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Unlocking the Undruggable with Targeted Protein Degradation

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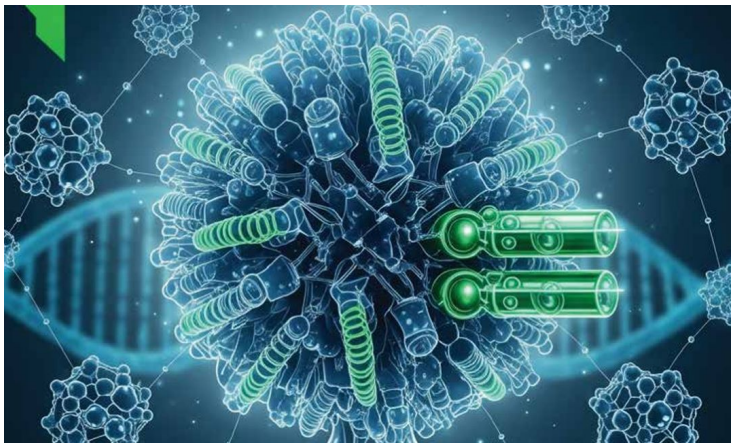
Targeted Protein Degradation (TPD) is an emerging therapeutic approach that allows the removal of disease-causing proteins once considered 'undruggable'. These proteins, which make up almost 80 per cent of the human proteome, cannot be addressed using traditional small-molecule binding strategies. By making it possible to eliminate such challenging targets, TPD is opening new opportunities for drug development in cancer, immune conditions, and other hard-to-treat diseases, and is increasingly viewed as a cornerstone for future drug discovery. Today, TPD boasts three approved therapies, nearly 60 clinical-stage assets, and around 200 active research programmes worldwide, according to a report from Nature. With big pharma pouring billions into partnerships, acquisitions, and platform deals, the field is entering a new phase of commercial maturity. In this story, we explore why TPD is commanding global attention from emerging biotech innovators in APAC to multinational players racing to secure the next blockbuster degrader.



Targeted protein degraders (TPD) are rapidly moving from niche science to mainstream drug development, with few therapies approved and many more advancing through late-stage trials.

TPD today rests on two pillars: PROTACs and molecular glues. PROTACs (proteolysis-targeting chimeras), proposed over two decades ago, work by bringing disease-causing proteins into proximity with the cell's degradation machinery. While none have yet reached the market, the field is gaining momentum with more than 40 candidates in clinical testing for cancers and autoimmune disorders, according to Biopharma PEG blog. These include inhibitors targeting the androgen receptor (AR), estrogen receptor (ER), Bruton's tyrosine kinase (BTK), and IRAK4. Three PROTACs are already in late-stage trials: Arvinas/Pfizer's ARV-471 (ER), Bristol Myers Squibb's BMS-986365 (AR), and BeiGene's BGB-16673 (BTK). Industry is closely watching Arvinas/Pfizer's ARV-471, with USFDA acceptance of its NDA in August 2025 and approval expected by June 2026. If approved, ARV-471 could become the first PROTAC therapy to reach the market, marking a major milestone for targeted protein degradation.

In contrast, molecular glues have already carved out a commercial foothold. These small molecules modulate protein–protein interactions to degrade, stabilise, or activate targets. Natural glues like thalidomide, discovered serendipitously, became the basis for multiple myeloma therapies developed by Bristol Myers Squibb (BMS). BMS remains the only company with approved molecular glue products—Revlimid, Pomalyst, and Thalomid—approved for adult multiple myeloma patients, though pediatric safety remains unconfirmed. The landscape has since expanded, with over 50 companies advancing more than 60 molecular glues, according to DelveInsight, a leading healthcare-focused market research and consulting firm. Leading candidates include BMS's mezigdomide and golcadomide, Eisai's E7820, Nurix's NX-5948 and NX-2127, and many

others.

Big Pharma bets on TPD

Big pharma has caught on in a big way in the TPD field. The space is now attracting multi-billion-dollar commitments from some of the world's largest drugmakers. From AbbVie and Takeda to Novartis and Biogen, major players are betting that molecular glues and degraders can finally unlock 'undruggable' targets in oncology and immunology.

