EXECUTIVE INSIGHTS

Is Biopharma Doing Enough to Advance Novel Targets?

Key takeaways

- About a quarter of the approximately 13,600 drug-target pairs in the current preclinical and clinical R&D pipeline are concentrated around just 38 unique biological targets — highlighting significant crowding around select mechanisms.
- Despite a threefold increase in early- and midstage venture capital investment over the past decade and a growing overall R&D pipeline, the number of novel biological targets being tested each year has declined sharply — from around 100 prepandemic to just 30 in 2024. This trend suggests a shift in biopharma's risk appetite and more stringent investment criteria for novel target exploration.
- While novel target R&D remains active in key therapeutic areas such as oncology, immunology, neuroscience and metabolism, there may still be room for more novel target investment across therapeutic areas given the level of pipeline crowding, the reduction in new pipeline target entry and the volume of unexplored biology.
- To enable the discovery of more innovative therapies with the potential for significant clinical impact, the biopharma industry needs to rebalance investment priorities toward underexplored novel targets that could drive greater clinical outcomes.

Introduction

R&D leaders devote substantial effort to selecting therapeutic targets, carefully assessing their associated risk profiles. A key strategic trade-off often emerges: develop drugs against well-established targets — with typically lower risk in early development but potentially higher commercial risk due to crowded competition — or pursue novel biological targets, which carry greater scientific uncertainty but offer stronger differentiation and the potential for first-to-market advantage.

In recent years, the biopharma industry appears to have leaned toward known targets, limiting investment in novel mechanisms. In this edition of *Executive Insights*, L.E.K. Consulting examines whether the industry is striking the right balance between refining known pathways and exploring uncharted biology to address unmet patient needs. We share findings that point to target crowding, outline limitations in recent target innovation and assess the strategic implications for future pipeline planning.

Concentrated R&D efforts on a few targets

By the end of 2024, approximately 10,000 drugs with known target activity were in the preclinical and clinical R&D pipeline. Accounting for drugs with multiple targets (e.g., bispecifics), this corresponded to around 13,600 unique drug-target pairs. To understand how these biological targets shape pharmaceutical R&D activity, all unique targets were extracted and categorized based on underlying drug activity.

About 2% of active R&D targets — 38 targets in total — were associated with 50 or more drugs. Despite representing a small number of total targets, the 38 highly developed targets account for roughly one quarter of the entire preclinical and clinical R&D pipeline — highlighting substantial crowding among a limited set of biological mechanisms (see Figures 1a and 1b).

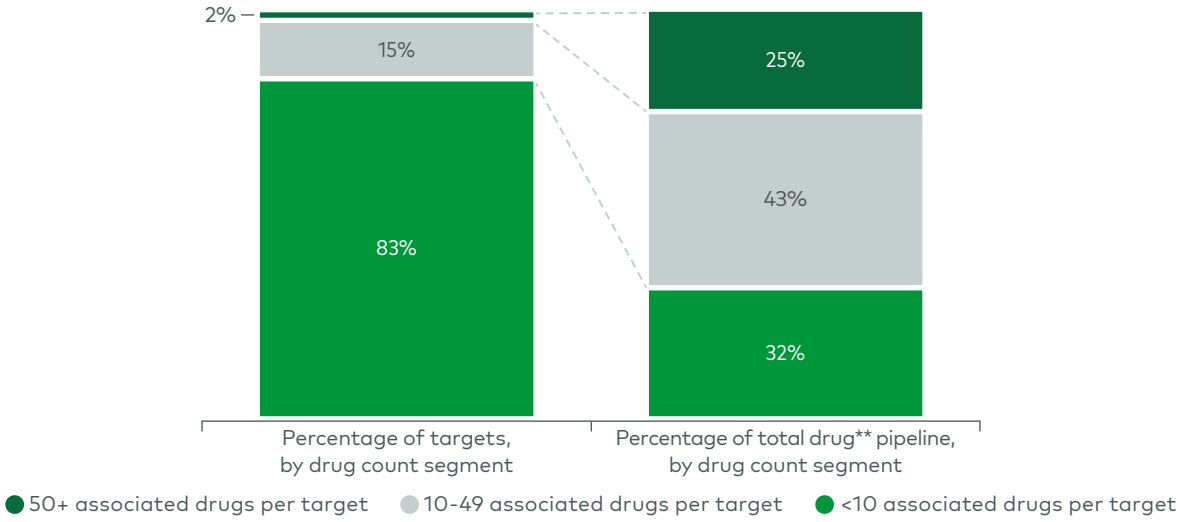
The concentration of drug development around a small number of established targets is likely driven by the high scientific risk of pursuing novel targets, coupled with the lower risk and greater clinical familiarity of known targets. These well-characterized targets serve as a foundation for continued innovation through scientific and clinical enhancements. As a result, the ecosystem around known targets has become increasingly crowded through various entry and expansion strategies, including:

