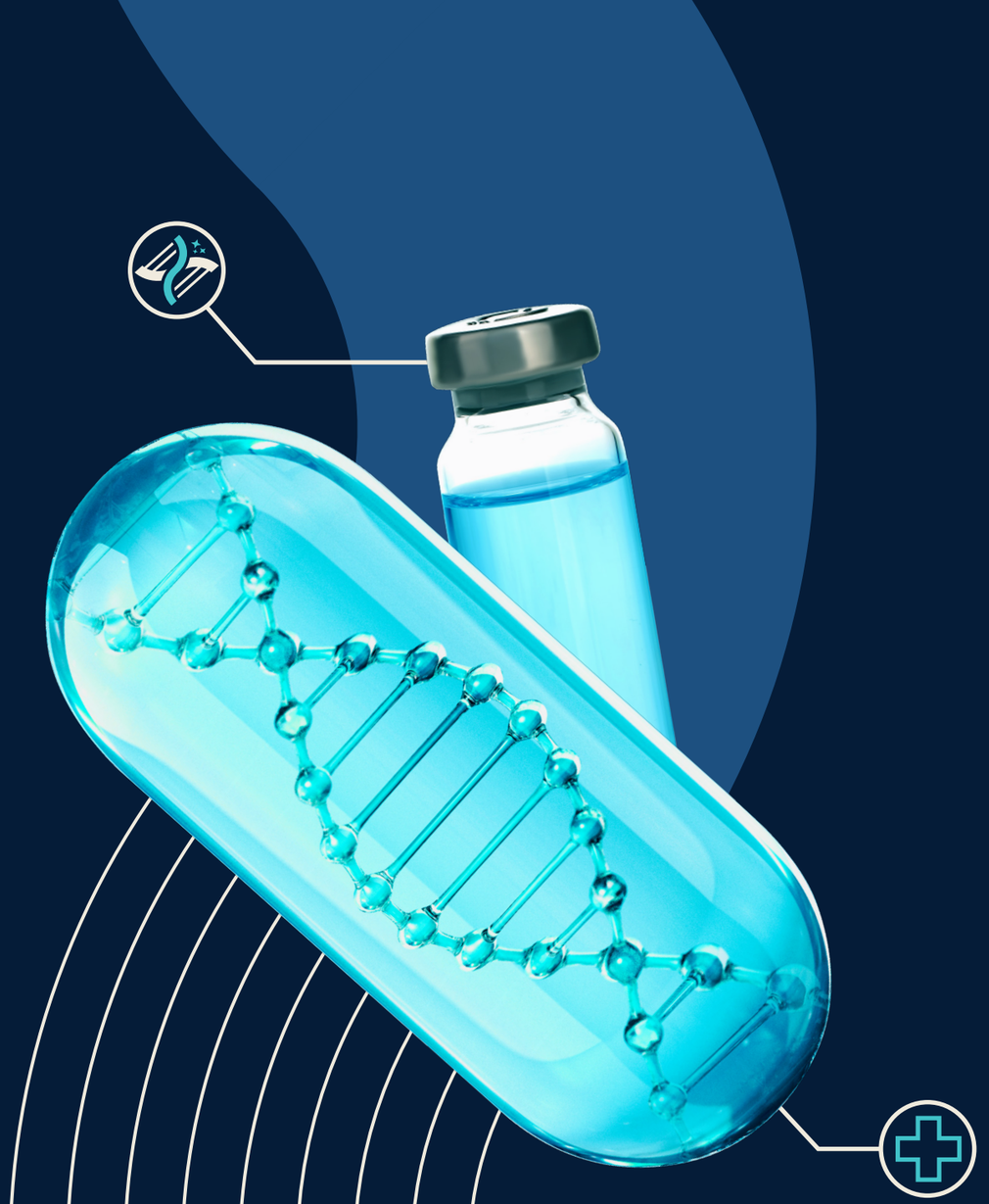
PitchBook

EMERGING TECH RESEARCH

Launch Report: Biopharma

VC trends and emerging opportunities

Q3 2023



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We are adding PitchBook Exit Predictor probabilities to our Emerging Technology Research reports. PitchBook's proprietary VC Exit Predictor estimates the probability that a startup, or VC-backed company, will successfully IPO, be acquired, or merge. The tool is available exclusively to PitchBook clients. Additionally, we have launched a pre-seed report methodology to more accurately and comprehensively capture deals from the earliest phase of venture. Going forward we will sunset "angel" as a specified stage of venture in all of PitchBook's venture-focused reports.

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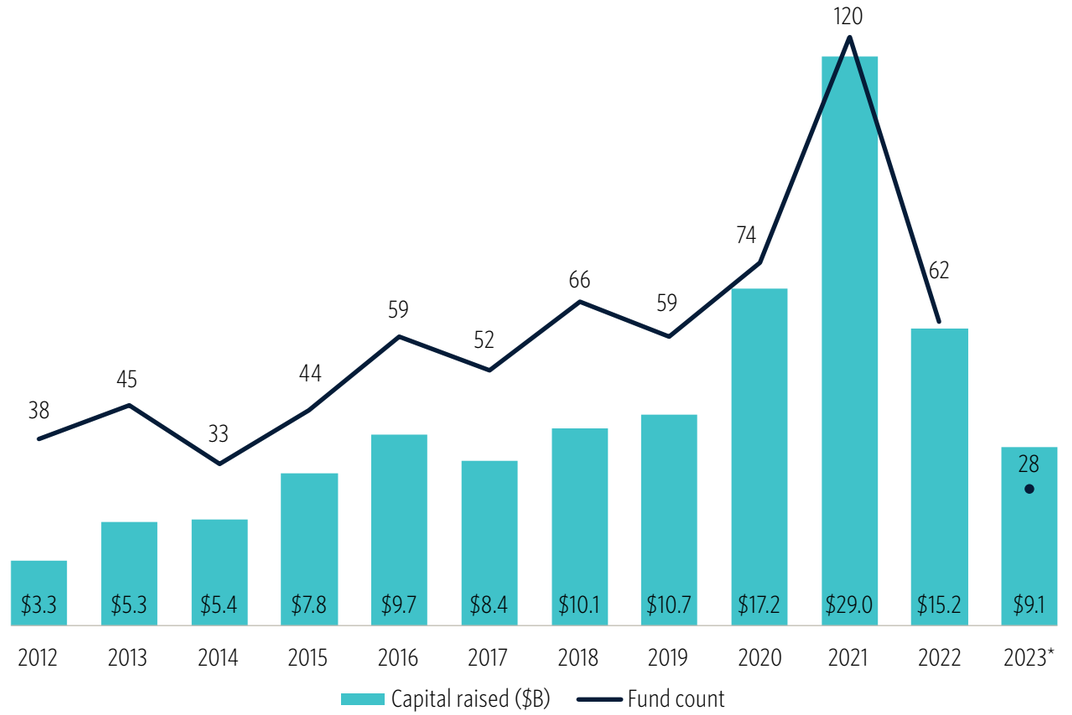
Vertical overview

Biopharma is a dynamic sector, targeting a diverse array of technologies and therapeutic areas. The sector has witnessed a significant shift in investment and research focus, moving from traditional small molecules and biologics to more advanced areas such as gene and cell therapies and tackling complex and chronic diseases. This diversification underlines the industry's commitment to innovation, targeting not just common chronic illnesses but also pursuing cures for more complex health conditions. Most recently, the biggest trends revolve around obesity treatments and artificial intelligence applications in drug development.

Investors in this field generally align with one of two primary focuses: new technologies or new biology. Those focusing on technology aim at developing new drug modalities to enable new functions, engineering platforms for molecules, or discovering molecules or biomarkers. Their objective is often to build a pipeline of molecules for various targets, thus diversifying and reducing risk. In contrast, biology-focused investors prioritize understanding disease pathways and applying suitable drug modalities for targeted treatment. Typically, such companies concentrate on a single asset, either designed or licensed for a specific indication. However, this approach can be less attractive to investors due to its "single shot on goal" nature. Yet, in recent years, some founders have adopted the hub-and-spoke model, creating portfolios of assets, each under its own company. This model, exemplified by companies like Biohaven Pharmaceuticals and Roivant Sciences, allows for multiple shots on goal with high capital funding, opening up large opportunities and exits.

Healthcare life sciences VC fundraising activity



Source: PitchBook • Geography: North America and Europe • *As of September 30, 2023

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VERTICAL OVERVIEW

The ideal scenario combines both approaches, with new modalities enabling the treatment of previously undruggable targets, such as using protein degraders to delete unwanted proteins. Also, the rise of other cutting-edge technologies, such as CAR-T cell therapies and CRISPR-Cas9 gene editing, is revolutionizing treatment paradigms, especially in oncology and genetic disorders. Messenger RNA (mRNA) technologies, initially crucial in pandemic responses for fast vaccine development, are now exploring broader therapeutic applications. The integration of AI in drug discovery is set to further revolutionize treatment development, offering more personalized approaches and shorter development timelines.

The market dynamics of biopharma are characterized by a blend of established pharmaceutical giants and innovative startups. Large firms dictate market trends and have substantial research & development (R&D) capabilities, while startups often spearhead groundbreaking therapies. This blend fosters rapid innovation, though the consolidation trend in the industry presents both opportunities and challenges. Mergers & acquisitions, often seen as strategic moves by larger firms to absorb innovative therapies, can benefit the industry by allowing smaller biotech firms to remain focused on developing high-risk, technologically advanced treatments.

Venture capitalists in this arena typically expect exits through M&A, either before or after an IPO. With high market valuations, VCs have opportunities to realize returns earlier—a necessary approach given their shorter operational timelines. However, building companies to be the next Gilead Sciences or Biogen is less practical for quick returns.

Investors face challenges such as regulatory oversight and intellectual property rights, particularly patents. Emerging therapies often encounter more intricate approval processes than traditional drug categories. Operational investments, especially in cell therapy and gene delivery, are substantial but can set industry standards if successful. Much of the current investment opportunities lie in pharmaceutical technology (pharmatech), whereas biotech investors need to navigate the dynamic interplay between traditional biopharma approaches and emerging technological innovations.

The sector's future is likely to witness increased collaborations between biopharma and tech companies, leveraging AI for therapeutics and precision medicine. However, the current market conditions have tightened fundraising for many biotech companies, with investors setting higher benchmarks for clinical data. This trend is leading to a focus on late-stage investments in clinical trials, ultimately rejuvenating the fundraising environment for early-stage ventures. As the biopharma landscape evolves, stakeholders must focus on innovation, regulatory navigation, and emergent technologies to maintain their competitive edge.

Q1 to Q3 2023 timeline

News

March 10

The collapse of Silicon Valley Bank significantly impacts early-stage biotech firms, leading to funding challenges and increased investment caution. This event exacerbates the ongoing decline in IPOs and VC funding, affecting biotech valuations and market confidence.

News

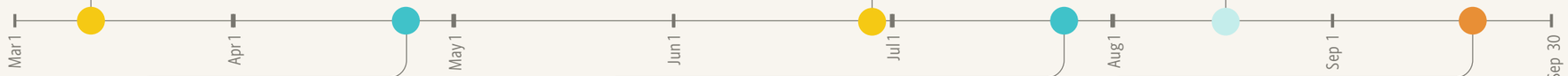
June 30

The US rolls out significant drug pricing reforms, including the Medicare Drug Price Negotiation Program set for 2026, as part of the Inflation Reduction Act (IRA). This critical event influences the pharmaceutical industry's pricing strategies and market dynamics.

M&A

August 14

Eli Lilly's strategic acquisition of Versanis Bio, which focuses on bimagrumab for metabolic diseases, marks a notable event with high-value potential payouts, signaling strategic growth in the metabolic disease sector.



VC deal

April 26

Orbital Therapeutics, specializing in RNA medicines, completes a $270 million Series A. This funding demonstrates growing investor interest in RNA-based therapeutic solutions, buoyed by the success of mRNA vaccines.

VC deal

July 26

Kriya Therapeutics raises over $150 million in a Series C. This capital injection, part of a total of $600 million raised to date, accelerates the development of its gene therapies, underlining significant investor confidence in gene therapy innovation.

IPO

September 19

RayzeBio's successful $358 million upsized IPO focusing on radiopharmaceuticals for solid tumors indicates a reinvigoration of the biopharma IPO market and investor confidence in innovative cancer treatments.

Q3 VC deal count summary

178
total deals

-19.8%
QoQ growth

-25.2%
2023 YoY growth

-26.7%
2023 YTD growth

Q3 VC deal value summary

$6.5B
total deal value

4.2%
QoQ growth

-3.9%
2023 YoY growth

-35.8%
2023 YTD growth

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Biopharma landscape

1. Cell therapy
2. Chemistry
3. Gene therapy
4. Biologics
5. Emerging therapy
6. Oncology
7. Neurology
8. Cardiovascular & metabolic disease
9. Immunology & infectious disease
10. Digestive & renal systems disorder
11. Systemic & structural disorder
12. Specialty disease

Drug modality VC ecosystem market map

Click to view the interactive market map on the PitchBook Platform.

Market map is a representative overview of venture-backed or growth-stage providers in each segment. Companies listed have received venture capital or other notable private investments.

Chemistry

Small molecule

nimbus THERAPEUTICS · Valo · KALLYOPE · TREELINE BIOSCIENCES

Degrader

AMPHISTA THERAPEUTICS · VICINITAS THERAPEUTICS · Photys · Avilar THERAPEUTICS · stablix protein stabilization therapeutics

Radiopharma

RadioMedix · ARICEUM · 药明博锐 BoomRay · Radionetics Oncology · Nucleus RadioPharma

Cell therapy

Immune cell

SONOMA BIOTHERAPEUTICS · ArsenalBio · REPERTOIRE IMMUNE MEDICINES · A2 bio · IASO

Tissue/biomaterial

Fesarius Therapeutics · VERIGRAFT · bioaesthetics · Videregen Bringing tissue repair to life · Pandorum Building blocks of life

Stem cell

ALTOS · orcabio · AURION BIOTECH · Aspen Neurosciences · Heartseed

Biologics

Antibody

ITBMed · OriCell Therapeutics 原启生物 · EpimAb Biotherapeutics · ARCH ONCOLOGY · TrueBinding · LIGHTCHAIN · AGOMAB THERAPEUTICS · Umoja BIOPHARMA · UpstreamBio · HEMOB

ADC/conjugates

Rakuten Medical · Crescendo biologics · ProfoundBio · SOLVE THERAPEUTICS · ALTRUBIO · MBRACE THERAPEUTICS · 浙江康佰生物医药有限公司 NovoCodex Biopharmaceuticals Co.,Ltd. · DualityBio 映恩生物 · ORUM THERAPEUTICS

Protein/peptide

WORG 百明信康 · ERA THERAPEUTICS · Enterome · Synthekine · MBX Biosciences · NEURELIS · Cerapedics · FOG · AMPHARMA · ODYSSEY THERAPEUTICS

Vaccine

新合生物 NeoCura · 嘉晨西海 immorna · MAXVAX 迈威康生物 · INNOVENA 深信生物 · nouscom · Tecon Pharmaceutical · Imvax · Advaccine · Leyden Labs · Juntuo Biomedical

Gene therapy

mRNA

ReCode THERAPEUTICS · NUTCRACKER · capstan therapeutics · METiS 附壹医药 · RVAC MEDICINES · etherna · REDONA THERAPEUTICS · COMBINED THERAPEUTICS · REJUVENATION TECHNOLOGIES · ENVISAGENICS

Oligos/RNA

TRAND THERAPEUTICS · 舶望制药 Argo Biopharma · MINA Therapeutics · Inceptive · alltrna · Atalanta THERAPEUTICS · ISARNA THERAPEUTICS · LYCANAbio · CAMP4 · QurAlis

Gene editor

EXCISION · 克睿基因 · BIOMENTA · Tome BIOSCIENCES · nvelop therapeutics · LOCUS BIOSCIENCES · scribe THERAPEUTICS · TUNE THERAPEUTICS · EDIGENE 博雅辑因 · CHROMA MEDICINE

Gene delivery

affinia THERAPEUTICS · JAGUAR GENE THERAPY · FRONTERA THERAPEUTICS · ensoma · Ring THERAPEUTICS · NEUROGENE · Encoded THERAPEUTICS · CAPSIDA BIOTHERAPEUTICS · FORGE BIOLOGICS

Emerging therapy

Bacteriotherapy

microbiotica · DermBiont · OxThera · adaptive phage THERAPEUTICS · prokarium · FEDERATION BIO · Siolta Therapeutics · Artizan BIOSCIENCES · BiomeBank · exeliom biosciences

Oncolytic virus

accession therapeutics · ImmVirX Powered by Targeted Oncolytic Viruses · FluGen · tilt BIOTHERAPEUTICS · GENEMEDICINE · ABALOS THERAPEUTICS · THERAVECTYS · ICONOVIR BIO · ImmVira · VYRIAD

Exosome

evox · Diasome · anjarium · Vesigen THERAPEUTICS · ExoCoBio · MANTRA BIO · carmine THERAPEUTICS · ARUNABIO · STRM·BIO · VESICURE Therapeutics

Nanotech

Intrance MEDICAL SYSTEMS · SN BioScience · virometix VACCINES · haima therapeutics · Cellics Therapeutics · COUR · AMORPHICAL · AVICEDA THERAPEUTICS · MonTa Biosciences · HOPEWELL Therapeutics

Therapeutic area VC ecosystem market map

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Market map is a representative overview of venture-backed or growth-stage providers in each segment. Companies listed have received venture capital or other notable private investments.

Oncology

Neurology

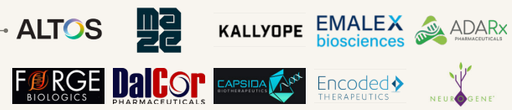
Cardiovascular & metabolic disease

Immunology & infectious disease

Digestive & renal system disorder

Systemic & structural disorder

Specialty disease

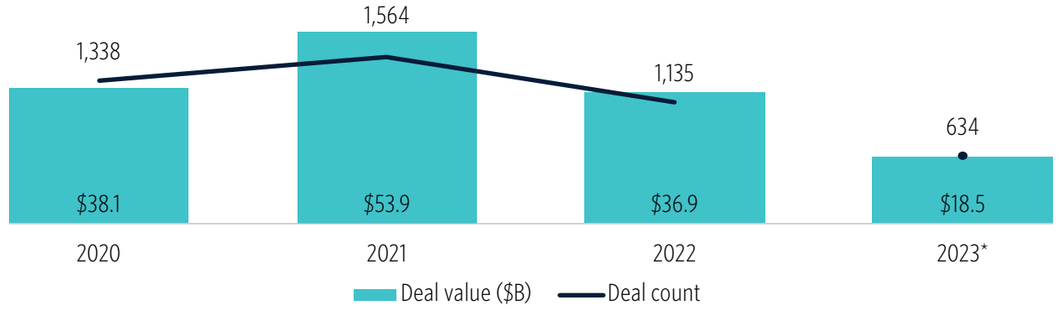


VC activity

Venture capital dynamics in the biopharma industry present a nuanced narrative in 2023, with projections suggesting deals might exceed $24 billion across roughly 840 transactions by year's end—a modest rise from the previous quarter. This uptick contrasts with the year's overall downward trend in dealmaking. It is starkly different from the high-water marks of 2020 through 2022, when annual values reached $38.1 billion, $53.9 billion, and $36.9 billion, respectively. On the exit activity front, the number of acquisitions plummeted from the 2021 high of 200 deals totaling $86.4 billion to the low of 77 deals totaling $23.4 billion in 2022. Currently, 2023 is projected to have around 84 deals totaling $17.9 billion. The greatest loss for exits was in the IPO market, with a 71% drop in deal count from 154 to 45, while acquisitions experienced a 28% decrease from 45 to 32 during the 2021-to-2022 market shift. The exit split by the end of 2023 does not differ greatly from 2022, with projections of 55 IPOs and 29 acquisitions. Overall, the current climate indicates a recalibration toward pre-pandemic investment norms, despite the sector's explosive growth amid COVID-19.

