442 CD38 x CD47 BEAT® 2.0 bispecific antibody	IND-Enabling Studies	Relapsed/Refractory Multiple Myeloma
ISB 2001 TREAT™ trispecific antibody	Discovery	Hematologic Malignancies
ISB 2004 BEAT® 2.0 bispecific antibody	Discovery	Hematologic Malignancies/ Solid Tumors
ISB 2005 TREAT™ trispecific antibody	Discovery	Hematologic Malignancies

OVERVIEW OF SELECT ONCOLOGY COMPOUNDS

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 biweekly dosing was closed in March 2020 following clinical pharmacology evaluation in 29 subjects.
  - Enrollment of patients receiving a weekly dosing regimen is ongoing.
  - Number of sites participating in the study was recently expanded to enhance enrollment. New locations in the US were added and six sites have opened for enrollment in France.
- 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.

- Orphan Drug Designation for multiple myeloma was granted by the FDA in September 2019.
- 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 CD38 x CD47 biparatopic bispecific antibody 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 CDC and ADCC, enabled by the architecture and engineered Fc of the molecules.
- IND-enabling studies are proceeding, and a Phase 1/2 first-in-human dose-finding study of ISB 1442 in relapsed/refractory multiple myeloma is currently planned to start in mid-2022.
- Preclinical data on ISB 1442 were selected for an oral presentation at the 2021 American Society of Hematology Meeting on December 11, 2021. (abstract)
- The first bulk drug substance batch to support IND filing and early clinical studies was manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland during this past quarter.

ISB 2001 TREAT™ TRISPECIFIC ANTIBODY

- Based on BEAT® 2.0 technology, ISB 2001 trispecific antibody (TREAT™) represents a first-in-class potential treatment for hematologic malignancies and is designed to extend therapeutic durability.
- Identification and amino acid sequence lock of the top two candidates was achieved this past quarter. Preclinical evaluation of in vivo efficacy, PK/PD correlation, additional biophysical properties description, late pharmacology studies and other attribute-defining studies are ongoing, and the results will inform the selection of the clinical lead.
- Manufacturability development is ongoing at the Ichnos site in La Chaux-de-Fonds, Switzerland.

ICHNOS TO OUT-LICENSE ASSETS IN AUTOIMMUNE DISEASE

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS
ISB 830 Telazorlimab OX40 Antagonist Antibody	Atopic Dermatitis	Phase 2b	Achieved the primary endpoint of EASI[2] score, % change from baseline to Week 16, at the two highest doses tested (300 mg and 600 mg q 2 weeks) versus placebo. Numerical improvements were also seen at the two higher dose arms of telazorlimab for the secondary endpoints of EASI-75[3] and Investigator Global Assessment[4] as compared to placebo, but most of these differences were not statistically significant.
	Other autoimmune diseases, including Rheumatoid Arthritis	US IND for RA and other autoimmune indications is active.	
ISB 880 IL-1RAP Antagonist Monoclonal Antibody	Autoimmune Diseases	Pre-clinical	IND-enabling studies and the dossier are complete and IND filing is on track for end of calendar year 2021.

AUTOIMMUNE DISEASE

ISB 830 (TELAZORLIMAB, OX40 ANTAGONIST)

- The ISB 830-204 Phase 2b clinical study is now complete and the database was locked in October 2021. This study, which was conducted in the US, 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.

[2] EASI: Eczema Area and Severity Index
[3] Proportion of patients with ≥75% improvement in EASI score from baseline to Week 16
[4] Proportion of patients with Investigator Global Assessment of clear or almost clear (0 or 1) and ≥2-point reduction from baseline at Week 16

	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 ongoing follow-up period of this study are available and were recently 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 US IND to conduct studies of telazorlimab in autoimmune diseases, including Rheumatoid Arthritis (RA), is active.
- Licensing discussions are ongoing.

ISB 880 (IL-1RAP ANTAGONIST)

- ISB 880, a fully human, high-affinity, monoclonal antibody blocking IL-1RAP signalling, 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 IND filing by end of calendar year 2021.
- 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.
- Licensing discussions are ongoing.