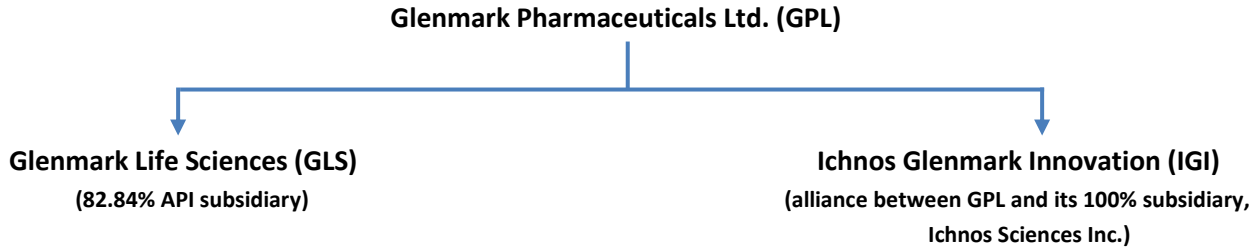
Management Discussion & Analysis
for the Third Quarter of FY 2023-24

Glenmark group operates its key businesses through the following structure



Each of these three businesses operate independently with separate management teams

Revenue Figures for Glenmark Pharmaceuticals Ltd. (Consolidated)

(In Rs. Million)

	For the third quarter ended December 31			For the nine months ended December 31		
	FY 2023-24	FY 2022-23	Growth (%)	FY 2023-24	FY 2022-23	Growth (%)
India	2,622	10,745	-75.6%	24,482	32,014	-23.5%
North America	7,629	8,373	-8.9%	23,105	22,534	2.5%
Europe	6,357	4,932	28.9%	18,086	12,016	50.5%
Rest of the World[1]	7,250	6,541	10.8%	20,086	16,921	18.7%
API	4,129	3,756	9.9%	11,828	10,751	10.0%
Total	**27,987**	**34,347**	**-18.5%**	**97,587**	**94,236**	**3.6%**
Other Revenue	1,109	291	280.6%	1,404	1,928	-27.2%
Consolidated Revenue	**29,096**	**34,639**	**-16.0%**	**98,991**	**96,164**	**2.9%**

1. Asia, Middle East and Africa (MEA), Russia + CIS (RCIS), and Latin America (LATAM)

Average conversion rate in 9M FY 2023-24 considered as INR 82.69 / USD 1.00

Average conversion rate in 9M FY 2022-23 considered as INR 79.58 / USD 1.00

USD figures are only indicative

Review of Operations for the Quarter ended December 31, 2023

For the third quarter of FY24, Glenmark's consolidated revenue from operations was at Rs. 29,096 Mn (USD 349.1 Mn) as against Rs. 34,639 Mn (USD 422.6 Mn) in the corresponding quarter last year, recording overall year-on-year (YoY) decline of 16%. The lower sales in the current quarter was mainly on account of a one-time impact on the Company's India business. Excluding this impact, Glenmark's consolidated revenue in Q3 FY24 would have been approximately Rs. 37,796 Mn, with an approximate growth of 9% over previous year. For the nine months of FY24, Glenmark's consolidated revenue was at Rs. 98,991 Mn (USD 1,197 Mn) as against Rs. 96,164 Mn (USD 1,208 Mn), recording a year-on-year growth of 2.9%

GLENMARK PHARMACEUTICALS LTD. (GPL)

GPL is primarily focused on building a global formulation business with Branded, Generics, and OTC segments 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 third quarter of FY24 was at Rs. 2,622 Mn (USD 30.8 Mn) as against Rs. 10,745 Mn (USD 130.7 Mn) in the corresponding quarter last year, recording a decline of 75.6%. During the third quarter, the Company implemented changes in its overall distribution model, through consolidation of stock points and rationalization of channel inventories. This has led to a one-time impact in sales for the India business in this quarter. However, this will help the Company in improving operating margins and overall working capital in the future. The changes in the India distribution system will also help accelerate the Company's Anti-Counterfeit packaging roll-out and ensure that it reaches faster to the patients.

