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Life Sciences Practice

What early-stage investing reveals about biotech innovation

Public funding for biotech remains tenuous, but in 2022 and 2023 venture capitalists have continued to pour money into innovative platforms that could revolutionize the sector.

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In recent years, biotech public markets have struggled to stage a meaningful comeback. The S&P Biotechnology Select Industry Index entered fourth quarter 2023 more than 50 percent lower than its peak in February 2021, and only 30 biotechs have undergone an IPO in the first three quarters of 2023 versus 114 IPOs in 2021 (Exhibit 1).[1] Total biotech IPO funding has dropped dramatically, with only $3.4 billion raised in the first three quarters of 2023 versus $16.0 billion in the first three quarters of 2021.[2] In response to this difficult environment, more than 250 biotechs have initiated layoffs in 2022 and 2023. Many of these companies have also streamlined their project pipelines to safeguard their available cash runway.[3]

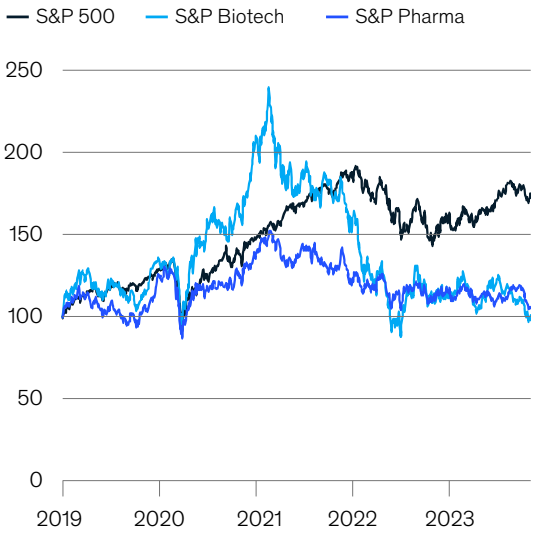
Amid a challenging public-market environment, venture capital (VC) funding has provided a much-needed lifeline to fuel biotech innovation. Despite also registering a decline after peaking in 2021, with several investments occurring in down or flat rounds,[4] VC funding has consistently remained

[1] S&P Capital IQ, accessed October 2023.
[2] Ibid.
[3] Annalee Armstrong, Max Bayer, and Gabrielle Masson, "Fierce Biotech Layoff Tracker 2023: Novavax to cut more staff in new $300M savings plan; Regenxbio, Gilead and more," Fierce Biotech, November 9, 2023.
[4] Gabrielle Masson, "After pandemic sugar rush, a market 'hangover' opens biotech to funding approaches steeped in stigma," Fierce Biotech, October 9, 2023.

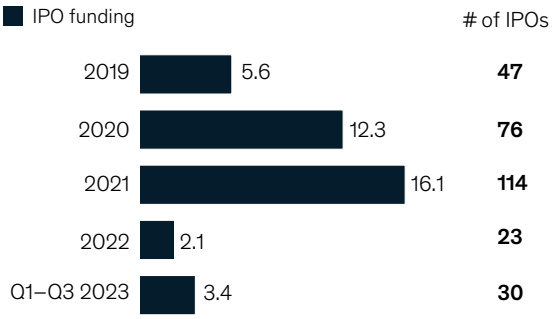
Exhibit 1

Biotech stock valuations and IPO funding have declined significantly since peaking in 2021.

