

Global Pharmaceutical Patent Intelligence

Connecting the dots between technology, targets, and therapies

CAS
A division of the
American Chemical Society

Unlocking the future of pharmaceutical innovation through patent intelligence.

Five years of global pharmaceutical patent data reveal a field in fundamental transition: therapeutic platforms multiplying, molecular targets expanding well beyond traditional proteins, and disease focus shifting toward previously intractable conditions. The patterns show not just where innovation is concentrating, but where genuine opportunity remains open.



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Executive summary: Unlocking the future of pharmaceutical innovation through patent intelligence

In an industry where R&D costs exceed USD $2.3 billion per approved drug, patent intelligence has evolved from legal necessity to strategic imperative for identifying innovation trajectories, white space opportunities, and competitive positioning. This report harnesses the comprehensive global patent data encompassed in the CAS Content Collection™ and advanced natural language processing (NLP) capabilities guided by scientists to decode emerging trends shaping pharmaceutical R&D. By systematically analyzing over 368,000 patent filings across 90+ global patent offices from 2020-2025, this analysis transforms vast patent datasets into actionable competitive intelligence for pharmaceutical executives, R&D scientists, and investment decision-makers.

This report delivers unprecedented integration of modality, target, and disease area intelligence. Throughout this report we present multiple comprehensive CAS TrendScape maps that organize the emerging therapeutic landscape with each map integrating patent frequency data with growth rate metrics to provide quantitative and qualitative perspectives on innovation patterns.

The modality assessment encompasses six major platforms including small molecules, biologics, cell/gene therapies, and transformative technologies like PROTACs, RNA therapeutics, and AI-driven drug discovery, alongside a deep analysis of leading and emerging patent assignees revealing acquisition strategies and technology transfer patterns.

The molecular target landscape maps 2,000+ targets dominated by protein targets, with growing emphasis on novel mechanisms and tissue-selective modulation extending beyond traditional kinases and GPCRs to previously undruggable transcription factors, protein-protein interactions, and degradation pathways.

The disease landscape maps 1,700+ diseases revealing that while oncology dominates absolute volumes, the breadth spans 17 categories with striking diversification, especially fibrotic diseases and genetic disorders.showing exceptional emergence across organ systems, metabolic conditions demonstrate highest growth rates, and infectious/urological diseases show constrained innovation reflecting mature landscapes.

Geographic and institutional analysis distinguishes academic pioneers from commercial developers, enabling identification of collaboration opportunities and revealing that China dominates academic patents while the U.S. excels in commercial translation, with critical implications for partnership and acquisition targeting.

Critical Findings and Strategic Takeaways

1. Modality Diversification as Competitive Imperative

The 850+ therapeutic modality topics mapped across four CAS TrendScape maps reveal fundamental transformation in platform selection strategies. Small molecules constitute approximately 60% of patent activity but plateau in relative growth, indicating market maturity where innovation emphasizes refinement through enhanced selectivity and novel mechanisms like targeted protein degradation. The most pronounced growth trajectories appear in RNA therapeutics (rising to ~8% of patents) and AI/ML applications (accelerating from 9% in 2020 to nearly 24% in 2025), reflecting their evolution from specialized tools to foundational platforms reshaping the entire drug discovery pipeline.

Leading pharmaceutical innovators now patent across five to seven distinct therapeutic modalities versus only two to three a decade ago, reflecting strategic diversification to match appropriate platforms with specific target biology. **Biologics** innovation concentrates on next-generation formats such as bispecific antibodies, antibody-drug conjugates, and engineered variants, with our analysis identifying leading patent assignees and acquisition patterns. **Cell and gene therapies** show CAR-NK cells demonstrating notable commercial patent growth as off-the-shelf alternatives to CAR-T, while CRISPR advances toward next-generation base and prime editing with improved precision. **Targeted protein degradation** represents transformative capability validated by U.S. FDA approval of vepdegestrant (Arvinas/Pfizer), with patent activity spanning PROTAC variants and molecular glues.

2. The Expanding Druggable Universe

The 2,000+ molecular targets mapped across eight CAS TrendScape maps demonstrate unprecedented expansion of the druggable genome, dominated by protein targets but increasingly emphasizing novel mechanisms and tissue-selective modulation. Innovation extends beyond traditional orthosteric inhibition of kinases and GPCRs toward previously intractable target classes including transcription factors, scaffolding proteins, protein-protein interactions, and targets amenable to degradation rather than inhibition. This expansion enables the disease area diversification documented across 14 CAS TrendScape disease maps, as novel modalities unlock therapeutic intervention in conditions previously lacking druggable targets.

3. Disease Area Diversification Beyond Oncology Dominance

While oncology maintains largest absolute patent volumes across all 14 disease-focused CAS TrendScape maps, the pharmaceutical landscape reveals strategic diversification into precision-defined patient populations rather than broad indications. **Oncology** itself demonstrates evolutionary patterns, with innovation concentrated in rare lymphoma subtypes and molecularly defined tumor categories rather than major cancer types like lung cancer, melanoma, and AML, indicating that subtype specificity drives differentiation in mature oncology markets.

The most striking emergence appears in **non-oncological categories** where novel modalities enable previously impossible interventions. Notably, infectious and urological diseases show minimal emergence compared to other branches, with growth rates predominantly 1.0-1.1X indicating mature therapeutic landscapes where innovation faces commercial and scientific constraints.

How to Leverage This Report

The CAS TrendScape maps are designed to serve multiple purposes: For executives, they provide a strategic overview of innovation patterns that can inform corporate development, licensing, and M&A activities. For discovery scientists, they highlight areas of intense research activity that may suggest competitive threats or collaborative opportunities. For medicinal chemists and pharmacologists, they identify disease areas where mechanistic understanding is expanding, potentially revealing novel targets or underexplored chemical space.

Patent intelligence, when analyzed through the comprehensive lens provided by CAS data and advanced analytics, illuminates the path forward. Organizations that master this intelligence will lead the next era of pharmaceutical innovation. This report provides the foundation for such strategic decision-making, grounded in data spanning millions of patent documents and decoded through scientific expertise.

1. Introduction

Patents represent far more than legal instruments. They are strategic signals of where pharmaceutical innovation is headed. Patent intelligence occupies a critical middle ground in the pharmaceutical innovation timeline: innovations mature enough to warrant intellectual property protection yet early enough to reveal emerging trends before they become obvious to competitors. Unlike scientific publications that capture exploratory research or clinical trials that reflect late-stage development, patent data provides systematic, quantifiable records of innovation hotspots, technology convergence, and the organizations shaping medicine's future.

This report analyzes over 368,000 pharmaceutical patents filed globally between 2020 and 2025, leveraging advanced natural language processing (NLP) and data analytics to extract insights impossible through manual review and resulting in more than 25 comprehensive CAS TrendScape maps (**Figure 1**). This comprehensive framework reveals not just what is being patented, but how the innovation landscape is evolving across biological targets, disease applications, therapeutic platforms, geographic regions, and institutional ecosystems.

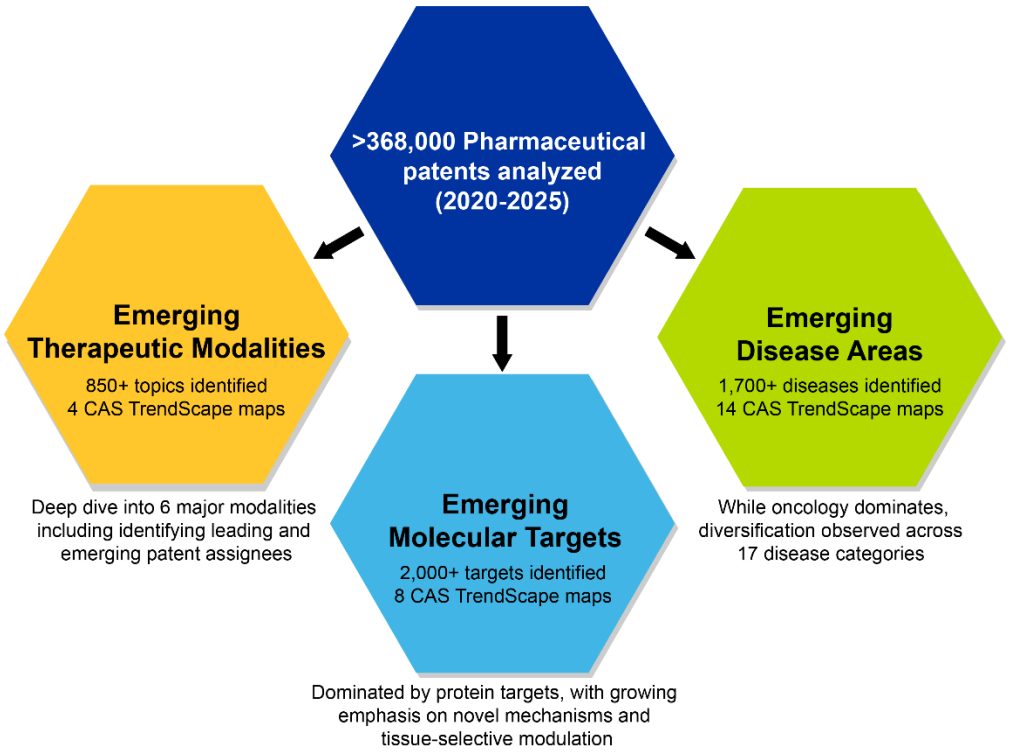


Figure 1. Schematic showcasing the contents of the report with a focus on emerging therapeutic targets, modalities, and disease areas.

The timing of this analysis captures pharmaceutical R&D at an inflection point. The COVID-19 pandemic accelerated the validation of non-traditional therapeutic platforms, most dramatically mRNA technology, which progressed rapidly from academic curiosity to global healthcare solution. This success has catalyzed investment across multiple frontier modalities: targeted protein degraders (PROTACs validated by the recent U.S. FDA approval of vepdegestrant in May 2026), cell therapies beyond CAR-T, RNA therapeutics beyond vaccines, and radiopharmaceutical theranostics.

Simultaneously, technological revolutions in structural biology (AlphaFold), computational chemistry, and artificial intelligence have fundamentally altered drug discovery paradigms. Targets once dismissed as "undruggable" (such as transcription factors lacking enzymatic pockets, protein-protein interactions (PPIs) with extensive binding surfaces, scaffolding proteins without catalytic activity) are now viable therapeutic opportunities through molecular glues, allosteric modulators, and proximity-induced degradation strategies. These advances enable the disease area diversification documented in this report, where fibrotic diseases, genetic disorders, and rare metabolic conditions show exceptional patent emergence as novel modalities unlock previously intractable biology.

These scientific advances intersect with evolving competitive dynamics. China has emerged as a major pharmaceutical patent filer with distinct specialization patterns, though the United States maintains superior commercial translation. Academic institutions increasingly pursue patent protection alongside traditional publications. Leading pharmaceutical companies have shifted from modality-focused organizations (small molecule companies vs. biologics companies) to platform-agnostic innovators that select optimal approaches based on target biology rather than historical competency.

Our methodology combines traditional patent analytics with sophisticated NLP techniques to extract meaningful scientific terms from patent text including titles, abstracts, claims, and CAS indexed terms from the CAS Content Collection™. This analysis leverages our unique position as the world's most comprehensive source of disclosed scientific information. Our approach integrates multiple CAS capabilities: the chemist-curated substance registry accessible via CAS REGISTRY®, extensive biological target databases accessible via CAS BioFinder®, and decades of indexing expertise accessible via CAS SciFinder® and CAS IP Finder, powered by STN™.

This data foundation, analytics approach, and our scientific knowledge in pharmaceutical research allow us to move beyond simple patent counts to understand and deliver insights about the actual technological content of innovations, identify interesting co-occurrence patterns, and track the evolution of scientific concepts over time, and reveal white space opportunities where unmet scientific needs intersect with emerging technological capabilities. The 26 CAS TrendScape maps developed for this report visualize the multidimensional patent landscape, revealing not only which technologies are growing but how they relate to one another.

The report is divided into several sub-sections and progresses from foundational competitive analysis to granular scientific insights to therapeutic area applications. Competitive analysis examines geographic filing patterns, institutional ownership dynamics, and temporal trends. Modality assessment provides deep dives into six major platforms—small molecules, biologics, peptides, cell/gene therapies, targeted protein degradation, and advanced delivery systems—identifying leading patent assignees and companies with robust patenting activities that reveal technology access priorities. Target analysis maps the 2,000+ molecular targets demonstrating unprecedented expansion of the druggable genome beyond traditional kinases and GPCRs. Disease area analysis presents 14 comprehensive CAS TrendScape maps spanning 17 disease categories, revealing striking diversification where fibrotic diseases and genetic disorders show exceptional emergence while infectious and urological diseases demonstrate constrained innovation reflecting mature therapeutic landscapes.

In an industry where R&D costs exceed USD $2.3 billion per approved drug (as estimated in 2024[1]) and development timelines span 10-15 years, strategic intelligence is imperative. Understanding where innovation is concentrating, which technologies are maturing, and where white space opportunities exist provide competitive advantage for pharmaceutical companies

navigating modality selection and therapeutic area prioritization, guides academic research toward translational impact in areas showing commercial momentum, informs investment strategies, and accelerates the development of medicines that improve and extend human life.

This report represents the most comprehensive analysis of recent pharmaceutical patent trends available, combining breadth of coverage with depth of scientific insight. The pharmaceutical innovation landscape documented here reveals an industry simultaneously diversifying across all three dimensions. Organizations that master this integrated three-dimensional patent intelligence will lead the next era of pharmaceutical innovation.

The future of pharmaceutical innovation is being written in patent filings today. This report, powered by unparalleled scientific information infrastructure and analytical capabilities at CAS, decodes that future.

2. Methodology

2.1 Search Strategy

This analysis leverages the CAS Content Collection™, utilizing our proprietary indexing system that categorizes substances based on their functional roles in pharmaceutical applications. Our search strategy specifically targeted patent documents containing substances indexed with pharmaceutical-relevant role codes, including therapeutic (THU) for compounds with direct therapeutic applications, pharmacological (PAC) for substances with defined pharmacological activity, pharmacokinetic (PKT) for compounds studied in the context of absorption, distribution, metabolism, and excretion, and diagnostics (DGN) for diagnostic and theranostic applications. This role-based approach ensures comprehensive coverage of pharmaceutical innovation while filtering out non-relevant chemical patents, providing a focused dataset that accurately represents drug discovery and development activities.

2.2 Data Scope and Extraction

The study encompasses patent documents published between January 2020 and December 2025. Our dataset comprises patent documents from 108 global patent authorities, including major jurisdictions such as the United States Patent and Trademark Office (USPTO), European Patent Office (EPO), World Intellectual Property Organization (WIPO) via the Patent Cooperation Treaty (PCT), and patent offices across Asia, including China (CNIPA), Japan (JPO), and South Korea (KIPO), among others.

For each patent document, we extracted comprehensive bibliographic and technical information, including patent assignees, geographic filing locations, patent family relationships to track related filings across jurisdictions, titles, abstracts, and claims text, and temporal data including priority dates and publication years. Beyond raw patent text, we utilized CAS expert indexing to access scientifically validated concepts and applications associated with each patent, CAS Registry Numbers® providing unique identifiers for specific chemical substances, detailed chemical structures, and functional role annotations describing how substances are utilized within the invention context.

2.3 Data Analysis

Our analytical framework combined targeted keyword searching with the controlled vocabulary of CAS indexing to identify relevant patent subsets. We developed comprehensive search queries centered around specific therapeutic modalities (e.g., "monoclonal antibodies," "CRISPR," "mRNA"), target classes (e.g., "kinase inhibitors," "GPCR modulators"), and disease areas (e.g., "oncology," "neurodegenerative diseases"). These searches were refined using CAS indexed concepts, which provide standardized scientific terminology independent of variations in patent language across different jurisdictions and filing entities. This approach mitigates the inherent challenges of patent text analysis, including the use of deliberately broad or obfuscated language, variations in terminology across countries and languages, and inconsistent naming conventions for chemical entities and biological targets.

2.4 NLP Methodology

To complement structured indexing, we employed advanced natural language processing (NLP) techniques to identify emerging topics and patterns within the patent corpus. Our NLP pipeline extracted candidate phrases ranging from single terms to six-word expressions from patent abstracts, titles, and claims sections. These candidate phrases underwent initial classification using machine learning algorithms trained to recognize pharmaceutical concepts, followed by multiple rounds of expert validation by domain specialists in medicinal chemistry, pharmacology, and biotechnology to ensure scientific accuracy and relevance. For a detailed description of the NLP methodology, please refer to Iyer et al.[2]

The validated emerging topics are presented through CAS TrendScape maps: interactive visualizations that convey multiple dimensions of scientific interest simultaneously, including publication volume, growth trajectories, and conceptual relationships between topics. These maps enable the identification of rapidly growing research areas, mature fields with sustained activity, and emerging niches that may represent future innovation hotspots, providing quantitative metrics and qualitative context for understanding the pharmaceutical patent landscape.

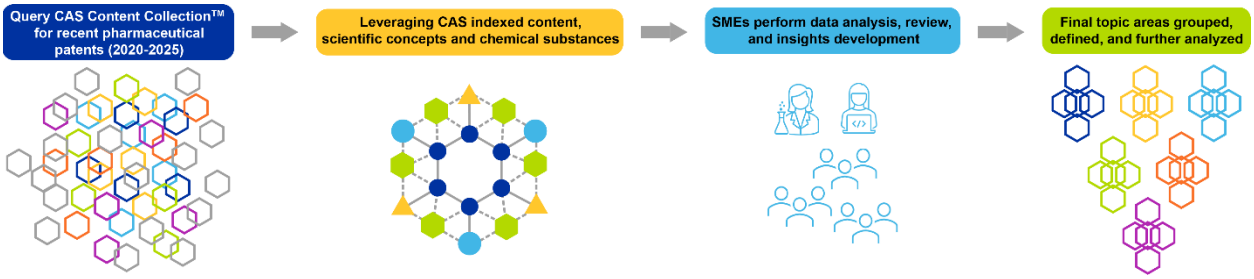


Figure 2. Schematic showing representative steps in the methodology for data analysis and NLP-based analysis.

3. Patent landscape

The intellectual property landscape provides critical insight into pharmaceutical innovation trends and competitive positioning within therapeutic areas. Patent activity serves as a leading indicator of research investment, strategic focus, and the maturation of drug discovery programs. Understanding these patterns enables identification of emerging therapeutic modalities, assessment of competitive intensity, and anticipation of potential freedom-to-operate challenges. We analyzed pharmaceutical patent publications from the CAS Content Collection spanning 2020 to 2025 to characterize recent trends in intellectual property generation and filing strategies within the pharmaceutical sector.

Analysis of pharmaceutical patent publications from 2020 to 2025 reveals distinct patterns in volume (**Figure 3**). The difference between stable patent family counts and expanding individual patent numbers suggests increased jurisdictional filing strategies and continued development of existing patent families.

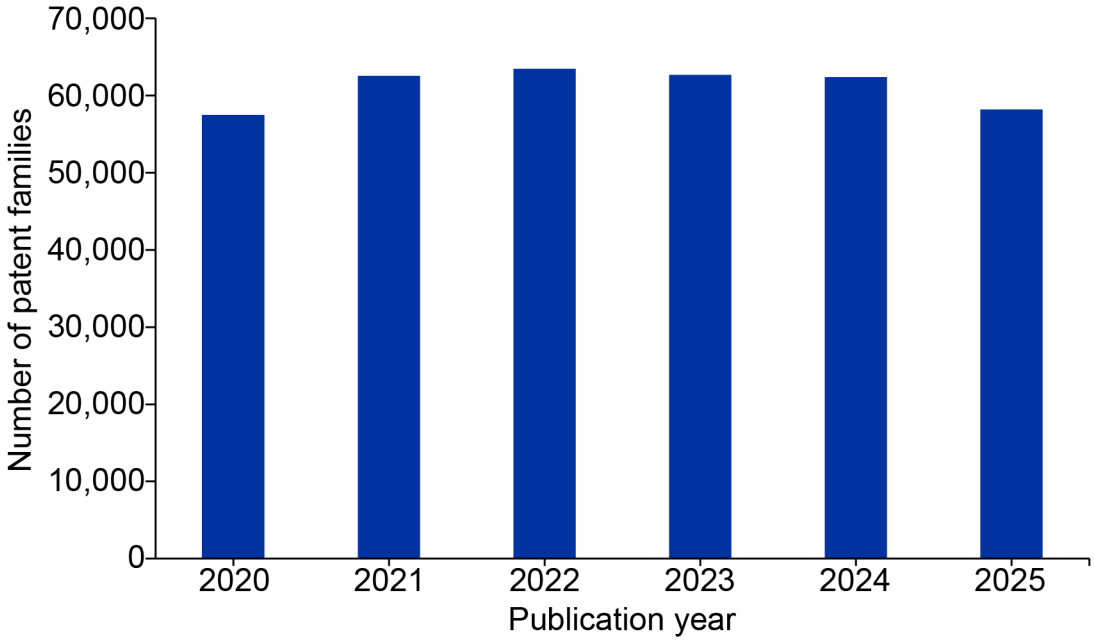


Figure 3. Annual pharmaceutical patent family publications from 2020 to 2025 from the CAS Content Collection.

3.1 Patent processing times and regional variations

Patent examination timelines directly impact the effective patent life available for pharmaceutical products and influence strategic decisions regarding jurisdictional filing priorities. We analyzed examination durations from application to grant across eight major patent offices, revealing substantial differences in processing times differences that can shape global pharmaceutical patent strategy.

The examination timeline for pharmaceutical patents varies across major patent offices worldwide, with significant implications for drug development strategies and market exclusivity planning (**Figure 4A**). The United States Patent and Trademark Office (USPTO) demonstrates the most expedited processing time at an average of two years from application to grant, followed closely by the Korean Intellectual Property Office (KIPO) at 2.9 years and the China National Intellectual Property Administration (CNIPA) at three years. Notably, **Figure 4A** highlights minimum processing times across modalities, with the USPTO achieving grants in as little as 0.2 years for certain applications. Analysis of modality-specific timelines reveals that advanced drug delivery systems and small molecules are granted faster than average in the United States (1.5 and 1.6 years, respectively), reflecting streamlined examination pathways for these established technology areas. These relatively brief timelines enable pharmaceutical companies to secure patent protection more rapidly in these jurisdictions, accelerating market entry and commercial planning. In contrast, the Canadian Intellectual Property Office exhibits the longest processing period at five years, with the European Patent Office (EPO) requiring 4.3 years. The intermediate processing times observed in India (3.3 years), Australia (3.6 years), and Japan (3.6 years) reflect the substantial examination burden faced by these offices. Such marked differences require careful coordination in global patent filing approaches, as extended examination timelines in major

pharmaceutical markets can significantly reduce the effective exclusivity period and undermine returns on drug development investments.

3.2 Global distribution and trends in pharmaceutical patent activity

The distribution of pharmaceutical patent applications and grants across major jurisdictions reflects market size considerations and regional innovation ecosystems. Analyzing the ratio of granted patents to total applications provides insight into examination stringency, applicant filing strategies, and the maturity of regional pharmaceutical innovation landscapes.

The global pharmaceutical patent landscape is dominated by three major jurisdictions, though distinct patterns emerge when examining granted versus total applications (**Figure 4B**). China leads substantially in the total number of patent applications, followed by the United States and the European Patent Office. However, the ratio of granted to total patents varies considerably, suggesting different applicant filing strategies across jurisdictions. Japan, South Korea, Australia, Canada, and India represent secondary but significant markets for pharmaceutical patent protection. China dominates with 22% of overall pharmaceutical patents applications which represents 42% of all patent families. While this shows greatly diversified patent activity, the percentage of patents that are granted is only around 10%. In contrast, the United States comprises roughly 6% of all patent families but 17% of all overall pharmaceutical patent applications (**Figure 5A**, and **5D**), showing more changes and refinements of technologies within patent families with a granted patent percentage of around 28%.

3.3 Patent publication trends reveal emerging markets drive recent patent publication growth

Temporal analysis of patent publications provides insight into the evolution of pharmaceutical innovation intensity and shifting strategic priorities across major patent offices. Comparing trends in patent families versus individual applications reveals how companies balance initial innovation disclosure with subsequent geographic expansion strategies.

Patent publication trends from 2020-2025 reveal distinct patterns across jurisdictions (**Figure 5**). For patent families (**Figure 5B**), most major offices, including China, the United States, Japan, and the EPO, show relatively stable publication rates (5,000-25,000 annually), with China exhibiting a peak around 2022-2023 followed by stabilization. India and, to a lesser extent, Russia demonstrate sustained upward trajectories in patent families, likely driven by increased small molecule innovation.

Individual patent applications show more dynamic trends (**Figure 5E** and **5F**). The United States, EPO, Japan, India, Australia, and South Korea all exhibit upward growth trajectories through 2025, reflecting expanding domestic pharmaceutical innovation sectors and strategic global filing strategies. These divergent patterns reflect the interplay of patent examination capacity, R&D investment shifts, and multinational filing strategies for novel therapeutics.

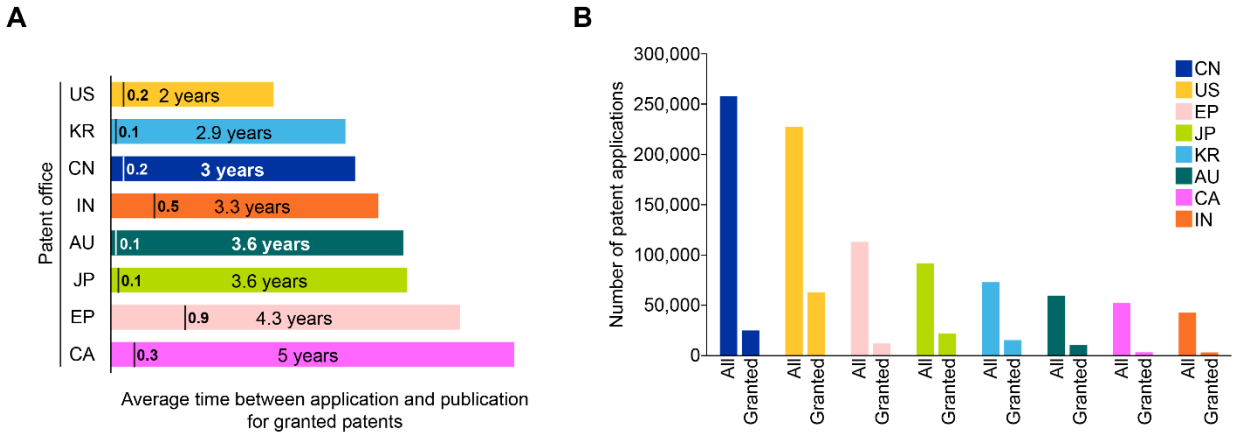


Figure 4. (**A**) Average examination time from application to grant for pharmaceutical patents across major patent offices. The horizontal line indicates the fastest times for granting. (**B**) Total applications versus granted patents by jurisdiction. CN, China; US, United States; EP, European Patent Office; JP, Japan; KR, South Korea; AU, Australia; CA, Canada; IN, India.

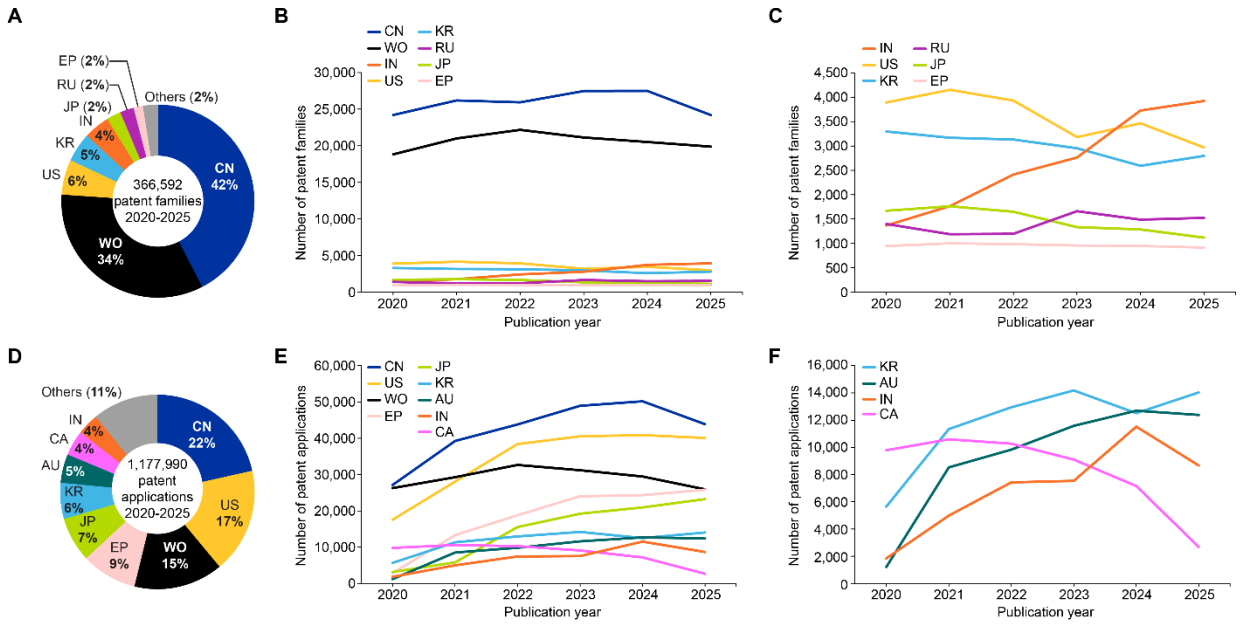


Figure 5. (**A** and **D**) Geographical distribution in terms of patent offices, and (**B**, **C**, **E** and **F**) yearly trends for selected patent offices – China (CN), World Intellectual Property Organization (WO), India (IN), United States (US), South Korea (KR), Russia (RU), Japan (JP), and European Patent Office (EP). The upper and lower panels correspond to patent families and individual patent applications, respectively.

3.4 Institutional origin and commercialization patterns in pharmaceutical patents

The institutional origin of patent applicants provides critical insight into the structure of pharmaceutical innovation ecosystems and the relative contributions of academic versus commercial sectors across different regions. Analyzing applicant geography across non-commercial and commercial entities reveals distinct national strategies for pharmaceutical research investment and technology transfer pathways.

The geographical distribution of pharmaceutical patent applicants reveals distinct patterns between overall filings, non-commercial research entities, and commercial organizations (**Figure 6**). In the general landscape (**Figure 6A**), China dominates with 47% of all pharmaceutical patent applications, followed by the United States at 16%, and South Korea at 7%, with remaining contributions from Japan, India, Russia, and European nations. When examining non-commercial applicants (**Figure 6B**), China's dominance becomes even more pronounced at 61% compared to 13% for the United States, suggesting robust pharmaceutical research activity within Chinese academic and governmental sectors. The commercial patent landscape (**Figure 6C**) exhibits notably different proportions, with China maintaining a leading but reduced position at 40% while the United States increases substantially to 21%, reflecting its robust private-sector pharmaceutical industry. European nations show modest increases in their commercial share, with Germany (3%), Switzerland (2%), the United Kingdom (2%), and France (2%) collectively representing a stronger presence than in non-commercial filings. This shift in relative contributions between sectors reflects varying innovation ecosystem structures, technology transfer efficiency, and national strategies for translating basic research into commercial pharmaceutical products, with China demonstrating exceptional academic patenting activity while the United States and Europe maintain stronger positions in commercial drug development.

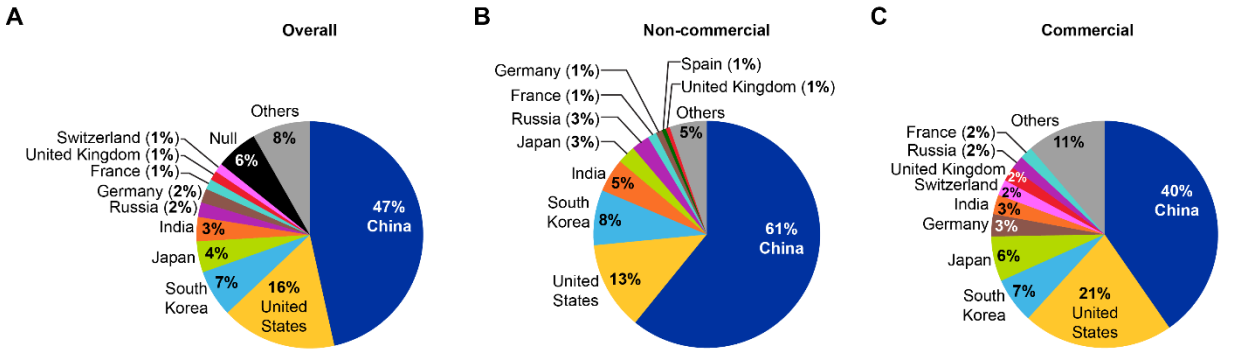


Figure 6. Percentage distribution of pharmaceutical patent families by assignee geography, indicating relative regional contributions for (**A**) overall, (**B**) research and academic institutions, and (**C**) corporate enterprises.

3.5 Patent portfolios reflect divergent innovation and acquisition strategies

Analysis of patent ownership patterns reveals the concentration of pharmaceutical intellectual property among specific organizations and their distinct approaches to portfolio development through internal innovation versus external acquisition. Understanding these organizational strategies provides insight into competitive positioning, therapeutic area focus, and technology transfer dynamics within the pharmaceutical industry.

Patent ownership is highly concentrated among Chinese entities (**Figure 6**). China accounts for 40% of all patent families filed by corporate enterprises, followed by the United States (21%) and South Korea (7%). The top patent holders include Jiangsu Hengrui Medicine (>1,200 families), Gilead Sciences (>1,200 families), and numerous Chinese pharmaceutical companies and research institutes. Patent acquisition strategies vary considerably across organizations, with some entities showing high percentages of patents acquired from other companies (~15-20% for certain organizations; **Figure 7**), indicating active in-licensing and patent portfolio consolidation strategies. In contrast, many major holders maintain predominantly internally developed patent portfolios. This landscape reflects organic innovation capacity and strategic intellectual property acquisition in the global pharmaceutical sector.

Notably, Novo Nordisk, best known for its leadership in GLP-1 receptor agonists and insulin therapeutics has been among the more active acquirers of externally developed patents, with a substantial share directed toward RNA interference (RNAi) and gene silencing technologies, multi-receptor agonist along with oral GLP-1 formulations, and Metabolic Dysfunction-Associated Steatohepatitis (MASH) therapeutics to build their capabilities beyond its core peptide franchise. Similarly, Sino Biopharmaceutical shows a comparatively elevated proportion of acquired patents, with its external portfolio concentrated on antibody-drug conjugates (ADCs) and next-generation immuno-oncology biologics, modalities that complement its traditional small molecule pipeline. These acquisition patterns suggest that even well-resourced organizations are increasingly relying on external innovation to access platform technologies outside their historical core competencies.

Leading pharmaceutical companies exhibit divergent patent publication trajectories from 2020-2025 (**Figure 8A**). Roche maintains the highest absolute patent output (~200-230 families annually), followed by Johnson & Johnson, which shows a declining trend. Jiangsu Hengrui Medicine demonstrates notable growth, peaking around 2022 (~200 families) before stabilizing. The others maintain relatively stable outputs ranging from 60-150 families annually.

When normalized to their total patents (**Figure 8B**), all companies appear to exhibit similar temporal fluctuations with Sanofi and AstraZeneca showing distinct upward trajectories. Despite differences in absolute patent volumes, these companies maintain comparable relative contributions to the overall pharmaceutical innovation landscape.

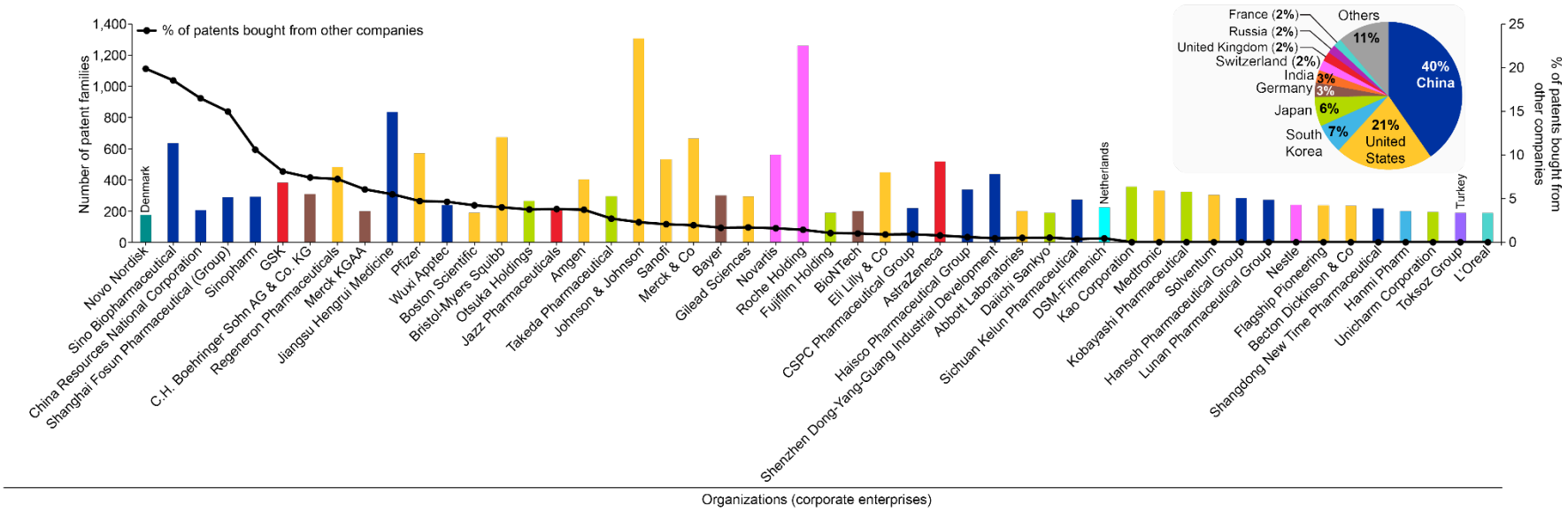


Figure 7. Leading organizations (corporate enterprises) in the number of patent families and the percentage of patents bought from other organizations. The inset pie chart shows the geographic distribution of organizations.

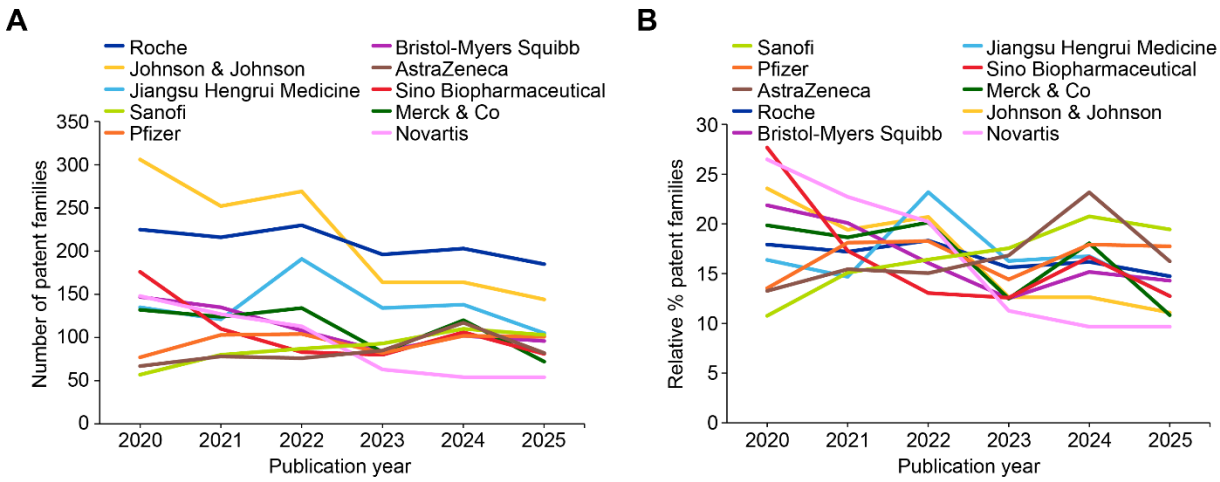


Figure 8. (**A** and **B**) Yearly patent trends for selected leading organizations (corporate enterprises). Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

3.6 U.S. Pharmaceutical patent activity demonstrates strong corporate and academic leadership

The United States demonstrates substantial pharmaceutical patent activity across diverse therapeutic modalities, including advanced drug delivery systems, antibody therapeutics, cell and gene therapies, and RNA therapeutics. This innovation landscape reflects contributions from corporate enterprises and academic institutions driving pharmaceutical research across multiple technology platforms.

The U.S. pharmaceutical patent landscape is characterized by strong contributions from established leaders and emerging innovators (**Figure 9** and **Figure 10**). Among established corporate enterprises (**Figure 9A**), Johnson & Johnson leads, followed by Roche and Merck. Regeneron, Bristol-Myers Squibb, and Pfizer form a substantial second tier, with Amgen, Eli Lilly & Co, and Gilead Sciences comprising a third tier of established innovators.

At the portfolio level, these leading companies exhibit distinct but overlapping areas of innovation across biologics, small molecules, and precision medicine approaches (**Table 1**).

Table 1. Summary of patent portfolio focus for a few leading U.S. pharmaceutical companies

Company	Patent portfolio summary
Johnson & Johnson	Johnson & Johnson's portfolio is highly diversified across therapeutics and medical technologies, with strong capabilities in biologics, small molecules, and delivery systems. It emphasizes combination therapies, biomarker-guided treatment, and next-generation modalities such as cell therapies and vaccines.
Roche	Roche's portfolio centers on oncology and diagnostics, combining advanced biologics with genomic and companion diagnostic technologies. It reflects a strong precision medicine approach integrating therapy and patient stratification.
Merck	Merck's portfolio is driven by immuno-oncology, vaccines, and infectious disease therapeutics, with strong emphasis on checkpoint inhibitors and combinations. It integrates biologics, small molecules, and biomarkers to expand therapeutic reach.
Regeneron	Regeneron's portfolio centers on advanced antibody engineering and biologics platforms across key therapeutic areas. It emphasizes precision medicine, combination strategies, and next-generation protein and gene-based modalities.
Bristol Myers Squibb	Bristol Myers Squibb's portfolio is centered on immuno-oncology, with innovations in checkpoint inhibitors, antibody therapies, and combination regimens. It also includes small molecules and emerging modalities supporting precision medicine approaches.

This company-level differentiation reinforces the broader landscape described above:

- **Johnson & Johnson and Roche** demonstrate breadth and integration across modalities and diagnostics.
- **Merck and Bristol-Myers Squibb** are strongly anchored in immuno-oncology and combination strategies.
- **Regeneron** stands out for its deep specialization in antibody engineering and biologics platforms.

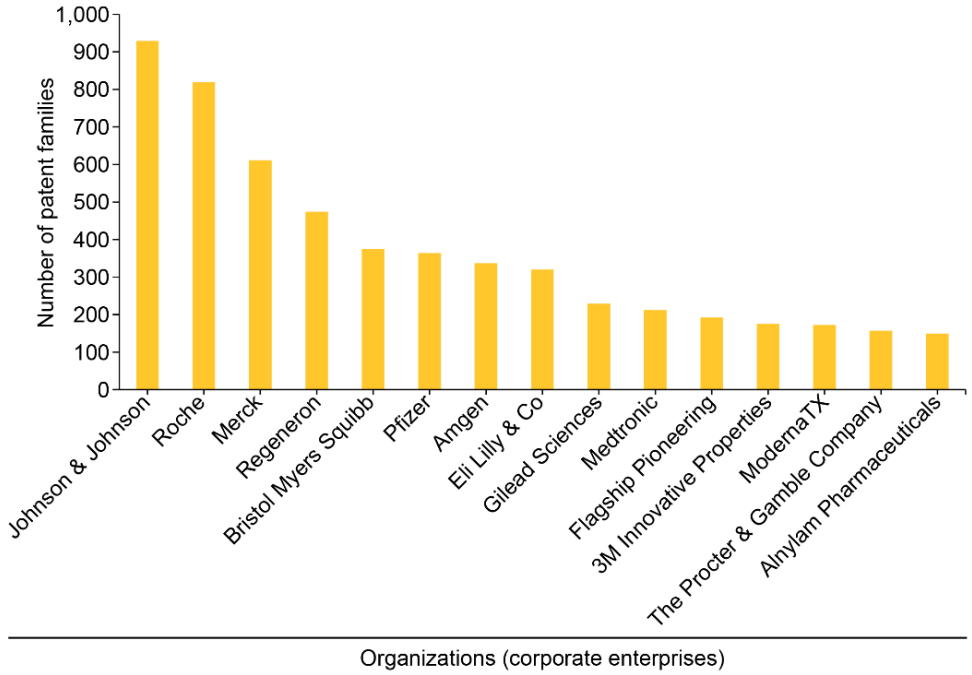
Together, these top five companies highlight a clear trend toward diversified innovation models that integrate biologics, small molecules, and advanced modalities such as cell therapies and precision diagnostics, alongside increasing emphasis on combination strategies and biomarker-driven approaches across therapeutic areas.

Temporal analysis reveals dynamic growth among emerging companies (**Figure 10A** and **10B**). Gilead Sciences shows the most pronounced late-stage growth, with a notable increase after 2023, while Boston Scientific Scimed demonstrates steady expansion with strong gains in recent years. Other emerging players, including Genzyme, Guardant Health, Foundation Medicine, and Voyager Therapeutics, exhibit consistent upward trajectories with moderate but sustained increases in annual patent activity. Additional organizations such as Neurocrine Biosciences and CaaMTech show lower but steadily rising activity toward the end of the period (**Figure 10A**).

Among academic and research institutions (**Figure 10B**), The Board of Regents of the University of Texas System demonstrates the strongest overall growth, while Memorial Sloan Kettering Cancer Center shows a pronounced surge in later years. Additional institutions, including the University of Pittsburgh, University of Massachusetts, and Mayo Foundation for Medical Education and Research, display steady upward trends. Other organizations such as Rutgers, The State University of New Jersey, The Texas A&M University System, and the University of Connecticut contribute to a broader base of sustained but moderate growth.

Academic and research organizations show high absolute output and emerging growth patterns (**Figure 9B**). The University of California system dominates, followed by The University of Texas System and Stanford University. The Johns Hopkins University, University of Pennsylvania, and Columbia University form a substantial second tier. This robust academic patenting activity, encompassing major research universities and specialized institutions, underscores the critical role of U.S. research institutions in pharmaceutical innovation alongside the corporate sector.

A



B

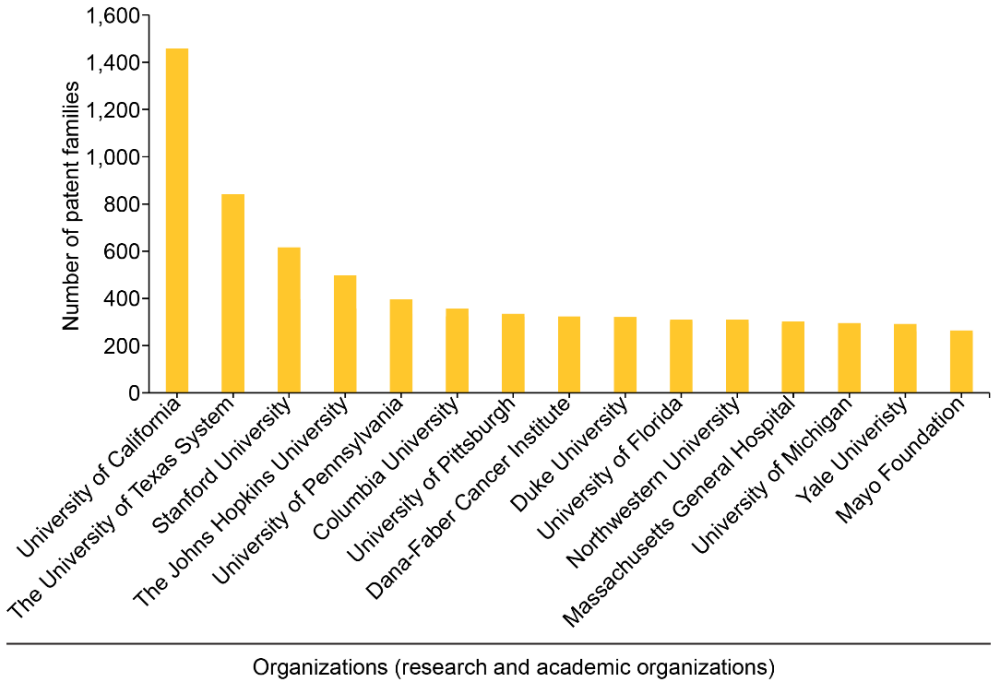


Figure 9. Leading organizations divided into (**A**) corporate enterprises and (**B**) research and academic institutions located in the United States based on patent assignee data. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

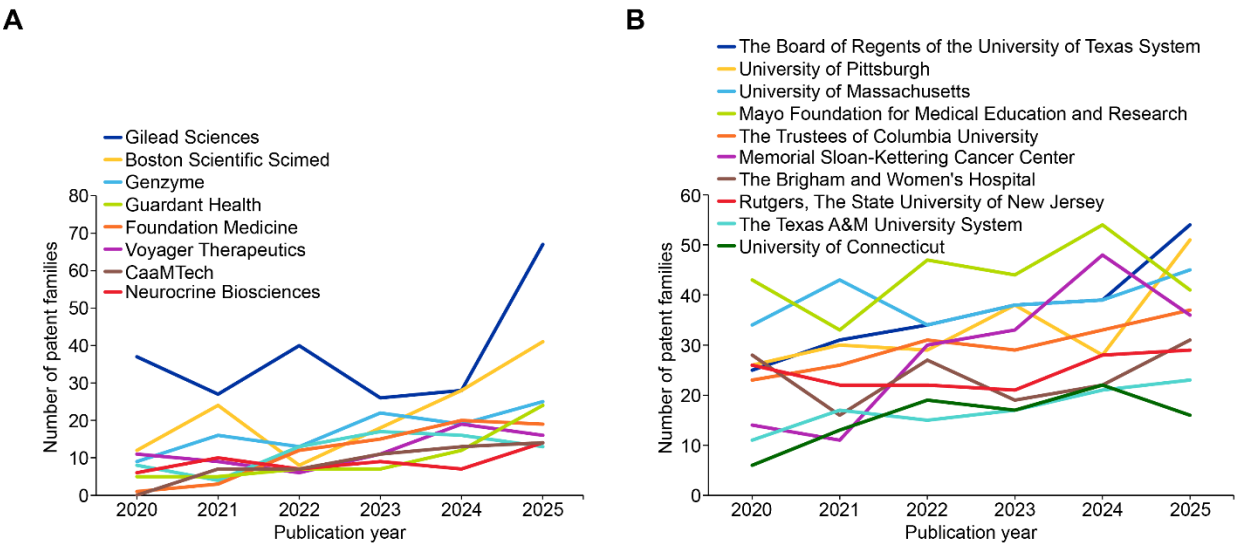


Figure 10. Yearly patent trends for selected organizations in terms of (**A**) corporate enterprises and (**B**) research and academic organizations headquartered/located in the United States based on patent assignee data. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

3.7 China's pharmaceutical patent ecosystem exhibits exceptional growth and distribution across corporate and academic sectors

China demonstrates substantial pharmaceutical patent activity across diverse therapeutic modalities and organizational structures. This innovation landscape reflects contributions from traditional pharmaceutical companies, academic institutions, and specialized patent-holding entities driving pharmaceutical research across multiple technology platforms.

China's pharmaceutical patent landscape demonstrates exceptional scale and strong distribution across both corporate and academic sectors (**Figure 11-13**). Leading corporate entities (**Figure 11A**) are dominated by Jiangsu Hengrui Medicine, followed by Chia Tai Tianqing Pharmaceutical Group and Lunan Pharmaceutical Group. A broad middle tier, including Haisco Pharmaceutical Group, Hansoh Pharmaceutical Group, and multiple Shenzhen- and Shanghai-based pharmaceutical companies, highlights a highly distributed corporate ecosystem in which many firms maintain substantial portfolios.

Chinese academic institutions (**Figure 11B**) show exceptionally high patent output, with China Pharmaceutical University and the Chinese Academy of Sciences leading, followed by Zhejiang University and Sichuan University. A strong second tier including Shandong University, Sun Yat-Sen University, and Shenyang Pharmaceutical University reinforces a highly productive and broadly distributed academic innovation base.

At the portfolio level, leading Chinese corporate players show strong emphasis on small-molecule therapeutics, translational drug development, and increasingly biologics and RNA-related modalities, with expansion into AI-driven and gene-based approaches among emerging firms (**Table 2**).