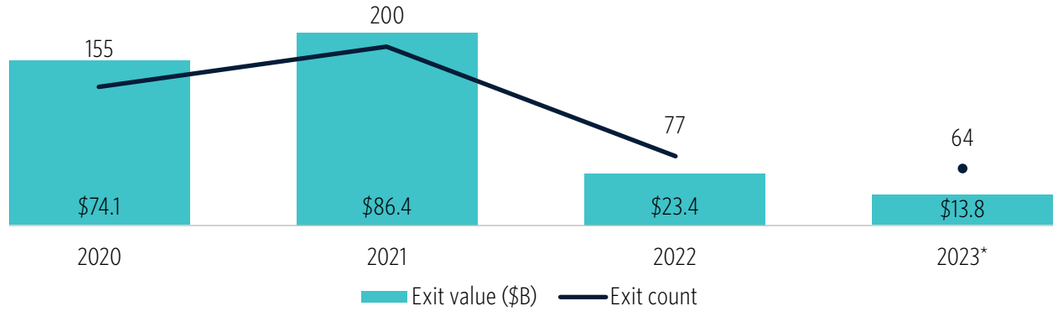
In the biopharma investment landscape, a strategic shift is evident, with a trend toward fewer but more significant deals, which is indicative of a prudent investment approach that prioritizes larger and potentially more stable investments. This could be attributed to various strategies such as reinforcing reserves for existing portfolios, optimizing the timing for IPOs, pursuing exit strategies to raise new funds, or adapting to an economic downturn impacting the availability of startup leadership. In this climate, strategic patience emerges as a key virtue for investors looking to fully capitalize on the prolific pandemic-era investments. Analyzing the investment distribution across clinical trial phases, there was a notable uptick in funding for companies initiating phase 1 trials from 2020 to 2021, with a subsequent dip in 2022 and a slight rebound in 2023. This fluctuation stems largely from the dynamic availability of capital and the appetite for risk, particularly for novel high-stakes modalities like gene and cell therapies. In contrast, investments in companies

Biopharma VC deal activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Biopharma VC exit activity



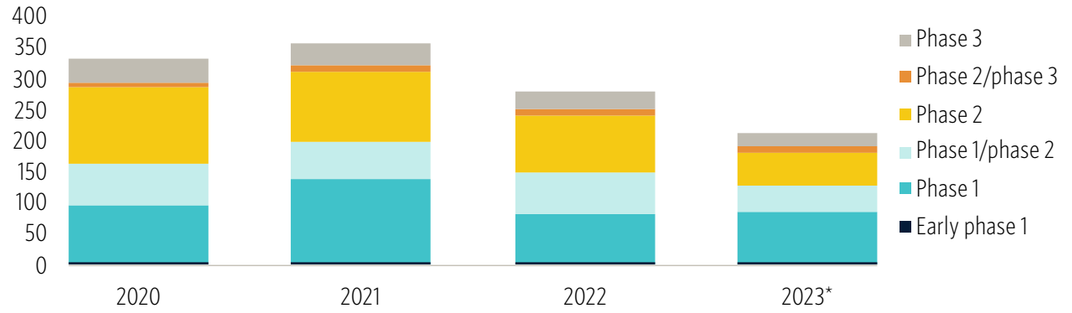
Source: PitchBook • Geography: Global • *As of September 30, 2023

heading into phase 2 trials have seen a steady decline, potentially hindered by the need for trial maturation or a dearth of compelling advancement opportunities. Transactions involving companies moving from phase 2 to phase 3, however, exhibit a consistency, possibly due to the relatively small number of drug candidates progressing to this pivotal stage prior to public market debut or acquisition.

On the international end, China's biopharma landscape is witnessing significant investment, with heavy funding for infrastructure development companies like Dongyangguang and Abogen Biosciences. Simultaneously, notable investments in platform technology firms such as Eikon Therapeutics and Insitro demonstrate a continued inclination toward technology-centric ventures. Conversely, substantial funding, the recent $2.7 billion Roche acquisition and canceled IPO for Carmot Therapeutics, and the completed IPO of Structure Therapeutics indicate a renewed confidence in biology-driven investments, inspired by recent pharma successes in the cardiovascular domain.

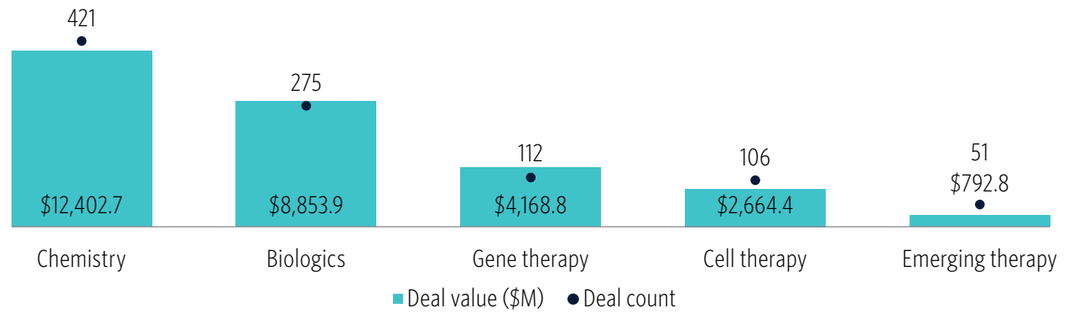
The VC outlook remains cautiously optimistic, with a heightened focus on clinical outcomes and the successes of late-stage and public ventures, prompting a more selective investment strategy. However, there is a clear gravitation toward platforms with the potential to pioneer new modalities, target elusive biological entities, or unveil novel pathways. Hence, amid this discerning landscape, strong deals persist, benefiting industry-leading venture builder firms and founder-led startups alike, and suggesting a balanced environment that values both proven leadership and innovative potential.

Biopharma VC deal count (#) by highest phase



Source: PitchBook • Geography: Global • *As of September 30, 2023

Trailing 12-months (TTM) biopharma VC deal activity by segment*



Source: PitchBook • Geography: Global • *As of September 30, 2023

Segment overview

Chemistry

The small-molecule drug domain, foundational to pharmaceuticals, is characterized by its traditional role and continued dynamism, integrating novel biological findings and advanced technologies like AI & machine learning (AI & ML) for innovative drug discovery and development.

Biologics

This key biopharma industry segment is characterized by diverse, complex products like monoclonal antibodies and vaccines, wherein established companies lead in commercialization, while startups drive innovation—particularly evident in the rapid development of COVID-19 vaccines.

Gene therapy

This rapidly evolving biopharma sector utilizes gene-based technologies like CRISPR and mRNA therapies, with both established companies and disruptive startups making strides in disease treatment and prevention.

Cell therapy

This burgeoning field leverages advancements in synthetic biology, immunology, and regenerative medicine to offer novel treatments, with major players and new investors alike contributing to its growth and therapeutic potential.

Emerging therapy

This segment spearheads novel treatment development across diverse technologies like nanotechnology, bacteriotherapy, oncolytic viruses, and exosomes, and aims to address unmet needs with precision treatments and reshaping medical practice.

Therapeutic areas

The biopharma industry develops treatments across several key segments wherein companies are engaging with novel targets, indications, and unexplored medical cases.

Chemistry

Overview

The chemistry segment focuses on small-molecule drugs, which are a traditional yet dynamic component of the pharmaceutical industry. These drugs are low-molecular-weight compounds that can easily diffuse across cell membranes to exert their biological effects. Small-molecule drugs are the basis for many classic therapeutic drugs and remain vital due to their ease of administration, capacity for oral dosing, and generally straightforward manufacturing process.

The landscape of legacy incumbents in this domain includes virtually all prominent pharmaceutical entities such as Pfizer, AbbVie, Merck, Johnson & Johnson, Novartis, Bristol Myers Squibb, and Roche. These companies have long held sway over the segment, leveraging extensive R&D resources and sophisticated infrastructures to lead small-molecule drug discovery and market entry.

Emerging from the wealth of new biology identified in academic settings, startups in the small-molecule space typically fall into one of two categories: One group focuses on advancing single assets or a portfolio of targeted assets stemming from novel biological discoveries. The other is characterized by its platform-based approach, aiming to establish a robust pipeline of drugs. These platforms often harness AI & ML for novel target identification, biomarker discovery, or the engineering of innovative molecules. A subset of these platforms pioneers new functions within small molecules, such as protein degraders or the therapeutic and diagnostic applications of radiopharmaceuticals.

Subsegments

- **Small molecules:** These are the foundational inhibitors or activators of specific enzymes or receptors and constitute the majority of pharmaceuticals in the market.
- **Degraders:** Representing a novel class, these bifunctional molecules recruit the body's own protein degradation machinery to selectively dismantle pathogenic proteins. This category includes proteolysis targeting chimeras (PROTACs).
- **Radiopharma:** These are compounds that are conjugated with radioactive isotopes, serving dual roles in both targeted diagnostic imaging and as therapeutic agents for conditions like cancer.

Industry drivers

- **New functions for small molecules:** Beyond traditional roles as enzyme or receptor inhibitors, small molecules are being engineered to perform complex biological functions. Companies like Vividion Therapeutics and RayzeBio are pioneering this shift. Vividon Therapeutics, which was acquired by Bayer for $1.5 billion, was developing small molecules that can modulate protein degradation, signaling pathways, and gene expression. RayzeBio, with a recent $358 million IPO, is pushing the space of radiopharma forward with its targeted radioisotope technology. This expansion of capabilities is enabling the development of highly targeted therapies with the potential to address diseases that have been challenging to treat with conventional small-molecule drugs.

- **AI & ML-enhanced drug discovery:** The integration of AI & ML into drug discovery processes is driving transformation in the small-molecule segment. Leveraging exponential growth in Big Data and high-throughput screening capabilities, companies such as Exscientia and Insilico Medicine are at the vanguard due to their AI drugs in clinical trials. They use AI & ML to significantly shorten drug discovery timelines, improve the prediction of drug efficacy and safety, and reduce overall R&D costs. AI & ML is not just accelerating the discovery of new drugs but is also redefining the ways in which chemical compounds are designed and optimized. Additionally, despite challenges such as Exscientia's drug failure in phase 1 and 2 studies, the investments continue and at premium valuations, with Genesis Therapeutics' $200 million Series B as a prime example. Ultimately, the difference lies in the details, which may solve costly issues in the leading AI & ML companies.

- **Precision medicine approach:** The trend toward precision medicine is fueling the development of small-molecule drugs tailored to the genetic and molecular profiles of individual patients. This approach aims to enhance the specificity and efficacy of treatments while minimizing adverse effects. The industry is shifting from a one-size-fits-all paradigm toward more personalized therapies, and small molecules, due to their versatility and ease of modification, are well suited to lead this shift. Recent raises include Actio Biosciences, which raised a $55 million Series A focusing on new mouse model technology to develop rare disease drugs, and Engine Biosciences, which raised $27 million to advanced oncology drugs with a computational platform utilizing CRISPR screening technologies.

Business model

In the biopharma industry, companies specializing in small-molecule drugs represent a significant segment, adhering to a traditional pharma development model. This sector is marked by a standardized process with a clear trajectory from drug discovery to market. Small-molecule drug companies generate revenue primarily through milestone payments and drug sales post-clinical development and regulatory approval. Additional revenue streams include upfront payments and royalties from out-licensing drugs to pharma partners for further development and commercialization.

Small-molecule startups typically operate under two main business models: platform companies and asset-focused companies. Platform companies build capabilities around technologies such as AI & ML, high-throughput biology, or molecular engineering. These capabilities are utilized both to advance internal pipelines and to partner on additional programs. Conversely, asset-focused companies tend to source or develop individual promising drug candidates, often with a focus on a specific therapeutic area or target. Recently, some asset-centric companies have adopted a hub-and-spoke model, creating separate subsidiaries for each key program to mitigate risk. The core distinction between these models lies in lead generation. Platform companies leverage computational or biological innovations for drug discovery, whereas asset-focused companies generally derive candidates from academic research or existing pharma pipelines. Ultimately, revenue for these startups hinges on advancing candidates to clinical validation and approval, thereby enabling them to realize milestones, royalties, and product sales.

The small-molecule sector is attractive for several reasons. It offers a more traditional, well-charted path to drug development, making market predictions and regulatory strategies more straightforward compared to newer biologic therapies. However, this space is not without its challenges. Small-molecule startups must navigate regulatory hurdles, intense competition, and the pressure of advancing drug candidates through the clinical and approval processes successfully. Opportunities for growth and expansion lie in new markets and emerging technologies that could enhance drug discovery and development processes.

VC activity

Chemistry VC activity peaked in Q1 2021 and subsequently declined into 2023, reflecting broader industry patterns. However, the chemistry segment witnessed a resurgence Q3 2023, with a 25% increase in funding to $3.4 billion—albeit coupled with a decline in the number of deals. This indicates a strategic pivot by VCs toward larger, late-stage investments, moving away from the earlier trend of seed funding. Furthermore, the sector's key deals, particularly the IPO of Neumora in neurology with a phase 3 drug, underscore a shift in investment strategy. VCs are now prioritizing early clinical validation over the potential of new technologies at preclinical stages, which is a marked change from previous years. Concurrently, the sector experienced a spike in exit activity, both in terms of deal value and count, suggesting a maturing landscape with investments made in recent years now coming to fruition.

Looking ahead, the sector is ripe for transformation, with companies specializing in AI and weight loss drugs, such as Insilico Medicine and Carmot Therapeutics, demonstrating high potential IPOs. However, acquisitions are also likely, especially depending on the outcomes of phase 2 clinical trials—but exceptions are driven by highly valued competitive assets, which was the case for Carmot's acquisition by Roche. Despite similar strategies to competing peptides and oral drugs, Carmot Therapeutics was attractive to large pharma acquisition for either consolidation or entry into the obesity market. The trends within specific subsectors like radiopharma and degraders indicate a growing early-stage fascination with new technologies, which are setting the stage for future pharmaceutical M&A once proven in clinical trials. A notable case is Point Biopharma's $1.4 billion exit to Eli Lilly driven by late-stage trials for its radiopharma drugs. This evolving landscape, however, is not without its challenges, as the regulatory impacts of the IRA are prompting a strategic shift from small molecules to biologics among early-stage investors. Despite these challenges, opportunities abound, driven by advancements in AI and novel drug modalities.

Chemistry VC deal activity

Source: PitchBook • Geography: Global • *As of September 30, 2023

Chemistry VC exit activity

Source: PitchBook • Geography: Global • *As of September 30, 2023

Key chemistry VC deals over the past year*

Company	Close date (2023)	Subsegment	Stage	Deal value ($M)	Lead investor(s)	Valuation step-up
Cardurion Pharma	July 12	Small molecule	Late-stage VC	$300.0	N/A	1.5x
Genesis Therapeutics	August 25	Small molecule	Early-stage VC	$224.0	Andreessen Horowitz	1.4x
Nimbus Therapeutics	August 7	Small molecule	Late-stage VC	$210.0	Atlas Venture, GV, SR One Capital Management	N/A
Avenzo Therapeutics	May 26	Small molecule	Early-stage VC	$196.5	N/A	N/A
Avalyn Pharma	September 27	Small molecule	Late-stage VC	$189.2	Eventide Asset Management, Perceptive Advisors, SR One Capital Management	N/A
Mariana Oncology	August 25	Radiopharma	Early-stage VC	$173.9	Deep Track Capital, Forbion	1.4x
ArriVent Biopharma	March 17	Small molecule	Early-stage VC	$155.0	General Catalyst, Sofinnova Investments	1.1x
Sinotau	July 3	Small molecule, antibody	Late-stage VC	$153.4	N/A	N/A
Pathalys Pharma	January 13	Small molecule	Early-stage VC	$150.0	Abingworth	N/A
Alkeus Pharmaceuticals	June 5	Small molecule	Late-stage VC	$150.0	Bain Capital Life Sciences	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Key chemistry VC exits over the past year*

Company	Close date (2023)	Subsegment	Exit value ($M)	Exit type	Acquirer(s)/index	Post-money valuation ($M)
Neumora	September 15	Small molecule	$2,333.1	Public listing	NASDAQ: NMRA	$2,583.1
Inversago Pharma	August 10	Small molecule	$1,075.0	Acquisition	Novo Nordisk	$1,075.0
Adlai Nortye	September 29	Small molecule, antibody, oncolytic virus	$860.0	Public listing	NASDAQ: ANL	$922.5
Laekna Therapeutics	June 16	Small molecule	$517.1	Public listing	02105.HK	$618.0
Mineralys	February 9	Small molecule	$432.9	Public listing	NASDAQ: MLYS	$624.9
Structure Therapeutics	February 4	Small molecule	$413.7	Public listing	NASDAQ: GPCR	$599.0
Sagimet Biosciences	July 14	Small molecule	$269.8	Public listing	NASDAQ: SGMT	$354.8
XinThera	May 9	Small molecule	$200.0	Acquisition	Gilead Sciences	$200.0
MIRA Pharmaceuticals	August 3	Small molecule	$94.3	Public listing	NASDAQ: MIRA	$103.2
Flame Biosciences	January 17	Small molecule	$79.0	Acquisition	Leap Therapeutics	$79.0

Source: PitchBook • Geography: Global • *As of September 30, 2023

Opportunities

Treatment with oral option alternatives to biologics: Small-molecule drugs are emerging as viable oral administration alternatives to traditionally injectable biologics. These drugs, with their potential for oral bioavailability, are opening new possibilities in treatment, particularly in areas where biologics have reigned supreme due to their superior targeting capabilities. This evolution is especially pertinent in the context of precision medicine and the development of new small-molecule modalities. The market for these innovative therapies is gradually expanding, capturing a segment of the share traditionally held by established biologic products. This growth reflects a rising interest in exploring oral alternatives in treatment, thus offering a new dimension to patient care and therapy accessibility.