Performance of the S&P Biotech index 2019–H1 2023,[1] total gross return, index (Jan 2019 = 100)



Biotech IPO funding 2019–Q3 2023, total investment, $ billion



Note: Chart includes IPOs > $10 million during 2019–Q3 2023, filtered for biotechnology industry; excludes nontherapeutic biotechs such as contract and research services, industrial biotechnology, and food and agriculture.
[1]Tickers include SPX (S&P 500), XPH (SPDR S&P Pharmaceuticals ETF) and XBI (SPDR S&P Biotech ETF)
Source: McKinsey analysis based on PitchBook, Inc. and S&P Capital IQ data, accessed Oct 2023; has not been reviewed by Pitchbook or Capital IQ analysts

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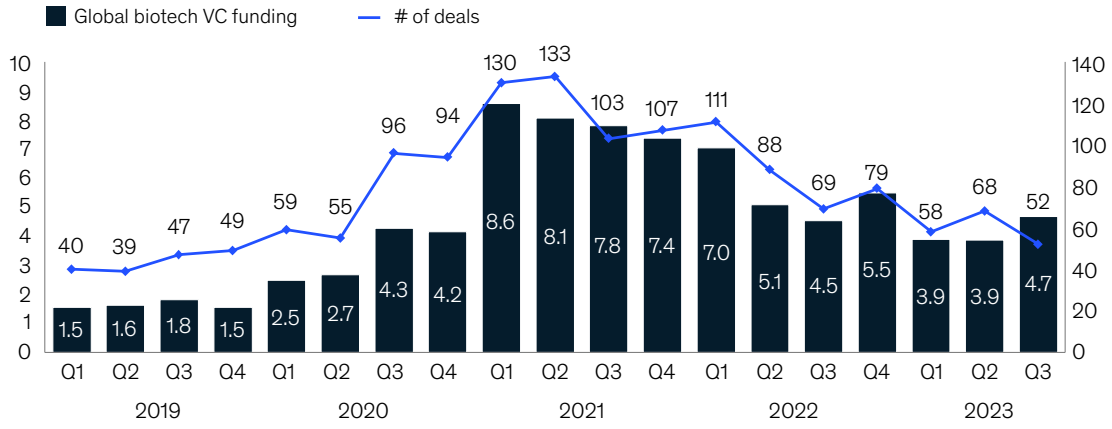
robust and elevated above prepandemic levels (Exhibit 2). In 2022, start-ups secured more than $22 billion in funding across early- and late-stage rounds from venture capitalists; 2023 is also shaping up to be a solid year, with more than $12 billion raised through quarter three. Overall declines have largely been driven by a lower number of deals, while median deal size has remained consistent. Investors continue to favor innovation, with Series A funding rounds accounting for almost half of all deals (Exhibit 3).

Innovative platform technologies such as drug discovery enabled by machine learning (ML), cell therapies, and gene therapies have dominated biotech funding over the past few years because they typically promise to address a broad array of

Exhibit 2

Biotech venture capital funding has declined from all-time highs but remains above prepandemic levels.

Biotech venture capital (VC) funding Series A onwards, 2019–Q3 2023, total investment, $ billion; # of deals



Note: Chart includes deals > $10 million from Series A to Series I in privately held companies during 2019–Q3 2023; excludes nontherapeutic biotechs such as contract and research services, industrial biotechnology, and food and agriculture.
Source: McKinsey analysis based on PitchBook, Inc. data, accessed Oct 2023; has not been reviewed by Pitchbook analysts