In terms of secondary sales, Glenmark's India business continued to outperform the overall industry in terms of growth. As per IQVIA December 2023 data, Glenmark's India formulation business recorded growth of 11.9% in the third quarter, and 11.4% growth as of MAT December 2023. In comparison, the Indian Pharmaceutical Market (IPM) grew at 8.2% in the third quarter and 9.5% as of MAT December 2023. Glenmark continues to outperform the market in the key therapy areas of Cardiac, Dermatology and Respiratory as shown in the table below:

	IPM		GLENMARK	
SUPERGROUP	VALUE GROWTH % (MAT DEC'23)	VALUE GROWTH % (OCT'23-DEC'23)	VALUE GROWTH % (MAT DEC'23)	VALUE GROWTH % (OCT'23-DEC'23)
CARDIAC	10.7	9.8	19.5	21.8
DERMA	6.2	3.5	9.9	4.9
RESPIRATORY	9.9	5.5	18.7	14.8
DIABETES	7.0	7.8	-14.5	-18.9

Glenmark's India business continues to be ranked 14th with a market share of 2.13% (IQVIA MAT December 2023). The Company continues to have 9 brands in the IPM Top 300 Brands in the country on the basis of IQVIA MAT December 2023. In terms of key therapeutic areas, Glenmark is ranked 2nd in both the Respiratory and Dermatology segments. In addition, Glenmark is ranked 5th in the Cardiac segment and 17th in the Diabetes segment. Glenmark also has improved its market share in the key therapy areas on the back of higher growth compared to the overall industry:

	GLENMARK	
SUPERGROUP	MARKET SHARE % MAT DEC'22	MARKET SHARE % MAT DEC'23
CARDIAC	5.06	5.45
DERMA	7.24	7.49
RESPIRATORY	5.35	5.78
DIABETES	2.39	1.91

In October 2023, Glenmark launched, in India, the first triple-drug, once-daily, fixed-dose combination (FDC) of the widely used DPP4 inhibitor Teneligliptin (20mg), the SGLT2 inhibitor Dapagliflozin (10mg), and Metformin SR (500mg/1000mg) under the brand name Zita® DM. In January 2024, Glenmark also became the first company to launch a biosimilar of the popular anti-diabetic drug Liraglutide, in India, under the brand name Lirafit™. This launch will sharply lower the daily cost of therapy by around 70%, making the drug more accessible to a larger number of patients in the country. The Company continues to have a healthy pipeline of differentiated products across the key therapy areas which it plans to launch in the market going forward.

INDIA – GLENMARK CONSUMER CARE (GCC)

Primary sales for GCC in Q3 FY24 was Rs. 482.4 Mn with a YoY growth of ~18%. The Company's flagship brand Candid Powder™ delivered revenue growth of 20% for Q3 FY24. La Shield™ portfolio delivered YoY revenue growth of 20%, while Scalpe+™ portfolio witnessed YoY revenue growth of 12.2% in Q3 FY24. For nine months of FY24, the GCC business recorded sales of Rs. 1,898 Mn with a YoY growth of 16%.

NORTH AMERICA

The North America business registered revenues from the sale of finished dosage formulations of Rs. 7,629 Mn (USD 91.6 Mn) for the third quarter of FY24 as against revenue of Rs. 8,373 Mn (USD 102.3 Mn) for the third quarter of FY23, and Rs. 7,392 Mn (USD 89.4 Mn) for the second quarter of FY24. This translates in to a YoY decline of 8.9% and a quarter-on-quarter (QoQ) growth of 3.2%. Q3 sales were impacted due to continued price erosion in the base business and lack of significant new product launches in the preceding quarters.