Table 2. Summary of patent portfolio focus for a few leading Chinese pharmaceutical companies

Company	**Patent Portfolio Summary**
Jiangsu Hengrui Medicine	Jiangsu Hengrui Medicine's portfolio is centered on oncology, anesthesia, and innovative small-molecule therapeutics, with growing investments in biologics and immunotherapy. The company emphasizes translational drug development and lifecycle expansion through formulation, delivery, and combination strategies.
Chia Tai Tianqing Pharmaceutical Group	Chia Tai Tianqing's portfolio focuses on liver disease, oncology, and anti-infectives, with strong capabilities in both generic and novel drug development. It integrates small-molecule innovation with biologics and formulation optimization to expand therapeutic reach.
Lunan Pharmaceutical Group	Lunan Pharmaceutical's portfolio spans cardiovascular, oncology, and anti-infective therapeutics, with a foundation in small-molecule drugs and increasing activity in biologics. The company emphasizes scalable manufacturing and incremental innovation through formulation and delivery improvements.
Haisco Pharmaceutical Group	Haisco's portfolio focuses on specialty therapeutics including anesthetics and CNS-related drugs, alongside emerging oncology assets. It demonstrates strong recent growth and emphasizes targeted small molecules and clinical-stage pipeline expansion.
Hansoh Pharmaceutical Group	Hansoh Pharmaceutical's portfolio is driven by oncology, CNS disorders, and metabolic diseases, combining small-molecule innovation with biologics development. It emphasizes targeted therapies and strategic expansion into next-generation modalities.

This company-level differentiation reinforces the broader landscape described above:

- **Jiangsu Hengrui Medicine** anchors the landscape with scale and breadth, reflecting leadership in small-molecule innovation with expanding biologics capabilities
- **Chia Tai Tianqing Pharmaceutical Group** and **Lunan Pharmaceutical Group** demonstrate strong, established portfolios rooted in small molecules, with increasing integration of biologics and translational development strategies
- **Haisco Pharmaceutical Group** and **Hansoh Pharmaceutical Group** represent a rapidly advancing tier, characterized by targeted therapeutics, specialty disease focus, and sustained portfolio growth

Together, these top five companies highlight a clear trend toward small-molecule foundations evolving into biologics-driven and more innovative therapeutic portfolios, alongside increasing diversification across disease areas and modalities.

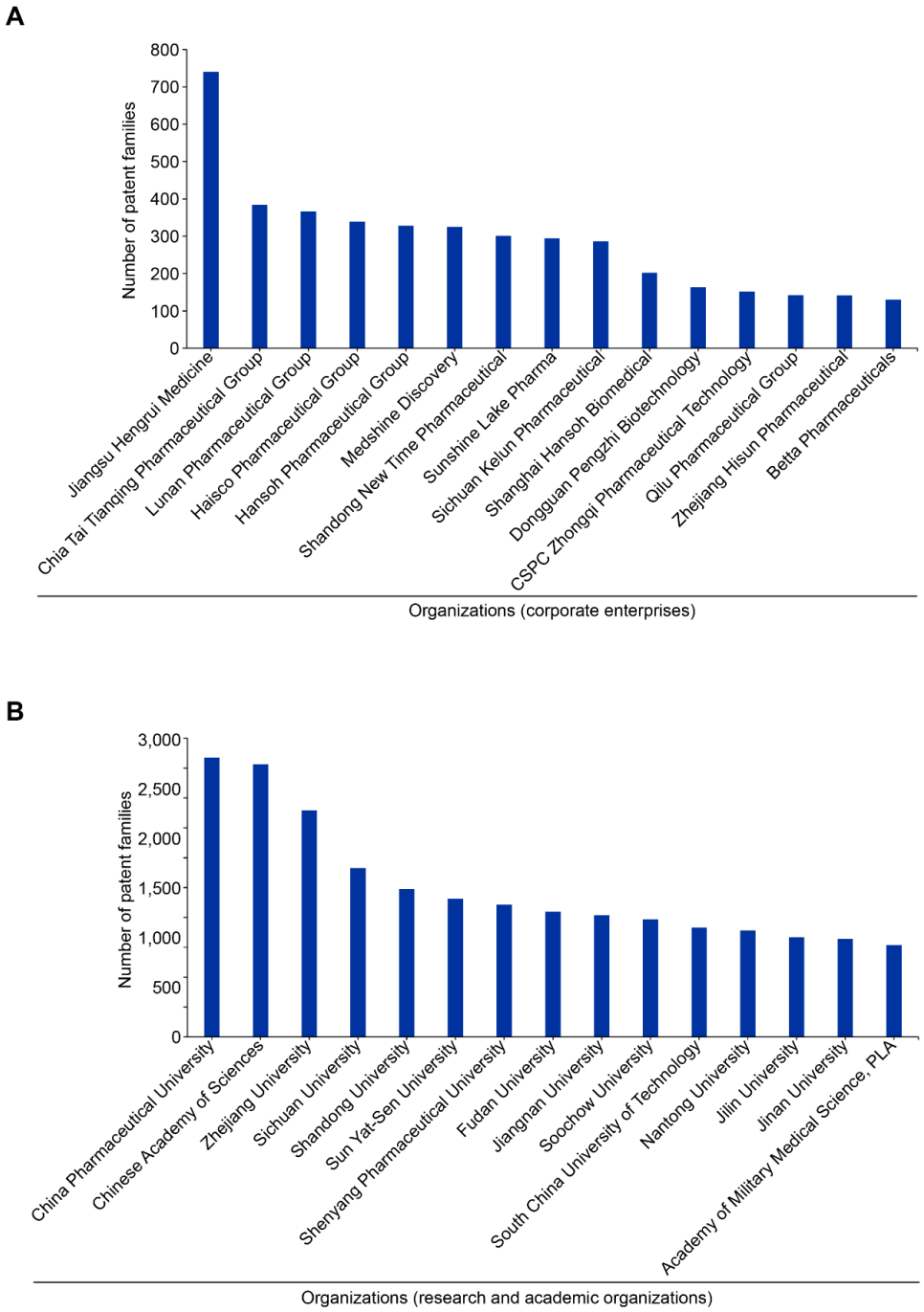


Figure 11. Leading organizations divided into (**A**) corporate enterprises and (**B**) research and academic institutions located in China based on patent assignee data. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Temporal analysis reveals sustained and accelerating growth across corporate entities (**Figure 12**). Companies such as Qilu Pharmaceutical, Wuhan Humanwell Innovative Drug Research and Development Center, and Changchun GeneScience Pharmaceutical show clear upward trajectories, with several organizations reaching consistent high annual output by 2024–2025. Additional firms, including Shanghai Qilu Pharmaceutical, Biocytogen Pharmaceuticals (Beijing), and Hefei TG Immunopharma, demonstrate late-stage acceleration with pronounced increases in the final years of the observed period, indicating rising innovation intensity.

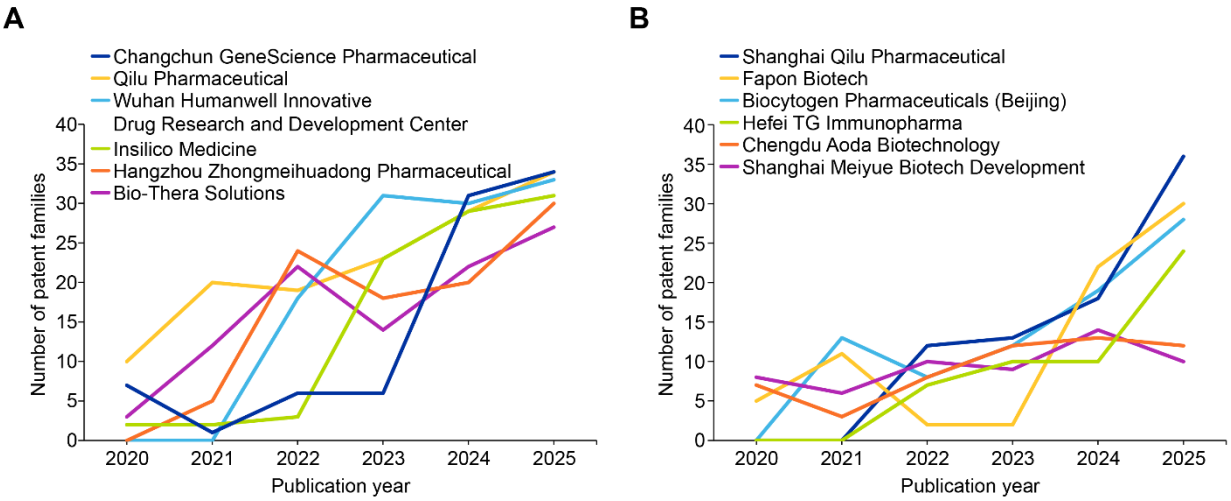


Figure 12. (**A** and **B**) Yearly patent trends for selected corporate enterprises headquartered/located in China based on patent assignee data. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Academic institutions (**Figure 13**) exhibit similarly strong growth dynamics. Chongqing Medical University and Ocean University of China show the most pronounced increases, with sharp rises after 2022, while PLA Air Force Medical University and South China Agricultural University maintain steady upward trajectories. Additional institutions such as Kunming University of Science and Technology, Nanjing University of Chinese Medicine, and Xinjiang Medical University demonstrate consistent growth, reflecting broad participation across major and regional research centers.

This multi-institutional and multi-sector growth pattern, spanning national academies, leading universities, and a broad corporate base, demonstrates China's systematic expansion of pharmaceutical innovation capacity, characterized by scale and broad distribution across organizational types.

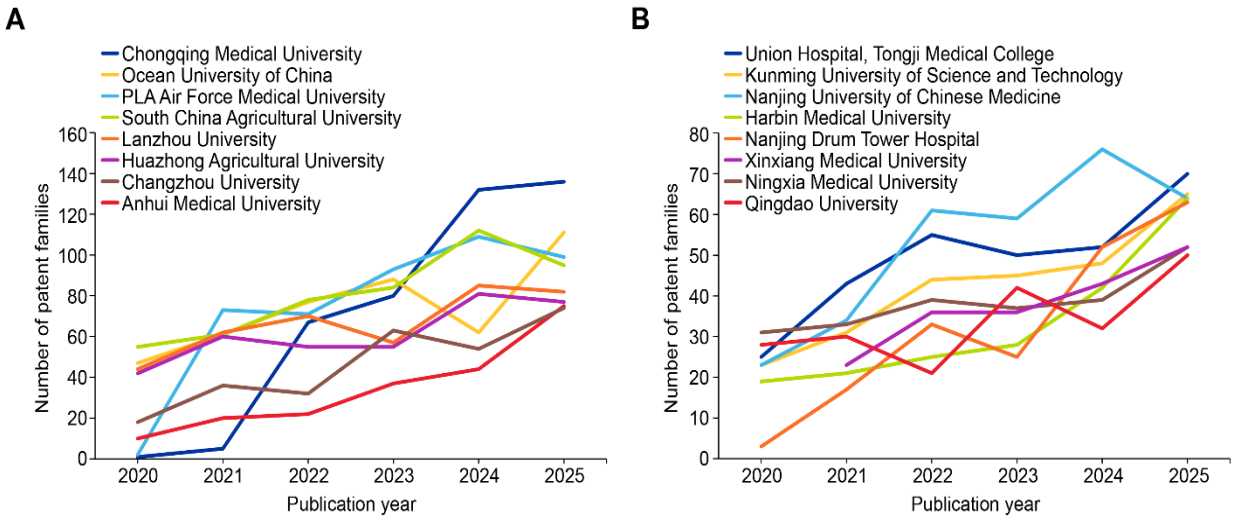


Figure 13. (**A** and **B**) Yearly patent trends for selected academic and research organizations in located in China based on patent assignee data. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

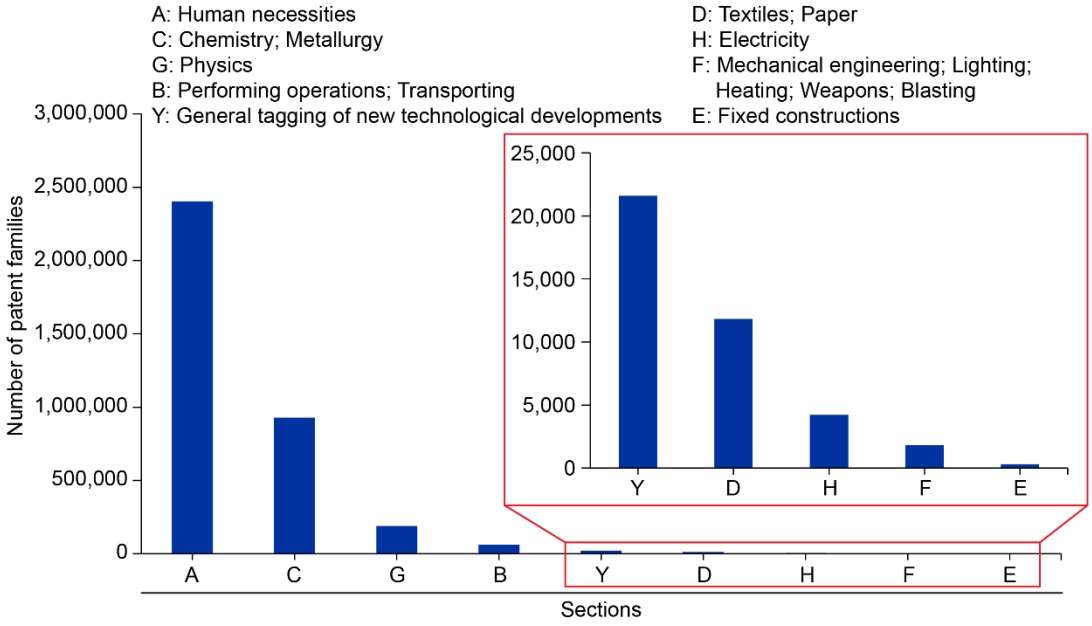
3.8 Pharmaceutical patent classifications show innovation concentrated in oncology

The International Patent Classification (IPC) and Cooperative Patent Classification (CPC) systems are hierarchical frameworks used globally to categorize patents by technical domain and function, enabling systematic organization and retrieval of patent information across jurisdictions.

In pharmaceutical patent analysis, IPC/CPC code distribution reveals key innovation trends: therapeutic focus areas, technological approaches, delivery mechanisms, and formulation strategies. Temporal shifts in code frequencies indicate emerging research priorities, such as transitions toward personalized medicine or novel therapeutic modalities. Cross-code analysis identifies technological convergence—for example, combining drug delivery systems with specific therapeutic classes—highlighting multidisciplinary innovation patterns and potential competitive landscapes within pharmaceutical R&D.

Our analysis of IPC/Code codes of recent pharmaceutical patents shows pronounced concentration in Section A (Human Necessities, ~2.4 million patent applications) and Section C (Chemistry; Metallurgy, ~950 thousand patent applications) (**Figure 14A**). Within Section A, the A61P subclass (Specific Therapeutic Activity of Chemical Compounds or Medicinal Preparations) categorizes patents by intended therapeutic application rather than chemical structure, enabling identification of drug development trends across disease areas and providing insights into therapeutic priorities and emerging treatment landscapes. Our analysis of the A61P subclass (**Figure 14B**), reveals that antineoplastic agents dominate globally across all major patent offices, followed by anti-infectives.

A



B

	Patent offices						
	CN	WO	US	KR	IN	EP	RU
Alimentary tract or the digestive system disorders	37,007	5,249	668	1,797	518	360	725
Metabolism disorders	29,452	6,507	807	2,020	718	320	237
Endocrine system disorders	2,975	827	74	47	58	50	66
Blood or the extracellular fluid disorders	9,287	1,805	267	365	142	110	349
Cardiovascular disorders	33,062	5,190	616	1,143	472	389	391
Respiratory disorders	19,880	3,867	395	644	222	244	291
Urinary system disorders	9,533	2,074	219	356	153	130	157
Genital or sexual disorders; Contraceptives	11,106	988	166	402	122	117	249
Dermatological disorders	30,494	4,998	797	2,788	697	543	615
Skeletal disorders	20,187	2,810	366	1,095	255	218	321
Muscular or neuromuscular disorders	4,256	1,539	233	594	39	132	52
Anaesthetics	700	190	60	22	6	22	148
Nervous disorders	48,061	14,829	2,302	2,623	**1,112**	**970**	670
Senses	9,568	2,890	548	701	186	255	365
Non-central analgesic, antipyretic or antiinflammatory agents	29,742	4,940	569	2,076	658	331	421
Antiinfectives, i.e. antibiotics, antiseptics, chemotherapeutics	**57,251**	12,309	**3,202**	**3,159**	**1,278**	**1,098**	**1,752**
Antiparasitic agents	2,647	639	142	86	70	113	66
Antineoplastic agents	**93,200**	**29,038**	**3,793**	**4,457**	**1,377**	**1,333**	953
Immunological or allergic disorders	22,706	6,462	624	1,005	230	339	261
General protective or antinoxious agents	11,739	695	202	496	128	59	168
Drugs used in surgical methods	138	83	24	24	3	6	81
Drugs for specific purposes	9,890	3,440	131	589	350	170	352

Figure 14. (**A**) Overall distribution of pharmaceutical patents as per sections (A-H and Y) and (**B**) breakdown of pharmaceutical patents across the A61P (Specific Therapeutic Activity of Chemical Compounds or Medicinal Preparations) subclass based on their IPC/CPC codes.

The Chinese patent office leads across all major therapeutic areas, with substantial patent applications in nervous disorders, alimentary/digestive disorders, cardiovascular disorders, and metabolism disorders. The United States PTO shows relative strength in nervous disorders and antineoplastics, while India focuses on anti-infectives and antineoplastics, reflecting distinct national pharmaceutical priorities. This distribution highlights the global emphasis on oncology and infectious diseases as primary pharmaceutical innovation targets, with notable regional variations in therapeutic area focus.

This patent landscape reveals a rapidly evolving pharmaceutical innovation ecosystem shaped by convergence and competition, as small-molecule foundations expand into biologics, gene-based therapies, and precision medicine. Distinct regional trends emerge, with the United States driving translational integration and China scaling innovation across a broad and highly distributed base. Together, these dynamics define an increasingly competitive intellectual property environment that will shape the pace, direction, and global leadership of future drug development.

4. Innovations in therapeutic modalities and targets

4.1 Platform Diversification Reflects Biology-Driven Modality Selection

The pharmaceutical industry's innovation portfolio reflects a strategic diversification beyond traditional small molecule therapeutics, signaling a fundamental shift in drug discovery and development approaches. Analysis of therapeutic modality distributions reveals the continued strength of established platforms and emergence of transformative technologies that are reshaping R&D investment priorities and competitive strategies.

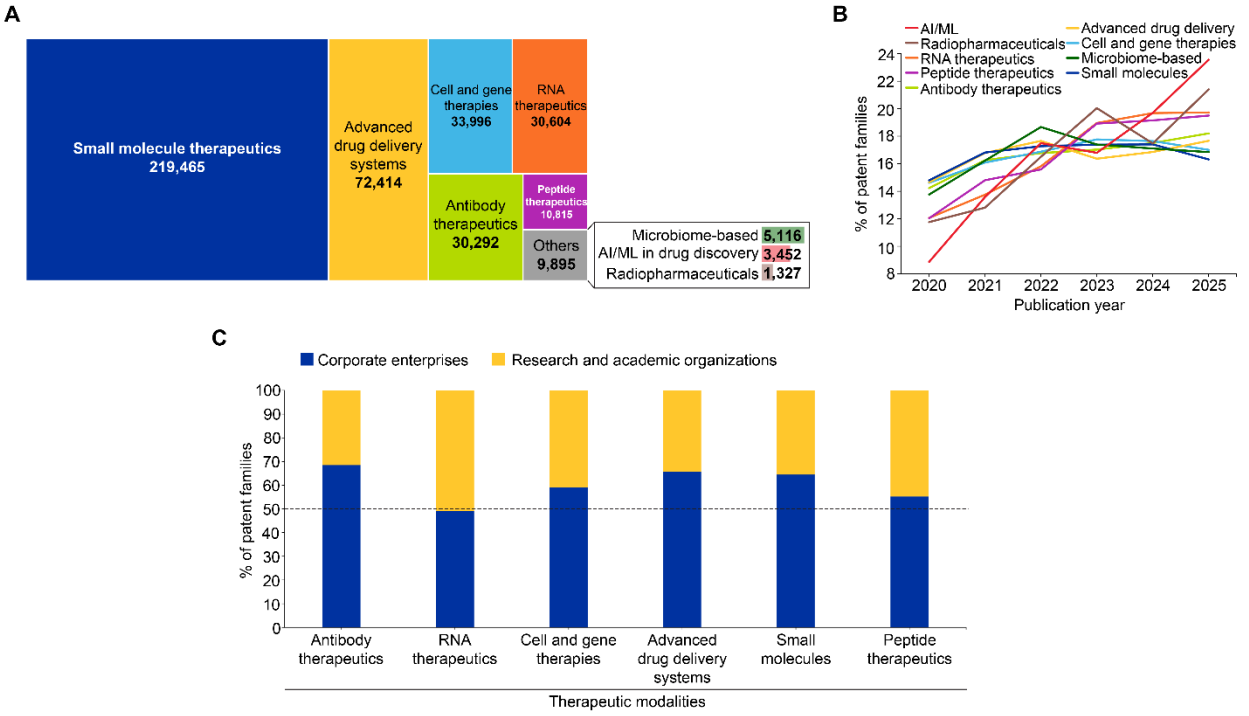


Figure 15. (**A**) Distribution of pharmaceutical patents across therapeutic modalities and (**B**) their yearly trends. (**C**) Distribution of pharmaceutical patents filed by corporate enterprises and research and academic institutions across therapeutic modality types. Data includes pharmaceutical patents from the CAS Content Collection for the period 2020-2025.

Small molecule therapeutics constitute most of the pharmaceutical patent activity, representing approximately 60% of all filings (**Figure 15A**). This sustained dominance reflects the inherent advantages of small molecules in reaching intracellular targets, achieving oral bioavailability, and penetrating challenging biological barriers such as the blood-brain barrier. However, the relative stability of small molecule patent proportions over the past few years (**Figure 15B**) indicates a mature market where innovation is focused on refinement rather than expansion, including enhanced target selectivity, improved drug-like properties, and novel mechanisms such as targeted protein degradation (including PROTACs).

The most pronounced growth trajectories are observed in **RNA therapeutics** and **peptide therapeutics**, both demonstrating sustained rapid expansion since 2020 (**Figure 15B**). The acceleration in RNA therapeutics (8%, **Figure 15**) extends well beyond mRNA vaccine applications, reflecting fundamental technological advances in chemical stabilization, delivery systems (particularly lipid nanoparticles), and tissue-specific targeting. This growth pattern indicates that RNA modalities are transitioning from specialized applications toward mainstream therapeutic platforms capable of addressing targets that have been historically difficult to target through traditional approaches. The platform enables diverse mechanisms including gene silencing (siRNA), protein replacement (mRNA), and splice modulation (antisense oligonucleotides; ASOs), expanding the druggable genome significantly.

Similarly, the rise in peptide therapeutics (3%, **Figure 15**) reflects breakthrough solutions to historical limitations around metabolic stability and membrane permeability. Advances in peptide engineering including cyclization, incorporation of non-natural amino acids, and constrained peptide architectures have transformed peptides into viable drug candidates capable of disrupting protein-protein interactions that remain inaccessible to conventional small molecules. This capability addresses a critical gap in the therapeutic landscape, as protein-protein interactions represent a large class of biologically validated but traditionally "undruggable" targets.

Antibody therapeutics (8%, **Figure 15A**) display modest but consistent growth throughout the analysis period (**Figure 15B**). This measured expansion reflects market maturation rather than declining innovation, as the field emphasizes next-generation formats that extend capabilities beyond simple target binding. Patent activity is shifting toward bispecific antibodies that simultaneously engage multiple targets such as antibody-drug conjugates (ADCs) that deliver cytotoxic payloads with precision and engineered variants with improved tissue penetration or extended half-life.

The most striking growth pattern emerges in frontier technologies: **artificial intelligence (AI)/machine learning (ML)** applications in drug discovery demonstrate the steepest trajectory of any modality (**Figure 15**), rising from approximately 9% of patents in 2020 to nearly 24% in 2025. This dramatic acceleration reflects the integration of computational approaches across the entire drug discovery pipeline from target identification and lead generation to property optimization and clinical trial design. The growth trajectory suggests that AI/ML has evolved from an experimental tool to a foundational technology with implications for development timelines, success rates, and the competitive value of proprietary chemical and biological datasets. **Radiopharmaceuticals**, though representing a smaller volume (0.3%, **Figure 15A**), exhibit similar strong upward momentum. This growth is driven by advances in targeted radionuclide therapy (particularly α-emitting isotopes), theranostic approaches that link diagnostic imaging with therapeutic intervention, and improved conjugation chemistry that enables stable attachment of isotopes to various targeting molecules.

Figure 15C shows the proportion of patent families contributed by corporate enterprises (blue) versus research/academic organizations (yellow) across different therapeutic modalities. Overall, companies dominate most areas (often ~60-70%), especially in antibody therapeutics, advanced drug delivery systems, and small molecules, while academic/research contributions are relatively higher in RNA therapeutics and peptide therapeutics, where the split is closer to 50-50%.

These trends collectively indicate a pharmaceutical innovation landscape undergoing fundamental transformation. The simultaneous growth of multiple modalities suggests that the industry is moving toward a strategy where therapeutic mechanism and target biology drive modality selection, rather than relying on a single platform approach. This platform diversification, enabled by AI-driven integration and optimization, represents an evolution toward precision medicine where therapeutic modality becomes a strategic variable optimized for each specific biological context rather than a constraint imposed by historical expertise.

4.2 Emerging opportunities in therapeutic modalities across platforms and drug classes

This section leverages NLP-based CAS TrendScape maps to visualize patent clustering and growth dynamics within each modality category, revealing which specific approaches are driving overall platform growth versus maintaining baseline activity.

TrendScape visualizations employ size (patent volume) and color (growth rate) to convey current market position and future trajectory simultaneously. This enables the identification of crowded competitive spaces, emerging high-growth niches, and underexplored white space opportunities. The following analyses dissect how modality innovation is diversifying: traditional modalities such as small molecules continue to demonstrate robust patent activity refining their capabilities (**Figure 16**), breakthrough mechanisms gaining validation (PROTACs transitioning from academic curiosity to clinical reality; **Figure 17**), frontier technologies emerging (circular RNA, CAR-NK cells, molecular glues; **Figure 18**), while also showcasing increasing diversification into biologics, peptide therapeutics, radiopharmaceuticals etc. (**Figure 17-19**). These granular patterns provide actionable intelligence for portfolio strategy, partnership evaluation, and competitive positioning within the rapidly evolving modality landscape.

4.2.1 The landscape of small molecule: sustained innovation in traditional drug classes and breakthrough mechanisms

Small molecules continue to dominate pharmaceutical patent activity, representing approximately 60% of all filings, though their evolution reflects a strategic shift from broad-spectrum agents toward precision-targeted inhibitors addressing previously intractable biology and resistance mechanisms. The patent landscape reveals the sustained productivity of validated target classes and remarkable diversification into novel mechanisms spanning protein degradation, epigenetic regulation, and cellular homeostasis pathways (**Figure 16**).

Kinase inhibitors (1X) are amongst those maintaining large patent volumes among small molecule therapeutics, reflecting over two decades of clinical validation with ~100 U.S. FDA-approved agents.[3] However, growth is concentrating in previously underexplored kinases: *Casein kinase 2 (CK2)* (>2X) exhibits exceptional acceleration as a pleiotropic kinase regulating cell survival, circadian rhythm,[4] and viral replication.[5] Its growth reflects oncology applications (overexpressed in multiple cancers, promoting cell proliferation and suppressing apoptosis)[6] and emerging roles in neurodegenerative diseases[7] where CK2 phosphorylates tau and α-synuclein.[8] *DNA-dependent protein kinase (DNA-PK)* (1.5X) shows strong growth as a DNA damage response kinase whose inhibition synergizes with radiotherapy and poly(ADP-ribose) polymerase (PARP) inhibitors through synthetic lethality in DNA repair-deficient cancers.[9,10] *PIKfyve* (1.6-1.9X), a phosphoinositide kinase generating PI(3,5)P2 for endolysosomal function, demonstrates high growth driven by viral entry inhibition (including SARS-CoV-2),[11-13] cancer,[14] and neurological applications[15,16] exploiting endolysosomal trafficking dependencies.[17] *Src family kinases* (1.6-

1.9X) show renewed growth following early disappointments with pan-Src inhibitors (dasatinib, bosutinib etc.), with more selective approaches and specific tumor contexts (triple-negative breast cancer[18]) driving resurgent interest. *Hematopoietic progenitor kinase 1 (HPK1)* (1.3X) as a negative regulator of T cell receptor signaling represents an emerging immune checkpoint target,[19] whose inhibition enhances anti-tumor immunity, positioning HPK1 inhibitors as potential combination partners for existing immunotherapies.[20-22] *Fibroblast growth factor receptor (FGFR)* (1.3X) within receptor tyrosine kinases shows continued growth with multiple recently approved agents (erdafitinib,[23] pemigatinib,[24] futibatinib[25]) for FGFR-altered cancers validating the target class and spurring next-generation molecules addressing resistance mutations.

Established kinase pathways maintain robust baseline activity: *MAPK pathway* (1X) including RAF,[26] MEK,[27] and ERK inhibitors[28] for cancer; *PI3K/AKT/mTOR pathway* (1X) with multiple clinical-stage agents (e.g., gedatolisib by Celcuity,[29] ipatasertib by Genentech (Roche)[30] etc.) and recently approved drugs (e.g., inavolisib,[31] alpelisib[32]) across cancer and metabolic indications; *Bruton's tyrosine kinase (BTK)* (1X) thoroughly validated in B-cell malignancies with multiple approved inhibitors (ibrutinib,[33] zanubrutinib,[34] tirabrutinib,[35] pirtobrutinib[36]) including as recently as February 2026 (acalabrutinib[37]) and continued innovation addressing resistance and improving selectivity; *Janus kinase (JAK)* (1.1X) with pan-JAK (delgocitinib[38] for eczema, baricitinib for rheumatoid arthritis[39] and alopecia areata,[40] etc.) and selective JAK1/2/3/TYK2 inhibitors (e.g., filgotinib[41]) approved across autoimmune and inflammatory diseases; *rho-associated protein kinase (ROCK)* (1.1X) for glaucoma,[42] cardiovascular disease,[43] and fibrosis;[44] and *signal transducer and activator of transcription (STAT) 3* (1.1X) as a challenging but validated oncogenic transcription factor target.

DNA damage response inhibitors (1.2X) represent one of the most successful recent therapeutic strategies, exploiting synthetic lethality in DNA repair-deficient tumors. Within this category, PARP inhibitor subclasses show differential growth: *PARP1 inhibitors* (1.2X) maintain steady activity as the validated clinical approach with multiple recently approved drugs (olaparib,[45] rucaparib,[46] niraparib,[47] talazoparib,[48] pamiparib[49]) for BRCA-mutant cancers, with ongoing efforts to expand beyond homologous recombination deficiency. Remarkably, *PARP7 inhibitors* (>2X) exhibit exceptional growth as PARP7 (also called TIPARP) regulates type I interferon signaling and immune responses. PARP7 inhibition enhances anti-tumor immunity and shows synergy with checkpoint inhibitors,[50] representing a mechanistically distinct approach from PARP1/2 inhibition.[51-53] Similarly, *poly(ADP-ribose)glycohydrolase (PARG) inhibitors* (>2X) show dramatic acceleration as PARG reverses PARP1 activity by hydrolyzing poly(ADP-ribose) chains with PARG inhibition potentially offering orthogonal therapeutic effects to PARP1 inhibition with distinct toxicity profiles, potentially addressing PARP inhibitor resistance mechanisms.[54,55] *ATR (ataxia telangiectasia and rad3-related) kinase* responds to replication stress, with clinical candidates (berzosertib,[56] elimusertib[57]) demonstrating activity in combination with chemotherapy or as monotherapy in ATM-deficient tumors,[58] possibly accounting for the brisk growth in ATR inhibitor patents (1.2X).[59,60]

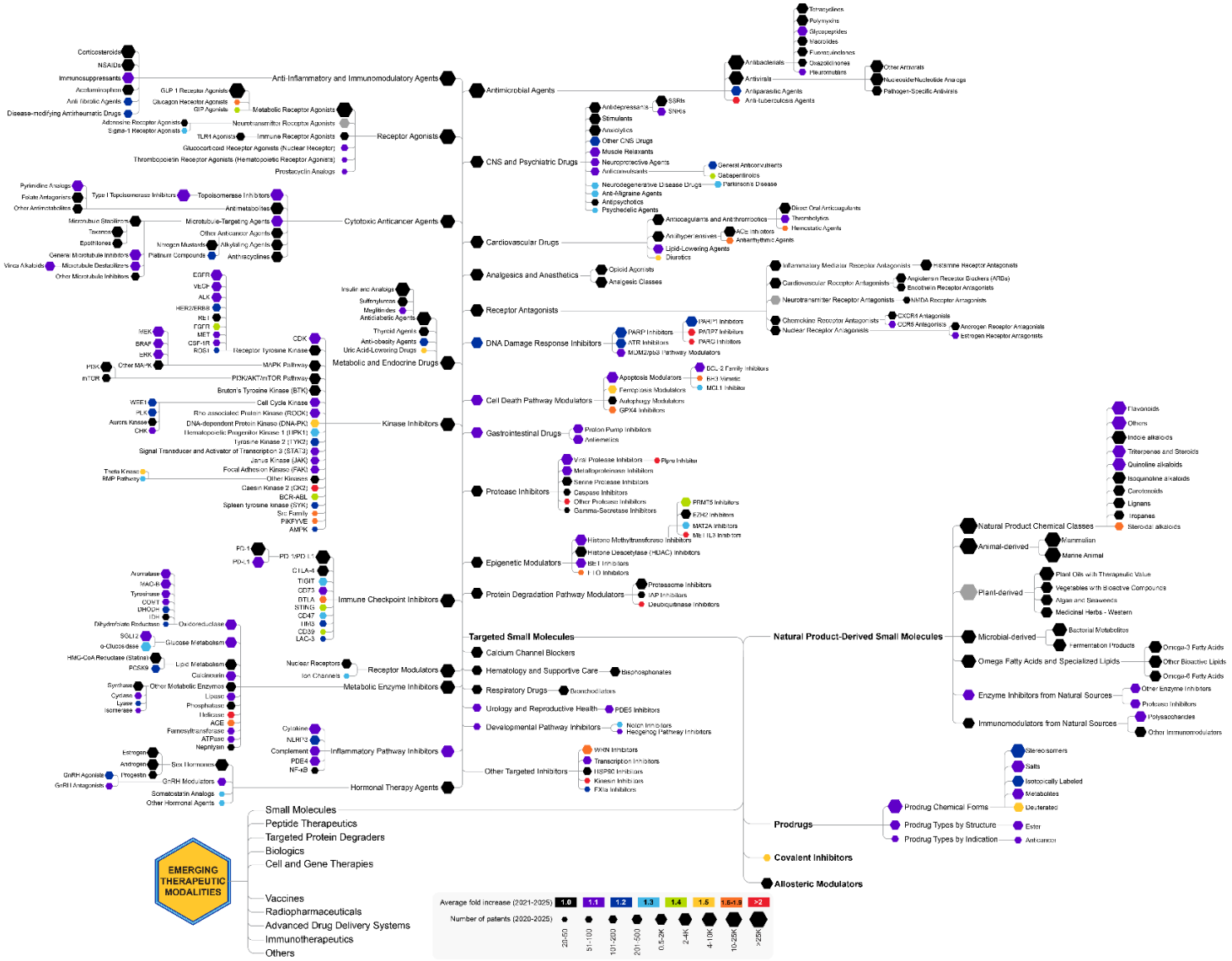


Figure 16. CAS TrendScape map of emerging topics in terms of therapeutic modalities focused on small molecules identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Epigenetic modulators demonstrate strong growth across multiple enzymatic mechanisms. *Histone deacetylase (HDAC) inhibitors* (1X) maintain activity with four approved drugs for hematologic malignancies, though dose-limiting toxicities of pan-HDAC inhibitors drive development of isoform-selective agents.[61] *BET (bromodomain and extra-terminal) inhibitors* (1.1X) targeting BET family bromodomain proteins (BRD2/3/4) maintain activity despite clinical setbacks,[62,63] with continued innovation in selectivity and combination strategies. Within methylation machinery, *histone methyltransferase inhibitors* (1.1X) show moderate growth with EZH2 inhibitors (tazemetostat,[64] valemetostat[65]) approved for specific cancers. High-growth components with this branch include *METTL3 (methyltransferase-like 3) inhibitors* (>2X), targeting the catalytic subunit of the m^{6}A RNA methyltransferase complex.[66,67] METTL3's roles in mRNA stability, translation, and cancer stem cell maintenance position it as a master regulator of post-transcriptional gene expression, with inhibitors showing preclinical efficacy across hematologic[68] and solid tumors.[69] *PRMT5 (protein arginine methyltransferase 5) inhibitors* (1.4X) demonstrate strong growth[70] as PRMT5 catalyzes symmetric dimethylation of histones and spliceosomal proteins,[71] with multiple clinical candidates (PRT543[72]) exploiting synthetic lethality in MTAP-deleted cancers.[73] *MAT2A (methionine adenosyltransferase 2α) inhibitors* (1.3X) show accelerating growth[74] as MAT2A inhibition depletes S-adenosylmethionine (SAM), the universal methyl donor, indirectly affecting all methyltransferases, with synthetic lethality in MTAP-deleted tumors creating therapeutic windows.[75] *FTO (fat mass and obesity-associated protein) inhibitors* (1.6-1.9X) exhibit high growth as FTO erases m^{6}A RNA methylation, regulating mRNA stability and translation, with FTO inhibitors showing activity in AML.[76]

Protein degradation pathway modulators represent transformative approaches to eliminate rather than inhibit proteins. *Deubiquitinase (DUB) inhibitors* (>2X) show exceptional growth (e.g., US20240294467 A1) as DUBs reverse ubiquitination, with over 90 DUBs in the human genome regulating protein stability, localization, and signaling.[77] DUB inhibitors offer opportunities to enhance degradation of oncoproteins or modulate immune signaling.[78] This growth complements the established interest in E3 ligase modulators and PROTACs (discussed in **section 4.2.2**), reflecting comprehensive interest in manipulating the ubiquitin-proteasome system.

Cell death pathway modulators demonstrate strong growth in alternative cell death mechanisms beyond traditional apoptosis. *Ferroptosis modulators* (1.5X) show accelerating interest as ferroptosis (iron-dependent lipid peroxidation-driven cell death) represents a non-apoptotic pathway relevant in cancer cells with altered metabolism.[79,80] *GPX4 (glutathione peroxidase 4) inhibitors* (1.6-1.9X) exhibit high growth as GPX4 protects against lipid peroxidation and ferroptosis with GPX4 inhibition inducing ferroptotic cancer cell death,[81] particularly in therapy-resistant contexts where apoptotic machinery is compromised.[82,83] Within apoptosis modulators, *BH3 mimetics* (1.6-1.9X) show strong growth as these molecules mimic BH3-only proteins to activate apoptosis, with venetoclax (a BCL-2 inhibitor) approved for CLL and AML[84] validating the approach. *MCL-1 inhibitors* (1.3X) demonstrate growth as MCL-1 (myeloid cell leukemia-1) represents the most common resistance mechanism to BCL-2 inhibition,[85] with multiple clinical candidates addressing this unmet need in hematologic malignancies. Examples of recent patents about MCL-1 inhibitors include design of ADCs,[86] combination therapy[87] and macrocyclic inhibitors.[88]

Immune checkpoint inhibitors (ICIs, 1X) for small molecules show steady activity, with growth concentrating beyond validated antibody targets: *TIGIT (T cell immunoreceptor with Ig and ITIM domains)* (1.3X) shows fast-paced growth as an inhibitory receptor on T cells and NK cells, with small molecule approaches complementing antibody development.[89-92] *CD47* (1.3X) demonstrates growth as a "don't eat me" signal that inhibits macrophage phagocytosis and while antibodies dominate this space small molecules disrupting CD47-SIRPα interaction offer potential

advantages.[93-95] *BTLA (B and T lymphocyte attenuator)* (1.6-1.9X) exhibits high growth as an underexplored checkpoint with similarities to CTLA-4 and PD-1 pathways.[96] *STING (stimulator of interferon genes)* (1.4X) shows strong growth as STING agonists activate innate immunity and enhance anti-tumor responses, positioning them as immunotherapy adjuvants or monotherapies (e.g., NCT06022029[97]) with recent patents exploring potential as protein degraders.[98] *CD39* (1.4X) demonstrates growth as an ectonucleotidase degrading immunostimulatory ATP to immunosuppressive adenosine with CD39 inhibition blocking adenosine generation and relieving immunosuppression in the tumor microenvironment (TME).[99,100] *TIM-3* (1.2X) and *LAG-3* (1.2X) show moderate growth as next-generation checkpoints with antibodies in clinical development and small molecule[99,101-103] and peptide therapeutic efforts emerging.[104,105] Established checkpoints *PD-1/PD-L1* (1X) and *CTLA-4* (1X) maintain patent activity dominated by antibodies, though small molecule PD-L1 inhibitors have reached clinical stages (e.g., INCB086550,[106] CCX559[107]).

Protease inhibitors (1X) maintain steady activity across multiple protease classes. *Viral protease inhibitors* (1.1X) show modest growth, with *PLpro (papain-like protease) inhibitors* (>2X) exhibiting exceptional acceleration likely driven by SARS-CoV-2 PLpro as a drug target. PLpro cleaves viral polyproteins and removes ubiquitin and ISG15 from host proteins to suppress innate immunity, making it attractive for direct antiviral activity and immune modulation.[108] *Serine protease inhibitors* (1X) maintain patent activity encompassing metalloproteinase, caspase, and other protease inhibitors. *Metalloproteinase inhibitors* (1.1X) show modest growth with matrix metalloproteinases (MMPs),[109] a disintegrin and metalloproteinases (ADAMs),[110] and other zinc-dependent proteases as targets in cancer and inflammation.

Cardiovascular drugs demonstrate growth in specific subclasses despite mature markets. *Anticoagulants and antithrombotics* (1X) show steady patent activity with *hemostatic agents* (1.6-1.9X) exhibiting high growth with efforts around incorporating hemostatic agents' wound dressings.[111, 112] *FXIa (Factor XIa) inhibitors* (1.2X) represent an emerging anticoagulant class targeting factor XIa to prevent thrombosis while potentially preserving hemostasis better than current anticoagulants, with candidates in phase 2/3 trials (e.g., abelacimab[113]). Within *antihypertensives*, *antiarrhythmic agents* (1.6-1.9X) show high growth reflecting renewed interest in rhythm control for atrial fibrillation and other arrhythmias, with novel mechanisms beyond traditional sodium/potassium channel blockers.[114] *Diuretics* (1.5X) demonstrate strong growth despite being one of the oldest drug classes, likely driven by novel mechanisms (e.g., SGLT2 inhibitors with diuretic effects showing cardiovascular benefits[115]), natural product based,[116] combination formulations,[117] and renewed appreciation for volume management in heart failure. *Lipid-lowering agents* (1.1X) maintain steady activity with statins thoroughly validated as do *calcium channel blockers* (1X) as established antihypertensives and antianginal agents.

Metabolic and endocrine drugs (1X) show differential growth by subclass. While *antidiabetic agents* (1X) maintain steady activity with multiple established mechanisms and incretin-based therapies dominating recent innovation,[118] *uric acid-lowering drugs* (1.5X) exhibit strong growth addressing gout and hyperuricemia, with novel mechanisms beyond allopurinol (xanthine oxidase inhibitor[119]) and emerging understanding of uric acid's roles in cardiovascular and metabolic disease.[120]

Receptor agonists (1X) demonstrate explosive growth in metabolic applications. *Glucagon receptor agonists* (1.6-1.9X) show high growth as components of dual and triple agonists (GLP-1/glucagon,[121] GLP-1/glucagon/gastrin[122]) that enhance weight loss and improve metabolic parameters beyond GLP-1 alone. These multi-agonists represent next-generation obesity and metabolic syndrome therapeutics. *GIP (glucose-dependent insulinotropic polypeptide) agonists* (1.3X) demonstrate growth validated by tirzepatide (GLP-1/GIP dual agonist) approval for diabetes and obesity,[123] with ongoing investigation of whether GIP agonism, antagonism, or balanced activity offers optimal metabolic benefits. *GLP-1 receptor agonists* (1X) maintain baseline growth as an established, highly successful class for diabetes (exenatide, liraglutide, dulaglutide, semaglutide) and obesity (semaglutide, liraglutide), with the market now mature but innovation continuing in combination therapies[124] and longer-acting versions.[125] *Sigma-1 receptor agonists* (1.3X) within *neurotransmitter receptor agonists* show growth as sigma-1 receptors modulate calcium signaling, ER stress, and neuroplasticity,[126] with potential applications in neurodegenerative diseases, neuropathic pain, and psychiatric disorders.[127,128]

Gastrointestinal drugs (1.1X) maintain steady activity across multiple mechanisms. *Proton pump inhibitors* (1.1X) show modest growth despite market saturation, with innovation focusing on on-demand dosing,[129] reduced drug interactions, and potassium-competitive acid blockers (P-CABs like vonoprazan) offering faster onset and longer duration than traditional proton pump inhibitors. *Antiemetics* (1.1X) demonstrate steady activity for chemotherapy-induced nausea and vomiting, postoperative nausea, and other indications, with 5-HT_3 antagonists,[130] NK1 antagonists,[131] and other well-established mechanisms.

CNS and psychiatric drugs demonstrate growth across multiple indications. *Parkinson's disease* agents, *anti-migraine agents*, and *psychedelic agents* all show similar fast-paced growth rates (1.3X). *Parkinson's disease* patent activity reflects novel mechanisms beyond dopamine replacement (adenosine A2A antagonists like istradefylline,[132] GLP-1 agonists showing neuroprotection[133]).[134,135] *Anti-migraine agents* have been revolutionized by calcitonin gene-related peptide (CGRP)-targeted therapies (gepants for acute and preventive treatment, though antibodies dominate prevention), with growth reflecting this therapeutic breakthrough.[136] *Psychedelic agents* including psilocybin, MDMA, ketamine, and related compounds show strong growth driven by breakthrough therapy designations for treatment-resistant depression, PTSD, and other psychiatric conditions,[137,138] representing a paradigm shift toward neuroplasticity-promoting therapies. Within *anticonvulsants* (1.1X), *gabapentinoids* (1.4X) show accelerated growth beyond traditional epilepsy indications, with gabapentin and pregabalin widely used for neuropathic pain,[139] anxiety,[140] and other off-label applications with novel gabapentinoids[141] and related calcium channel modulators continuing to be developed.[142]

Antimicrobial agents show differential growth by pathogen class. *Antibacterials* (1X) and *antivirals* (1X) maintain baseline activity reflecting the constant need for new agents addressing resistance and emerging pathogens, though breakthrough innovation remains challenging economically. Within this category, *antiparasitic agents* (1.2X) demonstrate moderate growth driven by neglected tropical diseases, malaria resistance to artemisinin-based therapies,[143] and renewed attention to parasitic infections in immunocompromised populations.[144] Most dramatically, *anti-tuberculosis agents* (>2X) exhibit exceptional growth reflecting the urgent need for shorter treatment regimens, drugs active against multidrug-resistant (MDR), extensively drug-resistant (XDR) TB, latent forms of TB, and novel mechanisms.[145,146] Approvals in the last decade (bedaquiline, delamanid, pretomanid) targeting ATP synthase and cell wall synthesis have provided first new TB drug classes in decades, spurring continued investment in this historically neglected area.

Inflammatory pathway inhibitors (1.1X) show steady baseline growth with *cytokine inhibitors* (1.1X) and *PDE4 (phosphodiesterase 4) inhibitors* (1.1X) maintaining activity for inflammatory diseases, though biologics dominate many cytokine-targeting approaches. *NLRP3 (NOD-like receptor protein 3)* inflammasome inhibitors (1.2X) show moderate growth as NLRP3 activation drives IL-1β and IL-18 release in autoinflammatory diseases, gout,[147] Alzheimer's disease,[148] and metabolic disorders[149] with multiple small molecule NLRP3 inhibitors in clinical development (e.g., dapansutrile, inzomelid) addressing multiple diseases with an inflammatory component.[150,151]

Developmental pathway inhibitors (1.1X) targeting embryonic signaling pathways reactivated in cancer show modest growth. *Notch inhibitors* (1.3X) demonstrate fast-paced growth, primarily as gamma-secretase inhibitors (GSIs) that block notch processing. While early GSIs faced dose-limiting gastrointestinal toxicity (notch regulates intestinal cell fate), more selective approaches, specific cancer contexts, and combination therapy[152] likely drive continued interest.

Metabolic enzyme inhibitors (1X) encompass diverse targets with differential growth. Within *glucose metabolism*, *α-glucosidase inhibitors* (1.3X) show fast-paced growth as oral antidiabetic agents (e.g., acarbose, voglibose, miglitol) that delay carbohydrate absorption are continually developed with innovation addressing improved tolerability and potential applications in prediabetes.[153,154] *Oxidoreductases* feature *dihydroorotate dehydrogenase (DHODH)* inhibitors (1.2X) showing growth likely for autoimmune diseases[155,156] and emerging applications in cancer,[157,158] along with *dihydrofolate reductase* inhibitors (1.2X) as established chemotherapy (methotrexate) and antimicrobial agents with continued optimization.[159] Within *lipid metabolism*, *advanced glycation end-product (AGE)* inhibitors (1.6-1.9X) show high growth as AGEs contribute to diabetic complications,[160] cardiovascular disease,[161] and aging-related pathologies[162] with RAGE inhibitors[163,164] representing potential disease-modifying therapies. *Proprotein convertase subtilisin/kexin type 9 (PCSK9)* inhibitors (1.2X) show brisk growth, though the validated mechanism is dominated by antibodies (evolocumab, alirocumab) and siRNA (inclisiran), small molecule approaches[165] continue to seek oral PCSK9 modulation for cholesterol reduction.[166]

Other targeted inhibitors demonstrate diverse high-growth opportunities. *WRN (Werner syndrome RecQ helicase-like) inhibitors* (1.6-1.9X) show high growth as WRN represents a synthetic lethal target in microsatellite instability-high (MSI-H) cancers with approximately 15% of cancers exhibiting MSI-H with defective mismatch repair, creating dependency on WRN helicase for survival.[167,168] *WRN inhibitors* selectively kill MSI-H cancer cells while sparing normal tissues, representing a precision oncology approach for colorectal, gastric, endometrial, and other MSI-H tumors.[169,170] *Kinesin inhibitors* (>2X) exhibit exceptional growth as kinesins are motor proteins driving mitosis and intracellular transport.[171] Kinesin spindle protein (KSP/Eg5) inhibitors reached clinical trials (e.g., ispinesib,[172] filanesib[173]) as mitotic inhibitors with potentially reduced neurotoxicity compared to traditional tubulin inhibitors, while other kinesin family members represent emerging targets in cancer and neurological diseases.

The small molecule patent landscape reveals a mature yet dynamically evolving field where innovation increasingly targets previously intractable biology through novel mechanisms (protein degradation, epigenetic regulation, ferroptosis), exploits synthetic lethality vulnerabilities, and addresses resistance mechanisms. The exceptional growth rates (>2X) in seemingly disparate targets reflect technological advances enabling new target classes and disease-driven urgency. The sustained activity in established mechanisms (e.g., MAPK inhibitors, JAK inhibitors, GLP-1 agonists) demonstrates that even mature drug classes continue generating patent activity through incremental improvements in selectivity, pharmacokinetics, and safety profiles. This dual dynamic, breakthrough mechanisms achieving exceptional growth rates while validated targets maintain steady innovation, characterizes a small molecule landscape that remains the

pharmaceutical industry's foundation while expanding into frontier biology previously accessible only to biologics or gene therapies.

4.2.2 Targeted protein degraders: PROTACs, molecular glues, and emerging degrader modalities

Targeted Protein Degraders, including proteolysis-targeting chimeras (PROTACs), molecular glues, and E3 ligase modulators, have evolved from academic curiosities to major patent clusters, signaling strong commercial validation of targeted protein degradation as a therapeutic modality. The first PROTAC approval was granted on May 1, 2026, to Arvinas's Veppanu (vepdegestrant)[174] and more approvals are anticipated soon based on current clinical trial progress. This approach offers potential advantages including catalytic mechanism of action (substoichiometric dosing), ability to target "undruggable" proteins lacking enzymatic or binding pockets, and applicability to scaffolding proteins, transcription factors, and other non-enzymatic targets previously inaccessible to traditional small molecules. Patent activity reveals the maturation of PROTAC platforms and the rapid emergence of alternative degradation mechanisms (**Figure 17**).