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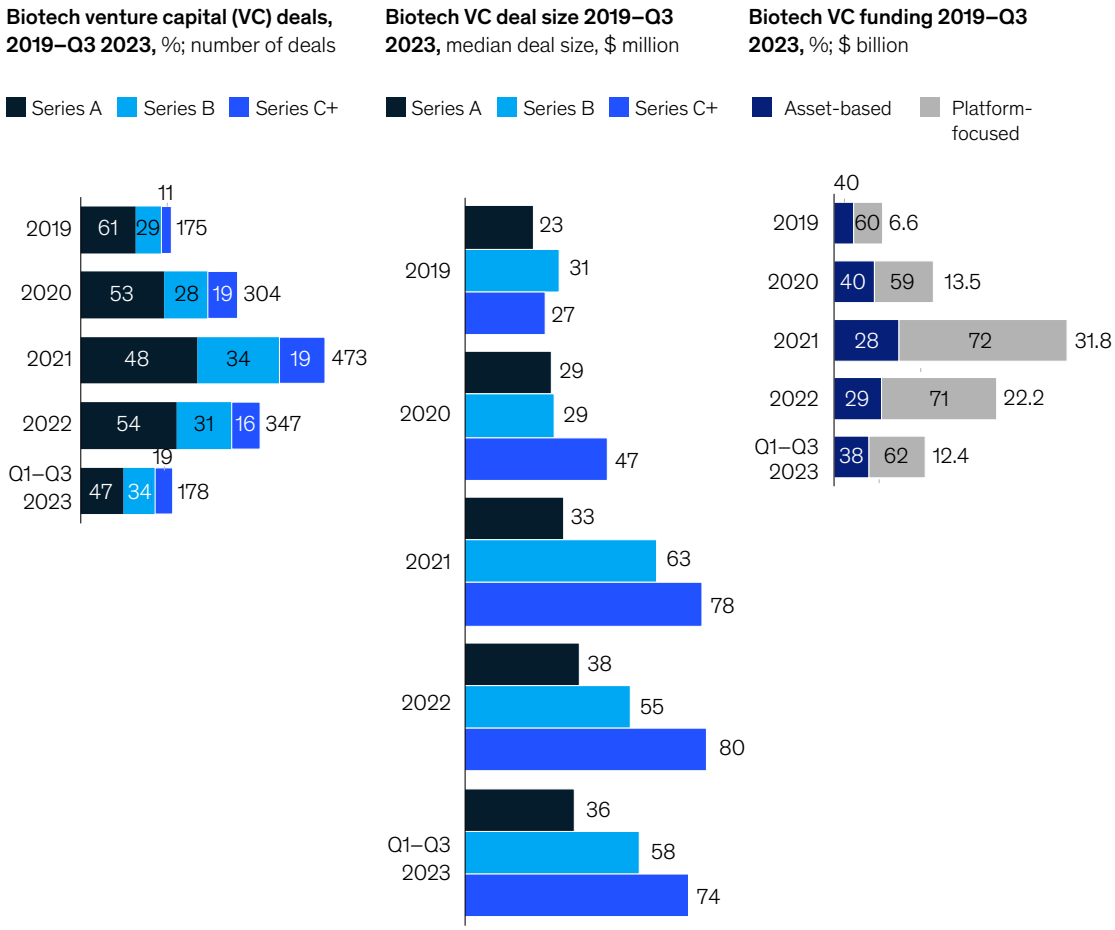
Innovative platforms secured a substantial $15.5 billion in funding, constituting more than two thirds of total biotech VC investment.

Exhibit 3

The venture capital funding landscape remained strong in 2022, but a return to prepandemic norms may be under way.



Note: Figures may not sum to 100%, because of rounding. Chart includes deals > $10 million from Series A to Series I in privately held companies during 2019–Q3 2023; excludes nontherapeutic biotechs such as contract and research services, industrial biotechnology, and food and agriculture.
Source: McKinsey analysis based on PitchBook, Inc. as of Oct 2023; has not been reviewed by Pitchbook analysts

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indications over time (Exhibit 4).[5] In 2022, these innovative platforms secured a substantial $15.5 billion in funding, constituting more than two-thirds of total biotech VC investment, a trend similar to what McKinsey's 2021 analysis uncovered.[6] This commitment to platforms stands in stark contrast to the $6.5 billion that was allocated in 2022 toward more traditional asset-based biotechs, which primarily concentrate on developing specific drugs. Although VC funding has faced some fluctuations, VC investors appear to still be excited about the sector's long-term potential.

