# August 2025 Update

## About Ichnos Glenmark Innovation (IGI)

IGI, Inc. is a global, fully integrated clinical-stage biotechnology company focused on developing innovative biologics in oncology. Headquartered in New York, NY, IGI is advancing a robust pipeline of novel, first-in-class Multispecifics™ aimed at addressing complex diseases and treating patients holistically. Powered by its proprietary BEAT® technology platform, IGI is committed to delivering breakthrough, curative therapies to improve and extend the lives of patients battling hematological malignancies and solid tumors. For more information, visit IGInnovate.com.

At IGI, there are three engines of innovation. Company headquarters in the United States in New York City, a biologics research center in Lausanne, Switzerland, and early discovery center in Navi Mumbai, Maharashtra, India.

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.

[1]Bispecific Engagement by Antibodies based on the TCR

# Oncology and Immunology Pipeline

IGI's multispecific antibody and small molecule immune modulator pipeline for oncology, consists of three assets. This includes ISB 2001 (BCMA x CD38 x CD3), which received orphan drug and fast track designations by the U.S. Food and Drug Administration (FDA) and is currently in dose expansion Phase 1 Part 2 clinical study for relapsed/refractory multiple myeloma (TRIgnite-1). GRC 65327 (Cbl-b inhibitor small molecule) is awaiting regulatory approval for initiating clinical development in India for solid tumors. ISB 2301 (NK-Cell Engager) is in the discovery stage for application in solid tumors. Updates of note in the last quarter are outlined below:

+ In a major strategic milestone (press release), IGI entered into a global licensing agreement with AbbVie for its lead asset, ISB 2001, a first-in-class trispecific T cell engager currently in Phase 1 clinical development for relapsed/refractory multiple myeloma. Under the terms of the agreement, AbbVie will receive exclusive rights to develop, manufacture, and commercialize ISB 2001 across North America, Europe, Japan, and Greater China, for oncology and autoimmune diseases. Subject to regulatory clearance, IGI will receive an upfront payment of $700 million and is eligible to receive up to $1.225 billion in development, regulatory, and commercial milestone payments, along with tiered, double-digit royalties on net sales

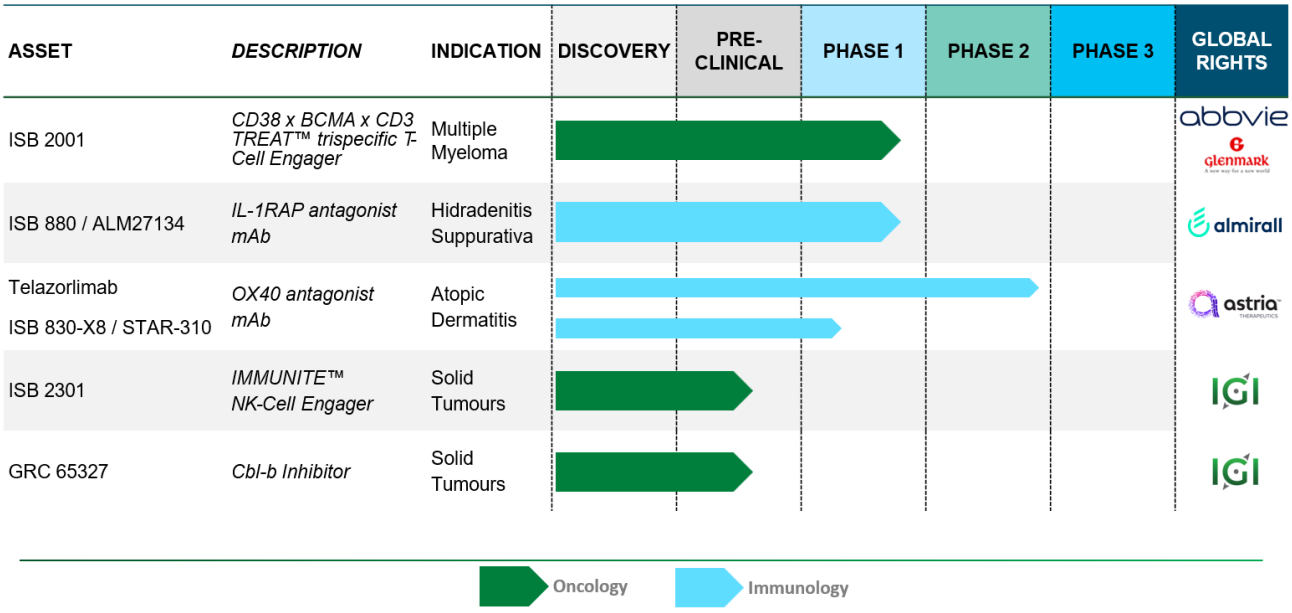
+ ISB 2001 Phase 1 study Part 2 (Dose Expansion) study initiated in Apr 2025 is enrolling rapidly

