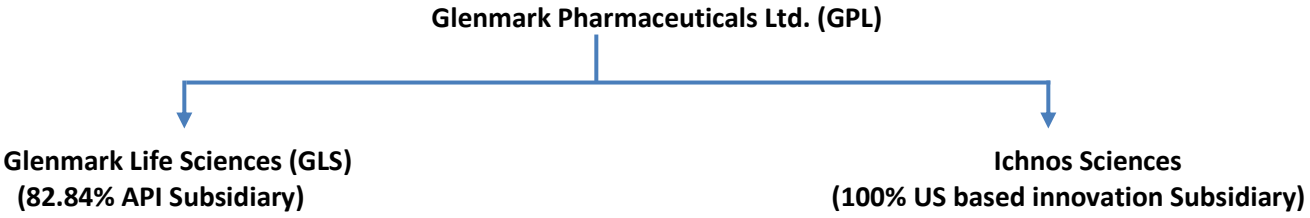
Management Discussion & Analysis for the Fourth Quarter of FY 2021-22

Glenmark operates its businesses through three separate entities



Each of these three entities operate independently with separate Management Teams and Board of Directors.

Revenue Figures for Glenmark Pharmaceuticals Ltd. (Consolidated)

(Rs. In Millions)

	Fourth Quarter ended March 31			For the Year ended March 31		
	FY 2021-22	**FY 2020-21**	**Growth (%)**	**FY 2021-22**	**FY 2020-21**	**Growth (%)**
India	8,847	8,238	7.4%	40,855	35,365	15.5%
North America	7,378	8,012	-7.9%	30,366	30,764	-1.3%
Europe	4,968	4,223	17.6%	15,218	13,276	14.6%
Rest of the World[1]	5,479	4,641	18.1%	21,672	16,855	28.6%
API	3,283	3,311	-0.9%	12,709	12,074	5.3%
Total	**29,955**	**28,425**	**5.4%**	**1,20,820**	**1,08,334**	**11.5%**
Other Revenue	237	174	36.5%	2,229	1,106	101.6%
Consolidated Revenue	**30,191**	**28,599**	5.6%	**1,23,049**	**1,09,439**	12.4%

1. Asia, Middle East and Africa, RCIS and LATAM

Average conversion rate in 12M FY 2021-22 considered as INR 74.38/USD 1.00

Average conversion rate in 12M FY 2020-21 considered as INR 74.02/USD 1.00

USD figures are only indicative

Review of Operations for the quarter ended March 31, 2022

For the Fourth Quarter of FY 2021-22, Glenmark's consolidated revenue was at Rs. 30,191 Mn (USD 402 Mn) as against Rs. 28,599 Mn (USD 392 Mn) recording an increase of 5.6% YoY.

For the year ended Mar 31, 2022, Glenmark's consolidated revenue was at Rs. 123,049 Mn (USD 1,654 Mn) as against Rs. 109,439 Mn (USD 1,479 Mn) recording an increase of 12.4% YoY.

Key Highlights during the year

1. Glenmark listed its wholly owned API subsidiary, Glenmark Lifesciences Ltd on the Indian exchanges. The IPO which consisted of a fresh issue of Rs 10.6 bn and offer for sale of up to 6.3 mn shares by the company was subscribed over 44 times.

2. Glenmark was listed in the prestigious Dow Jones Sustainability Index (DJSI) for the fourth consecutive year. The company is among only 15 companies from India to be listed on the DJSI Emerging Markets Index this year**.** Company's inclusion in the list is a validation of its commitment to sustainability and ESG principles and reiterates its consistent performance across all sustainability indicators.
   Also, Glenmark was the first domestic pharma company to raise sustainability linked loans (SLL), by raising USD 228 Mn in SLLs during the year

   A detailed ESG profile of the company is available under the investor section on our website.

