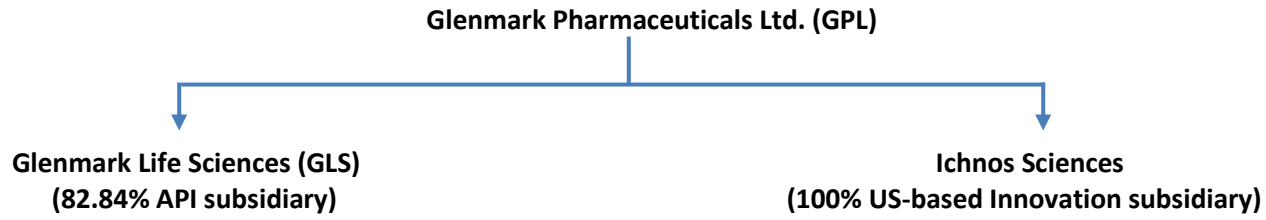
Management Discussion & Analysis
for the First Quarter of FY 2023-24

Glenmark operates its businesses through three separate entities



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

Revenue Figures for Glenmark Pharmaceuticals Ltd. (Consolidated)

(Rs. in Million)

	For the first quarter ended June 30		
	FY 2023-24	FY 2022-23	Growth (%)
India	10,643	10,352	2.8%
North America	8,085	6,628	22.0%
Europe	5,732	3,300	73.7%
Rest of the World[1]	5,512	4,226	30.4%
API	3,769	3,251	16.0%
Total	**33,740**	**27,757**	**21.6%**
Other Revenue	276	16	1616.9%
Consolidated Revenue	**34,016**	**27,773**	**22.5%**

1. Asia, Middle East and Africa, Russia + CIS, and Latin America

Average conversion rate in 3M FY 2023-24 considered as INR 82.15 / USD 1.00

Average conversion rate in 3M FY 2022-23 considered as INR 76.98 / USD 1.00

USD figures are only indicative

Review of Operations for the Quarter ended June 30, 2023

For the first quarter of FY24, Glenmark's consolidated revenue from operations was at Rs. 34,106 Mn (USD 414.1 Mn) as against Rs. 27,773 Mn (USD 360.8 Mn) in the corresponding quarter last year, recording overall year-on-year (YoY) growth of 22.5%.

GLENMARK PHARMACEUTICALS LTD. (GPL)

GPL is primarily focused on building a global formulations 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 formulations business in India for Q1 FY24 were at Rs. 10,643 Mn (USD 129.6 Mn) as against Rs. 10,352 Mn (USD 134.5 Mn) in Q1 FY23, recording a YoY growth of 2.8%. The lower growth was mainly on account of the full impact of divestment of few non-core brands and some impact of the NLEM price revisions. The India business contribution was at 31.3% in Q1 FY24 compared to 37.3% in Q1 FY23.

Glenmark's India business continued to significantly outperform industry growth rates. As per IQVIA Q1 FY24 data, Glenmark's India formulations business recorded a growth of 10.7%, compared to the industry growth of 8.1%. Furthermore, as per IQVIA MAT June 2023, Glenmark's India business grew by 13.1% compared to the overall industry growth of 10.3%. Glenmark's India business continues to be ranked 14th with a market share of 2.12% (IQVIA MAT June 2023). The Company also continues to have 9 brands in the IPM Top 300 Brands in the country on the basis of IQVIA MAT June 2023.

In Q1 and MAT June 2023, contribution from Chronic therapeutic segments for Glenmark was at 47% and 45% respectively. In terms of key therapeutic areas, Glenmark is ranked 2nd in, both, the Respiratory and the Dermatology segments. In addition, Glenmark is ranked 5th in the Cardiac segment and 17th in the Diabetes segment. During the quarter, Glenmark's India business also considerably improved its market share in its key therapeutic areas. As per IQVIA MAT June 2023, the Dermatology segment market share increased to 7.42% from 7.28% last year; the Company's share in the Respiratory market increased to 5.65% from 5.19%, while the Cardiac segment market share increased to 5.23% from 4.89%. Glenmark's share in the Diabetes market was 2.21% as per IQVIA MAT June 2023. This market share gain has been led by higher-than-industry growth across most of the core therapeutic areas.

