February 2025 Update

About IGI

IGI Inc., a global fully integrated clinical-stage biotech company developing multispecifics™ in oncology, with the aim to accelerate new drug discovery in cancer treatment. IGI combines research and development proficiencies in novel biologics with those in new small molecules to continue developing cutting-edge therapy solutions that treat hematological malignancies and solid tumors. Harnessing the combined proficiency of over 100 scientists and a robust pipeline of novel molecules, IGI looks to leverage the capabilities of its centers of innovation spread across the USA, Switzerland and India to propel Innovation. For more information, visit https://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 150 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.

The proprietary BEAT® technology platform[1] is one of the bases 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.

Oncology Pipeline

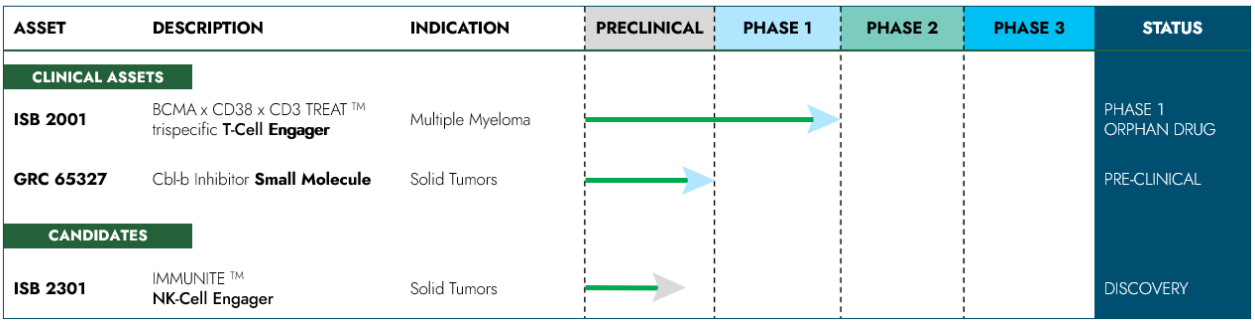
IGI's multispecific antibody pipeline consists of three assets. This includes ISB 2301 which is in the discovery stage for application in solid tumors, ISB 2001 and ISB 1442, which has orphan drug designated by the U.S. Food and Drug Administration (FDA). ISB 2001 is currently in Phase 1 clinical

[1] Bispecific Engagement by Antibodies based on the TCR

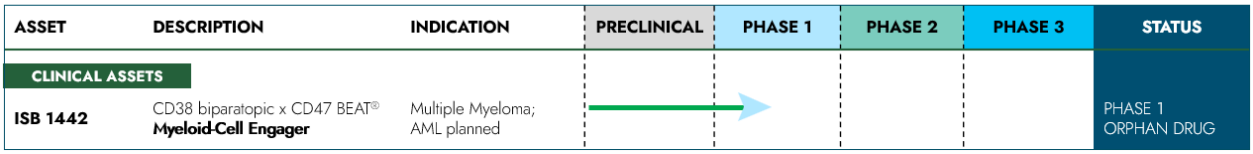
study for relapsed/refractory multiple myeloma. ISB 1442 development has been discontinued and the asset prepared for out-licensing. GRC 65327 (Cbl-b inhibitor) is awaiting regulatory approval for initiating clinical development in India for solid tumors. Updates of note in the last quarter are outlined below:

+ ISB 2001 abstract was accepted at ASH2024 and presented in 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 ISB 2001 ASH Presentation.
+ ISB 2001 continues to enroll fast in the escalation phase and expansion on track to start in H1, 2025.
+ ISB 1442 abstract was accepted and presented at ASH2024 as a poster presentation of the clinical data.

Oncology-Focused Pipeline to Drive Long-Term Value Growth



Partnering-Ready Asset 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 Oncology Candidates in Development

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 in 2024 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 Festivals of Biologics in Basel in October 2024 and at PEGS Europe in Barcelona in November 2024, the antibody engineering, pharmacology and cell line development of ISB 2001 were presented in several presentations.
- In April 2023, IGI 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 the 9th and last dose level being evaluated in the dose escalation phase. The dose expansion is scheduled to be initiated 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 was presented in an oral presentation at ASH 2024 on December 9th, 2024 (press release) and showed:
  - + ISB 2001 is well tolerated with no dose limiting toxicities up to 1200 µg/kg, low grade cytokine release syndrome, no neurological Adverse Events or ICANs, low infection and hematological toxicity rates, no Adverse Events leading to discontinuation.
  - + Early, deep and sustained responses were observed across effective dose levels (DL3 to DL7) with antimyeloma activity from 50 µg/kg (MRD negative sCR) and higher
  - + Overall Response rate (ORR) was 83% (22% Complete response (CR) or better, 50% Very Good Partial Response (VGPR) and 11% Partial Response (PR). The ORR was 75 % in patients pretreated with CAR-T or bispecific T cell engagers and 90 % in patients who had not been treated with T-cell directed therapies.
  - + Dose proportional PK with long half-life supports less frequent dosing and T cell activation observed at effective doses

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 were presented at ASH 2024 and a publication describing the molecular architecture of the molecule was published in mAbs.
- 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 discontinue the ISB 1442-101 study due to portfolio prioritization and make this program available for licensing.

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 the Drugs Controller General of India (DCGI) on October 30, 2024. The meeting with the oncology subject matter expert committee (SEC) happened on December 13, 2024. Queries from DCGI SEC received on January 7, 2025, were addressed on January 9, 2025. The committee recommended the approval of the Phase 1 protocol with the condition of initiating the study with a 10 mg dose cohort and submitting data of the first subject of the same cohort before initiation into the second subject to the Central Drugs Standard Control Organization (CDSCO) for further deliberation by the committee. A formal approval of NOC is awaited.
- Drug substance and drug product manufacturing activities will be initiated before the Phase 1 study starts.
- An abstract entitled 'Discovery of GRC 65327: A Best-in-Class, Selective and potent Cbl-b E3 ligase inhibitor for the treatment of advanced solid cancers' was submitted to the AACR 2025 and confirmation expected by mid-February 2025.
- 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 is 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.	
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ISB 880 / ALM27134 (IL-1RAP ANTAGONIST)

- IGI 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. IGI 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)

- IGI entered an exclusive global licensing agreement for ISB 830 and its follow-on ISB 830-X8 with Astria Therapeutics in October 2023.

- On January 23, Astria announced initiation of a phase 1a trial of STAR0310, a potential best-in-class monoclonal antibody OX40 antagonist for the treatment of atopic dermatitis. This would trigger the payment of a development milestone to IGI upon dosing of the first human subject.

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