PROTACs maintain the largest patent volume within targeted degraders, reflecting intensive optimization since their conceptual validation in the early 2000s and recent clinical translation (ARV-110 for prostate cancer, ARV-471 for breast cancer, and multiple other candidates in trials) exhibiting fast-paced growth (1.3X). The PROTAC architecture comprises three essential components: a ligand binding the protein of interest (POI), a ligand recruiting an E3 ubiquitin ligase, and a chemical linker connecting them. PROTAC acting as a heterobifunctional molecule brings POI and E3 ligase into proximity, enabling POI ubiquitination and subsequent proteasomal degradation.

Linkers, an essential **PROTAC component**, demonstrate the strongest growth (1.5X), reflecting recognition that linker chemistry profoundly influences PROTAC properties beyond simple tethering. Linker length, flexibility, composition (alkyl, polyethylene glycol (PEG), aromatic), and cleavability determine the geometry of the ternary complex (POI-PROTAC-E3 ligase), affecting degradation efficiency, selectivity, and pharmacokinetic properties. Innovations include stimulus-responsive linkers (pH-sensitive,[175] protease-cleavable[176]) enabling tissue-specific or tumor-selective degradation, rigid linkers preorganizing optimal ternary complex geometry,[177] and hydrophilic linkers improving aqueous solubility and oral bioavailability,[178] all of which have been major PROTAC limitations.

E3 ligase binding moieties (1.2X) show moderate growth, though the field remains dominated by cereblon (CRBN) binders (derived from thalidomide/lenalidomide/pomalidomide) and von Hippel-Lindau (VHL) binders (VH032 and derivatives), which together constitute the most commonly used E3 ligase binders in PROTACs.[179] Patent activity reflects efforts to expand beyond these two E3 ligases to access the ~600 E3 ligases in the human genome. Alternative E3 ligases offer tissue-specific expression patterns, distinct ubiquitination mechanisms, and potential to avoid resistance mechanisms that emerge through cereblon (CRBN) or VHL mutations/downregulation. Novel E3 ligase recruiters under investigation include IAP (inhibitor of apoptosis protein) antagonists,[180] mouse double minute 2 (MDM2) ligands,[181] and DDB1- and CUL4-associated factor (DCAF) ligands,[182] each offering unique advantages for specific targets or tissue contexts.

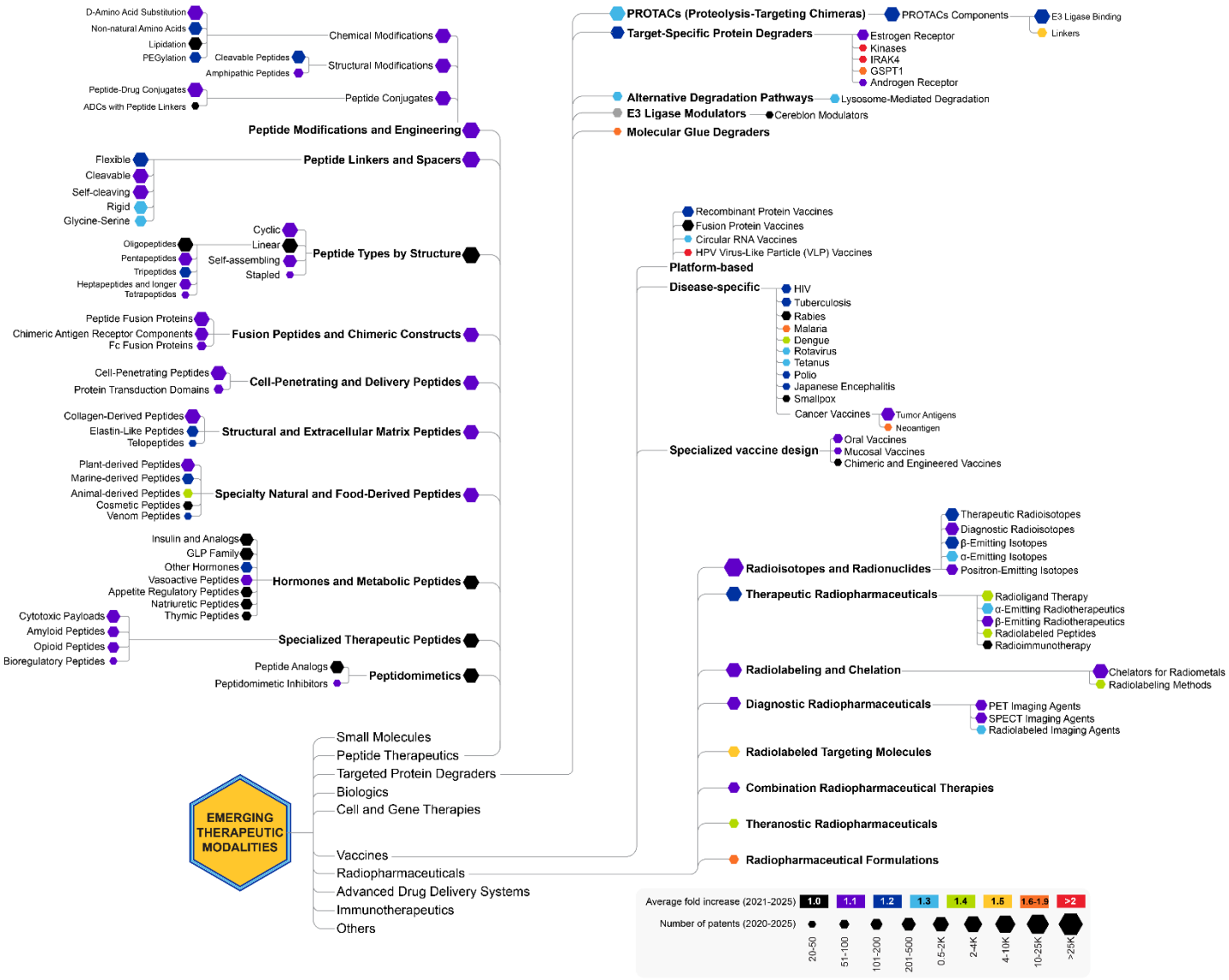


Figure 17. CAS TrendScape map of emerging topics in terms of therapeutic modalities focused on peptide therapeutics, targeted protein degraders, vaccines, and radiopharmaceuticals identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Target-specific protein degraders (1.2X) demonstrate differential growth by target class, revealing validated applications and emerging opportunities. *Estrogen receptor (ER)* and *androgen receptor (AR)* degraders maintain steady activity (1.1X) as the most clinically advanced PROTAC applications. These nuclear hormone receptors provide proof-of-concept for PROTAC efficacy in humans and continue generating patent activity around next-generation molecules addressing resistance, improved pharmacokinetics, and specific mutant receptors. Remarkably, *kinase*-targeting degraders (>2X) exhibit exceptional growth despite kinase inhibitors being the most successful small molecule drug class historically. This dramatic acceleration reflects multiple drivers: degraders can eliminate scaffolding functions of kinases independent of catalytic activity; degraders may overcome resistance mutations that affect inhibitor binding but not degrader recognition; degraders enable targeting of pseudokinases (catalytically inactive but biologically important); and degraders offer prolonged target suppression versus reversible inhibition. The kinase degrader portfolio spans receptor tyrosine kinases (EGFR, HER2, ALK, RET), non-receptor kinases (BCR-ABL, BTK, JAK), and serine/threonine kinases (CDK, BRAF, MEK), essentially recapitulating the entire kinase inhibitor field through the degradation lens. Clinical data emerging for BTK degraders and other kinase-targeting PROTACs are validating the approach's therapeutic potential. BTK degraders have rapidly advanced into the clinic, with multiple candidates targeting relapsed or refractory B-cell malignancies. Clinical-stage BTK PROTACs include BGB-16673, now in a Phase 3 head-to-head study versus pirtobrutinib in CLL/SLL (NCT06973187[183]), alongside ABBV-101 (NCT05753501[184]), AC676 (NCT05780034[185]), NX-2127 (NCT04830137[186]), NX-5948 (NCT05131022[187]), TQB3019 (NCT06943677[188]), and UBX-303061 (NCT06590961[189]), all of which are being evaluated in Phase I trials, primarily for relapsed or refractory B-cell malignancies. Complementing these trials, preclinical studies such as PTD10,[190] a sub-nanomolar BTK degrader with enhanced selectivity and apoptosis induction, and structure-guided efforts to improve oral bioavailability of BTK PROTACs,[191] collectively support BTK degradation as a promising strategy to overcome resistance to conventional BTK inhibitors. Other kinase-targeting PROTACs in clinical development include CFT1946, a BRAF V600 degrader in Phase 2 trials for mutant solid tumors (NCT05668585[192]), BG-60366, an EGFR degrader in Phase 1 evaluation for EGFR-mutant NSCLC (NCT06685718[193]), and BTX-9341, a CDK4/6-targeting PROTAC being assessed in Phase 1 studies for advanced or metastatic breast cancer (NCT06515470[194]).

Interleukin-1 receptor-associated kinase 4 (IRAK4) degraders (>2X) show exceptional growth as IRAK4 represents a critical node in TLR/IL-1R signaling driving inflammatory and autoimmune diseases.[195-197] IRAK4 degradation offers advantages over kinase inhibition: IRAK4's scaffolding functions independent of kinase activity contribute to pathway activation, and degradation eliminates catalytic and non-catalytic functions. Clinical candidates demonstrate efficacy in models of hidradenitis suppurativa, atopic dermatitis, and other inflammatory conditions, positioning IRAK4 degraders as potentially disease-modifying therapies. Early clinical-stage degraders include LT-002-158 (NCT06932003[198] – Phase I/II) being evaluated in patients with hidradenitis suppurativa, BGB-45035 (NCT06342713[199] – Phase I) being assessed across healthy volunteers and patients with autoimmune dermatologic diseases, KT-413 (NCT05233033[200] – Phase I) which has demonstrated pharmacodynamic IRAK4 degradation and early clinical activity in relapsed or refractory B-cell non-Hodgkin lymphoma. Early clinical-stage degraders include LT-002-158 (NCT06932003[198]), being evaluated for safety, tolerability, pharmacokinetics, and efficacy in patients with hidradenitis suppurativa, BGB-45035 (NCT06342713[199]), assessed across healthy volunteers and patients with autoimmune dermatologic diseases, and KT-413 (NCT05233033[200]). In parallel, several preclinical studies describe potent IRAK4 PROTACs such as Jh-XIII-05-1,[201] LZ-07,[202] and SIM0711[203] that achieve nanomolar IRAK4 degradation, robust suppression of pro-inflammatory cytokines, and improved

efficacy and safety profiles, collectively underscoring the promise of IRAK4 degraders as disease-modifying therapies across inflammatory and immune-mediated diseases.

GSPT1 (G1 to S phase transition 1) degraders (1.6-1.9X) exhibit high growth reflecting an interesting therapeutic strategy.[204,205] GSPT1 is a translation termination factor whose degradation causes nonsense-mediated mRNA decay and apoptosis selectively in cancer cells with specific genetic contexts (e.g., MYC amplification). This represents neo-substrate degradation where the degrader creates a synthetic lethal vulnerability rather than targeting an oncogenic protein directly.

Molecular glue degraders[206] (1.6-1.9X) demonstrate high growth as conceptually distinct from PROTACs, these small molecules induce protein-protein interactions (PPIs) between E3 ligases and neo-substrates (proteins not normally degraded by that E3 ligase), functioning through an allosteric mechanism rather than simple tethering. The paradigm was established by immunomodulatory drugs (IMiDs: thalidomide, lenalidomide, pomalidomide) that induce cereblon to bind and degrade IKZF1, IKZF3, and other zinc finger transcription factors. This "molecular glue" mechanism explained IMiDs' therapeutic effects in multiple myeloma and other hematologic malignancies decades after their clinical use began. Recent rational design of molecular glues (e.g., targeting cyclin K for cancer, GSPT1 degraders mentioned above) has validated that this mechanism can be prospectively engineered, not discovered serendipitously. Molecular glues offer potential advantages over PROTACs including smaller molecular weight (better drug-like properties), simpler synthesis, and potentially novel mechanisms accessing targets impossible for bivalent molecules. The high growth rate reflects intense interest in discovering and designing molecular glues for diverse targets, representing a complementary degradation modality to PROTACs. Some notable patents in this field include KR2025178250 A,[207] WO2024015855 A1,[208] CN121717822 A,[209] and WO2026051373 A1.[210]

Lysosome-mediated degradation (1.3X) shows accelerating interest through multiple mechanisms: LYTACs (lysosome-targeting chimeras) that conjugate target proteins with glycan moieties recognized by lysosome-targeting receptors, inducing endocytosis and lysosomal degradation, which is useful for extracellular and membrane proteins inaccessible to cytoplasmic PROTACs;[211] autophagy-targeting chimeras (AUTACs) that hijack selective autophagy machinery to deliver target proteins to lysosomes; and chaperone-mediated autophagy inducers. These approaches complement PROTACs by accessing different subcellular compartments and leveraging distinct quality control machinery.[212]

The patent data suggests that targeted protein degradation has evolved from a single modality (PROTACs) to a diverse platform encompassing multiple mechanisms (PROTACs, molecular glues, lysosome-targeting, autophagy-based), each with distinct advantages for different targets and therapeutic contexts. The high growth indicates this is not merely an alternative approach for difficult targets but a potentially superior strategy for many well-validated targets. As the first wave of degraders inches towards regulatory approval and clinical experience accumulates, the field appears positioned for continued rapid expansion across therapeutic areas, target classes, and degradation mechanisms. This fundamentally expands the druggable proteome beyond what inhibition-based approaches could access.

4.2.3 The peptide renaissance: Engineering approaches and applications

Peptide therapeutics represent a rapidly evolving modality that bridges the gap between small molecules and large biologics, offering the specificity of antibodies with improved tissue penetration and synthetic accessibility. The patent landscape reveals interest across multiple dimensions of peptide drug development (**Figure 17**). *Peptide modifications and engineering* dominates as one of the largest clusters, encompassing strategies to overcome the traditional limitations of peptides such as proteolytic instability, poor bioavailability, and rapid clearance. Within this domain, chemical modifications (D-amino acid substitution,[213] non-natural amino acids,[214] PEGylation[215]) and structural modifications (cyclization,[216,217] stapling[218,219]) are extensively patented, reflecting the field's maturation beyond natural peptide sequences. The prominence of *cyclic peptides* as a distinct sub-category underscores their therapeutic advantages: enhanced metabolic stability, improved binding affinity through conformational constraint, and better membrane permeability compared to linear counterparts.

Innovation in *peptide conjugates* including peptide-drug conjugates (PDCs) and antibody-drug conjugates (ADCs) with peptide linkers, demonstrates the integration of peptides into targeted delivery strategies, leveraging their receptor-binding capabilities to achieve tissue-specific drug delivery.[220] Valine-citrulline linker is used in multiple approved ADCs and continues to be the benchmark due to its cathepsin B cleavable mechanism and strong clinical validation, as reflected in patents such as WO2022032020 A1[221] and WO2022237666 A1.[222] Emerging peptide linker designs including Phe-Lys dipeptides and more stable tripeptide systems such as Val-Ala and Ala Ala-Asn demonstrate efforts to fine-tune protease-mediated cleavage and improve tumor selectivity and stability, as highlighted in patents WO2024133763 A2[223] and WO2025098391 A1.[224] Recent patent activity also highlights next-generation innovations such as dual-cleavage and hybrid oligosaccharide peptide linkers,[225,226] which are designed to improve pharmacokinetics, enable higher drug loading, and support more precise, site-specific conjugation strategies.

The *cell-penetrating and delivery peptides* cluster highlights ongoing efforts to address intracellular target access, a critical challenge for peptide therapeutics. Notably, *specialized therapeutic peptides* encompass diverse applications from hormones and metabolic peptides (insulin analogs,[227] GLP-1 family[228]) to specialized categories like antimicrobial and cytotoxic peptides.[229,230] The emergence of *peptidomimetics*, molecules that mimic peptide structure while incorporating non-peptidic elements, represents a strategic approach to retain biological activity while improving drug-like properties.[231, 232]

4.2.4 Vaccine platform innovation: Beyond infectious disease to cancer and chronic conditions

The ***vaccine*** landscape has undergone transformative innovation during the 2020-2025 period, catalyzed by the COVID-19 pandemic but extending far beyond infectious disease applications. Our analysis of recent pharmaceutical patents reveals *platform-based vaccine technologies* as the fastest-growing segment, with *circular RNA (circRNA) vaccines*[233] and *HPV virus-like particle (VLP) vaccines* demonstrating exceptional growth rates, 1.3X and >2X, respectively (**Figure 17**). *Circular RNA (circRNA) vaccines* represent a natural evolution from the successful deployment of linear messenger RNA (mRNA) vaccines, offering enhanced stability through their closed-loop structure that resists exonuclease degradation, potentially enabling lower dosing and improved duration of antigen expression.[234] The prominence of recombinant protein vaccines[235] and fusion protein vaccines[236,237] reflects continued refinement of established technologies, now enhanced

by rational design approaches and structural biology insights that enable optimized immunogen presentation.

Within *disease-specific vaccines*, traditional targets like HIV,[238] tuberculosis,[239] and rabies[240] maintain substantial patent activity, but notable acceleration is evident in neglected tropical diseases including malaria, dengue, Zika as illustrated by recent vaccine patent filings in these indications.[241-243] Similarly, emerging and reemerging threats such as Japanese encephalitis and smallpox are increasingly represented in the patent landscape, reflecting heightened preparedness efforts.[244,245] The cancer vaccines branch featuring tumor antigens and neoantigens signals the convergence of vaccinology with immuno-oncology, leveraging personalized medicine approaches to generate patient-specific immune responses. *Specialized vaccine design* innovations encompass oral vaccines for improved patient compliance, mucosal vaccines[246] targeting pathogen entry sites, and chimeric/engineered vaccines[247] that combine antigens from multiple pathogens or optimize immune recognition. This diversification reflects technological maturation and expanding ambition: from preventing acute infections to managing chronic diseases and cancer, vaccines are evolving into versatile immunomodulatory platforms with applications across the therapeutic spectrum.

4.2.5 Radiopharmaceuticals: Theranostic approaches and targeted therapy

Radiopharmaceuticals represent one of the most dynamic growth areas in therapeutic innovation, combining advances in nuclear medicine, molecular targeting, and precision oncology. The patent landscape reveals *therapeutic radiopharmaceuticals* as the dominant cluster by volume (**Figure 17**), with strong activity in *α-emitting radiotherapeutics* and *radioligand therapy*, reflecting the clinical success of agents like lutetium-177[248] and actinium-225-based[249] therapies in treating metastatic cancers. α-Emitters are attractive due to their high linear energy transfer and short tissue penetration range, enabling potent cytotoxicity while minimizing damage to surrounding healthy tissue, a critical advantage in treating micrometastases and minimal residual disease.[250,251] The *β-emitting radiotherapeutics* category exhibits substantial patent activity, indicating continuous commercial interest in a more established therapeutic approach with proven agents targeting neuroendocrine tumors and prostate cancer.[252,253]

Radiolabeling and chelation technologies show brisk growth rates (1.1X), underscoring their foundational importance. Effective chelators must stably bind radioisotopes under physiological conditions while maintaining the targeting molecule's biological activity. Innovation in *chelators for radiometals* (1.1X) and *radiolabeling methods* (1.4X) enables the expanding radioisotope palette beyond traditional options.[254-256] The *diagnostic radiopharmaceuticals* branch featuring PET, SPECT, among other general radiolabeled imaging agents demonstrates the theranostic paradigm's growing adoption, where the same molecular target is exploited for disease detection and therapy, enabling patient selection and treatment monitoring as seen by the 1.4X increase in patenting activity of *theranostic radiopharmaceuticals*.[257,258] *Combination radiopharmaceutical therapies* represents an emerging frontier, integrating targeted radiation with immunotherapy, chemotherapy, or other modalities to overcome resistance mechanisms and enhance therapeutic efficacy, positioning radiopharmaceuticals as versatile platforms in precision medicine's arsenal.[259,260]

4.2.6 Engineered antibodies, RNA therapeutics, and cell therapies: Next-generation biologics

The ***Biologics*** patent landscape reflects a sector in rapid transition, with established *antibody therapeutics* maintaining substantial volume while *RNA therapeutics* represents the fastest-growing biologics segment (**Figure 18**). Patent activity in antibody therapeutics continues to expand, particularly across engineered formats and functional enhancements, with antibody–drug conjugates (ADCs) emerging as a key area of innovation.[261] Notably, increasing patent filings highlight advances in linker chemistries[262] and site-specific conjugation approaches,[263] enabling improved stability, controlled drug release, and enhanced therapeutic precision, alongside the incorporation of next-generation payloads.[264] *Immune checkpoint antibodies* remain an emerging category with continued diversification beyond PD-1/PD-L1 and CTLA-4 to targets like LAG-3, TIM-3, and TIGIT,[265-267] reflecting efforts to overcome resistance and identify synergistic combination strategies. Notably, *nanobodies and single-domain antibodies* (1.2X), along with *bispecific* and *multispecific* antibody formats (1.1X) show accelerating patent activity[268-270] enabling simultaneous engagement of multiple targets for enhanced therapeutic effects, particularly in immuno-oncology applications.

RNA Therapeutics represents the fastest-growing biologics segment, catalyzed by multiple RNA modalities including *messenger RNA (mRNA) therapeutics* (1.6-1.9X), *self-amplifying RNAs* (saRNAs; 1.5X), *small nucleolar RNA* (snoRNA; 1.5X), *circular RNAs* (circRNAs; 1.3X), *small nuclear RNAs* (snRNA; 1.3X), and *piwi-interacting RNA* (piRNA; 1.3X) at the forefront (**Figure 18**). *Messenger RNA (mRNA) therapeutics* now encompasses protein replacement, cancer immunotherapy, and regenerative medicine applications, with significant innovation in *circRNA*[271,272] and *saRNA*[273] platforms that promise enhanced stability and prolonged expression. *Small interfering RNA* (siRNA; 1.1X) maintains brisk patent activity with improvements in delivery systems and chemical modifications enabling tissue-specific targeting.[274] *MicroRNA (miRNA) therapeutics* and *ASOs* (1.1X) demonstrate sustained innovation, addressing previously undruggable targets through gene silencing mechanisms.[275,276] *Guide RNA* (gRNA) for gene editing underscores CRISPR's clinical translation,[277] while emerging modalities like *RNA interference (RNAi) agents* (1.1X) and *catalytic RNA* (ribozymes; 1.1X) expand the RNA therapeutic toolkit beyond conventional mechanisms.[278-280]

Cell and Gene Therapies represent the vanguard of personalized medicine, with patent activity revealing the maturation of pioneering approaches and the emergence of next-generation platforms. *Chimeric antigen receptor (CAR) therapy* dominates by volume (**Figure 18**), reflecting its clinical validation in hematologic malignancies, with innovation now focusing on CAR structure and components to enhance efficacy, reduce toxicity, and expand beyond CD19 targeting.[281,282] Next-generation CAR designs incorporate costimulatory domain optimization, logic-gated activation systems,[283] and armored CARs secreting immunomodulatory payloads.[284] *CAR-T cell therapy* (1.1X) remains the established leader, while *CAR-macrophages* (1.6-1.9X) and *CAR-NK Cells* (1.3X) emerge as high-growth alternatives, offering potential advantages including allogeneic "off-the-shelf" products, reduced cytokine release syndrome risk, and activity against solid tumors through enhanced tumor infiltration and microenvironment remodeling.[285,286]

Gene editing technologies exhibit brisk growth (1.1X), with *CRISPR-cas systems* (1.2X) and *nuclease-based gene editing* (1X) representing the primary approaches for precise genomic modification.Innovations span base editors for single-nucleotide changes, prime editors enabling targeted insertions and deletions without double-strand breaks,[287] and epigenetic editors for reversible gene regulation.[288,289] *Viral vectors* (adeno-associated virus (AAV), lentiviral, adenoviral, retroviral) appear to be maintaining substantial patent volume and brisk growth (1.1X)

despite well-established technology, reflecting ongoing optimization of tissue tropism, immunogenicity reduction, and packaging capacity. *Non-viral gene delivery* (1.2X) methods show accelerating growth as alternatives addressing manufacturing scalability and safety concerns.[290-292] *Stem cell therapies,* which includes mesenchymal, hematopoietic, and pluripotent stem cells, demonstrates sustained patent activity (1.1X) for regenerative applications, while *tumor-infiltrating lymphocyte (TIL) therapy* (1.1X) and *macrophage cell therapy* (encompassing M1, M2, and engineered macrophages; 1.2X) represent emerging frontiers in cellular immunotherapy beyond engineered T cells.[293,294]

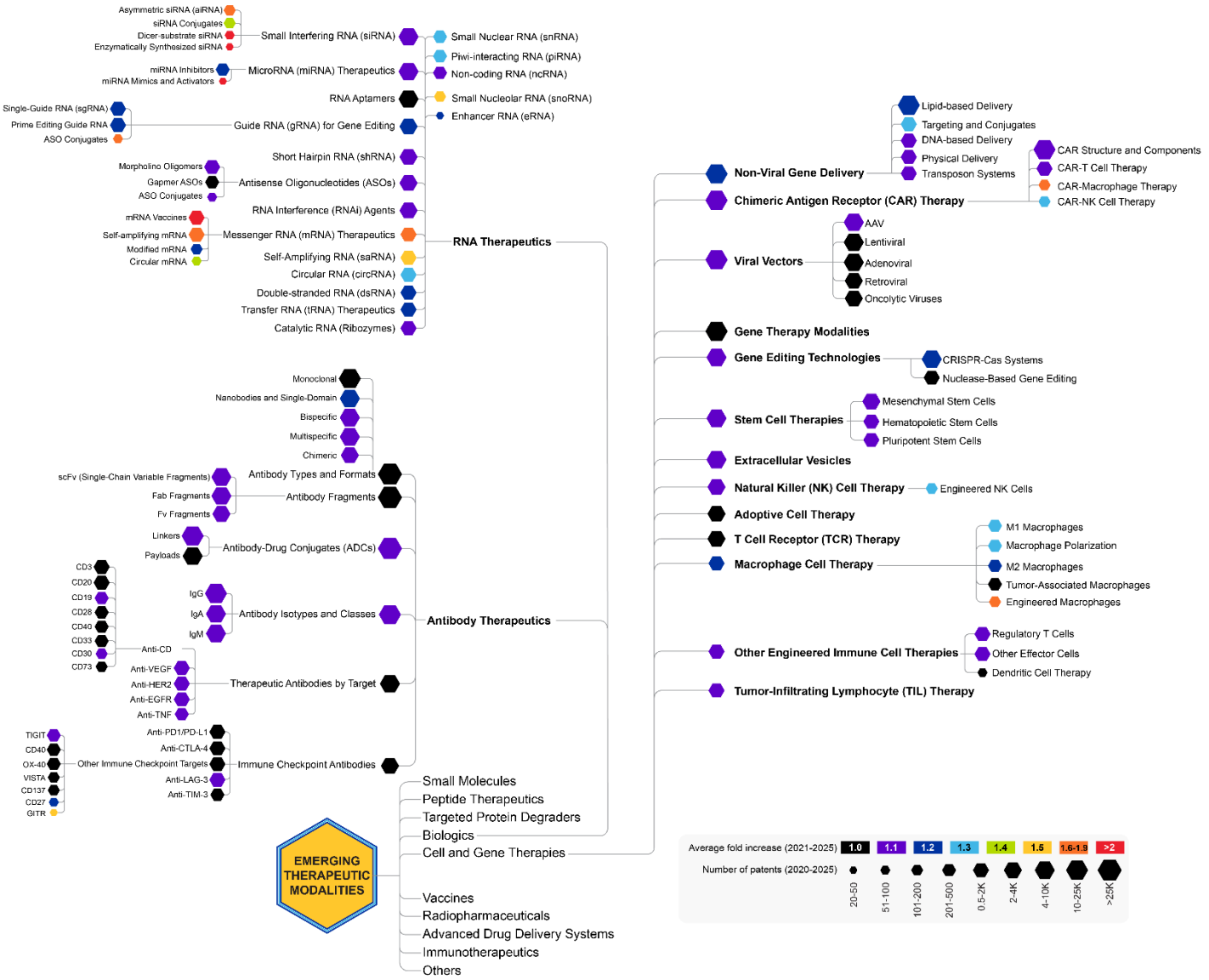


Figure 18. CAS TrendScape map of emerging topics in terms of therapeutic modalities focused on biologics (antibody and RNA therapeutics) and cell and gene therapies identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.2.7 Advanced delivery systems: Enabling technologies across modalities

Advanced drug delivery systems represent a critical enabler for emerging therapeutic modalities, with our analysis of patent activity revealing sophisticated approaches to overcome biological barriers, enhance targeting specificity, and control drug release kinetics (**Figure 19**).

Lipid-based drug delivery systems exhibit exceptional growth (1.5X), likely driven by mRNA vaccine success that validated lipid nanoparticles (LNPs) as clinical-grade delivery vehicles.[295] Innovations focusing on *ionizable and cationic LNPs*[296,297] (1.3X) that enable endosomal escape, *specialized LNPs* (1.5X) including cubosomes, niosomes, and transferosomes among others[298,299] for tissue-specific targeting, and *nanostructured lipid carriers* (1.3X) center around using cell-penetrating peptides and receptor-specific ligands[300] and surface modifications.[301] Traditional *liposomes* maintain substantial patent volume and modest growth (1.1X), reflecting their versatility across multiple therapeutic applications. *Surface modification and functionalization strategies* (1.1X) including *PEGylation*[302] and *ligand conjugation*[303] to extend circulation time and enhance cellular uptake also exhibit substantial patenting activity.

Among **inorganic nanoparticles**,[304] *metal-organic frameworks* (MOFs; 1.3X) are emerging as platforms combining high drug loading with stimulus-responsive release[305] along with *metal oxide nanoparticles* (1.2X) besides the more well-known/established nanoparticles such as gold, silica, etc.[306, 307] **Protein and biological nanoparticles** (1.1X) including *viral vectors* and *extracellular vesicles*[308] exhibit steady growth (1.1X) while *protein-based*[309] (1.2X) and *biomimetic nanoparticles*[310] (1.5X) show accelerating growth, leveraging biological machinery for improved biocompatibility and targeting. **Polymeric drug delivery systems** (1X) remain foundational,[304] with steady patent activity in *biodegradable polymers* (1X) and *PLGA-based systems* (1X) and brisk activity in *polymeric nanogels*[311] (1.1X) and *polymeric micelles*[312] (1.1X), the latter reflecting their established clinical utility. *Polymeric complexes* (1.2X) utilize ionic interactions between polyelectrolytes and oppositely charged therapeutics to create stable nanocarriers, with utility for gene delivery applications where cationic polymers complex with anionic nucleic acids to facilitate cellular uptake and endosomal escape.[313]

Pulsatile and sequential release systems nestled in the **controlled and sustained release systems** branch demonstrate strong growth (>2X). So do *stimuli-responsive systems* (pH, temperature, enzyme-triggered) that enable spatiotemporal control.[314] **Transdermal and topical delivery** innovations, particularly *microneedles* (1.1X), offer non-invasive alternatives with improved patient compliance.[315]

This patent activity reflects a maturing delivery technology landscape where platform diversity, functional integration, and stimulus-responsive control collectively address the complex requirements of modern therapeutics across multiple modalities and administration routes.

4.2.8 Other emerging therapeutic modalities

Photodynamic therapy (PDT) and related light-activated treatments exhibit brisk growth rates (1.1X), leveraging *photosensitizers* (1.1X) that generate reactive oxygen species upon light exposure for spatially controlled tumor ablation[316] and antimicrobial[317] applications despite being an application-limited modality. *PDT combination therapies* (1.1X) appear to be emerging integrating photodynamic approaches with immunotherapy or chemotherapy to enhance efficacy and overcome resistance mechanisms.[318,319] Applications extend beyond oncology to *dermatology* (1.2X) and *ophthalmology* (1X), where accessible tissue sites enable practical light delivery.

4.2.9 Strategic takeaways: Navigating the multimodal innovation landscape

The modality-level patent analysis reveals pharmaceutical innovation transitioning from platform-constrained to biology-driven therapeutic design. Exceptional growth clusters in targeted protein degraders, circRNA vaccines, CAR-NK cells, and α-emitting radiopharmaceuticals signal technologies moving from academic validation toward commercial implementation, while established modalities (kinase inhibitors, checkpoint antibodies, GLP-1 agonists) maintaining steady growth demonstrate sustained value extraction from mature platforms through incremental optimization.

Organizations should maintain diversified modality portfolios spanning breakthrough technologies (high risk, differentiation potential), emerging platforms (validated mechanisms with growth momentum), and established modalities (near-term revenue, lifecycle management). They must also invest in enabling technologies, particularly AI-driven design, advanced drug delivery systems, and manufacturing innovations, that create competitive advantages across multiple modalities rather than betting exclusively on single platforms. Furthermore, they must develop modality-agnostic target assessment frameworks where biological mechanism determines therapeutic format rather than organizational legacy constraining target selection. The convergence patterns observed (e.g., ADCs, mRNA-LNPs vaccines, CAR-engineered innate cells) suggest future success requires integration capabilities spanning chemistry, biology, engineering, and data science rather than deep expertise in isolated modalities. Organizations building these cross-disciplinary platforms while maintaining a strategic focus on differentiated targets are positioned to capture disproportionate value as the druggable universe expands and modality boundaries blur.

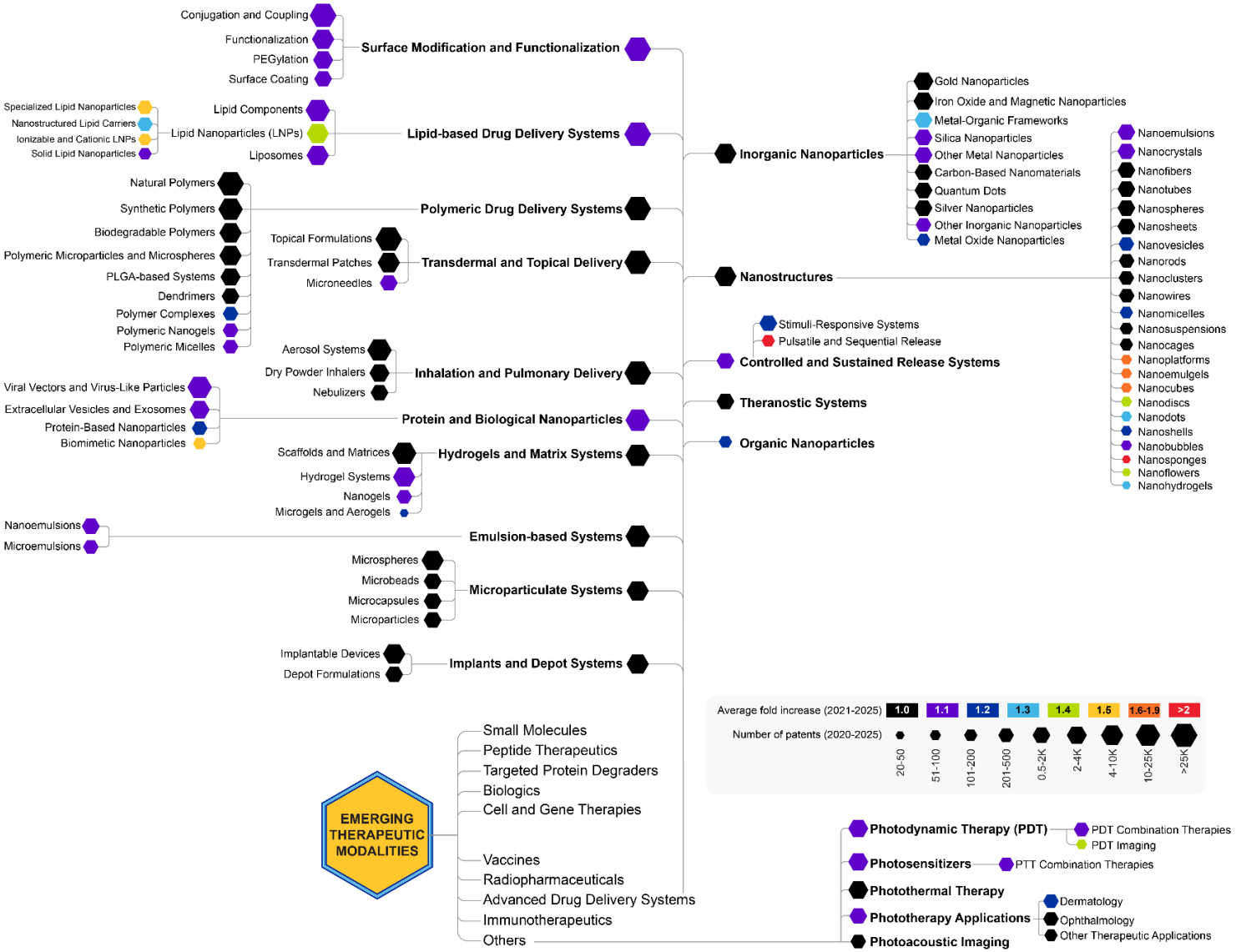


Figure 19. CAS TrendScape map of emerging topics in terms of therapeutic modalities focused on advanced drug delivery systems and others identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.3 Emerging opportunities in therapeutic targets across proteins, cells, and pathogens

The pharmaceutical innovation landscape can be understood through two complementary lenses: the therapeutic *modalities* employed (how we intervene) and the biological *targets* engaged (where we intervene). Having examined modality evolution in **section 4.2**, this section employs the same NLP-based patent analysis to identify which specific targets are experiencing accelerating innovation, revealing pharmaceutical R&D's evolving biological focus across specific proteins, cells, and pathogens whose modulation drives therapeutic benefit. Target patent growth rates serve as proxies for emerging therapeutic opportunities, revealing where recent biological insights, technological advances, or urgent clinical needs are driving concentrated innovation.

These growth patterns often reflect the dynamic interplay between modality capabilities and target accessibility. Transcription factors, long deemed "undruggable" by small molecules, now show accelerating patent activity enabled by targeted protein degradation technologies. CRISPR-Cas gene editing systems have transformed genetic mutations from permanent disease drivers into correctable targets, spawning entire therapeutic programs addressing previously intractable monogenic disorders. Innate immune cell populations demonstrate rapid growth as CAR-engineering expands beyond conventional T cells. Coronavirus proteins exhibit dramatic patent surges following COVID-19, validating our methodology's ability to capture real-world research shifts. This section maps the biological terrain where pharmaceutical innovation is advancing the most, providing strategic intelligence on which molecular mechanisms, cellular pathways, and infectious threats represent tomorrow's validated drug targets and where the most promising opportunities for therapeutic intervention may lie.

4.3.1 Protein targets: From classical druggable targets to emerging undruggable space

4.3.1.1 The receptor target spectrum: Classical pathways and emerging immune checkpoints

The receptor target landscape reveals both the continued dominance of validated target classes and the rapid emergence of immunological receptors reflecting the immuno-oncology revolution. *G-protein coupled receptors (GPCRs)* maintain their position as one of the largest target class by patent volume, encompassing diverse subfamilies including *somatostatin receptors* (SSTR2,[320] 1.3X), *melanocortin receptors* (1.3-2X),[321] *orexin receptors*[322] (1.6-1.9X) and others driving patent growth. The GPCR superfamily's sustained patent activity reflects its proven druggability and ongoing opportunities for subtype-selective modulation, particularly for *orphan GPCRs*[323, 324] (1.3X) whose biological functions are newly elucidated. *Receptor tyrosine kinases (RTKs)* similarly demonstrate substantial volume, with the *EGFR family* (EGFR, ERBB2/HER2, ERBB3/HER3) and *VEGF receptor family* remaining prominent, alongside *FMS-like tyrosine kinase 3 (FLT3)* and *FGFR family* members, established oncology targets with continued innovation in selectivity profiles and resistance mutation coverage.

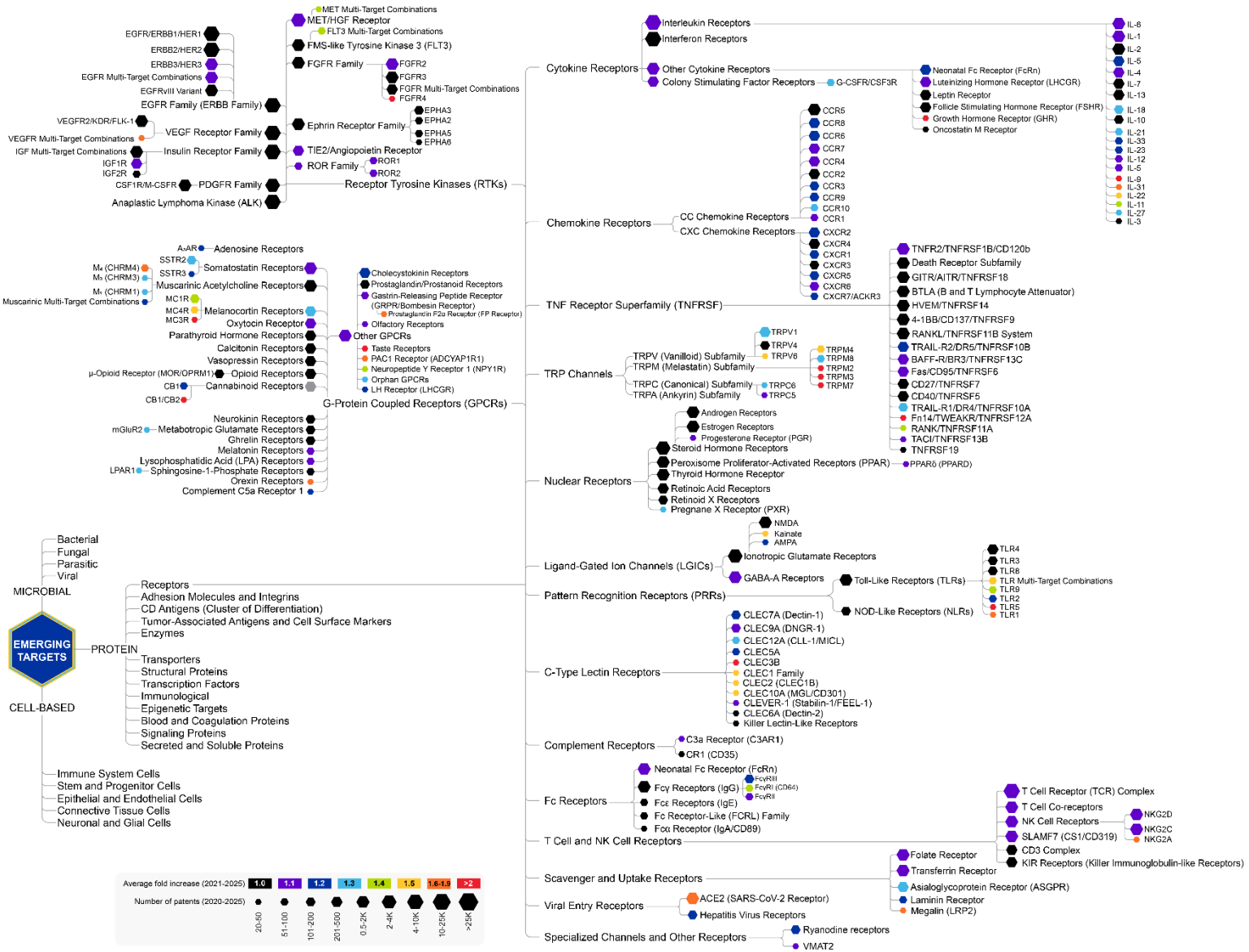


Figure 20. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – receptors, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

The most striking growth appears in *cytokine receptors*, where *interleukin receptors* (IL-18, IL-21, IL-33, IL-23, IL-9, IL-31, IL-22, IL-11 and IL-27)[325,326] show exceptional patent acceleration, reflecting therapeutic opportunities in autoimmune disorders, inflammatory diseases, and cancer immunotherapy. Specific members of the *TNF receptor superfamily (TNFRSF)* like *TNFR2*[327,328] (1.1X) and *death receptor subfamilies* (DR4, DR3)[329,330] branch exhibits robust growth, offering apoptosis modulation opportunities.

Nuclear receptors including *peroxisome proliferator-activated receptors* (PPARs), *steroid hormone receptors* including *estrogen receptors* and *androgen receptors* maintain steady activity in metabolic and hormonal disorders. Other emerging receptor targets include *pattern recognition receptors* (PRRs) such as *toll-like receptors* (TLRs)[331,332] and *C-type lectin receptors* (CLEC9A,[333] CLEC12A,[334] etc.), reflecting interest in innate immunity modulation for vaccines and immunotherapies.

The receptor target landscape reveals that while classical families (GPCRs, RTKs, etc.) sustain innovation through selectivity refinement, exceptional growth concentrates in immunological targets such as cytokine receptors, pattern recognition receptors, and chemokine receptors, reflecting the pharmaceutical industry's strategic pivot toward immune modulation across oncology, autoimmune, and inflammatory diseases.

4.3.1.2 Emerging opportunities in adhesion molecules, CD antigens, and transporter proteins

Cell surface and membrane-associated proteins beyond classical receptors represent rapidly expanding therapeutic target classes (**Figure 21**), particularly for antibody-based therapies and targeted drug delivery. *Adhesion molecules and integrins* demonstrate substantial patent activity, with the *immunoglobulin superfamily cell adhesion molecules* (IgCAMs) encompassing diverse members including *ICAM-1/CD54*,[335] *VCAM-1/CD106*,[336] and *L1CAM/CD171*.[337] Integrins maintain robust activity through *integrin heterodimers* (LFA-1/αLβ2) and *specific integrin β subunits* (*integrin β6*, *integrin β1*) and *integrin α subunits* (*integrin αE*, *integrin αL*), reflecting their roles in cancer metastasis, angiogenesis, and immune cell trafficking.[338-340] These adhesion molecules serve dual purposes: as direct therapeutic targets to disrupt pathological cell-cell or cell-matrix interactions, and as delivery vehicles for antibody-drug conjugates.

Tumor-associated antigens and cell surface markers represent a large cluster by patent volume, reflecting intense interest in cancer immunotherapy and targeted biologics. Established *carcinoma-associated antigen* targets include *prostate-specific membrane antigen* (PSMA),[341] *epithelial cell adhesion molecule/CD326* (EpCAM),[342] *mesothelin* (MSLN),[343] *carcinoembryonic antigen* (CEA),[344] and mucins: antigens with restricted normal tissue expression but overexpression in malignancies, which makes them attractive for CAR-T therapies, ADCs, and radioimmunotherapy.

CD antigens (cluster of differentiation) encompass the most extensively characterized cell surface markers, with distinct patent activity patterns across functional categories. *T cell CD markers* include established targets like CD8,[345] CD28,[346] CD3,[347] as well as emerging ones such as CD2, CD7, CD25, alongside *co-stimulatory CD molecules* (*CD278/ICOS*, *CD40/TNFRSF5*, *CD154*, *CD70*, *CD276/B7-H3*, *CD30/TNFRSF8*) that are focal points for cancer immunotherapy agonist antibodies. *B cell CD markers* feature *CD19*,[348] *CD79*,[349] *CD22*,[348] and *CD179a/VPREB1* as validated targets for hematologic malignancy therapies. *Myeloid CD markers* (*CD33*, *CD38*, *CD1*) and *NK cell CD markers* (*CD56/NCAM*, *CD16*) reflect cell-type-specific therapeutic strategies. Emerging growth areas also include specialized markers *CD133/prominin-1*[350] and *CD117/c-Kit* for targeting cancer stem cell populations.

Transporters represent a relatively underexploited target class with accelerating patent activity, particularly in overcoming drug resistance and exploiting tumor-specific metabolic dependencies. The *solute carrier (SLC) superfamily* dominates transporter patents, with *glucose transporters* (particularly SLC5A2/SGLT2[351] and SLC5A1/SGLT1[352]) targeted for metabolic disorders and cancer metabolism modulation. *Amino acid transporters*, including *SLC7A5/LAT1* and *SLC7A1/CAT-3*, attracting interest in disrupting cancer cell nutrient uptake. Monoamine transporters (SLC6 family) which include dopamine transporters (DAT/SLC6A3; 1.2X) and norepinephrine transporters (NET/SLC6A2; 1.1X) continue to garner significant patenting activity and interest likely in the context of psychiatric disorders. High-growth areas include *GLT-1/EAAT2/SLC1A2*[353] and other *excitatory amino acid transporters* as well as the *vesicular transporter VMAT2/SLC18A2*.[354]

These emerging target classes demonstrate strategic expansion beyond classical receptor pharmacology: adhesion molecules and tumor antigens enable ADCs and CAR-T therapies exploiting restricted tissue expression, while CD markers provide cell-type-specific immune modulation across T cells, B cells, myeloid cells, and NK cells.

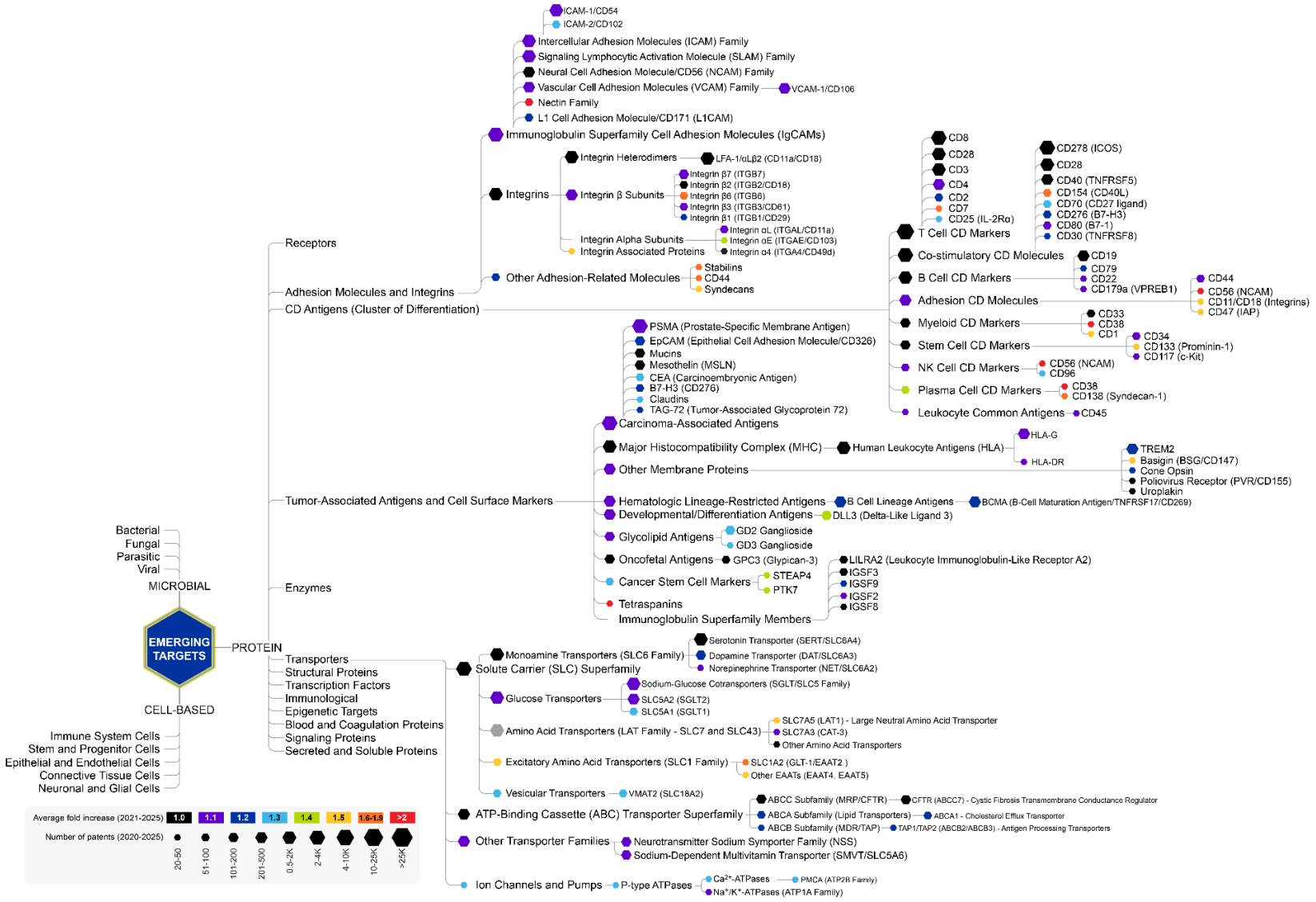


Figure 21. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets including adhesion molecules and integrins, CD antigens, tumor-associated antigens and cell surface markers, and transporters identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.3.1.3 Kinase maturation, epigenetic expansion, and metabolic enzymes emergence: Insights enzyme target evolution

Enzymes represent the most targeted protein class, with patent activity reflecting both the maturation of established mechanisms and the rapid emergence of novel catalytic targets enabled by structural biology and chemical biology advances (**Figure 22**).

