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# ICHNOS SCIENCES INC.

## **FEBRUARY 2021 UPDATE**

Ichnos Sciences aims to shift the way the world thinks about innovation in medicine by developing potentially transformative biologic treatments in oncology. The company, headquartered in New York City, with discovery and manufacturing at two sites in Switzerland, has approximately 200 employees and strong capabilities in the research and development of new biological entities (NBEs).

The first wave of Ichnos' multispecific oncology pipeline consists of seven programs, including two clinical-stage T cell engager assets: ISB 1342 (CD38 x CD3) in relapsed refractory multiple myeloma and ISB 1302 (HER2 x CD3) in metastatic HER2+ breast cancer.

Ichnos' proprietary BEAT<sup>®</sup> technology platform<sup>1</sup> will enable 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 potential first-in-class therapeutics addressing autoimmune disease and pain. These include ISB 830 (telazorlimab, OX40 antagonist) in Phase 2b, and ISB 880 (anti-IL-1RAP antagonist) in IND-enabling studies, which both have potential in a range of autoimmune diseases, and ISC 17536 (TRPA1 antagonist) which has completed a Phase 2a study in pain associated with diabetic peripheral neuropathy. Ichnos is currently in discussions with pharmaceutical companies to license out ISB 830, ISB 880, and ISC 17536. In addition, Ichnos is planning to out-license ISC XXXXX, a small molecule HPK1 inhibitor in IND-enabling studies for undisclosed oncology indications.

Officially launched on 15 October 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.

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<sup>1</sup> Bispecific Engagement by Antibodies based on the T cell receptor



## QUARTERLY HIGHLIGHTS

Ichnos is continuing the separation process from Glenmark and is in the process of building and transitioning to distinct systems for human resources and finance. A Series B financing round is in process.

Both clinical- and preclinical-stage assets have continued to progress. Enrollment in Phase 1 studies for both ISB 1342 and ISB 1302 is ongoing and preclinical-stage assets focused on CD38 x T cell engagers and macrophage modulators are advancing.

The opening of the global headquarters in New York is still pending due to the pandemic. US-based colleagues will work remotely until the situation improves, with the goal of opening the office later in calendar year 2021.

## UPDATE ON ICHNOS ONCOLOGY BIOLOGICS PIPELINE

MOLECULE MECHANISM/CLASS	PHASE/STATUS	POTENTIAL INDICATIONS
ISB 1342 CD38 x CD3 BEAT® bispecific antibody	Phase 1 Enrolling	Relapsed/Refractory Multiple Myeloma
ISB 1908 CD38 x CD3 BEAT® bispecific antibody	Pre-IND	Relapsed/Refractory Multiple Myeloma
ISB 1909 BEAT® T cell engager bispecific antibody	Discovery	Undisclosed
ISB 1442 CD38 x CD47 BEAT® bispecific antibody	Pre-IND	Hematologic Malignancies
ISB 2004 BEAT® bispecific antibody	Discovery	Undisclosed
ISB 2001 BEAT® trispecific antibody	Discovery	Undisclosed
ISB 1302 HER2 x CD3 BEAT® bispecific antibody	Phase 1 Enrolling	Metastatic HER2+ Breast Cancer

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**OVERVIEW OF CLINICAL-STAGE ONCOLOGY ASSETS**

**ISB 1342 (CD38 X CD3 BISPECIFIC ANTIBODY)**

- A Phase 1/2, first-in-human study of ISB 1342 to determine the MTD with biweekly and weekly dosing regimens in patients with refractory multiple myeloma is ongoing. Enrollment of patients receiving biweekly dosing was closed in March 2020 following evaluation of safety/efficacy and PK/PD of 11 cohorts.
- Enrollment of patients receiving a weekly dosing regimen is ongoing.