In January 2025, AbbVie struck a partnership with U.S. biotech Neomorph, giving it an option to license molecular glue degraders across oncology and immunology. The deal, valued at up to $1.64 billion, will see Neomorph lead early discovery while AbbVie takes forward clinical development and commercialisation. During the same period, HealZen Therapeutics, working with China's Shanghai Institute of Materia Medica, signed a global licensing agreement with Johnson & Johnson to develop BTK degraders for multiple diseases. Around the same time, Denmark's LEO Pharma entered into a $1.7 billion alliance with Gilead Sciences to advance STAT6 inhibitors and degraders for inflammatory diseases, while Magnet Biomedicine partnered with Eli Lilly in March 2025 in a tie-up worth $1.25 billion to apply its TrueGlue platform in oncology. In April 2025, Nurix Therapeutics also out-licensed an undisclosed degrader programme to Sanofi for autoimmune conditions, a deal that could bring in up to $465 million in milestones plus royalties.

Several high-profile agreements in late 2024 paved the way for these blockbuster transactions. Takeda committed up to $1.2 billion in May 2024 for a collaboration with China's Degron Therapeutics. In August 2024, Eisai struck a $1.5 billion-plus research pact with SEED Therapeutics. In October 2024, Novartis secured global rights to Monte Rosa's MRT-6160, a phase 1 molecular glue degrader, paying $150 million upfront with the potential to exceed $2.1 billion in milestones. In the same month, Biogen entered into a $1.45 billion collaboration with Neomorph to access its glue discovery platform. Companies such as Merck, Roche, and Novo Nordisk were early movers in the targeted protein degradation space, signing initial agreements to explore the technology way back in 2022–23.

The APAC Landscape

In the Asia-Pacific region, China and South Korea are emerging as leading hubs for TPD research and development, while Japan, Australia, and Singapore are also actively exploring opportunities in this space. South Korea, in particular, has seen its major pharmaceutical players actively expand into this space through acquisitions, partnerships, and pipeline building.

SK Biopharmaceuticals entered TPD by acquiring a 60 per cent stake in Proteovant Sciences (now SK Life Sciences Labs). The subsidiary is focused on developing novel anti-cancer and central nervous system (CNS) therapies, leveraging an AI-enabled target identification platform, degrader drug-hunting expertise, and its proprietary MOPED molecular glue screening technology.

Yuhan Corporation has taken a partnership-driven approach, collaborating with biotech firms such as Uppthera, Cyrus Therapeutics, Kanaph Therapeutics, Ubix Therapeutics, and Fraser Therapeutics to access new TPD technologies and expand its pipeline.

Daewoong Pharmaceutical also entered the field in 2023 through a partnership with Pin Therapeutics, a biotech developing novel E3 ligases and molecular glue degraders. Pin's lead candidate, PIN-5018 — a first-in-class CK1? molecular glue degrader cleared for IND in May 2025 is being advanced for colorectal cancer, adenoid cystic carcinoma (ACC), and relapsed/refractory AML.

Dong-A ST has been expanding its research footprint with both acquisitions and partnerships. The company acquired ADC firm Abtis in 2023 and in August 2025 partnered with an AI drug discovery company XtalPi to strengthen its R&D in immunology and inflammation, while also exploring new directions in degrader-based drug discovery.

Beyond the large pharma groups, several South Korean biotech firms are progressing their own TPD pipelines. Ubix Therapeutics received IND approval for UBX-303-1 from the U.S. FDA in December 2023 and the Korean MFDS in September 2023, and is now conducting global clinical trials. The company has signed multiple partnerships with both large pharma and smaller firms, the most recent in February 2025 with Y-Biologics to co-develop degrader antibody conjugates.

Orum Therapeutics, which raised ?50 billion in a Korea Exchange IPO in February 2025, is developing ORM-1153, a GSPT1 degrader for acute myeloid leukaemia, with preclinical data expected this year and an IND filing in 2026. Orum gained international attention when Bristol Myers Squibb acquired rights to its oncology asset ORM-6151 in late 2023.

