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Advancing Affordable Indigenous Immunotherapies

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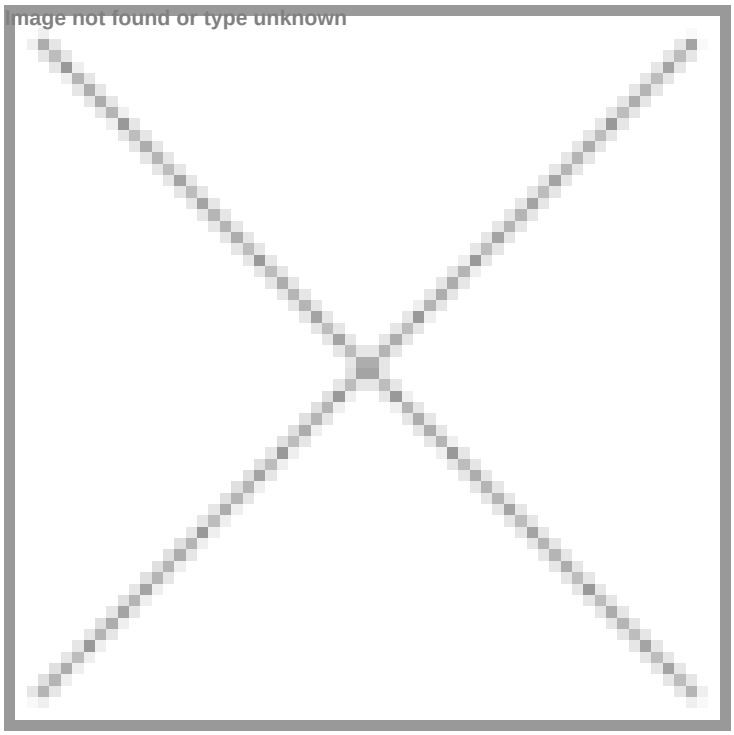
Immunotherapy is transforming modern medicine by offering targeted, effective, and less toxic treatments for cancer, autoimmune disorders, and infectious diseases. As global demand for these therapies grows, India is rapidly positioning itself as a key player in their development and large-scale production. We shall take a deep dive into India's immunotherapy research pipeline—what's driving it, what's holding it back, and whether the country can truly emerge as a global hub for affordable immunotherapy.



India is emerging as a key player in global immunotherapy, backed by strong government support, skilled talent, and growing biotech capacity. A major milestone came in 2023 with the approval of NexCAR19, the country's first indigenous CAR-T therapy. This was followed in January 2025 by the approval of Qartemi from Bengaluru-based Immuneel Therapeutics—a CAR-T cell therapy for patients with relapsed or advanced B-cell Non-Hodgkin Lymphoma—marking India's second approved CAR-T product.

"From 2015 to 2025, the market is projected to grow from $0.5 billion to $4 billion. This momentum is being driven by research efforts sparked by COVID-19, innovations in cancer-focused immunotherapies and biosimilar products, as well as the growing adoption of CAR-T cell technologies and AI-based diagnostic tools—solidifying its role as an emerging centre for cutting-edge biologics and personalised medicine. However, compared to global leaders like the U.S., EU, and China, India is still in a developmental phase, with several critical capabilities under maturation," said **Shalini Tanwar, Team Lead-Immunotherapy, Aurigene Pharmaceutical Services**.

There has been a flurry of activity in India's immunotherapy landscape in recent months. In June 2025, Zydus Life Sciences acquired rights to Agenus' BOT/BAL cancer immunotherapy for India and Sri Lanka. Earlier, in March, Delhi-based Cellogen

Therapeutics secured a patent for what is reportedly the world's first indigenously developed bi-specific 3rd generation CAR-T cell therapy. In January, CytoMed Therapeutics partnered with SunAct Cancer Institute to initiate a proposed phase 2 trial of Gamma Delta T cell therapy for solid tumours. This followed Mankind Pharma's December 2024 collaboration with Innovent Biologics to bring the PD-1 inhibitor sintilimab to India.

