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ICHNOS SCIENCES INC.

NOVEMBER 2020 UPDATE

Ichnos Sciences aims to shift the way the world thinks about innovation in medicine by developing potentially transformative treatments in oncology and autoimmune disease. The company, with its global headquarters in New York City, and discovery and manufacturing at two locations in Switzerland, has strong capabilities in the research and development of new biological entities (NBE). Ichnos is also engaged in the discovery of new chemical entities (NCE) to treat cancer through an agreement with Glenmark Pharmaceuticals, Ltd. for work being conducted at its research facility in the Mumbai, India area.

Ichnos currently has four molecules in clinical development: two in oncology, one in autoimmune disease, and one in pain management. With a patented BEAT® technology platform[1] for development of novel biologic drugs, along with drug pioneering teams, Ichnos Sciences has a mission to provide breakthrough, potentially curative therapies that will hopefully extend and improve lives, writing a new chapter in healthcare.

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 while additional investors are secured during calendar year 2020 and beyond.

HIGHLIGHTS

Ichnos has taken numerous steps toward becoming an independent company over the past few months. Many services that were shared with Glenmark were recently transitioned to new, cloud-based Ichnos systems, including those for email, legal, security and analytics. The network separation from Glenmark will be completed in November 2020 and additional projects are underway to implement new Ichnos systems for finance and human resources operations.

In mid-September, Ichnos began a financing round and worked with an investment bank to schedule and host a series of non-confidential meetings with potential healthcare investors. Many of these investors have now advanced to confidential discussions, and Ichnos is aiming to complete this financing round by end of calendar year 2020. In addition, Ichnos expanded its Board of Directors in September with the appointment of Lawrence Olanoff, M.D., Ph.D. as an Independent Director. The Board is now comprised of nine members, five of whom are non-executive directors.

1 Bispecific Engagement by Antibodies based on the T cell receptor

Both clinical- and preclinical-stage assets have continued to progress, and top-line results from the double-blind portion of Part 2 of the Phase 2b study of the OX40 antagonist antibody ISB 830 in Atopic Dermatitis are now available. Preclinical studies to support further clinical development of oral analgesic ISC 17536 are underway, and partnership discussions for this asset are continuing.

Ichnos filed Intellectual Property (IP) for three new assets this quarter: 1) ISB 1908, a CD38 x CD3 BEAT® bispecific antibody for multiple myeloma; 2) ISB 1442, a CD38 x CD47 BEAT® bispecific antibody for hematologic malignancies; and 3) ISB 880, an IL-1RAP antagonist monoclonal antibody for autoimmune disease. Ichnos is on track to initiate IND-enabling studies for these three assets later this calendar year.

Although Ichnos completed the relocation of its global headquarters to New York at the end of June, the office has not yet opened due to the ongoing COVID-19 pandemic. US-based colleagues continue to work remotely and, depending on the course of the pandemic, the office will open in calendar year 2021. Offices and laboratories in Switzerland are open and continue to operate within the guidelines set forth by the local authorities.

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UPDATE ON ICHNOS PIPELINE OF CLINICAL STAGE DRUGS

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS (DATES ARE IN CALENDAR YEAR)
AUTOIMMUNE DISEASE			
ISB 830 OX40 Antagonist Antibody	Atopic Dermatitis (AD)	Phase 2b	Top-line results for Part 2 of this study showed that the primary efficacy endpoint was met: a statistically significant improvement in percent change from baseline in Eczema Area and Severity Index (EASI) was observed for ISB 830 versus placebo. Improvements in the secondary efficacy endpoints were also observed, but the changes were generally not statistically significant versus placebo. These results are consistent with what was observed for the highest dose of ISB 830 tested in Part 1 of the same study.
	Rheumatoid Arthritis (RA)	Phase 2b	US IND for RA and other indications is active. Timing of study start dependent on pandemic.
PAIN			
ISC 17536 TRPA1[2] Oral Antagonist	Painful Diabetic Peripheral Neuropathy	Phase 2a	Phase 2a study was previously completed. Primary endpoint was not met for the overall study population, but a statistically significant reduction in pain was seen in a pre-specified subgroup of patients with preserved small nerve fiber function. Additional preclinical studies have started this year and a formulation study in healthy volunteers is expected to be completed in early 2021.
ONCOLOGY			
ISB 1302 HER2 x CD3 Bispecific Antibody	Breast Cancer	Phase 1	Enrolling
ISB 1342 CD38 x CD3 Bispecific Antibody	Multiple Myeloma	Phase 1	Enrolling

2 Transient receptor potential ankyrin-1

AUTOIMMUNE DISEASE
ISB 830 (OX40 ANTAGONIST)

- The double-blind portion of the multinational Phase 2b study of ISB 830 (anti-OX40 monoclonal antibody) in adults with Atopic Dermatitis (AD) was recently completed. This was a two-part, randomized, controlled study that assessed four doses and dosing schedules of ISB 830 versus placebo in adult patients with moderate-to-severe AD across study sites in the US, Canada, Germany, Czech Republic, and Poland. Results for the primary efficacy endpoint, percent change from baseline in the Eczema Area and Severity Index (EASI) score compared to placebo at week 16, are shown in the table below.