Meanwhile, newer biotech entrants are moving toward clinical readiness. Cyrus Therapeutics is advancing CYRS1542, a GSPT1 molecular glue degrader (US IND 174397), for multiple neuroendocrine cancers including small cell lung cancer, large cell neuroendocrine carcinoma, neuroendocrine prostate cancer, and metastatic castration-resistant prostate cancer. Prazer Therapeutics is similarly building a pipeline based on TPD technology, with early-stage drug discovery efforts underway.

Besides Korea, China too is rapidly establishing itself as a hub for TPD, with several firms actively developing innovative therapies, some of which are already in late-stage trials.

BeiGene is advancing its Chimeric Degradation Activation Compound (cDAC) for patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL). The candidate is currently in phase 3 clinical trials, with several other candidates at various stages of development.

Kintor Pharma has pioneered GT20029, claimed to be the world's first dermatological topical AR degrader, which in September 2024 met its Phase II primary endpoint in China, showing significant efficacy in treating male androgenetic alopecia (AGA). The company is now preparing for Phase III trials.

Jiangsu HengRui is developing HRS-5041, an ER-targeting degrader for metastatic castration-resistant prostate cancer (mCRPC), and HRS-1358, an AR-targeting degrader for breast cancer, with both candidates currently in Phase II trials.

Ranok Therapeutics is advancing RNK-05047, a BRD4-targeting degrader for advanced solid tumours, including diffuse large B-cell lymphoma (DLBCL), which is currently in phase II trials.

Hinova Pharma is leveraging PROTAC and deuteration technologies to develop therapies for cancers and metabolic syndromes. Its pipeline includes HP518, an orally bioavailable chimeric degrader targeting AR, which has completed phase I trials for metastatic castration-resistant prostate cancer (mCRPC).

Gluetacs Therapeutics, the first biotech incubated by ShanghaiTech University, focuses on small-molecule oral protein degraders. Officially operational since March 2021, Gluetacs has advanced two candidates into clinical trials, demonstrating the efficiency of its GlueTacs platform. The company has independently developed molecular glue (GLUE) and bifunctional degrader (GLUETAC) platforms, filed and received over 100 patents globally, and established AI-driven virtual screening, in vitro drug screening, pharmacokinetic, proteomics, and in vivo efficacy testing platforms to cover the full drug discovery process.

GluBio Therapeutics Inc., a clinical-stage TPD biotech, has completed phase I of its trial for GLB-002, an IKZF1/3-selective molecular glue degrader, in patients with relapsed or refractory non-Hodgkin lymphoma. The trial demonstrated strong pharmacokinetics, pharmacodynamics, safety, and target degradation. Phase II is now open for patient recruitment.

Degron Therapeutics is preparing a phase I study of its HuR-targeting degrader DEG6498 following US IND clearance.

US-based Photys Therapeutics in-licensed HPB-143 from Hangzhou Polymed Biopharmaceuticals in February 2025, securing global rights outside Greater China and Southeast Asia for its Phase 1-ready IRAK4 degrader. Kangpu Biopharma is advancing molecular glue-based candidates through its NeoMIDES, gDACS, and X-SYNERGY platforms.

Several other Chinese companies also have phase I targeted protein degradation candidates, including Qilu Pharmaceutical (SMARCA2 for prostate cancer), JAR (SHR-3591 for mCRPC), Simcere Pharma (SIM-0270 for ER+?/HER2? breast cancer), and Chia Tai Tianqing Pharmaceutical (TQB-3019 targeting BTK in advanced malignant tumours).

In Japan, several firms are actively advancing targeted protein degradation (TPD) programmes. Leading among them is Astellas, which has integrated state-of-the-art AI, molecular simulation, and robotics into its drug discovery efforts. Its lead TPD asset, ASP3082, a phase 1 protein degrader targeting KRAS G12D, was discovered and optimised in significantly shorter timelines than historical precedent. Robotics-driven synthesis has further streamlined development, enabling the company to respond with agility to the unique challenges of TPD.