Demand for more convenient treatment options has been driven by growing attention to both infectious and chronic diseases. The COVID-19 pandemic highlighted this need acutely, as it underscored the limitations in clinical access and the challenges posed by supply chain disruptions in vaccine and antibody distribution. This scenario brought oral treatments like Pfizer's Paxlovid into the limelight. The competitive landscape for these therapies features both established pharmaceutical companies and agile startups. For instance, startups employing innovative structural design technologies, such as Anagenex's small-molecule directed evolution platform, are pushing the boundaries of drug development. Meanwhile, the quest for oral obesity therapies, stimulated by the success of injectable GLP-1 drugs, underscores the ongoing challenge of developing effective oral solutions. Companies like Structure Therapeutics are finding value in the relative ease of prescribing, manufacturing, and distributing small molecules, setting the stage for future advancements in the field. The ongoing development of more precise targeting methods, like those seen in degraders, promises to further enhance the appeal and efficacy of small-molecule alternatives.

Beyond PROTAC degraders for new technologies: The realm of small-molecule drugs is witnessing significant evolution, particularly with the development of small-molecule degraders, which have broadened the functional scope of these therapeutics beyond merely serving as inhibitors. This in turn allows for more versatile and targeted therapeutic approaches. PROTACs have been at the forefront of this transformation, emerging as a rapidly growing segment within the field of small-molecule innovation. Their ability to offer greater precision in drug targeting without compromising key oral advantages, such as in the case of antibody-drug conjugates (ADCs), marks a pivotal advancement in drug design.

Leading the charge in this innovative landscape are companies like Arvinas, which raised over $639 million, and industry giants like GSK, which have been instrumental in paving the way for PROTACs. This burgeoning field has attracted substantial investment, as evidenced by Gate Bioscience's $20 million Series A for its gate molecule technology and Lycia Therapeutics' $70 million Series B for its lysosome-driven degrader technology. These developments underscore the unique advantages of these new modalities, including the potential to target previously undruggable molecules and the opportunity for new patent protections around these innovations. The regulatory path for these drugs is like traditional small molecules, making them attractive to investors due to lower risks in

manufacturing. The adoption and implementation of these therapies are straightforward, though potential challenges may arise in oral delivery, especially if the PROTACs are peptide-like in size. Looking to the future, the continued interest in bifunctional modalities and the need for innovative molecule design, combined with new biological insights, suggest a dynamic and evolving landscape for small-molecule drugs.

Risks and considerations

Inflated valuations for AI-powered biotech: In the biopharma industry, the hype and subsequent overvaluation of AI technologies in drug discovery, particularly for small-molecule drug development, pose significant risks. The initial promise of AI-generated drugs, with trials underway, has not yet definitively proven their superiority over traditional methods. Despite industry expectations of a richer pipeline and more efficient development processes, several AI-designed drugs have underperformed in clinical trials. Notable examples include Exscientia's cancer drug candidate and BenevolentAI's dermatitis drug, both of which have faced setbacks. Even Recursion Pharmaceuticals, which has not encountered direct trial failures, has faced clinical challenges. This trend has led to skepticism about AI's efficacy in boosting drug discovery success rates and questions about the future of AI investments in biotech. Despite these issues, AI companies, some achieving unicorn status, continue to be highly valued.

The sector's response to these challenges involves evolving strategies to mitigate risks. Companies are now incorporating more human tissue samples into their research and enlisting experienced clinical personnel. This in turn underscores the need to advance organoid sciences, wherein pharmatech players like Xilis are leading the way. While there is acknowledgment that AI has improved speed and cost in preclinical stages, proving its effectiveness in enhancing clinical trial success is a longer journey. First-generation companies, in collaboration with major drugmakers, remain committed to exploring AI's role in drug discovery. They are adapting to these challenges, suggesting a cautious but continued interest in the potential of AI technologies in the biopharma sector. Despite the setbacks and market downturn affecting stock prices, new AI startups are still attracting substantial funding, indicating an ongoing belief in AI's future role in biopharma.

Compound mining disappointment: In biopharma, the pursuit of new small molecules through compound mining has encountered significant challenges. The initial excitement surrounding the discovery of novel natural compounds, often derived from diverse bacterial sources like soil, sea, or the human body, has not yielded the expected fruitful outcomes. This is despite advancements in genomics technologies, which led to a surge in startups dedicated to this endeavor. Instead, traditional compound screening methods continue to dominate drug discovery, suggesting that the future might not diverge drastically from established practices. The field is increasingly recognizing that many easily discoverable compounds may have already been identified, leaving

the sector reliant on serendipitous discoveries. An illustrative example of this trend is Lodo Therapeutics, which, despite forming high-stake partnerships, failed to create significant value and was eventually acquired by Zymergen.

To navigate these risks, some pharmatech startups are adopting alternative strategies. For instance, companies like Brightseed are focusing on forming partnerships to explore bioactive compounds with drug potential, rather than building their internal pipelines. This approach reduces the inherent risks by leveraging external collaborations and expertise, thereby creating a more sustainable model amid the uncertainties of natural compound mining. By adapting in this way, these startups are finding a balance between innovative exploration and the practicalities of the current drug development landscape. This strategy provides a pathway for continued exploration in compound mining while acknowledging and addressing the challenges that have emerged in this ambitious yet unpredictable field.

Biologics

Overview

Biologics, representing a forefront segment in the biopharmaceutical industry, encompasses a diverse array of products derived from living organisms. This segment is distinguished by its complexity in development and manufacturing, often requiring cutting-edge technologies for successful commercialization. Innovations such as monoclonal antibodies (mAbs), therapeutic proteins, peptides, ADCs, and vaccines constitute the core of this sector. These biologics offer targeted therapeutic interventions, often for conditions inadequately addressed by small-molecule drugs, marking a significant evolution in personalized medicine.

Key legacy incumbents, such as Roche, Novartis, Pfizer, and Merck, have established robust pipelines and extensive market presence, often leading in revenue generated from biologics. Their entrenched positions are supported by comprehensive infrastructures for R&D, production, and distribution, as well as strong regulatory expertise.

However, the biologics landscape is also witnessing burgeoning growth from innovative startups. These startups are catalyzing industry disruption, challenging the incumbents with more agile and innovative approaches to therapeutic development—particularly highlighted by the swift development of COVID-19 vaccines.

Subsegments

- **Antibodies:** These are immune system proteins created in the lab. They are designed to bind to specific targets found on cancer cells, viruses, or other pathogens, offering precision in treatment.
- **Proteins & peptides:** These are engineered macromolecules that mimic natural ones in the body. They play a pivotal role in treating metabolic and genetic disorders, among other conditions.
- **Antibody-drug conjugates (ADCs) & other conjugate technologies:** These are targeted cancer drugs that link monoclonal antibodies to cytotoxic agents, providing targeted delivery of chemotherapy to cancer cells while sparing healthy tissue.
- **Vaccines:** These biologic preparations provide active acquired immunity to infectious diseases. The focus on vaccine technology has intensified, with mRNA and viral vector vaccines being at the center of innovation.

Industry drivers

- **Technological advances in drug development:** The biologics sector is experiencing significant growth driven by breakthroughs in technology, such as high-throughput screening and next-generation sequencing, which enhance the discovery and development of new biologic entities. These advancements enable the identification of novel drug targets and the development of antibodies, proteins, and peptides with greater specificity and efficacy. This technological evolution is attracting substantial interest from pharma, with acquisitions like Amgen's purchase of TeneoBio for $1.3 billion driven by its new multispecific antibody engineering platform.

- **Personalized medicine:** As the global burden of chronic diseases such as cancer and autoimmune disorders increases, the demand for more effective and personalized treatments is rising. Biologics offer tailored therapies based on individual genetic profiles, which leads to better patient outcomes. This shift toward personalized medicine is creating new investment opportunities, with startups such as Loxo Oncology, which was acquired by Eli Lilly for $8 billion, demonstrating significant value now paving the way for the space.

Business model

Biotech startups specializing in biologics, a sector characterized by large-molecule drugs derived from living cells, are revolutionizing the treatment of various diseases such as cancer and autoimmune disorders. These companies are at the forefront of the shift toward personalized medicine, leveraging the specificity and efficacy of biologics to address unmet medical needs. With the industry gravitating toward these innovative treatments, these startups have adopted a B2B2C business model, targeting health systems and large payers while ultimately serving the end patients. This approach ensures steady revenue streams through reimbursable services, possibly supplemented by cash pay or subscription models. The aim is to create a significant market impact by addressing the unmet medical needs that are ripe for innovation.

The market for biologics has many opportunities for partnerships, especially in novel biologics platforms such as data-driven protein engineering using AI & ML methods. These collaborative efforts can help de-risk the platform, which will be crucial for future fundraising and scaling up. Biologics, owing to their targeted delivery mechanisms, are often preferred over small molecules, particularly in scenarios wherein minimizing side effects is critical. However, navigating insurance coverage, including Medicare and private insurance, is a vital aspect of market access. Regulatory approvals from entities like the Food and Drug Administration (FDA) and decisions from bodies like the Centers for Medicare & Medicaid Services (CMS) are pivotal in shaping market strategies. Thus, these startups must strategically tailor their coverage approaches to suit different markets and regulatory environments. The delivery of these biologics, which often requires clinical settings for injections or infusions, especially for antibody methods, or using peptide injection pens, underscores the specialized nature of these treatments.

Biologics startups face challenges such as navigating complex regulatory landscapes, managing high development costs, and competing with established industry players. However, the opportunities for growth are significant, especially in expanding into new markets and leveraging emerging technologies. Adapting to evolving payer coverage models and aligning with future trends, such as advancements in biologic therapies and shifts in healthcare policies, will be crucial for these companies. A focus on precision medicine, with an aim to *design* rather than *discover* biologics, and a strong emphasis on biomanufacturing innovations, are shaping the future of these startups.

VC activity

In the biologics sector, funding trends have mirrored the broader industry, with a significant upsurge in 2020, followed by a decline through to 2023, with Q3 2023 in particular witnessing a notable decrease in funding. This trend highlights the sector's sensitivity to research outcomes and market dynamics, wherein funding is as influenced by clinical results as it is by speculative investment.

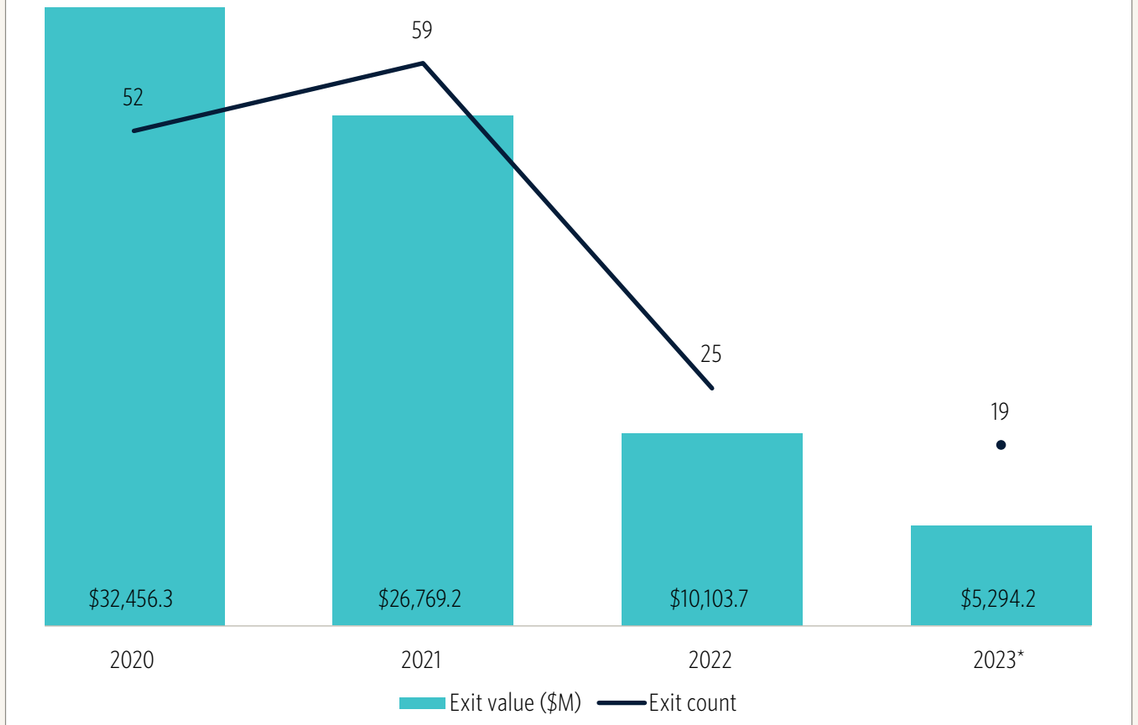
Key deals in the biologics sector underscore a strategic focus on emerging technologies and market expansion. Significant investments such as Generate Biomedicine's $273 million Series C and MBX Biosciences' $115 million Series B demonstrate investor confidence in data-driven platforms and innovative therapies. Internationally, significant investments in Chinese firms like Dongyangguang and Abogen Biosciences reflect sector creation needs for a robust biotech infrastructure.

Looking forward, the biologics sector shows potential for growth despite challenges. The emergence of ADCs as a promising subsector and the pivot toward precision medicine indicate new directions for investment and innovation. While the sector is currently dominated by larger pharmaceutical firms, particularly in areas like weight loss therapies, significant potential exists for early-stage ventures, especially those leveraging AI in protein engineering. Challenges in deal activities are countered by an increase in exit activities, suggesting a maturing market. This is reflected by the 86% increase in deal value from Q2.

Biologics VC deal activity

Source: PitchBook • Geography: Global • *As of September 30, 2023

Biologics VC exit activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Key biologics VC deals over the past year*

Company	Close date (2023)	Subsegment	Stage	Deal value ($M)	Lead investor(s)	Valuation step-up
Generate Biomedicines	September 6	Protein/peptide	Late-stage VC	$273.0	N/A	1.2x
Orbital Therapeutics	April 26	Vaccine, oligos/RNA	Early-stage VC	$270.0	ARCH Venture Partners	1.9x
Upstream Bio	June 6	Antibody	Early-stage VC	$200.0	Enavate Sciences, Venrock	1.7x
Aera Therapeutics	February 16	Protein/peptide	Early-stage VC	$193.0	ARCH Venture Partners, GV, Lux Capital	N/A
TORL BioTherapeutics	April 10	ADC/conjugate	Late-stage VC	$158.0	Goldman Sachs Asset Management	N/A
Abcuro	August 11	Antibody	Late-stage VC	$155.0	Bain Capital Life Sciences, Redmile Group	1.6x
Worg Pharmaceuticals	June 28	Protein/peptide	Late-stage VC	$154.0	N/A	N/A
Sinotau	July 3	Small molecule, antibody	Late-stage VC	$153.4	N/A	N/A
ROME Therapeutics	September 12	Protein/peptide	Early-stage VC	$149.0	N/A	2.3x
Bitterroot Bio	June 7	Protein/peptide	Early-stage VC	$145.0	ARCH Venture Partners, Deerfield Management	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Key biologics VC exits over the past year*

Company	Close date (2023)	Subsegment	Exit value ($M)	Exit type	Acquirer(s)/index	Post-money valuation ($M)
Kelun Biotech	July 11	ADC/conjugate	$1,496.7	Public listing	06990.HK	$1,670.5
ACELYRIN	May 5	Antibody	$1,128.6	Public listing	NASDAQ: SLRN	$1,668.6
Adlai Nortye	September 29	Small molecule, antibody, oncolytic virus	$860.0	Public listing	NASDAQ: ANL	$922.5
Cutia Therapeutics	June 9	Protein/peptide	$788.7	Public listing	02487.HK	$848.0
Apogee Therapeutics	July 13	Antibody	$509.4	Public listing	NASDAQ: APGE	$809.5
YZY Bio	September 25	Antibody	$371.3	Public listing	02496.HK	$397.1
Luzhu Biotech	May 5	Vaccine	$119.5	Public listing	02480.HK	$162.9
Bird Rock Bio	August 18	Antibody	$20.0	Acquisition	Skye Bioscience	$20.0
Emergence Therapeutics	July 12	ADC/conjugate	N/A	Acquisition	Eli Lilly	N/A
Qwixel Therapeutics	February 6	Antibody	N/A	Acquisition	Nammi Therapeutics	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Opportunities

Data-driven protein engineering: Data-driven protein engineering, at the intersection of computational methods and biophysical protein data, heralds a new era in the development of biologics. Leveraging advancements in machine learning, AI, protein databases, and high-throughput biology methods, this approach is poised to revolutionize the way protein structures and functions are predicted and manipulated. However, despite the advancements, developers still face challenges in creating biologic drugs that precisely target select molecules in disease pathways. The reliance on experimental methods to screen candidate libraries remains a hurdle, with functional response filtering, a crucial design objective, occurring only after several rounds of optimization and screening.

The field has seen substantial investor interest, particularly in the applications of AI in biotech. Companies are adopting different strategies, with some focusing on partnering models, as seen with BigHat Biosciences and LabGenius, while others like Absci and Protillion Biosciences are building their own pipelines. This interest is driven by the potential to significantly shorten development timelines and enhance the specificity of biologic therapeutics. Regulatory bodies are adapting to these changes, with AI & ML enabling richer pipelines to be taken into clinical trials without altering the downstream path. However, widespread adoption of these technology platforms is still in its infancy, and the industry is keenly awaiting the first clinical success story. Data-driven methods are set to become the standard in protein engineering, but there's a growing need for more accurate methods that can integrate biophysical data on a larger scale, promising a future wherein precision and efficiency in biologics development are greatly enhanced. Additionally, it is crucial for companies in this field to focus on addressing unmet medical needs, as ultimately, the real-world clinical value of these innovations will be a key determinant of their success in the public markets, rather than the theoretical potential of AI. Those focusing solely on partnerships or entering overcrowded target markets may find themselves at a disadvantage if they lose sight of this critical aspect of drug development.

Direct protein drug delivery: A technique that directly transports functional proteins to targeted cells, direct protein drug delivery represents a significant advancement in treating diseases characterized by compromised protein expression or function. By delivering proteins directly, this method circumvents the need for endogenous cellular production. The technology encompasses a range of delivery mechanisms, including nanoparticle-based systems, viral vectors, and innovative nonviral methods. While the field is emerging, with no clear market leader yet, it holds immense potential for a variety of therapeutic applications, especially in genetic disorders and certain cancers. However, challenges such as ensuring protein stability and bioactivity during delivery, avoiding immune responses, and achieving efficient and safe cell targeting remain significant hurdles. Current efforts in this area are predominantly focused on small molecules or nucleic acids.

Innovative companies are leading the charge in this space, with Moderna and BioNTech making strides in mRNA delivery, which results in indirect protein production. Despite these companies' success, limitations in dosing and protein size have restricted the broader application of mRNA technologies beyond vaccines. On the investment front, notable developments include Entrada

Therapeutics' $182 million IPO for a delivery platform using cyclic peptide conjugates, and Incisive Genetics' $9.4 million seed funding for lipid nanoparticles encapsulating the CRISPR protein and nucleic acid complex. These advancements hint at improved specificity in biologics and new applications in cellular entry. In the future, direct protein drug delivery could have an impact comparable to that of ADC technology, which revolutionized the delivery of small molecules to challenging targets. The ability to deliver high-value protein systems like the CRISPR complex might soon surpass current gene delivery methods, indicating a significant shift in the landscape of molecular medicine and biotechnology.