1. **Alternative target modulation** — Using similar compounds to engage different regions of a protein (e.g., targeting distinct epitopes or developing allosteric vs. competitive inhibitors) to optimize efficacy and safety
2. **New modalities or delivery systems** — Developing a new therapeutic agent to more successfully modulate a disease target, leading to a stronger clinical outcome (e.g., using a new modality to perturb a disease target or pathology at a different macromolecular or cellular stage, developing a more patient-friendly route of administration, or developing a fixed-dose combination that reaches multiple targets in one therapy)

3. **Precision medicine approaches** — Applying detailed patient stratification based on genetic or biomarker profiles to match therapies with those most likely to benefit, increasing efficacy and reducing risk

4. **Indication and therapeutic area expansion** — Extending known targets into new indications or disease areas to meet additional unmet needs, whether through life cycle management of existing drugs or development of new ones in novel settings

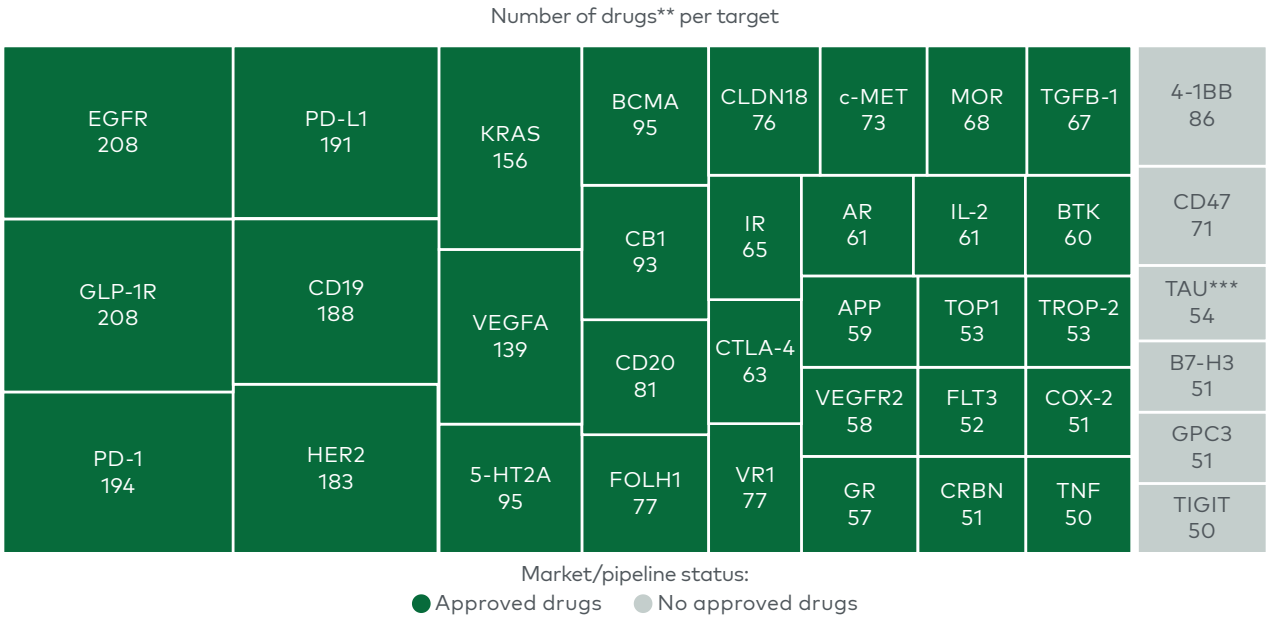
Figure 1a
Worldwide preclinical and clinical R&D pipeline activity* (2024)



