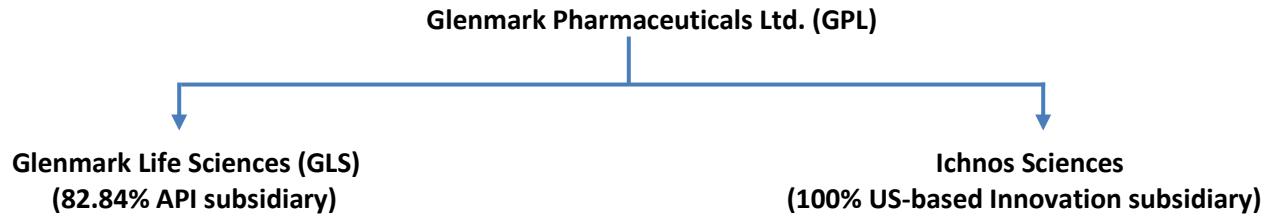
Management Discussion & Analysis
for the Fourth Quarter of FY 2022-23

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 Million)

	For the fourth quarter ended March 31			For the twelve months ended March 31		
	FY 2022-23	FY 2021-22	Growth (%)	FY 2022-23	FY 2021-22	Growth (%)
India	8,284	8,847	-6.4%	40,298	40,855	-1.4%
North America	8,507	7,378	15.3%	31,041	30,366	2.2%
Europe	6,078	4,968	22.3%	18,094	15,218	18.9%
Rest of the World[1]	6,856	5,479	25.1%	23,777	21,672	9.7%
API	3,831	3,283	16.7%	14,582	12,709	14.7%
Total	**33,555**	**29,955**	**12.0%**	**127,791**	**120,820**	**5.8%**
Other Revenue	183	237	-23.0%	2,110	2,229	-5.3%
Consolidated Revenue	**33,737**	**30,191**	**11.7%**	**129,901**	**123,049**	**5.6%**

1. Asia, Middle East and Africa, Russia + CIS, and Latin America
2. Average conversion rate in 12M FY 2022-23 considered as INR 80.22 / USD 1.00
   Average conversion rate in 12M FY 2021-22 considered as INR 74.38 / USD 1.00
   USD figures are only indicative

Review of Operations for the Quarter ended March 31, 2023

For the fourth quarter of FY23, Glenmark's consolidated revenue from operations was at Rs. 33,737 Mn (USD 411 Mn) as against Rs. 30,191 Mn (USD 402 Mn) in the corresponding quarter last year, recording overall year-on-year (YoY) growth of 11.7%.

For the twelve months of FY23, Glenmark's consolidated revenue from operations was at Rs. 129,901 Mn (USD 1,619 Mn) as against Rs. 123,049 Mn (USD 1,654 Mn), recording an overall YoY growth of 5.6%.

Key Highlights for the Year FY23:

1. **As per IQVIA MAT March 2023, Glenmark was ranked 2nd in the Respiratory segment of the Indian Pharmaceutical Market, with 1.5x higher value growth compared to the overall Respiratory market. Glenmark is now ranked 2nd across Dermatology and Respiratory segments in India.**

2. **Glenmark's Europe business recorded revenues of USD 225+ Mn, continuing the strong growth momentum over the last two years.**

3. **Glenmark's ROW business recorded 20%+ growth across all sub-regions, driven by key product launches in Respiratory and Dermatology.**

4. **Ryaltris® was approved in the USA and was launched by Hikma, Glenmark's commercial partner.**

5. **In FY23, Ryaltris® was launched in 12 markets on our own / through a partner; in totality, Ryaltris® has now been commercialized in 27 markets across the globe.**

6. **Proof-of-Concept (PoC) studies were initiated for four clinical oncology assets which are a part of the Glenmark / Ichnos development pipeline – study read-outs in FY24 for all four molecules.**