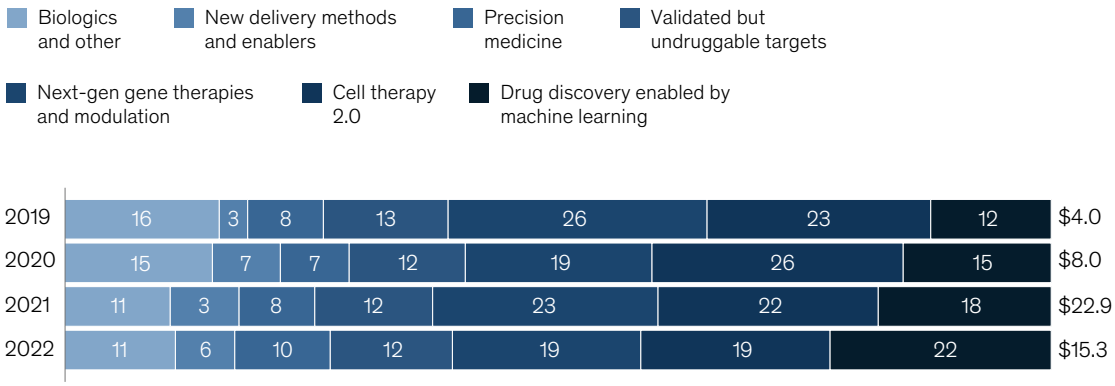
[5] McKinsey defines platform companies as those that are developing a base or infrastructure for further therapeutic development.
[6] Olivier Leclerc, Michelle Suhendra, and Lydia The, "What are the biotech investment themes that will shape the industry?," McKinsey, June 10, 2022.

Uncertainty remains over the trajectory of the current gap between public and private markets, underscoring the challenges of valuing early-stage innovation. To address this uncertainty, we have outlined some emerging trends in these dominant platform technologies by diving into Series A–funded companies in 2022 (see sidebar "Methodology"). We also briefly discuss trends in asset-based companies, with a growing interest in immunology assets emerging in 2022, and touch on some key questions for biotechs and investors as they continue to navigate a shifting environment.

Exhibit 4

Biotechs focused on machine learning have been capturing an increasing share of venture capital funding.

Venture capital funding, $ billion, %



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Source: McKinsey analysis based on PitchBook, Inc. data, accessed Oct 2023; has not been reviewed by Pitchbook analysts

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Methodology

McKinsey analysis included biotech companies receiving venture capital funding from Series A to Series I with deal sizes greater than $10 million from the beginning of 2019 to quarter three 2023. We categorized companies as either focused on developing differentiated platform technologies (a base or infrastructure for therapeutic development such as machine learning–enabled drug discovery, cell therapies, and gene therapies) or advancing distinctive traditional assets for a focused therapeutic purpose.[1] We then further subdivided these companies by the types of platforms they are developing or by the therapeutic focus of their assets. Analysis excluded nontherapeutic companies such as those focused on medical devices, advanced research tools, and contract research and services.

[1] McKinsey defines traditional assets as those with a specific treatment focus and limited ability to be reprogrammed for another use—for example, small-molecule or antibody drugs with a specific mechanism of action or target forming the basis for investment versus a cell therapy platform that could be adapted for many different blood cancers in the future.

Innovative platform technologies drawing VC interest

With more than $15 billion raised in VC funding for platform biotechs in 2022, investors have been attracted to areas such as the integration of large omics data sets, investigation of regenerative medicines, and unlocking of large-scale genomic edits. These areas of development indicate where innovative biotech may be heading

ML-enabled drug discovery

Between 2019 and 2022, VC investors poured more than $9 billion into start-ups focused on ML-enabled drug discovery. These start-ups promise to upend the stubbornly expensive and time-consuming R&D process for biopharma drugs.[7] ML models may improve the ability to select molecules with a higher probability of success and enable fit-for-purpose molecular design for newly identified disease targets. The field has yet to prove itself; most companies are still at the preclinical stage. Nonetheless, interest in the technology is growing rapidly, and ML is being incorporated across the pharma value chain (see sidebar "The future of biotech and AI").