Risks and considerations

Consolidation in weight loss biologic drugs: The biologics market for obesity is highly consolidated, with significant control wielded by major pharmaceutical corporations like Eli Lilly and Novo Nordisk. This dominance raises concerns about the sector's growth, as it potentially limits market diversity and the entry of innovative treatments from smaller entities. Such a lack of diversity could stifle innovation, leading to slower development of new and more effective obesity treatments. Moreover, the reduced competition could result in higher prices for these biologics, impacting both the industry and patients seeking treatment. Despite this market concentration, collaborations and partnerships between large pharma companies and smaller biotech firms can drive innovation. A notable example of such successful collaboration is the partnership between Boehringer Ingelheim and Zealand Pharma in developing novel peptide-based medicines. Additionally, recent issues with compounding pharmacies trying to market weight loss peptides highlight the potential future fights on the biosimilar end to prolong the arrival of generics.[1] This demonstrates the need for these large consolidators to protect their assets from loopholes with strong patent portfolios.

Vaccine market limitations: The biologics segment's vaccine market, which experienced a surge in investment due to COVID-19 and the development of cancer vaccine technologies, is now facing substantial practical challenges. During the pandemic, government partnerships with companies were crucial for developing COVID-19 treatments and significantly boosted investment in this sector. However, as the world transitions toward postpandemic normalcy, the same level of governmental support and investment in vaccine development for other diseases has significantly decreased. This reduction in support is creating a riskier environment for vaccine-centric firms, which may struggle to find a clear direction in the post-COVID-19 era. This uncertainty is exacerbated by the fact that patients without health insurance may be unable to afford vaccines, thus further impacting market sustainability.

1: "Weight-Loss Drug Shortages Prompt Copycats and Counterfeits," ChemistryWorld, Royal Society of Chemistry, Anthony King, November 16, 2023.

BIOLOGICS

The vaccine market's profitability is often contingent upon government subsidies and support, making it an unstable area for ongoing investment. Startups and companies in this space must strategically plan and diversify to navigate these changes. A viable mitigation strategy is to expand beyond vaccines, possibly exploring other biologics or therapeutic areas. For instance, BioNTech, known for its mRNA COVID-19 vaccine, is also an immunology company developing multiple platforms beyond mRNA. In contrast, Moderna's future seems more dependent on the success of its mRNA technology in other therapeutic areas or on potentially using its COVID-19 vaccine profits to acquire new technologies. As the industry evolves, vaccine-focused firms must seek innovative ways to maintain their operations and contribute to public health advancements, thereby ensuring their adaptability and relevance in the changing landscape of biopharma.

Gene therapy

Overview

The gene therapy segment in biopharma represents a cutting-edge convergence of genetics and therapeutics. This segment is distinguished by its focus on modifying genetic material to treat or prevent disease. The technologies within this segment include sophisticated methods for gene editing, such as CRISPR and transcription activator-like effector nucleases (TALENs), and gene delivery systems, including viral vectors like adeno-associated viruses (AAVs), which serve as delivery vehicles to introduce therapeutic genes into patients' cells. mRNA therapy, made famous by its role in COVID-19 vaccines, is another hallmark of this segment; it enables cells to produce proteins that may counteract or prevent disease.

Legacy incumbents in this space include companies like Novartis, Gilead Sciences, and Spark Therapeutics, which have set a precedent in terms of investment and innovation in gene therapies focused on delivery. However, the landscape is rapidly evolving, with gene editing and mRNA startups like CRISPR Therapeutics, Moderna, and BioNTech gaining ground and potentially disrupting the industry with their rapid growth, propelled by advancements in technology and successful application in treatments. Most recently, the UK approval of Casgevy, which was developed from a collaboration between CRISPR Therapeutics and Vertex Pharmaceuticals for treating sickle cell disease and beta thalassemia, is a major milestone for gene editing.[2]

Subsegments

- **Oligos/RNA therapy:** This subsegment focuses on manipulating RNA to influence gene expression. Therapies involve the use of small interfering RNA (siRNA) to silence genes responsible for disease.
- **mRNA therapy:** mRNA therapies deliver messenger RNA molecules that encode for disease-fighting proteins, essentially turning the patient's body into its own medicine producer.
- **Gene delivery:** Key to gene therapy, this involves methods to deliver corrected genes into patient cells. Viral vectors are the most common delivery method, with nonviral methods being actively explored.
- **Gene editing:** This category encompasses technologies that allow for direct editing of the DNA within a patient's cells, with CRISPR-Cas9 being the most widely recognized technique that makes it possible to add, remove, or alter genetic material at particular locations in the genome.

2: "Sickle-Cell Treatment Created With Gene Editing Wins UK Approval," New York Times, Gina Kolata, November 16, 2023.

Industry drivers

- **Scientific advances enabling new therapeutic approaches:** The biopharma industry has seen significant advancements with improved gene editing tools like CRISPR-Cas9, optimized mRNA technologies, and better delivery mechanisms overcoming long-standing technical hurdles. These innovations are not just theoretical but are being actively implemented by startups such as Chroma Medicine, which closed on $135 million to build the next-generation gene editing platform focused on epigenetics. These developments represent a transformative shift in how we approach the treatment of previously intractable diseases, offering more precise, effective, and personalized medical solutions.

- **First approvals generating excitement and validation:** The biopharma sector is witnessing a surge in enthusiasm and validation following the first approvals of novel therapies in rare diseases. This trend is exemplified by former VC-backed companies like CRISPR Therapeutics, Alnylam Pharmaceuticals, and bluebird bio. CRISPR Therapeutics is leveraging CRISPR technology to develop gene-edited therapies for genetic disorders, resulting in the world's first gene-editing product approval. Alnylam's pioneering work in RNAi therapeutics has led to the approval of drugs targeting rare genetic conditions, while bluebird bio's gene therapies offer potential cures for genetic diseases. The success of these companies in navigating clinical trials to approval has fueled investment and interest in RNA and gene delivery therapeutics. The industry is now more optimistic about the prospect of durable, potentially curative therapies, thus marking a new era in medicine wherein genetic and rare diseases can be effectively targeted and treated.

Business model

In biopharma, gene therapy companies are rapidly gaining prominence by offering innovative treatments for genetic disorders. These companies, utilizing advanced techniques like nucleic acid delivery and gene editing, are pivotal in the movement toward personalized medicine. Their business models, which are primarily B2B2C, target health systems, large payers, and sometimes direct consumers. Revenue generation comes from various strategies, including reimbursable services, cash pay, subscription models, and royalties from licensing deals and collaborations with larger biopharma partners for late-stage development and commercialization. These models, especially in gene editing, face potential regulatory hurdles similar to other biologics and RNA therapies.

The gene therapy market's appeal stems from its ability to treat previously unaddressable genetic conditions. Crucial partnerships with insurance companies and health systems are vital in managing the high costs of gene therapy products, which often exceeds $1 million. These alliances are essential for market access and expanding patient reach. However, the regulatory environment poses significant challenges, with FDA approvals and CMS coverage greatly influencing market access. This necessitates flexible coverage strategies in various markets, considering the significant costs and manufacturing complexities. For instance, gene therapy companies such as bluebird bio have been leaders in developing value-based purchasing agreements that put up to 80% of a treatment's list price at risk depending on clinical outcomes.[3] Additionally, the success of mRNA vaccines indicates that scaling production could eventually lead to more accessible pricing.

3: "Recode the Status Quo," bluebird bio, n.d., accessed November 10, 2023.

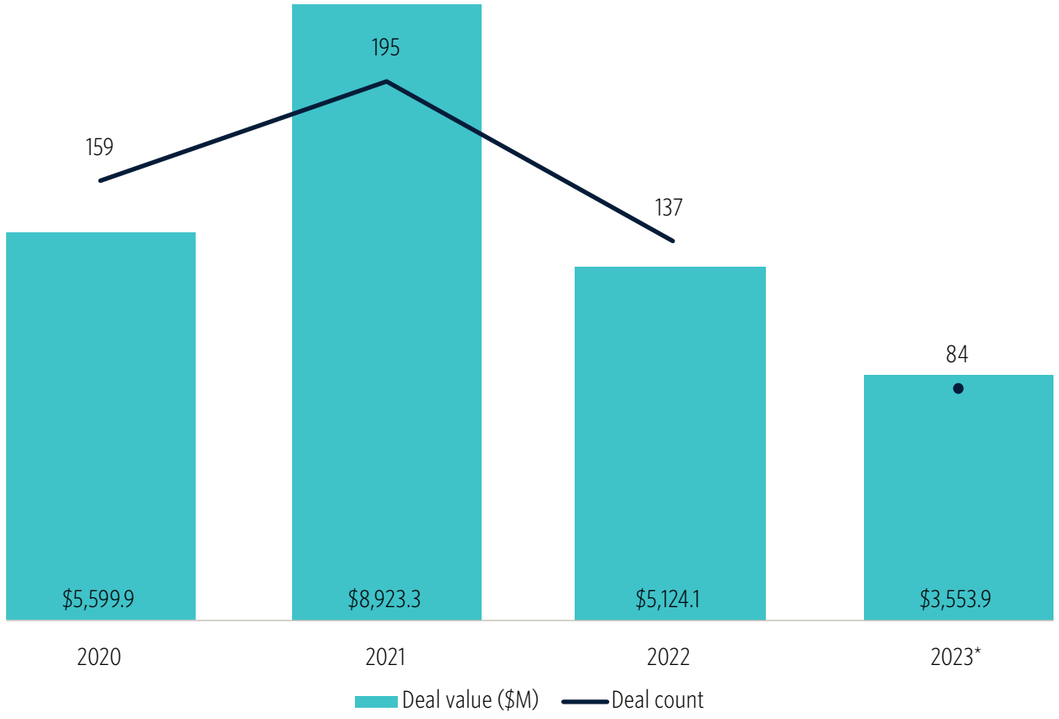
VC activity

The gene therapy sector has experienced a notable shift in funding trends, with a decline from its peak in 2021 as it entered 2023. However, there was a resurgence in Q3 2023, when funding increased by 46.6% from Q2. This uptick indicates renewed investor interest and potential in the field, suggesting a complex and dynamic funding environment for gene therapy.

Key deals in the gene therapy sector, such as Kriya Therapeutics' $430 million Series C for its RNA therapeutics hub and Orbital Therapeutics' $270 million Series A for RNA therapeutic development, underscore the sector's vitality. These significant investments highlight the sector's focus on emerging modalities, with capital flowing to various innovative areas. Gene therapy remains a hotbed for investment, attracting funds across multiple new platforms and technologies. This diversity of investment indicates a robust and innovative sector, ripe with opportunities for new therapeutic approaches and technological advancements.

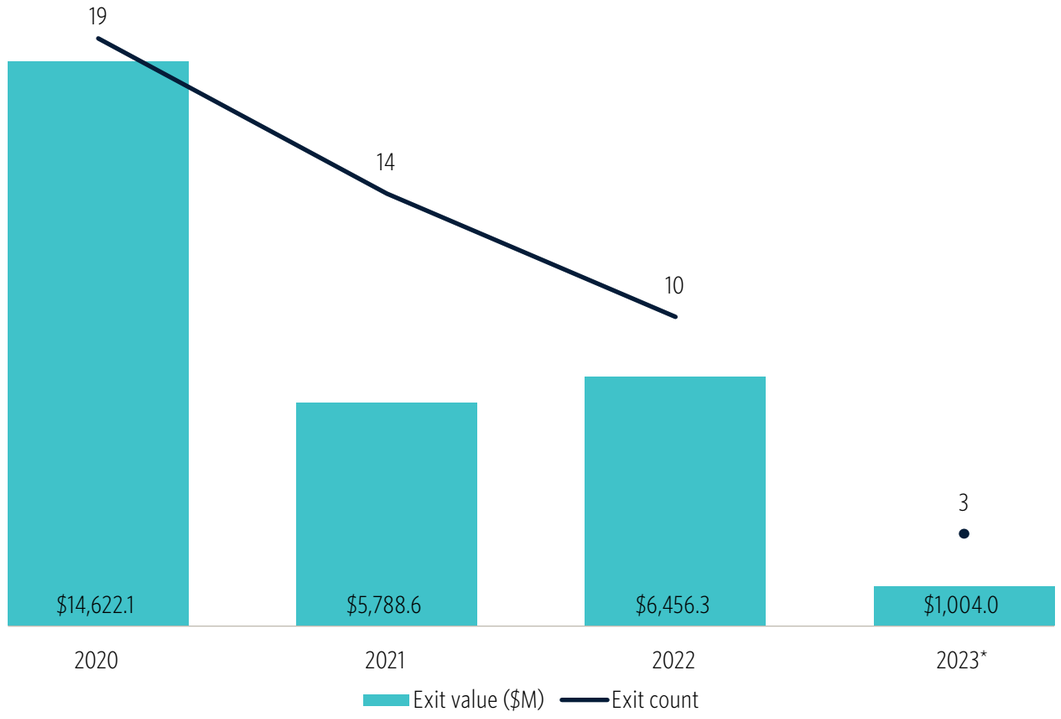
Looking toward the future, gene therapy faces both challenges and opportunities. The regulatory pathway for new modalities in gene therapy is not fully developed, thus presenting a significant challenge that could affect venture capital activity. However, the potential for growth is immense, especially if breakthroughs are achieved in gene editing or novel mRNA methods. These advancements could significantly expand funding and interest in the sector. While early-stage investment is currently high, we anticipate a shift toward late-stage focus due to the need for exits and the high capital requirements of later development stages. In a downturn with funding gaps, this shift would be a combination of maintaining large cash reserves, insider rounds, and downsizing startup operations until clinical milestones show promise. In other cases, shutting down is the only way if the funding gap is too large, with no excitement from investors even at discounted rates probably due to lack of technical development or clinical results.

Gene therapy VC deal activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Gene therapy VC exit activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Key gene therapy VC deals over the past year*

Company	Close date (2023)	Subsegment	Stage	Deal value ($M)	Lead investor(s)	Valuation step-up
Kriya Therapeutics	July 26	Gene delivery	Late-stage VC	$430.0	Patient Square Capital	1.3x
Metagenomi	January 5	Gene editor, immune cell	Late-stage VC	$275.0	Catalio Capital Management, Farallon Capital Management, Leaps by Bayer, Moderna, Novo Holdings, PFM Health Sciences, Revival Healthcare Capital, SymBiosis Capital Management	N/A
Orbital Therapeutics	April 26	Vaccine, oligos/RNA	Early-stage VC	$270.0	ARCH Venture Partners	1.9x
ReCode Therapeutics	September 19	mRNA	Late-stage VC	$260.0	Blockchange Ventures, Leaps by Bayer, Matrix Capital Management, Pfizer Ventures	3.0x
ADARx Pharmaceuticals	August 2	Gene editor	Late-stage VC	$200.0	Bain Capital Life Sciences, TCG Crossover Management	1.3x
Ensoma	May 16	Gene delivery, immune cell, stem cell	Early-stage VC	$135.0	5AM Ventures, Arix Bioscience	1.2x
Chroma Medicine	March 1	Gene editor	Early-stage VC	$135.0	GV	1.3x
Tune Therapeutics	March 9	Gene editor	Early-stage VC	$120.0	New Enterprise Associates	1.7x
Alltrna	August 9	Oligos/RNA	Early-stage VC	$109.0	N/A	N/A
Immorna	February 27	Vaccine, mRNA, oligos/RNA	Early-stage VC	$100.0	N/A	N/A

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Key gene therapy VC exits over the past year*

Company	Close date (2023)	Subsegment	Exit value ($M)	Exit type	Acquirer(s)/index	Post-money valuation ($M)
DTx Pharma	July 17	Oligos/RNA	$1,000.0	Acquisition	Novartis	$1,000.0
StrideBio	April 5	Gene delivery	$4.0	Acquisition	Ginkgo Bioworks	$4.0
Dynacure	March 2	Oligos/RNA	N/A	Acquisition	Flamingo Therapeutics	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Opportunities

Next-generation mRNA therapeutics: Next-generation mRNA therapeutics represent a transformative leap in medical science by harnessing messenger RNA to turn the body's cells into efficient protein production units. Originally catapulted into the limelight by their critical role in COVID-19 vaccines, these technologies are now branching out into broader applications including treatments for chronic diseases, cancer therapies, and advanced gene-editing techniques. The market for mRNA therapeutics, while still in its infancy, is experiencing rapid growth, driven by substantial investments and pioneering research into novel mRNA methodologies. This expansion is underscored by significant financial moves like Sanofi's $3.2 billion acquisition of Translate Bio, along with substantial funding rounds for startups like Replicate Bioscience and Orna Therapeutics, which are developing self-amplifying RNA and circular RNA platforms, respectively.

The unique appeal of mRNA therapies lies in their ability to use the body's own machinery to produce therapeutic proteins, offering a potentially more efficient and less invasive alternative to conventional drug therapies. This agility also facilitates swift development and adaptation, as evidenced by the rapid rollout of mRNA COVID-19 vaccines. However, the path to widespread adoption of mRNA therapeutics is strewn with challenges, including stabilizing the mRNA molecules, minimizing inflammatory reactions, and ensuring effective and targeted protein expression. Regulatory frameworks for these novel therapies, particularly for nonvaccine applications, are still under development, with agencies working to establish guidelines for chronic diseases and cancer treatments. The future of mRNA therapeutics is bright, with expectations of significant advances in mRNA stability, delivery mechanisms, and targeted therapies. These innovations, alongside the convergence with other biomedical technologies, could revolutionize personalized medicine and tackle previously untreatable conditions.

Advances in new gene editing methods beyond CRISPR-driven gene editing: RNA editing, a process that alters RNA sequences in cells to modify protein structure or quantity, offers a distinct approach in gene therapy compared to DNA editing. This emerging technology provides a reversible and transient alteration of genetic information, positioning it as a versatile tool for therapeutic applications. Despite its discovery nearly four decades ago, RNA editing gained commercial momentum only after the advancements in DNA editing technologies like CRISPR. The market is currently at an early stage but shows significant promise, driven by the need for targeted, reversible medical interventions. However, challenges such as the transient nature of RNA edits, which necessitates more frequent treatment administration, and the development of simplified delivery methods, remain unaddressed.

The field is witnessing substantial investment and innovation, with key players like Wave Life Sciences and ProQR Therapeutics leading the charge in clinical applications and technological development. Newer companies like Amber Bio and AIRNA have attracted significant funding, highlighting the growing belief in RNA editing's potential. The regulatory landscape is evolving, as RNA editing begins to enter clinical trials, thus setting the stage for future adoption and implementation in therapeutic contexts. RNA editing could revolutionize personalized medicine, as it offers new solutions for various diseases where temporary genetic modification is desirable. This emerging field is poised to unlock new therapeutic possibilities and address challenges in medical treatments that were previously insurmountable.

