November 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 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 200 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, Executive Director 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

ROBERTO GIOVANNINI, Ph.D.
Chief Process & Manufacturing Officer

DEAN THOMAS, LLM
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

Pfizer, Allogene, Bristol Myers Squibb, Roche, Legend Biotech, Novartis, sanofi, Aurigene Oncology, Debiopharm, Boehringer Ingelheim, glenmark

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 platform[1] 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

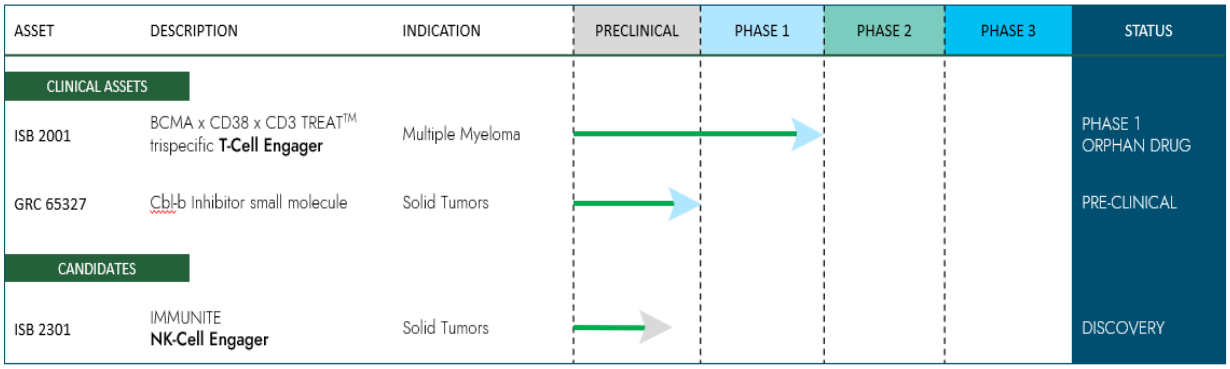
Collaboration propels innovation

Oncology Pipeline

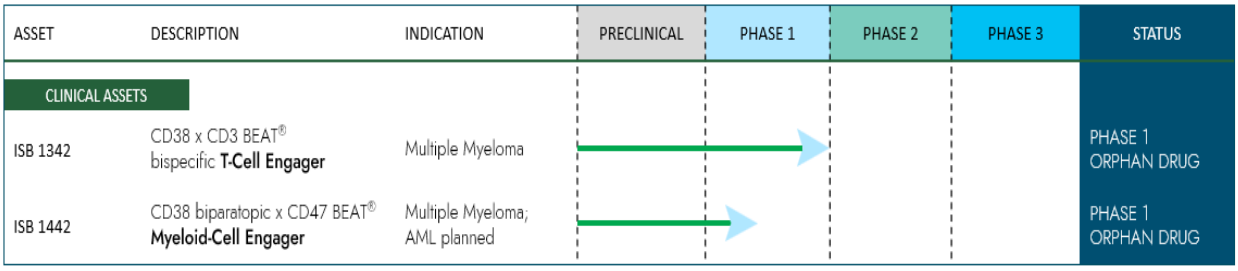
IGI's multispecific antibody pipeline consists of four assets. This includes ISB 2301 which is in the discovery stages for application in solid tumors and ISB 2001, ISB 1342 and ISB 1442, each of which are orphan drug designated by the U.S. Food and Drug Administration (FDA) and currently in Phase 1 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 classes and recently working on protein degradation. Updates of note in the last quarter are outlined below:

+ The preclinical data package for ISB 2001 was recently published in Nature Cancer
+ ISB 2001 abstract was accepted at ASH2024 for an oral presentation of the first clinical data in the section of: Multiple Myeloma: Pharmacologic Therapies: Into the Future: New Drugs and Combinations in Multiple Myeloma
+ The ISB 2001-101 clinical Ph1 study is enrolling patients rapidly and a protocol amendment was recently approved to explore two additional higher doses.
+ ISB 1442 abstract was accepted at ASH2024 for a poster presentation of the clinical data
+ The IND for the clinical candidate GRC 65327 was submitted to DCGI on October 30, 2024
+ ISB 1342 is in active discussions for out licensing in oncology and non-oncology