In the third quarter of FY24, Glenmark launched Prochlorperazine Maleate Tablets USP, Fluphenazine Hydrochloride Tablets USP and Benazepril HCl and Hydrochlorothiazide Tablets USP. In the upcoming quarter, Glenmark plans to file up to five new ANDAs.

During the quarter, Glenmark has significantly expanded its injectable portfolio through exclusive product partnerships. Some of the notable launches in the injectable segment include Fosphenytoin Sodium Injection USP, Octreotide Acetate Injection, Posaconazole Injection, 300 mg/16.7 mL (18 mg/mL), and Ketorolac Tromethamine Injection USP, 15 mg/mL and 30 mg/mL. The Company now has 5 injectable products commercialized in the market and these launches are likely to positively impact the US business from Q4 FY24 onwards. The Company is hoping to re-start commercialization of further injectable products from the Monroe manufacturing site, from FY25 onwards.

Glenmark has also leveraged its strong development capabilities in the Respiratory therapeutic area to build a portfolio for the USA market. The Company has filed two ANDAs for generic nasal sprays and is awaiting approval for the same. In addition, the ongoing clinical trial for generic Flovent® pMDI has been completed, and the Company expects to file the ANDA for the same in Q1 FY25. Glenmark also plans to file at least one more generic respiratory pMDI in the U.S. in FY25 and continue filing momentum beyond FY25.

Glenmark's marketing portfolio through December 31, 2023 consists of 194 generic products authorized for distribution in the U.S. market. The Company currently has 51 applications pending in various stages of the approval process with the US FDA, of which 21 are Paragraph IV applications.

EUROPE

Glenmark Europe operations' revenue for the third quarter of FY24 was at Rs. 6,357 Mn (USD 76.4 Mn) as against Rs. 4,932 Mn (USD 60.5 Mn) recording a growth of 28.9%.

Glenmark's European operations continued their strong trajectory, driven by a robust uptick of the branded business and sustained growth in the generics business. The Western European business clocked ~20% growth for Q3 mainly led by the United Kingdom (UK), Spain and Germany. Glenmark continues to be ranked 16th in the generic market of Germany as per IQVIA MAT November 2023 data. Multiple product launches

across the Western European region aided the growth in Q3. Key markets across the CEE region recorded strong double-digit growth in the quarter. The Czech recorded 40%+ growth compared to previous year, Poland recorded 20%+ secondary sales growth, and Slovakia also recorded 15%+ growth in Q3. The Respiratory portfolio launched by Glenmark in Europe continues to do well. Key brands such as RYALTRIS® and Salmex® / Asthmex® continue to sustain their market share, both, in terms of volume as well as value, across the CEE markets.

ROW REGION (ASIA, MEA, LATAM & RCIS)

For the third quarter of FY24, revenue from the ROW region was Rs. 7,250 Mn (USD 87.2 Mn) as against Rs. 6,541 Mn (USD 80.1 Mn) for the corresponding quarter last year, recording a growth of 10.8%. The Company continues to witness growth in the base business across all sub-regions of the ROW market.

As per IQVIA Q3 FY24 and MAT December 2023 data, Glenmark's Russia business recorded 7% and 18% growth in value, respectively. In terms of key therapeutic areas, Glenmark recorded growth of 20% in value in the Dermatology segment versus the overall Dermatology market growth of 8% as per MAT December 2023. Amongst the Dermatology companies in Russia, Glenmark ranks 9th as per MAT December 2023. Amongst the companies present in the Expectorants market in Russia, Glenmark continues to maintain a strong position, ranking 2nd as per MAT December 2023. Key recent launches in Russia in the nine months of FY24 include Ascoril LS™ (ambroxol + guaifenesin + levosalbutamol) solution, Fenismart™ (Dimetindene gel) and Phelisans™ (phenasone + lidocaine) ear drops. RYALTRIS® also continues to gain market share in 9M FY24.