3. In 3QFY22, Ichnos entered into an exclusive licensing agreement with Almirall SA for the IL-1RAP antagonist ISB 880. Under the agreement, Almirall is granted global rights to develop and commercialize this monoclonal antibody for autoimmune diseases. Ichnos retains the rights for antibodies acting on the IL-1RAP for oncology indications. Ichnos received an upfront payment of Eur 20.8 Mn and will receive additional development and commercial milestone payments and tiered royalties based upon future global sales.

4. As per IQVIA, In April '21, Fabiflu became the highest selling drug in the Indian Pharma market amongst all therapies. The success of Fabiflu is a testament to the end-to-end capabilities of Glenmark to offer patients quality medicines with affordable access.

5. Glenmark was selected for the Production Linked Incentive (PLI) scheme aimed at improving India's manufacturing capabilities and enhancing exports. Glenmark is one of the 11 companies under group A and is well placed to meet the objectives and guidelines of the scheme thereby helping in the "Aatmanirbhar Bharat" strategy of the government.

6. Europe business achieved significant milestone of USD 200 mn annual revenues for the first time

7. Glenmark had several successes in its core respiratory franchise during the year. The company received USFDA approval for its NDA product Ryaltris in the US and marketing approval in all 17 markets across EU and UK during the year.

GLENMARK PHARMACEUTICALS LTD. (GPL)

GPL is primarily focused on building a global Generics, Specialty, and OTC business in the therapy areas of Dermatology, Respiratory and Oncology. It also has strong regional/country-specific presence in other therapeutic areas like diabetes, cardiovascular and oral contraceptives.

India

Sales from the formulation business in India for the Fourth Quarter of FY 2021-22 was at Rs. 8,847 Mn (USD 118 Mn) as against Rs. 8,238 Mn (USD 113 Mn) in the previous corresponding quarter, recording growth of 7.4% YoY. The India business contribution was at 29% of the total revenues in Q4FY22 similar to Q4FY21.

As per Jan-Mar '22 IQVIA data, the non-COVID base portfolio grew 15.5% as compared to the non-COVID IPM growth of 10.6% during the quarter.

The India business continues to significantly outperform industry growth rates, continuing the trend of the past several years. As per IQVIA data, Glenmark was the one of the fastest growing companies in the industry among the Top 20 players on a MAT March 2022 basis with growth of 23.8% as compared to IPM (Indian Pharma market) growth of 17.4%. For the year, Glenmark's India Formulation business is ranked 13th, up 1 rank from last year and its market share has increased to 2.47% as compared to 2.34% last year.

In terms of market share, Glenmark's India business further strengthened its position in its core therapy areas such as Cardiac and Respiratory. As per IQVIA MAT March 2022, the Cardiac segment market share increased to 4.96% as compared to 4.76% last year; the respiratory segment market share increased to 5.43% as compared to 4.96% last year while the derma segment changed from 8.54% to 8.10%. The company was ranked 2nd in Derma segment, 4th in respiratory segment and 6th in cardiac segment during the year.

The India formulation business has achieved several important milestones during the current financial year. As per IQVIA MAT Dec '22, Fabiflu® was the sixth largest brand across all brands in India during the period. Ascoril D Plus became the 10th brand of Glenmark to enter the IPM 300 brand league. The company now has 10 brands in the top IPM 300 brands in the country up from 6 brands last year.

The company launched seven new products during the quarter and 31 products during the year. Amongst key launches during the quarter, the company launched the novel Zita Plus Pio which contains Teneligliptin (20 mg) + Pioglitazone (15 mg), to be taken once a day, and is the first of its kind in India; offering a world-class and affordable treatment option to adult diabetic patients.

India – Glenmark Consumer Care Business

GCC business recorded revenue of Rs. 619 Mn in the fourth quarter and Rs 1,790 Mn in FY22 with secondary sales growth of 23.4% in Q4 and 12.6% YoY in FY22 respectively. This growth was led by new product launches, especially Candid Cream where secondary sales grew 30% YoY annually while La Shield recorded secondary sales growth of 95% YoY. Candid Powder faced headwinds during the year due to COVID impact in the beginning of the year. The brand continued to maintain its dominant market leadership status with a market share of 63% in the current financial year. The company also

launched Candid Prickly Heat Powder during the quarter where the response has been encouraging.