Applications of ML are not limited by modality, and as the technology matures, it may become an integral part of all biopharmaceutical research rather than a distinct category of biotechs. McKinsey analysis saw an increasing number of biotechs across platform areas integrating machine learning into their R&D processes.[8] Early-stage AI biotech start-ups funded in 2022 have focused on areas including the following:

Integrated omics. Researchers continue to lack a complete understanding of the factors involved in complex polygenic diseases such as heart disease and cancer. Very large omics data sets have been collected (for example, UK Biobank), but identifying actionable insights from this data remains challenging. ML models can

[7] "AI in biopharma research: A time to focus and scale," McKinsey, October 10, 2022.
[8] For more on the potential impact of machine learning and AI in life sciences, see "The future of biotech: AI-driven drug discovery," McKinsey, accessed November 10, 2023.

The future of biotech and AI

A discussion about the future of biotech would be incomplete without addressing the potential of artificial intelligence and machine learning (ML) to completely change the sector. Companies founded on accelerating drug development with this technology are maturing to the clinical stage. Large pharmaceutical companies are increasingly interested in enhancing their own R&D capabilities via internal investments and partnerships with AI firms.

Additionally, the boom of excitement around generative AI has the biopharma industry questioning the relevant use cases and their impact. So far, there has been significant activity in R&D applying gen AI to use cases such as accelerating drug discovery with de novo drug design across modalities and enhancing indication finding. But gen AI also presents opportunities to solve problems in other pharma domains—including commercial, medical, manufacturing, and other supporting functions—through use cases such as generating insights on patient and physician activity to refine the understanding of drug performance or improving patient experience with virtual support services.

As AI and ML technology gains a foothold throughout the industry, several important questions remain unanswered:

- What will be the real payoff in clinical timelines and probability of success in biotech?
- Will smaller biotechs be able to sustain the investments required to establish and iterate AI and ML models with new clinical data?
- Who will own the clinical data that will be necessary to innovate AI and ML models in the future?

Both biotechs and investors might consider these questions moving forward. Answers to these questions will determine how the sector interacts with AI and ML and where value will accrue in the next few years.

integrate these large data sets to gain a deeper understanding of disease mechanisms and uncover new molecular targets. Several biotechs have also been incorporating advanced microscopy and imaging technologies in hopes of better visualizing disease processes in real time and incorporating these findings into their models. Others are tackling the remaining questions about the function of the dark, or noncoding, genome in disease pathology. Start-ups focusing on these efforts attracted more than $500 million in Series A funding in 2022.

Computational chemistry. Early-stage biotechs are researching ML models to bridge the gap between lab experimentation and computer simulation. The hope is to enable fit-for-purpose chemical and biologics design that supplants inefficient and expensive library screening methods. Data from physical experimentation can be fed into models that then predict novel chemical-protein or protein-protein interactions for targets of interest. Start-ups are designing automated systems that can feed precise biochemical data into models for training. Some approaches are even trying to simulate the entire cellular environment when designing bespoke therapeutic molecules. Series A companies in this space raised more than $350 million in 2022.

Cell therapies

According to McKinsey analysis of data from Evaluate Pharma, cell therapies brought in more than $3 billion in sales in 2022, supported by indication expansion of chimeric antigen receptor (CAR) T-cell therapies within hematological malignancies (that is, approval in multiple myeloma and second-line large B-cell lymphoma). Sales are projected to rise to more than $21 billion by 2026, supported not only by CAR T but also by various stem-cell and immune-cell therapies expected to come to market in the coming years. The patient impact of cell therapies is expected to continue to grow as therapies stretch into earlier lines of treatment in cancer and expand into new therapeutic areas, such as diabetes.

Despite their early success, cell therapies still require significant work to improve their safety and reach. Improving the immunogenic profiles of therapies and reducing the burden of complex manufacturing and long treatment timelines will require innovation. This area attracted more than $3 billion in VC funding in 2022. The following stood out as focus areas among early-stage players in the field:

Regenerative medicines. Expanding on the success of cell therapy in hematological malignancies, investors put $300 million in 2022 toward cell therapies that can tackle the effects of complex degenerative conditions such as chronic liver and kidney diseases. Start-ups are developing engineered macrophages and regulatory T cells that may reverse the immune drivers of disease. Others are hoping to reverse fibrotic damage and promote new tissue growth in damaged organs using reprogrammed stem cells.