7. **Ichnos' partnered asset in immunology, ISB 880, progressed to Phase 1 studies which were initiated by Glenmark's development partner, Almirall.**

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 fourth quarter of FY23 was at Rs. 8,284 Mn (USD 100 Mn) as against Rs. 8,847 Mn (USD 118 Mn) in the previous corresponding quarter, recording a decline of -6.4%. The decline was mainly on account of the impact of divestment of few non-core brands, some impact of the NLEM price revisions as well as returns of Covid-related products. Adjusted for these impacts, the India business recorded YoY growth of 5.1% in Q4 FY23. The India business contribution was at 31% in FY23 compared to 33% in FY22.

Glenmark's India business continued to significantly outperform industry growth rates. As per IQVIA Q4 FY23 data, Glenmark's India formulation business recorded growth of 18.2%, compared to the industry growth of 14.4%. Furthermore, as per IQVIA MAT March 2023, excluding the Covid portfolio, Glenmark's India business grew by 12.3% compared to the overall industry growth of 9.5%. Glenmark's India business is ranked 14th with a market share of 2.12% (IQVIA MAT March 2023).

In terms of key therapeutic areas, Glenmark is now ranked 2nd in the Respiratory segment, continues to be ranked 2nd in the Dermatology segment, 5th in the Cardiac segment and 14th in the Diabetes segment. The Company continues to have 9 brands in the IPM Top 300 Brands in the country on the basis of IQVIA MAT March 2023. During the quarter, Glenmark's India business also considerably improved its market share in its key therapeutic areas. As per IQVIA MAT March 2023, the Dermatology segment market share increased to 7.35% from 7.12% last year; the Company's share in the Respiratory market increased to 5.59% from 5.44% last year, while the Cardiac segment market share increased to 5.17% from 4.66% last year. Glenmark's share in the Diabetes market was 2.31% as per IQVIA MAT March 2023.

The Company launched multiple new products during the quarter and continued to gain market share in some of the key launches across segments. In Q4, Glenmark became the first Company to introduce Lobeglitazone + Metformin (LOBG-M®) in India for the treatment of type 2 diabetes in adults, particularly for insulin-resistant diabetic individuals. Earlier in FY23, Glenmark also launched Fixed-Dose Combination (FDC) of Teneligliptin (20 mg) + Pioglitazone (15 mg) + Metformin (500mg/1000mg) SR under the brand name Zita®-PioMet. Glenmark also launched other FDCs of Teneligliptin including its combinations with Pioglitazone (Zita Pio™) and Dapagliflozin (Zita-D™), Sitagliptin (Sitazit®) and its FDCs as well as

Lobeglitazone (LOBG®), emphasizing its overall strong focus on the Diabetes segment.

In the Cardiac segment, Glenmark launched Sacubitril + Valsartan under the brand name, Sacu V™ for the treatment of heart failure. The sacubitril-valsartan combination belongs to the class ARNI (Angiotensin receptor neprilysin inhibitor). This drug helps reduce the risk of cardiovascular related deaths and hospitalizations. 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 Q4 FY23 was Rs. 672 Mn with a growth of 9%, which was mirrored by strong double digit secondary growth of 15%. This growth was driven primarily by increasing volume growth of key brands Candid Powder™ and La Shield™. New products such as La Shield Pollution Protect, La Shield Probiotic Moisturizer & Scalpe Pro Shampoo also contributed to the growth in the business. For the twelve months of FY23, GCC revenue stands at Rs. 2,330 Mn with YTD growth of 30%. Our flagship brand Candid Powder™ delivered revenue growth of 17% for FY23. La Shield™ portfolio delivered 53% growth in Q4 FY23 and 73% growth in FY23. Finally, Scalpe+™ portfolio recorded 13% growth in Q4 FY23 and 13% growth in FY23.