Immunotherapy research pipeline

Most CAR?T products have roots in public research. *NexCAR19*, India's first approved CAR-T product, is a prime example, developed by IIT Bombay in collaboration with Tata Memorial Centre. *Qartemi*, launched by Immuneel Therapeutics, was licensed from Hospital Clínic de Barcelona, highlighting the role of international technology transfer in advancing Indian immunotherapy. Similarly, IIT Kanpur is set to transfer several gene therapy assets to Laurus Labs through an in-licensing arrangement, backed by a research grant to support preclinical development.

Several key research projects funded by the Department of Biotechnology (DBT), Government of India have been instrumental in building the country's immunology and cell therapy pipeline, from advancing CAR-T cell technologies to pioneering gene-editing strategies and developing indigenous manufacturing capabilities. Given this deep academic foundation, it's only fair to take a closer look at some of the DBT funded research projects powering India's next generation of immune-based therapies.

anti-CD19 CAR-T cell therapy: This, India's first indigenously developed CAR-T cell therapy, *talicabtagene autoleucel* (Tali-cel), is currently undergoing a multi-centre phase II trial involving 50 paediatric patients with relapsed/refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL). Developed through a project funded by Tata Memorial Centre, the therapy was initially evaluated in a phase I/Ib open-label single-arm study. This early-stage trial demonstrated a favourable safety profile, manageable toxicities, and promising durable remissions in heavily pretreated patients. A key objective of the programme is to provide an affordable and scalable alternative to costly global CAR-T treatments, which remain largely inaccessible in low- and middle-income countries due to high manufacturing costs, limited local production, and clinical management challenges. Based on findings from the initial study, a recommended dose of 5–10?×?10? CAR-T cells/kg was identified to balance efficacy and safety. The product is being manufactured and co-sponsored by ImmunoACT, with the ongoing Phase II trial aimed at supporting regulatory registration.

Unlike traditional therapies reliant on costly, frequent Factor VIII replacement, this first-in-human trial involved autologous haematopoietic stem cells (HSCs) transduced with a lentiviral vector carrying the Factor VIII gene—an alternative to the widely used AAV-based systems. The therapy offers a long-term, potentially curative approach to a disorder for which India bears the world's second-largest burden (~1.36 lakh cases). The results, published in the *New England Journal of Medicine* , mark a significant milestone for accessible gene therapy in low-resource settings.

Human gene therapy for Hemophilia A: India's first gene therapy using a lentiviral vector for severe Hemophilia A has demonstrated landmark results in a single-centre study led by the Centre for Stem Cell Research (CSCR) at CMC Vellore, supported by the Department of Biotechnology (DBT). All five participants achieved zero annualised bleeding rates over a cumulative 81-month follow-up, with sustained Factor VIII production, eliminating the need for repeated infusions.

Gene editing based strategies for treatment of Thalassemia and Sickle Cell Disease (SCD): Another pioneering project initiated by the CSCR, Vellore, and funded by DBT focuses on applying genome editing technologies to treat ?-haemoglobinopathies, including SCD and ?-thalassemia. Leveraging the precision of CRISPR/Cas9, the project aims to modify a patient's own HSCs to serve as a renewable source of healthy red blood cells following autologous bone marrow transplantation.

The therapeutic strategy is centred on reversing the fetal-to-adult hemoglobin switch, thereby increasing fetal haemoglobin (HbF) production—known to mitigate clinical symptoms in both SCD and ?-thalassemia. The team is targeting BCL11A, a key repressor of gamma-globin, along with other regulatory regions associated with Hereditary Persistence of Fetal Haemoglobin (HPFH) mutations. This approach not only aims to reduce sickled haemoglobin in SCD patients but also compensates for defective beta-globin in ?-thalassemia by promoting the expression of gamma-globin.

Unlike hydroxyurea or HDAC inhibitors, this gene-editing platform offers a potentially curative solution by permanently reprogramming the patient's own stem cells. The CSCR-DBT collaboration represents a significant step forward in developing affordable, gene-based therapies tailored to Indian patients with haemoglobin disorders.