Note: *Based on preclinical and clinical pipeline activity. Unspecified / Not applicable targets excluded from analysis (~11,000 associated drugs with Unspecified or Not applicable target pairs). CD3 (~240 associated drugs) excluded from the since CD3 mechanism is not commonly the primary target of drug (e.g., bispecific molecules); **Drugs with multiple targets are counted individually for each associated target. ~10,000 unique drugs are associated with known targets. The ~10,000 drugs represented here along with the drugs having Unspecified / Not applicable targets sum to the ~21,000 drugs in the R&D pipeline
Source: Citeline Pharmaprojects (January 2025)

Figure 1b

Worldwide preclinical and clinical R&D pipeline targets with 50+ associated drugs* (2024)



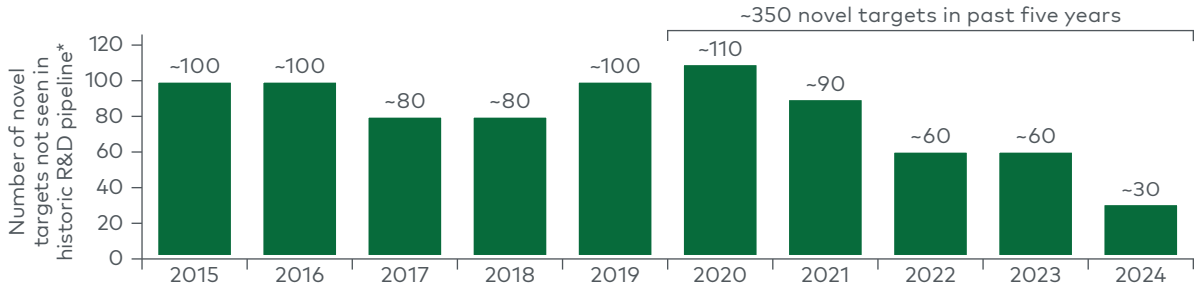
*Based on preclinical and clinical pipeline activity; unspecified/not applicable targets excluded from analysis (~11,000 associated drugs with unspecified or not applicable target pairs); CD3 (~240 associated drugs) excluded from the since CD3 mechanism is not commonly the primary target of drug (e.g., bispecific molecules)
**Drugs with multiple targets are counted individually for each associated target; ~10,000 unique drugs are associated with known targets; the ~10,000 drugs represented here along with the drugs having unspecified/not applicable targets sum to the ~21,000 drugs in the R&D pipeline
***Not including approval of a diagnostic tau product
Source: Citeline Pharmaprojects (January 2025)

Pipeline gap in novel targets

The annual rate at which novel targets enter the pipeline has dropped significantly — from around 100 a decade ago to just 30 in 2024. This decline in early-stage innovation isn't due to a lack of new drugs in development or reduced early-stage venture capital funding. In fact, the overall R&D pipeline has nearly doubled in size, growing from approximately 11,000 active drug programs in 2015 to about 21,000 by the end of 2024, even after accounting for product launches, program pauses and terminations. At the same time, Series A investment in early-stage life sciences companies has grown steadily, averaging around 18% annual growth over the past 10 years, with increasing average investment across a smaller number of companies being funded (see Figure 2).