The Asia region recorded 20% growth in secondary sales which was driven by markets like the Philippines, Malaysia, Sri Lanka and Vietnam. As per IQVIA, Glenmark is growing faster (17%) than the covered market (7%) in Q3 FY24. Top contributing brands in the Dermatology and the Respiratory segments have registered strong growth in the third quarter. Glenmark received approvals for 10 new products in the region, mainly in the Dermatology, Respiratory and Oncology therapeutic areas. RYALTRIS® continues to do well in Australia, South Korea and Malaysia.

The Middle East and Africa region recorded 15% growth in sales during the third quarter of FY24. The Company continued to achieve strong secondary sales growth in Kenya, South Africa, Saudi Arabia and other African markets. Respiratory and Dermatology together contributed ~70% to the overall sales of the MEA region. RYALTRIS® was launched in Saudi Arabia in Q1 FY24 and the product has received good response in the market. RYALTRIS® continues to be the leading nasal spray for Allergic Rhinitis in South Africa, and the product was launched in four additional middle eastern markets in the third quarter.

LATAM witnessed strong growth of 30% in Q3 FY24. The Respiratory portfolio remains the key contributor

for Glenmark in this region. Glenmark Brazil achieved strong double-digit growth in the covered market as per IQVIA YTD December 2023. The Company maintained its rank in the top-10 amongst the top companies in the covered market of the chronic respiratory segment in Brazil as per IQVIA MAT December 2023. Secondary sales growth remained strong in Mexico, and the Company achieved its highest market share in the respiratory market during the quarter. Within the covered market, Glenmark continues to rank in the top-10 as per IQVIA MAT December 2023 data.

CREATING GLOBAL BRANDS

RYALTRIS®

- As of the end of the third quarter of FY24, marketing applications for RYALTRIS® have been submitted in more than 70 countries across the world. The product has been commercialized in 31 markets, including major markets like the USA, Canada, Europe (the UK and multiple markets across the EU), Australia, Russia, South Africa, South Korea and Saudi Arabia.
- Further, the product has been approved in 18 other markets where it will be launched over the course of the next 3-6 months.
- Glenmark's commercial partner in the USA, Hikma, continued to see strong new prescriptions with a full strength field force focusing on high prescribing physicians
- Glenmark's partner in Mainland China, Grand Pharmaceutical (China) Co. Ltd., is progressing with the application and registration process and expects to launch the product in mid-2025.
- Below are the value market shares of RYALTRIS® across key geographies (Top 10 products within "R1A1 – Nasal Corticosteroids without Anti Infectives" category as per IQVIA + RYALTRIS®):

MARKET	MARKET SHARE
Australia	18.1%
Czech	19.1%
South Africa	19.7%
Poland	12.0%
Italy	13.1%
Austria	7.7%
France	5.8%
Spain	6.0%
Ireland	4.8%
Peru	5.9%
Ecuador	4.8%
Russia	2.3%

**Data as of, for each respective market: Australia – May 2023; South Africa, Peru, France – September 2023; Poland, Czech – November 2023; Italy, Austria, Spain, Ireland – August 2023; Russia – December 2023

RESPIRATORY INNOVATIVE ASSET

GRC 39815

GRC 39815 (RORγt inhibitor) is the Company's respiratory pipeline asset for treatment of mild-to-moderate Chronic Obstructive Pulmonary Disorder (COPD). It is currently under Phase 1 clinical development in the U.S., and the Company is evaluating deprioritizing further development of this asset.

GLENMARK LIFE SCIENCES LTD. (GLS)

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

External sales for GLS in Q3 FY24 were at Rs. 4,129 Mn (USD 49.6 Mn) as against Rs. 3,756 Mn (USD 45.8 Mn) in Q3 FY23, recording a growth of 9.9% YoY.