North America

North America registered revenue from the sale of finished dosage formulations of Rs. 7,378 Mn (USD 98.2 Mn) for the quarter ended March 31, '22 as against revenue of Rs. 8,012 Mn (USD 109.8 Mn) for the previous corresponding quarter, recording de-growth of (7.9)% YoY and (2.5)% QoQ. North America business contributed 24% of the total revenues in Q4FY22 as compared to 28% in Q4FY21.

In the fiscal year 2021-22, Glenmark was granted approval of 9 Abbreviated New Drug Applications (ANDA), comprised of 7 final approvals and 2 tentative approvals. Additionally, Glenmark was granted a 2nd tentative approval on a Prior Approval Supplement (PAS) for the 0.25 mg strength for Fingolimod Capsules. Notable approvals include: Lacosamide Tablets USP, Clindamycin Phosphate Foam, 1% and, Theophylline Extended-Release Tablets USP, 300 mg and 450 mg. The Company filed a total of 19 ANDA applications with the U.S. FDA throughout the fiscal year including 4 filings from Monroe in FY22 and plans to file 14-15 ANDAs in FY23.

Glenmark completed the successful launches of 10 new products during fiscal year 2021-22, consisting of a mix of semi-solid preparations, delayed- and immediate-release oral solids. Notable launches include Lacosamide Tablets USP (Generic Vimpat® tablets) and Rufinamide Tablets USP (Generic Banzel® tablets), where Glenmark was one of the first generics available for launch.

In the fourth quarter of fiscal year 2021-22, Glenmark was granted final approval and launched Bisoprolol Fumarate and Hydrochlorothiazide Tablets USP, Metronidazole Vaginal Gel, 0.75% and Lacosamide Tablets USP. In addition, Glenmark introduced a previously approved product, Esomeprazole Magnesium Delayed-Release Capsules USP, which was approved in 2019.

Glenmark Canada filed two ANDS applications with the Canadian Health Authorities this quarter.

Glenmark's marketing portfolio through March 31, '22 consists of 174 generic products authorized for distribution in the U.S. market. The Company currently has 46 applications pending in various stages of the approval process with the US FDA, of which 20 are Paragraph IV applications.

Europe

Glenmark Europe's operations revenue for the fourth quarter of FY 2021-22 was at Rs. 4,968 Mn (USD 66 Mn) as against Rs. 4,223 Mn (USD 58 Mn.) recording growth of 17.6 % YoY and 30.5% QoQ. Europe business contributed 16% of the total revenues in Q4FY22 as compared to 15% in Q4FY21.

The company witnessed healthy growth in both its key markets of Western Europe and Central Eastern Europe during the quarter. With the continued easing of Covid restrictions, growth in Western Europe was strong, led by double digit growth in key markets like Netherlands, Spain and the Nordic countries. The Central Eastern European region maintained its strong growth trajectory especially in markets like Poland. Amongst the key launches, the company launched four products in Germany, three in UK and two products in Czech Republic respectively. Slovakia and Germany launched one product each during the quarter respectively.

Glenmark has a comprehensive plan to grow its European business going ahead, including geographical expansion in new markets and expand its product portfolio to leverage launches in key therapeutic segments like respiratory and dermatology.

Asia, MEA, LATAM and RCIS Region (RoW)

For the fourth quarter of FY 2021-22, revenue from RoW was Rs. 5,479 Mn (USD 73 Mn) as against Rs. 4,641 Mn. (USD 64 Mn) for the previous corresponding quarter, recording growth of 18.1% YoY. ROW business contributed 18% of the total revenues in Q4FY22 as compared to 16% in Q4FY21.

The company witnessed healthy growth in base business in the region across all its key geographical segments.

As per IQVIA Jan-Mar'22 secondary sales grew 31% YoY in value terms in Russia. As per IQVIA MAT '22, Russia segment grew 27.6% in value terms as compared to retail market growth of 21.6%. The company recently received approval for Ambroxol Solution and the overall response to Ryaltris and Ryaltris Mono has been very encouraging in the market. The company has various strategic initiatives to strengthen the respiratory franchise in the region going ahead.