Glenmark is expecting the business growth to remain stable in spite of a recent slowdown in certain acute segments of the industry, such as Respiratory and Anti-Infectives. The Company launched multiple line extensions during the quarter and continued to gain market share in some of the key launches across the core therapeutic segments. The Company continues to have a healthy pipeline of differentiated products which it plans to launch in the market going forward.

INDIA – GLENMARK CONSUMER CARE (GCC)

Primary sales for GCC in Q1 FY24 were Rs. 781 Mn with a growth of 21.3%, which was mirrored by strong double-digit secondary growth of 17%. The Company's flagship brand Candid Powder™ delivered revenue growth of 29% for Q1 FY24. The La Shield™ portfolio delivered 2% growth in Q1 FY24, which was low primarily due to a high-base effect. The Scalpe+™ portfolio recorded 58% growth in Q1 FY24.

NORTH AMERICA

The North America business registered revenues from the sale of finished dosage formulations of Rs. 8,085 Mn (USD 98.4 Mn) for Q1 FY24 as against revenue of Rs. 6,628 Mn (USD 86.1 Mn) for Q1 FY23, and Rs. 8,507 Mn (USD 104 Mn) for Q4 FY23. This translates to a YoY growth of 22.0% and a quarter-on-quarter (QoQ) decline of 5.0%. For Q1 FY24, the North America business contribution was at 23.8% compared to 23.9% in Q1 FY23.

In the first quarter of FY24, Glenmark launched Clindamycin Hydrochloride Capsules USP, which was approved in the previous quarter. Additionally, Glenmark filed two ANDAs in the first quarter. The Company plans to file 2-3 applications in the forthcoming quarter and a total of 10-12 ANDAs in FY24.

Glenmark's marketing portfolio through June 30, 2023 consists of 183 generic products authorized for distribution in the U.S. market. The Company currently has 50 applications pending in various stages of the approval process with the U.S. FDA, of which 21 are Paragraph IV applications.

EUROPE

Glenmark Europe operations' revenue for Q1 FY24 was at Rs. 5,732 Mn (USD 69.8 Mn) as against Rs. 3,300 Mn (USD 42.9 Mn) in Q1 FY23 recording a YoY growth of 73.7%. The Europe business contributed 16.9% to the total revenues in Q1 FY24 compared to 11.9% in Q1 FY23.

The strong growth in the region was driven by an uptick in the base business as well as new product launches during the quarter. The Western European business clocked high double-digit growth for Q1, with markets like the United Kingdom (UK) and Spain growing significantly. Amongst the key markets, the UK recorded

strong growth on the back of key launches in the generics business. Key markets in Central and Eastern Europe, such as the Czech and Poland, recorded strong secondary sales growth during the quarter.

Glenmark's respiratory portfolio in Europe has also been a key factor for the strong performance in Q1 FY24. The Company has seen a strong uptake in Soprobec® across markets. In addition, RYALTRIS® continues to exhibit strong growth across markets in which both Glenmark and, partner, Menarini have launched the product. Salmex® / Asthmex® also continues to sustain its market share across the CEE markets, in terms of volume as well as value. The Company has filed four additional Respiratory products in the EU markets in Q4 FY23, which would be launched over the next two-three years. As mentioned in the last quarter's notes, Glenmark has also entered the Italian market and will be expanding across the country in the forthcoming quarters.

ROW REGION (ASIA, MEA, Russia+CIS & LATAM)

For Q1 FY24, revenue from the ROW region was Rs. 5,512 Mn (USD 67.1 Mn) as against Rs. 4,226 Mn (USD 54.9 Mn) for Q1 FY23, recording a YoY growth of 30.4%. For Q1 FY24, the ROW business contribution was at 16.2%, compared to 15.2% in Q1 FY23.