In September 2023, Glenmark announced that it has entered into a definitive agreement with Nirma Limited to divest 75% stake in its subsidiary, Glenmark Life Sciences Limited (GLS) at a price of Rs. 615/- per share for an aggregate consideration of Rs. 56,515 Mn, subject to closing adjustments. Glenmark would own 7.84% in GLS after the divestment. The transaction is subject to customary closing conditions precedent, including receipt of regulatory and shareholder approvals.

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

ICHNOS GLENMARK INNOVATION (IGI)

The Company and its global fully integrated, clinical-stage biotech subsidiary, Ichnos Sciences Inc. (Ichnos), recently announced the launch of their alliance – Ichnos Glenmark Innovation – to accelerate new drug discovery in cancer treatment. This alliance combines Glenmark's research and development proficiencies in small molecules with those of Ichnos in novel biologics to continue developing cutting edge therapy solutions that treat hematological malignancies and solid tumors. The newly formed IGI features a robust pipeline of three innovative oncology molecules targeting multiple myeloma, acute myeloid leukemia and solid tumors currently undergoing clinical trials. Two of these molecules have received orphan drug designation from the U.S. FDA. Additionally, IGI has two autoimmune disease assets that have been out licensed to leading companies. Going forward, all of Glenmark group's investments on innovative assets will be channelized through the IGI alliance.

GRC 54276

GRC 54276 (HPK1 Inhibitor) is being developed as an orally administered IO-adjuvant treatment for patients with solid tumors. Hematopoietic progenitor kinase 1 (HPK1), is a negative regulator of T and B cell receptor signaling and an attractive therapeutic strategy for immuno-oncology based treatment in cancers. GRC 54276 is a novel, orally active HPK1 inhibitor that demonstrates stand-alone efficacy and enhances current immunotherapy efficacy. It is currently being evaluated in the First in Human (FIH) Phase 1 clinical study. This asset will now be a part of the IGI alliance.

Part 1a monotherapy phase of the study is ongoing in India since July 2022. Additional subjects are being recruited in the 50 mg monotherapy backfill cohort of the study to further assess safety, and tolerability for GRC 54276 monotherapy. The Phase 1, Part 1b combination study of GRC 54276 with pembrolizumab and atezolizumab was initiated in India and the U.S. in Q1 FY24 and Q2 FY24 respectively. As of Q3 FY24, two dose cohorts of GRC 54276 with pembrolizumab and atezolizumab have been completed, and patient recruitment and dosing is ongoing for the third cohort.

For further updates on IGI, including the biologic pipeline assets, please log on to https://www.iginnovate.com/

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ICHNOS SCIENCES INC.

FEBRUARY 2024 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 research and manufacturing operations at two sites in Switzerland. As a fully integrated biotechnology company with approximately 151 employees following the recent restructuring of the Research group, 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.

CYRIL KONTO, M.D. President and Chief Executive Officer	**LIDA PACAUD, M.D.** Chief Medical Officer	**EUGENE ZHUKOVSKY, Ph.D.** Chief Scientific Officer
PATRICIA JAQUET Head of Human Resources	**ROBERTO GIOVANNINI, Ph.D.** Chief Process and Manufacturing Officer	**DEAN THOMAS, DPhil, LLM** General Counsel

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

Ichnos' multispecific antibody pipeline consists of four assets. This includes ISB 2301, which is in the discovery stages for application in solid tumors, and ISB 2001, ISB 1342 and ISB 1442, each of which are orphan drug designated by the U.S. Food and Drug Administration (FDA) and currently in Phase 1 clinical studies for relapsed/refractory multiple myeloma. Updates of note in the last quarter are outlined below:

- Each clinical-stage asset was the subject of a poster presentation at the 65th ASH Annual Meeting on December 9-12, 2023, in San Diego, California, and available online here.
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MOLECULE MECHANISM/CLASS	PHASE/STATUS	LEAD INDICATION
ISB 1342 CD38 x CD3 BEAT® bispecific antibody[2]	Phase 1	Relapsed/Refractory Multiple Myeloma; T-Cell Acute Lymphoblastic Leukemia(T-ALL) is also under consideration
ISB 1442 CD38 x CD47 BEAT® bispecific antibody	Phase 1	Relapsed/Refractory Multiple Myeloma; Phase 1 study in Acute Myeloid Leukemia (AML) is planned by early 2024
ISB 2001 BCMA x CD38 x CD3 TREAT™ trispecific antibody[3]	Phase 1	Relapsed/Refractory Multiple Myeloma
ISB 2301 NK-cell engaging multispecific platform	Discovery[1]	Solid Tumors

1. Lead optimization initiated in December.

Ichnos is looking for asset-level and platform-level collaboration partners in development and research. For more information, visit the partnership webpage.

[1] Bispecific Engagement by Antibodies based on the TCR
[2] Future clinical development will be advanced by a partner
[3] Trispecific Engagement by Antibodies based on the TCR

OVERVIEW OF SELECT ONCOLOGY DRUG PRODUCT CANDIDATES

ISB 1342 (CD38 X CD3 BEAT® BISPECIFIC ANTIBODY)

- A Phase 1, open-label, dose-escalation, first-in-human study of ISB 1342 in patients with relapsed/refractory multiple myeloma.
  - The study has been suspended and the strategy is to out-license the asset and allow a potential partner to continue the escalation/expansion now that clinical proof-of-mechanism and clinical activity have been established with acceptable immunogenicity on pair with other bispecifics.
  - Database lock and site closures are ongoing while preparing for a potential out licensing and handover to a partner.
  - The first partial response in this study was observed in Cohort 109 intravenous (dose level 8 µg/kg) and two partial responses were observed in Cohort 110 intravenous (dose level 16 µg/kg). The responses are supported by translational data, where higher T-cell activation has been observed with increasing doses.
- 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 the anti-myeloma activity of ISB 1342 according to the International Myeloma Working Group response criteria (Part 2 dose expansion).
- Clinical safety remains on par with earlier results presented in a poster session at the 2022 as of October 2023 (American Society of Hematology (ASH) Annual Meeting in December 2023) (link) with data cut-off October 26, 2022:
  - Observed CRS events were moderate and manageable with supportive care
  - No increased risk of infection has been observed
  - Proof-of-Mechanism with evidence of T-cell activation was noted following treatment with ISB 1342
    - Dose escalation continues with participants enrolling in additional cohorts two parallel dose escalations IV and SQ
  - Further dose-escalation (to 32 and 64 µg/kg) is warranted based on manageable safety profile, anti-myeloma activity observed, and supported by PK profile as well as T-cell activation biomarkers with current dose of 16 µg/kg IV.
- ISB 1342 was granted Orphan Drug Designation for multiple myeloma by the U.S. Food and Drug Administration in 2019.

- The bulk drug substance is manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland.
- In July 2023, a research article, Preclinical characterization of ISB 1342, a CD38 × CD3 T-cell engager for relapsed/refractory multiple myeloma, was published in Volume 142, Issue 3, of the American Society of Hematology's *Blood* journal.
  + One of the figures from this publication was prominently featured on the cover of the print edition of the journal.
- Additional information on the Phase 1 was presented at the 2023 ASH Annual Meeting:
  + **Dose Escalation of ISB 1342, a Novel CD38xCD3 Bispecific Antibody, in Patients with Relapsed / Refractory Multiple Myeloma (RRMM)**
  + Sunday, December 10, 2023, 6:00 PM-8:00 PM
    San Diego Convention Center, Halls G-H
    Session Name: 652. Multiple Myeloma: Clinical and Epidemiological: Poster II
    Publication Number: 3339

ISB 1442 (CD38 X CD47 BEAT® BISPECIFIC ANTIBODY)