	PART 1				PART 2	
	ISB 830 300 MG Q2W (N=76*)	ISB 830 300 MG Q4W (N=78*)	ISB 830 75 MG Q4W (N=77*)	PLACEBO (N=80*)	ISB 830 600 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.

- For both Part 1 and Part 2, larger numerical improvements were seen for the higher dose arms of ISB 830 compared to placebo in the secondary endpoints of EASI-75[3] and Investigator Global Assessment[4], but the differences were generally not statistically significantly different from placebo.

- In the blinded period of Part 1, no deaths, malignancies, or thromboembolic events were reported, and the most commonly reported serious adverse event was atopic dermatitis (1.3% vs 1.3% for placebo).

- In the blinded period of Part 2, there were no thromboembolic events, and one death due to pre-existing hypertension was reported in the ISB 830 group. There were no other serious adverse events reported.

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

- In Part 1, the most commonly reported treatment-emergent adverse events for ISB 830 (>5%) were: atopic dermatitis (21.2% vs 22.5% for placebo); nasopharyngitis (8.2% vs 8.8% for placebo); upper respiratory tract infection (7.4% vs 5.0% for placebo); and headache (5.6% vs 10.0% for placebo).

- In Part 2, the most commonly reported treatment-emergent adverse events for ISB 830 (>5%) were similar to those reported in Part 1: atopic dermatitis (17.3% vs 16.2% for placebo); nasopharyngitis (8.0% vs 9.5% for placebo); upper respiratory tract infection (5.3% vs 6.8% for placebo); and headache (6.7% vs 6.8% for placebo).

- Ichnos is considering a range of options for clinical development of ISB 830, including partnering with other companies to further develop the compound. Additionally, a US IND to conduct studies of ISB 830 in additional indications, including Rheumatoid Arthritis (RA), is active.

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 pain was seen for ISC 17536 compared to placebo in the pre-specified subgroup of patients with preserved small nerve fiber function.

- At a Type C meeting with FDA in March 2020, agreement was reached regarding the preclinical plan to enable a randomized, double-blind, placebo-controlled, Phase 2b, dose-range finding study for painful DPN. The preclinical studies are ongoing/ planned, and a formulation study in healthy volunteers is expected to be completed in early 2021.

ONCOLOGY

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 bi-weekly 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.

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.

UPDATE ON ICHNOS PRECLINICAL NBE PIPELINE AND NCE PRECLINICAL CANDIDATES, UNDER AGREEMENT WITH GLENMARK

Ichnos will continue to leverage its capabilities in NBEs, particularly through the BEAT® platform, and will continue to advance NCEs in oncology through an agreement with Glenmark. The Company is planning to advance to IND-enabling studies for a number of candidates in 2020 and beyond.

NEW BIOLOGIC ENTITY (NBE) AND NEW CHEMICAL ENTITY (NCE) ASSETS

CATEGORY/CANDIDATE	PRECLINICAL	IND-ENABLING STUDIES	
ONCOLOGY NBE		**CY 2020**	**CY 2021**
ISB 1908	**CD38 x CD3 BEAT® bispecific antibody**	2H 2020	
ISB 1909	**BEAT® T-cell engager**		1H 2021
ISB 1442	**CD38 x CD47 BEAT® bispecific antibody**	2H 2020	
AUTOIMMUNE DISEASE NBE			
ISB 880	**IL-1RAP antagonist monoclonal antibody**	2H 2020	
ONCOLOGY NCE			
ISC XXXXX	**HPK1 inhibitor**	2H 2020	

Ichnos continues to advance additional biologic and small molecule candidates with its discovery teams in Switzerland and through an agreement with Glenmark, respectively.

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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**
• Optimize molecular attributes of ISB 1342 (CD38 x CD3) T-cell engager • Deliver a competitive MM portfolio by advancing next wave of T-cell engagers and innate immune engagers (e.g., NK, macrophages)	• Accelerate delivery of innovative concepts by leveraging trispecific T-cell and innate immune engagers (e.g., NK, macrophages)	• Optimize molecular attributes of ISB 1302 (HER2 x CD3) T-cell engager