Risks and considerations

Regulatory and reimbursement hurdles: Gene therapies face considerable regulatory and reimbursement challenges that impact their development and adoption. Stringent FDA regulations and exacting international trial standards can significantly lengthen development timelines and escalate costs. Moreover, the high cost of gene therapy treatments presents obstacles for patient access, with insurers often hesitant to cover these expensive treatments, especially when long-term efficacy and safety data is incomplete. This hesitancy can limit the adoption of gene therapies and has a substantial impact on the industry. The rigorous regulatory environment and the challenges in securing reimbursement can slow the progress of new gene therapies, thus potentially impeding the growth of this promising sector.

In response to these challenges, companies are adopting mitigation strategies focused primarily on downsizing to reduce burn rates and reallocating resources toward achieving clinical milestones, while limiting expenditures in R&D. For example, Beam Therapeutics has downsized and redirected its focus to core products with higher potential upsides upon validation.[4] Despite its CAR-T product being a reasonable demonstration of its CRISPR technology, the success of its CAR-T product alone would not significantly advance the industry's ambitions in ex vivo treatment. In contrast, the success of Verve Therapeutics, which licensed Beam's platform for cardiovascular applications, brings confidence to this approach. This strategy of focusing on core products and leveraging partnerships highlights how gene therapy companies are navigating the complex landscape of regulatory and reimbursement challenges to sustain their operations and contribute to advancements in the field.

Technical challenges in gene therapy: Gene therapy, a rapidly evolving segment in biopharma, is grappling with substantial technical obstacles that impede its progress. Key challenges include ensuring targeted and efficient delivery of therapies into patient cells and managing immune responses to gene editing components or vectors. These technical difficulties can significantly compromise treatment efficacy and patient safety. As a result, they can lead to setbacks in clinical trials, challenges in regulatory approvals, and reduced patient acceptance.

To address these hurdles, mitigation strategies are focused on investing in R&D and fostering collaborations with academic institutions and other companies to pool knowledge and resources. Pharmatech companies do not develop internal pipelines but focus heavily on technology development and transfer much of the clinical risks and costs to partners. For example, Bayer focused on partnering with Mammoth Bio, a pharmatech company, to work with the latest gene-editing technologies for developing drugs. Similarly, pharmatech startups like Dyno Therapeutics are tackling delivery issues by optimizing viral vectors and forming strategic partnerships with giants such as Roche.

4: "Beam Lays Off About 100 Employees, Deprioritizes Car-T Programs to Push Runway Into 2026," Fierce Biotech, Max Bayer, October 19, 2023.

Cell therapy

Overview

Cell therapy represents a dynamic, innovative domain within biopharma, characterized by the use of living cells for therapeutic purposes. This field has experienced a surge in growth, fueled by breakthroughs in immunology and regenerative medicine. Cell therapies encompass immune cell therapies, which utilize the body's own immune system to combat diseases, and stem cell therapies aimed at tissue regeneration and repair through the unique capabilities of stem cells. Additionally, tissue engineering integrates cells with biomaterials to regenerate tissues and organs, presenting new treatment avenues.

The therapeutic promise offered by cell therapies, particularly for diseases that have previously defied conventional treatments, has catalyzed significant investment and focus within the sector. In the realm of immune cell therapy, prominent players include Novartis, Gilead Sciences through its acquisition of Kite Pharma, and Bristol Myers Squibb, following its acquisition of Celgene. These companies have been trailblazers in the CAR-T cell therapy arena, establishing benchmarks for therapeutic efficacy and safety profiles. While stem cell therapy is still nascent and lacks established leaders, pharmaceutical giants like Bayer and Eli Lilly are investing heavily and could emerge as disruptors, poised to redefine the landscape of biopharma with their novel approaches and advanced technologies.

Subsegments

- **Immune cell therapies:** Uses the body's immune cells, often modified ex vivo, to treat diseases. A prominent example is CAR-T therapy, wherein patients' T cells are engineered to target cancer cells.
- **Stem cell therapies:** Utilizes stem cells' ability to differentiate into various cell types, which aids in tissue regeneration, repair, and treatment of degenerative diseases. This includes both embryonic and adult stem cell therapies.
- **Tissue engineering therapies:** Uses biomaterials and cells to develop functional tissue constructs that can repair or replace damaged or diseased tissues in the body.

Industry drivers

- **Cell therapy as a cure:** Previous efforts in immune cell therapy suffered from lackluster results in the early efforts of Dendreon's first approved cell-based immune therapy. This changed with the clinical success of CAR-T, which led to large investment exits for Juno Therapeutics and Kite Pharma. There exists a range of diseases with limited or no effective treatment options. Conditions like certain aggressive cancers, genetic disorders, and degenerative diseases have remained therapeutic challenges. Cell therapies, especially those involving immune cells and stem cells, present a beacon of hope for these conditions. The initial CAR-T clinical breakthrough enabled the massive ongoing investor interest to fund cell therapy across the board, including bets on CAR-T, next-generation immune cell engineering modalities, and stem cell therapies.

- **Advancements in precision medicine:** Precision medicine allows treatments to be tailored to individual patients based on their genetic, biomarker, phenotypic, or psychosocial characteristics. As our understanding of genetics and molecular pathways involved in diseases expands, so does our ability to target these pathways with cell therapies. For instance, CAR-T therapies are customized for each patient using their cells. This personalized approach enhances the efficacy of treatments and reduces adverse side effects, thus driving demand for such therapies. Despite potential cost challenges downstream, the precision medicine mindset unlocked the fields of gene and cell therapy as a whole.

Business model

Cell therapy represents a groundbreaking paradigm in the biopharmaceutical industry, capitalizing on the therapeutic potential of human cellular material. This innovative sector, although currently a small portion of the healthcare market, is rapidly growing and poised to revolutionize patient treatment. The business model of cell therapy largely mirrors traditional biopharma processes, beginning with drug discovery and extending through rigorous R&D phases. This includes identifying cellular targets, engineering cells for therapeutic intervention, and conducting extensive preclinical and clinical trials to ensure safety and efficacy. Post-clinical phase, the focus shifts to manufacturing and market penetration strategies. However, cell therapy distinguishes itself by its emphasis on personalized treatments, which are often administered as a final therapeutic option. This involves a collaborative approach with healthcare providers, particularly hospitals, integrating cell therapy into patient care pathways, which is crucial given the high costs and complexities associated with insurance approvals.

The market attractiveness of cell therapy is anchored in its innovative approach to complex diseases and potential for personalized treatment solutions. Partnerships play a pivotal role in this landscape, involving collaborations with biotech firms, healthcare systems, and academic institutions for R&D, as well as VC firms for funding and technological advancements. However, the sector faces regulatory and insurance coverage challenges, due primarily to the high costs and personalized nature of treatments. Compliance with FDA regulations is essential for market access, and navigating

the intricacies of insurance coverage is crucial for patient affordability. The shift from autologous to allogeneic therapies, anticipated in the future, is expected to streamline manufacturing and reduce costs, although challenges in product availability and hospital administration remain.

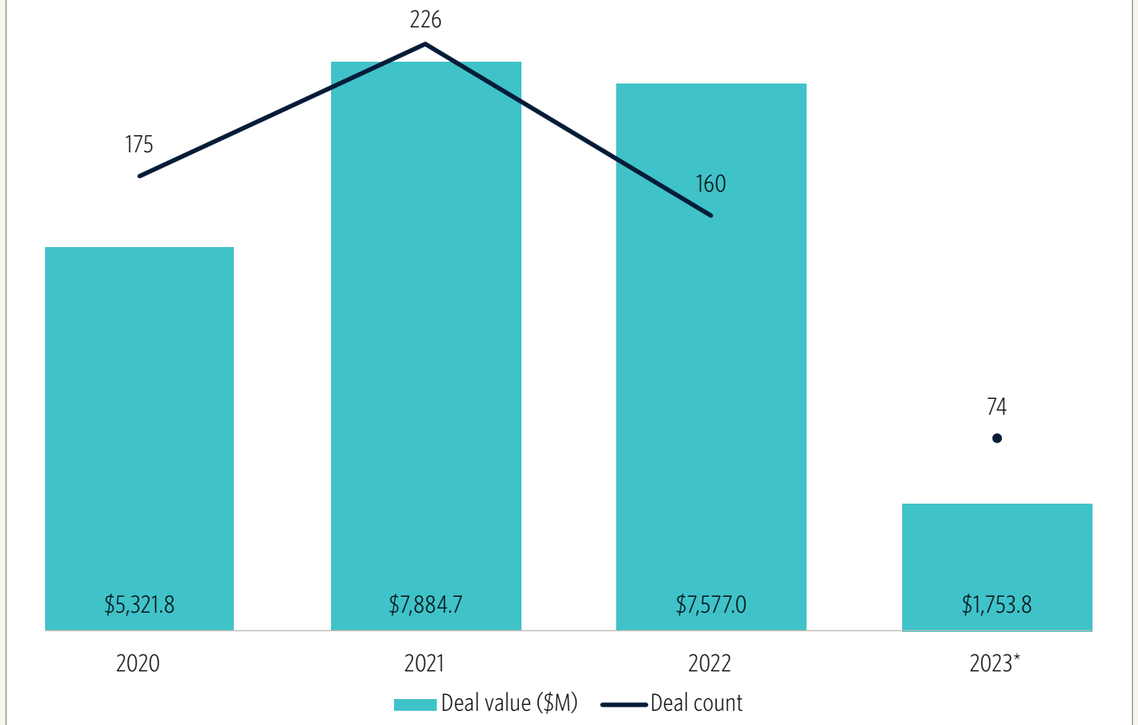
The sector must adapt to evolving scientific and technological advancements, especially as it transitions from more complex autologous therapies to potentially more scalable allogeneic ones. These developments will not only impact manufacturing processes but also influence patient access and treatment efficacy. To harness the full potential of cell therapies, companies must focus on building effective operating models and forging robust collaborations. This involves enhancing digital capabilities for better patient journey management, astutely navigating regulatory landscapes, and innovating revenue strategies to manage high treatment costs.

VC activity

The cell therapy sector has experienced a fluctuating funding landscape, which reached its deal value peak in 2021 at $7.8 billion, followed by a slight decline in 2022 to $7.6 billion and a more pronounced drop into 2023 to an estimated $2.2 billion. This trend is reflective of the evolving investor sentiment and market dynamics within the sector marked by mega-rounds and insider rounds at later stages for companies waiting for an IPO window. The third quarter of 2023 marked a significant low in funding since 2020, indicating a cautious approach from investors. Despite these challenges, notable deals in the sector, such as Altos Labs' $3 billion venture creation round, Lyell's $493 million Series B, and Sana Biotechnology's $435 million Series B, have demonstrated continued interest in innovative approaches to longevity, regenerative medicine, and cell therapy, especially for solid tumors and in vivo applications. These deals, driven by large investments, suggest that while overall funding has decreased, significant capital is still being directed toward groundbreaking and ambitious projects.

The cell therapy sector's outlook hinges on a combination of clinical success, exits, and transformative academic innovations. While the sector is currently dominated by a few deep-pocketed venture capitalists focusing on big bets, emerging areas like first-generation CAR-T therapies show promise due to their lower development costs and clearer market paths. However, the challenging fundraising environment still necessitates strong relationships with leading VCs, and companies must significantly differentiate from existing technologies to attract funding. Recent exits, including Sana Biotechnology's IPO at a $4 billion valuation and Legend Biotech's IPO at $2.5 billion, along with Tmunity's strategic exit to Gilead/Kite Pharma, demonstrate the sector's potential for lucrative exits as well as safety nets. The sector is poised for growth if it can navigate the current funding challenges, with companies like Sonoma Biotherapeutics showing promise for future IPOs based on technological advancements, and firms like Sana and Lyell potentially seeking exits to larger pharmaceutical companies to continue development amid funding constraints.

Cell therapy VC deal activity



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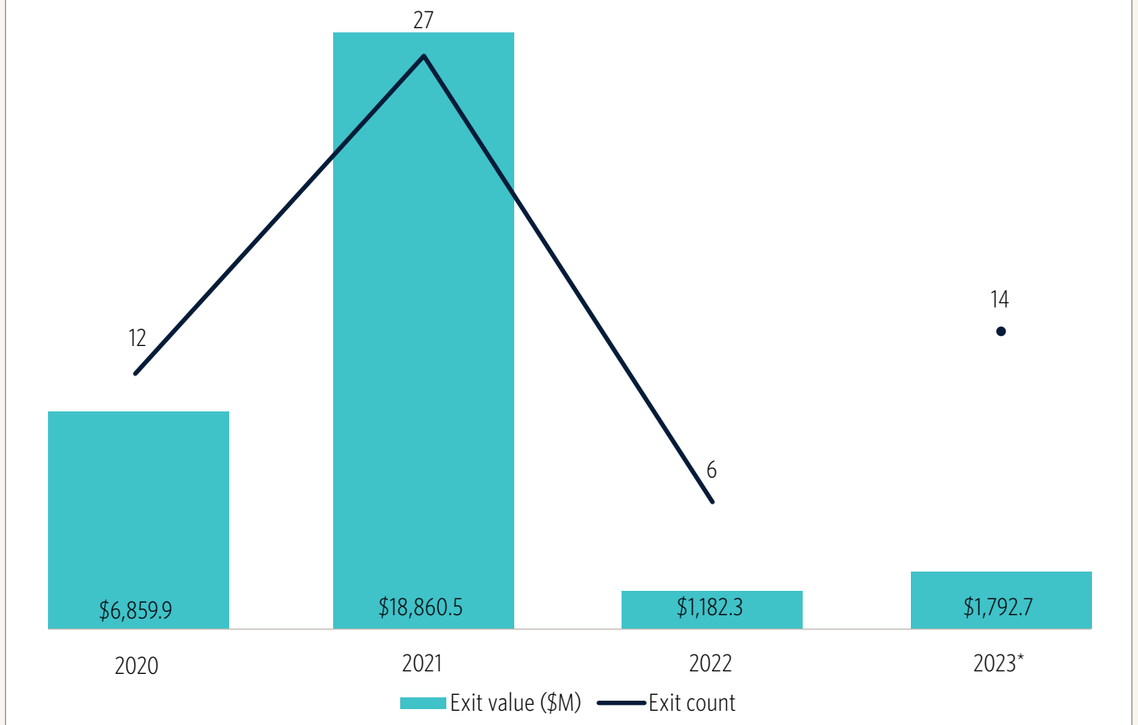
Cell therapy VC exit activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Key cell therapy VC deals over the past year*

Company	Close date (2023)	Subsegment	Stage	Deal value ($M)	Lead investor(s)	Valuation step-up
Metagenomi	January 5	Gene editor, immune cell	Late-stage VC	$275.0	Catalio Capital Management, Farallon Capital Management, Leaps by Bayer, Moderna, Novo Holdings, PFM Health Sciences, Revival Healthcare Capital, SymBiosis Capital Management	N/A
Cargo Therapeutics	February 9	Immune cell	Early-stage VC	$200.0	RTW Investments, Third Rock Ventures, Xontogeny	1.8
Ensoma	May 16	Gene delivery, immune cell, stem cell	Early-stage VC	$135.0	5AM Ventures, Arix Bioscience	1.2
Acepodia	June 6	Immune cell	Late-stage VC	$100.0	Digital Mobile Venture	N/A
Myeloid Therapeutics	May 4	Immune cell	Early-stage VC	$73.0	Hatteras Venture Partners	1.1
IASO Bio	January 15	Immune cell	Late-stage VC	$72.5	N/A	N/A
Tenpoint Therapeutics	July 12	Gene delivery, stem cell	Early-stage VC	$70.0	British Patient Capital, F-Prime Capital, Sofinnova Partners	N/A
Garuda Therapeutics	January 24	Stem cell	Early-stage VC	$62.8	Aisling Capital, Cormorant Asset Management, Northpond Ventures, OrbiMed	1.3
GRIT Biotechnology	September 8	Immune cell	Early-stage VC	$55.1	CICC Capital	N/A
BrainRepair	February 8	Stem cell	Late-stage VC	$54.2	N/A	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Key cell therapy VC exits over the past year*

Company	Close date (2023)	Subsegment	Exit value ($M)	Exit type	Acquirer(s)/index	Post-money valuation ($M)
Tmunity	February 22	Immune cell	$1,300.0	Acquisition	Kite Pharma	$1,300.0
Neogene Therapeutics	January 16	Immune cell	$200.0	Acquisition	AstraZeneca	$200.0
Turnstone Biologics	July 24	Immune cell	$186.3	Public listing	NASDAQ: TSBX	$266.3
CERo Therapeutics	June 7	Immune cell	$82.0	Public listing	NASDAQ: CERO	$145.0
CytoMed Therapeutics	April 17	Immune cell	$24.5	Public listing	NASDAQ: GDTC	$34.1
Carisma Therapeutics	March 7	Immune cell	N/A	Public listing	NASDAQ: TSBX	N/A
Teraimmune	June 29	Stem cell	N/A	Acquisition	Baudax Bio	N/A
Ambys Medicines	February 23	Stem cell	N/A	Acquisition	Cytotheryx	N/A
Carmell Therapeutics	July 14	Tissue/biomaterial	N/A	Public listing	NASDAQ: CTCX	N/A
Noile-Immune Biotech	March 29	Immune cell	N/A	Public listing	4893.TYO	N/A

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Opportunities

Off-the-shelf therapies: In the evolving landscape of immune cell therapies, a notable shift is occurring from traditional autologous methods, which utilize a patient's own cells, to the development of allogeneic, or "off-the-shelf," therapies. Despite being in the developmental phase, these allogeneic products mark a significant pivot in the industry. Current CAR-T products, such as Novartis' Kymriah and Gilead's Yescarta, are notably costly, with prices around $475,000 and $373,000, respectively. These high costs are driven by substantial investment and manufacturing expenses, as seen in Gilead's $11 billion acquisition of Kite Pharma and the estimated $100,000 manufacturing cost per dose.[5]

Leaders in the industry, including Novartis, Bristol Myers Squibb, and Gilead, continue to dominate the space with their initial foray into autologous cell therapy. From an investment standpoint, transitioning to allogeneic approaches is perceived as less risky after the success of autologous methods. Legend Biotech, which is valued at $2.1 billion, is at the forefront of this shift. The allogeneic CAR-T therapy presents unique features and advantages, potentially unlocking new targets and enabling wider patient adoption due to cost reductions. However, these therapies face new manufacturing challenges and a complex regulatory environment, as evidenced by the approval of Atara Biotherapeutics' Ebvallo for a rare post-transplant complication. Initially, these products will carry high costs due to significant initial investments and targeted development, but over time, the cost of developing allogeneic cell therapy is expected to decrease, thereby paving the way for large-scale adoption across various therapeutic areas.