- This first-in-class biparatopic bispecific antibody targeting CD38 and CD47 was generated 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 (ADCC) as well as complement-dependent cytotoxicity (CDC).
- After receiving approval from the HREC in Australia and the U.S. Food and Drug Administration, a Phase 1 / 2 first-in-human dose-finding study of ISB 1442 in relapsed/refractory multiple myeloma is now actively enrolling patients in Cohort 5 in both countries.
- Ichnos also plans to develop ISB 1442 in acute myeloid leukemia (AML).
- The preclinical data package for ISB 1442, which may be viewed at this link, shows:
  + 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 and low preclinical in vivo xenograft models

- Low on-target off-tumor binding with ISB 1442 compared to anti-CD47 mAb (hu5F9), 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 information on preclinical models in other hematologic malignancies were presented at the 2022 ASH Annual Meeting in December:

  - **Preclinical Evaluation of ISB 1442, a First-in-Class CD38 and CD47 Bispecific Antibody Innate Cell Modulator for the Treatment of AML and T-ALL**; Poster presentation that shows the rationale for advancing to a clinical study in relapsed/refractory AML (link), specifically:

    - In AML cell lines in multiple *in vitro* assays, ISB 1442 induces killing, including ADCP and ADCC

    - Superior activity to daratumumab in AML cell lines having intermediate or low CD38 expression

- ISB 1442 was granted Orphan Drug Designation for multiple myeloma by the FDA in March 2023.

- The bulk drug substance is manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland.

- Additional information on the ongoing Phase 1 was presented at the 2023 ASH Annual Meeting. Overall, treatment with ISB 1442 is well tolerated. CRS events observed were of low grade (1 or 2) and mostly resolved within one day. No neurotoxicity events have been observed to date. No signal of infections or anemia.

  - Proof of Mechanism observed based on biomarker changes, with increased macrophage-related markers among the first changes observed.

  - Dose escalation is ongoing.

  - **Initial Results from the Dose Escalation Phase1/2 of ISB 1442, a Novel CD38 Biparatopic x CD47 Bispecific Antibody, in Patients with Relapsed / Refractory Multiple Myeloma (RRMM)**

  - Monday, December 11, 2023, 6:00 PM-8:00 PM
    San Diego Convention Center, Halls G-H
    Session Name: 652. Multiple Myeloma: Clinical and Epidemiological: Poster III
    Publication Number: 4707

ISB 2001 TREAT™ TRISPECIFIC ANTIBODY

- ISB 2001 is the first-in-class T cell-engaging antibody that targets BCMA and CD38 on multiple myeloma cells. It is a trispecific antibody based on Ichnos' proprietary BEAT® platform, allowing maximal flexibility and excellent manufacturability of full-length multispecific antibodies. Additional ISB 2001 details include:
    + ISB 2001 combines three proprietary Fab 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 multiple myeloma cells. Its 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 for the treatment of 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 is expected to be more resistant to antigen escape associated with treatment of multiple myeloma patients.
- The preclinical data package for ISB 2001 was selected for a presentation (link) at the 2023 American Association for Cancer Research (AACR) Annual Meeting in April, as well as an oral presentation at the ASH Annual Meeting in December 2022:
    + In this presentation, **Overcoming Mechanisms of Escape from Treatments for Multiple Myeloma by ISB 2001, a first-in-Class Trispecific BCMA and CD38 targeted T Cell Engager,** the following data were highlighted:
        - Increased killing of tumor cells across variable levels of expression of both BCMA and CD38 compared to teclistamab, alnuctamab and EM-801
        - Higher potency *in vitro* when compared to the combination of daratumumab and teclistamab
        - Superior cytotoxicity over teclistamab in *ex vivo* assays with Multiple Myeloma cells from patients at different stages of progression of the disease
        - Superior efficacy over teclistamab in *in vivo* models with low level of expression of CD38 and BCMA demonstrating 100% complete responses

- In April 2023, Ichnos received approvals from HREC in Australia and the FDA to initiate a Phase 1 first-in-human study of ISB 2001 for the treatment of relapsed/refractory multiple myeloma. Ichnos is considering expansion of clinical studies to additional countries in parallel.