Protein kinases dominate enzyme patents by volume, underscoring decades of validated druggability. *Serine/threonine kinases* show substantial activity with emerging targets including mitotic kinase *TTK/MPS1*[355] (1.4X), *PKMYT1*[356] (1.6-1.9X), and eIF2α kinase *PERK*[357] (1.3X). *Tyrosine kinases* include non-receptor kinases (*SYK*, *FAK*) exhibiting steady interest. *Lipid kinases* (*DGK*, *SPHK1/2*) maintain substantial activity given central roles in cell signaling and metabolism. Continued kinase innovation targets resistance mutations, selectivity, and previously "undruggable" kinases through allosteric or covalent mechanisms.

Proteases and peptidases represent another major category. *Serine proteases* include *thrombin* (1X), *protein C/S* (1.3X), *proteinase-3* (>2X), and *chymase* (1.3X) potentially in cardiovascular diseases.[358] *Cysteine proteases* (*cathepsins*, *papain*; 1.1-1.3X) show brisk growth. *Metalloproteinases* (*MMPs*, *ADAMs* 1.2X, *ACE* 1.2X) and *aspartic proteases* (*BACE2* 1.1X, *renin* 1.1X) continue garnering significant interest.

Epigenetic enzymes exhibit exceptional growth. *HDACs* maintain the largest patent volume with ongoing innovation in dual target/multi-target inhibitors that combines HDAC modulation with kinase or epigenetic pathway inhibition (FLT3/HDAC;[359] KRAS/HDAC,[360] AR/HDAC6[361]). *Histone demethylases*, particularly *JmjC domain-containing demethylases*, demonstrate brisk acceleration (1.1X) as tools to pharmacologically manipulate gene expression patterns become available.

Metabolic enzymes represent increasingly attractive targets. *Amino acid metabolism* shows strong growth, with *aminotransferases*[362] (1.2X) enabling pathway intervention. *Tryptophan metabolism* features *kynureninase*[363] (1.4X) and *TDO2*[364] (1.5X) as immunometabolic targets. *Urea cycle* includes *ASL*[365] (1.2X) and *arginase*[366] modulating arginine availability.

Carbohydrate metabolism encompasses robust cancer metabolism targets. *Glycolysis* targets include *enolase*[367] (1.2X), *lactate dehydrogenase*[368] (1.3X), and *phosphoglycerate kinase* (1.2X).[369] *Pentose phosphate pathway* enzymes (*TKT*,[370] *PRPS*[371]) support nucleotide biosynthesis in rapidly proliferating cells and show exceptional growth (1.5-1.9X). Additional targets include *glycosidases* for lysosomal storage disorders and polysaccharide-degrading enzymes.

Lipid metabolism encompasses diverse enzymatic steps. *Fatty acid synthesis* features *FASN* (1.1X) as an established oncology target, alongside *acetyl-CoA carboxylase* (1.2X), *SCD* (1.2X), and rapidly growing *ELOVL* family[372] (1.4X) that controls fatty acid chain length and saturation. Fast growing targets in *cholesterol metabolism* include *LCAT*[373] (1.4X), *SQLE*[374] (1.4X), and *HMGCS1/2*[375] *(*1.3X). *Eicosanoid metabolism* features *COX/PTGS* as the established NSAID target. *Sphingolipid metabolism* offers emerging opportunities through *sphingomyelinases* (1.1X), *ceramidases* (1X), and *UGCG* (1X). *Lysosomal acid lipase*[376] (LAL; 1.3X) and *maltase* (acid alpha-glucosidase;[377] 1.3X) in triglyceride and glycerol metabolism emerge as fast-growing targets.

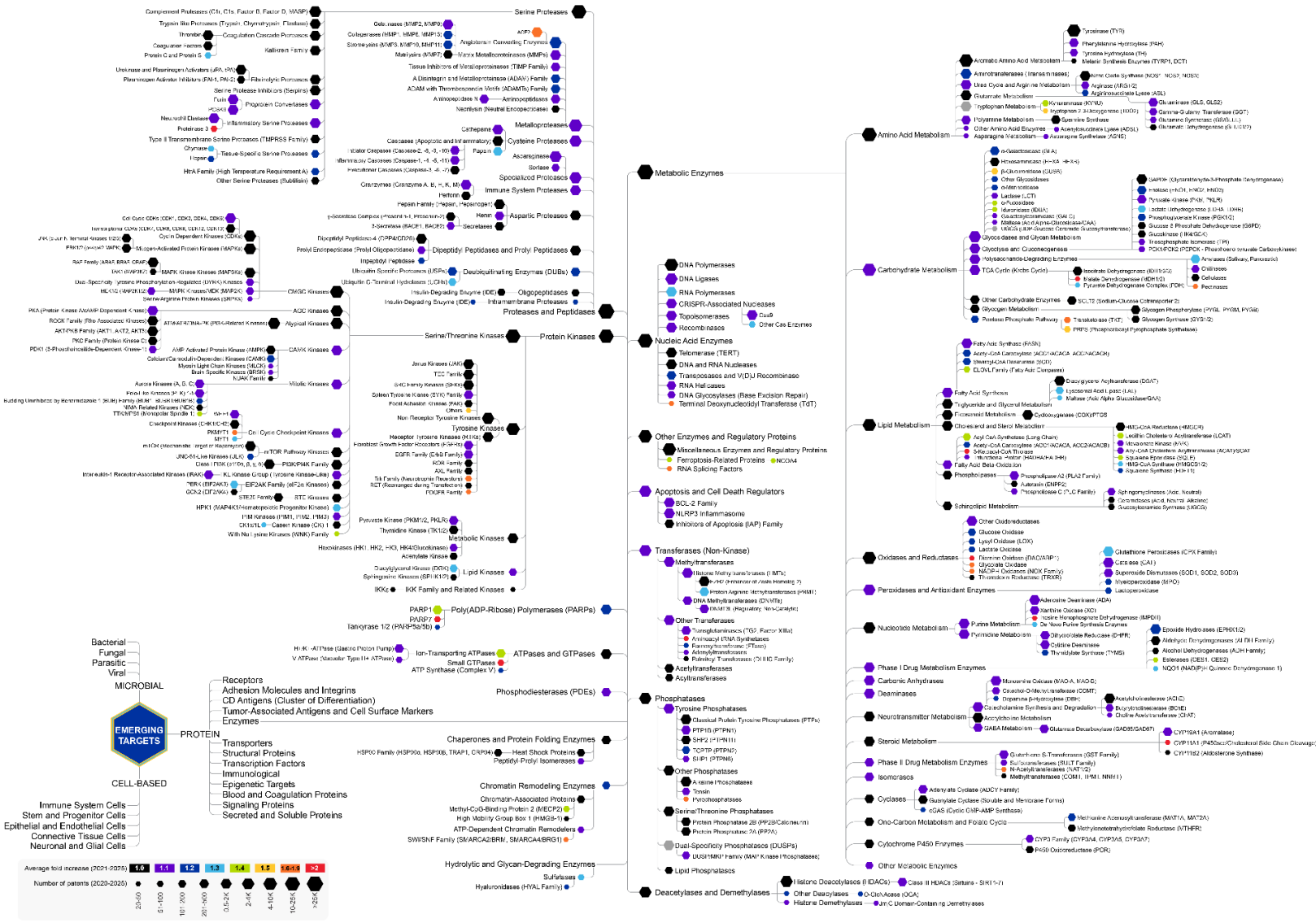


Figure 22. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – enzymes, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Oxidases and reductases show exceptionally strong growth. *NOX family* (1.6-1.9X) represents promising inflammatory disease and cancer targets.[378, 379] *Diamine oxidase* (*DAO/ABP1*) (>2X) demonstrates remarkable acceleration driven by urological and neurological interest.[380,381] *Glycolate oxidase* (1.6-1.9X) represents an emerging target in primary hyperoxaluria and calcium oxalate kidney stone prevention.[382,383] Additional targets include *glucose oxidase*[384] (1.2X), *lysyl oxidase*[385] (LOX; 1.2X) for fibrosis and cancer, *lactate oxidase* (1.2X) for therapeutic and diagnostic applications pertaining to cancer immunotherapy, biosensing, and wound healing,[386,387] and *thioredoxin reductase* (1X) in terms of small molecule inhibitors primarily for cancer treatment.[388]

Transferases (non-kinase) demonstrate growing therapeutic interest, including histone modifiers such as *PRMTs* (1.3X) and *PARPs* (1.2X), the latter validated through synthetic lethality in BRCA-mutant cancers.[389] The former appears to be primarily focused on developing PRMT5 inhibitors for cancer treatment, though non-oncological diseases are also being pursued.[390-392] *Hyaluronidases* (1.2X), in the *hydrolases and glycan-degrading enzymes* sub-branch, also show high growth with innovations around use of hyaluronidase to enable high-volume subcutaneous administration of monoclonal antibodies and dermatological applications.[393,394]

The enzyme landscape's breadth reflects the fundamental importance of catalytic function in cellular processes and the expanding toolkit for targeting previously intractable enzymatic mechanisms.

4.3.1.4 Transcription factors: Emerging druggability in gene regulation targets

Transcription factors have historically been considered "undruggable" due to their lack of defined binding pockets and nuclear localization, yet recent technological advances, including PROTACs, DNA-binding small molecules, and protein-protein interaction (PPI) inhibitors, are transforming this target class into viable therapeutic opportunities. Patent activity reveals sustained interest in validated targets and rapid emergence of developmental and stress-response regulators (**Figure 23**).

Among **oncogenic transcription factors**, *MYC family* members maintain the largest patent volume reflecting decades of interest in this master regulator of cell proliferation, though direct MYC inhibition remains challenging. *ETS family* transcription factors show accelerating activity, particularly *ETS1*[395] (1.4X) driven by its roles in cancer metastasis.

Lineage-specific transcription factors reveal tissue-restricted opportunities. The *myogenic transcription factors* branch highlights *MyoD* (MYOD1) and *myogenin* (MYOG) suggesting regenerative medicine applications in muscular dystrophies and sarcopenia.[396,397] *Neural transcription factors* include rapidly growing targets *OTX1* and *OTX2* (homeobox factors critical in brain development and medulloblastoma) with patents focused on detecting their levels as biomarkers[398,399] alongside *ASCL1/MASH1*[400] (neuronal differentiation) and the cardiac transcription factor *ISL1*[401] (1.3X). *Hematopoietic transcription factors* feature *IKZF Family* (IKAROS, HELIOS, AIOLOS) as validated targets in hematologic malignancies,[402-404] alongside *BCL6* (1.1X).[405]

Major developmental signaling pathway transcription factors demonstrate exceptional growth in previously underexplored regulators. Within the *NOTCH pathway*, *HEY family* (HEY1, HEY2, HEYL) members show strong patent acceleration (1.3X), reflecting their roles in stem cell maintenance, neurogenesis, and tumor cell fate determination.[406-408] *WNT/β-catenin pathway* components and *NOTCH ligands* (DLL1, DLL3, DLL4, JAG1, JAG2)[409-411] represent alternative intervention points.

Stress response and metabolic transcription factors feature the extensively studied *NRF2-KEAP1* (oxidative stress response) axis with substantial patent volume, representing a validated approach for cytoprotection in neurodegenerative diseases,[412] though also implicated in cancer therapy resistance.[413-416] The rapidly growing *NRF1* (NFE2L1) (>2X) offers an alternative oxidative stress modulator with distinct regulatory mechanisms.[417] *ATF6* within the unfolded protein response (UPR) pathway demonstrates strong growth (1.4X), reflecting interest in endoplasmic reticulum (ER) stress modulation for metabolic diseases, neurodegeneration, and cancer.[418,419] *HIF2α* (part of hypoxia response) represents a validated target in renal cell carcinoma with an approved inhibitor by Merck (belzutifan[420]).[421]

Established targets with substantial patent portfolios and brisk growth include *TEAD family* (TEAD1-4; 1.3X) as critical effectors of the Hippo pathway, particularly attractive given their obligate partnership with YAP/TAZ in driving oncogenic transcription, enabling disruption through PPI inhibition.[422,423] *STAT family* members, especially *STAT3* (1.1X) and *STAT6* (1.2X), maintain robust activity as signal transduction-activated transcription factors linking cytokine signaling to gene expression.[424,425] *Nuclear factor of activated T cells (NFAT) family* remains prominent for immunosuppression applications.[426]

Zinc finger transcription factors encompass the large *KRAB domain zinc fingers* family with established patent volume, alongside *KLF family* (KLF4) as pluripotency and differentiation regulators[427] with applications in anti-aging,[428] and *TWIST family (EMT regulators)* featuring the rapidly growing *TWIST1*, critical in epithelial-mesenchymal transition and cancer metastasis.[429,430]

Developmental transcription factors with growing patent interest include various *SOX groups* including the *SOXE group* (SOX8, SOX9, SOX10; 1.2X), important in neural crest development,[431-433] and *SOXB (SRY-box) family* members (1.1X). Additional fast-growing developmental factors include *TBX1* (>2X) within the *T-box (TBX) family* and *TGIF1* in TGF-β signaling regulation.[434] The *forkhead box (FOX) family* demonstrates diversity with *FOXO subfamily* members (FOXO1, FOXO3, FOXO4), *FOXP3* (Treg master regulator) for autoimmune diseases,[435,436] *FOXP1* (1.1X), and *FOXG1* (1X) showing recent growth.[437,438]

Our analysis of the transcription factor patent landscape demonstrates systematic progression from historically intractable master regulators toward mechanistically druggable nodes characterized by obligate protein partnerships, stress-response modularity, or tissue-restricted expression, enabled by PROTAC degraders and PPI inhibitors that circumvent traditional binding pocket requirements.

4.3.1.5 Emerging targets in complement, chemokines, and antigen presentation diversifying immunotherapy

The immunological target landscape is rapidly diversifying beyond established checkpoint inhibitors, with accelerating patent activity in innate immunity, complement modulation, and tissue-specific antigens reflecting cancer immunotherapy maturation and expansion into autoimmune and inflammatory indications (**Figure 24**). While *PD-1/PD-L1* and *CTLA-4* maintain large patent volumes (~5,000 patent families) as validated checkpoints, high-growth emerging targets suggest evolution toward combination strategies and novel immune modulation mechanisms.

Immune checkpoint molecules demonstrate growth beyond established players. *CD96* (1.3X),[439] an inhibitory receptor on NK and T cells competing with CD226 for CD155 binding, represents a promising target for enhancing anti-tumor immunity, particularly combined with PD-1 blockade. *TIGIT* (1X) shares this CD155 axis with robust activity. *CD80* (1.3X),[440] a ligand for

both CD28 (co-stimulatory) and CTLA-4 (co-inhibitory), offers selective pathway modulation opportunities. *Co-stimulatory molecules* (*4-1BB*, *GITR*, *ICOS*) as agonist antibody targets exhibit sustained patent interest.

Trophoblast antigens show exceptional growth, with *5T4*[441] and *PLAC1*[442] (1.4X) representing tumor-associated antigens with restricted normal expression limited to placental trophoblasts, attractive for ADCs and CAR-T therapies while minimizing off-tumor toxicity. *LAMP family*[443] (1.2X) members serve as tumor antigens and targets for modulating autophagy and lysosomal function.

Fcγ receptors[444,445] (1.1-1.4X) represent critical targets for antibody engineering and immunomodulation, mediating antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and immune complex clearance. Patent activity reflects therapeutic antibody optimization for enhanced FcγR binding (particularly activating FcγRIIIa) and inhibitory FcγRIIb antagonists to enhance anti-tumor responses.

Complement components show remarkable growth, particularly *complement C1q B chain*[446] (*C1QB*; 1.6-1.9X), part of the classical pathway-initiating C1 complex. Interest extends beyond rare diseases to cancer immunotherapy, where complement inhibition may enhance checkpoint inhibitor efficacy by reducing immunosuppressive myeloid cells and promoting T cell infiltration.

Chemokine receptors demonstrate strong growth across *CXCR family* members[447,448] (*CXCR2/3/1/7*, all 1.2X), controlling immune cell trafficking and TME composition. *CXCR2* antagonism reduces MDSC infiltration; *CXCR3* promotes T cell and NK cell recruitment. *CCR receptors* (*CCR5/4/8*) maintain substantial volume for HIV, cancer, and autoimmune applications.

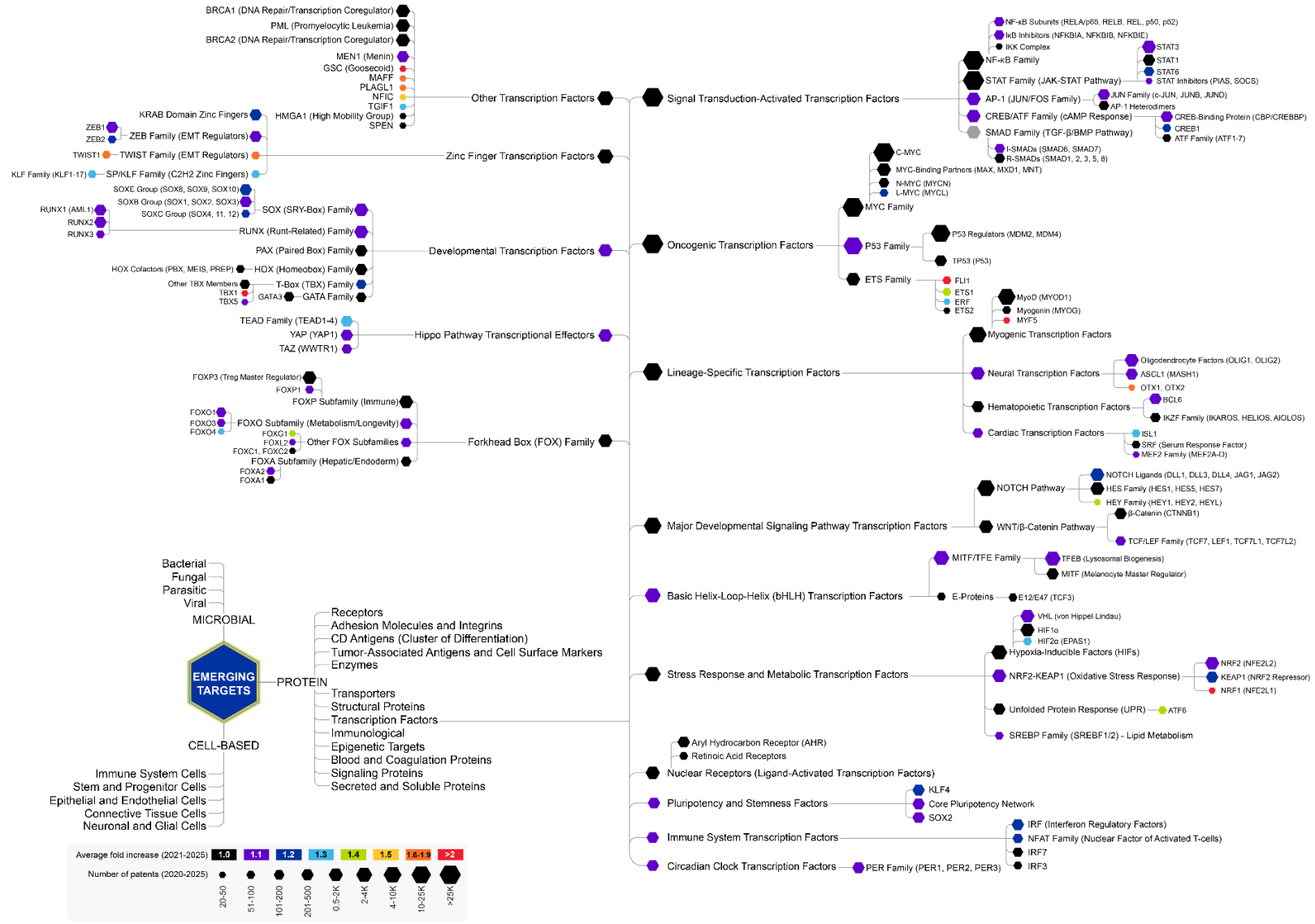


Figure 23. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – transcription factors, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

T cell markers reveal antigen presentation and activation opportunities. *CD1 family*[449] (1.3X) presents glycolipid antigens to specialized T cell subsets, which is relevant for mycobacterial infections and lipid-rich tumors. *CD25*[450] (1.3X) serves dual purposes: depleting Tregs to relieve immunosuppression or enabling selective IL-2 delivery. *CD3* maintains the largest volume as a universal T cell marker and bispecific antibody target.

MHC/HLA components show growing interest in antigen presentation modulation. *β2-Microglobulin*[451] (1.3X), MHC class I light chain, represents a target for modulating antigen presentation and enabling universal CAR-T cells. *HLA-G* maintains activity for checkpoint blockade and allograft applications.

B cell markers feature rapidly growing *CD23*[452] (1.6-1.9X), a low-affinity IgE receptor targeting allergic diseases, CLL, and autoimmune conditions. Established targets (*CD19/20/22*) maintain larger volumes. *BCMA* represents a validated multiple myeloma target.

TREM receptors (1.2X) represent emerging pattern recognition receptors modulating innate immunity. *TREM1*[453] targets sepsis and inflammatory diseases while *TREM2*[454] regulates microglial function in neurodegeneration and tumor-associated macrophage phenotypes, offering TME myeloid cell reprogramming opportunities.

Other immunological targets demonstrate diverse growth. *Lipoprotein receptors* (>2X) show exceptional growth in cardiovascular applications and immune cell metabolism. *Transferrin receptors* (1.3X) serve as proliferation markers and ADC delivery vehicles. *Fetal acetylcholine receptor* (1.2X) represents a tumor-specific antigen enabling neuromuscular-sparing immunotherapy. *Toxin and growth factor receptors* (1.3X) encompass immunotoxin construction and immunomodulatory functions.

Our analysis of the patent landscape reflects immunotherapy's maturation beyond single-agent checkpoint blockade toward combination strategies, innate immune modulation, and tissue-specific targeting expanding patient populations benefiting from immunological interventions.

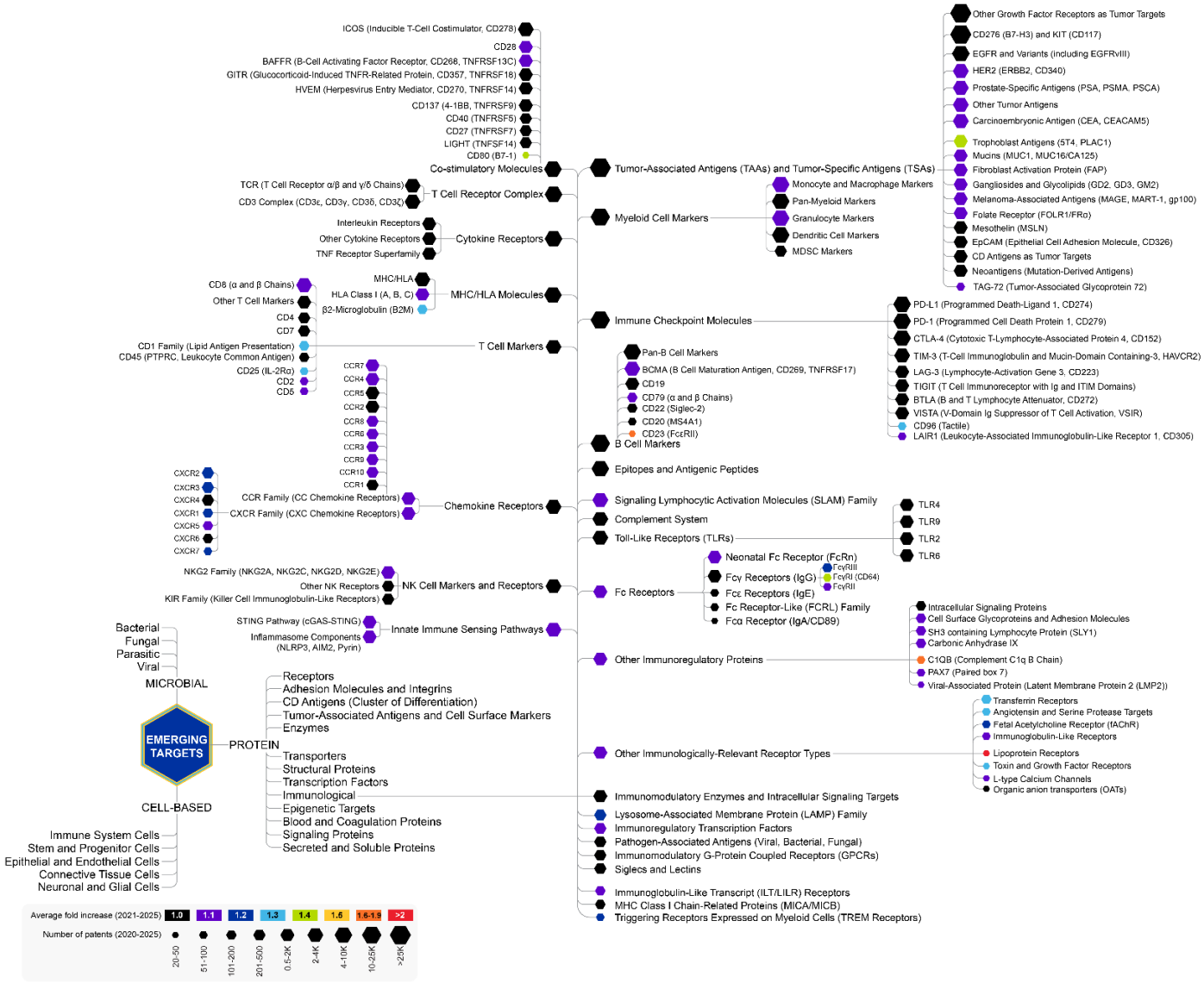


Figure 24. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – immunological, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.3.1.6 Diversifying epigenetic drug discovery portfolio beyond HDAC and DNMT inhibitors

Epigenetic targets represent one of the fastest-evolving areas, with patent activity reflecting clinical validation of first-generation inhibitors and emergence of sophisticated approaches targeting chromatin readers, remodelers, and RNA-mediated regulation (**Figure 25**). The field has matured beyond simple "writer" and "eraser" paradigms to encompass multi-protein complexes, architectural proteins, and regulatory RNAs orchestrating gene expression in cancer, neurological disorders, and developmental diseases.

Histone deacetylases (HDACs) (1X) maintain large patent volume reflecting two decades of optimization and four U.S. FDA-approved drugs (vorinostat, romidepsin, belinostat, panobinostat) for hematologic malignancies. Isoform-selective inhibitors show accelerating growth: *HDAC8* (1.2X, Class I) offers opportunities in cancer and diabetic neuropathy;[455] *HDAC9* (1.2X, Class IIa) plays a role in Alzheimer's and cancer immunotherapy.[456] **Class III HDACs** (**sirtuins**) demonstrate exceptional growth in specific isoforms: *SIRT3*[457] (1.2X) regulates mitochondrial metabolism and oxidative stress; SIRT4[458] (1.6-1.9X) controls fatty acid oxidation and insulin secretion with applications in metabolic syndrome, aging, and cancer metabolism.

Histone acetyltransferases (HATs/KATs) show growing interest as HDAC counterparts. *MYST family* (1.2X) features *MOZ*[459] (*KAT6A*) (1.3X) and *MOF*[460] (*KAT8*) (1.2X) as hematopoiesis and DNA damage response regulators. MOZ fusions drive AML, while MOF controls X-chromosome dosage compensation and DNA repair. The *GNAT family* (1.2X) includes *GCN5* (*KAT2A*; 1.3X) and *PCAF* (*KAT2B*; 1.2X) as transcriptional coactivators involved in metabolic regulation and cell cycle control.[461,462] The *CBP/p300 family* maintains substantial volume with recent successes in PROTAC and catalytic domain inhibitor suggesting renewed tractability.[463]

Bromodomain-containing proteins have emerged as highly druggable targets with the *BET family* maintaining high patent volume following discovery of selective inhibitors (JQ1, I-BET), validating the reader domain targeting paradigm. *Non-BET bromodomains* show strong growth as next-generation opportunities with potentially improved therapeutic windows: the *ZMYND family*[464] (1.6-1.9X) reads histone modification combinations and regulates transcriptional elongation and DNA damage response; *BPTF*[465] (1.3X), a NURF chromatin remodeling complex component, offers distinct biological functions and selectivity profiles as compared to BET proteins.

Histone lysine methyltransferases (KMTs) (1X) represent a diverse family with multiple clinical-stage inhibitors (enzomenib[466]) and recent approvals (ziftomenib,[467] revumenib[468]). *SMYD3* (>2X), an H3K4 methyltransferase with non-histone substrates and overexpressed in numerous cancers, shows exceptional growth reflecting oncology applications and emerging roles in transcriptional regulation. *KMT2B* (*MLL2*) (1.4X) and *KMT2A* (*MLL1*) (1.1X) are critical in leukemias with MLL translocations and represent targets for disrupting oncogenic MLL fusion protein complexes through menin-MLL interaction inhibitors[469,470] (some menin-MLL inhibitors are now in clinical trials: e.g., NCT04067336,[471] NCT06226571[472]). *ASH1L*[473] (1.3X), also a H3K4 methyltransferase, shows growth likely driven by roles in hematopoiesis and MLL-rearranged leukemia synthetic lethality. NSD3[474] (1.3X) is amplified in certain cancers and regulates transcriptional elongation; *SETDB1*[475] (1.2X) maintains heterochromatin with cancer immunotherapy implications. The *PRDM family* features *PRDM1*[476] (*BLIMP1*) (1.2X) as a transcriptional repressor critical for plasma cell differentiation.

Histone lysine demethylases (KDMs) represent the "eraser" counterparts to methyltransferases, with growth in specific subfamilies. *KDM5D*[477] (*JARID1D/SMCY*; 1.3X, H3K4 demethylase) the Y chromosome paralog with sex-specific biology and roles in drug resistance

through chromatin remodeling shows growth reflecting potential interest in sex differences in disease and therapy response. *KDM6B*[478] (*JMJD3*; 1.3X, H3K27 demethylase) opposes EZH2 with context-dependent roles as tumor suppressor and oncogene.

Protein arginine methyltransferases (PRMTs) show continued growth, with **PRMT5**[479] (1.3X) leading as a type II PRMT in clinical trials, particularly for MTAP-deleted tumors.

Polycomb group (PcG) complexes show accelerating activity in components beyond enzymatic cores. *Polycomb repressive complex 1* (*PRC1 complex*; 1.2X) mediates H2A ubiquitination and chromatin compaction, with *CBX family*[480] (1.4X) serving as chromodomain-containing readers recognizing H3K27me3 and recruiting the repressive machinery. *RING1A/B*[481] (*RNF2*; 1.6-1.9X) possesses E3 ubiquitin ligase activity showing exceptional growth likely as a potential target for reactivating tumor suppressor genes. *Polycomb repressive complex 2* (*PRC2 complex*) maintains higher volume of patents likely through validated *EZH2* (PRC2 catalytic subunit) and *EED* (PRC2 core component) as validated targets, with allosteric EED inhibitors offering an alternative to catalytic EZH2 inhibition.

ATP-dependent chromatin remodeling complexes (1X) alter nucleosome positioning and represent non-enzymatic targets with growing tractability. **SWI/SNF complexes**, mutated in 20% of malignancies, include *SMARCA4* (1.1X) and *SMARCA2* (1.2X) as mutually exclusive ATPases enabling synthetic lethality approaches as emerging targets.[482,483] Patents increasingly focus on degraders and synthetic lethal approaches.

DNA methylation machinery (1X) remains foundational with two U.S. FDA-approved DNMT inhibitors (azacitidine, decitabine) for myelodysplastic syndromes. *DNMT3L*[484] (1.6-1.9X), a catalytically inactive DNMT3 family member, shows growth reflecting interest in epigenetic reprogramming and developmental disorders. *DNA methylation cofactors* (1.6-1.9X) show exceptional growth, particularly *UHRF1*[485] (>2X) representing a more specific target than pan-DNMT inhibitors. *Thymine DNA glycosylase*[486] (*TDG*; 1.4X) initiates base excision repair and active demethylation, serving dual roles in genome stability and epigenetic reprogramming. *Methyl-CpG binding domain 2* (*MBD2*; 1.4X) shows strong growth as a potential therapeutic target for recruiting chromatin remodeling complexes to methylated DNA.

RNA-mediated epigenetic regulation is an emerging frontier. *Small regulatory RNAs* (1.1X) including *siRNA*, *miRNA*, and *shRNA* maintain growing activity validated by recent U.S. FDA-approved siRNA therapeutics (patisiran, givosiran, lumasiran, inclisiran). *Argonaute (AGO) proteins* and *RNA-induced silencing complex*[487] (RISC; both 1.2X) mediate gene silencing and chromatin modifications.

Other epigenetic regulators include *ADAR enzymes*[488] (1.5X) catalyzing RNA editing (adenosine-to-inosine editing) with emerging therapeutic strategies in immuno-oncology and genetic disease, and *KRAB zinc finger proteins*[489] (1.4X), represent the largest family of transcriptional repressors in mammals and their growth may reflect interest in controlling transposable element expression for cancer immunotherapy and understanding human-specific gene regulation.

Transcriptional coregulators beyond HATs/HDACs include *corepressor complexes* such as *nuclear receptor corepressor* (*NCoR*;[490] >2X), *NCoR/SMRT complex*, and *SIN3 complexes*[491] (1.2X) as scaffolds recruiting chromatin modifiers. *Chromatin architectural proteins* (*CTCF*, *cohesin*, *SMC2* >2X, *NIPBL* 1.6-1.9X) organize three-dimensional genome architecture, representing emerging targets for modulating long-range regulation with SMC2[492] and NIPBL[493] being patented as biomarkers.

Our analysis of the epigenetic target landscape reflects evolution from small molecule enzyme inhibitors toward sophisticated approaches: PROTACs for undruggable regulators, molecular glues redirecting corepressor complexes, allosteric modulators of multi-protein assemblies, and synthetic lethality strategies exploiting the interdependencies within chromatin regulatory networks. Exceptional growth in reader domains, auxiliary proteins, and regulatory RNAs suggests diversification beyond writer/eraser paradigms toward comprehensive chromatin state modulation.

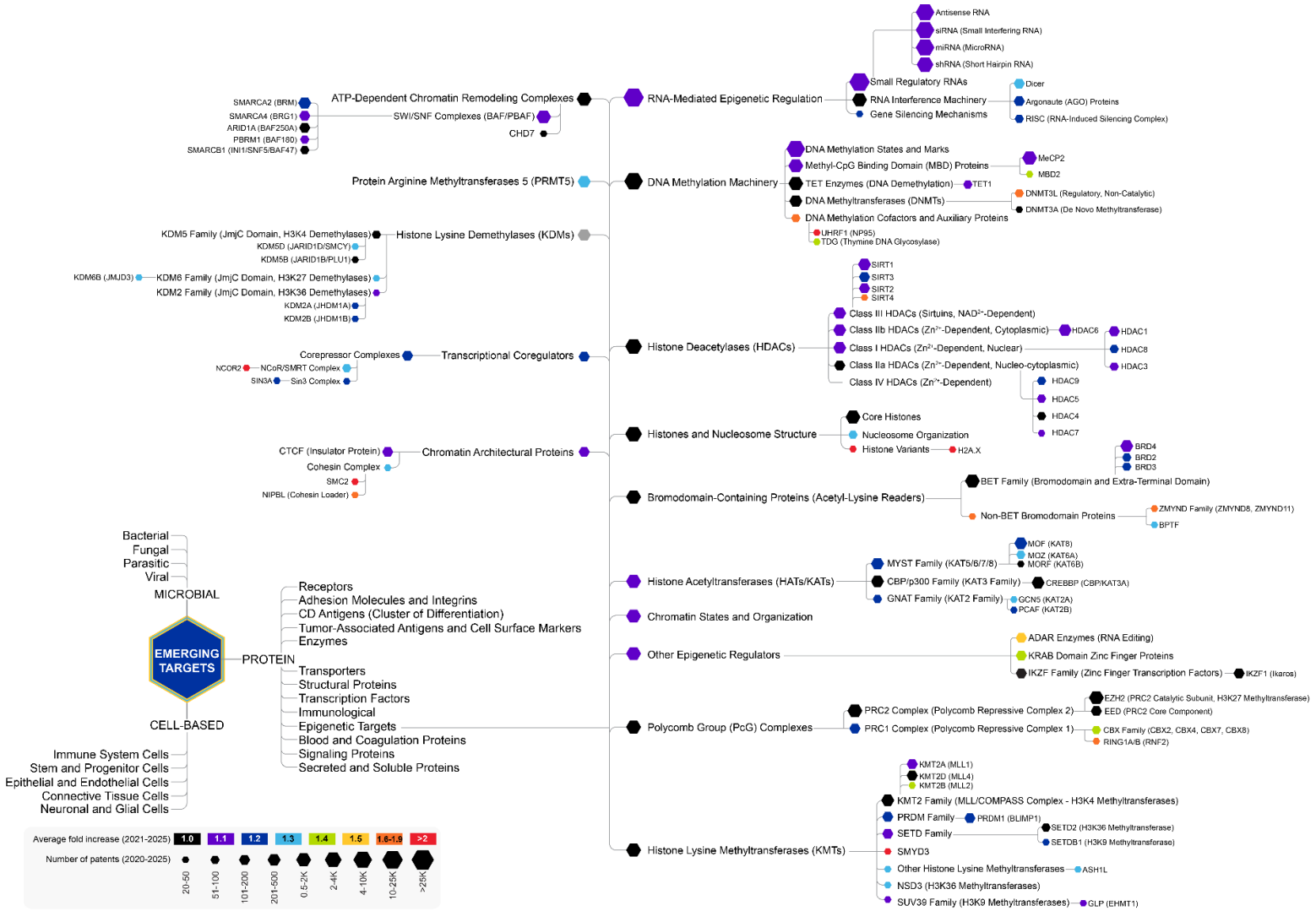


Figure 25. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – epigenetic targets, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.3.1.7 Expanding therapeutic opportunities in blood proteins, lipoproteins, and cardiac biomarkers

Blood and coagulation proteins represent highly validated targets with established anticoagulants generating tens of billions in annual revenue. The patent landscape reveals significant diversification beyond hemostasis toward lipid transport, iron homeostasis, cardiac biomarkers, and carrier proteins reflecting therapeutic and diagnostic innovations (**Figure 26**).

Coagulation and fibrinolysis proteins maintain large patent volumes, anchored by *thrombin (factor IIa)* (1X) as the most targeted protease with multiple direct oral anticoagulant classes (e.g., dabigatran), alongside the broader cascade encompassing *factors Xa*, *VIIa*, *IXa*, and *XIa*. High-growth targets include *ADAMTS13* (1.4X),[494] whose deficiency causes thrombocytopenic purpura. Patents reflect recombinant replacement therapies and cardiovascular biomarker applications. *Tissue factor pathway inhibitor*[495] (*TFPI*; 1.2X) represents an endogenous anticoagulant with therapeutic applications in hemophilia (through TFPI inhibition) and cardiovascular protection (through TFPI augmentation).

Platelet-derived proteins demonstrate exceptional growth. *Platelet-activating factor*[496] (*PAF*; >2X) shows highest growth, reflecting renewed interest in this potent inflammatory, thrombotic, and anaphylactic mediator with PAF antagonists targeting sepsis, acute respiratory distress syndrome (ARDS), and cardiovascular disease with complementary antithrombotic mechanisms. *Pro-platelet basic protein* (*PPBP, CXCL7*;[497] 1.3X), a platelet alpha-granule chemokine, shows strong growth related to inflammation, wound healing, and platelet activation biomarkers. *Platelet glycoproteins* maintain steady activity (1X), including *GPIIb/IIIa* and *P2Y12* as established antiplatelet targets.

Lipoproteins and apolipoproteins show strong activity (1.1X) reflecting cardiovascular disease burden and recent advances. *Apolipoprotein B* (*APOB*; 1.1X) maintains substantial volume with validated ASO (mipomersen) and siRNA (inclisiran) approaches. *Apolipoprotein D*[498] (*APOD*; 1.3X) shows accelerating growth for neurodegenerative diseases, metabolic disorders, and cancer applications. *Apolipoprotein E* (*APOE*) remains prominent given APOE4's Alzheimer's disease association and role in lipid metabolism.

Iron transport and storage proteins demonstrate strong growth driven by disorders of iron homeostasis. *Transferrin* (1.3X) serves dual roles: as iron transport protein enabling transferrin-drug conjugates exploiting TfR overexpression in cancer; and as therapeutic target in iron overload and anemias.[499,500] *Ferritin* (1.2X) stores intracellular iron and serves as a biomarker for iron status, inflammation, and specific diseases with recent innovations in ferritin nanocage drug delivery vehicles[501] and therapeutic targeting in iron overload and inflammatory diseases.[502] *Lactoferrin* (1.1X) maintains brisk activity likely for antimicrobial,[503] anti-inflammatory,[504] and immunomodulatory[505] applications.

Carrier and binding proteins reveal emerging opportunities in hormonal regulation. *Sex hormone-binding globulin* (*SHBG*; 1.6-1.9X) exhibits exceptional growth as primary testosterone/estradiol carrier, with implications for hormone-responsive cancers, metabolic syndrome, polycystic ovary syndrome (PCOS), and aging. Patents likely reflect diagnostic and therapeutic strategies to modulate hormone bioavailability.[506,507] *Retinol binding protein* (*RBP4*) maintains activity as a carrier for vitamin A and potential target for insulin resistance and metabolic disease.

Complement proteins show growth in specific regulatory components. *SERPING1*[508] (C1-INH) (1.3X) inhibits classical complement and contact pathways with deficiency causing hereditary angioedema. Multiple approved C1-INH replacement products are already available (e.g., Haegarda,[509] Cinryze,[510] etc.) with growing applications in complement-mediated kidney disease, transplant rejection, and inflammatory conditions. The broader complement *C1q complex* (1.2X) and *C3a receptor* (*C3AR1*; 1X) maintain activity for inflammatory and immunological applications.

Cardiac biomarker proteins demonstrate growth in established diagnostic markers and emerging therapeutic targets. *Cardiac troponins* (1.1X) remain gold standard myocardial injury biomarkers with sustained patent activity in high-sensitivity assays and point-of-care diagnostics. *Natriuretic peptides* (1X) maintain baseline activity as heart failure biomarkers (BNP, NT-proBNP) and therapeutic agents (nesiritide, sacubitril/valsartan targeting neprilysin to preserve endogenous natriuretic peptides). *Cardiac myosin*[511] (*MYH6/7*; 1.2X) shows breakthrough therapy validation with recent small molecule inhibitors (mavacamten, aficamten) for hypertrophic cardiomyopathy. *Phospholamban*[512] (*PLN*; 1.2X) regulates cardiac calcium handling, with therapeutic strategies including ASOs for mutant PLN reduction and small molecules modulating PLN-SERCA interaction for enhancing cardiac contractility in heart failure.

Hemoglobin-related proteins maintain substantial volume with *haptoglobin* and *globin genes* as targets for sickle cell disease and β-thalassemia, validated by recent U.S. FDA-approved gene therapies (betibeglogene autotemcel, exagamglogene autotemcel) and fetal hemoglobin inducers (voxelotor, crizanlizumab). *Serum amyloid proteins* maintain activity as inflammatory biomarkers and amyloidosis targets.

The patent landscape reflects maturation of anticoagulation therapies alongside emerging opportunities in metabolic proteins (apolipoproteins, iron carriers, hormone-binding globulins), cardiac targets transitioning from biomarkers to therapeutics (cardiac myosin, phospholamban), and complement modulation expansion into broader inflammatory applications. Exceptional growth in carrier proteins (SHBG, transferrin) and platelet mediators (PAF) suggests new therapeutic paradigms exploiting multifunctional blood component roles beyond classical hemostatic functions.

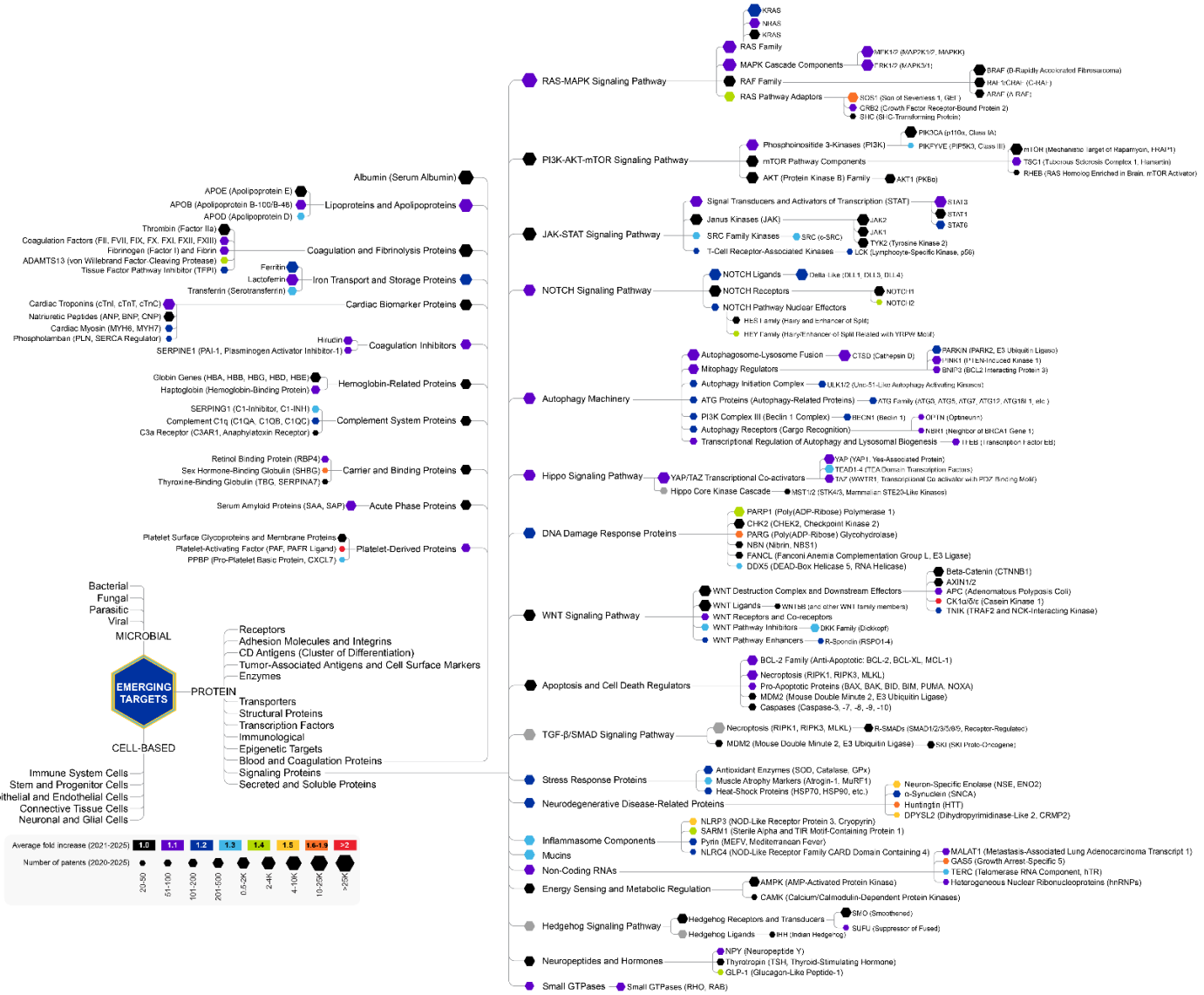


Figure 26. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on protein targets – blood and coagulation proteins and signaling proteins, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

4.3.1.8 Signaling protein therapeutics: From oncogenic pathways to autophagy, inflammation, and neuroprotection

Signaling proteins encompass vast intracellular communication networks transducing extracellular stimuli into cellular responses, representing productive therapeutic targets with kinase inhibitors alone generating over USD $50 billion annually.[513] Our patent TrendScape map (**Figure 26**) reveals continued refinement of established oncogenic pathways (RAS-MAPK, PI3K-AKT-mTOR, JAK-STAT) and dramatic growth in cellular homeostasis mechanisms (autophagy, stress response, proteostasis) reflecting evolving understanding of aging, neurodegeneration, and metabolic diseases as targetable through signaling modulation.

RAS-MAPK pathway maintains the largest volume as one of cancer's most frequently mutated pathways, with the *RAF family* (1X) including *BRAF* (validated by vemurafenib, dabrafenib), *CRAF*, and *ARAF* as established targets. *MEK1/2* (targeted by approved drugs such as trametinib, cobimetinib, binimetinib) and *ERK1/2* complete the core cascade. *RAS pathway adaptors* (1.4X) feature *son of sevenless 1*[514] (*SOS1*; 1.6-1.9X), a guanine nucleotide exchange factor activating RAS with SOS1 inhibitors representing breakthrough approaches targeting RAS-driven cancers with clinical-stage validation (BI 1701963). *KRAS G12C* covalent inhibitors (sotorasib, adagrasib) have validated RAS druggability for specific mutations, spurring broader efforts across RAS isoforms and mutations.

PI3K-AKT-mTOR pathway represents another extensively validated cascade with multiple U.S. FDA-approved inhibitors. *Phosphoinositide 3-kinases (PI3K)* encompasses Class I isoforms (targeted by alpelisib, idelalisib, copanlisib), with emerging interest in *PIKFYVE*[515] (1.3X) regulating endosomal trafficking, autophagy, and lysosomal function with activity in cancer and viral infections through distinct mechanisms. *AKT1*[516] (1X) remains the primary oncogenic isoform in the *AKT (protein kinase B) family* with allosteric and ATP-competitive inhibitors in development. While early allosteric inhibitors such as MK-2206[517] provided a proof-of-concept, and ATP-competitive agents like ipatasertib advanced into late-stage trials, clinical setbacks have led to discontinuation of several programs.[518] Current momentum has shifted toward newer ATP-competitive inhibitors such as capivasertib (NCT04862663[519]), which have demonstrated more consistent efficacy and progressed further clinically.

mTOR pathway components maintain significant interest, with *tuberous sclerosis complex 1* (*TSC1*; 1.1X) as a negative regulator with TSC loss validating mTOR inhibitors (everolimus, sirolimus) for TSC-associated tumors.

JAK-STAT pathway has been successful for autoimmune and inflammatory diseases. *Janus kinases* (*JAKs*; 1X) including *JAK1/2* and *TYK2* with multiple approved inhibitors (tofacitinib, baricitinib, upadacitinib, ruxolitinib) continue garnering activity. *Signal transducers and activators of transcription (STAT)* demonstrate isoform-specific growth: *STAT3*[520] (1.1X) maintains robust interest and high volume as a validated oncogenic transcription factor, while *STAT6*[521] (1.2X) shows acceleration in Th2 immunity, allergic diseases, and cancer. *SRC*[522] (1.3X), a part of *Src family kinases*, appears to be showing renewed growth following early disappointments with pan-SRC inhibitors. Selective approaches, specific tumor contexts (triple-negative breast cancer, bone metastases), and combination strategies are likely driving resurgent interest.

NOTCH pathway demonstrates strong growth across multiple pathway components reflecting its pleiotropic roles in development, stem cell maintenance, and cancer. *NOTCH1* (1X) is most studied with gamma-secretase inhibitors (GSIs) reaching clinical trials but facing dose-limiting gastrointestinal toxicity; *NOTCH2*[523] (1.4X) shows exceptional growth in specific therapeutic windows in certain cancers (B-cell malignancies, cholangiocarcinoma) and hepatic disorders

where NOTCH2 plays selective roles. *NOTCH ligands* (1.2X) include *delta-like (DLL1/3/4)* (1.2X) as alternative intervention points, with *DLL3* as attractive tumor-specific target in neuroendocrine cancers with ADCs validating the target and spurring next-generation therapeutics including BiTEs and CAR-T. *HEY family*[524] (1.4X) as transcriptional repressors downstream of NOTCH activation represent alternative intervention points in disrupting NOTCH transcriptional output.

Hippo pathway has emerged as a major cancer target following the discovery that YAP/TAZ transcriptional co-activators drive oncogenic programs. *TEA domain transcription factors*[525] (*TEAD1-4*; 1.3X) as DNA-binding partners required for YAP/TAZ transcriptional activity show fast growth, with TEAD-YAP/TAZ interaction representing the most druggable node in the pathway enabling small molecule disruption (VT3989, IAG933).