Next-generation modalities: Next-generation modalities in biopharma represent a pivotal shift that extends beyond traditional T cell therapies to encompass a diverse array of cell types, including stem cells, natural killer (NK) cells, macrophages, B cells, and advanced T cell technologies. Fueled by breakthroughs in genetic engineering, these novel therapies are set to address a wide range of conditions spanning from regenerative medicine and autoimmune diseases to solid tumors. This expansion in therapeutic approaches signals a major advancement, offering new, promising treatment avenues beyond conventional cell therapy methods. The cell therapy market, currently buoyed by the success of CAR-T products, is on the cusp of further expansion. The advent of next-generation methods is poised to significantly enlarge the market scope by enabling treatment for more varied targets and medical indications, heralding a new era of growth and development in cell therapy.

Despite the burgeoning potential, the field of next-generation modalities is still in its formative stages, with no established market leaders. Nonetheless, investment trends indicate a growing interest and belief in its future prospects. Notable examples include Be Biopharma, which raised $130 million in Series B funding for its work on engineered B cell modalities targeting solid tumors, and bit.bio, which secured a $141 million Series B to advance its cell-coding technology. These developments hint at the unique features and advantages of next-generation therapies, such as the potential for groundbreaking stem cell products in regenerative medicine and more efficient manufacturing techniques like blood and plasma harvesting for B cell engineering. However, the field is not without its challenges, as it faces significant technical, regulatory, and manufacturing hurdles. The focus on high-value targets becomes crucial to meet investor expectations and to successfully navigate these challenges. The adoption and implementation of these advanced therapies are largely propelled by their potential to address unmet medical needs, with companies like bit.bio leading efforts in areas like liver regeneration. As the field evolves, it is poised to make a substantial impact, driven by technological innovation and a strong focus on fulfilling critical medical needs.

5: "At $475,000, Is Novartis' Kymriah a Bargain—or Another Example of Skyrocketing Prices?" Fierce Pharma, Eric Sagonowsky, August 31, 2017.

Risks and considerations

Operational complexities: Operational complexities in manufacturing cell therapies pose significant challenges for the industry, due primarily to the intricate nature of scaling production while maintaining consistent quality. These complexities are further exacerbated by the high costs involved in the development and administration of these therapies, thus impacting market accessibility. To mitigate these issues, companies like Lyell, which raised a $141 million Series B in 2021, are streamlining operations, including cutting costs in areas like employees, R&D, and pipeline to focus on advancing products in clinical trials. Additionally, investors are increasingly channeling funds into pharmatech infrastructure to alleviate operational challenges. This trend is evident in the rise of biomanufacturing startups such as Cellares and Cellino Biotech, which raised $80 million and $71 million in Series B funding, respectively, for immune and stem cell therapy manufacturing. These investments are pivotal in decoupling manufacturing costs from drug development startups, marking a crucial strategy for addressing the operational hurdles in the cell therapy market.

Regulatory and safety concerns: These concerns are paramount in the development of cell therapies, particularly with potent modalities like CAR-T, which are associated with severe side effects such as cytokine release syndrome and neurotoxicity. These adverse events not only risk damaging public perception but also lead to stringent regulatory scrutiny, potentially impeding market adoption. The innovative nature of these therapies subjects them to rigorous regulatory pathways, thereby necessitating detailed safety and efficacy data. This regulatory rigor can significantly affect the commercial success of treatments, especially if clinical trials or approvals encounter setbacks. For instance, Beam Therapeutics, after facing several challenges, had to undergo substantial downsizing to conserve resources for clinical developments. The FDA's demanding requirements have led some companies to seek validation for their products in regions like Europe or China. In addressing these challenges, solutions might emerge from pharmatech innovations rather than traditional biopharma approaches. An example is Beacon Biosignals, which focuses on addressing neurotoxicity issues, highlighting the potential of technological advancements in mitigating critical safety concerns in cell therapy development.

Emerging therapy

Overview

The emerging therapy segment in biopharma is at the forefront of innovation. It focuses on the development of novel treatments that could revolutionize medical practice. This segment encapsulates a diverse range of technologies poised to address unmet medical needs with precision and efficiency. Nanotechnology in medicine offers targeted drug delivery, while bacteriotherapy, or the use of bacteria as treatment, is reshaping approaches to conditions like Clostridium difficile (C. diff) infections and is being explored for its potential in treating a variety of other diseases. Oncolytic viruses represent a new class of cancer therapeutics that selectively infect and destroy cancer cells while sparing normal tissues. Exosomes are another frontier, with their natural role as intercellular messengers being harnessed to deliver therapeutic molecules directly to specific cell types.

Key legacy incumbents in these various spaces, such as Amgen, with its pioneering oncolytic virus therapy Imlygic approved for melanoma, and startups like Seres Therapeutics in the bacteriotherapy domain, are making significant strides with approval of Vowst for C. diff infections. Meanwhile, companies such as Evox Therapeutics are gaining traction, potentially disrupting the industry with clinical validation in the exosome subsegment.

Subsegments

- **Nanotech medicine:** Utilizes nanoparticles for targeted drug delivery systems, thus enhancing the efficacy and reducing the side effects of treatments.
- **Bacteriotherapy:** Involves the use of live bacteria or their components to treat and prevent diseases, therebyopening avenues in the gut microbiome and beyond.
- **Oncolytic virus therapy:** Employs viruses that selectively infect and lyse cancer cells, offering a novel approach to cancer treatment.
- **Exosome therapeutics:** Uses exosomes as delivery vehicles for drugs, with potential applications ranging from regenerative medicine to cancer therapy.

Industry drivers

- **Precision synthetic biology:** Bioengineering advancements are catalyzing the development of precision medicine, with nanoparticles engineered for selective tissue targeting, microbes programmed for site-specific colonization, and the modification of viruses and exosomes to deliver custom payloads. These innovations are leveraging natural body systems and immune responses, such as using engineered cells and viruses to stimulate antitumor immunity or exploiting the microbiome for gastrointestinal and metabolic disorder treatments.
- **Targeted delivery systems:** The emerging therapy segment is capitalizing on the body's extracellular vesicles, like exosomes, or synthetic variants, like lipid nanoparticles, for targeted drug transport, which signifies a shift toward employing the body's innate mechanisms for therapeutic delivery. These breakthroughs in biological understanding and bioengineering are merging to create ultratargeted therapies that promise personalized treatment regimens, pushing beyond the limits of traditional pharmacological approaches and opening new frontiers in the manipulation of biological systems for healing.

Business model

Given the early stage of development, many emerging therapy companies generate minimal revenue today, but all more or less follow the biopharma's biologics FDA pathway to the market. The primary focus is on raising capital to advance pipelines through preclinical and early clinical research. Like the rest of biopharma, companies within the emerging therapy space generate revenue primarily through the development and commercialization of their proprietary technologies and therapeutic products.

VC activity

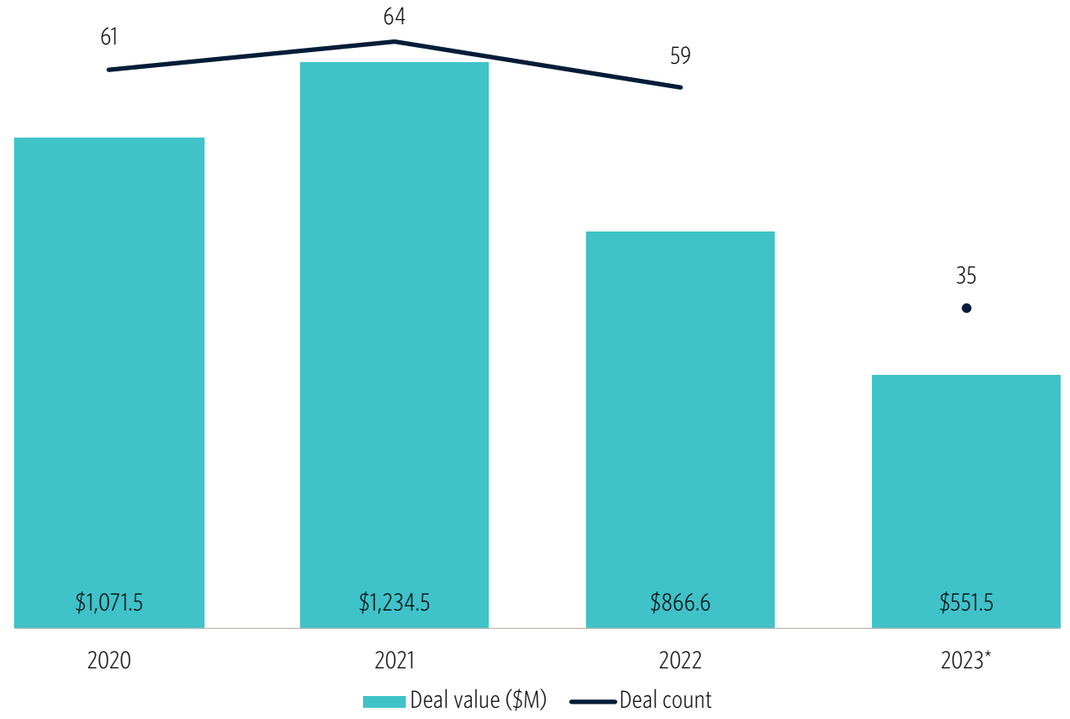
In the biopharma industry, VC activity for emerging therapeutics has mirrored broader industry trends, with an upsurge in funding in 2021 followed by a subsequent decline. However, due to the distinct characteristics of various modalities in this segment, these trends should be approached with caution. The unique features of each therapeutic approach impact deal activity, making a one-size-fits-all analysis less applicable.

Notable investments in this sector include CG Oncology's oncolytic virus platform, which raised over $520 million; Evox Therapeutics' exosome platform, with over $159 million in funding; and Microbiotica's microbiome adjuvant platform, which raised over $70 million. These deals underscore the trailblazing development of emerging technologies in the sector. Each represents a commitment to advancing novel therapeutic approaches, indicating a healthy interest in innovative biopharma technologies.

Recent exit activity has shown mixed results. For instance, Finch Therapeutics' $127 million IPO was undermined by the failure of its microbiome drug in clinical trials. Similarly, Codiak BioSciences' exosome platform reached IPO with an $82 million raise but ultimately faced bankruptcy—not due to technical hurdles, but because of costly clinical trials. These dynamics reflect the challenges inherent in bringing emerging therapeutics to market, where significant investments are often required to overcome technical and clinical trial barriers.

Specific subsectors within the market, such as oncolytic viruses and nanotechnology, are showing promise, particularly for their use in conjunction with other modalities as means for drug delivery. Conversely, investor focus on microbiome and exosome subsectors has waned due to recent high-profile failures. The sector is poised for a transformative breakthrough that could reignite investor interest. In terms of challenges, securing consistent funding remains a significant hurdle, particularly for technologies yet to demonstrate clinical success. However, growth opportunities exist, especially for therapies that can show clear clinical advantages or cost-effectiveness, and will potentially attract more VC investment in the future.

Emerging therapy VC deal activity



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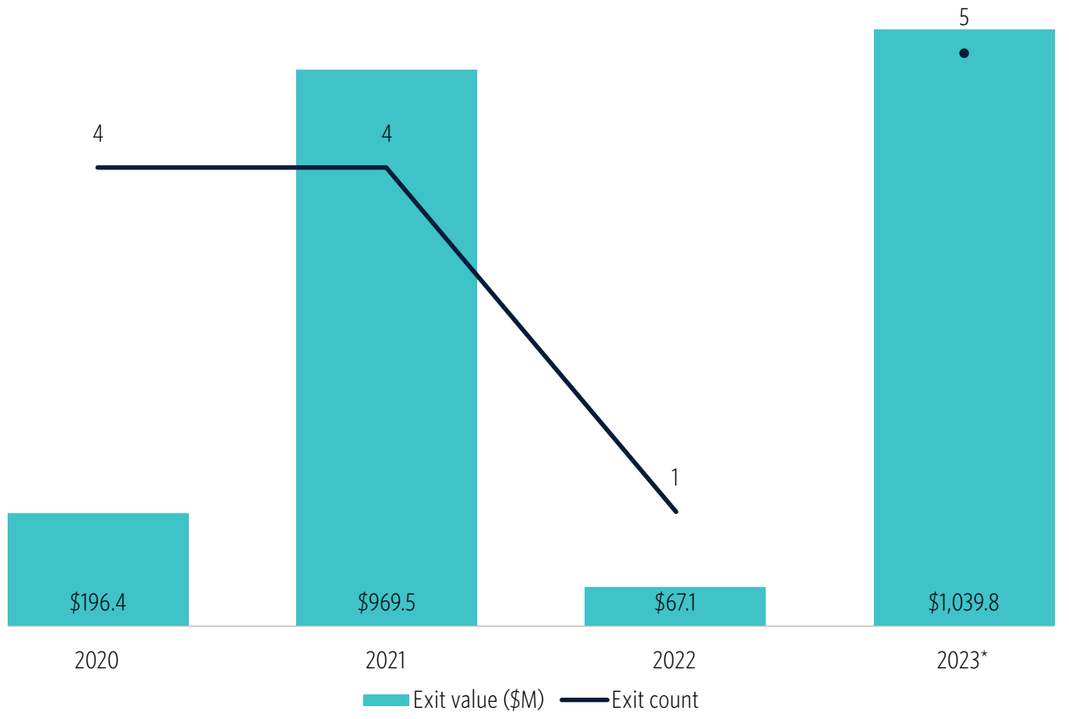
Emerging therapy VC exit activity



Source: PitchBook • Geography: Global • *As of September 30, 2023

Key emerging therapy VC deals over the past year*

Company	Close date (2023)	Subsegment	Stage	Deal value ($M)	Lead investor(s)	Valuation step-up
CG Oncology	August 2	Oncolytic virus	Late-stage VC	$105.0	Foresite Capital Management, TCG Crossover Management	1.3x
Elucida Oncology	June 15	Nanotech	Late-stage VC	$45.2	N/A	N/A
Capacity Bio	April 4	Small molecule, protein/ peptide, nanotech	Early-stage VC	$35.0	Insight Partners, RA Capital Management	N/A
Surge Therapeutics	May 24	Small molecule, nanotech	Late-stage VC	$32.0	Bioluminescence Ventures	1.8x
Prokarium	February 9	Bacteriotherapy	Late-stage VC	$30.0	N/A	N/A
BioTroy Therapeutics	March 7	Oncolytic virus	Early-stage VC	$26.2	Co-Win Ventures	N/A
Exeliom Biosciences	June 30	Bacteriotherapy	Late-stage VC	$26.0	CE-Ventures	N/A
Calidi Biotherapeutics	June 23	Oncolytic virus	Late-stage VC	$25.0	Jackson Investment Group	N/A
TILT Biotherapeutics	February 7	Oncolytic virus	Late-stage VC	$21.6	Lifeline Ventures	1.2x
IconOVir Bio	June 21	Oncolytic virus	Early-stage VC	$20.2	N/A	N/A

Source: PitchBook • Geography: Global • *As of September 30, 2023

Key emerging therapy VC exits over the past year*

Company	Close date (2023)	Subsegment	Exit value ($M)	Exit type	Acquirer(s)/index	Post-money valuation ($M)
Adlai Nortye	September 29	Small molecule, antibody, oncolytic virus	$860.0	Public listing	NASDAQ: ANL	$922.5
Genelux	January 26	Oncolytic virus	$126.9	Public listing	NASDAQ: GNLX	$141.9
Azitra	June 15	Bacteriotherapy	$52.9	Public listing	NASDAQ: AZTR	$60.4
Calidi Biotherapeutics	September 12	Oncolytic virus	N/A	Public listing	NASDAQ: CLDI	N/A
Ysopia Bioscience	June 13	Bacteriotherapy	N/A	Acquisition	Verb Biotics	N/A

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Opportunities

Next-generation biologic modalities: Emerging therapeutics in the biopharma industry are opening new frontiers, especially in the realm of next-generation biologic modalities. Technologies like oncolytic viruses and engineered bacteria show burgeoning potential for treating diseases, notably cancer. Startups like Oncorus are making strides with oncolytic viruses designed to selectively kill cancer cells and stimulate immune responses. Synlogic Therapeutics, meanwhile, is using synthetic biology to engineer therapeutic bacteria that perform specific functions in the body. These innovations represent a promising future for these novel modalities.

In the targeted drug delivery market, advancements in nanotechnology and exosome-based systems are revolutionizing how drugs are administered. This approach enables direct delivery of drugs to the disease site, which reduces systemic exposure and side effects. Leading this innovation, Alnylam Pharmaceuticals is utilizing RNAi therapeutics delivered through advanced nanoparticle systems. Codiak BioSciences is exploiting the natural targeting capabilities of exosomes to develop new biologic drugs, which will potentially transform treatments across various diseases. The market maturity and size for these emerging therapeutics are growing, driven by the pressing market need to address complex diseases more effectively and with fewer side effects. Investment trends are skewing toward these innovative approaches, reflecting their unique features and advantages. Regulatory and institutional contexts are evolving to accommodate these advancements, thus paving the way for broader adoption and implementation.

Risks and considerations

Novelty hurdles: Emerging therapeutics in the biopharma industry face significant regulatory and technical hurdles that pose challenges to their development and market entry. Novel therapies such as bacteriotherapy and exosome-enhanced drug delivery are pioneering new treatment methods, which often encounter uncharted regulatory pathways. This lack of precedent can lead to delays in clinical trials and heightened regulatory scrutiny. Moreover, the absence of established clinical efficacy for these innovative approaches necessitates rigorous trials to prove their safety and effectiveness—a process that can be both time-consuming and uncertain. These factors create a landscape filled with clinical and regulatory uncertainty, which impacts the speed at which these new therapies can be brought to market and gain acceptance.

The technical complexity involved in developing and manufacturing these therapies introduces further risks. Dealing with the intricacies of nanotechnology and exosome delivery systems requires expertise and presents considerable challenges, particularly in scaling up production and ensuring consistent quality. Additionally, the substantial funding required for research, development, and manufacturing of these advanced technologies often poses a significant barrier, especially for startups operating in a competitive investment landscape. To mitigate these risks, approaches such as forming strategic partnerships, engaging early with regulatory bodies, and seeking collaborative funding opportunities are essential. These strategies can help navigate the complex regulatory environment and manage the high costs associated with the development of emerging therapeutics, thereby enabling continued innovation and progress in this dynamic sector of biopharma.