Secondary sales in Asia grew 53% YoY led by positive momentum in key markets like Vietnam, Malaysia, and Philippines. After the successful launch of Ryaltris in Phillippines last quarter, the company expects to launch Ryaltris in Myanmar and Cambodia in FY23. The company successfully launched FabiSpray® in Singapore and Hong Kong this quarter under the brand name VirX® and the company has plans to launch in multiple markets in the region in the coming financial year.

The Middle East and Africa region recorded primary sales growth of 13% YoY during the quarter, with positive growth across major MEA markets like Kenya, South Africa and Saudi Arabia. The company expects the momentum to continue in FY23 as markets are witnessing signs of recovery due to the easing of lockdown measures.

In LATAM, while the company recorded positive growth momentum in some markets including Peru, Ecuador and Columbia during the quarter, overall the business has been impacted by Brazil where the market remained challenging for the company due to the pandemic. The company is witnessing signs of recovery and expects positive momentum in the market going ahead.

Respiratory – Creating global scale

Ryaltris – Innovative branded specialty nasal spray with focus to create global brand

a) North America - NDA approval received from USFDA – to be launched in FY23. Awaiting regulatory approval in Canada
b) Europe – Marketing approval received in all EU markets and UK; launched in UK, the Czech Republic, Poland, Italy; plan to launch in several markets in FY23 including Belgium, Ireland and Nordic countries
c) ROW – Launched in Australia, Russia, South Africa, Ukraine, Uzbekistan, Philippines, Peru, Ecuador, Namibia, Botswana. Awaiting regulatory approval in several markets including Brazil, Malayisa, South Korea, Cambodia etc in FY23
d) Grand Pharmaceutical (China) Co. Ltd., initiated the Phase 3 study in China in Q4 2022

Europe

a) Leverage existing branded portfolio of Soprobec® (Beclamethasone MDI), Salmex (Salmeterol/Fluticasone DPI), Tiogiva®/Tavulus® (Tiotropium DPI) and Ryaltris™ (olopatadine/mometasone nasal spray)
b) Plan to file at least 1-2 filings in FY23

US

a) Completed pivotal biostudy on Flovent pMDI & initiated clinical trial with 2,634 patients; Expect to file in CY23
b) Plan to file at least one more respiratory pMDI in CY23
c) Plan to continue the momentum and file more respiratory products beyond FY24

RoW

a) Top 5 player in respiratory segment in India as per IQVIA MAT '22
b) Leverage Ryaltris launch in multiple markets in Asia, MEA and LATAM
c) Ranked #3 in the expectorant market in Russia (IQVIA MAT '22)
d) Currently marketing 4 respiratory products in Brazil (Levolukast tablets, Salbutamol pMDI, Beclomethasone pMDI, Mometasone Nasal spray) on our own or through our partners. Additionally, we have filed 3 more products that are awaiting approval
e) Inked agreement with AstraZeneca to commercialize its product Pulmicort Respules® in Colombia

Innovative R&D Pipeline

GBR 310

Glenmark had announced successful Phase 1 results for GBR 310 that suggest similarity in pharmacokinetic, pharmacodynamic, safety and immunogenicity profiles between GBR 310, and the reference product, Omalizumab, marketed in the U.S. under the brand name Xolair®. Glenmark is in discussion with potential partners to out-license the product.

GRC 39815 (RORγt inhibitor)

GRC 39815 (RORγt antagonist) is the company's respiratory pipeline asset being developed as an inhaled therapy for treatment of mild to moderate COPD. It is currently under Phase 1 clinical development in the US with Phase 1 multiple ascending dose study planned in H1FY23.

GRC 17536

GRC 17536 (TRPA1 antagonist) is the company's pain pipeline asset being developed as an orally administered treatment for pain in patients with painful diabetic peripheral neuropathy. The Phase 2b study was initiated in Q2 FY22 and is currently ongoing in India with 238 patients randomized out of total 472 patients till date with Interim data for futility analyses is expected by Q2 FY23. GLP toxicology studies for metabolite qualification were completed in Q3 FY22. The company plans to hold discussions with the FDA to get feedback on the non-clinical package to support the clinical development up to NDA filing this year.