Figure 2

Worldwide preclinical and clinical R&D pipeline and life sciences Series A VC investment (2015-24)



	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Total R&D drug pipeline**	~10.8K	~12.1K	~13.0K	~13.5K	~14.8K	~15.8K	~17.1K	~18.4K	~19.4K	~20.8K
Series A biopharma investment***	$4B	$4B	$5B	$9B	$8B	$11B	$17B	$12B	$10B	$11B
Series A funded companies***	298	327	335	454	428	503	684	486	387	304

*A novel target is defined as a target first identified in the preclinical/clinical pipeline during the recorded year
**Represents the total number of drugs with active preclinical Phase 1, Phase 2 and Phase 3 presence
***Includes all completed and announced/in progress Series A, B and C global venture capital investor deals (primary investor type only) classified within the life sciences industry
Source: Citeline Pharmaprojects (January 2025); PitchBook Data Inc. (January 2025)

Roughly 350 novel targets entered the R&D pipeline between 2020 and 2024, with most being pursued in oncology, immunology, metabolism and neuroscience. A closer look reveals six core mechanistic categories driving this wave of biological innovation:

1. Cell fate and differentiation
2. Cell metabolism and clearance
3. Enzymatic modification
4. Immune cell balance
5. Neuron plasticity and activation
6. Protein catabolism

These mechanisms span diverse biological functions, but the targets associated with them remain largely early-stage — about 70% are still in preclinical development, including examples such as ALKBH5 and YTHDC1. The remaining approximately 30% have advanced to the clinic, primarily in Phase 1 trials, with targets such as LY6G6D and NEK7. As this biology continues to mature, deeper scientific assessment of these mechanistic areas is warranted to uncover high-potential innovation opportunities (see Figure 3).

Figure 3
Novel R&D targets by mechanism category (2020-24)

Mechanism category*	Example biological process**	Example notable target
1 Cell fate and differentiation	Chromatin remodeling	YTHDC1
	Negative regulation of cell differentiation	MYH10
2 Cell metabolism and clearance	Apoptotic cell clearance	TYROBP
	Regulation of autophagy	ALKBH5
3 Enzymatic modification	Protein phosphorylation	NEK7
	Regulation of catalytic activity	WARS1
4 Immune cell balance	Regulation of leukocyte-mediated immunity	CD84
	Stimulatory killer cell immunoglobulin-like receptor signaling pathway	LY6G6D
5 Neuron plasticity and activation	Neuron development	STMN2
	Regulation of axonogenesis	GRIK2
6 Protein catabolism	Positive regulation of catabolic process	STK11
	Positive regulation of proteolysis involved in catabolic process	QSOX1

Note: *Mechanism categories have been developed by leveraging a Gene Ontology (GO) Term analysis of 2020-2024 new R&D pipeline targets with the Panther 19.0 database. Identified GO biological processes were characterized and grouped into the six shown mechanism categories; **Targets may have biological overlap between different mechanism categories
Source: Citeline Pharmaprojects (January 2025); PubMed Journal Archive; Ashburner et al. Nat Genetics. 2000; The Gene Ontology Consortium. Genetics. 2023

Toward a more balanced R&D portfolio

Our data shows that the biopharma industry is becoming increasingly cautious in its clinical target selection. While refining known biology remains valuable, the current focus on a narrow set of well-characterized targets is leading to inefficient capital deployment. This crowding signals a broader imbalance — prioritizing familiar, lower-risk mechanisms over novel approaches that may offer greater long-term potential. As a result, even technically strong programs often struggle to differentiate clinically or commercially, with true differentiation emerging only after significant late-stage investment — raising the risk of redundancy.

The upside? There's still significant untapped potential in novel and underexplored targets. Despite persistent unmet needs, around 55% of the 4,500 druggable proteins in the human genome remain untouched by drug development (Finan et al., 2017). While not all will prove viable, scientific advances are steadily expanding the boundaries of druggable space.

Realizing this potential will require rigorous scientific vetting and targeted investment. Emerging technologies — such as artificial intelligence-driven discovery and in silico experimentation — provide powerful tools for derisking novel biology earlier and more cost-effectively. Equally critical is strategic collaboration among leading biopharma companies, emerging biotechs and academic institutions to foster smarter risk-taking and increase pipeline momentum around novel, first-in-class targets.

To remain competitive and deliver meaningful innovation, the industry must rebalance its approach — embracing bold science, advanced technologies and collaborative models that unlock the next wave of high-impact targets and transformative therapies.

For more information, please contact us.

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