- In July 2023, Ichnos received Orphan Drug Designation from the FDA for ISB 2001 for the treatment of multiple myeloma.

- First patient was dosed in November 2023 and is now actively enrolling patients in Cohort 4.

- The bulk drug substance is manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland.

- Additional information on the ongoing Phase 1 was presented at the 2023 ASH Annual Meeting:

    + **Trial in Progress: A Phase 1, First-in-Human, Dose Escalation and Dose-Expansion Study of a BCMAxCD38xCD3 Targeting Trispecific Antibody ISB 2001 in Subjects with Relapsed/Refractory Multiple Myeloma**

    + Sunday, December 10, 2023, 6:00-8:00 p.m.
    San Diego Convention Center, Halls G-H
    Session: 653. Multiple Myeloma: Prospective Therapeutic Trials: Poster II
    Publication Number: 3396

AUTOIMMUNE DISEASES

Ichnos has two monoclonal antibody drug product candidates addressing autoimmune diseases in the pipeline. To enhance the company's focus on oncology, future development of both assets will be overseen by out-licensing partners.

The first asset, ISB 880, an anti-IL-1RAP antagonist, was licensed to Almirall, S.A. in December 2021. The initiation of dosing in a Phase 1 study of ISB 880/ALM27134 was announced by Almirall in September 2022.

The second antibody, ISB 830 (telazorlimab), was licensed to Astria Therapeutics in October 20232. It is an OX40 antagonist that completed a Phase 2b study in moderate to severe atopic dermatitis in calendar year 2021. Both compounds have potential across a range of autoimmune diseases.

ASSETS IN AUTOIMMUNE DISEASES

MOLECULE MECHANISM/CLASS	POTENTIAL INDICATIONS	PHASE	STATUS
ISB 880 (ALM 27134) IL-1RAP Antagonist Monoclonal Antibody	Autoimmune Diseases	Phase 1	Licensed to Almirall S.A. in December 2021. Dosing of participants in the Phase 1 study was announced by Almirall in September 2022.
ISB 830 Telazorlimab OX40 Antagonist Antibody	Atopic Dermatitis	Phase 2b	Licensed to Astria Therapeutics in October 2023. Successfully completed a Phase 2b study in Atopic Dermatitis.
	Other autoimmune diseases, including Rheumatoid Arthritis	U.S. IND for Rheumatoid Arthritis 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 assumed full cost and responsibility for the global development and commercialization of the compound. Ichnos received an upfront payment of €20.8 million. The deal includes development and commercial milestone payments and tiered royalties based upon future global sales. As part of the agreement, Ichnos is also being paid to manufacture batches of ISB 880 to support early clinical studies to be sponsored by Almirall and realized revenue this year for drug supplies for the ongoing Phase 1 study.

- 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 enabled U.S. IND filing by Almirall, and a Phase 1 study is underway.

- 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.

- Ichnos retains rights for antibodies acting on the IL-1RAP pathway for oncology indications.

ISB 830 (TELAZORLIMAB, OX40 ANTAGONIST)

- Ichnos entered an exclusive global licensing agreement for ISB 830 in autoimmune diseases with Astria Therapeutics in October 2023.
- Previously, Ichnos had received FDA clearance to study Telazorlimab in seropositive autoimmune diseases (Rheumatoid Arthritis, Systemic Lupus Erythematosus, Sjogren's Syndrome, Multiple Sclerosis, Type I Diabetes Mellitus, Myasthenia Gravis).
- The database for the ISB 830-204 Phase 2b clinical study in atopic dermatitis was locked in October 2021, and the final results were posted on ClinicalTrials.gov. 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.
- Results from the double-blind portion of the study are summarized below:
    - **Efficacy:** The primary endpoint of the 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.
    - **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.
    - For more information, visit https://iginnovate.com/contact-us/