CAR-T cell therapy expressing BCMA-CAR and in vivo validation in the mouse model of multiple myeloma: This collaborative DBT-funded initiative, led by IIT Bombay's Department of Biosciences & Bioengineering in partnership with Tata Memorial Centre and ImmunoACT, focuses on developing a cost-effective, humanised CAR-T cell therapy targeting B-

cell maturation antigen (BCMA) for relapsed or refractory multiple myeloma. Using an in-house humanisation platform, the team designed four humanised BCMA CAR constructs (h1–h4), with h2 emerging as the most promising candidate. Preclinical studies demonstrated successful lentiviral production, robust in vitro CAR-T cell expansion, and optimal binding affinity for h2. In mouse xenograft models, h2-CAR T cells achieved complete tumor elimination, extended survival (median >123 days), and showed no systemic toxicity or organ damage. These findings mark a critical milestone in India's immunotherapy pipeline and position the h2-CAR candidate for potential translation into first-in-human clinical trials.

CD19 CAR-T Cell Therapy IMN-003A in B Cell malignancies: Varnimcabtagene autoleucel (IMN-003A), developed by Immuneel Therapeutics, is India's first industry-led CD19-directed CAR-T cell therapy for relapsed/refractory B-cell malignancies (RR BCM). This autologous product, which incorporates a 4-1BB co-stimulatory domain and a novel non-FMC63 A3B1 binder, is manufactured in India. Clinical development included a preclinical and Phase 1 study in Spain and a multicentre Phase 2 study (IMAGINE) in India. The therapy demonstrated a manageable safety profile with durable, deep responses and no severe neurotoxicity. The project is supported under the Biotechnology Industry Partnership Programme (BIPP) of the DBT, underscoring public-private efforts to advance indigenous cell therapies.

Single-Cell RNA-seq analysis of hCMV-specific T Cells: In a study published in Immunology, the Immunogenomics team at The National Institute of Immunology (NII) has characterised rare human Cytomegalovirus (hCMV) antigen specific memory T cells in an unbiased manner using high throughput single-cell multi-omics. The study shows that the hCMV-specific memory T cells are highly heterogeneous and consist of different flavors of long-term and effector memory T cells. The study can serve as a knowledge base for designing vaccines and therapeutic strategies to control hCMV infections, especially in immunocompromised individuals (patients undergoing organ transplant/chemotherapy for cancers, etc.), and infants born to hCMV-seropositive mothers.

GMP-grade plasmid and viral vector manufacturing: The First-in-India GMP-grade plasmid and viral vector manufacturing initiative aims to establish a domestic, high-quality production facility to support CAR-T cell therapy and other gene therapy applications. Backed by the DBT, this project addresses a critical infrastructure gap by enabling the local manufacture of clinical-grade plasmids and viral vectors—essential components for gene modification in cell therapies. The initiative is expected to accelerate indigenous development, reduce dependency on imports, and support clinical translation of advanced therapies in India, especially in oncology and rare genetic disorders.

Preclinical-grade CAR-T manufacturing process: The project titled 'Chimeric Antigen Receptor (CAR) T-Cells Technology for Cancer Treatment: Development of a Pre-clinical Grade Manufacturing Process as per Industry Standards' falls under the PACE (Promoting Academic Research Conversion to Enterprise) scheme of DBT. This initiative focuses on developing a robust and standardised pre-clinical manufacturing process for CAR-T cells to meet industry-grade requirements. The goal is to bridge the gap between academic research and commercial-scale production by establishing scalable, reproducible, and quality-controlled protocols. By doing so, the project aims to create a foundation for translational research and future clinical applications of CAR-T therapies developed indigenously in India.

Anti-Nipah monoclonal antibody (mAbs): A specialised programme on the discovery and development of novel anti-Nipah mAbs with an aim to create low-cost mAb products was initiated with BRIC-Translational Health Science and Technology Institute (THSTI), Faridabad under GCI. BRIC-THSTI in collaboration with BRIC-RGCB has invented novel monoclonal antibodies from B cells of recovered individuals infected with Nipah virus during October 2023 Kerala outbreak. Engineered spike G and F antigens of Nipah virus were used to sort and clone single memory B cells.

