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The landscape of top 10 global innovative drug targets 2015-2024

Cheng Tan,[1] Xingchen Wang,[1] Dingchen Ding,[2] and Pengfei Xu[1,3,*]

[1]Zhongnan Hospital of Wuhan University, Institute of Hepatobiliary Diseases of Wuhan University, Transplant Center of Wuhan University, School of Pharmaceutical Sciences, Wuhan University, Wuhan 430071, China

[2]Department of Biochemistry and Molecular Biology, Eberly College of Science, The Pennsylvania State University, University Park, PA 16802, USA

[3]Hubei Provincial Key Laboratory of Developmentally Originated Disease, Wuhan 430071, China

*Correspondence: pengfeixu@whu.edu.cn

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Dear Editor,

Over the past decade, the landscape of innovative drug development has been shaped by a core set of molecular targets that have consistently attracted global research and investment. From 2015 to 2024, transformative advances in immuno-oncology and precision medicine were driven by ten leading targets—CD19, BCMA, PD-1, CD3, PD-L1, CD20, HER2, EGFR, PSMA, and GLP-1R—resulting in breakthroughs across multiple therapeutic areas. Their prominence reflects not only the evolving priorities in drug discovery but also the remarkable adaptability and innovation potential of modern therapeutic platforms in addressing diverse disease contexts.

The identification and statistical analysis of these ten targets were based on global pipeline data integrated from the PharmCube NextPharma®, PharmaGO®, and TrialCube® databases covering 2015–2024.

COMPREHENSIVE TREND ANALYSIS

Regionally, China has experienced the most dramatic rise in innovative drug development over the past decade, with the number of active programs increasing from 124 in 2015 to 704 in 2024—surpassing that of the United States for the first time in 2021 (Figure 1A). The US maintained a high level of activity, peaking at 541 programs in 2022 before declining to 440 in 2024. In comparison, Europe and other regions showed moderate but steady increases, reaching 212 and 208 programs respectively in 2024. These patterns reflect a global shift from US-centric innovation to a more multipolar R&D landscape, with China emerging as a key contributor.[1]

While China's pipeline growth is striking, the quality dimension remains a key concern. Due to limited global annotation of first-in-class status within available databases, a formal cross-regional quantitative comparison could not be performed. Nevertheless, qualitative assessments indicate that China's expansion is accompanied by a relatively higher proportion of follow-on projects, suggesting an ongoing transition from imitation to innovation. This rise has been driven by strong policy incentives, increased capital investment, and advances in modalities such as monoclonal antibodies, chimeric antigen receptor T-cell (CAR-T) therapies, and bispecific antibodies (bsAbs). Despite this progress, challenges remain, including lower clinical success rates and fewer original target discoveries compared with the United States and Europe. This highlights that the emerging multipolar landscape reflects not only quantitative expansion but also qualitative diversity. Strengthening breakthrough therapy pathways, cross-sector collaboration, and clinical trial innovation may prove beneficial in reconciling the trade-off between quantity and quality, ultimately improving the success rates in late-stage development.

Between 2015 and 2024, the volume and stage distribution of global innovative drug development underwent substantial shifts (Figure 1B). The total number of projects increased from 736 in 2015 to 1,589 in 2024. Notably, the proportion of early-stage programs (Phase I and Phase I/II) rose sharply from 48% to 91%, with Phase I trials alone increasing by 366%, reflecting intensified early-stage exploration. In contrast, late-stage programs (Phase III, registration and approval) declined from 20% to just 2%. Most concerning, 2024 saw both a decrease in Phase III projects and a complete absence of drugs reaching registration or approval - indicating declining translational efficiency.