WNT pathway represents a major developmental and oncogenic cascade with growing intervention point diversity. *β-Catenin* (1X) maintains high patent volume as the central transcriptional effector, though direct inhibition remains challenging. *Casein kinase 1 (CK1α/δ/ε*; >2X) phosphorylates β-catenin for degradation with diverse applications in cancer, sleep disorders, and neurodegeneration and shows a high growth rate.[526] *TRAF2 and NCK-interacting kinase*[527] (*TNIK*; 1.2X) regulate WNT target gene expression through TCF4 phosphorylation. *DKK family* (1.3X) as WNT antagonists show therapeutic potential in bone diseases and cancer.[528] *R-spondin*[529] (1.2X) enhances WNT signaling with roles in intestinal stem cells and cancer.

Autophagy machinery (1.1X) demonstrates strong growth across multiple components, reflecting therapeutic interest in modulating cellular self-digestion for neurodegeneration, aging, cancer, and metabolic diseases. High interest targets include: *Unc-51-like autophagy activating kinases* (*ULK1/2*; 1.2X) serving as proximal autophagy regulators respond to nutrient and energy stress,[530] *beclin 1*[531] (*BECN1*; 1.2X) as a key component of the VPS34 lipid kinase complex generating PI3P for autophagosome nucleation, and *ATG family* (1.2X – CN119818678 A) comprising ubiquitin-like conjugation systems. *PARKIN*[532] (1.2X) ubiquitinates damaged mitochondria with mutations causing familial Parkinson's disease with PARKIN activation representing a therapeutic strategy for sporadic Parkinson's and other diseases with mitochondrial dysfunction.

DNA damage response proteins (1.2X) show strong growth across diverse targets. *Poly(ADP-ribose) polymerase 1* (*PARP1*; 1.4X) maintains high activity following clinical success in BRCA-mutant cancers. Ongoing innovation focuses on overcoming resistance, expanding to homologous recombination-proficient tumors, and combination strategies.[533-535] *Poly(ADP-ribose)glycohydrolase*[536] (*PARG*; 1.6-1.9X) shows exceptional growth as the enzyme reversing PARP1 activity, potentially offering orthogonal therapeutic effects. *DEAD-box helicase 5*[537] (*DDX5*; 1.3X), a type of RNA helicase, participates in DNA damage response through RNA processing and transcriptional regulation, representing an emerging target class beyond traditional DNA repair enzymes.

Apoptosis and cell death regulators maintain substantial volume with growing alternative cell death interest. *BCL-2 family* (1.1X) includes validated *BCL-2* (venetoclax) alongside *BCL-XL* and *MCL-1* as resistance mechanisms and alternative targets with ongoing drug discovery efforts (selective MCL-1 inhibitors are in clinical development). *Necroptosis* (*RIPK1/3,*[538] *MLKL*;[539] 1.1X) shows growth as a programmed necrotic pathway with RIPK1 inhibitors in clinical trials (e.g., eclitasertib,[540] ocadusertib,[541] etc.).

Stress response proteins (1.2X) demonstrate broad growth as well as considerable patent volume reflecting therapeutic interest in cellular adaptation mechanisms. *Heat-shock proteins* (1.2X) serve as molecular chaperones maintaining proteostasis with HSP90 inhibitors having been extensively studied in cancer (though clinical success has been limited). Newer approaches focus on selective inhibition of stress-induced HSP expression or targeting co-chaperones.[542,543] *Antioxidant enzymes* (1.2X) represent targets for augmentation (neuroprotection) and inhibition (cancer). *Muscle atrophy markers* (1.3X), including atrogin-1, are E3 ubiquitin ligases driving muscle protein degradation. Their growth likely reflects interest in preventing muscle wasting in cachexia, sarcopenia, and disuse atrophy through inhibition of these muscle-specific ubiquitin ligases.[544]

Neurodegenerative disease-related proteins (1.2X) exhibit exceptional growth across: *huntingtin* (1.6-1.9X) as the causative protein in Huntington's disease with ASOs and RNAi approaches reaching clinical trials (e.g., ASO Tominersen - NCT05686551,[545] miRNA AMT-130 - NCT04120493[546]), *DPYSL2* (1.5X) regulating axonal outgrowth in Alzheimer's and neuropathic pain, and *NSE* (1.5X) serving as neuronal injury biomarker.[547,548] *α-Synuclein* (1.2X) represents Lewy body component with aggregation inhibitors and antibody approaches.[549]

Inflammasome components (1.3X) demonstrate strong growth as innate immune signaling platforms collectively representing intervention points in autoinflammatory diseases, sterile inflammation, and infectious disease responses. *NOD-like receptor protein 3*[550] (*NLRP3*; 1.5X) is the fastest growing inflammasome sensor with inhibitors in clinical development for autoinflammatory diseases, gout (dapansutrile - NCT05658575[551]), Alzheimer's (ACI-19764[552]), and metabolic disorders (dapansutrile - NCT06047262[553]). *Sterile alpha and TIR motif-containing protein 1* (*SARM1*; 1.4X) executes axonal degeneration through NAD+ depletion, representing neuroprotection strategy for chemotherapy-induced peripheral neuropathy, traumatic brain injury, and glaucoma.[554] *Pyrin* (1.2X) and *NOD-like receptor family CARD domain containing 4* (*NLRC4*; 1.2X) respond to bacterial signals with implications in immune mediated diseases.[555]

Non-coding RNAs (1.1X) show accelerating growth as therapeutic targets and biomarkers. *Metastasis-associated lung adenocarcinoma transcript 1* (*MALAT1*; 1.1X), an abundant lncRNA regulating alternative splicing with cancer metastasis roles, has ASOs in preclinical development.[556]

Our analysis shows that the signaling protein landscape reflects the field's evolution from targeting individual kinases in linear pathways toward comprehensive modulation of interconnected signaling networks and cellular homeostasis mechanisms. The exceptional growth in autophagy machinery, inflammasome components, and neurodegenerative disease proteins, alongside continued innovation in established oncogenic cascades, demonstrates expanding therapeutic paradigms beyond cancer into aging, neurodegeneration, and metabolic disorders. Emerging druggability of historically intractable targets (RAS, β-catenin, transcription factors) through novel modalities (PROTACs, molecular glues, allosteric inhibitors) and the increasing focus on context-dependent signaling states rather than simple pathway inhibition suggest that signaling protein therapeutics will continue diversifying across disease areas while achieving greater precision in patient selection and combination strategies.

4.3.2 Cell-based therapeutics: From CAR-T dominance to NK cells, macrophages, and stromal engineering

Cell-based targets represent a paradigm shift from molecular to cellular pharmacology, with patent activity reflecting the clinical success of CAR-T cell therapies and the rapid expansion toward innate immune cells, tissue-resident populations, and stromal components that collectively shape disease pathogenesis and therapeutic responses (**Figure 27**).

Immune system cells dominate cell-based target patents, with *T cell targets and modulators* (1.1X) having one of the largest volumes of patents. Within this category, *regulatory T cells* (*Tregs*; 1.1X) show sustained activity with substantial volume as targets for depletion (cancer, infectious disease) to relieve immunosuppression[557] and expansion/infusion (autoimmune disease, transplant rejection, graft-versus-host disease) to enhance tolerance.[558-560] The bidirectional therapeutic potential of Tregs explains continued innovation in selective Treg modulators, ex vivo expanded Treg therapies, and CAR-Tregs engineered for antigen-specific suppression.[561,562] *Gamma-delta T cells* (1.2X) demonstrate accelerating growth as unconventional T lymphocytes recognizing antigens through non-MHC-restricted mechanisms (phosphoantigens, stress ligands). Their advantages include MHC-independent tumor recognition (enabling "universal" allogeneic therapies), innate-like rapid activation, and tissue-resident surveillance functions.[563,564] Gamma-delta CAR-T products and bispecific antibodies engaging gamma-delta T cells are in clinical development (prulacabtagene leucel,[565] cibisatamab[566]) for solid tumors where conventional alpha-beta T cells have struggled. *CD4+ helper* and *CD8+ cytotoxic T cells* maintain patent activity ranging from 1-1.1X.

NK cell targets and activators (1.1X) have emerged as major focus areas following recognition that NK cells offer advantages over T cells for certain applications: no MHC restriction (enabling allogeneic "off-the-shelf" products), inherent tumor-targeting through activating receptor-ligand interactions, reduced cytokine release syndrome and neurotoxicity risks compared to CAR-T, and activity against cancer stem cells.[567] Within this category, *innate lymphoid cells* (*ILCs*; 1.2X) show strong growth as tissue-resident innate immune populations that mirror T helper cell functions without antigen-specific receptors. ILCs regulate inflammation, tissue repair, and metabolic homeostasis in barrier tissues (gut, lung, skin), with therapeutic targeting in inflammatory bowel disease, asthma, and metabolic disorders. CAR-NK cells, NK cell engagers (bispecific/trispecific antibodies), and checkpoint inhibitors blocking NK inhibitory receptors (anti-KIR, anti-NKG2A) represent major innovation areas.[568-570] *Invariant NKT cells* (*iNKT*; 1.2X) bridge innate and adaptive immunity by recognizing glycolipid antigens presented by CD1d. Their rapid cytokine production and ability to transactivate other immune cells make them attractive for cancer immunotherapy and infectious disease, with alpha-galactosylceramide analogs as iNKT activators in clinical development.[571,572] *Mucosal-associated invariant T (MAIT) cells* (1.6-1.9X) exhibit exceptional growth as the most abundant innate-like T cell population in humans, recognizing microbial vitamin B metabolites presented by MR1. MAIT cells' roles in antibacterial immunity, inflammatory diseases, and cancer are driving therapeutic interest in MAIT activation for infections and vaccines, or MAIT suppression for autoimmune conditions.[573,574]

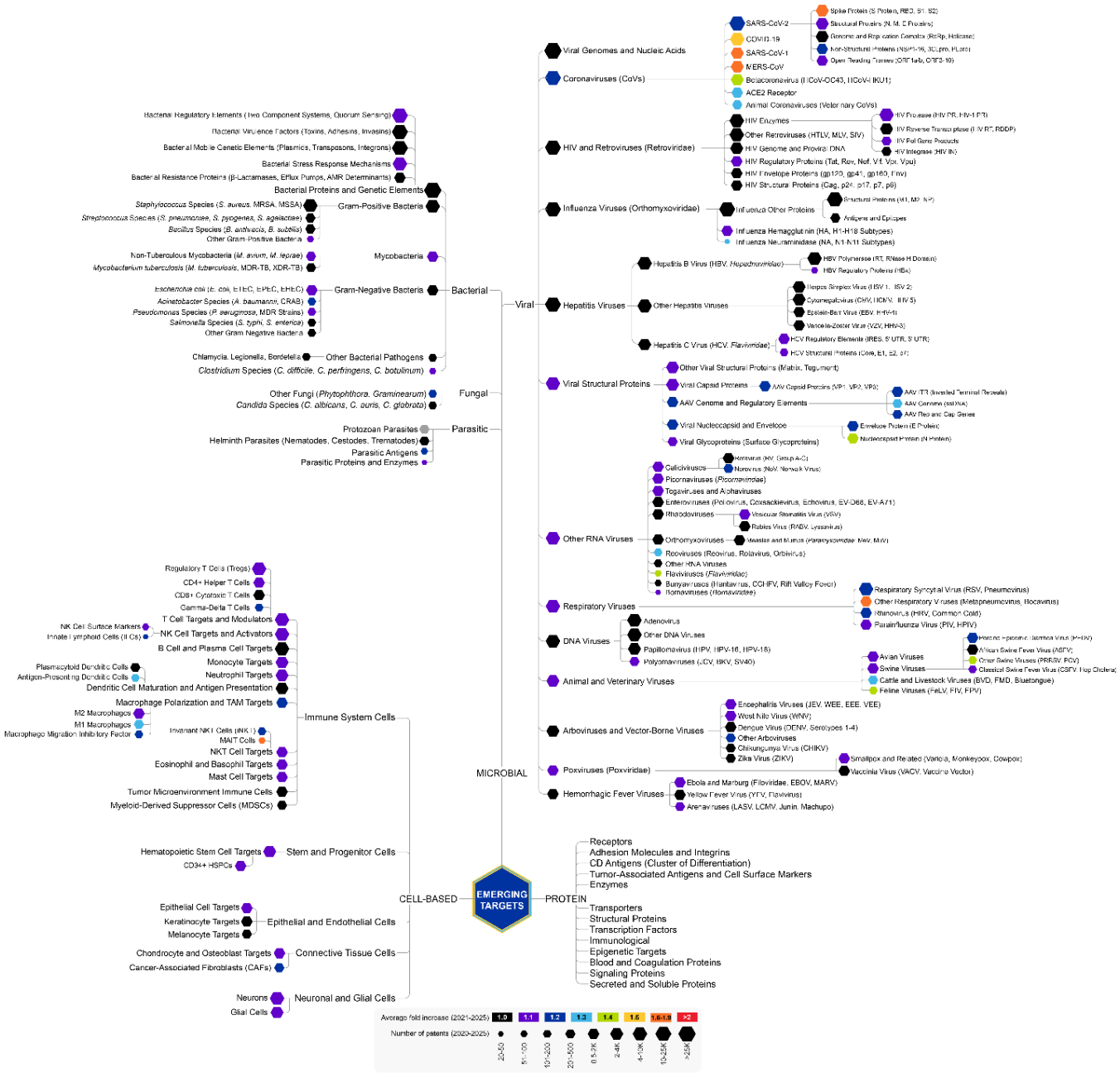


Figure 27. CAS TrendScape map of emerging topics in terms of therapeutic targets focused on cell-based and microbial targets, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Dendritic cell maturation and antigen presentation (1X) encompasses the professional antigen-presenting cells that initiate adaptive immunity. *Antigen-presenting dendritic cells* (1.3X) show strong growth reflecting DC-based cancer vaccines (sipuleucel-T, approved for prostate cancer, represents proof-of-concept), ex vivo DC loading with tumor antigens or mRNA, in vivo DC targeting with antibody-antigen conjugates, and DC activation strategies to enhance T cell priming.[575-578] Recent innovations include combining DC vaccines with checkpoint inhibitors[579] and using DCs engineered to present neoantigens[580] with various DC subsets (conventional DC1/DC2, plasmacytoid DCs), offering distinct immunological properties.[581]

Macrophage polarization and TAM targets (1.2X) address tumor-associated macrophages (TAMs) and their roles in cancer progression, immunosuppression, angiogenesis, and metastasis. *M1 macrophages* (1.3X) represent classically activated, pro-inflammatory, tumoricidal macrophages that therapeutic strategies aim to promote through polarization of M2-like TAMs. Approaches include CSF1R inhibition to deplete TAMs,[582] CD40 agonism to activate macrophages, and a blockade of "don't eat me" signals (CD47-SIRPα axis) to enhance phagocytosis.[583] *Macrophage migration inhibitory factor* (*MIF*; 1.2X) is a pleiotropic cytokine maintaining M2-like immunosuppressive macrophage phenotypes and promoting tumor growth. MIF inhibitors are in development for cancer[584] and inflammatory diseases. *M2 macrophages* represent alternatively activated, immunosuppressive macrophages enriched in tumors. TAMs, broader engineered macrophages (CAR-macrophages with tumor-targeting receptors), and various macrophage activation pathways maintain patent activity.[585] The macrophage field reflects a shift from depletion strategies toward repolarization approaches that convert immunosuppressive TAMs into anti-tumor effectors.

Myeloid-derived suppressor cells (**MDSCs**) maintain substantial volume as immunosuppressive populations expanded in cancer and chronic inflammation with MDSC depletion or functional inhibition strategies including targeting arginase, iNOS, COX-2, and MDSC recruitment pathways.[586,587] *Neutrophil targets* (1.1X) encompass tumor-associated neutrophils (TANs) with pro- or anti-tumor phenotypes, and neutrophils in inflammatory diseases. Interventions include modulating neutrophil recruitment (CXCR2 antagonism[588]), activation, or extracellular trap (NET) formation.[589] Eosinophil and basophil targets address allergic and parasitic disease contexts[590] while mast cell targets regulate allergic responses and inflammation.[591]

Stem and progenitor cells demonstrate strong activity across multiple lineages. *Hematopoietic stem cell targets* (1.1X) maintain robust patent activity for ex vivo expansion protocols,[592] mobilization strategies,[593] gene editing approaches (for sickle cell disease,[594] β-thalassemia,[595] SCID[596]) and niche modulation to enhance engraftment as shown by recent successes with gene-edited HSCs (CTX001, LentiGlobin) have validated this approach. *CD34+ HSPCs* serve as the primary HSC isolation marker and transplant product. *Mesenchymal stem cells* (*MSCs*) maintain high patent volume for regenerative medicine,[597] immunomodulation in graft-versus-host disease[598] and autoimmune conditions,[599] and as carriers for therapeutic proteins or oncolytic viruses. Despite widespread clinical investigation, efficacy remains debated with heterogeneity in MSC preparations complicating development.

Epithelial and endothelial cells show growing interest in tissue repair and disease modeling. *Epithelial cell targets* include applications in inflammatory bowel disease[600] (WO2024064879 A2) (intestinal epithelial barrier restoration), cystic fibrosis[601] (CFTR-expressing epithelial cells), and cancer (targeting cancer stem cells with epithelial properties[602]). *Endothelial cell targets* encompass anti-angiogenic strategies[603] (established through VEGF inhibitors), vascular repair and regeneration, and endothelial dysfunction in cardiovascular disease. *Keratinocyte targets* address dermatologic conditions and wound healing.[604] *Melanocyte targets* relate to vitiligo, melanoma, and pigmentation disorders.[605,606]

Connective tissue cells (1.1X) demonstrate growth in TME modulation. *Cancer-associated fibroblasts* (*CAFs*; 1.2X) show accelerating activity as key stromal cells that remodel the extracellular matrix, secrete growth factors and cytokines, suppress anti-tumor immunity, and mediate therapy resistance in solid tumors. CAF targeting strategies include FAP (fibroblast activation protein) inhibition, depletion with FAP-targeted therapies (antibodies, CAR-T cells, vaccines), and reprogramming CAFs to quiescent states.[607,608] CAF heterogeneity (inflammatory

CAFs, myofibroblastic CAFs, antigen-presenting CAFs) complicates therapeutic development but offers opportunities for subset-selective targeting. *Chondrocyte and osteoblast targets* (1.1X) maintain steady activity for osteoarthritis, bone regeneration, and skeletal disorders. Approaches include chondrocyte implantation, growth factor delivery (BMPs), and modulation of osteoblast/osteoclast balance in osteoporosis.

Neuronal and glial cells show sustained interest in neurodegenerative diseases and CNS disorders. *Neurons* (1.1X) are targeted for neuroprotection (antioxidants,[609] anti-apoptotics, neurotrophic factors[610]), neuroregeneration (stem cell-derived neurons, reprogrammed neurons), and circuit modulation (optogenetics,[611] chemogenetics[612]). *Glial cells* (1.1X) encompass *astrocytes* (reactive astrogliosis in neurodegeneration, stroke, trauma[613]), *microglia* the brain's resident macrophages implicated in Alzheimer's disease through phagocytic dysfunction and inflammatory activation,[614,615] and *oligodendrocytes* (remyelination in multiple sclerosis).[616,617] Microglial modulation strategies include CSF1R inhibitors to deplete dysfunctional microglia, TREM2 agonists to enhance phagocytic activity, and polarization toward homeostatic phenotypes. Astrocyte targeting addresses astrogliosis and glial scar formation that inhibit CNS regeneration.

Tumor microenvironment (TME) and immune cells represent the paradigm shift from targeting cancer cells alone to modulating the cellular ecosystem. The growth in CAFs, TAMs, MDSCs, and Tregs reflects recognition that immunosuppressive and tumor-promoting cell populations often outnumber cancer cells in solid tumors and represent critical therapeutic targets.[618-620] Combination approaches targeting multiple cell types (e.g., anti-PD-1 plus anti-CTLA-4, anti-PD-1 plus CSF1R inhibition, CAR-T plus macrophage activation) show synergistic efficacy, driving patent activity in rational combination strategies.

Our analysis of the cell-based target landscape reveals drug discovery expanding from molecules to cells as therapeutic agents (CAR-T, CAR-NK, DC vaccines, MSCs, engineered macrophages) and targets for depletion, activation, or repolarization. The exceptional growth in innate immune cells (gamma-delta T cells, MAIT cells, iNKT cells, ILCs, M1 macrophages) reflects efforts to harness rapid-acting, MHC-unrestricted immunity for "off-the-shelf" therapeutics. Stromal cell targeting (CAFs, endothelial cells) addresses the TME's physical and biochemical barriers to therapy. This cellular pharmacology paradigm—enabled by single-cell technologies revealing cellular heterogeneity, genetic engineering creating cell therapies, and antibodies/small molecules selectively modulating cell populations—promises interventions impossible through traditional molecular targeting, though faces unique challenges in manufacturing, delivery, and controlling complex cellular behaviors in vivo.

4.3.3 Anti-infective innovation: Bacterial pathogens, viral therapeutics, and the post-pandemic research agenda

The microbial target landscape reflects humanity's ongoing arms race against infectious diseases, with patent activity shaped by antibiotic resistance crises, pandemic preparedness following COVID-19, and the dual use of viruses as pathogens and therapeutic vectors (**Figure 27**). The 2020-2025 period captures unprecedented attention to viral threats alongside persistent bacterial resistance challenges and persistent interest in infectious diseases.

4.3.3.1 Methodology validation: Coronavirus target patent surge as NLP benchmark

The exceptional growth in **Coronaviruses** (**CoVs**) (1.2X) provides compelling validation of this report's methodology for identifying emerging therapeutic targets. Within this family, *SARS-CoV-2* shows dramatic patent acceleration with specific viral components demonstrating differential growth rates that mirror research priorities and therapeutic development: *spike protein S* (*S1/S2, S-Trimer*) maintains the highest volume as the primary target for vaccines (mRNA, protein subunit, viral vector) and neutralizing antibodies (bebtelovimab, sotrovimab), with its receptor-binding domain (RBD) enabling ACE2 engagement. COVID-19 as a disease indication generated an extraordinary patent surge across therapeutics (small molecule antivirals, monoclonal antibodies, immunomodulators), diagnostics (RT-PCR, antigen tests, serology), and vaccines. *SARS-CoV-1* and *MERS-CoV* maintain steady activity reflecting ongoing surveillance and cross-reactive therapeutic development.

Critically, coronaviruses exemplify how real-world events (the COVID-19 pandemic beginning in 2020) create massive patent acceleration in directly relevant targets, while our methodology successfully captured this growth signal (1.2X) against the baseline of all pharmaceutical patents. The detection of this known emerging threat validates the approach's ability to identify rising research areas, lending confidence that other high-growth targets identified similarly represent genuine emerging opportunities rather than analytical artifacts.

4.3.3.2 Bacterial targets: Addressing the antimicrobial resistance crisis

Gram-positive bacteria maintain substantial patent volume reflecting ongoing threats from resistant strains. *Staphylococcus species* (1X) represents one of the most studied bacterial pathogens with methicillin-resistant *S. aureus* (MRSA) driving continued antibiotic development. Recent innovations include novel cell wall synthesis inhibitors,[621] anti-virulence strategies (toxin neutralization, biofilm disruption),[622] and immunotherapies (vaccines, monoclonal antibodies against surface antigens). *Streptococcus species* (1X) maintain activity through pneumococcal vaccines (conjugate vaccines covering increasing serotype numbers)[623] and antibiotics for invasive streptococcal infections. *Mycobacterium tuberculosis* (*M. tuberculosis*, *MDR-TB*, *XDR-TB*) maintains high patent volumes given the global tuberculosis burden and emergence of extensively drug-resistant strains. New regimens (bedaquiline, delamanid, pretomanid) targeting ATP synthase and cell wall synthesis have provided first novel TB drugs in decades.

Gram-negative bacteria show accelerating growth in multidrug-resistant pathogens representing critical unmet needs. *Acinetobacter species* (1.2X) exhibits strong growth as carbapenem-resistant *A. baumannii* (CRAB) has become a leading cause of hospital-acquired infections with limited treatment options. Innovations include beta-lactamase inhibitor combinations (cefiderocol), novel antibiotic classes (polymyxins, sulbactam combinations), and anti-virulence approaches targeting biofilm formation and immune evasion.[624,625] *Pseudomonas species* (1.1X) maintains steady growth as an opportunistic pathogen that is problematic in cystic fibrosis and immunocompromised patients with therapeutic approaches including anti-biofilm agents, quorum sensing inhibitors,[626] and bacteriophage therapy[627] gaining renewed interest. *Escherichia coli* (*E. coli*, ETEC, EPEC, EHEC; 1.1X) encompasses commensal strains and pathogenic variants causing diarrheal disease (ETEC), hemolytic uremic syndrome (EHEC/STEC), and urinary tract infections (uropathogenic *E. coli*). Vaccines against enterotoxigenic and Shiga toxin-producing *E. coli* are in development.[628,629] Other gram-negative priorities include *Klebsiella pneumoniae* (carbapenem-resistant strains), *Salmonella*, and *Shigella* species.

Other gram-positive bacteria include *Clostridioides difficile* with fecal microbiota transplantation validated as therapy[630] alongside newer antibiotics (fidaxomicin, bezlotoxumab), *Enterococcus* (VRE), and various anaerobes. The *Rhizobiaceae species* and other environmental bacteria

maintain lower patenting activity. *Bacterial cell wall synthesis* inhibitors (β-lactams, glycopeptides) represent the most validated antibiotic class.[631] *Bacterial DNA replication and repair* (fluoroquinolones, rifamycins) and *bacterial protein synthesis inhibitors* (aminoglycosides, macrolides, tetracyclines, oxazolidinones) maintain steady patent activity, reflecting ongoing optimization and resistance circumvention efforts.

Bacterial proteins and genetic elements show growing interest in non-traditional targets. *Bacterial regulatory elements* (*two-component systems*, *quorum sensing*; 1.1X) represent anti-virulence strategies that disarm pathogens without killing them, potentially reducing selection pressure for resistance. Quorum sensing inhibitors disrupt bacterial communication systems controlling biofilm formation, toxin production, and virulence factor expression.[632] *Bacterial stress response mechanisms* (1.1X), including heat shock proteins,[633] oxidative stress defenses, and stringent response pathways, offer targets a way to sensitize bacteria to immune clearance or enhance antibiotic efficacy. *Bacterial toxins and virulence factors* maintain activity through toxoid vaccines and neutralizing antibodies. *Bacterial cell membrane and efflux pumps* represent targets for overcoming antibiotic resistance.[634]

4.3.3.3 Viral targets: From pandemic response to broad-spectrum therapeutics

Viral genomes and nucleic acids attract substantial attention for diagnostic and therapeutic purposes. The various genome types (dsRNA, ssRNA positive-sense, ssRNA negative-sense, ssDNA, dsDNA) across viral families represent fundamental replication machinery targetable by polymerase inhibitors and nucleoside/nucleotide analogs.

Influenza viruses (orthomyxoviridae) maintain high patent volume reflecting annual vaccination needs and pandemic preparedness. *Influenza neuraminidase* (NA, N1-N11 subtypes) (1.3X) shows strong growth as the target of neuraminidase inhibitors (oseltamivir, zanamivir, peramivir, baloxavir) with continued innovation addressing resistance mutations and next-generation inhibitors with improved pharmacokinetics.[635,636] *Influenza hemagglutinin* (HA, H1-H18 subtypes) serves as the primary vaccine antigen with universal influenza vaccine efforts targeting conserved HA stem regions.[637] The *M2 ion channel* (targeted by amantadine, rimantadine, now largely obsolete due to resistance) and polymerase (cap-dependent endonuclease inhibited by baloxavir marboxil) represent validated targets.

HIV and retroviruses (retroviridae) maintain the second-largest viral patent volume reflecting decades of antiretroviral therapy development. *HIV enzymes* (1X) encompass the extensively validated *HIV protease* (targeted by 10+ protease inhibitors), *HIV reverse transcriptase* (nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs)), and *HIV integrase* (integrase strand transfer inhibitors: raltegravir, elvitegravir, dolutegravir, bictegravir, cabotegravir).[638] HIV structural proteins (Gag, Env gp120/gp41, Pol) serve as vaccine targets. *HIV entry inhibitors* (maraviroc blocking CCR5, enfuvirtide inhibiting fusion) and the capsid[639] protein represent additional intervention points. Long-acting formulations and broadly neutralizing antibodies[640] represent recent innovations toward functional cure.

Hepatitis viruses show sustained activity. *Hepatitis B virus* (HBV, hepadnaviridae) (1X) maintains patent activity through nucleos(t)ide analogs (tenofovir, entecavir) suppressing viral replication and interferon-based therapies,[641] with ongoing efforts toward functional cure through targeting HBsAg production, cccDNA,[642] and enhancing immune responses. *Hepatitis C virus* (HCV, flaviviridae) achieved cure rates >95% with direct-acting antivirals (DAAs) targeting NS3/4A protease, NS5A, and NS5B polymerase[643] representing great success. **Other hepatitis viruses** (1X) garnering patenting activity includes *Hepatitis D virus* (HDV), *Hepatitis E virus*

(HEV), and, to a lesser extent, *Hepatitis A virus* (HAV). HDV, a defective RNA virus dependent on HBV co-infection, has attracted increasing interest with therapeutic strategies targeting viral entry (e.g., sodium/taurocholate cotransporting polypeptide (NTCP) inhibitors), replication, and host-virus interactions, reflecting unmet medical needs in chronic HDV infection.[644] HEV-related patent activity is more limited but focuses on antiviral compounds,[645] vaccine development,[646] and diagnostic approaches[647] given its relevance in immunocompromised populations and emerging zoonotic transmission concerns. In contrast, HAV, being an acute and vaccine-preventable infection, shows comparatively lower patent intensity, with innovation largely centered on vaccine formulations[648] and outbreak control strategies rather than therapeutic interventions.

Respiratory viruses demonstrate diverse growth patterns especially *other respiratory viruses* (metapneumovirus, bocavirus) (1.6-1.9X) showing exceptional growth likely reflecting heightened attention to respiratory pathogens post-COVID-19 and recognition of human metapneumovirus as a significant cause of lower respiratory tract infections in children and immunocompromised adults. While therapeutic development previously lagged due to limited surveillance, the pandemic infrastructure has enabled accelerated research. *Respiratory syncytial virus* (RSV, pneumovirus) maintains high patent volume and growth (1.2X) with recent approvals of RSV vaccines (arexvy by GSK,[649] abrysvo by Pfizer[650]) for older adults and maternal immunization, plus monoclonal antibody prophylaxis (nirsevimab) for infants validating decades of RSV research.[651,652] *Parainfluenza viruses* and *rhinoviruses* round out the respiratory virus portfolio achieving brisk patent growth (1.1-1.2X).[653,654]

Arboviruses and vector-borne viruses reflect growing concern over mosquito- and tick-transmitted infections. *Dengue virus* (DENV, Serotypes 1-4; 1X) maintains patent activity with dengue vaccine challenges (dengvaxia safety concerns) and need for therapeutics given 100-400 million annual infections.[655] Antibody-dependent enhancement complicates vaccine development requiring balanced immunity to all four serotypes.[656] *Chikungunya virus* (CHIKV; 1X) has expanded geographically causing epidemic arthralgia, driving vaccine development[657] (Valneva's VLA1553 recently approved by the U.S. FDA[658]). *Zika virus* (ZIKV; 1X) caused the 2015-2016 epidemic with congenital Zika syndrome (microcephaly), spurring vaccine development though disease burden has decreased. *West Nile virus* (WNV; 1.1X) and *encephalitis viruses* (JEV, WEE, EEE, VEE; 1.1X) maintain steady activity as causes of neuroinvasive disease with vaccine for Japanese encephalitis being available (ixiaro by Valneva[659]), while other encephalitis viruses lack approved vaccines. The broader flaviviruses cluster encompasses these threats plus yellow fever and tick-borne encephalitis. *Yellow fever virus* (YFV, flavivirus; 1X) maintains activity through the effective live-attenuated vaccine (YF-17D),[660] though urban yellow fever outbreaks persist in Africa and South America.

Other RNA viruses demonstrate diverse growth: *reoviruses* (reovirus, rotavirus, orbivirus) show fast growth (1.3X), with rotavirus vaccines (Rotarix, RotaTeq) achieving major public health impact reducing childhood diarrheal mortality, while reovirus shows oncolytic activity in cancer trials.[661] *Flaviviruses* (Flaviviridae; 1.4X) as a family show strong growth encompassing dengue, Zika, West Nile, hepatitis C, yellow fever, and emerging threats. *Norovirus* (NoV, Norwalk virus; 1.2X) maintains brisk growth as the leading cause of epidemic gastroenteritis with vaccine development challenged by antigenic diversity and short-lived immunity. Recent advances in VLP vaccines[662] and understanding of histo-blood group antigen binding offer hope. *Togaviruses and alphaviruses* maintain activity while emerging threats such as *bunyaviruses* (hantavirus, Rift Valley fever, Crimean-Congo hemorrhagic fever) attract limited patent attention.

Hemorrhagic fever viruses show steady activity reflecting biodefense priorities and outbreak responses. *Ebola and Marburg* (filoviridae, EBOV, MARV; 1.1X) maintain investment following the 2014-2016 West African Ebola epidemic and subsequent outbreaks with approved Ebola vaccines (Ervebo, Zabdeno/Mvabea) and therapeutics (monoclonal antibody cocktails: Inmazeb, Ebanga) validating extensive research,[663,664] while Marburg virus lack approved countermeasures. *Arenaviruses* (LASV, LCMV, Junín, Machupo; 1.1X) include Lassa fever virus causing endemic disease in West Africa with vaccine development ongoing[665] and South American hemorrhagic fever viruses (Junín with vaccine available, others lacking countermeasures). *Yellow fever virus* (YFV, flavivirus) also causes hemorrhagic fever. The biosafety level 4 requirements for many hemorrhagic fever viruses complicate research, but biodefense funding sustains activity.

DNA viruses show diverse activities. *Herpesviruses* maintain high volume with eight human herpesviruses causing latent infections and disease in immunocompromised hosts: herpes simplex virus (HSV-1, HSV-2), varicella-zoster virus (VZV), cytomegalovirus (CMV, with letermovir recently approved), Epstein-Barr virus (EBV, causing infectious mononucleosis and associated with lymphomas), human herpesvirus 6 (HHV-6), and Kaposi sarcoma-associated herpesvirus (KSHV/HHV-8) all attract therapeutic interest.[666-668] *Adenoviruses* serve as pathogens (epidemic keratoconjunctivitis, respiratory infections)[669] and vectors for gene therapy and vaccines. *Papillomaviruses* (HPV, HPV-16, HPV-18, etc.) maintain high activity likely through HPV vaccines (Gardasil, Cervarix) preventing cervical and other cancers, with therapeutic HPV vaccines under development for existing infections.[670]

Poxviruses (*Poxviridae*) demonstrate growing interest. *Smallpox and related* (variola, monkeypox, cowpox) (1.1X) show moderate growth driven by monkeypox (mpox) outbreaks in 2022-2023 creating demand for vaccines (JYNNEOS/Imvamune, ACAM2000) and antivirals (tecovirimat/TPOXX targeting orthopoxvirus VP37 envelope protein) with biodefense concerns about smallpox as bioterror agent likely maintaining research despite eradication.[671,672] **Vaccinia Virus** serves as smallpox vaccine and oncolytic virus platform.[673]

Viral structural proteins attract growing interest in therapeutic targeting and engineering for gene therapy applications. *Viral capsid proteins* include diverse structural components across virus families.[674] *Viral nucleocapsid and envelope* feature the aforementioned *nucleocapsid protein* (N protein; 1.4X) and *envelope protein* (E protein; 1.2X) showing strong growth across multiple virus families as diagnostic targets and potential therapeutic intervention points for disrupting virion assembly and release.[675]

AAV (adeno-associated virus) components show strong growth reflecting the explosion of AAV-based gene therapies. *AAV capsid proteins* (VP1, VP2, VP3; 1.2X) are being extensively engineered to alter tissue tropism, evade pre-existing neutralizing antibodies (a major limitation of AAV gene therapy), and enhance transduction efficiency with capsid engineering through rational design, directed evolution, and computational approaches likely driving this growth.[676, 677] Multiple U.S. FDA-approved AAV gene therapies (Luxturna for inherited retinal disease, Zolgensma for spinal muscular atrophy, Hemgenix for hemophilia B, plus others) validate the platform. *AAV genome* (ssDNA; 1.3X), *AAV ITR* (inverted terminal repeats; 1.2X), and *AAV rep and cap genes* (1.2X) within the **AAV genome and regulatory elements** category reflect patent activity in optimizing vector design. ITRs are required in cis for genome packaging and integration, while Rep proteins mediate replication and Cap proteins form the capsid. Different AAV serotypes (AAV1, AAV2, AAV5, AAV8, AAV9, AAVrh10, etc.) show distinct tissue tropisms, with AAV9 capable of crossing the blood-brain barrier making it attractive for CNS gene therapy.[678] The growth in AAV-related patents reflects the number of gene therapy programs in development

(hundreds in clinical trials) and the intellectual property landscape around improving what has become the dominant gene therapy vector platform.

Other Viral Structural Proteins include matrix proteins, nucleoproteins, and various structural glycoproteins across virus families. These components serve as vaccine antigens,[679,680] diagnostic targets, and potential points of therapeutic intervention through entry inhibitors or assembly disruptors.

4.3.3.4 Fungal targets: A persistent gap

Fungal targets show notably modest patent activity despite growing clinical concern over invasive fungal infections in immunocompromised populations and emerging antifungal resistance. *Candida species* maintain baseline activity with *Candida auris* emergence as a multidrug-resistant healthcare-associated pathogen, yet patent growth remains subdued.[681] *Aspergillus species* cause invasive aspergillosis in immunocompromised patients with high mortality. The established antifungal classes, azoles (targeting ergosterol synthesis), echinocandins (targeting beta-1,3-glucan synthase), and polyenes (binding ergosterol), show limited innovation compared to antibacterial and antiviral spaces.

The fungal target landscape reveals a critical gap: despite rising incidence of invasive fungal infections, limited new antifungal mechanisms, and emerging resistance (azole-resistant *Aspergillus*, echinocandin-resistant *Candida*), pharmaceutical innovation lags dramatically behind antibacterial development. This gap likely reflects economic factors (smaller market than antibacterials), technical challenges (fungi are eukaryotes sharing cellular machinery with humans, limiting selective targets), and historically lower attention from major pharmaceutical companies. The antifungal pipeline's weakness represents a critical unmet need as immunosuppressive therapies and immunocompromising conditions expand the at-risk population.

4.3.3.5 Parasitic targets: Patent trends in neglected tropical disease research

Parasitic targets maintain modest but steady patent activity, primarily supported by global health initiatives for neglected tropical diseases. *Protozoan parasites* include malaria (caused by *Plasmodium* species such as *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*) as the highest volume parasitic target with ongoing antimalarial development addressing artemisinin resistance,[682] leishmaniasis (caused by *Leishmania* species),[683] trypanosomiasis (*Trypanosoma brucei* causing African sleeping sickness,[684] *T. cruzi* causing Chagas disease[685]), toxoplasmosis (*Toxoplasma gondii*),[686] and various intestinal protozoans (*Giardia*, *Entamoeba*, *Cryptosporidium*).

Helminth parasites (nematodes, cestodes, trematodes) represent worm infections affecting billions globally[687] and includes nematodes (roundworms including soil-transmitted helminths *Ascaris*, *Trichuris*, *hookworms*, plus filarial worms *Wuchereria bancrofti*, *Brugia malayi*, *Onchocerca volvulus* causing river blindness), cestodes (tapeworms), and trematodes (flukes including schistosomiasis-causing *Schistosoma* species). Mass drug administration programs using albendazole, ivermectin, and praziquantel have reduced disease burden. Recent innovation includes next-generation anthelmintics such as emodepside,[688] which targets drug-resistant nematodes and represents a promising pipeline candidate.

Parasitic antigens (1.2X) show moderate growth as vaccine targets. Malaria vaccines (RTS,S/Mosquirix with modest efficacy,[689] R21/Matrix-M showing improved efficacy (NCT04704830[690])) represent major achievements given the parasite's complex life cycle and immune evasion. Schistosomiasis and hookworm vaccines are in development (NCT05658614,[691] NCT01385189[692]). Diagnostic antigens for serology and point-of-care tests drive additional patent activity.[693]

The parasitic disease portfolio reflects public health priorities (malaria killing ~600 thousand annually;[694] neglected tropical diseases affecting >1 billion[695]) and the challenging economics of tropical disease drug development, heavily dependent on philanthropic funding[696] (Gates Foundation, Welcome Trust) and product development partnerships (Medicines for Malaria Venture, Drugs for Neglected Diseases initiative). The modest patent growth rates suggest these diseases remain underserved relative to their global burden.

4.9.3.6 Cross-cutting themes

The microbial target landscape is shaped by several converging trends: (1) Pandemic preparedness following COVID-19 has elevated all respiratory virus research and created infrastructure (mRNA vaccine platforms, rapid diagnostic development, monoclonal antibody discovery) applicable to future outbreaks; (2) antimicrobial resistance in bacteria continues escalating with few novel antibiotic classes, driving traditional antibacterial approaches and anti-virulence/immunotherapy alternatives; (3) dual use of viruses as both pathogens requiring countermeasures and as therapeutic vectors (AAV for gene therapy, adenovirus/lentivirus/vaccinia for vaccines, oncolytic viruses) creates bidirectional patent activity in viral biology; (4) the mosquito-borne disease burden from flaviviruses and parasites reflects climate change expanding vector ranges and urbanization increasing transmission; (5) immunocompromised populations from HIV, cancer chemotherapy, organ transplantation, and autoimmune disease biologics face growing threats from opportunistic infections (CMV, *Pneumocystis*, *Aspergillus*, *Cryptococcus*, *Toxoplasma*) inadequately addressed by current therapeutics; (6) the substantial gap in antifungal innovation despite rising invasive fungal infections represents a critical and underappreciated threat and (7) neglected tropical diseases remain dependent on philanthropic funding with insufficient commercial incentives despite affecting over a billion people globally.

The COVID-19 pandemic's influence permeates the entire viral target landscape, accelerating not only coronavirus research but creating generalizable platforms (mRNA vaccines now being developed for influenza, RSV, HIV, malaria; rapid therapeutic antibody discovery applicable to any virus; sophisticated clinical trial networks for emerging infections) that promise faster responses to future pandemics. The detection of this massive research shift through growth metrics (coronavirus 1.2X, specific structural proteins up to 1.4X) validates the analytical methodology while highlighting how rapidly research priorities can pivot when faced with global health emergencies. This suggests the pharmaceutical industry now possesses unprecedented capability to respond to emerging infectious threats: a capability absent in previous pandemics and representing perhaps the most significant legacy of COVID-19 research investment.

4.4 Summary: The expanding target landscape

The emerging target landscape reveals pharmaceutical R&D's trajectory toward more sophisticated biological intervention. Exceptional growth rates (>2X) in previously intractable target classes signal that technological advances (protein degradation, gene editing, cell engineering, RNA therapeutics) are translating academic biology into druggable mechanisms faster than ever. Simultaneously, established targets maintain steady patent activity, indicating that validated mechanisms continue generating innovation through improved selectivity, pharmacokinetics, and resistance circumvention. This dual dynamic, breakthrough targets achieving exceptional growth while mature targets sustain steady innovation, characterizes a pharmaceutical landscape where frontier biology and incremental optimization create value. Organizations that systematically monitor target-level patent dynamics, maintain platform flexibility across modalities, and rapidly translate target validation into therapeutic programs are positioned to access the expanding therapeutic opportunity space that increasingly defines competitive advantage in pharmaceutical innovation.

5. Competitive intelligence across therapeutic modalities: A deep dive

For each modality, we examine the patent assignee landscape to identify market leaders and emerging innovators, analyze technological trends reflected in recent patent filings (nanobodies, cyclic peptides, PROTACs), and highlight scientific discoveries translating into intellectual property (tissue-selective delivery, in vivo gene editing, oral peptides, targeted radiopharmaceuticals). The competitive intelligence presented herein provides strategic insights into which organizations are positioned to capture value from next-generation therapeutics, which technological approaches are likely to attract the most investment, and which scientific breakthroughs are likely to reshape therapeutic paradigms across disease areas in the coming decade.

Across major pharmaceutical companies such as Johnson & Johnson, Roche, Bristol Myers Squibb, Eli Lilly, AstraZeneca, Pfizer, Novartis, Amgen, Merck & Co., GSK, and Boehringer Ingelheim, small molecules account for the largest share of patents, with more limited contributions from antibody therapeutics and emerging modalities such as RNA, peptide, and cell/gene therapies. While most organizations show a similar modality distribution, certain companies (e.g., Amgen, Roche, and Regeneron) demonstrate relatively higher diversification into biologics and newer platforms. It should be noted that the percentages may exceed 100% for some companies due to overlap, as individual patents can be classified under multiple therapeutic modalities. Overall, the data highlights both the continued dominance of small molecules and the gradual expansion into next-generation therapeutic approaches.

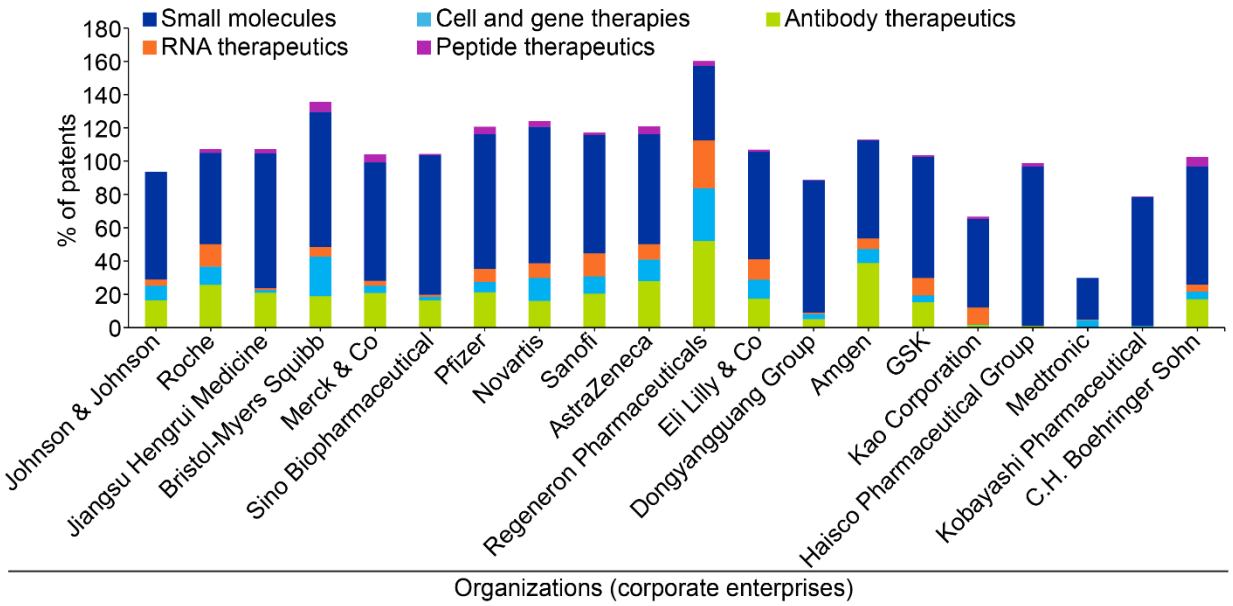


Figure 28. Distribution of patents across therapeutic modalities among leading pharmaceutical companies. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

5.1 Next-generation biologics: Patent trends in antibodies and RNA therapeutics

Biologics have evolved from first-generation monoclonal antibodies (mAbs) into diverse therapeutic platforms encompassing ADCs, multi-specific antibodies, and other antibodies. Antibody therapeutics maintain the largest commercial footprint with over 100 U.S. FDA-approved products generating approximately USD $200 billion annually, while RNA modalities, mRNA vaccines, siRNA therapeutics, and ASOs, have transitioned from experimental approaches to validated platforms with expanding disease applications beyond rare genetic disorders into oncology, cardiovascular disease, and infectious diseases.

5.1.1 Antibody therapeutics

Antibody therapeutics have matured beyond conventional IgG monoclonal antibodies (mAbs) toward engineered formats addressing historical limitations in tissue penetration, target specificity, and immune effector functions. The patent landscape reveals intensifying competition in bispecific and multispecific antibodies that simultaneously engage multiple targets (tumor antigens and T-cell receptors, or multiple disease mediators), antibody-drug conjugates[261] (ADCs) exploiting internalization for cytotoxic payload delivery, and antibody fragments (scFv, nanobodies, Fab) enabling access to cryptic epitopes and improved solid tumor penetration.

The patent landscape reveals how antibody engineering is evolving (illustrated in **Figure 29**), with newer formats gradually increasing their share alongside conventional mAbs. While mAbs remain foundational, the rise of engineered and hybrid formats reflects efforts to overcome the limitations of single-target therapies. Among these, ADCs show a clear upward trend, highlighting their role as precision delivery systems that couple antibody specificity with potent cytotoxic payloads to enhance efficacy while minimizing systemic toxicity. In parallel, bispecific and multispecific antibodies are gaining traction due to their ability to engage multiple antigens or pathways simultaneously. For instance, bispecific constructs can redirect immune effector cells (such as T cells) toward tumor cells or co-modulate signaling pathways, thereby amplifying therapeutic responses that cannot be achieved with traditional mAbs.

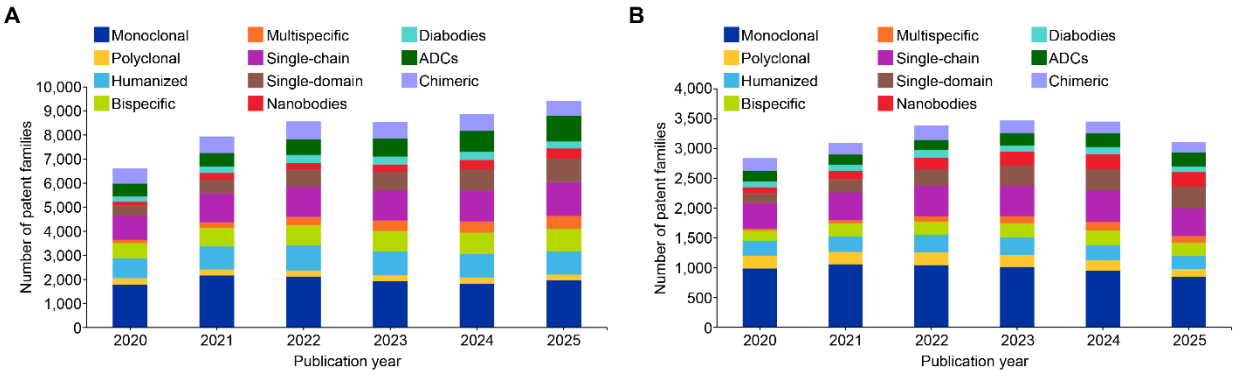


Figure 29. Distribution of various antibody modalities in patents filed by (**A**) corporate enterprises and (**B**) research and academic organizations. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Smaller engineered fragments, such as diabodies and nanobodies, are likewise increasing, driven by advantages in tissue penetration and tunable pharmacokinetics. Lacking the full Fc region, these formats can reduce immune-related effects while enabling better access to dense tissues like solid tumors. Overall, the expansion of ADCs, multispecifics, and fragment-based formats highlights a shift toward multifunctional, mechanism-driven biologics tailored to complex disease biology.

Leading assignees span established pharmaceutical companies with extensive antibody platforms and specialized biotechnology firms pioneering novel formats, with innovation focusing on manufacturing scalability, immunogenicity reduction, and combination strategies. Among established players, companies such as Roche, Amgen, and Regeneron dominate the antibody therapeutics landscape through advanced platforms and clinically validated portfolios (**Figure 28**). Amgen has been a pioneer in bispecific T-cell engager (BiTE) technology, exemplified by blinatumomab (CD19×CD3), the first approved bispecific antibody, and more recently tarlatamab (DLL3×CD3), which extends this approach into solid tumors. Roche has emerged as a global leader in bispecifics and ADCs, with a broad portfolio that includes emicizumab (a factor IXa/FX mimetic), mosunetuzumab, and glofitamab (both CD20×CD3 bispecifics), which together have generated multi-billion-dollar revenues and established Roche as a dominant force in hematology-focused bispecific therapies. Regeneron, leveraging its Veloci-Bi platform,[697] has advanced a diverse pipeline of bispecific and multispecific antibodies such as odronextamab (CD20×CD3) and BCMA-targeting constructs, while also exploring next-generation immune costimulatory approaches (e.g., CD28 bispecifics) designed to enhance responses in immune-resistant tumors. Pfizer has entered the space with assets such as elranatamab (BCMA×CD3), further validating the clinical and commercial viability of T-cell engaging bispecifics. Eli Lilly has struck multiple AI partnerships with companies like BigHat Biosciences,[698] XtalPi (Ailux),[699] and Chai Discovery[700] to use machine learning and generative AI for designing and optimizing next-generation (including bispecific) antibodies.