Antigen-specific B cell clones were then screened to identify ones that bind very strongly to Nipah F and G proteins and also able to neutralise a panel of pseudoviruses encoding F and G genes of Indian, Bangladeshi, Malaysian and Flying Fox Bat origins. BRIC-THSTI also established pseudovirus neutralisation assay in this period which can be useful for vaccine studies by other researchers as well. Two top neutralising monoclonals have been identified for further development as IND products through industry-academy collaboration. This is the very first invention from India and any LMIC.

Universal CAR-T cells: All existing CAR-T cell products available globally are autologous (made with same patient-derived T lymphocytes) to avoid severe alloimmune rejection due to a mismatch of MHC between the donor and the recipient. Various studies have been implemented through the DBT's support to advance CAR-T cell therapy for a broader spectrum of cancers and reducing therapy related toxicities.

One such study aims to develop ‘off-the shelf’ or ‘universal’ CAR-T cells from healthy donors using CRISPR/Cas9 technology with specific modifications in MHC genes. Concurrently, the project focused on designing and engineering “Inducible CARs” to mitigate cytokine release syndrome, a common adverse event associated with CAR-T cell therapy. Two constructs were designed, incorporating advanced features such as syn-NOTCH domains for context-specific activation and dual-plasmid systems enabling tight regulation of IL-6 secretion. T cells were efficiently isolated using CD4 and CD8 magnetic beads, and a mCherry-luciferase expressing Raji reporter cell line was developed to evaluate the efficacy of CAR-T cells

IL-15 Cytokine for cancer immunotherapy: Another promising lead is a Chimeric Interleukin-15 (IL-15) developed using tools of genetic engineering. IL-15 is a cytokine which is a multifunctional cytokine that targets many cell types and connects the innate with the adaptive immune system. Globally, among the cytokines, IL-15 has been identified as a top candidate for cancer immunotherapy. However, the major limitations in developing IL-15 as a therapeutic agent are its short-half life and poor bioavailability. To overcome these limitations, stable chimeric IL-15 (IL-15 coupled to IgG2 constant heavy chain) was developed with an increased half-life of 40 hours. Despite the development of a stable chimeric IL-15 with extended half-life and bioactivity, its full therapeutic potential remains to be explored. Current studies are in progress to elucidate 3D structure to investigate its role in combination therapy with checkpoint inhibitors for tumor regression and relapse prevention, as well as its potential as an adjuvant for formation of memory T and B cells. An Indian patent has been granted in 2024.

In 2024–25, DBT advanced several innovative cancer immunotherapy projects, including dual CAR-T cells, NK cell-based therapies, IL-15–enhanced CAR-T, oncolytic viruses, and RNA therapeutics. It also initiated Virtual Network Centres focused on off-the-shelf and inducible CAR-T platforms, glioblastoma-targeted T-cell therapies using non-genetically engineered MSCs, and a dedicated Cancer Immunotherapy Network to design affordable, indigenous cell-based therapies for Indian patients.

Key challenges

Despite the growing momentum, India faces several critical challenges that must be addressed to achieve commercial-scale readiness in immunotherapy manufacturing.

“One of the foremost barriers is the high capital investment required to establish GMP-compliant facilities. While biotech hubs such as Hyderabad and Bengaluru are witnessing infrastructure growth, India still lags behind the scale and technological sophistication seen in the U.S., EU, and increasingly, China. The financial burden of setting up advanced manufacturing units—including infrastructure, equipment, and quality systems—is particularly daunting for startups and small-to-medium enterprises (SMEs), which often struggle to secure funding due to long return-on-investment cycles and limited access to biotech-focused venture capital,” said Shalini.

Another significant constraint is the limited domestic availability of critical raw materials and enabling technologies. The production of immunotherapies relies heavily on imported reagents, viral vectors, and cell lines, making the supply chain both fragile and costly. The absence of a robust local ecosystem for these components creates bottlenecks that hinder scalability and responsiveness.