The Company witnessed healthy growth in the base business across all sub-regions of the ROW markets. As per IQVIA YTD June 2023 and MAT June 2023 data, Glenmark's Russia business recorded growth of 33.8% and 17.1%, respectively, in value. This has been driven by all key brands, including RYALTRIS®, Ascoril® and Montlezir™. In terms of key therapeutic areas, Glenmark recorded growth of 19.2% in value in the Dermatology segment versus the overall Dermatology market growth of 8.6% as per MAT June 2023. Amongst the Dermatology companies in Russia, Glenmark ranks 10th as per MAT June 2023. Amongst the companies present in the Expectorants market in Russia, Glenmark continues to maintain a strong position, ranking 2nd as per MAT June 2023. In June 2023, Glenmark launched Ascoril LS™ (ambroxol + guaifenesin + levosalbutamol) to further consolidate its leadership position in the Expectorants market.

The Asia region recorded 14% growth in secondary sales, which was driven by markets like the Philippines and Vietnam. Dermatology and Respiratory are key therapy areas for Glenmark in Asia, contributing significantly to the overall sales. RYALTRIS® was launched by Glenmark in the Malaysian market in Q1 FY24. RYALTRIS® holds 18.1% value market share in Australia across the top allergic rhinitis products; the product has also received strong response in South Korea post launch in Q3 FY23 by partner, Yuhan Corporation.

The Middle East and Africa (MEA) region recorded 20%+ growth in sales during the first quarter of FY24. Glenmark continued to be ranked 3rd in the overall Kenya Pharmaceutical Market. Further, the Company continued to achieve strong secondary sales growth in South Africa and UAE. RYALTRIS® was launched in

Saudi Arabia in Q1 FY24 and is expected to further drive growth in the Respiratory segment as the product gets launched across other MEA markets in FY24.

The Latin America (LATAM) region witnessed strong growth in Q1 FY24. The Respiratory portfolio remains the key contributor for Glenmark in the LATAM markets. Glenmark Brazil achieved 25%+ growth in the covered market. The Company maintained its rank amongst the top companies in the covered market of the chronic respiratory segment in Brazil as per IQVIA MAT June 2023. Secondary sales growth remained strong in Mexico; Glenmark's business grew by ~25% in value and ~15%+ in units (IQVIA MAT June 2023).

RYALTRIS®

- As of the end of Q1 FY24, marketing applications for RYALTRIS® have been submitted in more than 70 countries across the world.
- The product has been commercialized in 29 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.
- Menarini, Glenmark's partner in the EU, intends to launch the product in additional EU markets in FY24 and consolidate its position in the markets where the product has been already launched.
- Hikma, Glenmark's commercial partner in the USA, continued to see strong new prescriptions and repeat prescriptions growth as the allergy season progressed in the country.
- Grand Pharmaceutical (China) Co. Ltd., Glenmark's partner in Mainland China, aims to complete the on-going Phase 3 study in the country and submit the marketing authorization application in the second half of FY24.
- 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®):
    - Australia – 18.1%
    - South Africa – 15.2%
    - Czech Republic – 25%
    - Poland – 7.6%
    - Italy – 10.2%

Other Key Respiratory Products

- Clinical trial ongoing for generic Flovent pMDI; expect to file in FY24
- Plan to file at least one more generic respiratory pMDI in the U.S. in FY24 and continue filing momentum beyond FY24.

INNOVATIVE R&D PIPELINE

GRC 54276

GRC 54276, a novel HPK1 Inhibitor, is being developed as an orally administered immunotherapeutic agent 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. In pre-clinical studies, GRC 54276, when administered alone, has demonstrated substantial anti-tumor effects, which are further enhanced when administered in combination with currently available immunotherapy.

