

May 2024 Update

About IGI

Ichnos Glenmark Innovation (IGI) is an alliance between Ichnos Sciences Inc., a global fully-integrated clinical-stage biotech company developing multispecifics™ in oncology, and Glenmark Pharmaceuticals Ltd. (Glenmark), with the aim to accelerate new drug discovery in cancer treatment. IGI combines Ichnos' research and development proficiencies in novel biologics with those of Glenmark's in new small molecules to continue developing cutting-edge therapy solutions that treat hematological malignancies and solid tumors. Harnessing the combined proficiency of over 150 scientists and a robust pipeline of novel molecules, this collaboration will leverage the capabilities of its three global centers of innovation spread across the USA, Switzerland and India to propel Innovation. For more information, visit www.iginnovate.com.

Headquartered in New York City, IGI has research and manufacturing operations at two sites in Switzerland. As a fully integrated biotechnology company with approximately 258 employees, IGI has strong capabilities in research, antibody engineering, small molecule, CMC, and clinical development of biotechnologies.

IGI is guided by an accomplished management team with experience developing immune cell engagers and small molecules within the biopharmaceuticals industry, and is led by Cyril Konto, M.D., President and Chief Executive Officer.

Highly Experienced Leadership Team



LEADERSHIP

CYRIL KONTO, M.D. President and Chief Executive Officer
LIDA PACAUD, M.D. Chief Medical Officer
MARIO PERRO, Ph.D. Head of Biologics Research
NAGARAJ GOWDA, Ph.D. Head of Small Molecule Research
DEAN THOMAS General Counsel
SEBASTIEN CHENUET, Ph.D. Head of Business Development
EVA YUEN Head of Finance
KARISHMA SIPAHIMALANI, Ph.D. Head of Human Resources

PREVIOUS EXPERIENCE



BY THE NUMBERS

110+ Years combined experience in biotech and pharmaceuticals
30+ Products developed or launched
40+ Mergers, acquisitions, IPOs and other transactions

The proprietary BEAT® technology platform¹ is one of the basis for IGI's 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.

¹ Bispecific Engagement by Antibodies based on the TCR



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Oncology Pipeline

IGI's 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. Small molecule research group in India has experienced research group and facility to work on challenging targets across different class and recently working on protein degradation. Updates of note in the last quarter are outlined below:

- + ISB 2001 was the subject of an oral presentation at the American Association of Cancer Research (AACR) 2024 on April 7, 2024, in San Diego, California and available online [here](#).

MOLECULE MECHANISM/CLASS	PHASE/STATUS	LEAD INDICATION
ISB 2001 BCMA x CD38 x CD3 TREAT™ trispecific antibody ²	Phase 1	Relapsed/Refractory Multiple Myeloma
ISB 1442 CD38 x CD47 BEAT® biparatopic bispecific antibody	Phase 1	Relapsed/Refractory Multiple Myeloma; Phase 1 study in Acute Myeloid Leukemia (AML) is planned by early 2024
ISB 1342 CD38 x CD3 BEAT® bispecific antibody ³	Phase 1	Relapsed/Refractory Multiple Myeloma; T-Cell Acute Lymphoblastic Leukemia (T-ALL) is also under consideration
GRC 65327 Cbl-b Inhibitor	IND-enabling	Solid Tumors

IGI is looking for asset-level and platform-level collaboration partners in development and research. For more information, visit <https://IGInnovate.com/contact/>.

Overview of Select Oncology Drug Product Candidates

ISB 2001 TREAT™ TRISPECIFIC ANTIBODY

- ISB 2001 is a first-in-class T cell-engaging antibody that targets BCMA and CD38 on multiple myeloma cells. It is a trispecific antibody based on IGI's proprietary BEAT® platform, allowing maximal flexibility and excellent manufacturability of full-length multispecific antibodies.

² Trispecific Engagement by Antibodies based on the TCR.

³ Asset available for in-licensing. Future clinical development will be advanced by a partner.



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- 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.
- 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.
- At the recent AACR Annual Meeting 2024, an oral presentation showcased the results of ISB 2001 anti-myeloma activity in bone marrow aspirates from patients who were either newly diagnosed or suffer from r/r MM following multiples lines of treatment, including patients relapsing after CD38 and BCMA targeted therapies. This pre-clinical study shows the promise of ISB 2001 trispecific antibody targeting BCMA and CD38 against multiple myeloma, and CD3 on T cells.
 - + ISB 2001, a BCMA and CD38 dual targeting T cell engager, demonstrates superior cytotoxicity relative to teclistamab in the samples of patient relapsing from CD38 and BCMA targeted immunotherapies.
- 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. IGI 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.
- In April 2024, IGI received approval from DCGI in India to expand the clinical Phase 1 study into India.
- The bulk drug substance is manufactured in La Chaux-de-Fonds, Switzerland.