“Regulatory complexity further compounds these challenges. Navigating approvals from multiple agencies such as the Central Drugs Standard Control Organisation (CDSCO), DBT, and the Indian Council of Medical Research (ICMR) can be time-consuming and lacks harmonisation. While efforts are underway to streamline biologics approval pathways, India’s regulatory framework is still evolving. In contrast, regulatory bodies in the U.S. and EU benefit from decades of experience and integrated innovation ecosystems that facilitate faster approvals and clearer guidance for novel therapies like CAR-T and gene editing,” said Shalini.

The skill gaps in specialised areas also poses a barrier. Although India has a strong foundation in bioprocessing and engineering, expertise in niche domains such as viral vector production, gene editing, and advanced analytics remains limited. Industry-academia collaboration for hands-on training and workforce development is still in its early stages and needs significant scaling.

“Logistical challenges, particularly in cold chain and last-mile delivery, remain a concern. Immunotherapies require stringent temperature control, which is difficult to maintain in rural and remote regions. Fragmented logistics networks and the lack of real-time monitoring systems increase the risk of compromising product integrity during transport,” said Shalini.

She further added, “The innovation ecosystem remains fragmented. Many startups and academic labs lack access to pilot-scale facilities and structured tech transfer mechanisms. This disconnect between lab-scale innovation and commercial production delays the time-to-market for promising therapies.”

Capitalising on opportunities

India is rapidly laying the groundwork to become a major player in global immunotherapy manufacturing. Building on its established strengths in generics and vaccines, the country is now making strategic moves into the more complex arena of biologics and cell therapies. This transition brings both challenges and significant opportunities.

One example is the cost of CAR-T therapy. While globally the treatment can cost upwards of Rs 2–3 crore per patient, India’s indigenously developed alternatives are being offered at a much lower price point—from Rs 25 to Rs 50 lakh.

“To bridge the gap between research and commercialisation, the Government of India, through the DBT, has launched the BioRIDE initiative. This includes the development of Biofoundries, Bio-AI Hubs, and Biomanufacturing Hubs - shared platforms designed to accelerate innovation and scale-up,” said Shalini.

Biopharmaceutical clusters are emerging in cities like Hyderabad, Bengaluru, and Pune, with Hyderabad’s Genome Valley becoming a focal point for biologics and cell therapy infrastructure. Across the country, GMP-compliant facilities are being established to support the production of biologics and cell-based therapies at scale. At the same time, India has significantly upgraded its cold chain logistics to support the transport of temperature-sensitive immunotherapies, although last-mile delivery in rural and tier-2/3 cities remains a logistical hurdle.

“India’s scientific ecosystem is also evolving to support the full lifecycle of immunotherapy development. Leading research institutions are actively engaged in immunotherapy R&D, and the country has hosted clinical trials for CAR-T therapies and monoclonal antibodies, including homegrown innovations. A major milestone was the approval of NexCAR19, India’s first indigenous CAR-T therapy, which marked a leap in local manufacturing capabilities. The country is also nurturing a growing talent pool in bioprocessing, cell culture, and downstream processing, though there remains a need for specialised training in areas like viral vector manufacturing and gene editing,” said Shalini.

Public–private partnerships are playing a catalytic role in this transformation. Initiatives like BioNEST and BIRAC are supporting biotech startups with infrastructure, mentorship, and funding. The National Biopharma Mission, co-funded by the World Bank and DBT, is driving the development of biopharmaceuticals through support for translational research and manufacturing scale-up.

“Academic collaborations with institutions such as IIT Bombay, IISc, and Tata Memorial Centre are further accelerating the co-development of CAR-T therapies and novel delivery systems. Additionally, the Production-Linked Incentive (PLI) scheme is incentivising investment in high-end biomanufacturing infrastructure, reinforcing India’s position as a rising global player in immunotherapy,” said Shalini.

“While full commercial-scale readiness is still evolving, the foundation being built today signals a future where India plays a central role in the global immunotherapy ecosystem,” signs off Shalini.

India is progressively building the foundation to establish itself as a global center for cost-effective and scalable immunotherapy solutions. With strategic investments, regulatory reforms, and a growing talent base, the country is poised to transform not only its own healthcare landscape but also contribute significantly to global health equity.

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