Clinical attrition remains the key bottleneck, with many Phase III trials failing due to insufficient efficacy or concerning safety signals. Regulatory reforms, including tighter FDA accelerated-approval standards, have raised entry barriers. Consequently, the pipeline has become increasingly front-loaded, with surging early exploration but limited late-stage conversion. Recent analyses suggest that late-stage failures are often linked to the lack of predictive biomarkers, patient heterogeneity, and emergent safety liabilities, with attrition rates approaching 90% in Phase II–III studies.[2] These observations underscore the importance of biomarker-guided stratification, adaptive and decentralized trial designs, and earlier regulatory engagement to improve translational efficiency and clinical success rates. In oncology, several checkpoint inhibitors and kinase-targeted therapies have failed in pivotal trials when efficacy did not exceed the standard of care or when biomarker stratification was inadequate. Conversely, adaptive trial designs and early biomarker integration have demonstrated improved efficiency and predictive accuracy.[3] To overcome these challenges, approaches such as biomarker-guided stratification, innovative trial designs, and earlier regulatory engagement are increasingly essential to improve late-stage success. Furthermore, the coronavirus disease 2019 (COVID-19) pandemic disrupted clinical trial timelines, causing widespread delays that likely compounded the observed reduction in late-stage programs after 2020.

An integrated analysis of annual trends from 2015 to 2024 further highlights the dynamic trajectories of the top ten innovative drug targets and the shared principles underlying their success (Figure 1C). Cluster of differentiation 19 (CD19) activity surged after 2018, peaking in 2020 with 47 candidates, reflecting the rapid adoption of CAR-T therapies. B-cell maturation antigen (BCMA)-targeted programs grew steadily since 2017, fueled by progress in multiple myeloma treatment. Programmed death-ligand 1 (PD-L1) and CD3 expanded rapidly during 2021–2022, coinciding with innovations in checkpoint inhibitors and bsAbs, whereas epidermal growth factor receptor (EGFR) remained stable, reflecting its maturity in lung cancer. Collectively, these temporal patterns illustrate how emerging technologies, such as CAR-T, bsAbs, and antibody-drug conjugates (ADCs), drive target-specific momentum.

These leading targets exhibit several key characteristics: robust mechanistic validation supported by biomarker or genetic evidence, adaptability across therapeutic platforms such as CD19 with CAR-T, EGFR with tyrosine kinase inhibitors, human epidermal growth factor receptor 2 (HER2) with ADCs, and programmed cell death protein 1 (PD-1) with mAbs, and cross-indication potential (glucagon-like peptide-1 receptor (GLP-1R)) in diabetes and obesity, CD20 in lymphoma and autoimmune disorders. Nonetheless, challenges remain, including drug resistance, off-target effects, high cost, and limited specificity in certain contexts. The temporal dynamics also reflect technology–indication co-evolution: the 2020 increase in CD19 programs followed CAR-T adoption in B-cell malignancies, PD-L1 expansion in 2021–2022 paralleled bispecific antibody innovation in solid tumors, while EGFR's plateau underscores its therapeutic saturation. Overall, these findings underscore the tight interplay between technology platforms, target biology, and clinical modalities in shaping global innovation trajectories.

GLOBAL DISTRIBUTION OF THE TOP TEN INNOVATIVE DRUG TARGETS, 2015–2024

The distribution of the top ten innovative drug targets reveals distinct therapeutic category patterns (Figure 1D). Immuno-oncology targets dominate the landscape, led by CD19 with 305 candidate drugs, followed by BCMA, PD-1, and CD3. Non-immuno-oncology cancer targets include HER2 and EGFR, while prostate-specific membrane antigen (PSMA)—representing other oncology targets—accounts for 108 candidates. In the metabolic disease category, GLP-1R has accumulated 86 candidate drugs, highlighting its growing clinical relevance. This distribution provides a foundation for target class–level analyses and underscores the central role of immuno-oncology