NORTH AMERICA

The North America business registered revenues from the sale of finished dosage formulations of Rs. 8,507 Mn (USD 104 Mn) for the fourth quarter of FY23 as against revenue of Rs. 8,373 Mn (USD 102 Mn) for the third quarter of FY23, recording a quarter-on-quarter (QoQ) growth of 1.6%. YoY growth for the North America business was 15.3%. For the twelve months of FY23, the North America business contribution was at 24% compared to 25% in FY22.

In the fiscal year 2022-23, Glenmark was granted approval of 10 Abbreviated New Drug Applications (ANDA), comprised of 6 final approvals, 2 Prior Approval Supplement approvals [for a new strength or formulation] and 2 tentative approvals. Notable approvals include: Sodium Phenylbutyrate Tablets USP, 500 mg; Nicardipine Hydrochloride Capsules; Clindamycin Hydrochloride Capsules. The Company filed a total of 6 ANDA applications with the U.S. FDA in the fourth quarter of FY23, and 8 ANDA applications throughout the fiscal year 2023. Further, the Company plans to file 2-3 applications in the forthcoming quarter and a total of 10-12 ANDAs in FY24.

Glenmark successfully launched 8 new products during fiscal year 2022-23, consisting of a mix of immediate-release oral solids and an injectable. Notable launches include Ezetimibe Tablets USP; Abiraterone Acetate Tablets USP, 500 mg; Fingolimod Capsules, 0.5 mg; Sodium Phenylbutyrate Tablets USP, 500 mg; Nicardipine

Hydrochloride Capsules. In the fourth quarter of fiscal year 2022-23, Glenmark launched Bumetanide Injection, 1 mg/4 mL (0.25 mg/mL) Single-Dose Vials and 2.5 mg/10 mL (0.25 mg/mL) Multi-Dose Vials, Nicardipine Hydrochloride Capsules, and Teriflunomide Tablets; Glenmark was one of the first generics to launch Teriflunomide (Aubagio®) Tablets. During this quarter, Glenmark also announced an exclusive distribution agreement with Cediprof for U.S. FDA-approved Mixed Amphetamines Immediate-Release Tablets.

Glenmark's marketing portfolio through March 31, 2023 consists of 183 generic products authorized for distribution in the U.S. market. The Company currently has 45 applications pending in various stages of the approval process with the U.S. FDA, of which 21 are Paragraph IV applications.

The Company and its US subsidiary (Glenmark Pharmaceuticals Inc., USA) have, subject to final documentation and approval of the Court, after the end of the accounting year, arrived at a settlement with Three Plaintiff Groups collectively representing all of the claims against the Company and Merck in relation to multiple antitrust and consumer protection lawsuits, including a class action, consolidated in the Eastern District of Virginia, U.S. (the "Court") for a total amount of US$ 87.5 million, payable over two financial years. The final settlements will be in accordance with the separate agreements entered into with each of the plaintiff groups and will be subject to the final approval by the Court. The settlements will make clear that the Company denies each and every one of the allegations against it and the settlements are not on the basis of the Company having conceded or admitted any liability, offence, wrongdoing or illegality.

EUROPE

Glenmark Europe operations' revenue for the fourth quarter of FY23 was at Rs. 6,078 Mn (USD 75 Mn) as against Rs. 4,968 Mn (USD 66 Mn) recording a growth of 22.3%. For the twelve months of FY23, the Europe business contribution was at 14% compared to 12% in FY22.

The strong European business growth was driven by markets in, both, Western Europe (WEU) and Central & Eastern Europe (CEE). Key markets in CEE, such as the Czech, recorded strong secondary sales growth of 20%+ during the quarter. Growth 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 Q4 with markets like the United Kingdom and Spain growing significantly. Amongst the key markets, the UK recorded strong growth on the back of key launches in the generics business. Glenmark ranks amongst the top 15 companies in the generics market of Germany. 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. The Company has filed four additional respiratory products in the EU markets in FY23 which would be launched over the next two-three

years. Glenmark has also entered the Italian market and will be expanding across the country in the forthcoming quarters.