Oncology-Focused Development Pipeline to Drive Long-Term Value Growth



Partnering-Ready Assets to Accelerate Short-Term Value Creation



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.
- 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.
- At the AACR Annual Meeting in 2024, an oral presentation showcased the results of ISB 2001 anti-myeloma activity ex-vivo in bone marrow aspirates from patients who have relapsed after CD38 and BCMA targeted therapies. ISB 2001 demonstrated superior cytotoxicity relative to teclistamab in the samples of patient relapsing from CD38 and BCMA targeted immunotherapies.
- The preclinical data package for ISB 2001 was recently published in Nature Cancer and shows that:
    + ISB 2001 can overcome resistance mechanisms by dual tumor targeting via binding and cytotoxicity of tumor cells with low expression of CD38 and/or BCMA.
    + ISB 2001's architecture is optimized to support robust killing of tumor cells while limiting CD38 on-target, off-tumor activity.
    + ISB 2001 demonstrated increased killing of tumor cells compared to BCMA-targeted T cell engagers in vitro, in vivo and ex vivo; induced complete tumor regression in humanized mouse models; and demonstrated superior potency compared to standard combination of therapies.
- The advantages of the trispecific ISB 2001 antibody was highlighted in the accompanying News and Views article written by S.R. Ruuls and P.W.H.I. Parren and was further emphasized in a Fierce Biotech article in which the mode of action of ISB 2001 and promise of IGI's BEAT® platform were described by IGI's CEO, Cyril Konto.
- At the recent Festivals of Biologics in Basel and at PEGS Europe in Barcelona, the antibody engineering, pharmacology and cell line development of ISB 2001 were presented in several presentations.
- 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 r/r MM. In April 2024, IGI received approval from DCGI to expand the clinical Phase 1 study into India. The phase 1 study is divided into a dose escalation part and a dose expansion part, with the latter being designed to meet the goals of FDA Project Optimus. First patient was dosed in November 2023 and the trial is now active in US, Australia and India with expansion scheduled to initiate in H1, 2025.
- In July 2023, ISB 2001 received Orphan Drug Designation from the FDA for the treatment of MM.
- IGI declared clinical Proof-of-Concept for ISB 2001 in r/r MM in July 2024, based on the data generated in the ongoing dose escalation phase, and has decided to accelerate the development of this asset.
- The first clinical data of the ongoing ISB 2001 trial will be presented in an oral presentation at ASH 2024 on December 9th, 2024 (press release).

Collaboration propels innovation

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-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, the U.S. Food and Drug Administration and the Drug Controller General of India, IGI is conducting a Phase 1 / 2 first-in-human dose-finding study of ISB 1442 in relapsed/refractory multiple myeloma and the dose escalation phase is active in all three countries.
- 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 February 2023.
- In addition to the information presented at the 2023 ASH Annual Meeting, more data will be presented at ASH 2024
- Proof of Mechanism in patients was declared based on increased macrophage-related markers among the other biomarkers changes observed.
- On November 1st, 2024, the decision was made to terminate the ISB 1442-101 study due to portfolio prioritization and ongoing development challenges with anti-CD47 therapeutics.

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 paused due to pipeline strategic reprioritization and the asset is available for licensing in oncology (proof-of-mechanism and proof-of-concept have been established in RRMM, with acceptable immunogenicity on par with other bispecifics) as well as autoimmune indications, observations of depletion of B cells with the CD38 targeting has been observed during the clinical trial.
  - The Database was locked in March 2024 and all sites closed. The Clinical Study Report is targeted for Q4, 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.

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 and NK cells activation in the absence of CD28 co-stimulation, regulate immune cells activity in PD-1, CTLA4, TIGIT etc positive cells. As an intracellular master regulator, Cbl/b inhibition may lead to robust immune cells activation in suppressed tumor microenvironment and induce strong single agent activity.

- The IND for the clinical candidate GRC 65327 was submitted to DCGI on October 30, 2024. The meeting with the oncology subject matter expert committee (SEC) is expected to happen on November 27, 2024, and the permission (DCGI CT-NOC) to initiate the clinical trial is expected before the end of December 2024.

- Activities for analytical tech transfer for API (drug substance) initiated for Ankleshwar plant for GMP batch manufacturing. GMP API batch manufacturing activities on-going at GLS. The drug substance and drug product for the Phase 1 clinical trial are expected by Q1 CY2025.

- A poster entitled 'GRC 65327, a novel small molecule selective oral Cbl-b inhibitor as IO therapy for patients with solid tumors' was presented at Society for Immunotherapy of Cancer (SITC) on 9 November 2024.

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 are 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.

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.	
	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. Almirall initiated a Phase I study in 2022, to evaluate the safety, pharmacokinetics, pharmacodynamics and clinical activity of the licensed asset.

- 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.

- Astria Therapeutics disclosed in their 10-Q form for the quarterly period ended March 31, 2024 that they anticipate submitting an investigational new drug application, or IND, to the FDA for STAR-0310 for the treatment of AD by year-end. If the IND clears, Astria Therapeutics anticipate initiating a Phase 1a clinical trial of STAR-0310 in healthy subjects in the first quarter of 2025 and reporting initial results from the Phase 1a clinical trial in the third quarter of 2025, including PK and PD data and early signals on safety and tolerability. Assuming positive results from the Phase 1a clinical trial, Astria Therapeutics plan to initiate a Phase 1b clinical trial of STAR-0310 in patients with AD in the second half of 2025 and would expect to report results from such trial in the second quarter of 2026.

- 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/.

Collaboration propels innovation