**ISB 1302 (HER2 X CD3 BISPECIFIC ANTIBODY)**

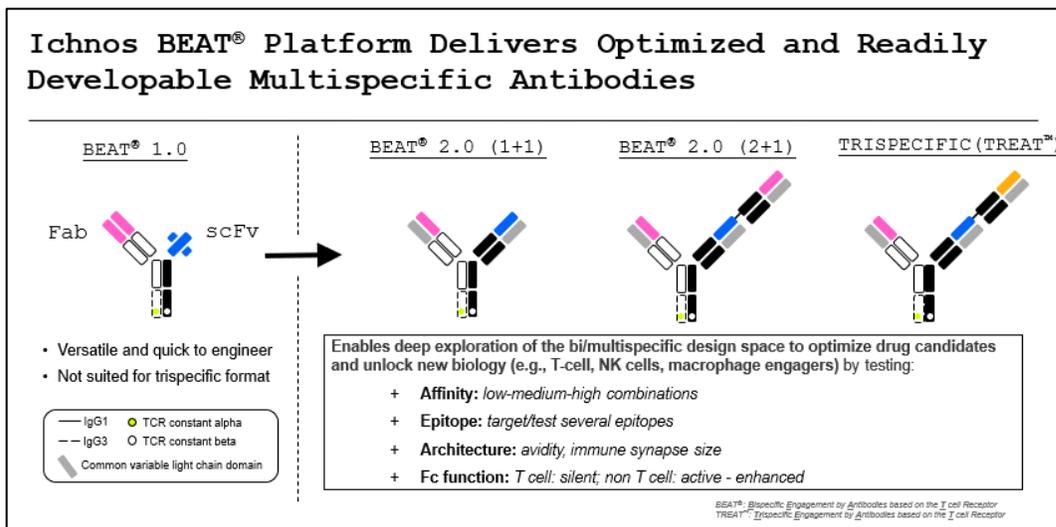
- A Phase 1/2, first-in-human study of ISB 1302 to determine the maximum tolerated dose (MTD) with biweekly dosing in patients with HER2-positive cancers completed enrollment in the US and Germany in May 2019.
- A Phase 1/2 study of ISB 1302 to evaluate a weekly dosing regimen is ongoing.

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**UPDATE ON ICHNOS DISCOVERY NBE ONCOLOGY PIPELINE**

Ichnos will continue to leverage its capabilities in NBEs to expand the portfolio. With the BEAT® platform, Ichnos Discovery is positioned to fully explore the design space, and to engineer and optimize multispecific antibodies. The company is planning to advance to IND-enabling studies for a number of candidates in 2021 and beyond.

**BEAT® Platform Delivers Optimized and Readily Developable Multispecific Antibodies**



**Strategic Priorities for Biologics Discovery Research in Immuno-Oncology**

**FOCUS ON DISEASE-CENTRIC APPROACH AND LEVERAGE BEAT® ANTIBODY ENGINEERING PLATFORM TO DELIVER FIRST-IN-CLASS CANDIDATES**

MULTIPLE MYELOMA (MM)	HEMATOLOGICAL MALIGNANCIES	SOLID TUMORS
<ul style="list-style-type: none"> <li>• Optimize molecular attributes of ISB 1342 (CD38 x CD3) T cell engager</li> <li>• Deliver a competitive MM portfolio by advancing next wave of T cell engagers and innate immune engagers (e.g., NK, macrophages)</li> </ul>	<ul style="list-style-type: none"> <li>• Accelerate delivery of innovative concepts by leveraging trispecific T cell and innate immune engagers (e.g., NK, macrophages)</li> </ul>	<ul style="list-style-type: none"> <li>• Optimize molecular attributes of ISB 1302 (HER2 x CD3) T cell engager</li> </ul>