ROW REGION (ASIA, MEA, LATAM AND RCIS)

For the fourth quarter of FY23, revenue from the ROW region was Rs. 6,856 Mn (USD 84 Mn) as against Rs. 5,479 Mn (USD 73 Mn) for the previous corresponding quarter, recording a growth of 25.1%. For the twelve months of FY23, the ROW business contribution remained at 18%, similar to that in FY22.

The Company witnessed healthy growth in the base business across all sub-regions of the ROW markets. As per IQVIA YTD March 2023 and MAT March 2023 data, Glenmark's Russia business recorded growth of 10.3% in value versus the overall retail market growth of 1.8%. This has been driven by all key brands, including Ryaltris®, Ascoril® and Montlezir™. Ryaltris® continued to sustain its momentum and gained further market share during the quarter. Across the year, four new products were introduced in the market including Fenismart™ (dimetindene) gel and Phelisans™ (phenasone + lidocaine) ear drops. In terms of key therapeutic areas, Glenmark recorded growth of 12% in value in the Dermatology segment versus the overall Dermatology market growth of 6.7% as per MAT March 2023. Amongst the Dermatology companies in Russia, Glenmark ranks 11th as per MAT March 2023. Amongst the companies present in the Expectorants market in Russia, Glenmark continues to maintain a strong position, ranking 2nd as per MAT March 2023.

The overall environment remained challenging across Asian markets such as Sri Lanka, Myanmar, Vietnam and Cambodia. Amongst the key markets in the Asia region, the Philippines continued to record double-digit secondary growth. 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 Q4 FY23. It continues to gain value market share in Australia with 18.1% share across the top allergic rhinitis products. Launched in South Korea in Q3 FY23 by Glenmark's partner, Yuhan, Ryaltris® has shown strong pickup in a short time span with double digit share in the allergic rhinitis combination market.

The Middle East and Africa region recorded 20%+ growth in secondary sales during the fourth quarter of FY23. During the year FY23, the Kenya market was impacted by macroeconomic instability and currency devaluation, however, Glenmark's business remained resilient and the Company 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 Saudi Arabia. Respiratory and Dermatology together contributed ~60% to the overall sales of the MEA region. Ryaltris® is expected to further drive growth in the Respiratory segment as the product gets launched across multiple MEA markets in the first half of FY24.

LATAM witnessed strong growth for Q4 as well as for the full year FY23. The Respiratory portfolio remains

the key contributor for Glenmark in the LATAM markets. Glenmark Brazil achieved the highest growth rate among the Top 20 Companies 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 March 2023. Secondary sales growth remained strong in Mexico, with Glenmark's business growing by 60%+ in value and 50%+ in units (IQVIA MAT March 2023), while the overall Mexican Pharmaceutical Market grew at ~7% and the growth in the covered market was ~17%.

RESPIRATORY – CREATING GLOBAL SCALE

Following are the key business updates for Glenmark's global respiratory business in Q4 FY23:

Ryaltris®

- As of the end of the fourth quarter of FY23, marketing applications for Ryaltris® have been submitted in more than 70 countries across the world. The product has been commercialized in 27 markets, including major markets like the USA, Europe (the UK and multiple markets across the EU), Australia, Russia, South Africa, and South Korea.
- Glenmark's partner in the EU, Menarini, initiated the commercial launch in Austria, Belgium, France, and Spain in the fourth quarter, and intends to launch the product in additional EU markets in FY24.
- Glenmark's commercial partner in the USA, Hikma, continued to see strong new prescriptions and repeat prescriptions growth as the allergy season progressed in the country. Hikma also recently held a clinical advisory board and received positive feedback on Ryaltris® from 14 senior allergy physicians in the USA.
- Glenmark Canadian partner, Bausch Health, launched Ryaltris® in April 2023.
- Glenmark's partner in Mainland China, Grand Pharmaceutical (China) Co. Ltd., aims to complete the on-going Phase 3 study in China 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 – 10.3%
    - Czech Republic – 15.6%
    - Poland – 5.6%