Therapeutic areas

Overview

In addition to the diverse modality segments detailed above, the biopharma industry can also be scoped in terms of therapeutic areas, each distinguished by unique technology profiles, research focus, and key players. We divide the VC biopharma landscape into several therapeutic areas:

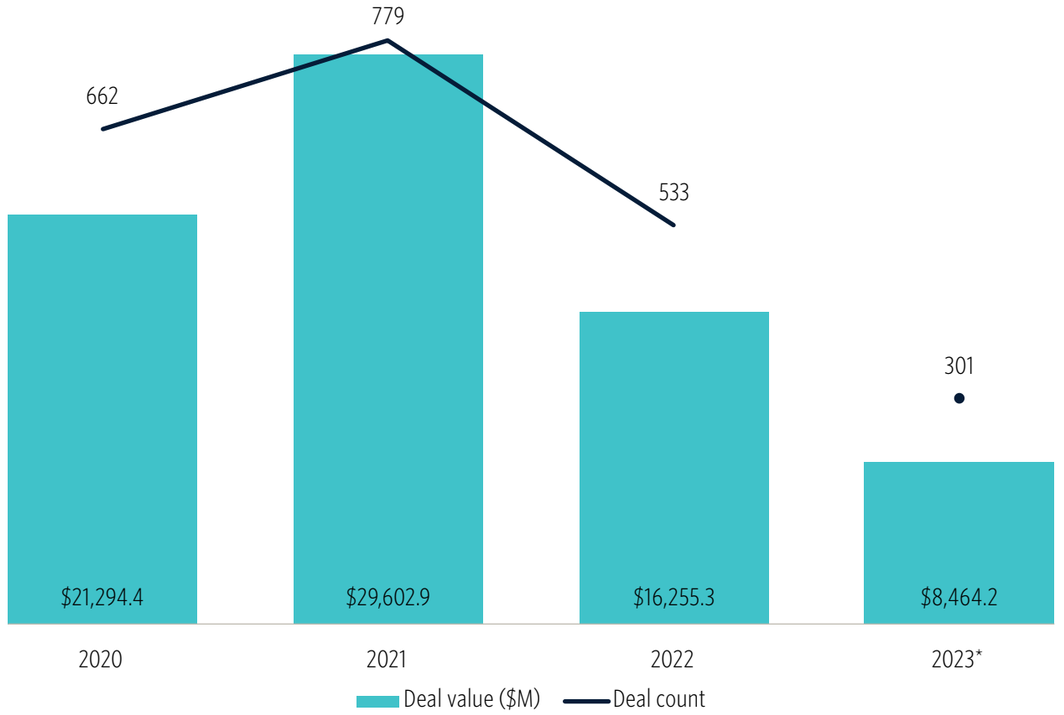
- **Oncology:** This segment encompasses all aspects of cancer research and treatment, including solid tumors and immuno-oncology, or immunotherapy.
- **Neurology:** The segment covers a range of diseases and disorders related to neurology, psychology, and psychiatry. It includes the R&D of treatments for mental health disorders, neurological conditions, and brain health.
- **Cardiovascular & metabolic disease:** This segment is dedicated to cardiovascular, metabolic, and endocrinological diseases. It involves the development of treatments for heart diseases, diabetes, and other metabolic disorders.
- **Immunology & infectious disease:** Covering autoimmune disorders, allergies, and anti-infective treatments, this segment deals with diseases related to the immune system and infectious diseases.
- **Digestive & renal systems disorder:** This segment includes the development of treatments for conditions related to gastroenterology, hepatology, nephrology, and urology, focusing on the digestive and renal systems.
- **Systemic & structural disorder:** This segment covers a broad range of conditions including hematology, dermatology, musculoskeletal disorders, respiratory diseases, and ophthalmology.
- **Specialty disease:** Focused on aging, rare and orphan diseases, genetic disorders, and animal health, this segment deals with specialized, often less common diseases and offers targeted and niche therapeutic solutions.
- **Unknown & stealth:** This segment includes biopharma companies that are either working on unknown targets or operating in stealth mode, which often involves groundbreaking and undisclosed research areas in biopharma.

Oncology

In biopharma, oncology remains at the center of investment, with significant competition across targets and indications. It has accounted for approximately 44% of investment dollars in 2023. This dominant position underscores the critical importance and potential of cancer research and treatment. The trend in VC activity within oncology closely mirrors the broader industry trends, having peaked in 2021 and subsequently declined. Advances in gene and cell therapy are fueling optimism for potential cures for cancer. The field faces the ongoing challenge of treating solid tumors, a significant area of unmet medical need. As our understanding of cancer biology evolves, new opportunities are emerging to target previously "undruggable" areas, thus reinforcing oncology as a sector with substantial revenue potential.

Despite the opportunities, the oncology sector is not without its risks. Cancer vaccines, for example, remain largely unproven and carry considerable market risks, especially when compared with infectious disease vaccines. The intense competition in this field is also a significant factor, with many companies pursuing similar targets in a race to be best in class. Oncology is witnessing the emergence of new modalities that are reshaping the approach to cancer treatment. Highlighting this trend are major deals like Vividion Therapeutics' acquisition by Bayer for $1.5 billion in 2021, which emphasized the promise of degraders in oncology. Further, the acquisitions of Affinivax by GSK for $3 billion and VelosBio by Merck for $2.7 billion demonstrate the potential of ADCs, which combine antibody precision with small molecules for more targeted cancer treatment.

Oncology VC deal activity



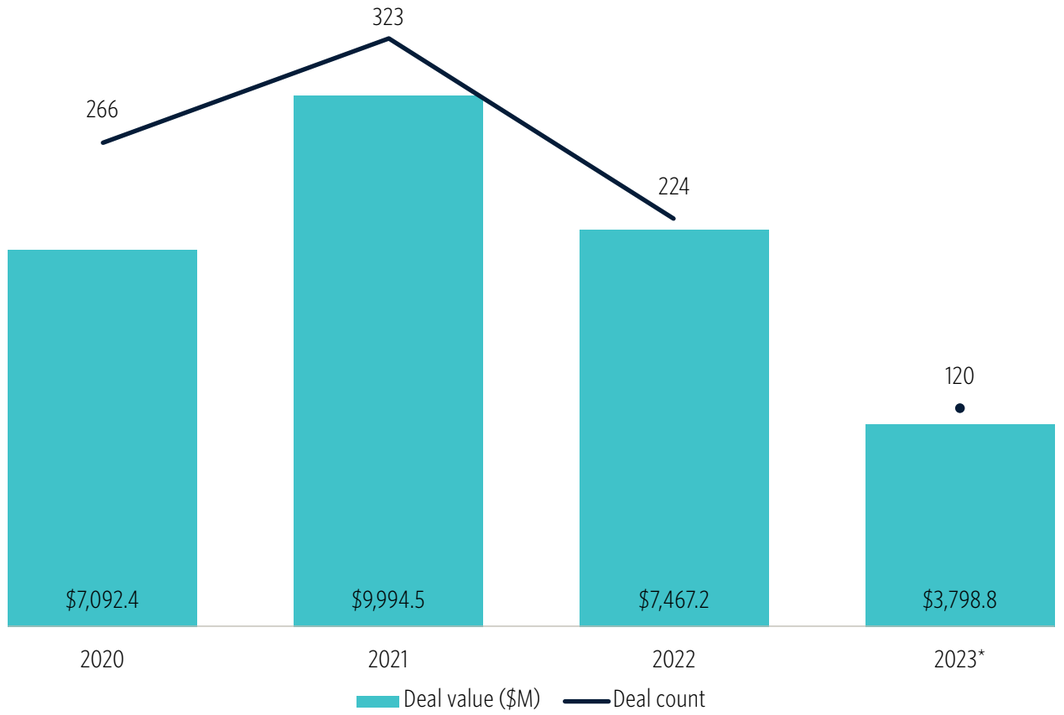
Source: PitchBook • Geography: Global • *As of September 30, 2023

Neurology

Neurology remains a challenging space for pharma and startups like, but the field is moving forward, with victories such as Biogen's Leqembi drug for Alzheimer's disease that help drive continued investor interests for new bets. Technology-wise, in neurology, small molecules have historically dominated due to the challenges posed by the blood-brain barrier. However, biologics and nucleic-acid-based methods are showing increasing promise as drug delivery techniques improve. Particularly notable is the potential role of stem cells in repairing the nervous system. New technologies are emerging that facilitate the discovery of gene and protein biomarkers, which can significantly aid in the treatment of neurological disorders. Advances in methods for delivering therapeutic molecules to the brain are also opening up new treatment avenues. Furthermore, advancements in stem cell research may offer novel approaches to combating neurodegeneration.

However, this field is not without its challenges. Monitoring patients over the course of treatment poses a significant hurdle, as there are few standardized methods to measure neurological health beyond questionnaires. Further, clinical trials for neurological diseases can run long, such as the clinical trials for Denali Therapeutics' Parkinson's drug lasting until 2031. Despite these challenges, significant investments are being made in neurology. Neumora Therapeutics, with a $250 million IPO valuing the company at $2.3 billion, represents a major investment in this space. The company focuses on a variety of psychological disorders and neurodegenerative conditions through a multiplatform approach. Scribe Therapeutics, having raised a $100 million Series B, is exploring the potential of gene editing for neurological disorders using its CRISPR platform. Additionally, Neurona Therapeutics recently raised a $72 million Series D, underscoring the growing interest in stem cell products for regenerative medicine applications in neurology.

Neurology VC deal activity



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Cardiovascular & metabolic disease

The cardiovascular & metabolic disease sector is currently experiencing a surge in the weight loss treatment market while continuing to address the persistent need for diabetes care. This trend highlights the increasing awareness of obesity's role in exacerbating cardiovascular diseases and diabetes. An opportunity lies in developing treatments that are easier to use and have better form factors, as these advancements can significantly improve patient compliance and the effectiveness of therapies. However, the sector faces challenges—notably the uncertainty in improving existing treatments, which are often considered inadequate. Moreover, the dominance of major pharmaceutical companies creates a large barrier to entry, even at the seed stage, which potentially hinders innovation and limits opportunities for new market entrants.

In terms of market dynamics, Big Pharma companies like Novo Nordisk and Eli Lilly are strategically positioned for short-term dominance. These companies are likely to strengthen their positions through strategic M&A. VC investors in general have stayed away from the cardiovascular markets due to the supreme dominance of the industry leaders. However, opportunities are evidenced by the fundraising success of Carmot Therapeutics for its $150 million Series E and its $2.7 billion exit to Roche. Furthermore, the sector is witnessing significant M&A, highlighted by Eli Lilly's acquisition of Versanis Bio and Novo Nordisk's purchase of Inversago Pharma, which underscores a focus on expanding portfolios in this therapeutic area.

Cardiovascular & metabolic disease VC deal activity

Source: PitchBook • Geography: Global • *As of September 30, 2023

Immunology & infectious disease

The immunology & infectious disease sector continues to spark significant investor interest—a trend further amplified in the wake of the COVID-19 pandemic. The urgent global response to infectious diseases has led to a resurgence in the field, with an emphasis on innovative treatment approaches. Immunology, in particular, has broad therapeutic implications, with considerable unmet needs in areas such as oncology, neurology, and cardiovascular diseases. New modalities, especially in autoimmune diseases, are emerging. For example, Sonoma Biotherapeutics recently raised $120 million to advance CAR-T cell therapies for rheumatoid arthritis—a promising step toward targeted autoimmune treatments. In another example, Excision BioTherapeutics is developing CRISPR methods to treat and cure patients with HIV.

However, the sector's growth faces challenges. The future of vaccines, in particular, appears heavily dependent on government backing, thereby underscoring a crucial need for sustained public sector support to maintain momentum in vaccine development and distribution.

In terms of notable startups, Moderna's triumph in mRNA vaccine development for COVID-19 has positioned it as a leader in the field. This success has not only been transformative for the fight against the pandemic but has also paved the way for mRNA technology to be considered for other diseases. On the autoimmune front, Mozart Therapeutics attracted attention with an $80 million Series A in May to focus on new biology to discover immune engagers that address pathogenic immune responses. Additionally, Odyssey Therapeutics' $168 million Series B is propelling its efforts to combat inflammatory diseases through a data-driven platform aimed at new target discovery. These startups represent the innovative edge of immunology and infectious disease research, which promises to reshape treatment paradigms across a spectrum of conditions.

Immunology & infectious disease VC deal activity

Source: PitchBook • Geography: Global • *As of September 30, 2023

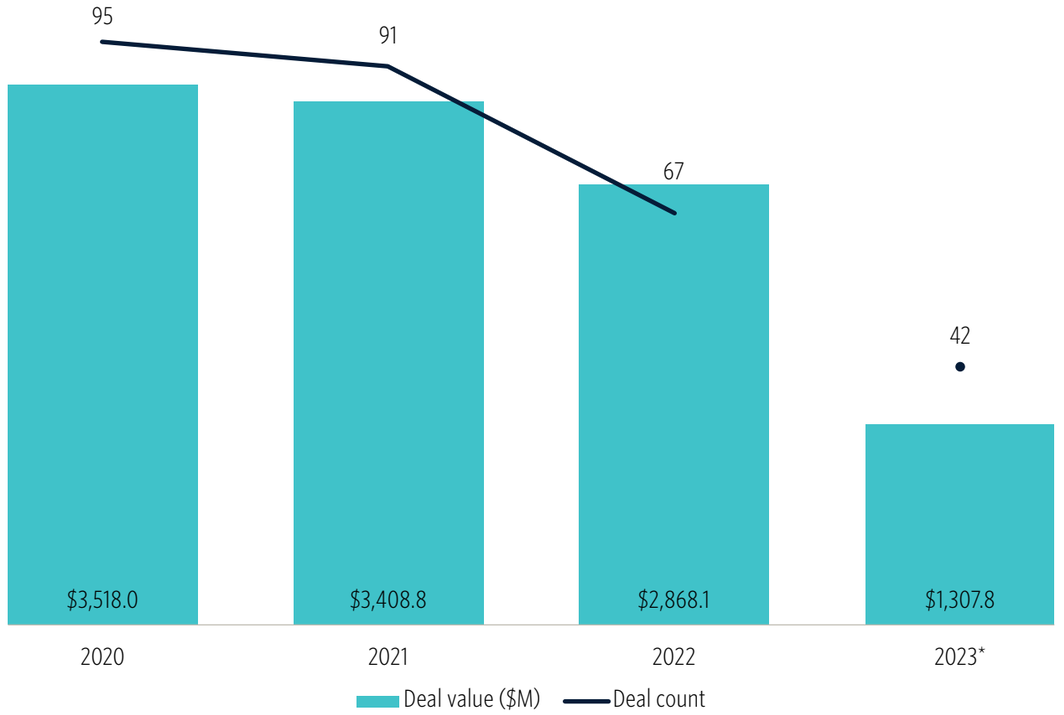
Digestive & renal systems disorder

In biopharma, digestive & renal systems disorder has seen a downturn in investments since 2020, which can be attributed to the complex nature of diseases affecting the gut, liver, kidney, and urinary tract. This decline is exacerbated by the current gaps in biomarker discovery and a comprehensive understanding of disease biology, which is complicated by the intricate interactions across organ systems. Additionally, these areas have seen relatively little pharma M&A activity.

Despite these challenges, substantial opportunities exist in this domain. Nonalcoholic steatohepatitis (NASH) represents a significant unmet medical need within liver diseases and has attracted investor interest due to its considerable market potential. Kidney-related disorders are also seeing significant investment, as exemplified by Walden Biosciences' $51 million Series A aimed at kidney disease treatment. In gastroenterology, the exploration of microbiome therapeutics holds the potential to revolutionize treatment approaches, with companies like Seres Therapeutics at the forefront. Moreover, Kallyope's $236 million Series D underscores the promise of its gut-axis platform in developing treatments for gastrointestinal diseases by deepening the understanding of underlying biology.

However, targeting the specific organs implicated in these diseases remains a formidable challenge and poses a risk to the development and efficacy of potential treatments. As such, the digestive & renal systems disorder space is marked by a high-risk, high-reward dynamic, with the possibility of significant breakthroughs should these hurdles be overcome.

Digestive & renal systems disorder VC deal activity



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Systemic & structural disorder

The biopharma industry's approach to systemic & structural disorder has evolved notably since 2020, which marked the start of a downtrend in investment. This is largely due to the complex nature of disease biology and a decrease in M&A activity in this field. Hematology stands out as an area ripe for innovation, with significant unmet needs being addressed through biologics and gene therapies. Companies like Editas Medicine and Rallybio are at the forefront of these efforts, focusing on conditions such as sickle cell disease and rare blood disorders. Ophthalmology also continues to be a focal point, especially for gene therapy developments, leveraging its "closed-system" nature to validate new, high-risk platforms. Concurrently, the musculoskeletal disorders market, though niche, is poised for growth with the aging population.

On the opportunity front, dermatology presents a niche market with high patient needs, particularly due to its aesthetic dimensions, which make it an attractive area for investment. The respiratory sector is also witnessing a significant influx of capital, with companies like Upstream Bio, Avalyn Pharma, ReCode Therapeutics, and Aiolos Bio raising substantial funds, indicating a robust interest in developing new treatments. However, the sector faces challenges. Many startups are compelled to focus narrowly on specific targets, which limits their ability to expand across various therapeutic areas. This specialization, necessitated by the complexity of these disorders, poses a risk to the scalability and versatility of these companies, thus potentially impacting their long-term growth and ability to diversify their therapeutic portfolios.

Systemic & structural disorder VC deal activity

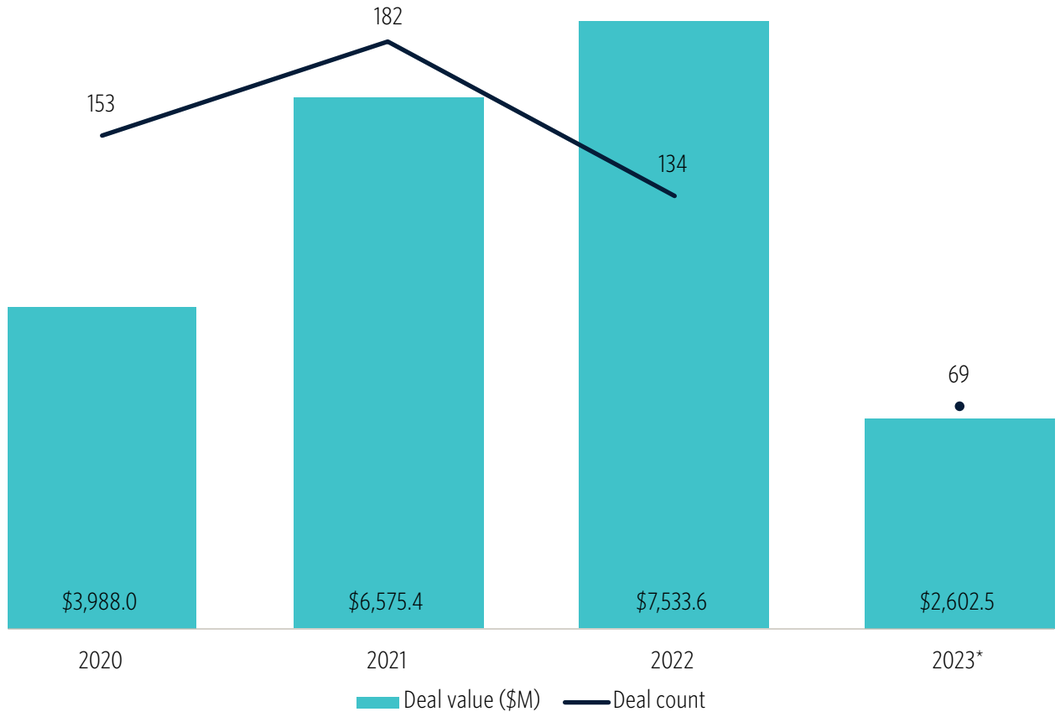
Source: PitchBook • Geography: Global • *As of September 30, 2023

Specialty disease

The specialty disease segment in the biopharma industry encompasses a range of emerging therapeutic areas, including genetic diseases, rare or orphan diseases, aging-related conditions, and animal health. These niche sectors, while serving a smaller patient population, offer immense value due to the significant unmet medical needs they address. 2020 to 2022 saw a surge in investments in this domain, but there was a notable decline at the onset of 2023, due primarily to stagnation in clinical advancements. Genetic diseases have become a central focus, particularly in gene therapy research aiming to develop definitive “one-shot” cures. Meanwhile, rare and orphan diseases continue to play a crucial role in platform development, offering the advantage of accelerated FDA approval timelines, thus helping to de-risk new technologies.