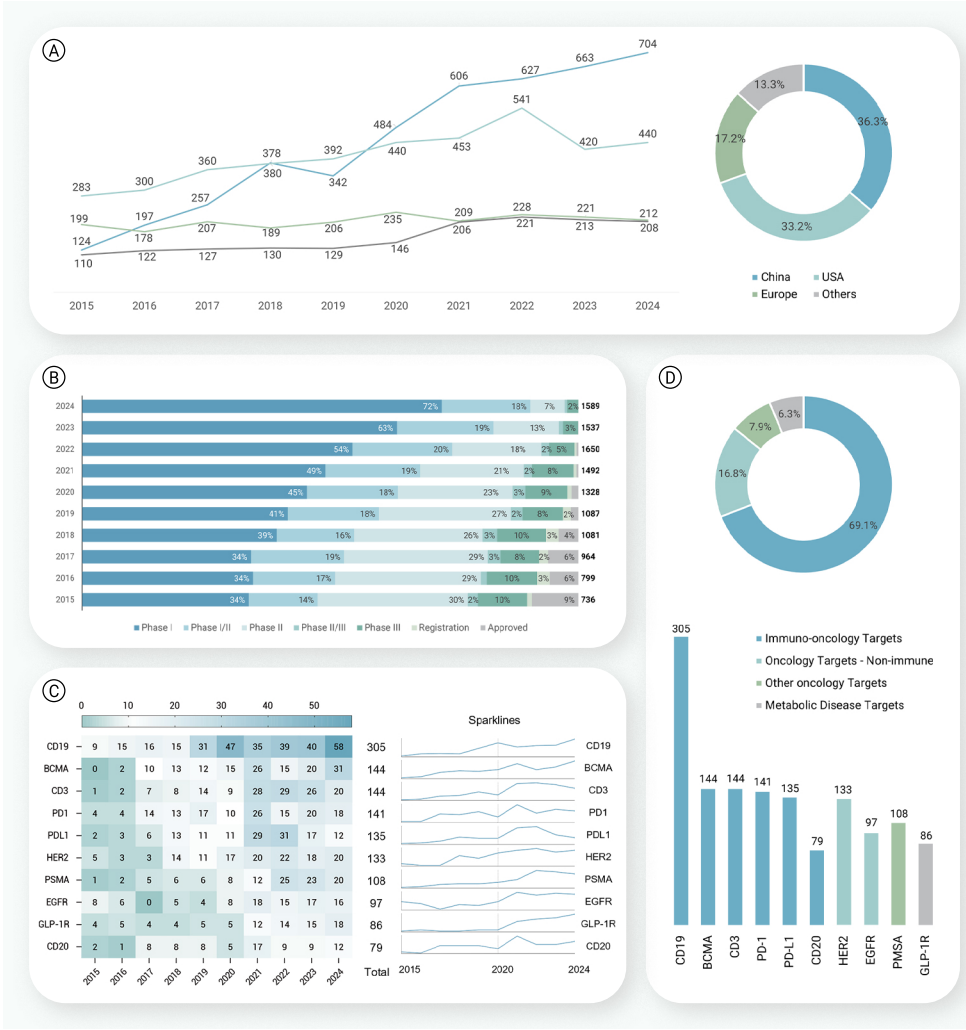

Figure 1. Global trends in innovative drug development, 2015–2024 (A) Regional distribution of innovative drug development programs, showing rapid growth in China and stable activity in the US, with moderate increases in Europe and other regions. (B) Distribution of development stages, with a rising proportion of early-stage programs and a decline in late-stage projects over time. Percentages indicate stage shares by year; total program numbers are shown on the right. (C) Global activity of the top 10 drug targets, shown as annual counts (heatmap) and temporal trends (sparklines). (D) Disease-area classification of the top 10 targets, highlighting the dominance of immuno-oncology alongside emerging non-immuno-oncology and metabolic targets.

in shaping global drug innovation priorities.

IMMUNO-ONCOLOGY TARGETS: THE CENTRAL DRIVERS OF INNOVATION

Among the top ten innovative drug targets, immuno-oncology represents the largest cluster. CD19 leads in candidate volume, owing to its pivotal role in B cell malignancies and notable progress across three therapeutic modalities: CAR-T cell therapies, bsAbs, and ADCs.[4] BCMA–targeted therapies, primarily ADCs and CAR-T cells, have shown strong efficacy in treating multiple myeloma by targeting BCMA-positive plasma cells.[5] PD-1 and PD-L1, as immune checkpoint targets, have demonstrated clinical success in solid tumors such as melanoma and non-small cell lung cancer, and more recently in bispecific and combination strategies.[6] CD3 enables T cell redirection through bsAbs, with indications expanding from hematologic malignancies to autoimmune diseases.[7] CD20 bridges oncology and autoimmunity, evolving from mAbs to bsAbs and CAR-T therapies. Collectively, these advances highlight immune modulation as a central driver of oncology innovation, despite challenges such as resistance and immune-related toxicities, including cytokine release syndrome.