Other key 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 (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. GRC 54276 is a novel, orally active HPK1 inhibitor. 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 (GRC 54276-101). Part 1a monotherapy phase of the study is ongoing in India since July 2022 and no dose limiting toxicities have been observed during the DLT period to-date. Acceptance of IND by U.S. FDA was received in Q4 FY23. Initiation of the Part1b of the study for GRC 54276 in combination with pembrolizumab and atezolizumab in India and the U.S. is planned in Q1 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. 6,213 Mn as against Rs. 5,141 Mn, recording a YoY growth of 21%. Generic API revenues in Q4 FY23 increased by 10.4% QoQ and increased by 15.5% YoY. The business witnessed steady growth momentum across regulated as well as emerging markets. CDMO revenues in Q4 FY23 doubled sequentially and grew by 30.4% YoY in Q4 FY23. DMF/CEPs filing continued across major markets in Q4 FY23, taking the total cumulative filings to 468 as on March 31, 2023. Multiple projects are completed / ongoing for capacity expansion across the Ankleshwar and Dahej facilities.

External sales for Glenmark Life Sciences in Q4 FY23 were at Rs. 3,831 Mn (USD 47 Mn) as against Rs. 3,283

Mn (USD 44 Mn) in Q4 FY22, recording a growth of 16.7% YoY.

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

ICHNOS SCIENCES Inc.

Glenmark invested Rs. 1,906 Mn (USD 24 Mn) in the fourth quarter of FY23 compared to Rs 1,640 Mn (USD 22 Mn) in the corresponding quarter last year. For the twelve months of FY23, Glenmark invested Rs. 6,833 Mn (USD 85.2 Mn) compared to Rs. 6,627 Mn (USD 89.1 Mn) invested in the corresponding period of the previous financial year.

For further updates on the pipeline and the organization, please log on to www.ichnossciences.com. The pipeline update for the fourth quarter of FY23 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.

MAY 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.

CYRIL KONTO, M.D. President and Chief Executive Officer	**ROBERTO GIOVANNINI, Ph.D.** Chief Process and Manufacturing Officer	**PATRICIA JAQUET** Head of Human Resources
ASHOK MARÍN General Counsel	**MICHAEL D. PRICE** Chief Financial Officer	**EUGENE ZHUKOVSKY, Ph.D.** Chief Scientific Officer

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

[1] Bispecific Engagement by Antibodies based on the TCR

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. Ichnos also 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.

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

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]	IND-Enabling Studies	Relapsed/Refractory Multiple Myeloma
ISB 2004 BEAT® bispecific antibody	Discovery	Hematologic Malignancies
NK-cell engaging multispecific platform (newly ISB 2301)	Discovery	Solid Tumors

[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 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.
  - The first partial response in this study was observed in Cohort 109 (intravenous). In parallel, a new lyophilized formulation was filed and is now used in a subcutaneous dose-escalation. Clinical proof of concept is anticipated in the third quarter of calendar year 2023.
- 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.

ISB 1442 (CD38 X CD47 BEAT® BISPECIFIC ANTIBODY)

- This first-in-class biparatopic bispecific antibody targeting CD38 x 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.
- 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 first bulk drug substance batches to support IND filing and the ongoing Phase 1/2 dose escalation and expansion study 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 Ichnos' proprietary BEAT® 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 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 oral presentation (link) at the 2023 American Association for Cancer Research (AACR) Annual Meeting in April:
    + 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 U.S. 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.

- The first bulk drug substance batches to support IND filing and the Phase 1 dose escalation and expansion study were manufactured at the Ichnos site in La Chaux-de-Fonds, Switzerland in 2022.

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)

- 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.