However, the specialty disease sector also faces considerable risks, especially in the aging & longevity segment. Despite the potential for substantial impact, there is a lack of validation in this area. Significant investments in companies like Altos Labs, Calico, Human Longevity, and Unity Biotechnology have yet to show major breakthroughs, which suggests that the field may still be too immature for its ambitious goals. Animal health, albeit a smaller market, offers unique opportunities for testing and refining novel gene and cell therapies, which could potentially pave the way for their application in human medicine.

Specialty disease VC deal activity



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Appendix

Top VC-backed biopharma companies by total VC raised to date*

Company	VC ($M) raised to date	Segment	Category	IPO probability	M&A probability	No exit probability
Dongyangguang	$1,235.6	Chemistry, biologics	Small molecule, antibody	N/A	N/A	N/A
AbogenBio	$1,135.5	Biologics, gene therapy	Vaccine, mRNA	N/A	N/A	N/A
Eikon Therapeutics	$806.6	Chemistry	Small molecule	N/A	N/A	N/A
Magpie Pharmaceuticals	$768.9	Chemistry	Small molecule	N/A	N/A	N/A
Generate Biomedicines	$693.0	Biologics	Protein/peptide	73%	25%	2%
Rakuten Medical	$654.7	Biologics	ADC/conjugate	64%	34%	2%
insitro	$643.2	Chemistry	Small molecule	95%	3%	2%
Nimbus Therapeutics	$637.0	Chemistry	Small molecule	94%	4%	2%
Kriya Therapeutics	$617.6	Gene therapy	Gene delivery	84%	14%	2%
Tessera Therapeutics	$580.0	Gene therapy	Gene editor	84%	14%	2%

Source: PitchBook • Geography: Global • *As of September 30, 2023
Note: Probability data is based on PitchBook VC Exit Predictor methodology.

Top strategic acquirers of biopharma companies since 2020*

Investor	Deal count	Investor type
Eli Lilly	8	Corporation
Merck & Co.	6	Corporation
Novartis	6	Corporation
Centessa Pharmaceuticals	5	Corporation
Gilead Sciences	4	Corporation
Novo Nordisk	3	Corporation
Pfizer	3	Corporation
Boehringer Ingelheim	3	Corporation
Takeda Pharmaceutical Company	3	Corporation
Bayer	3	Corporation

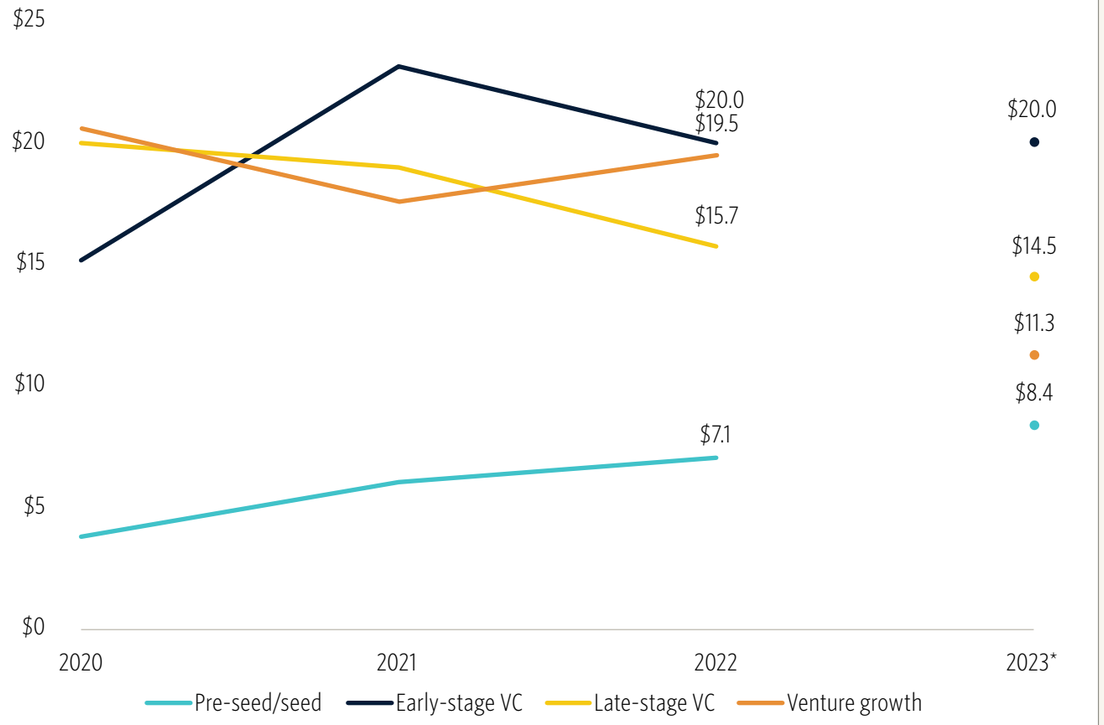
Source: PitchBook • Geography: Global • *As of September 30, 2023

Top VC investors in biopharma companies since 2020*

Investor	Deal count	Pre-seed /seed	Early-stage VC	Late-stage VC	Venture growth
RA Capital Management	161	10	79	60	12
Alexandria Venture Investments	115	4	78	29	4
ARCH Venture Partners	86	6	58	19	3
Lilly Asia Ventures	81	3	44	30	4
Casdin Capital	78	2	53	20	3
Samsara BioCapital	73	5	42	22	4
GV	67	2	42	17	6
HongShan	64	3	38	22	1
HBM Healthcare Investments	60	0	28	24	8
Qiming Venture Partners	56	2	33	16	5

Source: PitchBook • Geography: Global • *As of September 30, 2023

Median biopharma VC deal value ($M)



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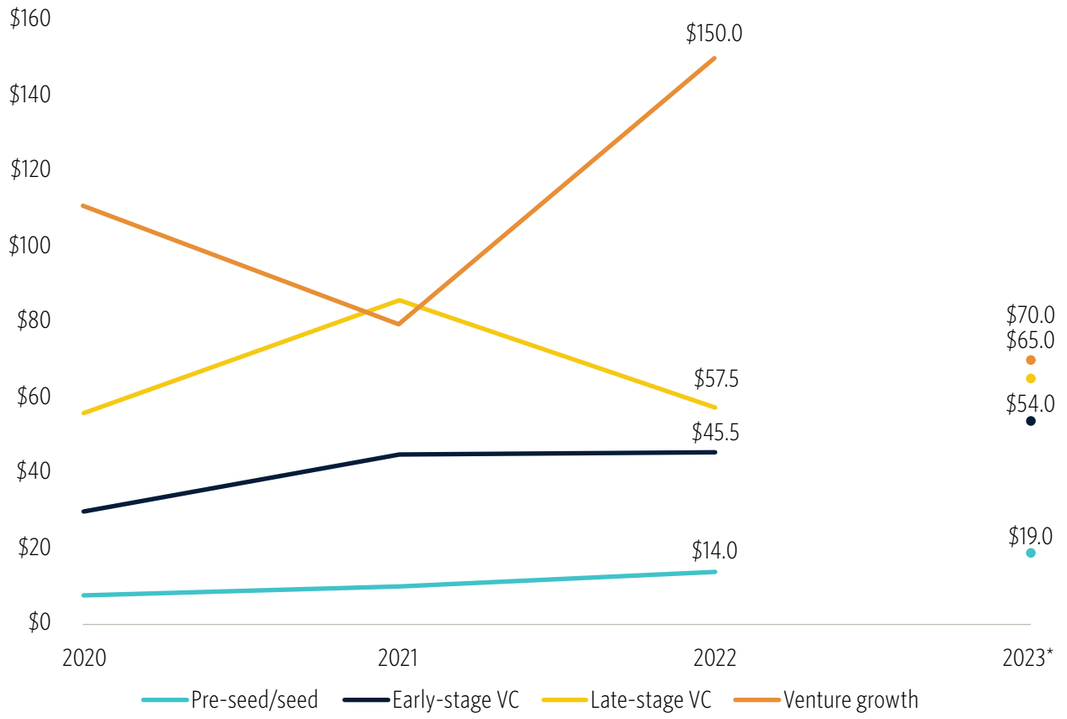
Median biopharma pre-money valuation ($M)



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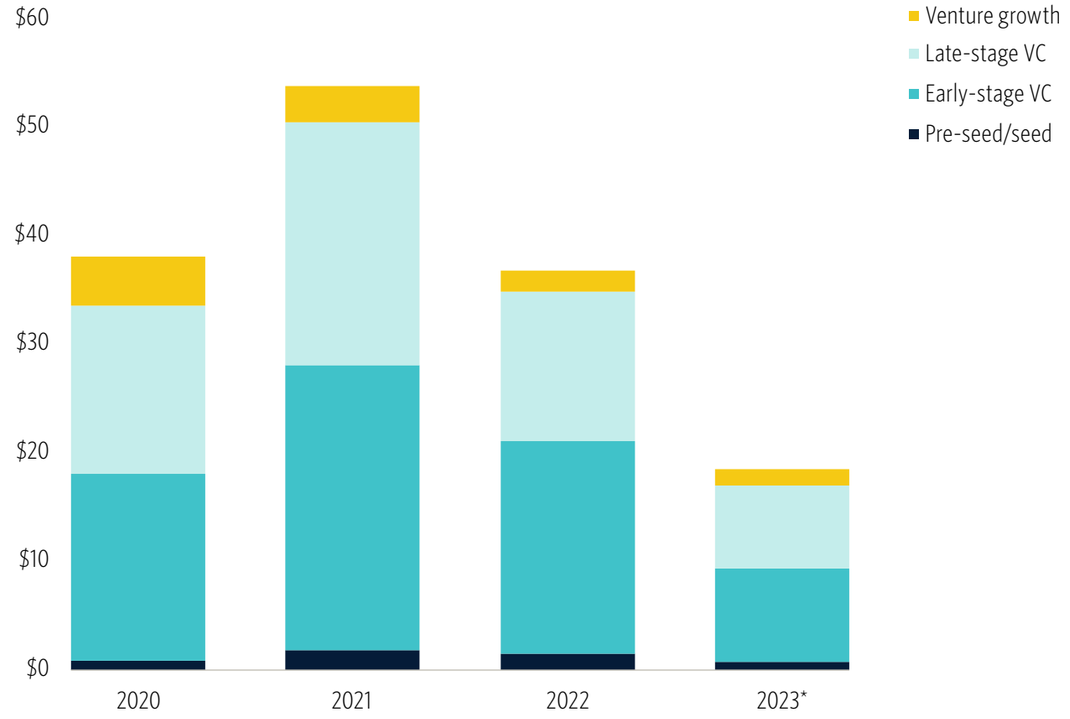
Biopharma VC deal value ($M) by stage



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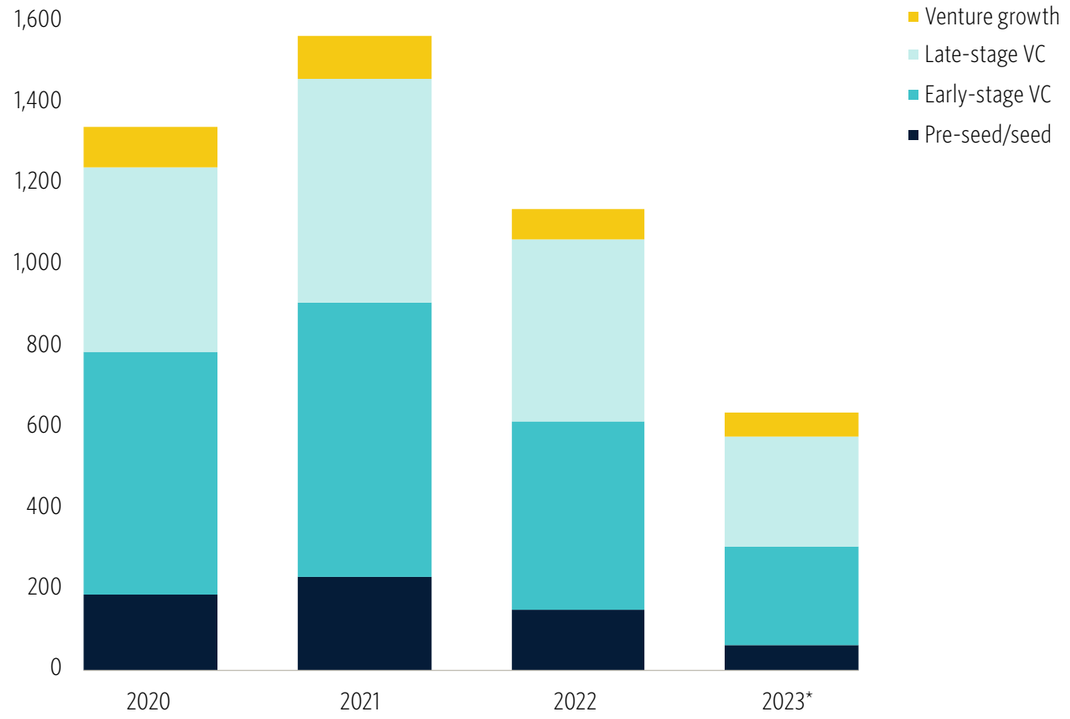
Biopharma VC deal count by stage



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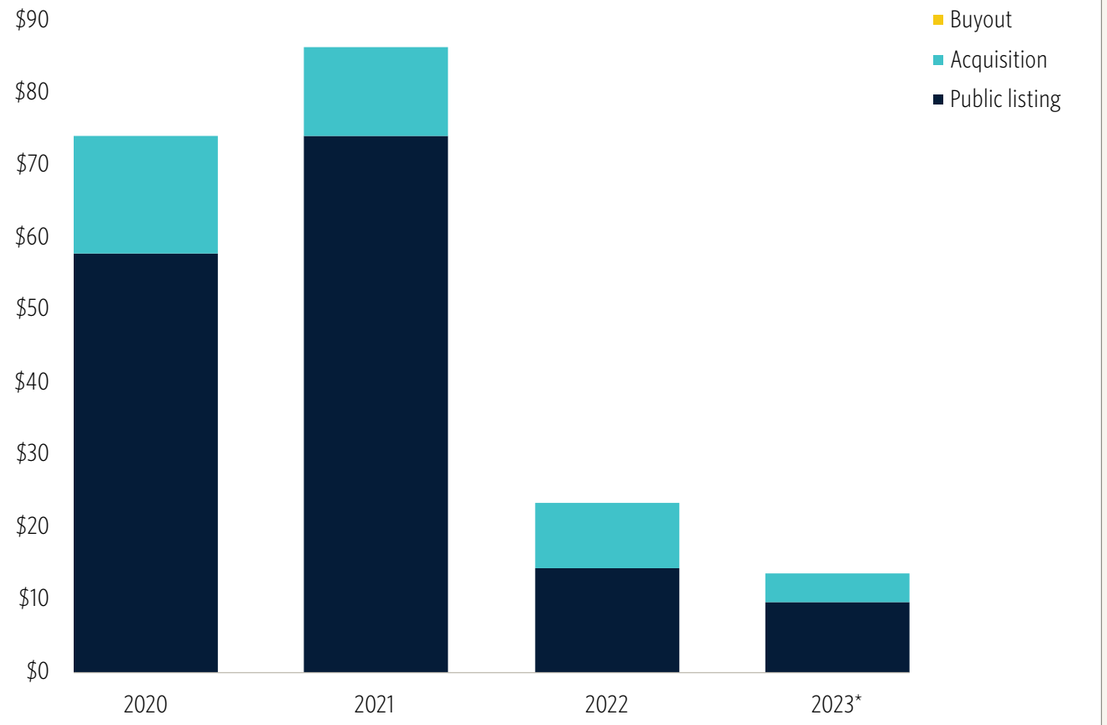
Biopharma VC exit value ($M) by type



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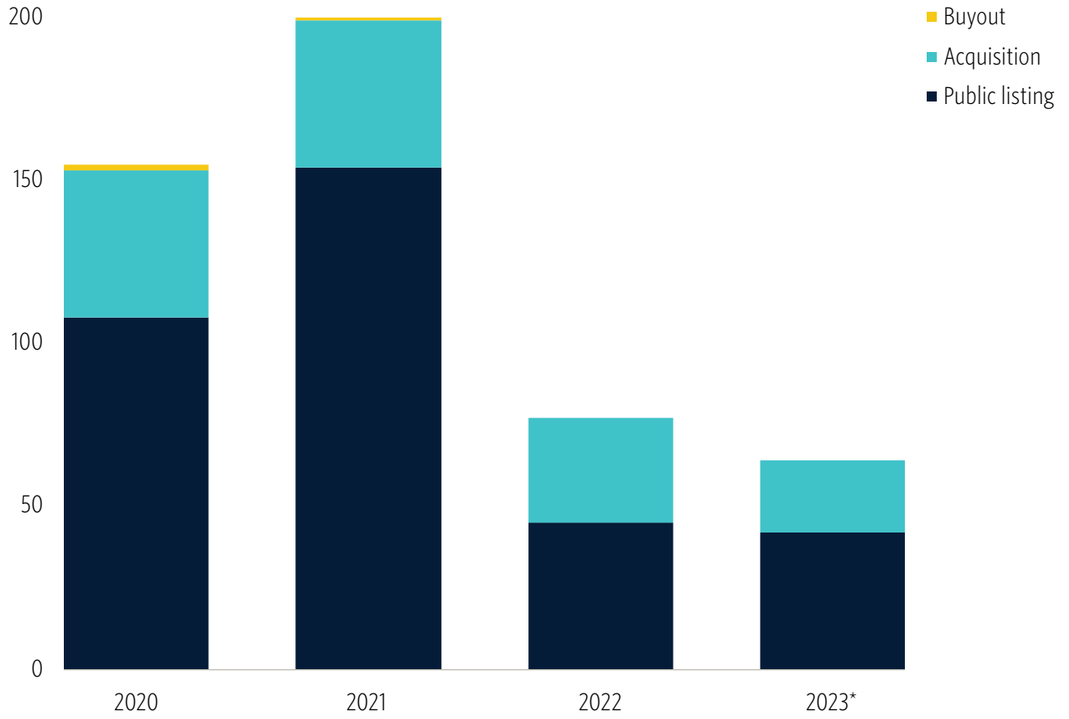
Biopharma VC exit count by type



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