**ICHNOS TO OUT-LICENSE ASSETS IN AUTOIMMUNE DISEASE, PAIN, AND ONCOLOGY SMALL MOLECULES**

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS
<b>AUTOIMMUNE DISEASE BIOLOGICS</b>			
ISB 830 Telazorlimab OX40 Antagonist Antibody	Atopic Dermatitis (AD)	Phase 2b	Achieved the primary endpoint of EASI <sup>2</sup> 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 <sup>3</sup> and Investigator Global Assessment <sup>4</sup> as compared to placebo, but most of these differences were not statistically significant.
	Other autoimmune diseases, including Rheumatoid Arthritis (RA)	US IND for RA and other autoimmune indications is active.	
ISB 880 IL-1RAP Antagonist Monoclonal Antibody	Autoimmune Diseases	Pre-clinical	IND-Enabling Studies
<b>PAIN SMALL MOLECULE</b>			
ISC 17536 TRPA1 <sup>5</sup> Oral Antagonist	Painful Diabetic Peripheral Neuropathy	Phase 2a	A Phase 2a study in patients with painful diabetic peripheral neuropathy was previously completed. The primary endpoint was not met for the overall study population, but a statistically significant reduction in pain was seen in a prespecified subgroup of patients with preserved small nerve fiber function. Additional preclinical toxicology studies and a formulation study in healthy volunteers have both recently been completed.
<b>ONCOLOGY SMALL MOLECULE</b>			
ISC XXXXX HPK1 Inhibitor	Not Disclosed	Pre-clinical	Pre-IND

<sup>2</sup> EASI: Eczema Area and Severity Index

<sup>3</sup> Proportion of patients with ≥75% improvement in EASI score from baseline to Week 16

<sup>4</sup> Proportion of patients with Investigator Global Assessment of clear or almost clear (0 or 1) and ≥2-point reduction from baseline at Week 16

<sup>5</sup> Transient receptor potential ankyrin-1

## AUTOIMMUNE DISEASE

ISB 830 (TELAZORLIMAB, OX40 ANTAGONIST)

- The double-blind portion of a two-part, randomized, controlled, multicenter, Phase 2b clinical trial, assessing four doses and dosing schedules of telazorlimab versus placebo in adults with moderate-to-severe atopic dermatitis (AD), has been completed. An open-label extension is ongoing across study sites in the US, Canada, Germany, Czech Republic, and Poland.
- 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

\*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. There was one death due to pre-existing hypertension in a patient in the telazorlimab group, considered by the investigator to be unrelated to study drug.
- A US IND to conduct studies of telazorlimab in additional autoimmune diseases, including Rheumatoid Arthritis (RA), is active and Ichnos plans to out-license this asset for further development.

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## ISB 880 (IL-1RAP ANTAGONIST)

- ISB 880 is a fully human, high-affinity, monoclonal antagonist antibody against human IL-1RAP that blocks signalling via three key disease drivers, IL1R, IL36R, and IL33R, reducing downstream inflammatory responses. ISB 880 is expected to impact diseases where multiple cytokines may concurrently play a role and, thus, has the potential to deliver superior and sustained clinical efficacy in a broad range of indications.
- A US IND in autoimmune disease indication(s) is targeted for the second half of calendar year 2021.

## **PAIN**

### ISC 17536 (TRPA1 ANTAGONIST)

- A Phase 2a proof-of-concept (PoC) study of the oral inhibitor of transient receptor potential ankyrin-1 (TRPA1), ISC 17536, was previously completed at sites in Europe and India in adult patients with painful diabetic peripheral neuropathy (DPN).
- While the primary endpoint of change from baseline to week 4 in average pain intensity was not met in the overall study population, a statistically significant reduction in this endpoint was seen for ISC 17536 compared to placebo in the prespecified subgroup of patients who had preserved small nerve fiber function at baseline.
- At a Type C meeting with FDA in March 2020, agreement was reached regarding the proposed preclinical plan that would enable a randomized, double-blind, placebo-controlled, Phase 2b, dose-range-finding study for painful DPN. A preclinical toxicology study in dogs and a formulation study in healthy volunteers have recently been completed.
- Intellectual property rights and oversight of future development of ISC 17536 are being transferred to Ichnos' parent company, Glenmark. Future out-licensing activities for the product will be conducted by Glenmark Business Development.

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**ONCOLOGY SMALL MOLECULES**

ISC XXXXX HEMATOPOIETIC PROGENITOR KINASE 1 (HPK1, MAP4K1)  
INHIBITOR

- Multiple immunogenic syngeneic models have demonstrated (in vivo) anti-tumor activity associated with HPK1 gene deletion, kinase dead HPK1, and small molecule inhibitors.
- Enhanced anti-tumor efficacy may be achieved by combining HPK1 inhibition with checkpoint inhibitors (CPIs) like anti-PD-1, anti-PD-L1, or anti-CTLA4 antibodies.
- Ichnos plans to focus on biologics for the treatment of cancer and will out-license this program prior to starting IND-enabling studies.