Emerging companies (**Figure 30**), particularly from China and innovative biotech ecosystems, are playing an increasingly important role in shaping the future landscape. BioNTech, traditionally associated with mRNA technologies, is rapidly expanding into antibody therapeutics with a strong emphasis on multispecific designs and ADCs. Its lead bispecific candidate (developed in collaboration with Bristol Myers Squibb), BNT327 (PD-L1×VEGF-A),[701] is currently in late-stage clinical development and exemplifies a new generation of molecules that combine immune checkpoint inhibition with anti-angiogenic targeting to enhance therapeutic efficacy. Similarly, Innovent Biologics has developed a broad and diversified pipeline of antibody-based therapeutics, including bispecific antibodies (e.g., IBI389 targeting CLDN18.2×CD3), ADCs (e.g., IBI343 targeting CLDN18.2), and novel immunocytokine-like constructs such as IBI363 (PD-1×IL-2), reflecting a strategy centered on modality convergence.[702] Platform-driven companies such as Biocytogen are contributing to the ecosystem by enabling high-throughput discovery of bispecific antibodies and bispecific ADCs, including dual-target constructs like TROP2-EGFR and EGFR-MET, highlighting the increasing importance of scalable antibody engineering technologies.[703]

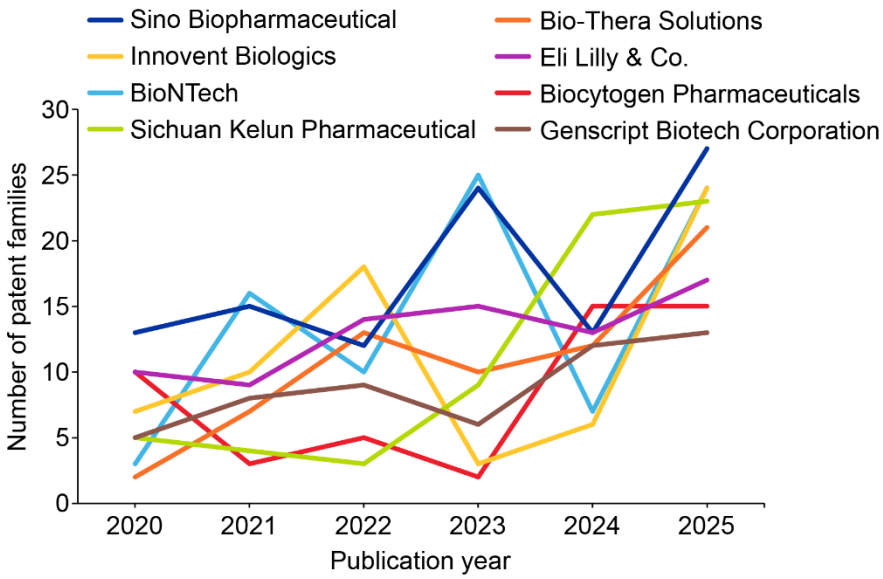


Figure 30. Publication trends for selected companies active in the antibody therapeutics space based on patent activity. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Established players such as Roche continue to lead in ADC commercialization, while emerging companies like Sichuan Kelun Pharmaceutical,[704] Bio-Thera,[705] and Sino Biopharmaceutical[706] are rapidly advancing ADC pipelines and forming global partnerships, positioning China as a key hub for ADC innovation. Nanobodies and diabodies represent important fragment-based extensions of the antibody therapeutics landscape, particularly in enabling next-generation multispecific designs. Nanobodies, pioneered by Ablynx (Sanofi), are small single-domain antibodies with superior tissue penetration and stability, exemplified by caplacizumab (Cablivi[707]), the first approved nanobody drug for thrombotic thrombocytopenic purpura. Beyond Ablynx, companies such as Biocytogen and GenScript are developing nanobody discovery platforms and incorporating them into multispecific constructs and cell therapies. Diabodies, while less prominent as standalone therapeutics, served as critical building blocks for bispecific formats. Notably, Amgen's BiTE platform[708] is based on diabody-like architectures, and other antibody engineering companies are similarly using diabody scaffolds to design compact bispecifics with improved tumor penetration and manufacturability.

Overall, the field is transitioning toward a paradigm in which antibody therapeutics are no longer simple targeting agents but rather programmable, multi-functional biologics capable of orchestrating complex biological responses. This shift is expected to define the next decade of innovation, with bispecific and multispecific antibodies, ADC hybrids, and modular antibody formats collectively shaping the future of precision medicine.

5.1.2 RNA therapeutics

RNA therapeutics have achieved clinical and commercial validation following the COVID-19 mRNA vaccine success and multiple U.S. FDA-approved siRNA and ASO drugs, establishing nucleic acid medicines as mainstream modalities.

The patent landscape showing the evolution of RNA-based therapeutics is highlighted in **Figure 31**, with mRNA[709] and siRNA clearly emerging as the dominant modalities. Their leading share reflects strong clinical validation and scalable delivery platforms. Our analysis indicates that RNA interference related modalities, microRNA, shRNA, and siRNA, are driving more pronounced

growth in patents filed by corporate enterprises, suggesting sustained industry investment and translational focus. In contrast, patent activity by research and academic organizations for these modalities appears relatively stable, indicating slower expansion in early-stage or academic innovation compared with industry-led development.

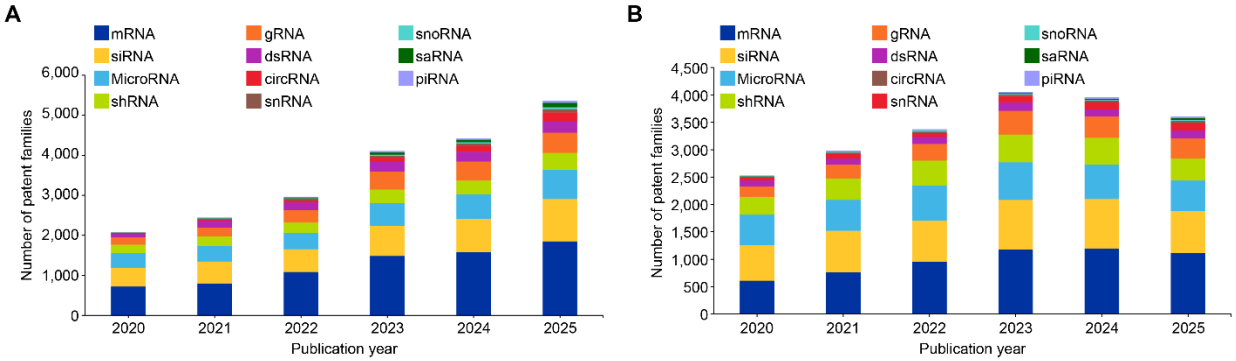


Figure 31. Publication trends of various RNA modalities with respect to patents filed by (**A**) corporate enterprises and (**B**) research and academic organizations. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

In parallel, RNA editing and gene-modulating approaches, including guide RNA-based systems and emerging CRISPR-associated RNA formats, are gradually gaining representation. Although smaller in share as compared to established platforms, their steady growth indicates strong momentum as technologies mature. Emerging RNA classes such as circular RNA (circRNA) and self-amplifying RNA (saRNA) are beginning to appear as small but noteworthy segments. These formats aim to address some of the limitations of conventional RNA therapeutics, such as stability and duration of expression, and their gradual rise underscores ongoing innovation in RNA engineering.

Overall, the expansion across mRNA, siRNA, gene-editing RNAs, and next-generation constructs highlights a broader transition toward multifunctional, programmable RNA therapeutics. Much like the evolution seen in antibody engineering, the field of RNA therapeutics is shifting from single-mechanism interventions to a diverse toolkit of modalities designed to precisely manipulate biological pathways, improve durability, and adapt therapeutic strategies to the complexity of disease biology.

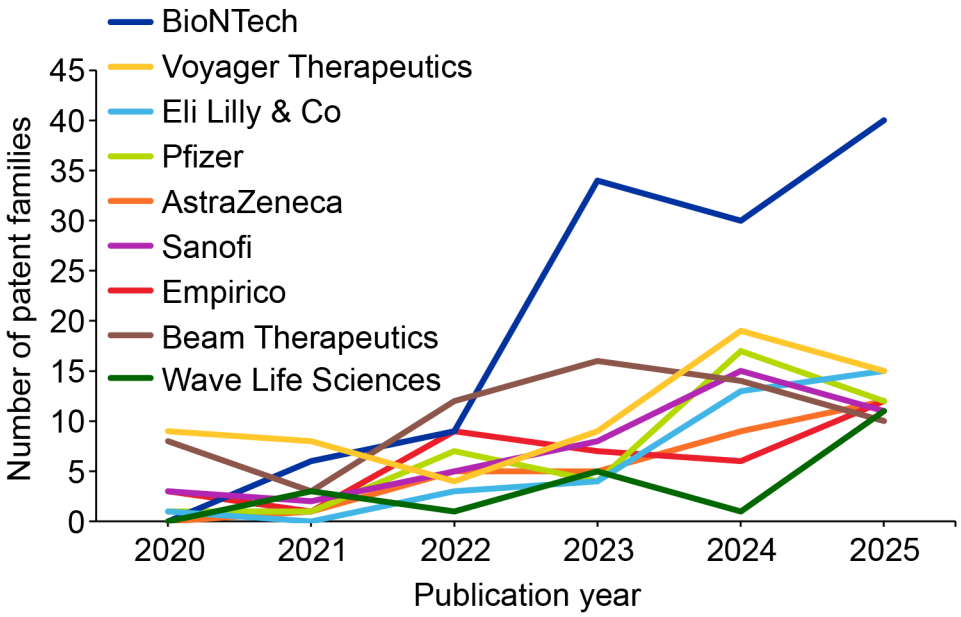


Figure 32. Publication trends of selected companies active in the RNA therapeutics space based on patent activity. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

The RNA therapeutics field is increasingly shaped by a mix of large, established pharmaceutical companies and emerging, innovation-driven biotech firms, with clear modality-specific specialization across players. While traditional leaders such as Roche, Sanofi, Regeneron, and Eli Lilly maintain broad biologics portfolios, their RNA strategies are more selective and often focused on clinically validated approaches or partnerships. In contrast, emerging and hybrid players including BioNTech, Beam Therapeutics, Wave Life Sciences, Voyager Therapeutics, AstraZeneca, Pfizer, and Empirico are driving innovation across next-generation RNA platforms (**Figure 32**).

RNA interference remains one of the most mature and commercially validated RNA modalities. Large pharma players such as Roche and Sanofi have historically engaged in RNAi through collaborations, while Eli Lilly has expanded into RNA-based therapeutics via partnerships and internal programs. Among emerging players, Wave Life Sciences is a key contributor, focusing on stereopure RNAi and ASOs, with candidates such as WVE-003 (Huntington's disease).[710] AstraZeneca (via its collaboration with Silence Therapeutics) is advancing siRNA programs targeting cardiometabolic diseases.

BioNTech and Pfizer remain dominant forces in mRNA, leveraging their COVID-19 vaccine success to expand into oncology (e.g., BNT111, BNT122)[711] and individualized cancer vaccines. Sanofi is also rebuilding its mRNA capabilities through partnerships and internal investments. Self-amplifying RNA (saRNA), which enables prolonged expression at lower doses, is gaining traction. Companies like BioNTech and AstraZeneca are exploring this space for vaccines and infectious disease applications, although pipelines remain in earlier stages compared to conventional mRNA. Gene-editing RNA modalities are driven by specialized biotech firms. Beam Therapeutics is a leader in base editing, using guide RNA to direct precise nucleotide changes, with pipeline programs such as BEAM-101 (sickle cell disease).[712] Pfizer has partnered in gene-editing efforts, while AstraZeneca is also investing in CRISPR-based therapeutics. These approaches represent a shift from transient silencing to precise, potentially curative genome modification, although clinical maturity is still evolving. Additionally, Eli Lilly's collaboration with

ProQR on ASOs for chronic pain and neurological disorders represents important therapeutic applications of RNA editing technology. snoRNA-based therapeutics and other niche RNA classes remain relatively underrepresented but are gaining early traction in rare genetic and splicing-related disorders. Companies like Wave Life Sciences and Empirico are contributing to novel RNA-targeting strategies, often leveraging computational biology and AI-driven target discovery. Voyager Therapeutics plays a key role in RNA delivery, particularly for CNS applications, using engineered capsids to enhance tissue-specific delivery of RNA therapies. This highlights delivery innovation as a core differentiator across RNA modalities.

The RNA therapeutics landscape is increasingly bimodal: large pharma companies continue with selective participation, partnerships, and focus on de-risked platforms and emerging companies are driving modality innovation and expanding into next-generation RNA technologies.

5.2 Cell and gene therapies: CRISPR, CAR-T, and beyond

Cell and gene therapies represent the convergence of biological engineering precision with transformative clinical potential, spanning regenerative medicine, immunotherapy, and genetic correction. The patent landscape reveals strategic shifts from established CAR-T and stem cell platforms toward next-generation modalities including CAR-NK cells, CRISPR-based editing, and emerging immune cell platforms, reflecting industry prioritization of scalability, safety profiles, and manufacturing feasibility alongside therapeutic efficacy.

Stem cells and CAR-based approaches remain a major component in patents filed by corporate enterprises and research and academic organizations. However, CAR-NK cell therapies show a noticeable upward trend, particularly in commercial patents (**Figure 33**), reflecting increasing interest in off-the-shelf and potentially safer alternatives to CAR-T.

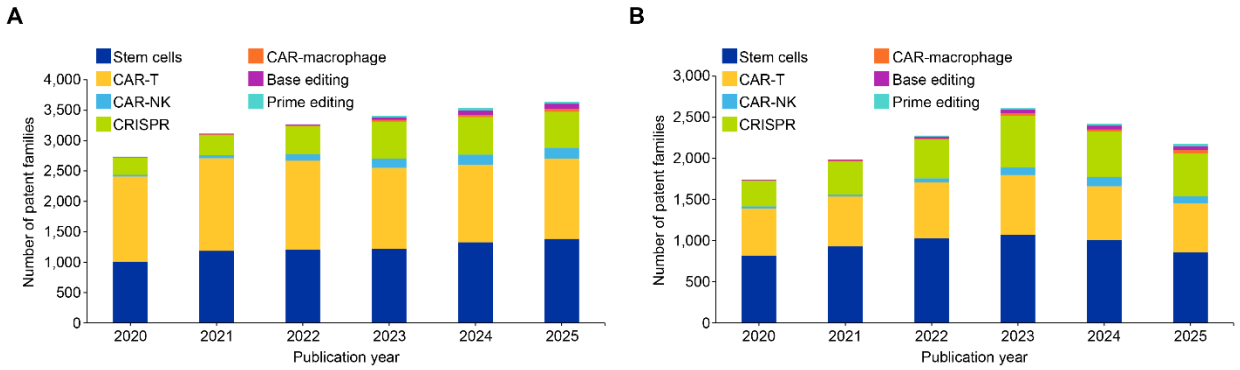


Figure 33. Distribution of various cell and gene therapy modalities in patents filed by (**A**) corporate enterprises and (**B**) research and academic organizations. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

CRISPR-based approaches[713] appear prominently across patents filed by corporate enterprises as well as research and academic organizations, with a modest increase in the former reflecting growing translational momentum (**Figure 33B**). Emerging next-generation editing approaches, including base editing and prime editing, while accounting for a modest number of patents, are nonetheless steadily increasing, highlighting early-stage innovation gaining traction within the commercial space. Additionally, CAR macrophage-based therapies appear as a minor but emerging segment, suggesting expanding exploration of alternative immune cell platforms beyond T and NK cells.

Overall, while non-commercial patents continue to demonstrate broader exploratory research across modalities, commercial activity is increasingly concentrated on scalable, translatable technologies, with CAR-NK and CRISPR leading this transition and newer editing tools gradually entering the innovation pipeline.

5.2.1 Gene editing (CRISPR)

CRISPR-based technologies have rapidly evolved into a central pillar of gene editing, with a combination of established biotech leaders and large pharmaceutical companies driving innovation and commercialization. Key players include CRISPR Therapeutics, Editas Medicine, and Intellia Therapeutics, which have pioneered early clinical applications, alongside Beam Therapeutics and Verve Therapeutics (**Figure 34**), involved in advancing next-generation precision editing platforms. Large pharmaceutical companies such as Regeneron, Novartis, and Eli Lilly & Co. are also active through partnerships and internal programs, reflecting growing confidence in the modality.

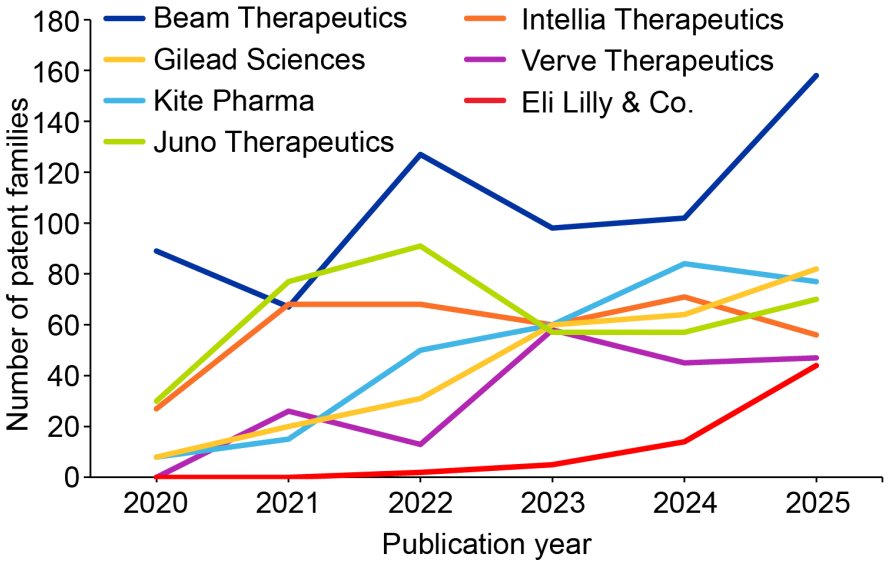


Figure 34. Publication trends of selected companies active in cell and gene therapy based on patent activity. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Recent innovation in the field has moved beyond traditional CRISPR-Cas9 nuclease-based editing toward more precise and potentially safer approaches. Base editing, led by companies like Beam Therapeutics, enables single-nucleotide changes without introducing double-strand breaks. For example, BEAM-101 targets sickle cell disease through precise hemoglobin gene modification. Similarly, prime editing, developed by Prime Medicine, allows versatile “search-and-replace” editing, significantly expanding the scope of correctable mutations.

Clinical translation is accelerating, with *in vivo* CRISPR therapies demonstrating promising progress. For example, NTLA-2001, developed by Intellia Therapeutics, targets transthyretin (ATTR) amyloidosis via systemic CRISPR-mediated gene knockout in the liver, marking a major milestone in *in vivo* editing.[714] Similarly, VERVE-101, developed by Verve Therapeutics, applies base editing to disrupt the PCSK9 gene for cardiovascular disease, highlighting the potential of one-time, durable treatments for chronic conditions.[715] Patent activity reflects these trends, with

increasing filings around delivery systems, Guide RNA (gRNA) optimization, and editing specificity. Emerging CRISPR epigenetic silencing approaches, such as Tune Therapeutics' TUNE-401[716] and nChroma Medicine's CRM-1001,[717] are expanding the toolbox beyond gene editing toward programmable and potentially reversible gene regulation.

5.2.2 CAR-T and beyond

CAR-based cell therapies continue to evolve beyond traditional T cell approaches, with growing diversification into NK and macrophage platforms. CAR-T therapies remain the most established, led by major players such as Gilead Sciences (via Kite Pharma), Novartis, and Bristol Myers Squibb, with approved therapies including Yescarta[718] and Kymriah.[719] Innovation in this space focuses on improving persistence, reducing toxicity, and enabling allogeneic ("off-the-shelf") CAR-T products, supported by patents around gene editing (e.g., CRISPR-enabled T cell engineering) and safety switches.

In parallel, CAR-NK cell therapies are gaining significant traction, driven by their potential for improved safety profiles, lower risk of cytokine release syndrome, and allogeneic use. Companies such as Fate Therapeutics, Nkarta, and Takeda, along with academic collaborations, are advancing CAR-NK pipelines. Recent innovation includes the use of induced pluripotent stem cell (iPSC)-derived NK cells and multiplex gene editing to enhance activity and persistence, with increasing patent filings reflecting efforts to optimize NK cell expansion and targeting.

Emerging more recently, CAR-macrophage therapies represent a novel approach to targeting solid tumors. Carisma Therapeutics and Senti Biosciences are key players in this space, developing macrophages engineered to enhance phagocytosis and modulate the TME. These therapies leverage macrophages' natural tumor infiltration capabilities, with patents focusing on improved antigen presentation and immune activation. Additionally, emerging approaches such as CAR-engineered mucosal-associated invariant T (MAIT) cells are gaining attention. Although still at an early stage with limited patent activity, these innate-like T cells offer advantages including allogeneic applicability and reduced risk of graft-versus-host disease, positioning them as a potential next-generation cell therapy modality.

5.3 Peptide therapeutics: Chemical innovation and cyclic peptide renaissance

Peptide therapeutics represent a well-established yet rapidly evolving modality, anchored by major pharmaceutical players such as Bristol Myers Squibb, Pfizer, AstraZeneca, and Merck, alongside specialized innovators like PeptiDream and Beiersdorf A.G. These companies maintain strong pipelines across metabolic diseases, oncology, endocrinology, and dermatology, leveraging peptides for their high target specificity and favorable safety profiles. Recent innovation has focused on overcoming inherent limitations such as rapid degradation and poor bioavailability through advances in stability engineering, half-life extension, and delivery technologies.

A key trend is the development of long-acting peptide analogs via chemical modifications, including lipidation and PEGylation, to enhance pharmacokinetics, as seen in cardiometabolic pipelines at Pfizer and AstraZeneca. In parallel, there is growing emphasis on peptidomimetics, which incorporate non-natural amino acids or backbone modifications to improve stability and receptor selectivity.

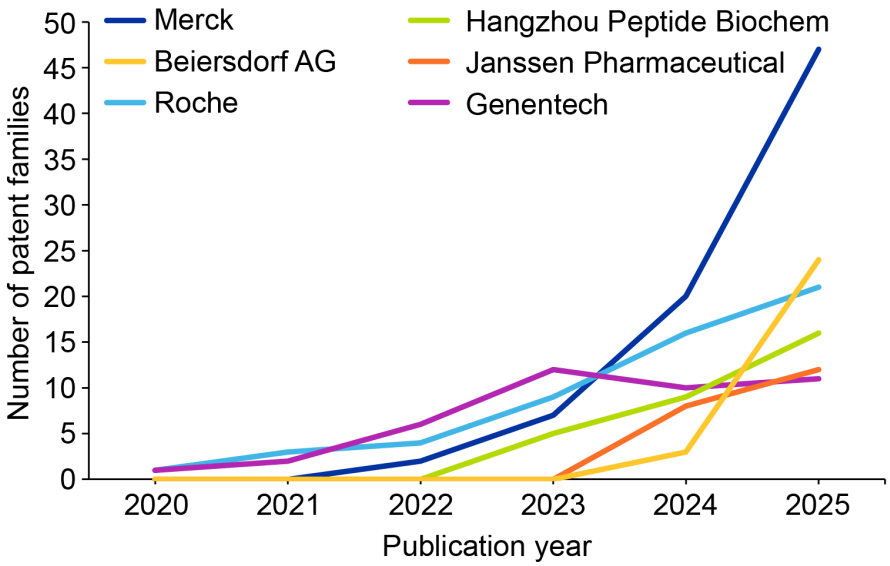


Figure 35. Publication trends of selected companies active in peptide therapeutics based on patent activity. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

In oncology, peptide-drug conjugates (PDCs) are gaining traction as a complementary approach to ADCs, offering improved tumor penetration and tunable pharmacokinetics. Bristol Myers Squibb and Merck are advancing targeted peptide-based delivery strategies, including peptide radioconjugates and cytotoxic payload conjugates, with innovation focused on cleavable peptide linkers and spacers for controlled payload release. These efforts are supported by platform technologies capable of generating structurally diverse and high-affinity peptide ligands.

PeptiDream plays a central role in this landscape through its proprietary Peptide Discovery Platform System (PDPS),[720] enabling the generation of diverse macrocyclic and constrained peptides for therapeutic and conjugate applications. The company has established multiple high-profile collaborations with global pharmaceutical leaders to expand the use of peptide-based technologies. Notably, PeptiDream has entered into a collaboration and license agreement with Genentech[721] to discover and develop novel peptide-radioisotope drug conjugates, highlighting the increasing importance of targeted radiotherapeutics. The company has also partnered with Janssen Pharmaceutica NV,[722] where its PDPS technology is being leveraged to identify constrained peptides against multiple targets of interest. In addition, PeptiDream maintains an ongoing alliance with Bristol Myers Squibb,[723] under which discovery programs have progressed to key milestones. In one such program, Bristol Myers Squibb designated a collaboration compound as a candidate for exploratory clinical development, advancing it into IND-enabling studies and underscoring the clinical potential of PDPS-derived peptides.

Peptide innovation is also expanding into adjacent sectors such as dermatology. Beiersdorf A.G., for example, has partnered with Macro Biologics, Inc. in a multi-year collaboration[724] to develop biodegradable antimicrobial peptides with broad applications in skin care and healthcare, reflecting the versatility of peptide platforms beyond traditional pharmaceutical indications.

5.3.1 Cyclic peptides

Cyclic peptides represent a distinct and high-potential class within peptide therapeutics, offering improved structural stability, target binding affinity, and resistance to proteolysis compared to linear peptides. Key innovators in this space include Bicycle Therapeutics and Entrada Therapeutics, both of which are advancing proprietary platforms to develop constrained peptide scaffolds for targeted delivery and intracellular access.

Bicycle Therapeutics is notable for its Bicycle® platform,[725] which generates bicyclic peptides with antibody-like specificity but smaller size, enabling better tissue penetration. Its pipeline includes bicycle toxin conjugates, such as BT8009, targeting nectin-4 in oncology. Entrada Therapeutics focuses on intracellular delivery of peptides, particularly for neuromuscular and genetic disorders, using its endosomal escape vehicle (EEV™) platform.[726]

An important emerging trend is the development of orally bioavailable cyclic peptides, addressing one of the long-standing limitations of peptide therapeutics. Advances in conformational constraint and permeability engineering are enabling cyclic peptides to achieve sufficient stability and absorption for oral dosing. Notably, Merck's MK-0616,[727] an oral macrocyclic peptide targeting PCSK9 for cardiovascular disease, represents a key example of this progress and highlights the potential for convenient, non-injectable peptide-based therapies.

Patent activity in cyclic peptides highlights innovations in constrained peptide design, linker chemistry, and targeted payload delivery, particularly in oncology and rare diseases. Although still smaller in share compared to traditional peptides, cyclic peptides are rapidly gaining traction, driven by their ability to bridge the gap between small molecules and biologics, and are positioned as a key emerging modality in next-generation therapeutics.

5.4 Small molecule evolution: PROTACs, covalent inhibitors, and precision chemistry

Small-molecule therapeutics are undergoing a major shift, driven by new target classes and new design paradigms. These include the ability to tackle previously "undruggable" biology using approaches like targeted protein degradation, parallelly, researchers are moving beyond proteins toward RNA as a drug target, opening a new frontier for small molecules to modulate gene expression with the scalability and oral availability that biologics often lack. The most transformative development has been in oncology, particularly with KRAS inhibitors representing a major breakthrough after decades of this target being considered "undruggable". Major pharmaceutical companies such as Merck,[728] Roche/Genentech, and Bristol-Myers Squibb are investing in next-generation RAS-targeted therapies, including pan-RAS and pan-KRAS inhibitors. Several clinically advanced pan-RAS inhibitors, such as daraxonrasib (RMC-6236),[729] originate from specialized biotech companies, with some programs involving collaborations with larger pharmaceutical partners.

While these mutation-agnostic inhibitors show strong potential to overcome resistance and broaden patient coverage beyond allele-specific KRAS inhibitors,[730] they remain largely in clinical development.

Our analysis of pharmaceutical patents resulted in identification of emerging companies in the field of small molecule therapeutics (**Figure 36**). Across these companies, the key trend is a shift from traditional small-molecule drug development (simple enzyme inhibitors) to highly

engineered, mechanism-driven therapeutics that expand what small molecules can do biologically. Insilico Medicine is a biotech company that uses AI and generative models to discover novel drug targets and design small-molecule drugs, particularly in areas like fibrosis, oncology, and aging-related diseases.[731] They have collaborated with major pharma companies such as Eli Lilly & Co. and Sanofi. Chinese players like Changchun High-Tech, Haisco, Huadong, Hansoh, and BeOne Medicines are at the forefront of this change. They are building large pipelines of small-molecule assets but with a strong emphasis on novel biology and differentiated mechanisms for example, targeting specific cancer mutations like TP53 with structure-guided molecules,[732] developing protein degraders (PROTACs/molecular glues),[733] and advancing oral metabolic therapies such as GLP-1 agonists for diabetes and obesity.[734] At the same time, large global pharma companies like AstraZeneca, Gilead, and Sanofi are doubling down on small molecules by integrating AI, structure-based design, and new target classes into discovery workflows. Their innovation focus includes areas like highly selective pathway modulation (e.g., PARP1), and immunology signaling pathways, along with partnerships that use advanced platforms like chemoproteomics to discover new binding pockets on difficult targets.

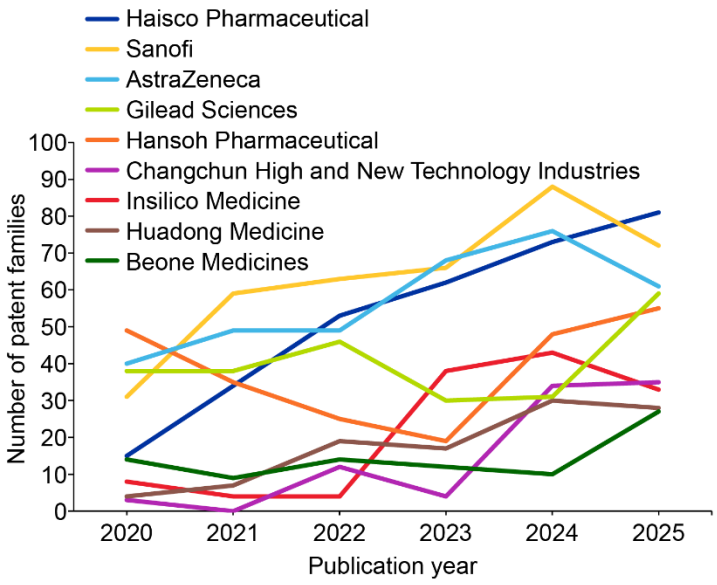


Figure *36*. Publication trends of selected companies active in small molecule therapeutics based on patent activity. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

5.4.1 U.S. FDA approval validates PROTACs as transformative degradation platform

PROTACs represent a transformative approach to targeted protein degradation. Recent innovations have focused heavily on optimizing this architecture, particularly linker design and E3 ligase selection, to enhance ternary complex stability and degradation efficiency. Beyond conventional constructs, the field is advancing toward more sophisticated designs and variations[735] as shown in **Figure 37**.

Dual-PROTACs typically refer to constructs designed to degrade two distinct protein targets simultaneously by incorporating two different target-binding ligands, whereas dual-ligand PROTACs more generally describe molecules containing two ligands (either for the same protein to enhance avidity or for different proteins), enabling improved binding, selectivity, or cooperative ternary complex formation rather than necessarily dual target degradation. bioPROTACs replace the small-molecule framework with engineered biological constructs, such as fusion proteins that combine a target-binding domain (e.g., nanobody) with an E3 ligase component but still operate via the same ubiquitin-proteasome pathway. PHOTACs or AP-PROTACs introduce light-sensitive elements, typically within the linker region, allowing external control over PROTAC activation so that ternary complex formation and degradation occur only upon light exposure allowing spatiotemporal control.

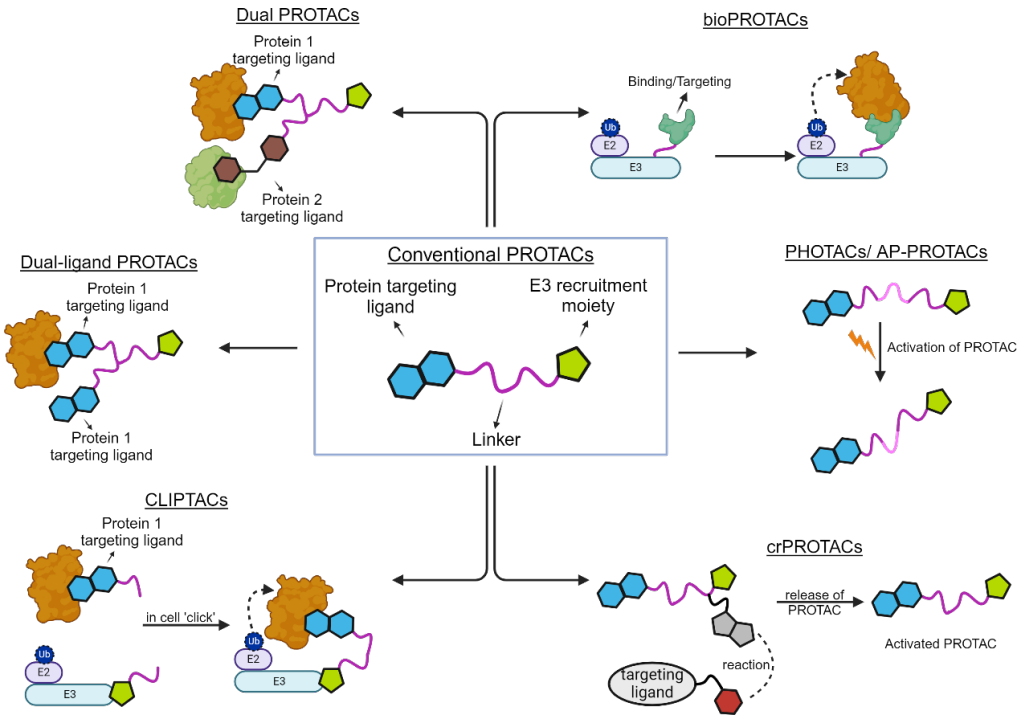


Figure 37. Schematic showing the variations of PROTACs being pursued. Figure generated using www.BioRender.com.

Further modifications include crPROTACs, which stands for click-release PROTACs, involves administration of a PROTAC prodrug that undergoes activation to release the active PROTAC. CLIPTACs divide the PROTAC into two smaller precursor molecules: one targeting the protein and the other recruiting the E3 ligase that assemble intracellularly via click chemistry to form the active degrader, thereby addressing permeability and size limitations associated with the intact molecule shown in the figure. Across all these innovations, the fundamental mechanism remains unchanged, while modifications to the ligand regions, linker, or mode of assembly enable improved selectivity, control, pharmacokinetics, and target scope, transforming PROTACs into a highly versatile and programmable degradation platform.

A defining milestone in the field is the recent U.S. FDA approval of VEPPANU (vepdegestrant)[174] by Arvinas and Pfizer, marking the first approved PROTAC therapy. This drug targets the estrogen receptor in patients with ER+/HER2–, ESR1-mutated advanced or metastatic breast

cancer, demonstrating clinical efficacy where traditional endocrine therapies often fail. This approval validates PROTACs as a viable therapeutic modality and underscores their ability to target previously "undruggable" proteins such as transcription factors. The broader pipeline reflects strong industry momentum, with leading companies including Arvinas, Pfizer, Kymera Therapeutics, Sanofi, and Genentech advancing candidates across oncology and immunology. Notable programs include ER degraders such as vepdegestrant and androgen receptor degraders, as well as non-oncology targets like Kymera's IRAK4 degrader (KT-474), which demonstrates the applicability of PROTACs in inflammatory and autoimmune diseases. Recently, GT20029, the first topical PROTAC entered Phase II clinical trial for the treatment of alopecia.[736]

Beyond these advances, key studies continue to expand the scope and sophistication of PROTAC technology. Clinical and preclinical work on ER-targeting degraders has shown improved outcomes compared to conventional SERMs and SERDs, driven by complete protein removal rather than inhibition. Additionally, emerging research into next-generation degradation strategies including alternative E3 ligase recruitment, molecular glues, and lysosome-targeting chimeras (LYTACs) is broadening the range of addressable targets. The field is also seeing increased emphasis on precision design principles, such as structure-guided ternary complex formation and cooperative binding effects, to enhance selectivity and reduce off-target toxicity. Collectively, these innovations position PROTACs as a rapidly maturing therapeutic class that bridges small molecules and biologics, with the potential to redefine drug discovery paradigms.

5.4.2 Expanding the small molecule toolkit: Allosteric modulation, covalent chemistry, and natural product innovation

Modern small molecule drug discovery has evolved beyond traditional active site inhibition to embrace sophisticated modulation strategies that exploit diverse binding modes and mechanisms. **Allosteric modulators** offer the ability to regulate protein function through binding at sites distinct from the orthosteric active site which are typically less conserved that enable higher selectivity and reduced likelihood of off-target effects making them attractive for precision medicine. Recent advances have expanded the applicability of allosteric modulation to a wide range of challenging targets, with the notable example of KRAS G12C inhibitor.[737] Importantly, the field is moving beyond simple modulation toward more complex mechanisms, including biased signaling[738] and ago-allosteric modulation.[739]

In the case of **covalent inhibitors**, the field has progressed significantly from early concerns around toxicity and off-target reactivity toward highly selective and tunable chemistries. Modern covalent inhibitor design[740] emphasizes the rational incorporation of electrophilic "warheads" (e.g., acrylamides, nitriles, and boronic acids) that selectively react with nucleophilic residues such as cysteine, while carefully tuning intrinsic reactivity to achieve high target specificity and minimize off-target interactions.[741] At the same time, there is a strong shift toward reversible covalent inhibitors,[742] which combine the durability of covalent binding with improved safety and pharmacokinetic control, representing a key innovation in the field.

Natural product-derived small molecules continue to play a central and evolving role in drug discovery, serving both as direct therapeutic agents and as inspiration for synthetic design. Despite advances in synthetic chemistry, natural products remain foundational, with estimates indicating that around half of approved drugs are natural products or their derivatives. Recent breakthroughs highlight the integration of natural products with modern technologies such as genome mining,[743] synthetic biology, and AI-driven discovery,[744] which enable the identification of previously inaccessible chemical scaffolds and the efficient generation of analogues.

Overall, unified paradigms are emerging in which small molecules are no longer viewed merely as inhibitors of active sites, but rather adaptable tools capable of modulating complex biological systems. Together, these latest innovations are enabling the targeting of previously inaccessible biological mechanisms including RNA regulation, protein-protein interactions, and dynamic conformational states, redefining the scope and potential of small molecule therapeutics.

5.5 Advanced drug delivery systems: Enabling technologies across modalities

Advanced drug delivery systems have evolved from passive carriers to sophisticated enabling technologies that fundamentally expand the therapeutic potential of diverse modalities, including small molecules, biologics, nucleic acids, and cell therapies.

The comparative analysis of patents filed by corporate enterprises and academic and research organizations in drug discovery highlights steady growth across both domains, with more pronounced and sustained expansion in commercial filings (**Figure 38**). Lipid-based systems such as lipid nanoparticles (LNPs), liposomes, and related nanocarriers show the most striking trend, with a sharp increase in commercial patents and a comparable, though slightly less steep, rise in non-commercial activity, indicating strong academic-to-industry translation. Polymeric systems remain dominant in both categories but exhibit relatively moderate growth, suggesting a more mature and established technology base.

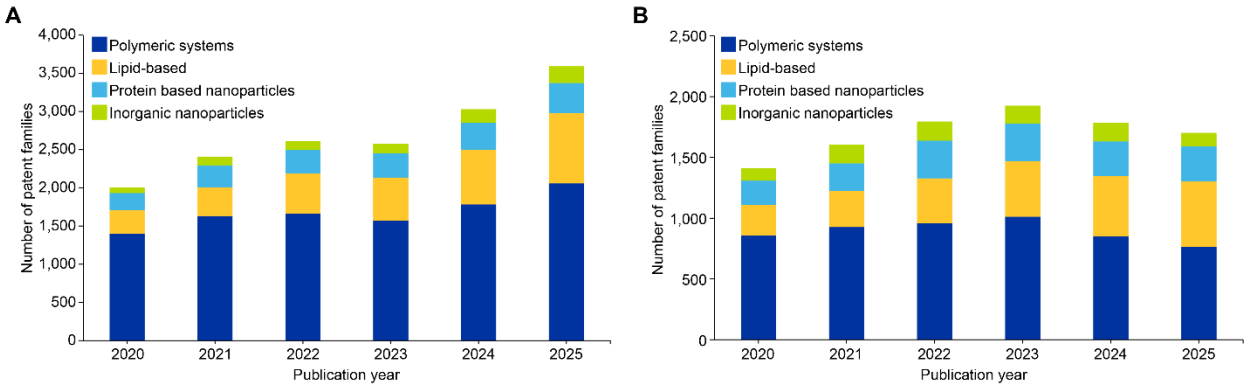


Figure 38. Distribution of various *advanced* drug delivery systems in *patents filed by* (**A**) *corporate enterprises* and (**B**) *academic and research organizations.* Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

In contrast, protein-based systems (e.g., viral vectors, virus-like particles (VLPs), extracellular vesicles, and exosomes) and inorganic systems (e.g., metal-organic frameworks, inorganic nanoparticles, and metal oxide nanoparticles) show slightly stronger growth in the commercial space compared to non-commercial research, reflecting increasing industry interest in biologics and advanced nanomaterials. In later years, commercial activity continues to rise or stabilize at higher levels, whereas non-commercial trends show mild plateauing, indicating a shift from exploratory research toward translation and application-driven innovation, driven by lipid-based platforms.

Advanced drug delivery systems are undergoing a rapid transformation, with a clear shift toward precision, programmability, and clinical translatability. One of the most prominent innovations is the continued evolution of lipid-based systems, particularly lipid nanoparticles, which have moved beyond mRNA vaccines into siRNA, CRISPR delivery, and targeted oncology applications, with

companies like Moderna, BioNTech, and Alnylam expanding platforms for tissue-specific delivery. In parallel, inorganic and hybrid systems, including metal-organic frameworks and stimuli-responsive nanoparticles, are being explored for controlled release, imaging integration, and combination therapies, particularly in oncology and theranostics.

A major frontier is the integration of smart, stimuli-responsive systems and AI-driven design, where delivery vehicles respond to pH, enzymes, or tumor microenvironment cues to achieve site-specific activation. Big pharma and biotech are investing in multifunctional platforms that combine targeting ligands, imaging capability, and therapeutic payloads. Additionally, there is strong momentum toward next-generation biologically derived carriers, such as engineered exosomes and synthetic cells, which promise lower immunogenicity and improved biodistribution. Large pharmaceutical companies including Novartis, AstraZeneca, and Roche are expanding into these areas through partnerships and acquisitions, while niche biotech firms are driving innovation in modular delivery systems and precision targeting. Overall, the field is moving toward intelligent delivery systems that integrate targeting, sensing, and therapeutic action, positioning advanced drug delivery as a critical enabler of next-generation therapeutics.

5.6 Other emerging modalities: Microbiome, AI-designed therapeutics, and radiopharmaceuticals

5.6.1 Microbiome-based

Microbiome-based therapeutics have rapidly evolved over the past decade from exploratory concepts into a clinically validated and commercially active field. Early approaches such as fecal microbiota transplantation and probiotics laid the foundation, but the field is now transitioning toward defined, standardized, and engineered microbiome interventions. This includes the development of live biotherapeutic products, which represent a major share of current pipelines and are designed to function as pharmaceutical-grade treatments rather than crude biological mixtures. Alongside this, advances in sequencing, metagenomics, and bioinformatics have enabled a much deeper understanding of microbiome-host interactions, driving the development of precision microbiome medicine where therapies are tailored based on individual microbial profiles. FDA approvals of microbiome-based therapies like Rebyota[745] (by Ferring Pharmaceuticals) and VOWST[746] (by Seres Therapeutics), have validated the field and opened a regulatory pathway for future products. In parallel, emerging approaches such as engineered bacteria, bacteriophage therapies, and microbiome-derived metabolites are reshaping the field.

Current patents in this field are focused on innovations such as bacterial consortia, therapeutic mechanisms, and diagnostic biomarkers. Major patent clusters include bacterial therapeutics, disease-specific applications, and microbiome-based diagnostics, with bacterial-based interventions accounting for nearly half of all filings. One notable example is WO2022178193,[747]which focuses on microbiome modulation to enhance cancer immunotherapy. The patent describes methods to identify patients with favorable microbial profiles, develop microbiome-based biomarkers for predicting treatment response, and optimize fecal microbiota transfer strategies. This represents a significant advancement in precision oncology by integrating microbiome science directly into immunotherapy decision-making and treatment optimization. Another example of an important development is WO2024206308,[748] which introduces AI-driven donor selection for fecal microbiota transplantation in inflammatory bowel disease. This patent leverages metagenomics to classify patients based on microbial taxa enrichment profiles and match them with suitable donors. WO2025054086 describes next-generation microbiota restoration therapies for recurrent *Clostridioides difficile* infection. Given the high recurrence rates

of this infection following antibiotic treatment, this approach offers a potentially curative strategy by restoring microbial balance rather than simply eliminating pathogens.

Overall, these developments demonstrate that microbiome therapeutics are moving from an exploratory phase toward a mature, translational discipline. The convergence of microbiology, genomics, AI, and precision medicine is enabling the development of next-generation therapeutics with clear clinical utility and strong commercial potential, supported by a rapidly expanding pipeline and significant global investment.

5.6.2 AI/ML in drug discovery

Recent patent activity highlights how AI has evolved from a supportive tool to a central driver of innovation in modern drug discovery workflows. Latest patents in the field are strongly focused on core workflows such as structure-based design, virtual screening, QSAR, and molecular docking, with a clear shift toward integrated, end-to-end platforms. A major trend is the rise of generative AI for de novo drug design, using transformer and diffusion models to create novel molecules rather than just predict properties.[749] In parallel, AI-powered structure-based drug design platforms are combining docking, virtual screening, and pharmacokinetics modeling for lead optimization,[750] while deep learning approaches such as protein language models are advancing protein structure and binding prediction.[751]

Additional innovations include the use of graph neural networks for drug-target interaction and repurposing,[752] and the integration of QSAR with machine learning for rapid activity prediction and compound screening.[753] Emerging areas such as AI-driven RNA-targeted drug discovery[754] and recursive transformer models for protein interactions[755] highlight the expansion beyond traditional protein targets. Overall, the field is transitioning from isolated predictive models to multi-modal, AI-integrated platforms combining generative design, prediction, and optimization, marking a shift toward fully computational, data-driven drug discovery pipelines.

5.6.3 Radiopharmaceuticals

Radiopharmaceuticals have emerged as a transformative modality in modern medicine, particularly within oncology, where they enable highly targeted delivery of radiation directly to tumor cells. At the core of this progress is the concept of theranostics, which integrates diagnostic imaging and therapy into a single platform. This has significantly enhanced precision medicine by enabling patient selection, real-time monitoring, and individualized dosing strategies. Over the past decade, radiopharmaceutical therapy has moved from niche applications to a mainstream oncology strategy, fueled by advances in molecular targeting, radionuclide chemistry, and clinical validation, including approvals of agents such as ^{177}Lu-PSMA-617[756] and ^{177}Lu-DOTATATE.[757]

Current research trends highlight a rapidly expanding radiopharmaceutical pipeline with extensive clinical activity, reflecting strong scientific momentum and growing commercial interest. While β-emitters such as lutetium-177 remain dominant, the field is shifting toward α-emitters and combination strategies, alongside expansion into diverse cancers through new molecular targets like HER2 and PD-L1. Major players such as Novartis have engaged in extensive patent enforcement, indicating the transition from early innovation to high-value commercialization. Patent activity is focused on targeting ligands, radionuclide-chelator systems, dosimetry optimization, and isotope production technologies, reflecting the complex and multidisciplinary nature of radiopharmaceutical development.

Several recent patent examples illustrate how innovation is addressing practical and clinical challenges in radiopharmaceutical therapy:

1. US20260115337 A1[758] describes an improved formulation of ^{177}Lu-PSMA I&T for metastatic castration-resistant prostate cancer, featuring extended shelf life and high radiochemical purity. This innovation addresses key supply chain limitations of short-lived isotopes, enabling centralized production, wider distribution, and improved patient access to effective PSMA-targeted therapies.
2. RU2853908 C1[759] introduces ^{225}Ac-PSMA radioligand therapy for brain meningiomas, extending PSMA-targeted treatment beyond prostate cancer into neuro-oncology.
3. IN202541102453 A[760] describes an AI-driven dual-tracer PET platform that integrates PSMA and FDG imaging with advanced machine learning models to generate predictive biomarkers and guide therapy selection in prostate cancer.

Radiopharmaceuticals are transitioning into a mature yet rapidly expanding field at the intersection of nuclear medicine, oncology, and precision therapeutics. With growing clinical validation and ongoing advances in targeting and isotopes, radiopharmaceuticals are likely to play an important role in future cancer therapy.

6. Innovations across major disease areas

6.1 Emerging therapeutic areas drive innovation across disease categories

The pharmaceutical innovation landscape is experiencing rapid evolution, with R&D efforts focused on previously underserved therapeutic areas and novel disease mechanisms. Our comprehensive analysis of more than 368,000 recent pharmaceutical patents revealed over 1,700 distinct disease areas demonstrating significant growth trajectories, reflecting expanding scientific understanding and evolving unmet medical needs.

The emerging therapeutic areas identified in this analysis span the full spectrum of human disease, from oncological indications to complex systemic disorders. Growth rates range from steady expansion (1-1.2X) to explosive innovation (>2X), with these metrics serving as quantitative indicators of research intensity, competitive interest, and potential therapeutic impact. Areas experiencing accelerated growth often represent convergence points where technological advances, mechanistic insights, and clinical needs align to create fertile ground for pharmaceutical innovation. Mid-tier growth rates (1.3-1.5X) frequently characterize established therapeutic areas undergoing meaningful innovation, such as the application of novel drug classes to well-studied diseases or the refinement of existing therapeutic approaches through improved selectivity, pharmacokinetics, or patient stratification strategies. Modest growth rates (1-1.2X) may indicate either mature therapeutic categories or areas where innovation faces significant scientific, technical, or regulatory challenges.

This section presents 14 comprehensive CAS TrendScape maps that systematically organize the emerging therapeutic landscape. One map (**Figure 39**) is dedicated exclusively to oncological disease areas, reflecting cancer's unique complexity and the substantial proportion of pharmaceutical R&D investment directed toward oncology. The remaining 13 maps (**Figure 40-53**) address major non-oncological disease categories including neurological, metabolic, autoimmune, among many others.

6.1.1 Oncology: A mature landscape with subtype-specific opportunities

The oncology patent landscape reveals a strategic focus on rare tumor subtypes and lymphoma heterogeneity despite dominant cancer types maintaining substantial volumes (**Figure 39**). Rare T-cell lymphomas demonstrate exceptional growth, with *subcutaneous panniculitis-like T-cell lymphoma* (SPTCL) and *intestinal T-cell lymphoma* (ITCL) both expanding at 1.6-1.9X, alongside *MALT lymphoma*[761] (1.4X; e.g.) and *marginal zone lymphoma*[762] (1.3X). These patterns reflect precision oncology's maturation, where molecularly defined subtypes enable targeted therapeutic development previously impossible in heterogeneous disease categories.

Thoracic malignancies show differentiated innovation: *Pleural cancer*,[763] *bronchial cancer*,[764] and *thymic tumors*[765] (all 1.2X) attract focused attention, while *lung cancer*[766] and *mesothelioma*[763] maintain substantial patent activity growing at a sedate pace (1X) in competitive immunotherapy and targeted therapy landscapes.

Notably, oncology demonstrates fewer ultra-high-growth areas (>2X) compared to non-oncological categories (e.g., metabolic (**Figure 41**), fibrotic (**Figure 51**), and genetic (**Figure 53**)

diseases) exhibiting more explosive emergence. This contrast likely reflects oncology's mature innovation ecosystem with established checkpoint inhibitors, CAR-T platforms, and targeted therapies, versus non-oncological areas where novel modalities are opening previously intractable therapeutic spaces. Major cancer types (such as melanoma, AML, cervical cancer, diffuse large B-cell lymphoma (DLBCL), and ovarian cancer) maintain substantial volumes, indicating continued refinement through resistance mechanisms, combination strategies, and biomarker-driven patient selection rather than paradigm-shifting breakthroughs characterizing emerging non-cancer indications.