GRC 54276

GRC 54276 (HPK1 Inhibitor) is the company's oncology pipeline asset being developed as an orally administered IO-adjuvant treatment for patients with solid tumors in oncology. IND enabling studies

were completed with a Phase I submission to the DCGI in Q4 FY22. The company has recently received approval for initiation of Phase 1 study and the first patient visits are planned from Q1FY23.

GLENMARK LIFE SCIENCES LTD. (GLS)

Glenmark Life Sciences primarily includes manufacturing and marketing of Active Pharmaceutical Ingredient (API) products across all major markets globally. It also includes captive sales (i.e. use of API by GPL for its own formulations).

Revenues from operations including captive sales were Rs. 5,140.6 Mn as against Rs. 4,671.6 Mn, growing at 10% YoY for Q4 FY22 and Rs. 21,232.1 Mn for FY 22, a growth of 12.6%. During FY22, revenues from the regulated markets witnessed a healthy growth of 21.4% YoY, whereas revenues from the emerging markets declined by 6.3% YoY due to high base of COVID products sales last year. EBITDA was at Rs. 1,473.1 Mn for Q4FY22 with margin at 28.7% and ₹ 6,307.6 Mn for FY22 with margin at 29.7%.

External sales for Glenmark Life Sciences were at Rs. 3,283 Mn as against Rs. 3,311 Mn in Q4 FY21, recording decline of (0.9) % YoY and 8.3% growth QoQ.

The company is in the process of executing brownfield and greenfield capacity expansion projects to support strategic growth levers.

For further updates on the organization, please log on to www.glenmarklifesciences.com.

ICHNOS Sciences Inc.

Glenmark has invested Rs 1,640Mn (USD 21.9 Mn) in the fourth quarter of the financial year as compared to Rs1,880 mn (USD 26 mn) in 4QFY21. Thus, for the entire financial year, Glenmark invested Rs. 6,627 mn (USD 89.4 mn) as compared to Rs. 7,570 Mn (USD 102.3 Mn).

For further updates on the pipeline and the organization, please log on to www.ichnossciences.com. The pipeline update for the fourth quarter is published on this site.

Key objectives for FY23

- Revenue growth of 6-8%% during the year
- Sustain EBITDA margin performance at similar levels of FY22
- Capex of Rs. 7-8 Bn
- Strategic priority to enhance free cash generation for further debt reduction
- Close 1-2 out-licensing agreements in innovation pipeline

Leadership Changes

Brendan O'Grady will be joining the company as the **Chief Executive Officer – Global Formulations Business** with effect from **10th** June 2022. Brendan will lead the Commercial Business Units for GPL and provide strategic leadership for bringing greater focus and alignment across all regions and therapeutic areas. Brendan comes with over three decades of rich experience in the pharmaceutical industry, spread across both Generics and Specialty segments wherein he has successfully led and transformed businesses for growth across multiple

geographies globally. In his last engagement prior to Glenmark, Brendan was the Chief Growth & Commercial Officer for Amwell, Inc. wherein he provided strategic leadership to Amwell's global business operations. Prior to that, he was associated with Teva Pharmaceuticals, Inc. as the President & CEO, Teva USA and EVP, North America Commercial.
Brendan spent over two decades at Teva during which he was instrumental in stabilizing and growing the North American business, revitalizing the Global Specialty strategy, and making significant contributions to market access strategies, brand acquisitions, and integrations. He also had significant and successful stints with Sanofi Pharmaceuticals and SC Johnson (Wax) & Son at the beginning of his career.

Mr. Robert Crockart, Chief Commercial Officer, has decided to pursue opportunities outside Glenmark. We wish to thank him for his valuable contributions to the organization during his tenure and wish him the best for his future endeavours.

Disclaimer

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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 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** 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.