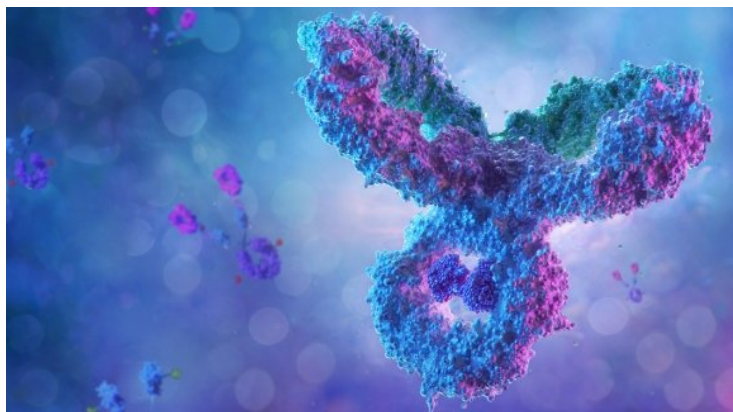


The Third Dimension of Antibody Therapy

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Trispecific antibodies are emerging as the next frontier in antibody therapeutics. Building on the success of bispecific antibodies, these next-generation molecules have attracted growing interest from Big Pharma, fuelled billion-dollar licensing and acquisition deals, and are advancing rapidly through the clinical pipeline. As researchers seek to overcome the limitations of current immunotherapies, trispecific antibodies are being explored for their potential to deliver greater precision, stronger efficacy and broader therapeutic applications. Here is why the industry is shifting towards trispecifics, the advantages they offer, and how this rapidly evolving field is shaping the future of immunotherapy.



Bispecific antibodies have transformed treatment by simultaneously targeting two molecules, delivering significant clinical success across oncology and other therapeutic areas. However, as researchers attempt to overcome tumour resistance, improve efficacy in solid tumours and minimise treatment escape mechanisms, the limitations of engaging only two targets have become increasingly evident.

Trispecific antibodies build on the success of bispecifics by incorporating a third functional target, enabling more precise immune activation, enhanced tumour selectivity and the ability to address multiple disease pathways simultaneously. Trispecific T-cell engagers (TCEs) represent the next evolution of antibody therapeutics, rapidly evolving from a promising immunotherapy modality into an important pillar of modern immuno-oncology, particularly for difficult-to-treat solid tumours.

"Traditional immunotherapies, including checkpoint inhibitors, rely on patients' pre-existing tumour-reactive T cells and often struggle to activate immune responses in immunosuppressive 'cold' tumours, resulting in limited efficacy and widespread treatment resistance in solid tumours," said **Dr Lei Fang, Co-founder, Chairman and CEO of Excalipoint Therapeutics.**

Explaining the advantages of trispecific antibodies, Dr Fang said, "While the TCE modality achieved definitive clinical validation through the approval of Tarlatamab in 2024, establishing bispecific TCEs as a clinically proven therapeutic approach for solid tumours, they still face several bottlenecks, including tumour antigen escape, insufficient and unsustained T-cell activation, T-cell exhaustion, and suboptimal selectivity leading to off-tumour toxicities. Trispecific antibody platforms overcome these limitations by integrating a third functional binding domain into a single molecular scaffold, enabling multidimensional precision immune regulation that dual-target bispecific formats cannot achieve."

One of the biggest advantages of trispecific antibodies is their ability to bind multiple tumour-associated antigens simultaneously, helping overcome target antigen loss and tumour heterogeneity—two of the leading causes of acquired resistance and treatment failure in conventional immunotherapies.

Clinical Pipeline Gaining Momentum

Although no trispecific antibody has yet received regulatory approval, more than 100 trispecific antibody candidates were in development worldwide as of May 2026, according to ScienceDirect.

Among the most advanced programmes are Merck's Restoret (MK-3000) and Innovent Biologics' IBI3003. Restoret (MK-3000, formerly EYE103), being developed by Merck and EyeBio for ophthalmic applications, is the first trispecific antibody to enter a Phase 2b/3 clinical trial. The candidate is being evaluated for diabetic macular oedema (DME), a condition that poses a significant threat to vision and quality of life.

Innovent Biologics has also dosed the first patient in TriadicMM-1, a pivotal Phase 3 trial evaluating IBI3003, a GPRC5D/BCMA/CD3 trispecific antibody, in patients with relapsed or refractory multiple myeloma. The programme is only the second trispecific antibody globally to reach pivotal Phase 3 development in this indication and the first with independently owned intellectual property in China.