Beyond individual targets, the interplay among immune pathways has become increasingly important. PD-1/PD-L1 inhibitors are often combined with CD19- or CD3-directed therapies, reflecting synergy between checkpoint blockade and T-cell redirection. Concurrently, overlapping modalities including CAR-T cells, bsAbs, and ADCs, converge on shared targets like CD19 and BCMA, underscoring the need for optimized sequencing and patient stratification. Resistance remains a major limitation, particularly for PD-1/PD-L1 therapies. Next-generation bsAbs, CAR-T combinations, and biomarker-guided regimens are emerging to overcome resistance and improve treatment durability.

NON-IMMUNO-ONCOLOGY TARGETS: SUSTAINED RELEVANCE

Non-immuno-oncology targets, such as HER2 and EGFR, continue to play a pivotal role in cancer treatment. Over the past decade, HER2-targeted therapies have achieved significant advances, with ADCs emerging as the dominant modality.[8] Their indications have expanded beyond single tumor types, establishing HER2 as a benchmark for pan-tumor targeted therapy. EGFR, one of the earliest oncology targets to enter clinical development, remains a milestone in the history of targeted therapy. Its indications now extend beyond lung cancer to multiple solid tumors, encompassing both common mutations and rarer variants, reinforcing EGFR as a sustained driver of precision oncology.[9] HER2 and EGFR are both receptor tyrosine kinases that serve as important therapeutic targets in precision oncology.

OTHER ONCOLOGY TARGETS: A FOCUS ON PRECISION

Among other oncology targets, PSMA stands out, with 108 candidate therapies in development—reflecting the growing emphasis on tumor-specific precision approaches. PSMA has become a foundational target in prostate cancer, with agents such as Pluvicto significantly improving progression-free survival in advanced disease.[10] This class exemplifies the increasing integration of molecular imaging and biomarker-guided strategies to enhance tumor specificity and therapeutic responses, underscoring the expanding potential of precision medicine in solid tumors.

METABOLIC DISEASE TARGETS: EXPANDING HORIZONS

GLP-1R has emerged as one of the most clinically and commercially promising targets in metabolic diseases with highly competitive drug development in this space. Ozempic, a leading GLP-1R agonist, has gained global regulatory approval for treating type 2 diabetes and obesity. GLP-1R is now recognized not only as a glycemic control target but also as a central node in systemic metabolic regulation across multiple indications. This new understanding has led to more targeted combination therapies, expanding GLP-1R's applications to various metabolic conditions.

LIMITATIONS AND FUTURE DIRECTIONS

This study has several limitations. First, database coverage bias may affect completeness, as early academic or regionally disclosed programs may be underrepresented. Second, inconsistencies in target classification or development-stage annotation across sources may introduce minor discrepancies. Future work should integrate databases, such as ClinicalTrials.gov and ChiCTR, for cross-validation. Expanding analyses to include target–modality relationships, AI-assisted trend prediction, and longitudinal validation could yield deeper insights into the evolving innovation landscape.

OUTLOOK

Over the past decade, the leading drug targets have spanned immuno-oncology, non-immuno-oncology, other oncology-related targets, and metabolic diseases, reflecting the evolution of drug discovery paradigms. While early progress was driven by single-mechanism antibody therapies, current trends emphasize combination regimens, cell-based therapies, and biomarker-guided precision medicine. Advances such as ADCs and CAR-T have sustained the relevance of established targets.

Looking ahead, emerging modalities will help address persistent challenges. AI-driven drug design may optimize GLP-1R therapy development; CRISPR-based engineering could improve the safety of CD19 and BCMA CAR-T; mRNA therapeutics offer flexible platforms for PD-1/PD-L1 modulation; and AI–RNA modeling may accelerate solutions to EGFR resistance. In addition, proteolysis-targeting chimeras (PROTACs) and RNA-based therapies hold promise for addressing "undruggable" targets. Together, these approaches are expected to expand the spectrum of targetable biology in the coming decade.

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AUTHOR CONTRIBUTIONS

Cheng Tan and Pengfei Xu conceptualized and supervised this work. Cheng Tan wrote the manuscript and created the figures. Xingchen Wang and Dingchen Ding contributed to discussions on the writing framework. All authors read and approved the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

ETHICAL STATEMENT AND PATIENT CONSENT

Not applicable.

DATA AND CODE AVAILABILITY

Not applicable.