GRC 54276 is currently being evaluated in the First in Human (FIH) Phase 1 clinical study. Part 1a monotherapy phase of the study is ongoing in India since July 2022 and no dose limiting toxicities have been observed. Based on the Phase 1 IND approvals received from DCGI and U.S. FDA in Q4 FY23, the Phase 1 Part 1b combination study of GRC 54276 with pembrolizumab and atezolizumab was initiated in India in Q1 FY24. Initiation of the study in the US is planned in Q2 FY24.

GRC 39815

GRC 39815 (RORγt inhibitor) is the Company's respiratory pipeline asset being developed as an inhaled therapy for treatment of mild-to-moderate Chronic Obstructive Pulmonary Disorder (COPD). It is currently under Phase 1 clinical development in the U.S.

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).

Revenues from operations including captive sales were Rs. 5,785 Mn as against Rs. 4,899 Mn, recording a YoY growth of 18.1%. Generic API revenues in Q1 FY24 increased by 13.3% YoY. The business witnessed steady growth momentum across regulated as well as emerging markets. CDMO revenues almost doubled with 91.3% YoY in Q1 FY24. DMF/CEPs filing continued across major markets in Q1 FY24, taking the total cumulative filings to 476 as on June 30, 2023. Detailed engineering work has started for the construction of 200 KL in phase 1 at Solapur; initially total capacity of ~500KL will be operational by FY26.

External sales for GLS in Q1 FY24 were at Rs. 3,769 Mn (USD 45.9 Mn) as against Rs. 3,251 Mn (USD 42.2

Mn) in Q1 FY23, recording a growth of 16.0% YoY.

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

ICHNOS SCIENCES Inc.

Glenmark's wholly owned subsidiary, Ichnos is an innovation biotech company focused on the development of novel biological molecules as potential treatment options for oncology.

Glenmark invested Rs. 1,417 Mn (USD 17.2 Mn) in Q1 FY24 compared to Rs. 1,682 Mn (USD 21.8 Mn) in Q1 FY23 and Rs. 1,906 Mn (USD 24 Mn) in Q4 FY23.

For further updates on the pipeline and the organization, please log on to www.ichnossciences.com. The pipeline update for the first quarter of FY24 is published on the Ichnos website.

KEY OBJECTIVES FOR FY24

- **Consolidated Revenue Growth: 10-11%**
- **Consolidated R&D Investment: 8-8.5% of total sales**
- **Consolidated EBITDA Margin: 19-20%+**
- **Consolidated Capex: INR 6-7 Bn**
- **Priority to enhance free cash generation for further debt reduction**
- **Close at least 1 out-licensing deal in innovation pipeline**

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ICHNOS SCIENCES INC.

AUGUST 2023 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 164 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.

In June 2023, Ichnos welcomed Lida Pacaud, M.D. as the company's new Chief Medical Officer.

CYRIL KONTO, M.D. President and Chief Executive Officer Allogene, Pfizer, Bristol Myers Squibb	**LIDA PACAUD, M.D.** Chief Medical Officer Legend Biotech, Novartis, Roche	**EUGENE ZHUKOVSKY, Ph.D.** Chief Scientific Officer Genentech, Xencor, Affimed, Biomunex, Boehringer Ingelheim
MICHAEL D. PRICE Chief Financial Officer AKCEA, novelion	**ROBERTO GIOVANNINI, Ph.D.** Chief Process and Manufacturing Officer Boehringer Ingelheim, glenmark	**ASHOK MARÍN** General Counsel sanofi, Gilead
PATRICIA JAQUET Head of Human Resources COVANCE		

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 programs are 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, and ISB 1442, a biparatopic bispecific antibody targeting CD38 and CD47, currently in a Phase 1/2 dose escalation/expansion study for the same indication. In April 2023, Ichnos received approval from the Human Research Ethics Commission (HREC) in Australia and the U.S. Food and Drug Administration (FDA) to initiate a first-in-human clinical study of ISB 2001, the company's first TREAT™ trispecific antibody targeting BCMA, CD38, and CD3, for the treatment of relapsed/refractory multiple myeloma. In July 2023, Ichnos was granted Orphan Drug Designation by the FDA for ISB 2001 for the treatment of multiple myeloma. Additionally, Ichnos selected targets for ISB 2301, the company's first NK-cell engaging mutlispecific platform, for the treatment of solid tumors.