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ISB 1442 (CD38 X CD47 BEAT® BISPECIFIC ANTIBODY)

- This first-in-class biparatopic bispecific antibody targeting CD38 and CD47 was generated by scientists in IGI's laboratories in Lausanne at the Biopole life sciences campus.
- ISB 1442 is designed to kill CD38-expressing tumor cells through inhibition of the CD47-SIRP α 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 6 (450 mg SQ weekly) in both countries. The DCGI in India has recently approved the study and enrollment in India was recently initiated.
- IGI is also considering the potential development of 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. Specifically, data showed the rationale for advancing to a clinical study in relapsed/refractory AML ([link](#)). ISB 1442 induces killing, including ADCP and ADCC, in AML cell lines in multiple in vitro assays. ISB 1442 also showed 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 in IGI's manufacturing plan in La Chaux-de-Fonds, Switzerland.
- Additional information on the ongoing Phase 1 was presented at the 2023 ASH Annual Meeting. Overall, treatment of low grade (1 or 2) CRS and mostly resolved within one day. No neurotoxicity events have been observed to date. No signal infections or anemia. <https://www.hematology.org/meetings/annual-meeting/abstracts>
 - + Proof of Mechanism in patients was declared based on increased macrophage-related markers among the other biomarkers changes observed.
 - + Dose escalation is ongoing.



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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 is available for partnerships due to pipeline strategic reprioritization. The out-licensing of this asset will allow a potential partner to continue the escalation/expansion now that clinical proof-of-mechanism and proof-of-concept have been established with acceptable immunogenicity on par with other bispecifics.
 - + The Database has been locked and all sites closed by Q2, 2024. The Clinical Study Report is targeted for H2, 2024.
 - + The first partial response in this study was observed in Cohort 109 intravenous (dose level 8 µg/kg) and additional 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 Phase 1 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 2023 American Society of Hematology (ASH) Annual Meeting in December ([link](#)) with data cut-off October 27, 2023:
 - + 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
 - + Further dose-escalation (to 32 and 64 µg/kg) is warranted based on the manageable safety profile, anti-myeloma activity observed, and supported by PK profile as well as T-cell activation biomarkers.
- ISB 1342 was granted Orphan Drug Designation for multiple myeloma by the U.S. Food and Drug Administration.
- The bulk drug substance is manufactured in IGI's manufacturing plant in La Chaux-de-Fonds, Switzerland.



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CASITAS B-LINEAGE LYMPHOMA B (CBL/B) PROGRAM

- Casitas B-lineage lymphoma b (Cbl/b) is an E3 ubiquitin ligase that has been identified as a key inhibitor of T cell activation in the absence of CD28 co-stimulation and considered as intracellular check point. Through a complex interaction of signal transducers, Cbl-b inhibits T cell transcriptional activity and promotes immune tolerance across innate and adaptive immunity. As an intracellular master regulator, Cbl/b inhibition may represent a more specific and efficient route toward broad immune activation regardless of upstream checkpoint signalling (i.e., PD-1, CTLA-4). Substantial preclinical evidence supports Cbl/b inhibition as a potent driver of anti-tumor immunotherapy.
- GRC 65327 is the clinical candidate. It has been identified as a novel nanomolar potent, selective, and orally bioavailable candidate with intuitive medicinal chemistry and computational chemistry approaches.
- IND-enabling studies are ongoing. The clinical formulation will be ready by mid-October 2024.
- The submission to the Drugs Controller General of India (DCGI) is planned at the end of CY24 and the FIH trial is expected to start in early 2025 and enroll patients with relapsed/refractory solid tumor indications.

Autoimmune Diseases

IGI 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) and its follow-on molecule ISB 830-X8, was licensed to Astria Therapeutics in October 2023. Telazorlimab is an OX40 antagonist that successfully completed a Phase 2b study in moderate to severe atopic dermatitis in 2021. Both compounds have potential across a range of autoimmune diseases.



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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. <u>Dosing of participants in the Phase 1 study was announced by Almirall in September 2022.</u>
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.
	Other autoimmune diseases, including Rheumatoid Arthritis		U.S. IND for Rheumatoid Arthritis and other autoimmune indications is active.

ISB 880 / ALM27134 (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
- For more information on this asset, please visit almirall.com

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).
- For more information, visit <https://IGInnovate.com/contact/>.



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