+ ISB 2001 EU CTA has been accepted by EU HA on 17 June 2025

+ ISB 2001 clinical abstract has been accepted at multiple conferences in H1 2025 and new clinical data has lately been presented in June 2025 at ASCO2025 in the Rapid Oral Abstract Session, followed by Poster Presentation at EHA2025 (encore) also in June 2025

+ During CY 2024-2025 IGI initiated a transitioning from in-house CMC manufacturing to a CDMO model to improve flexibility and scalability supporting the development of their assets from early to late phase development. The transition was fully completed by June 2025

## Diversity of Immune Cell Engagement and Indications Across Hematologic and Solid Tumours




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.
- 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. In June 2025, IGI received EU CTA acceptance to expand the trial in Europe (France, Italy, Spain, and Norway). The phase 1 TRIgnite-1 study is divided into a dose escalation (part 1) and a dose expansion (part 2), 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 dose expansion initiated in April 2025. Enrollment start in Europe is targeted for end of Q3 2025.
- In July 2023, ISB 2001 received Orphan Drug Designation from the FDA for the treatment of MM and in April 2025, FDA also granted Fast Track designation to ISB 2001 (press release).
- 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 decided to accelerate the development of this asset.

- At the **American Society of Hematology (ASH) Annual Meeting in December 2024**, IGI presented the first clinical results from its Phase I dose escalation TRIgnite-1 study:
  - **ORR: 83%** (n=18) at the therapeutic dose levels in a heavily pre-treated R/R MM population (median 6 prior lines of therapy, including CAR-Ts and bispecifics)[1]
  - **CR/sCR: 22%** (n=18) deep responses were seen across patients with or without prior BCMA targeted and/or T Cell Directed Therapies (bispecific and CAR-T)[1]
  - **Safety**; Mild CRS, No ICANS, well manageable neutropenia and infections, enabling continuation of study treatment[1]

- By **American Society of Clinical Oncology (ASCO) 2025**, expanded data from the TRIgnite-1 study dose escalation cohorts showed:
  - **ORR: 79%** (n=33) at the therapeutic dose levels in a heavily pre-treated R/R MM population (median 6 prior lines of therapy, including patient who failed prior CAR-Ts and bispecifics)[2]
  - **CR/sCR: 30%** (n=33), deep responses were seen across patients with or without prior BCMA targeted and/or T Cell Directed Therapies (bispecific and CAR-T)[2]
  - **Robust activity across key subgroups**: Effective regardless of prior CAR-T, TCEs, BCMA therapies, CD38-refractoriness, extramedullary disease, or high-risk cytogenetics, and ORR in subject with no prior CAR-T and/or TCE was 84%.[2]
  - **Durability of response**: Median DOR not reached at 9-month median follow-up[2]
  - **Safety**; Mild CRS, a single Grade 1 ICANS, well manageable neutropenia and infections, enabling continuation of study treatment[2]
  - **Pharmacokinetics:** Dose-proportional PK with a median half-life of 17 days supports less-frequent dosing[2]

[1] Quach H. et al., ASH2024, Oral Presentation
[2] Quach H. et al., ASCO2024, Oral Presentation

## GRC 65327: 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. 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 second set of queries from DCGI SEC received on March 21, 2025, were addressed on April 23, 2025. A third set of questions from DCGI SEC received on 4 June 2025 followed by face-to-face interaction on 15 July 2025. The amendment to protocol addressing questions is currently ongoing and it will be completed by 18 August 2025. A formal approval of NOC is awaited.

# Overview of Immunology Candidates in Development

- 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. Almirall completed Phase I single and multiple ascending doses in healthy volunteers, presenting the results at the recent AAD meeting. The antibody showed a favorable safety and tolerability profile, along with a low immunogenicity risk, supporting further development for treating immune-mediated inflammatory skin disorders. A Phase II study in Hidradenitis Suppurativa is planned for late 2025.

- The second antibody, ISB 830 (telazorlimab) and its follow-on molecule ISB 830-X8 (STAR-0310), 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. ISB 830-X8 (STAR-0310) is in development for the treatment of AD and potentially other indications. Phase 1 trial was initiated in the first quarter of 2025.

# 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 830-X8 (STAR-0310) | Atopic Dermatitis | Phase 1a | Next-generation version of ISB 830 with extended half-life and expected optimized affinity and safety profile. Phase 1 initiated in the first quarter of 2025. |

## 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. IGI received a milestone payment in March 2025.

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 (STAR-0310) 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. The phase 1a trial in healthy subjects started earlier this year and triggered the payment of a milestone to IGI in Q1 2025.

For more information on this asset, please visit astriatx.com