Scalable allogeneic therapies. One of the bottlenecks in currently approved autologous cell therapies is the expensive and time-consuming production of treatments derived from patient cells. Biotechs are addressing these challenges by exploring diverse

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cell types with limited immunogenic profiles that may be more suitable for off-the-shelf treatments. Emerging approaches include virus-specific T cells, NK cells, and macrophages. Alongside new cell types, start-ups are increasingly focused on optimizing and automating in-house manufacturing processes. This strategy may help with scaling the production of approved cell therapies in the future and avoiding manufacturing delays that affect CAR T-cells. Efforts to create scalable allogeneic cell therapy solutions pulled in more than $400 million in VC support in 2022.

Precision control and persistence. Despite success in hematological malignancies, existing cell therapies have struggled to address solid tumors and still carry risks of toxic immune responses. To address these concerns, start-ups continue to improve the binding specificity and persistence of cell therapies, powered by more than $450 million in funding in 2022. High-throughput screening techniques are being used to identify the next generation of improved CAR constructs for tumor cell targeting. Synthetic receptors and biological logic gates (that is, biological circuits designed from components such as proteins) are being tested to help cell therapies evade immunosuppressive signals in the tumor microenvironment.

Gene and oligonucleotide therapies

Hundreds of gene and oligonucleotide therapies are in clinical development,[9] and several have been approved over the past decade. Viral vector gene therapies are now used to treat diseases such as hemophilia B, retinal dystrophy, and spinal muscular atrophy. More recently, mRNA vaccines were pivotal in curbing the spread of COVID-19 and have further accelerated interest in the potential of oligonucleotide-based therapeutics. VC investors provided $3 billion in funding for this group in 2022.

As the impact of these platforms grows, early-stage start-ups are focusing their efforts on the following areas:

Optimizing mRNA technology. Given mRNA vaccines' significant contribution to curbing the COVID-19 pandemic, an interest in optimizing the platform continues to grow. Leaders in the space, such as Moderna and BioNTech, are spending billions to advance their mRNA pipelines in a wide set of indications. On top of these large investments, VC investors are betting on even more innovation in the field with almost $250 million in VC funding in 2022. Start-ups have been exploring new mRNA structures and self-replicating capabilities to overcome the current transient nature of treatment. Targeting molecules and synthetic switches are also being added to mRNA to improve tissue targeting and enable cell-specific expression. Start-ups and established companies hope that the technology will prove effective at tackling indications outside of infectious disease, with many programs focused on rare disease, immunology, and oncology.

Expanding gene editing technology. There is growing interest in expanding gene-editing technologies to facilitate larger-scale genomic edits than is currently possible with CRISPR-based technologies such as base editing and prime editing.[10] CRISPR fusion proteins and new nucleases are being investigated for their ability to facilitate site-specific integrations of large genetic sequences. Rather than repairing individual mutations, which may differ among patients with the same diseases, these approaches seek to fully replace larger faulty genomic sequences with corrected versions, potentially expanding the impact of gene editing to more diseases. Companies pursuing these technologies received $240 million in VC support in 2022.

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[9] *Gene, cell, & RNA therapy landscape: Q1 2023 quarterly data report*, American Society of Gene & Cell Therapy and Citeline, 2023.

[10] Base editing and primer editing approaches are built on CRISPR-Cas9 technology and are generally limited to single nucleotide edits or small insertions in the genome.

Targeting the transcriptome. Targeting the transcriptome has also become a popular approach for biotechs and attracted $230 million in VC funding in 2022. Rather than directly modifying the genome, this approach seeks to influence RNA expression for therapeutic benefit. This can bypass risks associated with permanent alterations to patients' genetic material while still offering the ability to correct genetically based disorders. Biotechs are approaching this from diverse angles, including RNA-binding small molecules and synthetic long noncoding RNAs. Another approach in this field has been to engineer transfer RNAs that can correct mutations during transcription.