Ichnos is looking for asset-level and platform-level collaboration partners in development and research. For more information, email us at Partnership@IchnosSciences.com.

[1] Bispecific Engagement by Antibodies based on the TCR

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 2004 BEAT® bispecific antibody	Discovery	Hematologic Malignancies
ISB 2301 NK-cell engaging multispecific platform	Discovery	Solid Tumors

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 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. Currently seven (7) sites in the US and eleven (11) sites in France are actively enrolling.
  - + The first partial response in this study was observed in Cohort 109 intravenous (dose level 8 µg/kg) and Cohort 110 intravenous (dose level 16 µg/kg) is now enrolling. In parallel, a new lyophilized formulation was filed and is now used in a subcutaneous dose-escalation arm, which is at Cohort 109 (dose level 8 µg/kg). Clinical proof of concept is anticipated in the third quarter of calendar year 2023.

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

- 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).
- Clinical safety remains on par with earlier results presented in a poster session at the 2022 American Society of Hematology (ASH) Annual Meeting in December (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
- ISB 1342 was granted Orphan Drug Designation for multiple myeloma by the U.S. Food and Drug Administration.
- 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.
- An abstract for the 2023 ASH Annual Meeting with the latest clinical data has been submitted:
  - **Dose Escalation of ISB 1342, a Novel CD38xCD3 Bispecific Antibody, in Patients with Relapsed / Refractory Multiple Myeloma (RRMM)**

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 4 in both countries.
- Currently four (4) sites in the US and four (4) sites in Australia are actively enrolling. The study is in cohort 4 (dose level 150mg).
- 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 the ongoing Phase 1 study and on preclinical models in other hematologic malignancies were most recently presented at the 2022 ASH Annual Meeting in December:
    + **A Phase 1/2, First-in-Human, Multicenter, Open-Label, Dose Escalation and Dose-Expansion Study of Single-Agent ISB 1442 in Patients with Relapsed/Refractory Multiple Myeloma**; Poster presentation that describes the design of the ongoing study may be viewed here (link).
    + **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.
- An abstract for the 2023 ASH Annual Meeting with the latest clinical data has been submitted:
    + **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)**

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

- ISB 2001 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.

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

- Two abstracts for the 2023 ASH Annual Meeting have been submitted. One describing the use of quantitative systems pharmacology (QSP) for determining the first in human (FIH) starting dose and the second one the trial design and specific mechanism of action:

  + **Integrated Preclinical data analysis of ISB 2001 enables optimal starting dose selection for a first in class trispecific T cell engager**

  + **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**

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 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), an OX40 antagonist that completed a Phase 2b study in moderate to severe atopic dermatitis in calendar year 2021, is in partnering discussions. 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	Successfully completed a Phase 2b study in Atopic Dermatitis. Exploring partnership(s).
	Other autoimmune diseases, including Rheumatoid Arthritis	U.S. IND for Rheumatoid Arthritis and other autoimmune indications is active.	

ISB 880 (IL-1RAP ANTAGONIST) almirall

- 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)

- 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.
- Ichnos has clearance from the FDA to study telazorlimab in seropositive autoimmune diseases (Rheumatoid Arthritis, Systemic Lupus Erythematosus, Sjogren's Syndrome, Multiple Sclerosis, Type I Diabetes Mellitus, Myasthenia Gravis), and is actively seeking a partner to further develop the drug in atopic dermatitis and other indications. For more information, email us at Partnership@IchnosSciences.com.