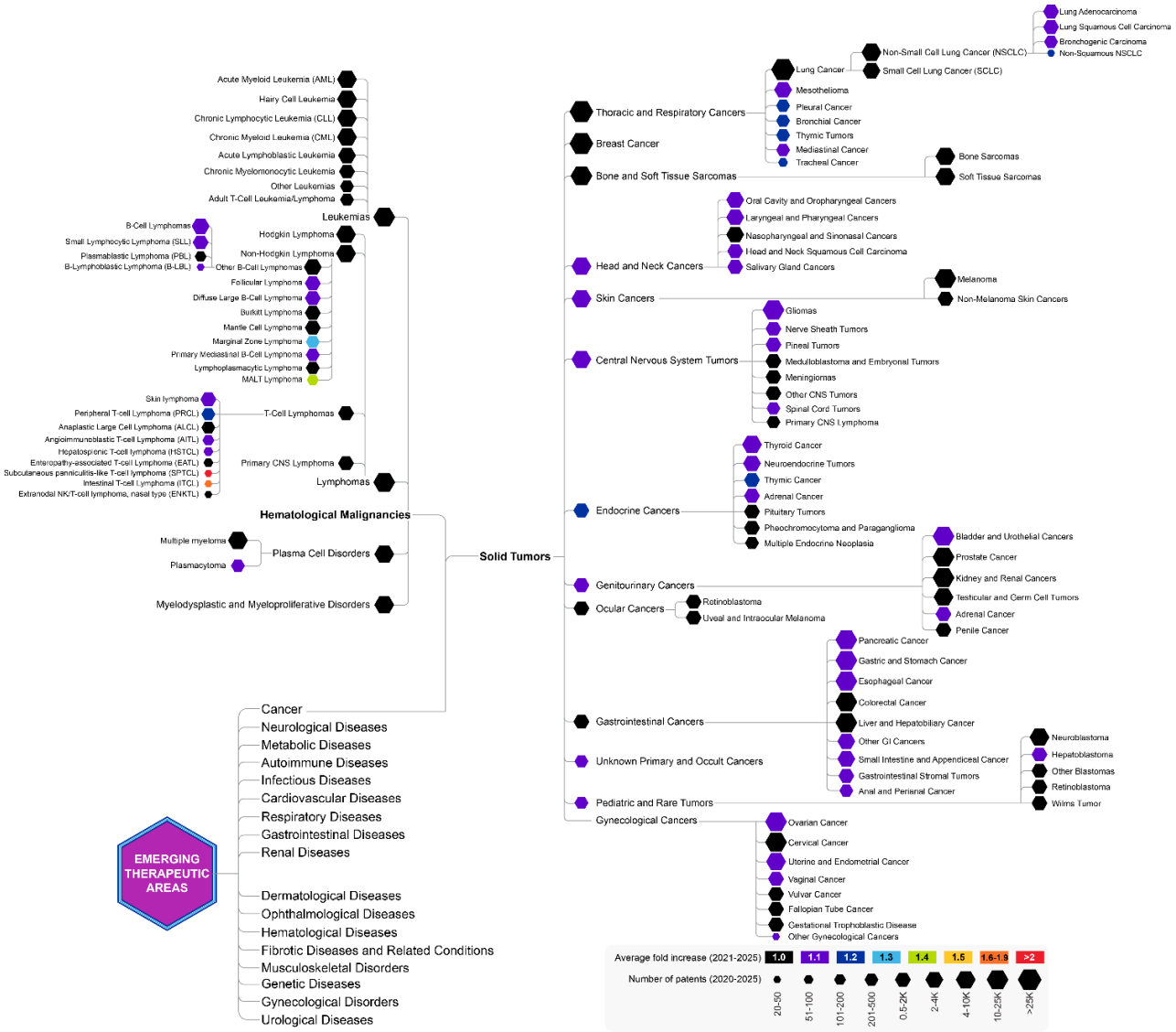


Figure 39. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on oncological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

6.1.2 Non-oncological innovation spans diverse therapeutic categories

Neurological Diseases: The neurological disease patent landscape reveals strategic diversification beyond traditional neurodegenerative targets (**Figure 40**). **Glial disorders** emerge as one of the highest growing areas (1.6-1.9X), reflecting increasing recognition of astrocytes, oligodendrocytes, and microglia as therapeutic targets rather than passive bystanders in neurological disease.[767,768] This growth parallels advances in understanding neuroinflammation and neuron-glia interactions.

Pain-related indications show robust growth, with *myalgic pain* (1.4X) and *peripheral neuropathy* (1.2X) attracting significant attention, likely driven by the opioid crisis and demand for non-addictive analgesics.[769] **Autoimmune neurological disorders** demonstrate sustained innovation, including *Guillain-Barré syndrome*[770] (1.3X), *myasthenia gravis*[771] (1.2X), and *neuromyelitis optica*[772] (1.2X), benefiting from advances in immunomodulatory therapies and biomarker-driven patient stratification.[773,774]

Movement disorders show moderate growth, with *tremor disorders* (1.3X) and *motor dysfunction* (1.2X) gaining traction. Notably, major **neurodegenerative diseases** such as *Alzheimer's*,[775] *Parkinson's*,[776] and *multiple sclerosis*,[777] all maintain substantial patent volumes despite modest growth rates (1.1X), indicating continued investment in these large-market indications even as innovation diversifies toward emerging mechanisms and underserved populations.

Metabolic Diseases: The metabolic disease landscape demonstrates remarkable diversification beyond traditional cardiometabolic targets (**Figure 41**). *Metabolic homeostasis* (>2X) and *microalbuminuria* (>2X) represent fast-growing areas, reflecting intensified efforts in early intervention and disease prevention.[778] *Syndromic obesity*[779] (1.6-1.9X) while having lower patent volumes appear to be growing fast likely driven by the clinical success of GLP-1 receptor agonists, which have transformed obesity treatment and stimulated innovation in related *eating disorders* (1.2X).

Dyslipidemia shows strategic shifts toward rare lipid disorders, with *hypolipoproteinemias*[780] (1.5X) and *sitosterolemia*[781] (both 1.6-1.9X) emerging alongside moderate growth in common dyslipidemias like *hyperlipoproteinemia*[782] and *chylomicronemia*[783] (both 1.3X). **Bone metabolism** disorders exhibit exceptional activity, particularly *osteomalacia*[784] (>2X) and *parathyroid disorders*[785] (1.6-1.9X), suggesting novel therapeutic mechanisms beyond traditional bisphosphonates.

Lysosomal storage diseases demonstrate consistent innovation, with *Krabbe disease*[786] and *metachromatic leukodystrophy*[787] (both 1.5X) showing accelerated growth, likely reflecting advances in gene therapy and enzyme replacement strategies. Established high-volume areas—*hypercholesterolemia*,[788] *PCOS*,[789] and atherosclerosis[790] (1-1.1X)—maintain substantial patent activity despite modest growth rates, indicating continued refinement of existing therapeutic paradigms.

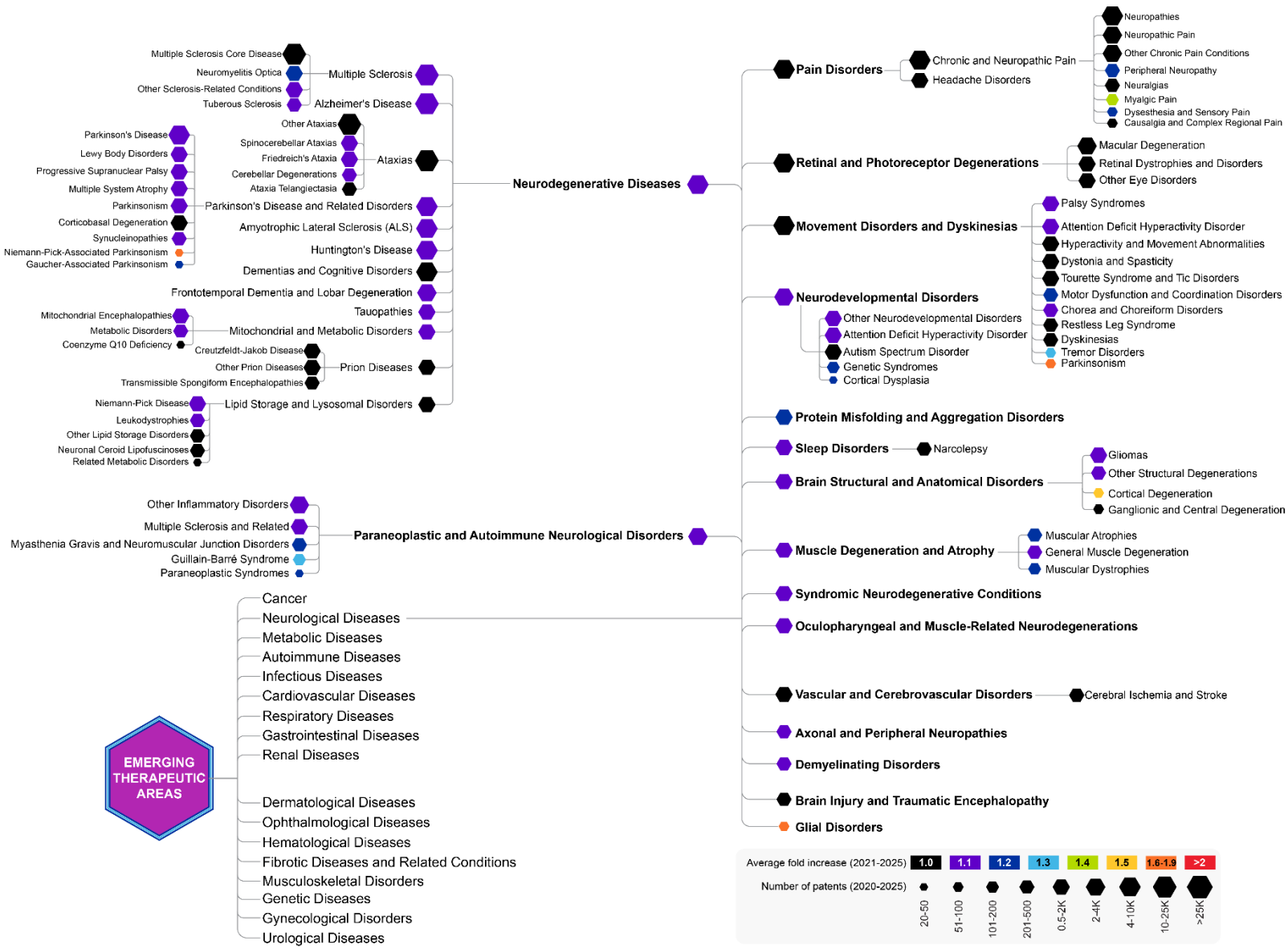


Figure 40. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on neurological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

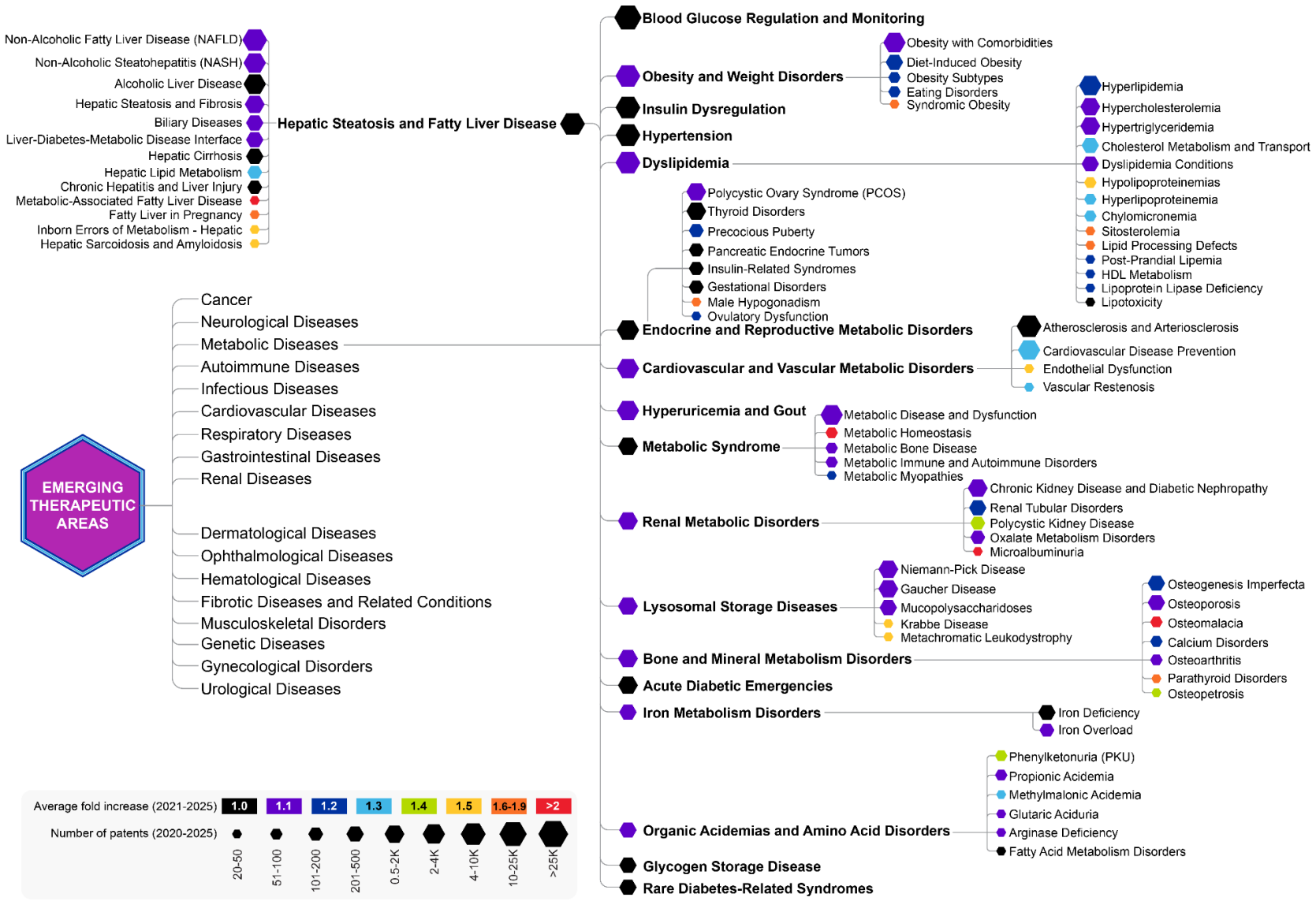


Figure 41. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on metabolic diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Autoimmune Diseases: The autoimmune disease patent landscape reveals strategic expansion into organ-specific manifestations and dermatological conditions beyond traditional systemic indications (**Figure 42**). *Progressive ossification* (1.5X) emerges as one of the highest-growing rheumatic areas, likely reflecting interest in fibrodysplasia ossificans progressiva[791] (FOP) and related rare bone formation disorders amenable to targeted therapies.

Dermatological autoimmune conditions demonstrate uniform moderate growth, with *alopecia*,[792] *hidradenitis suppurativa*,[793] and *vitiligo*[794] all expanding at 1.2X. This pattern suggests successful translation of immunological insights, particularly JAK inhibitors and biologics, to previously underserved inflammatory skin disorders.[795] **Systemic lupus erythematosus** (SLE)-related innovation focuses on specific organ manifestations, with both *lupus nephritis* and *cutaneous/discoid lupus* growing at 1.2X, reflecting precision approaches to heterogeneous disease presentations.[796, 797]

IBD innovation shows subtle differentiation, with *ulcerative colitis*[798] (1.2X) slightly outpacing *Crohn's disease*[799] (1X), potentially driven by distinct mechanistic insights or unmet medical needs. *Neuromyelitis optica* (1.2X) continues attracting attention within demyelinating diseases, benefiting from improved disease definition and targeted complement inhibition strategies.[772,800]

Established large-market autoimmune diseases including *rheumatoid arthritis*,[801] *multiple sclerosis*,[802] *psoriasis*,[803] and *osteoarthritis*,[804] maintain substantial patent volumes and modest growth (1-1.1X), indicating ongoing therapeutic optimization in competitive, biologics-dominated markets where differentiation increasingly requires novel mechanisms or improved pharmaceutical properties.

Infectious Diseases: The infectious disease patent landscape demonstrates notably limited emergence compared to other therapeutic areas, reflecting mature antibacterial markets, antibiotic stewardship concerns, and challenging commercial dynamics (**Figure 43**). No infectious disease areas achieve growth rates exceeding 1.3X, with innovation concentrated in niche pathogens and specific viral families rather than broad therapeutic breakthroughs.

Bacterial innovation focuses on specific underserved organisms, including *Bartonella* (e.g., WO2022256487 A1) (1.3X) and *Cutibacterium acnes*[805] (1.3X). The growth in *Lactobacillus* species (*L. rhamnosus* and *L. acidophilus* at 1.2X) likely reflects microbiome modulation and probiotic applications rather than traditional antimicrobial development.[806-808] **RNA virus infections** show selective activity in *Bunyaviridae*,[809] *Caliciviridae*,[810] and *Arteriviridae*[811] (all 1.2X), potentially driven by pandemic preparedness initiatives and broad-spectrum antiviral platforms.

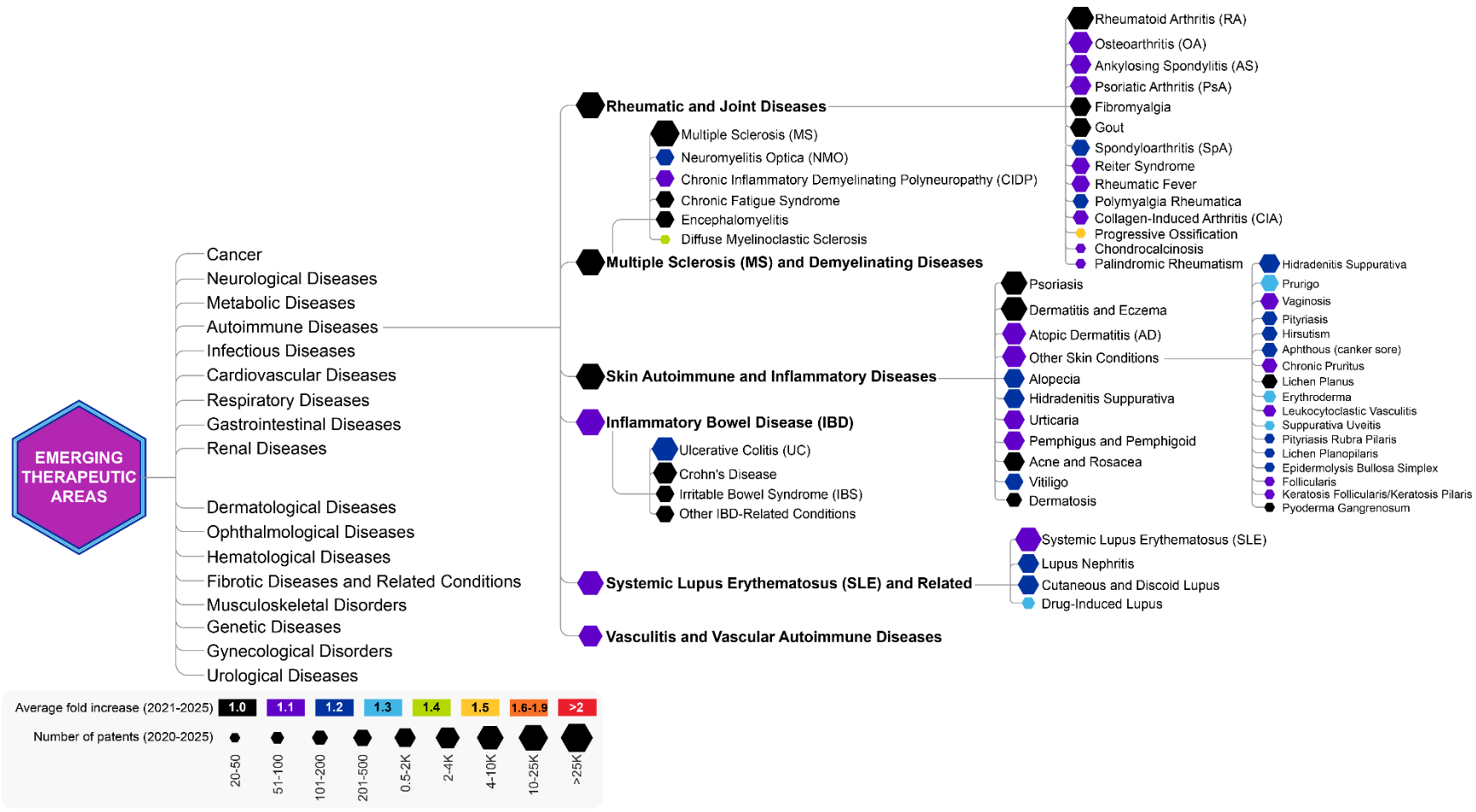


Figure 42. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on autoimmune diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Major bacterial pathogens maintain stable patent activity with minimal growth: *Staphylococcal*, *Streptococcal*, *Clostridial*, and *Enterococcal* infections all grow at 1X, while Mycobacterial infections remain flat despite ongoing tuberculosis burden. This pattern suggests that infectious disease innovation increasingly emphasizes resistance mechanisms, diagnostic approaches, and host-directed therapies over novel antimicrobial scaffolds, with limited commercial incentives dampening investment in traditional antibacterial drug discovery.

Cardiovascular Diseases: The cardiovascular patent landscape reveals strategic shifts toward pathophysiological mechanisms and phenotypic disease stratification beyond traditional organ-based classifications (**Figure *44***). *Calcification* emerges as one of the fastest-growing areas (1.6-1.9X), reflecting intensified efforts to address vascular and valvular calcification.[812]

Heart failure innovation demonstrates clear phenotypic differentiation, with *heart failure with preserved ejection fraction*[813] (HFpEF; 1.3X) outpacing *heart failure with reduced ejection fraction*[814] (HFrEF; 1.2X), mirroring clinical recognition that preserved ejection fraction represents distinct pathophysiology requiring targeted approaches beyond neurohormonal blockade. *Cardiotoxicity*[815] (1.4X) and *hyperplasia*[816] (1.3X) show robust growth, likely driven by oncology-cardiology intersection concerns and drug safety requirements as cancer therapies proliferate.

Mechanism-focused areas demonstrate consistent moderate growth: *Cardiac fibrosis*[817] (1.2X), **inflammatory cardiac conditions**[818] (1.2X), **vasculitis/arteritis**[819] (1.2X), and **valvular heart disease**[820] (1.2X) all reflect movement toward targeting specific pathological processes rather than symptomatic management. **Lipid-related cardiovascular conditions** (1.2X) continue evolving beyond traditional statins.

Established high-burden cardiovascular conditions maintain substantial patent activity with modest growth: *Stroke* subtypes, *ventricular arrhythmias*,[821] and *embolism*[822] (1.1X) indicate mature therapeutic landscapes where incremental improvements predominate, though their large patent volumes reflect continued commercial significance in prevention and acute management.

Respiratory Diseases: The respiratory disease patent landscape emphasizes fibrotic pathology, disease comorbidities, and infection-inflammation intersections (**Figure 45**). *Radiation-induced pulmonary fibrosis*[823,824] (1.5X) and *occupational fibrotic diseases* such as *silicosis*[825] and *asbestosis*[826] (both 1.3X) represent some of the fastest-growth areas, reflecting both increased oncology survivorship concerns and persistent occupational health challenges. These growth patterns suggest novel antifibrotic mechanisms beyond pirfenidone and nintedanib are being explored. Chronic obstructive pulmonary disease (COPD) and pneumonia innovation focuses on comorbid presentations: emergence of *COPD with cystic fibrosis* and *COPD with acute respiratory distress syndrome* (ARDS) (both 1.2X), alongside *pneumonia with sepsis* (1.3X), indicate shifting emphasis from monotherapy approaches toward managing complex, multifactorial respiratory disease. *Infectious bronchitis* (1.4X) show accelerated activity, potentially reflecting post-pandemic preparedness and improved understanding of host-pathogen interactions.[827]

Respiratory syncytial virus[828] (RSV; 1.2X), *eosinophilic conditions*[829] (1.2X), and *inflammatory lung diseases*[830] (ILD; 1.2X) demonstrate steady growth, with RSV particularly notable given recent regulatory approvals.[650,831,832] *Pleural mesothelioma*[833] and *obstructive sleep apnea*[834] (both 1.2X) represent persistent unmet needs. Major respiratory diseases maintain substantial patent volumes despite modest growth: *COPD*,[835] *cystic fibrosis*,[836] and *allergic rhinitis*[837] (1-1.1X) reflect mature markets, while *idiopathic pulmonary fibrosis*[838] (IPF) and *pulmonary arterial hypertension*[839] (1.1X) indicate continued refinement of recently established therapeutic classes.

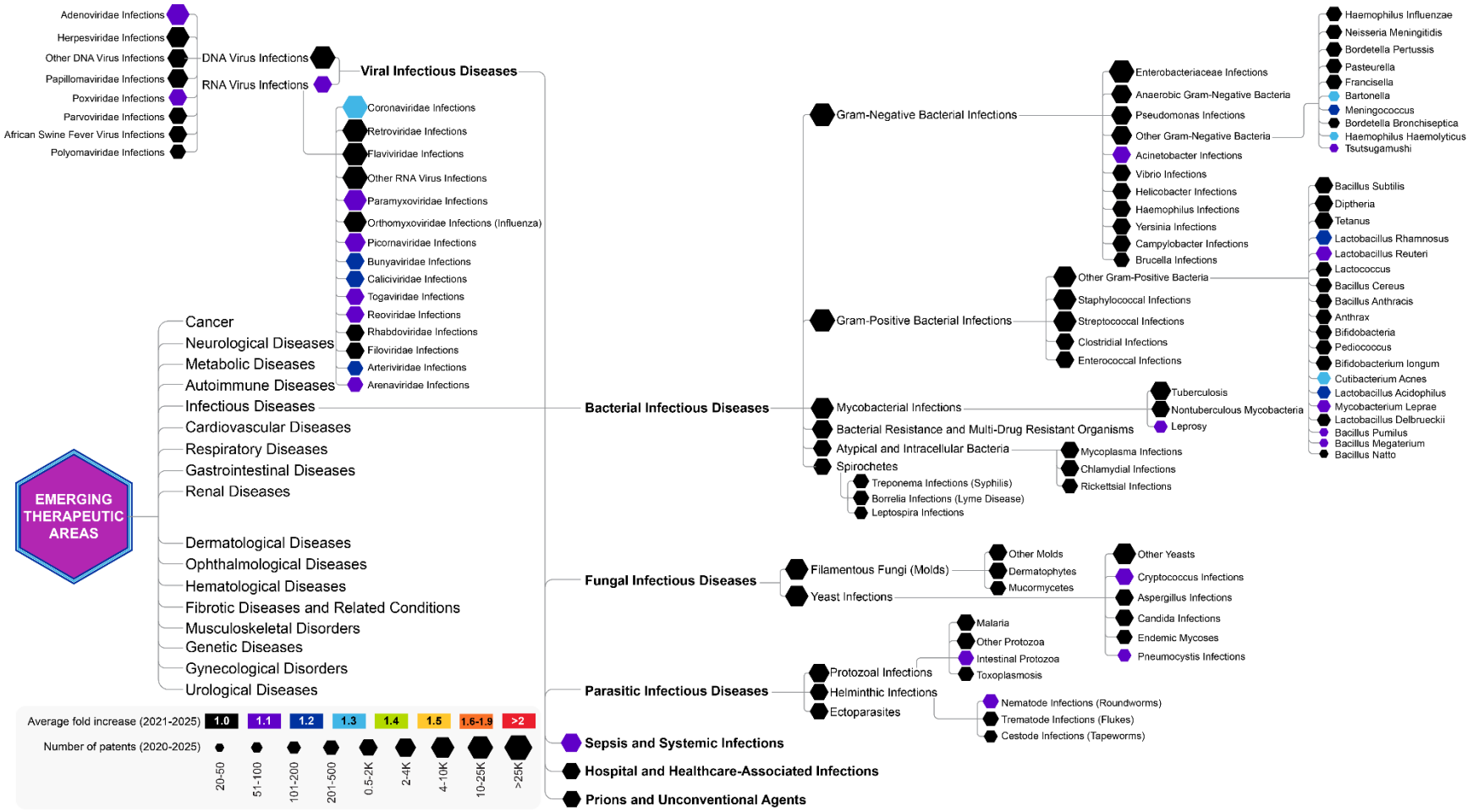


Figure 43. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on infectious diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

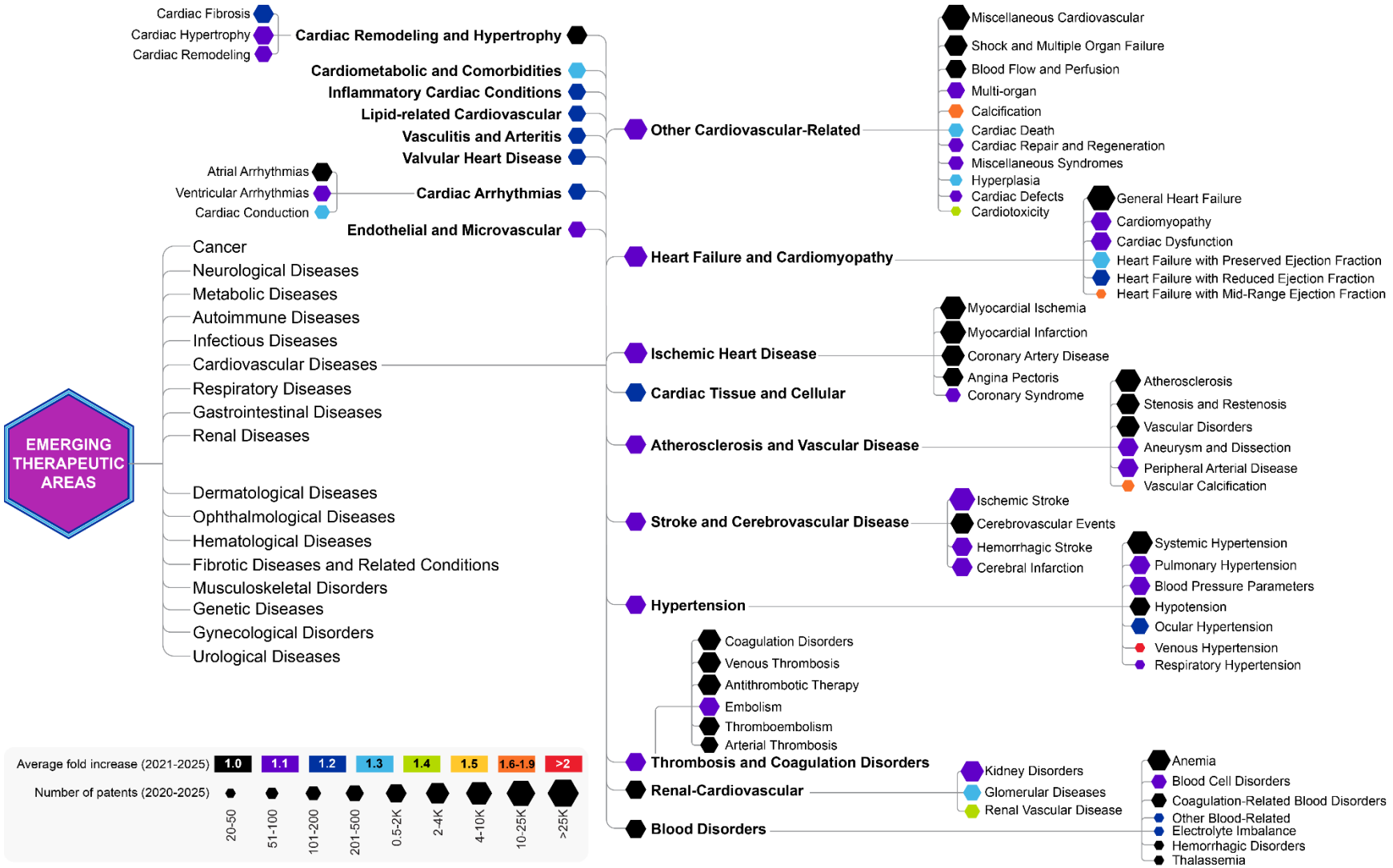


Figure 44. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on cardiovascular diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

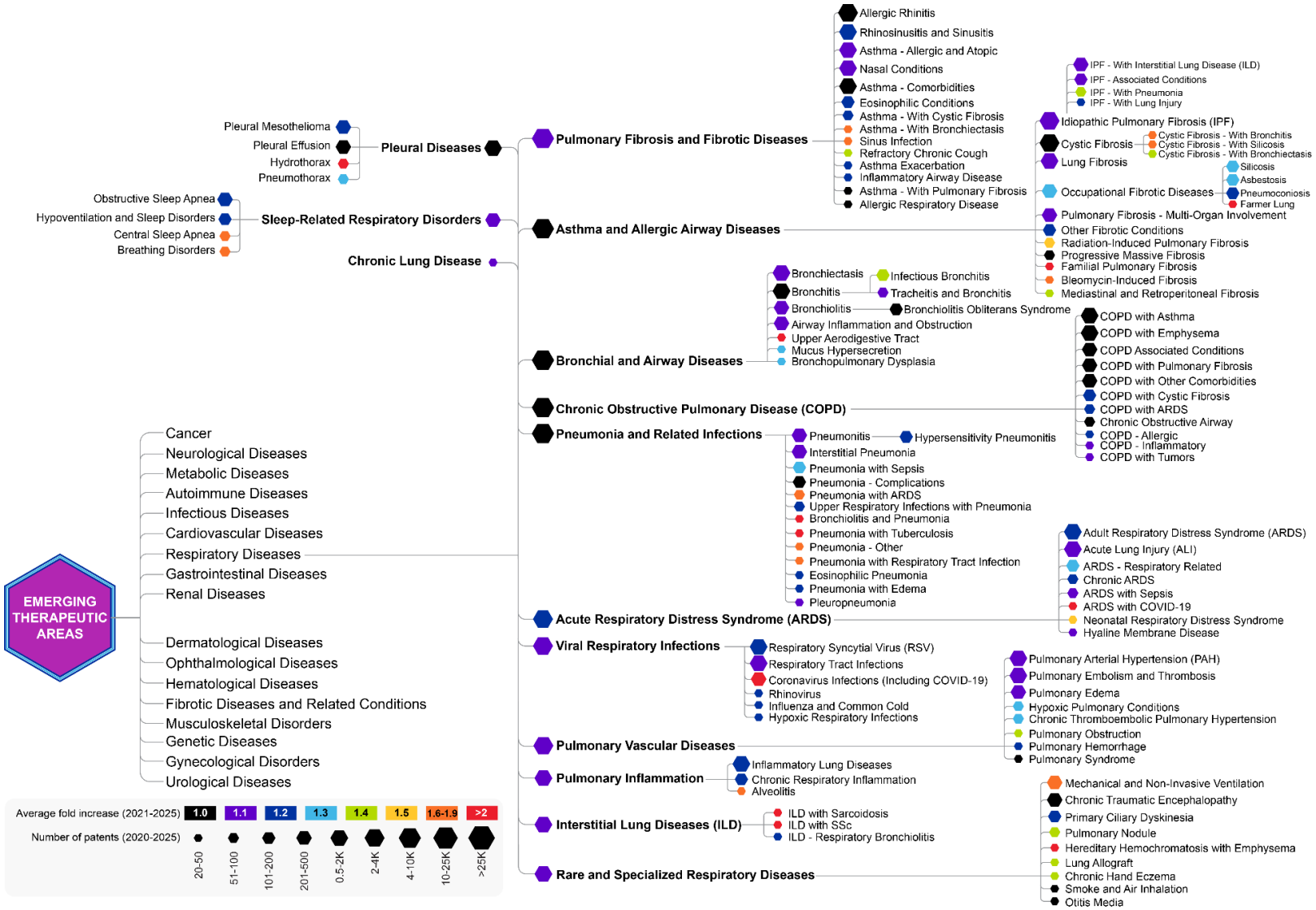


Figure 45. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on respiratory diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Gastrointestinal Diseases: The gastrointestinal disease patent landscape demonstrates concentrated innovation in hepatic disorders and limited emergence across other GI pathologies (**Figure 46**). Liver disease innovation shows dual focus on viral and metabolic etiologies: *Hepatitis* (1.2X) continues attracting investment despite direct-acting antiviral successes in HCV,[840] potentially reflecting efforts in HBV cure strategies and hepatitis-associated complications.[841,842] *Non-alcoholic fatty liver disease* (*NAFLD*)/*nonalcoholic steatohepatitis* (*NASH*) (1.2X) maintains moderate growth with substantial patent volumes, indicating a competitive landscape where numerous mechanisms including antifibrotics are being explored for this major unmet having only one approved drug (rezdiffa or resmetirom).[843-845] **Gastrointestinal fibrosis** (1.2X) emerges as a cross-cutting pathological target, reflecting broader pharmaceutical interest in fibrotic mechanisms affecting liver, intestinal, and pancreatic tissues, potentially leveraging insights from pulmonary and cardiac fibrosis programs.[846]

Major GI conditions demonstrate modest growth with significant patent volume: *Ulcerative colitis*[847,848] (1.1X), *gastroenteritis* (1.1X), *esophageal diseases*[849] (1.1X), and *biliary tract diseases*[850] (1.1X) reflect mature therapeutic areas where biologics and small molecules have established efficacy, requiring meaningful differentiation through novel targets, improved safety profiles, or oral bioavailability for competitive advantage.

Gynecological Diseases: The gynecological disease patent landscape reveals focused innovation in uterine pathophysiology and ovarian dysfunction, though overall growth rates remain modest compared to other therapeutic areas (**Figure 46**). *Premature ovarian failure/insufficiency* (1.3X) emerges as one of the fastest-growing ovarian disorder, reflecting increasing interest in preserving fertility and hormonal function through regenerative approaches and novel endocrine modulation strategies.[851,852]

Uterine disorders such as *uterine bleeding disorders*,[853] *intrauterine adhesion*[854] (both 1.3X), alongside *endometrial hyperplasia*[855] (1.2X), despite smaller patent volumes show fast growth rates indicating emerging therapeutic opportunities beyond traditional hormonal interventions. *Preeclampsia* (1.1X) shows moderate activity within pregnancy-related conditions,[856] likely reflecting improved understanding of angiogenic imbalance and endothelial dysfunction, though therapeutic options remain limited with innovations focused on biomarker research.[857,858]

High-prevalence gynecological conditions maintain stable patent activity: *Leiomyoma/uterine fibroids*[859] and *endometriosis*[860] (both 1X) generate substantial patent volumes despite sedate growth, indicating competitive markets where GnRH antagonists and other hormonal therapies dominate. *Ovulation disorders*, *pelvic organ prolapse*, and *premenstrual syndrome* (all 1X) similarly reflect mature therapeutic landscapes requiring differentiation through novel mechanisms or improved tolerability profiles.[861-863]



Figure 46. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on gastrointestinal and gynecological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Renal Diseases: The renal disease patent landscape reveals a strategic focus on immunologically mediated glomerular diseases and rare genetic kidney disorders (**Figure 47**). *Hemolytic uremic syndrome*[864] (HUS) (1.4X) emerges as one of the fastest-growing areas, with *atypical HUS*[865] (aHUS; 1.3X) demonstrating sustained innovation following complement inhibitor successes (e.g., eculizumab[866] and ravulizumab[867]), suggesting continued interest in alternative complement pathways and thrombotic microangiopathy mechanisms.[868]

Glomerular diseases show robust activity across multiple pathologies: *IgA nephropathy*[869,870] (1.3X) represents a common primary glomerulonephritis, while *glomerulonephritis*[871] more broadly (1.2X) reflects efforts targeting immune complex deposition, podocyte injury, and inflammatory mediators.

Autosomal dominant polycystic kidney disease (ADPKD; 1.2X) maintains moderate growth, suggesting continued innovation beyond tolvaptan including CRISPR.[872] **Acute kidney injury** (1.2X) represents a critical unmet need where therapeutic interventions remain largely supportive despite high clinical burden.[873]

Established renal conditions demonstrate modest growth with substantial patent volumes: *Glomerulosclerosis*[874] (1.1X), *renal ischemia-reperfusion injury*[875] (1.1X), and *hyperuricemia/gout*[876] (1.1X) reflect mature therapeutic areas where RAAS inhibition, immunosuppression, and urate-lowering therapies dominate, requiring novel approaches for meaningful clinical differentiation in progressive kidney disease management.

Dermatological Diseases: The dermatological disease patent landscape demonstrates diverse innovation across hair disorders, wound healing, and inflammatory skin conditions (**Figure 48**). *Telogen effluvium*[877] (>2X) represents a fast-growing area, though with limited patent volumes, reflecting emerging interest in stress-induced hair loss mechanisms and the intersection of dermatology with metabolic and inflammatory pathways. *Seborrheic alopecia* (1.5X) similarly shows accelerated growth in this underserved segment.[878]

Established alopecia subtypes maintain consistent moderate growth: *Alopecia areata*[879] and *androgenetic alopecia*[880] (both 1.2X) demonstrate sustained innovation, likely driven by JAK inhibitor successes in autoimmune alopecia and growing demand for medical hair loss treatments beyond traditional minoxidil and finasteride approaches.[881,882] Specialized inflammatory and fibrotic conditions show coordinated growth: *Hidradenitis suppurativa*,[793] *keloids*,[883] *diabetic wounds*,[884] and *dermatitis herpetiformis*[885] (all 1.2X) reflect targeted efforts in previously neglected dermatological conditions where biologics and precision approaches are enabling therapeutic intervention. *Pruritus and prurigo*[886,887] (1.3X) benefit from improved understanding of itch pathways, including peripheral and central neuroimmune mechanisms.[888]

High-volume dermatological conditions demonstrate market maturity: *Acne*,[889] *rosacea*,[890] *scleroderma*,[891] various *keratoses*,[892] and *allergic/seborrheic dermatitis*[893] (all 1-1.1X) maintain substantial patent activity with minimal growth, indicating competitive landscapes dominated by topical therapeutics, antibiotics, and retinoids where differentiation requires novel mechanisms or improved delivery systems.



Figure 47. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on renal diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

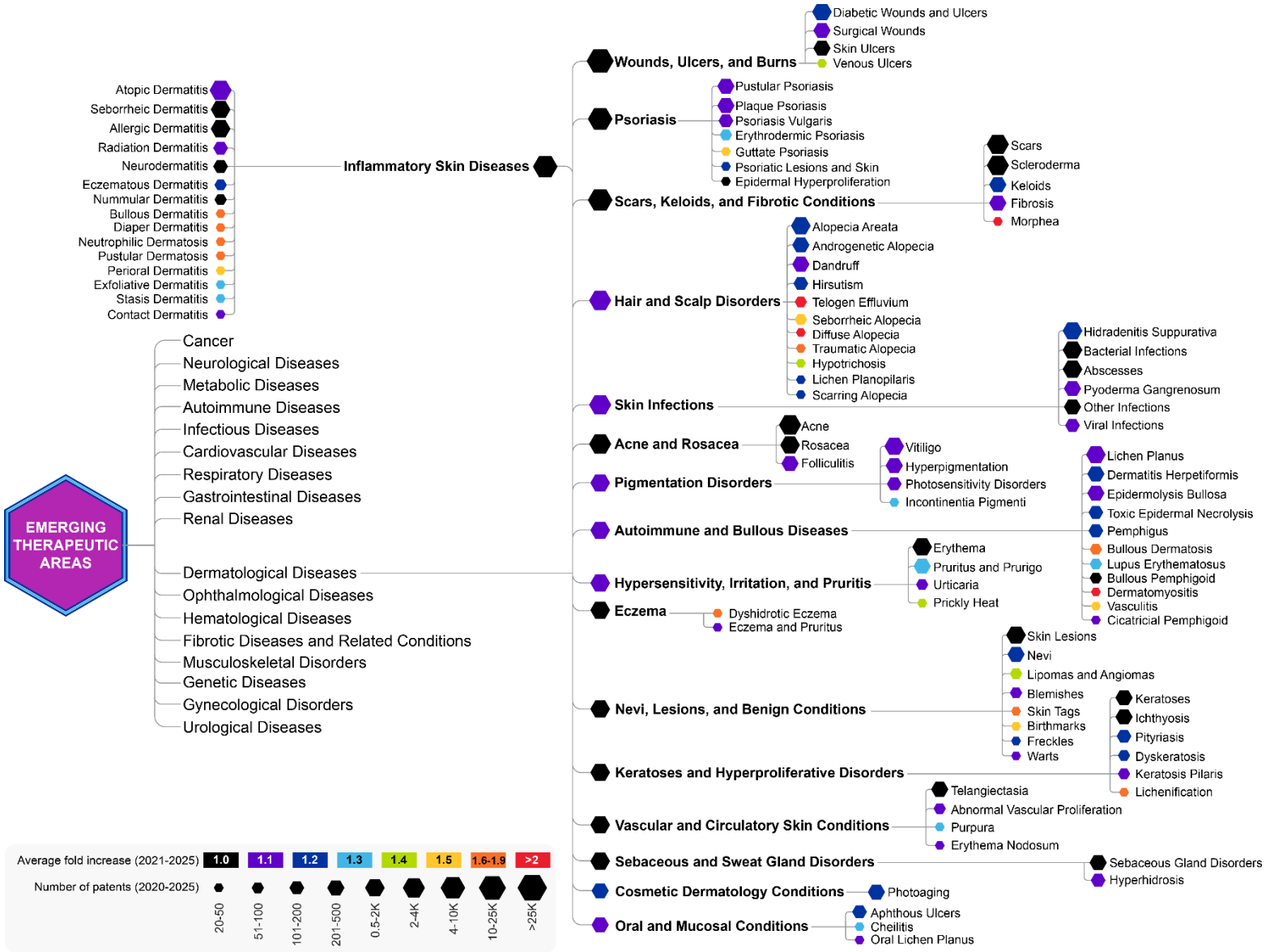


Figure 48. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on dermatological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Ophthalmological Diseases: The ophthalmological disease patent landscape reveals continued retinal focus alongside emerging attention to rare inflammatory and dystrophic conditions (**Figure 49**). *Sympathetic ophthalmia* demonstrates fast growth (1.4X), albeit with limited patent volumes, reflecting interest in this rare autoimmune condition following penetrating ocular trauma.[894,895] *Neovascular (wet) age-related macular degeneration* (AMD; 1.3X) and *fundus dystrophies* (1.3X) show sustained innovation,[896-898] with wet AMD activity likely extending beyond anti-VEGF therapies toward complement inhibition, gene therapy, and alternative angiogenic pathways.[899,900]

Glaucoma innovation focuses on pressure management: *Ocular hypertension*[901] (1.2X) suggests continued efforts in early intervention and neuroprotection beyond traditional intraocular pressure reduction. *Thyroid-associated orbitopathy*[902] (1.2X) reflects growing recognition of this debilitating TED manifestation, potentially benefiting from IGF-1 receptor antagonists and immunomodulatory approaches.

Major retinal diseases maintain substantial activity with modest growth: *Diabetic retinopathy*,[903] *retinal vascular diseases*,[904] and *macular edema*[905] (all 1.1X) generate significant patent volumes in competitive anti-VEGF and corticosteroid-dominated markets. *Corneal diseases* and choroidal diseases (both 1.1X) demonstrate steady innovation in surgical adjuncts, regenerative approaches, and inflammatory management.

Inherited retinal diseases show consistent moderate growth: *Stargardt disease*[906] and *Leber congenital amaurosis*[907] (both 1.1X) reflect ongoing gene therapy development and precision medicine approaches in previously untreatable genetic blindness, representing significant unmet needs despite relatively small patient populations driving orphan drug development strategies.

Urological Disease: The urological disease patent landscape demonstrates notably constrained innovation compared to other therapeutic categories, with minimal high-growth areas and predominantly stable patent activity (**Figure 49**). *Ovarian disorders* (1.3X) within **female reproductive and gynecological disorders** represents a fast-growing area, though this crosses traditional urological boundaries into gynecology. **Male infertility and reproductive disorders** (1.2X) shows moderate expansion, potentially reflecting increased attention to male factor infertility, hormonal therapies, and assisted reproduction technologies.[908] **Prostate disorders**[909] and **urolithiasis**[910] (both 1X) maintain substantial patent volumes despite flat growth, indicating continued refinement of existing approaches rather than paradigm-shifting innovations.

The paucity of emerging areas in urology likely reflects multiple factors: mature therapeutic landscapes dominated by established surgical interventions, limited novel drug development for common conditions, and the anatomical rather than mechanistic organization of many urological disorders. The overall pattern suggests urological innovation may be occurring more in other areas such as device development, surgical techniques, and diagnostics rather than novel pharmacological mechanisms, potentially explaining the limited patent growth in disease-focused analyses emphasizing therapeutic interventions over procedural innovations.

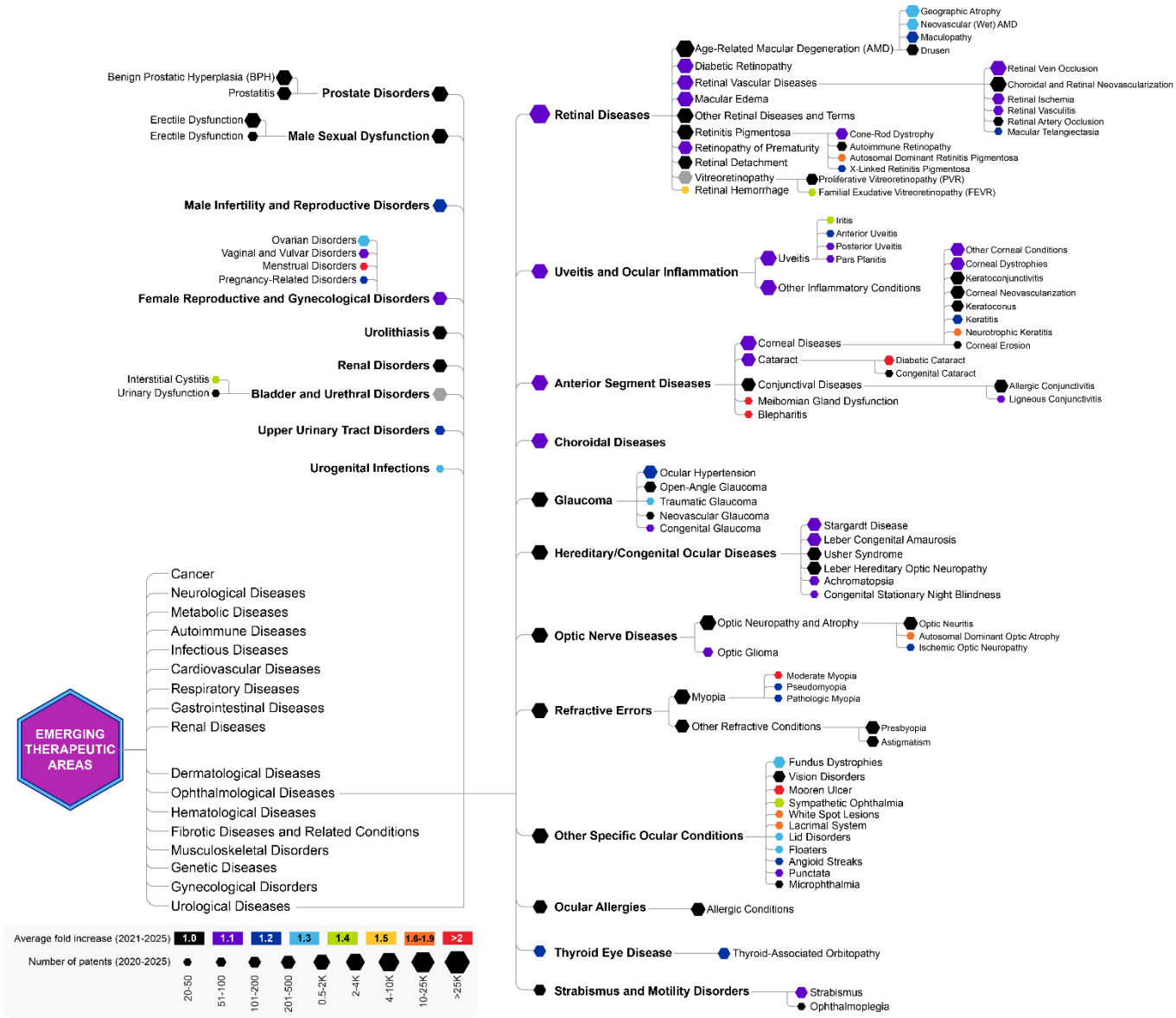


Figure 49. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on ophthalmological and urological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Hematological Diseases: The hematological disease patent landscape demonstrates focused innovation in rare blood disorders and complex coagulation abnormalities, with limited high-growth areas reflecting specialized therapeutic development (**Figure 50**). **Paroxysmal nocturnal hemoglobinuria** (**PNH**),[911] *Fanconi anemia*,[912] and *disseminated intravascular coagulation*[913] (DIC) all grow at 1.2X, representing distinct mechanistic opportunities. PNH's growth follows complement inhibitor successes with eculizumab and pegcetacoplan, suggesting continued interest in alternative complement targets and oral therapies.[914,915] *Fanconi anemia* (1.2X) reflects advances in bone marrow failure syndromes, potentially benefiting from gene therapy approaches[916] and improved understanding of DNA repair mechanisms in this rare inherited condition. *DIC* (1.2X) represents a critical coagulation emergency where therapeutic interventions remain largely supportive, indicating unmet needs in modulating pathological coagulation cascades and microvascular thrombosis.[917]

The overall modest growth rates across hematological disorders likely reflect the success of existing therapies such as erythropoiesis-stimulating agents for anemia, growth factors for neutropenia, and targeted therapies for myeloproliferative neoplasms, all of which create high bars for therapeutic advancement. Established hematological conditions maintain steady patent activity: *Hemolytic anemias*[918] and *aplastic anemia*[919] (both 1.1X), *neutropenia*[920] (1.1X), and *polycythemia vera*[921] (1X) generate substantial volumes in mature markets dominated by biologics and small molecules, where differentiation requires novel mechanisms addressing disease heterogeneity, improved safety profiles, or convenient administration routes in chronic conditions requiring long-term management.