Big Pharma Bets on Trispecifics

The rapid progress of trispecific antibodies has attracted considerable interest from major pharmaceutical companies. Johnson & Johnson, AbbVie, Pfizer and Sanofi have all invested heavily in promising trispecific programmes.

In March 2026, Sanofi licensed Kali Therapeutics' KT501, a CD3/CD19/BCMA trispecific T-cell engager for B-cell-mediated autoimmune diseases, in a deal worth \$180 million upfront. The candidate is currently being evaluated in a first-in-human trial for rheumatoid arthritis after demonstrating potent B-cell depletion and reduced cytokine production in preclinical studies.

AbbVie paid \$700 million upfront to Ichnos Glenmark Innovation (IGI) for ISB 2001, a CD38×BCMA×CD3 trispecific antibody being developed for multiple myeloma and autoimmune diseases.

Johnson & Johnson and Pfizer are also expanding trispecific development beyond oncology. Early Phase 1 data for Johnson & Johnson's JNJ-79635322 showed an overall response rate of 86.1 per cent, increasing to 100 per cent in patients who had not previously received BCMA- or GPRC5D-directed therapies, while demonstrating an encouraging safety profile.

Meanwhile, Pfizer reported positive Phase 2 results for its trispecific antibody candidate in patients with moderate-to-severe atopic dermatitis and plans to advance the programme into a pivotal Phase 3 trial later this year.

China Emerges as an Innovation Hub

Within the Asia-Pacific region, China is rapidly establishing itself as a global centre for trispecific antibody innovation.

Excalipoint Therapeutics launched in March 2026 with \$68.7 million in funding to develop next-generation T-cell engager therapies. Other Chinese companies advancing the field include CStone Pharmaceuticals, which is developing CS2009, a PD-1/VEGF/CTLA-4 trispecific antibody, and Akeso, which continues to expand its trispecific pipeline.

Huahui Health further demonstrated China's growing capabilities by signing a \$1.9 billion licensing and collaboration agreement with BeOne Medicines for HH160, a novel trispecific antibody for oncology immunotherapy.

"China is emerging as a global hub for engineered immunotherapy development, supported by mature clinical trial infrastructure, robust manufacturing capacity and unique patient access advantages. Its innovative ecosystem—combining cutting-edge platform technologies, efficient capital allocation and streamlined clinical development—will further accelerate the translation of complex trispecific therapies from laboratory to bedside," said Dr Fang.

The Next Generation of Immunotherapy

Excalipoint is among several companies developing proprietary trispecific platforms to overcome the limitations of existing immunotherapies. "At Excalipoint, we have built our proprietary differentiated platforms—EXCOPIA (co-stimulatory), EXiShield (immune shield) and EXPROMA (probody)—specifically to unlock the full potential of trispecific TCEs. Our technologies are engineered to remodel the immunosuppressive tumour microenvironment, convert immune 'cold' tumours into 'hot' tumours and target historically undruggable tumour antigens, addressing critical unmet needs in immuno-oncology. Our lead trispecific asset, EXP011 (DLL3/CD3/4-1BB), has already gained industry recognition through a clinical collaboration with Roche,

evaluating its combination with atezolizumab for DLL3-expressing solid tumours, including small-cell lung cancer," said Dr Fang.

Looking ahead, trispecific TCE-driven immunotherapy is expected to reshape treatment across several high-unmet-need disease areas. Oncology is likely to remain the primary beneficiary. Beyond improving outcomes in haematological malignancies such as lymphoma and multiple myeloma, trispecific TCEs are expected to deliver significant advances in refractory solid tumours—the long-standing challenge of cancer immunotherapy. Beyond oncology, this precision multispecific technology is also expected to expand rapidly into autoimmune diseases.

"The future of immuno-oncology will be defined by smart, precisely engineered multispecific TCEs, and Excalipoint will continue advancing our proprietary platforms and clinical pipeline to deliver next-generation immunotherapies to patients worldwide," concluded Dr Fang.

The race to develop trispecific antibodies is accelerating. As more candidates progress into late-stage clinical development and the technology continues to mature, these next-generation therapies have the potential to redefine immunotherapy across oncology, autoimmune diseases and other complex disorders.

Ayesha Siddiqui