Other Japanese companies are also making strides. PeptiDream and Ono Pharmaceutical are pursuing TPD programmes, with Ono forming multiple collaborations including a drug discovery agreement with Captor Therapeutics for small molecule degraders in neurodegenerative diseases and a partnership with Sibylla Biotech to generate novel candidates for neurological disorders. Eisai has advanced its own efforts, with investigator-initiated clinical studies planned following

confirmation of tumour shrinkage induced by its degrader E7820 in Japanese patient-derived tissue transplantation models (J-PDX). Mitsubishi Tanabe Pharma America Inc. is developing MT-4561, a BRD4-targeting degrader for advanced solid tumours, currently in phase I/II clinical trials. Meanwhile, FIMECS, founded in 2018 by Takeda researchers under its venture support programme, has pursued targeted proteolysis inducers for undruggable targets and was later acquired by RaQualia Pharma.

In Singapore, EDDC (Experimental Drug Development Centre) is collaborating with the Swiss biotech RDP Pharma AG to develop a monovalent degrader for anti-inflammatory therapies. Ligature, spun out of EDDC with Lightstone Singapore, has licensed A*STAR's protein degradation technologies to build its pipeline. Another company, Automera, launched in 2023, is advancing its AUTAC platform across multiple disease areas.

In Australia, the launch of Ternarx has marked a significant step in the country's entry into next-generation medicines. Spun out of WEHI, Ternarx is the first Australian company dedicated to developing targeted protein degrader therapeutics and technologies, with a focus on tackling hard-to-treat cancers.

What's driving TPD progress

The current momentum in TPD stems from foundational discoveries in the early 2000s and 2010s, particularly the identification of versatile binders to E3 ligases such as VHL (Von Hippel–Lindau,) and CRBN (Cereblon). These breakthroughs catalysed a wave of innovation, attracting new players and elevating research across the industry.

"We have made significant advances in our understanding of the chemical features governing neo-substrate recruitment with CRBN-based molecular glues and PROTACs, aiding more rational design of selective degraders. Additionally, advances in methods for proteomic and chemoproteomic profiling, combined with improvements in throughput and analysis, are enabling screening on the proteome scale," said Kristin Riching, Senior Research Scientist at Promega.

Building on this foundation, the field has begun to see proof in the clinic. Several TPD assets have shown clear efficacy, significantly boosting confidence and expanding interest across both biotech and pharma.

"There is explosive growth in novel degradation strategies that go beyond traditional PROTACs, expanding the modalities available for TPD and enhancing its versatility," said Chinatsu Sakata, Head of Oncology Research, Astellas Pharma, adding that "rapid advances in computational tools and AI are helping us design molecules that can not only form the ternary complex but also reach their targets deeper in tissues—two of the toughest challenges in TPD development."

These technological advances are complemented by the maturing ecosystem. "The rise of specialised CROs, particularly in Asia–Pacific, has shortened development cycles and lowered barriers for startups and smaller biotechs to enter the space. Together, these advances are propelling TPD into a new phase of growth," said Chinatsu.

What's next

The clinical landscape for targeted protein degradation (TPD) is beginning to take shape. As more TPD assets progress through trials and approach regulatory milestones, the modality is entering a decisive phase where real-world data will help define its potential. Oncology remains the most active area, but non-oncology indications are rapidly gaining traction.

Chinatsu noted that this phase will also sharpen scientific understanding. She said, "This next chapter will bring greater clarity on resistance mechanisms, informing more refined development strategies and helping identify optimal patient populations. Advances in molecular design and optimisation will produce assets with significantly improved pharmacological and safety profiles. We expect continued expansion of heterobifunctional molecules and growing interest in molecular glue-type degraders, both of which offer promising avenues for enhanced efficacy and broader disease applicability. These innovations will further accelerate progress and position TPD as a core small-molecule modality."

Looking ahead, experts believe the field is poised for a new wave of technical sophistication. Kristin highlighted advances in computational tools as a key driver. She said, "In the coming years, we will likely see expanded use of modelling approaches that integrate ternary complex docking and molecular dynamics simulations within the context of the full Cullin-RING ligase complex. These tools will enable more accurate prediction of ubiquitination and degradation efficiency, accelerating degrader discovery and optimisation."

Such scientific and technological progress is directly reflected in the market outlook. Currently valued at $1 billion, the global TPD market is expected to surge to $6.94 billion by 2035. With this rapid growth on the horizon, companies worldwide are

racing to establish themselves as leaders, developing innovative therapies and platforms to capture a larger share of the emerging market.

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