Fibrotic Diseases and Related Conditions: The fibrotic disease patent landscape reveals broad innovation spanning multiple organ systems, representing one of the more extensive maps with numerous emerging therapeutic areas (**Figure 51**). *Metabolic liver diseases*[922] and *metabolic syndrome/MASH*[923,924] both demonstrate highest growth (1.6-1.9X), reflecting the convergence of metabolic dysfunction and fibrogenesis as a dominant pharmaceutical focus. These areas benefit from improved understanding of lipotoxicity, inflammation, and stellate cell activation in hepatic fibrosis progression.

Cardio-renal fibrosis[925] (1.5X) exemplifies the growing emphasis on multi-organ fibrotic syndromes, recognizing shared pathophysiological mechanisms across tissues. *Muscle fibrosis and dystrophy*[926,927] (1.3X) and *bronchitis*[928,929] (1.3X) show accelerated activity, while *myocardial fibrosis* (e.g., CN121221743 A), *inflammatory bowel disease* (IBD),[930,931] and others expand at 1.2X, indicating systematic targeting of fibrotic pathways across anatomical locations.

The breadth of emerging fibrotic areas spanning pulmonary, hepatic, cardiac, renal, gastrointestinal, musculoskeletal, and dermal systems suggests the pharmaceutical industry's recognition that common pro-fibrotic mechanisms (TGF-β signaling, ECM remodeling, myofibroblast activation) may enable platform approaches applicable across diseases. This contrasts with historical organ-specific drug development. *NAFLD* and *NASH*[932,933] maintains substantial patent volumes (1.1X) despite modest growth, reflecting intense competition in this large-market indication where numerous mechanisms have advanced to late-stage development.

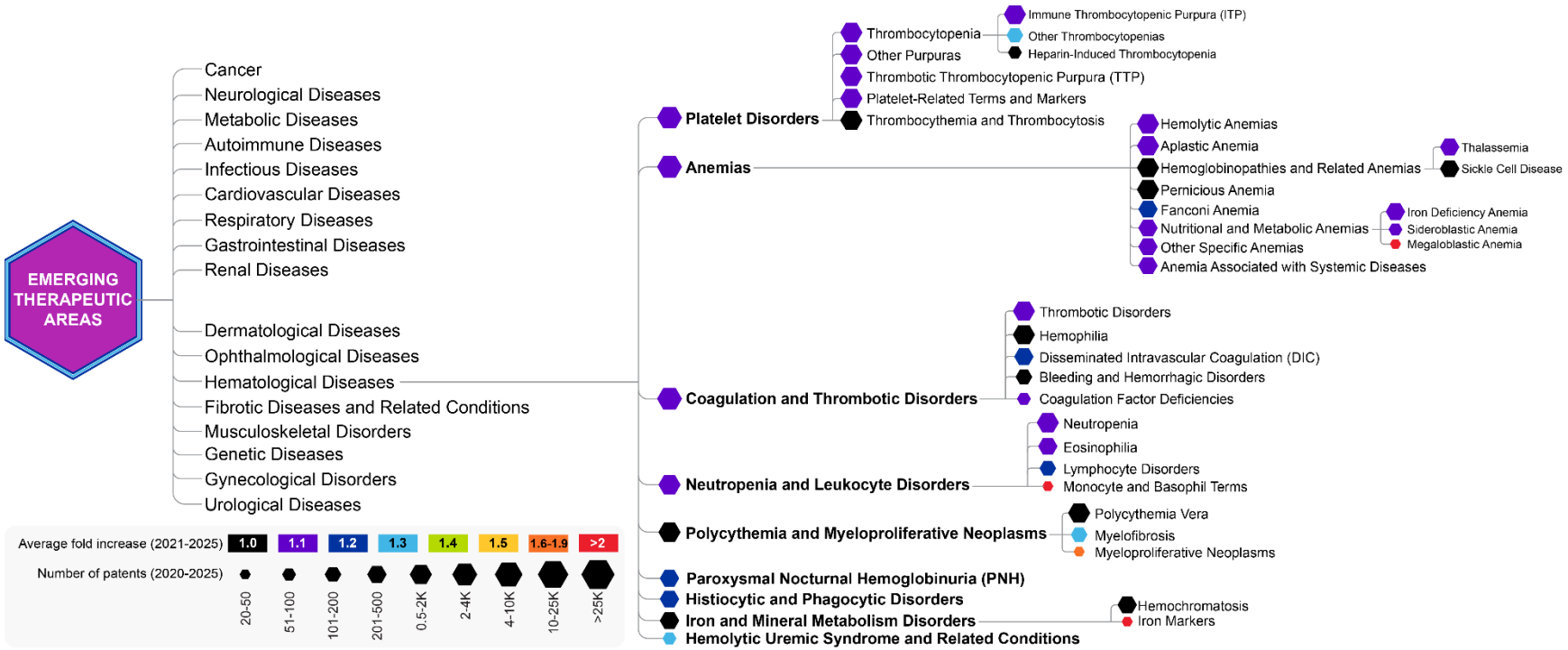


Figure 50. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on hematological diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

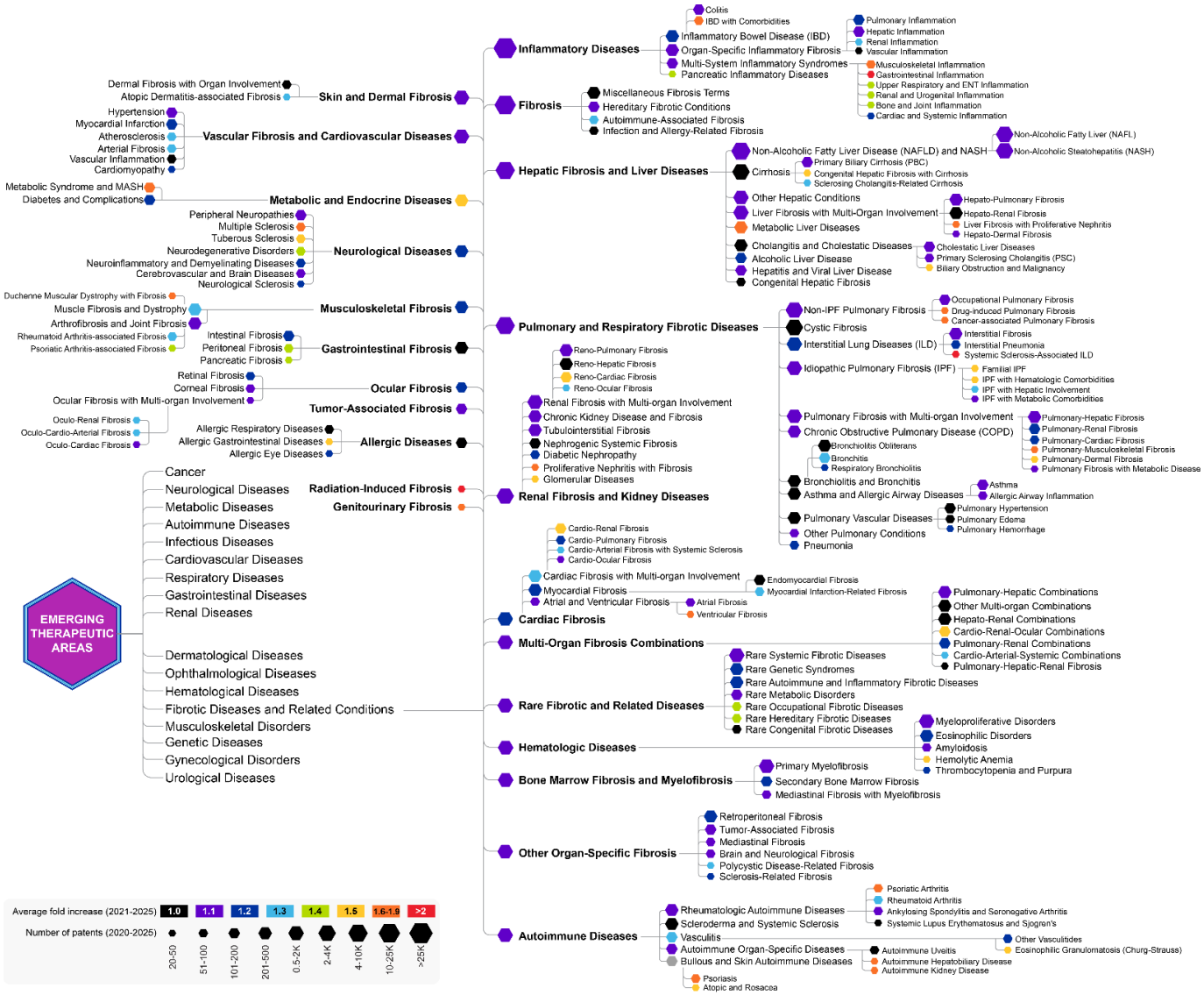


Figure 51. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on fibrotic diseases and related conditions, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Non-IPF pulmonary fibrosis (1.1X) similarly indicates continued refinement beyond pirfenidone and nintedanib, addressing progressive fibrosing phenotypes across interstitial lung disease spectrum.

Musculoskeletal Disorders: The musculoskeletal disorder patent landscape demonstrates strategic emphasis on rare genetic conditions and specialized inflammatory pathologies, with limited high-growth areas in common degenerative diseases (**Figure 52**). *Mooren ulcer*[934] (>2X) shows exceptional growth despite minimal patent volumes, representing a rare peripheral ulcerative keratitis with musculoskeletal autoimmune associations. *Myotonic dystrophy type 1*[935] (1.3X) and *juvenile idiopathic arthritis*[936] (1.3X) reflect focused innovation in genetic neuromuscular disease[935] and pediatric rheumatology,[937] respectively, where disease-modifying approaches remain limited.

Bone and muscle inflammatory conditions show consistent moderate growth: *Osteitis/hyperostosis/Paget's disease*,[938] *myositis/polymyositis*,[939] and *cartilage degeneration*[940] (all 1.2X) indicate targeted efforts in specific pathological mechanisms. Rare musculoskeletal disorders attract considerable attention, with *osteogenesis imperfecta*[941] and *familial adenomatous polyposis*[942] (both 1.2X) reflecting orphan drug development strategies where gene therapy, ASOs, and precision approaches enable previously impossible interventions.

Major musculoskeletal diseases maintain substantial volumes with minimal growth: *Osteoarthritis* (1.1X), *osteoporosis* (1X), *sarcopenia* (1X), and the entire **muscular dystrophy** branch (1X) reflect mature or challenging therapeutic landscapes. *Spinal muscular atrophy* (1.1X) shows modest growth despite transformative gene therapy and ASO successes,[943] suggesting market saturation following recent breakthrough approvals rather than declining interest.

Genetic Diseases: The genetic disease patent landscape demonstrates unprecedented innovation in ultra-rare conditions previously considered therapeutically intractable, likely enabled by gene therapy, ASOs, and enzyme replacement strategies (**Figure 53**). *Huntington's disease*[944,945] (>2X) represents a fast-growing area, reflecting multiple gene silencing approaches targeting HTT mRNA,[946] despite modest patent volumes in this devastating neurodegenerative condition lacking disease-modifying therapies.

Metabolic genetic disorders show exceptional activity: *Homocystinuria*[947] and *hypophosphatasia*[948] (both 1.6-1.9X), alongside *sulfatase deficiency*[949] and *lipid metabolism disorders*[950] (both 1.4X), demonstrate systematic targeting of inborn errors of metabolism through enzyme replacement, substrate reduction, and gene therapy modalities. Skeletal dysplasias attract intensified attention, with *chondrodysplasias*[951] (1.4X) benefiting from improved understanding of bone mineralization and growth plate biology.

Rare neurogenetic and lysosomal storage disorders show variable growth: *Kleine-Levin syndrome*[952] (1.6-1.9X), *fatal familial insomnia*[953] (1.5X), and specific *mucopolysaccharidoses* such as *Morquio*[954] and *Maroteaux-Lamy syndromes*[949] (both 1.2X) appear to be growing relatively fast indicating targeted development in rare populations where orphan designations and regulatory incentives enable commercial viability though patent volumes remain relatively small.

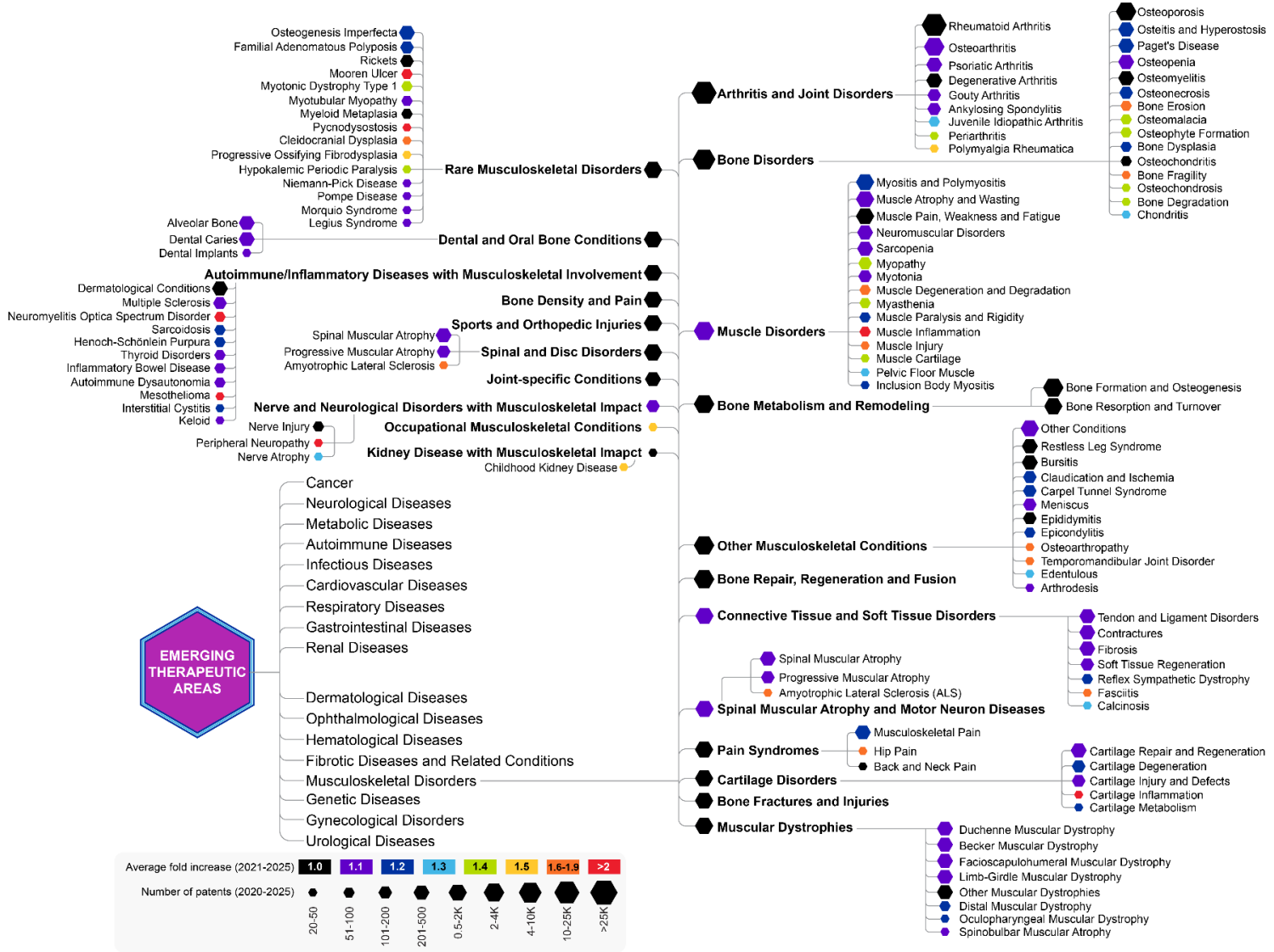


Figure 52. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on musculoskeletal diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

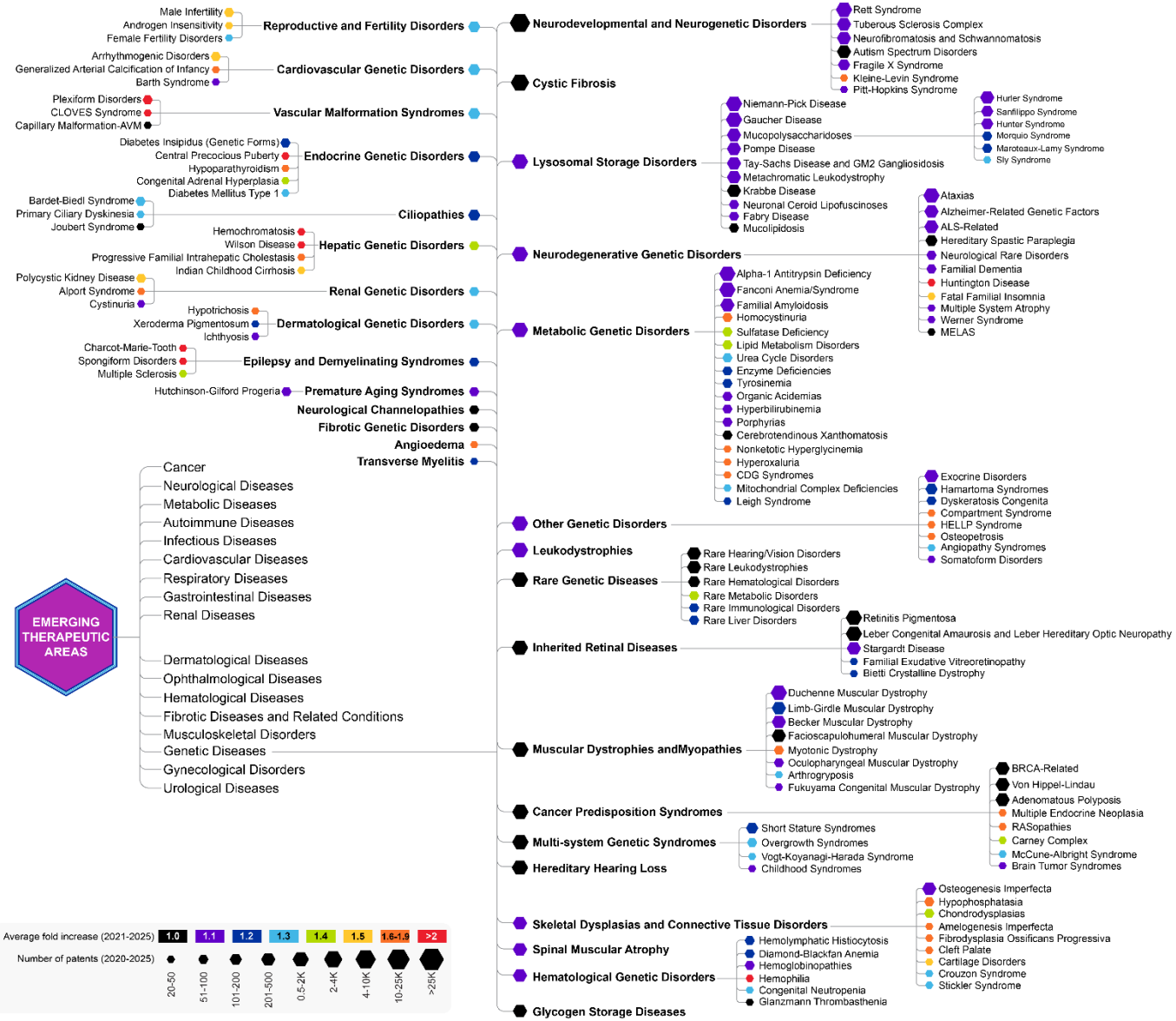


Figure 53. CAS TrendScape map of emerging topics in terms of therapeutic areas focused on genetic diseases, identified using NLP-based analysis of ~368 thousand patent publications from the CAS Content Collection for the period 2020-2025.

Established genetic disease programs maintain steady innovation: *Duchenne muscular dystrophy* (1.1X), major **lysosomal storage diseases** such as *Niemann-Pick*, *Gaucher*, *Pompe* (all 1.1X), and *α1 antitrypsin deficiency* (1.1X) demonstrate sustained refinement following first-generation therapies, pursuing improved efficacy, CNS penetration, and manufacturing efficiency in competitive rare disease markets.

Our comprehensive patent landscape analysis reveals a pharmaceutical innovation ecosystem undergoing fundamental transformation. The >1,700 emerging therapeutic areas identified demonstrate strategic diversification beyond traditional blockbuster targets toward precision medicine approaches, rare disease mechanisms, and previously intractable pathologies. High-growth areas concentrate in mechanistically defined conditions amenable to novel modalities including gene therapies, ASOs, targeted protein degradation, and advanced biologics.

The analysis reveals striking heterogeneity across therapeutic categories. Fibrotic diseases and genetic disorders exhibit exceptionally broad emergence spanning multiple organ systems, while infectious and urological diseases show constrained innovation reflecting mature therapeutic landscapes. Oncology, despite maintaining large patent volumes, demonstrates evolutionary rather than revolutionary growth, with innovation concentrated in rare lymphoma subtypes and molecularly defined tumor categories rather than major cancer types. Metabolic diseases and autoimmune conditions demonstrate differentiation strategies focusing on organ-specific manifestations and rare subtypes beyond established high-volume indications. Critically, major diseases maintaining modest growth rates with substantial patent volumes indicate continued commercial significance requiring meaningful differentiation.

6.2 Oncology patents lead as pharmaceutical innovation concentrates in major disease areas

Analysis of pharmaceutical patents by disease area provides a structured framework for examining patenting activity across therapeutic indications, enabling comparison of patterns across disease areas and over time.

The distribution of pharmaceutical patents across major disease categories reveals a clear concentration of innovation activity in a limited number of therapeutic areas (**Figure 54A**). Cancer constitutes the largest share of patent filings (approximately 15%), underscoring its continued prominence in pharmaceutical innovation. This pattern is consistent with high unmet medical need, favorable regulatory pathways, and strong commercial incentives associated with oncology drug development. Infectious diseases (9%), neurological disorders (8%), and immune-mediated diseases (7%) also represent substantial portions of the patent landscape, reflecting sustained efforts to address antimicrobial resistance, neurodegenerative conditions, and chronic inflammatory diseases.

Metabolic, gastrointestinal, respiratory, cardiovascular, endocrine, and musculoskeletal disorders each contribute moderate albeit smaller shares (approximately 5-6%), indicating continued innovation activity that is distributed across a broader range of therapeutic areas. In contrast, gynecological, oral and ENT, psychiatric, and nutritional disorders account for relatively smaller fractions of patent filings, likely reflecting variation in disease complexity, market size, and the anticipated commercial returns associated with drug development, which influence investment

priorities. In addition, innovation in certain areas is more frequently characterized by non-pharmaceutical interventions or incremental therapeutic improvements rather than the development of novel drug entities.

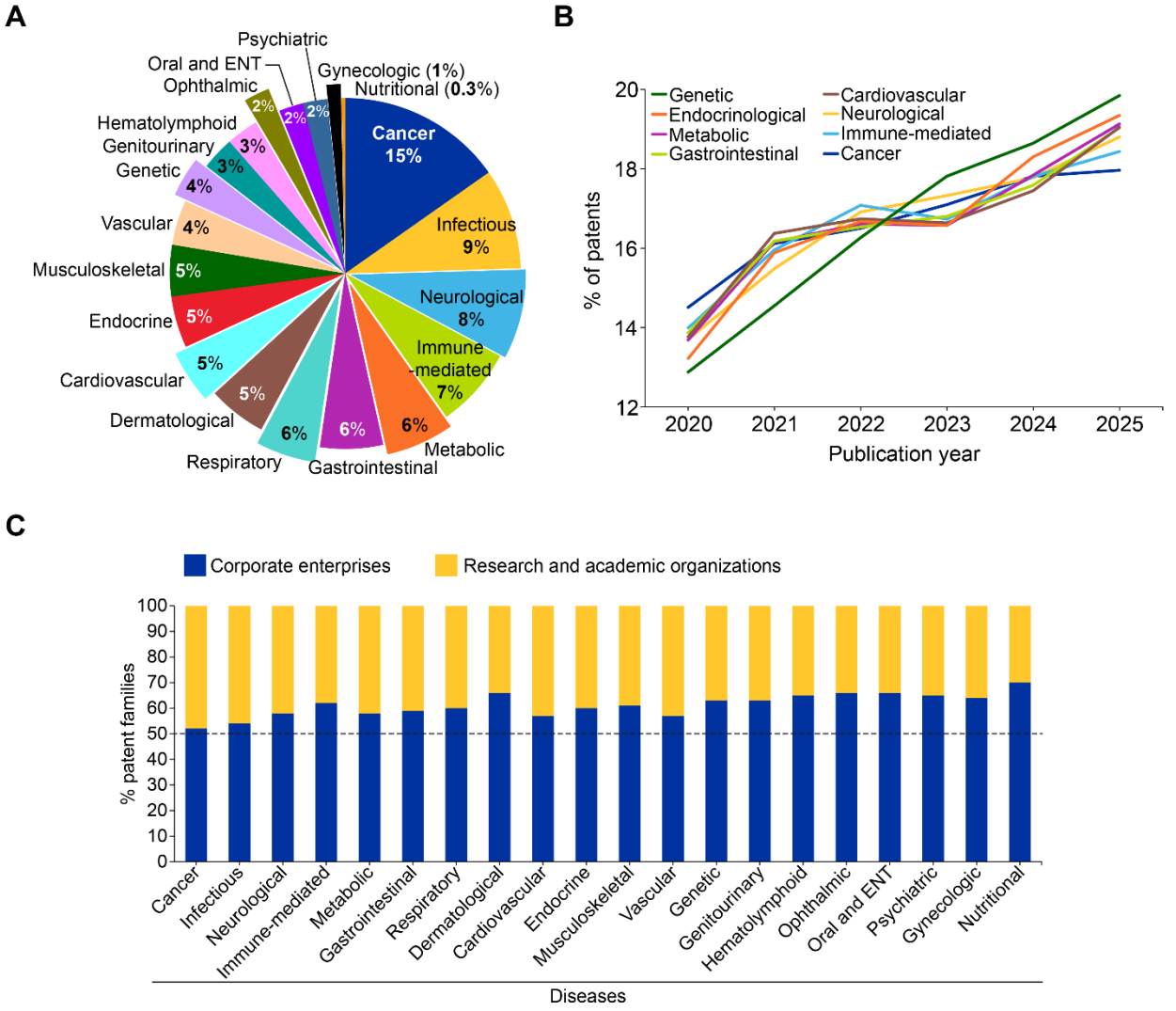


Figure 54. (**A**) Disease-wise distribution and (**B**) publication trends of pharmaceutical patents for selected diseases. (**C**) Distribution of pharmaceutical patents filed by corporate enterprises and research and academic institutions across disease categories. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Temporal analysis indicates that across major therapeutic indications, patenting activity follows a stable and progressive trajectory, suggesting continuity in research and development efforts rather than short-term fluctuations (**Figure 54B**). The absence of sharp inflection points or abrupt shifts among disease areas indicates that innovation has been sustained within established therapeutic domains, supported by incremental advances, platform refinements, and continued target exploration.

Analysis of patent assignees across disease categories provides insight into the relative contributions of different innovation stakeholders (**Figure 54C**). Across most disease areas,

corporate entities account for approximately 55-70% of patent filings, highlighting the central role of industry in advancing discoveries toward commercially viable therapies. This trend is evident in cancer, metabolic, and immune-mediated diseases, where high development costs and late-stage clinical translation demand substantial infrastructure and investment. At the same time, research institutes, including academic and public-sector research organizations, consistently contribute 30-45% of patent activity. Their involvement reflects the importance of early-stage research, particularly in disease areas driven by fundamental biology, target discovery, and platform innovation rather than immediate product development. This distribution underscores a pipeline continuum in which academic discoveries provide the foundation for subsequent industrial refinement, development, and commercialization.

Examining disease-area distributions within the patent portfolios of leading organizations offers insight into how their portfolios align innovation with strategic focus (**Figure 55**). Large multinational pharmaceutical companies such as Roche, Pfizer, Novartis, Johnson & Johnson, AstraZeneca, Eli Lilly & Co, Amgen, and Bristol-Myers Squibb display broad disease coverage, with prominent representation in cancer, immune-mediated, metabolic, and neurological disorders. This diversified distribution reflects long-standing R&D strategies and sustained investments in complex disease areas requiring extensive clinical development and global commercialization capabilities.

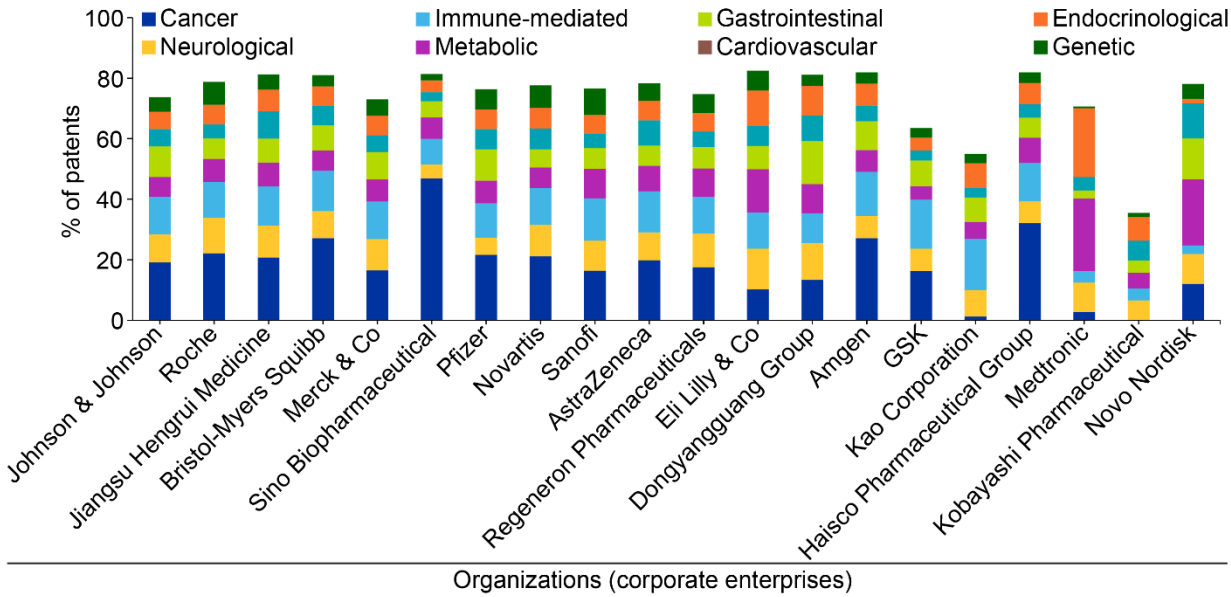


Figure 55. Distribution of patents across eight key disease areas for leading pharmaceutical corporate enterprises. Data includes pharmaceutical patent families from the CAS Content Collection for the period 2020-2025.

Several high patent-holding companies from rapidly expanding pharmaceutical markets, including Jiangsu Hengrui Medicine, Sino Biopharmaceutical, and Haisco Pharmaceutical Group, also demonstrate heterogeneous disease portfolios spanning oncology, metabolic, and infectious diseases. Sino Biopharmaceutical, however, exhibits a stronger emphasis on oncology, with patent activity focused on solid tumors such as lung, breast, and gastrointestinal cancers, reflecting a strategic prioritization aligned with high-incidence disease areas and targeted therapy development. Similarly, Shenzhen Dongyangguang Group shows a notable concentration in

gastrointestinal and hepatology-related diseases, particularly hepatitis-associated liver disorders and antiviral therapies, consistent with its research focus on infectious and liver diseases. Dongyangguang Group stands out for its high gastrointestinal patent share relative to its overall portfolio, indicating a distinct therapeutic concentration. This gastrointestinal component is primarily associated with hepatology-related diseases, particularly hepatitis-associated liver disorders and antiviral therapies, consistent with the company's broader focus on infectious and liver diseases. Such distributions are consistent with evolving R&D strategies shaped by regional healthcare needs and expanding innovation capacity. GSK's portfolio shows a significant emphasis on infectious diseases (approximately 28%), including viral and bacterial indications such as influenza, respiratory syncytial virus (RSV), HIV, and other vaccine-preventable infections. The remaining share is distributed across cancer, immune mediated, metabolic, and neurological disorders, indicating diversification beyond its traditional strength in vaccines and anti-infectives.

In contrast, companies such as Kao Corporation, Medtronic, and Kobayashi Pharmaceutical exhibit stronger patent representation in domains aligned with their core business areas rather than oncology. Kao Corporation's patent activity is concentrated in consumer products and specialty chemicals, including cosmetics, personal care formulations, surfactants, absorbent materials, and dermatology-related technologies. Medtronic's portfolio is dominated by endocrinology and metabolic disorders, driven by its leadership in diabetes management technologies, including insulin pump systems, continuous glucose monitoring (CGM) devices, and integrated or automated insulin delivery platforms. These device-based innovations are complemented by broader, minimally invasive, and implantable systems for managing chronic metabolic and cardiovascular conditions. Kobayashi Pharmaceutical focuses on over-the-counter medicines, supplements, gastrointestinal health, and lifestyle-related products, reflecting an emphasis on consumer healthcare and everyday health management. This strong orientation toward consumer health products, rather than high-intensity therapeutic areas such as oncology or complex chronic diseases, likely contributes to its lower representation across major disease categories in the figure.

These patterns illustrate how disease-area patent distributions among leading patent holders closely align with organizational focus and product portfolios.

Our disease-centric patent analysis reveals a pharmaceutical innovation landscape characterized by strategic concentration in high-value therapeutic areas, sustained growth trajectories across major disease categories, and complementary contributions from corporate and academic stakeholders.

7. Charting the future of pharmaceutical innovation through patent intelligence

The comprehensive analysis of 368,000 pharmaceutical patents filed between 2020 and 2025 presented in this report reveals fundamental shifts in pharmaceutical R&D characterized by unprecedented therapeutic modality diversity, expansion into previously "undruggable" target space, and integration of cutting-edge technologies reshaping drug discovery foundations.

The 2,000+ emerging molecular targets across eight CAS TrendScape maps demonstrate unprecedented expansion beyond traditional druggable proteins, with innovation extending to transcription factors, protein-protein interactions, and scaffolding proteins enabled by novel mechanisms including targeted degradation. The 1,700+ emerging disease areas spanning 17 therapeutic categories across 14 disease-focused CAS TrendScape maps reveal striking diversity: while oncology dominates absolute volumes, the fastest growth rates concentrate in non-oncological diseases such as fibrotic diseases, genetic disorders, and rare metabolic conditions where novel modalities unlock previously intractable biology. The 850+ therapeutic modality-related topics across four CAS TrendScape maps document accelerating diversification, with leading organizations now maintaining portfolios spanning five-to-seven distinct platforms versus two-to-three a decade ago, reflecting a strategic recognition that target biology rather than historical competency should drive modality selection. AI/ML applications accelerate from 9% of patents in 2020 to nearly 24% in 2025, evolving from experimental tools to foundational platforms reshaping target identification, lead optimization, and clinical trial design across all therapeutic areas.

7.1 Therapeutic modality diversification

The most striking finding is extraordinary therapeutic modality diversification shattering the traditional small molecule-biologics dichotomy into a spectrum of approaches, each with distinct advantages for specific targets and disease contexts.

Small molecules continue evolving beyond conventional enzyme inhibitors. Targeted protein degraders such as PROTACs represent genuine breakthroughs for previously undruggable targets lacking catalytic sites or binding pockets, validated by U.S. FDA approval of vepdegestrant in May 2026, with over 1,100 PROTAC-related patent families filed between 2020-2025 expanding from oncology into neurodegeneration, immunology, and metabolic disorders.

Biologics platforms have grown more sophisticated with antibody therapeutics evolving from simple mAbs into engineered constructs (bispecifics engaging two targets, trispecifics orchestrating complex cellular interactions, ADCs delivering potent payloads with exquisite selectivity). The ADC field alone accounts for over 5,600 patent families, with innovation distributed across targeting antibodies, cytotoxic payloads, and critical linker technologies. RNA therapeutics have exploded beyond COVID-19 mRNA vaccines, with patents covering mRNA for protein replacement, circRNA for sustained expression, RNAi for gene silencing, and ASOs with novel chemical modifications.

Cell and gene therapies represent radical departures from conventional paradigms. CAR-T therapies, while concentrated in hematologic malignancies, show patent expansion into solid tumors with engineering innovations addressing immunosuppressive microenvironments. Beyond CAR-T, the landscape reveals diversification into CAR-NK cells, TILs, TCR-T, and iPSC-derived

products. Gene therapy patents increasingly leverage CRISPR-Cas9 and next-generation base/prime editors for in vivo genetic correction.

Peptide therapeutics are experiencing a renaissance driven by chemical innovations overcoming poor pharmacokinetics and oral bioavailability limitations, exemplified by breakthrough oral formulations like Merck's MK-0616 addressing historical bioavailability limitations that confined peptides to injectable administration. Cyclic peptides, stapled peptides, and macrocyclic libraries feature prominently, with GLP-1 agonist success catalyzing investment in metabolic disease approaches using dual and triple agonist combinations.

Advanced delivery systems such as lipid nanoparticles for mRNA, refined viral vectors for gene therapy, and novel platforms including exosomes and VLPs command substantial patent activity as critical enabling technologies determining clinical viability of diverse payloads.

Emerging modalities including **microbiome-based therapeutics**, **radiopharmaceutical theranostics**, and **AI/ML in drug discovery** show remarkable early-stage patent activity.

7.2 Geographic innovation patterns and institutional dynamics

Patent filing patterns reveal distinct geographic specialization with strategic implications. China dominates accounting for nearly half of all pharmaceutical applications, with this dominance more pronounced in non-commercial filings, indicating robust academic research activity with evolving technology transfer efficiency. The United States represents a smaller fraction of total patents but shows greater contribution in terms of filings by corporate enterprises, reflecting superior translation from research to commercial products and stronger private-sector pharmaceutical infrastructure.

Leading patent holders demonstrate divergent strategies with organizations like Novo Nordisk show elevated external patent acquisition concentrated in RNAi technologies, multi-receptor agonists, and MASH therapeutics extending beyond core peptide franchises, while Sino Biopharmaceutical's external portfolio emphasizes ADCs and immuno-oncology biologics. These patterns indicate that even well-resourced organizations increasingly rely on external innovation to access platform technologies outside historical competencies, with acquisition analysis enabling identification of technology originators versus aggressive in-licensors.

The institutional diversity observed span Chinese pharmaceutical companies with government research institute origins, established Western multinationals, and specialized biotechnology firms creating a complex competitive landscape requiring sophisticated navigation of partnership, acquisition, and freedom-to-operate considerations.

7.3 Strategic imperatives for the next decade

1. Modality diversification is essential for addressing the full disease biology spectrum. Organizations maintaining capabilities across complementary platforms are likely to demonstrate greater resilience than single-platform competitors. The shift from platform-centric strategies tied to historical competencies toward target-driven approaches selecting optimal modalities based on biological mechanism represents a fundamental strategic evolution.
2. The expanding target landscape requires capabilities for difficult targets lacking obvious druggable features through innovative modalities like targeted protein degradation, molecular glues, and structure-guided peptide design. Organizations must invest in technologies and expertise enabling intervention beyond traditional orthosteric inhibition.
3. Data and computational capabilities represent increasingly important competitive differentiators. AI/ML's patent acceleration reflects integration across target identification, lead optimization, and clinical trial design. Organizations must invest in AI talent, infrastructure, and high-quality training data, with partnerships providing access to chemical and biological information breadth impossible to generate internally.
4. Geographic considerations are increasingly important, with China emerging as a major innovation center with distinct specializations and IP strategies requiring sophisticated navigation by global pharmaceutical companies.

As AI becomes increasingly embedded in drug discovery and invention workflows, it may introduce new complexities in pharmaceutical patenting. Recent legal decisions reaffirm that inventorship must be attributed to a natural person, even where AI contributes significantly to the inventive process. This highlights a potential misalignment between evolving innovation practices and current patent frameworks. In addition, as AI-generated output becomes more prevalent, practical considerations around disclosure and reproducibility may also emerge, influencing how future patent applications are drafted and assessed.

This report demonstrates how comprehensive patent intelligence, when integrated across the target-disease-modality framework and powered by the unique combination of exhaustive data coverage, scientific curation expertise, and advanced analytical capabilities at CAS, provides strategic insights essential for decision-making in an increasingly complex pharmaceutical landscape. Unlike conventional patent analytics focused on legal status and citation patterns, this approach extracts actionable intelligence from full patent specifications. Identifying specific protein targets being pursued, precise modality innovations being protected, and technology convergences signaling transformative opportunities.

The pharmaceutical innovation landscape documented here reveals an industry simultaneously diversifying across molecular targets, disease areas, and therapeutic modalities. The striking heterogeneity across diseases, modalities, and targets indicate that opportunities exist not uniformly but in specific niches. Organizations that master this integrated three-dimensional patent intelligence, understanding not just where competitors file patents but why certain disease-target-modality combinations demonstrate explosive growth while others plateau, will lead the next era of pharmaceutical innovation.

CAS is uniquely positioned to partner with pharmaceutical innovators in navigating this complexity, providing not just data but insights, analytics, and decision support tools that transform information into competitive advantage. The future of pharmaceutical R&D will be characterized by increasing diversity in modalities, targets, technologies, and geographic innovation centers, enabled by data and computation at unprecedented scales. With comprehensive patent intelligence grounded in scientific expertise, the patent landscape becomes not an obstacle, but a strategic map that reveals where the industry is headed and illuminating pathways to breakthrough innovation.

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List of Abbreviations

AAV	adeno-associated virus
ACE	angiotensin-converting enzyme
ADAM	A disintegrin and metalloproteinase
ADC	antibody-drug conjugate
ADCC	antibody-dependent cellular cytotoxicity
ADCP	antibody-dependent cellular phagocytosis
ADPKD	autosomal dominant polycystic kidney disease
AGE	advanced glycation end-product
AGO	argonaute
ALK	anaplastic lymphoma kinase
AMD	age-related macular degeneration
AML	acute myeloid leukemia
APO	apolipoprotein
AR	androgen receptor
ARDS	acute respiratory distress syndrome
ATR	ataxia telangiectasia and rad3-related
AUTAC	autophagy-targeting chimeras
B2M	β2-microglobulin
BCMA	B cell maturation antigen
BET	bromodomain and extra-terminal domain
bHLH	basic helix-loop-helix
BRAF	serine/threonine-protein kinase B-Raf
BTK	Bruton's tyrosine kinase
BTLA	B and T lymphocyte attenuator
C1QB	complement C1q B chain
CAF	cancer-associated fibroblast
CAR	chimeric antigen receptor
CD	cluster of differentiation
CDK	cylcin-dependent kinase
CEA	carcinoembryonic antigen
CGM	continuous glucose monitoring
CGRP	calcitonin gene-related peptide
CHIKV	Chikungunya virus
CHK	checkpoint kinase
circRNA	circular RNA
CK	casein kinase
CMV	cytomegalovirus
CNIPA	China National Intellectual Property Administration
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CRBN	cereblon
CRGP	calcitonin gene-related peptide
CRISPR	clustered regularly interspaced short palindromic repeats
CTLA-4	cytotoxic T-lymphocyte antigen-4
DAA	direct-acting antiviral
DAO	diamine oxidase
DAT	dopamine transporter
DCAF	DDB1- and CUL4-associated factors
DENV	Dengue virus
DGK	diacylglycerol kinase
DGN	diagnostics
DHODH	dihydroorotate dehydrogenase
DIC	disseminated intravascular coagulation
DLBCL	diffuse large B-cell lymphoma
DNA-PK	DNA-dependent protein kinase
DNMT	DNA methyltransferase
DPYSL2	dihydropyrimidinase-like 2
DR	death receptor
dsRNA	double strand RNA
DUB	Deubiquitinase
EAAT	excitatory amino acid transporter
EBOV	Ebola virus
EBV	Epstein-Barr virus
ECM	extracellular matrix
EGFR	epidermal growth factor receptor
ENT	ear, nose, and throat
EpCAM	epithelial cell adhesion molecule
EPO	European Patent Office
ER	estrogen receptor
FAK	focal adhesion kinase
FASN	fatty acid synthase
FGFR	fibroblast growth factor receptor
FLT3	FMS-like tyrosine kinase 3
FOP	fibrodysplasia ossificans progressiva
FOX	Forkhead box
FTO	fat mass and obesity-associated protein
GI	gastrointestinal
GIP	glucose-dependent insulinotropic polypeptide

GITR	glucocorticoid-Induced TNFR-Related protein
GLA	α-galactosidase
GPCR	G-protein coupled receptor
GPX4	glutathione peroxidase 4
GRB	growth factor receptor-bound
gRNA	guide RNA
GSI	gamma-secretase inhibitor
GSPT1	G1 to S phase transition 1
HAE	hereditary angioedema
HAT/KAT	histone acetyltransferase
HAV	hepatitis A virus
HBV	hepatitis B virus
HCV	hepatitis C virus
HDAC	histone deacetylase
HDV	hepatitis D virus
HER	human epidermal growth factor receptor
HEV	hepatitis E virus
HEY	hairy/enhancer-of-split related with YRPW motif
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HHV	human herpesvirus
HMG-CoA synthase	hydroxymethylglutaryl-CoA synthase
HPK1	hematopoietic progenitor kinase 1
HPV	human papilloma virus
HSC	hematopoietic stem cell
HSP	heat-shock protein
HSV	herpes simplex virus
HUS	hemolytic uremic syndrome
IBD	inflammatory bowel disease
ICI	immune checkpoint inhibitor
ICOS	inducible T-cell costimulator
IgA	immunoglobulin A
IgCAM	immunoglobulin superfamily cell adhesion molecule
ILC	innate lymphoid cell
ILD	inflammatory lung diseases
IMiD	immunomodulatory drugs
iNKT	invariant NKT cell
IPF	idiopathic pulmonary fibrosis
IRAK4	interleukin-1 receptor-associated kinase 4
ITCL	intestinal T-cell lymphoma
ITR	inverted terminal repeats
JAK	janus kinase
JPO	Japan Patent Office
KIPO	Korean Intellectual Property Office
KMT	histone lysine methyltransferase
KSHV	Kaposi sarcoma-associated herpesvirus
KSP	kinesin spindle protein
LAL	lysosomal acid lipase
LAMP	lysosome-associated membrane protein
LCAT	lecithin cholesterol acyltransferase
LNPs	lipis nanoparticles
LOX	lysyl oxidase
LYTAC	lysosome-targeting chimeras
MAIT	mucosal-associated invariant T cell
MALAT1	metastasis-associated lung adenocarcinoma transcript 1
MARV	Marburg virus
MAT2A	methionine adenosyltransferase 2α
MBD	methyl-CpG binding domain
MCL-1	myeloid cell leukemia-1
MDM2	mouse double minute 2
MDR	multidrug-resistant
MDSC	myeloid-derived suppressor cell
MEK	mitogen-activated protein kinase
METTL3	methyltransferase-like 3
MIF	macrophage migration inhibitory factor
miRNA	micro RNA
MMP	matrix metalloproteinase
MOF	metal-organic framework
mpox	monkey pox
mRNA	messenger RNA
MSC	mesenchymal stem cell
MSI-H	microsatellite instability-high
MSLN	mesothelin
NAFLD	non-alcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
NET	norepinephrine transporter
NFAT	nuclear factor of activated T cells
NK cell	natural killer cell
NLP	natural language processing
NLRC4	NOD-like receptor family CARD domain containing 4
NLRP3	NOD-like receptor protein 3
NNRTI	non-nucleoside reverse transcriptase inhibitors
NoV	Norovirus

NRTI	nucleoside reverse transcriptase inhibitors
NSE	neuron-specific enolase
NTCP	sodium/taurocholate cotransporting polypeptide
PAC	pharmacological
PAF	platelet-activating factor
PARG	poly(ADP-ribose)glycohydrolase
PARP	poly(ADP-ribose) polymerase
P-CAB	potassium-competitive acid blocker
PcG	polycomb group
PCOS	polycystic ovary syndrome
PCSK9	proprotein convertase subtilisin/kexin type 9
PCT	Patent Cooperation Treaty
PD-1	programmed death-1
PDC	peptide-drug conjugate
PDE4	phosphodiesterase 4
PD-L1	programmed death-ligand 1
PDPS	peptide discovery platform system
PDT	photodynamic therapy
PEG	polyethylene glycol
PET	Positron emission toimography
PI3K	phosphoinositide 3-kinase
piRNA	piwi-interacting RNA
PKT	pharmacokinetic
PLN	phospholamban
PLpro	papain-like protease
POI	protein of interest
PPAR	peroxisome proliferator-activated receptor
PPBP	pro-platelet basic protein
PPI	protein-protein interaction
PRC	polycomb repressive complex
PRMT	protein arginine methyltransferase
PROTAC	proteolysis targeting chimera
PRPS	phosphoribosyl pyrophosphate synthetase
PRR	pattern recognition receptor
PSMA	prostate-specific membrane antigen
RBP	retinol binding protein
RET	rearranged suring transfection
RISC	RNA-induced silencing complex
RNAi	RNA interference
ROCK	rho-associated protein kinase
RSV	respiratory syncytial virus
RTK	receptor tyrosine kinase
SAA	serum amyloid protein
SAM	S-adenosylmethionine
SARM1	sterile alpha and TIR motif-containing protein 1
saRNA	self-amplyfying RNA
SCD	stearoyl-CoA desaturase
SHBG	Sex hormone-binding globulin
siRNA	small interfering RNA
SLC	solute carrier
SLE	systemic lupus erythematosus
snoRNA	small nucleolar RNA
snRNA	small nuclear RNA
SOS1	son of sevenless 1
SPECT	single-photon emission computed tomography
SPHK	sphingosine kinase
SPTCL	subcutaneous panniculitis-like T-cell lymphoma
SQLE	squalene epoxidase
ssRNA	single strand RNA
STAT	signal transduction-activated transcription
STING	stimulator of interferon genes
SYK	spleen tyrosine kinase
TAM	tumor-associated macrophage
TAN	tumor-associated neutrophil
TB	tuberculosis
TBG	thyroxine-binding globulin
TDO2	tryptophan 2,3-dioxygenase
TFPI	tissue factor pathway inhibitor
THU	therapeutic
TIGIT	T cell immunoreceptor with Ig and ITIM domain
TIL	tumor-infiltrating lymphocytes
TIPARP	TCDD-inducible poly-ADP-ribose polymerase
TLR	toll-like receptor
TME	tumor microenvironment
TNFRSF	TNF receptor superfamily
Treg	regulatory T cells
TREM	triggering receptors expressed on myeloid cells
TSC	tuberous sclerosis complex
ULK	unc-51-like autophagy activating kinase
UPR	unfolded protein response
USPTO	United States Patent and Trademark Office
VEGF	vascular endothelial growth factor
VHL	von Hippel-Lindau

VLP	virus-like particle
VMAT	vesicular monoamine transporter
VZV	varicella-zoster virus
WIPO	World Intellectual Property Organization
WNV	West Nile virus
WRN	Werner syndrome RecQ helicase-like
XDR	extensively drug-resistant
YFV	Yellow fever virus
ZIKV	Zika virus

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