Trends in asset-based deals

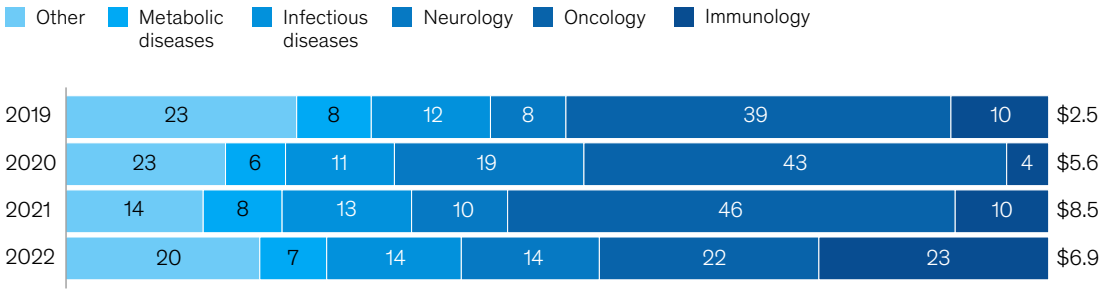
Asset-based biotechs—those that are developing more traditional assets for specific indications—accounted for the remaining third of VC funding in 2022. McKinsey analysis grouped asset-based companies according to their primary therapeutic area of focus or that of the lead asset. In 2022, immunology stood out as a clear area of heightened interest, capturing 23 percent of total asset-based company funding—a significant jump from previous years (Exhibit 5). Several immunology asset-based companies raised rounds of more than $100 million in 2022. This trend toward immunology aligns with the growing interest in regenerative cell therapies noted earlier, with most of those efforts focused on reversing immune drivers of disease. In 2022, VC funding supported a spectrum of immunology assets, ranging from companies focused on new therapeutic targets such as components of the inflammasome to those that offer improvements in tissue specificity and treatment administration of established targets such as IL-17 and TNF-alpha.

On the other hand, oncology dropped from 46 percent of asset-focused VC funding in 2021 to 22 percent in 2022. This trend may reflect tempered excitement in the immuno-oncology space because the field has yet to find the "next PD-L1 inhibitor"

Exhibit 5

Immunology has emerged as an area of heightened venture capital investment among asset-based biotechs in 2022.

Venture capital funding, $ billion, %



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and replicate its broad success.[11] Investors may have also turned their focus toward platform innovations such as cell therapies, patient-specific precision medicines, and engineered multispecific antibody platforms over more traditional small-molecule and antibody approaches. As understanding of the complexity of human cancers increases, complex biologic products may be able to take a more patient-centric and targeted approach.

Data from the first three quarters of 2023 shows VC funding continuing to level out from 2021 highs but remaining above prepandemic levels. This continued resilience contrasts starkly with public markets, which have remained hesitant about biotech throughout 2022 and 2023. Questions remain as to how long this bifurcation will continue and whether we will first see a slowdown in VC activity or an increase in public-market enthusiasm. It might be that public investors cannot tolerate the typically extended time horizons toward profitability in the sector, while VC investors are comfortable waiting for the results of biotech innovation.

As platform technologies continue to mature and the competitive arena grows increasingly crowded, biotechs will want to be able to clearly articulate the unique features that set them apart. Platform companies will also need to consider setting their sights beyond rare diseases toward more substantial areas of unmet medical needs. Biotech companies that prioritize investing in the key building blocks of a strong value proposition will likely stand out as the front-runners in attracting the significant VC funding essential for guiding transformational drugs to approval.

[11] Zihai Li et al., "Next-generation immuno-oncology agents: Current momentum shifts in cancer immunotherapy," *Journal of Hematology & Oncology*, 2020, Volume 13, Number 29.

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