2023 could be a rebound year for Biopharma M&A

An Amplity Health White Paper

Amplity HEALTH

INTRODUCTION

Last year was a down year for biopharma mergers and acquisitions (M&A). With a strong focus on licensing deals, we saw only <$100B in deal activity, down ~150% from its 2019 peak (Exhibit 1). Rising interest rates and an uncertain economy led many biopharma companies to take drastic action to conserve cash, including widespread layoffs and significant program cuts.

We expect increased deal activity in 2023 in light of the accelerating emergence of biosimilars to biologics markets, pending implementation of the Inflation Reduction Act's (IRA's) provisions, and significant scientific strides made in the cell and gene therapy spaces. These deals will be driven by a need to backfill pipelines that will include a strong focus on M&A and licensing agreements. We have already seen improved deal activity in Q1 of this year with biopharma's largest acquisition since 2019: Pfizer's $43B acquisition of Seagen, which will expand their oncology portfolio into the antibody–drug conjugate space, a unique technological area that enables more efficient therapeutic delivery. Given these factors, we're anticipating a stronger year for M&A in 2023 compared to 2022 and are already seeing signs of improvement, albeit in the shadows of an economy still on the verge of a recession.

2023 has the potential to be a rebound year for biopharmaceutical M&A. Amplity Consulting's M&A experts generated this report to enable our life science clients to keep moving at the pace of innovation.

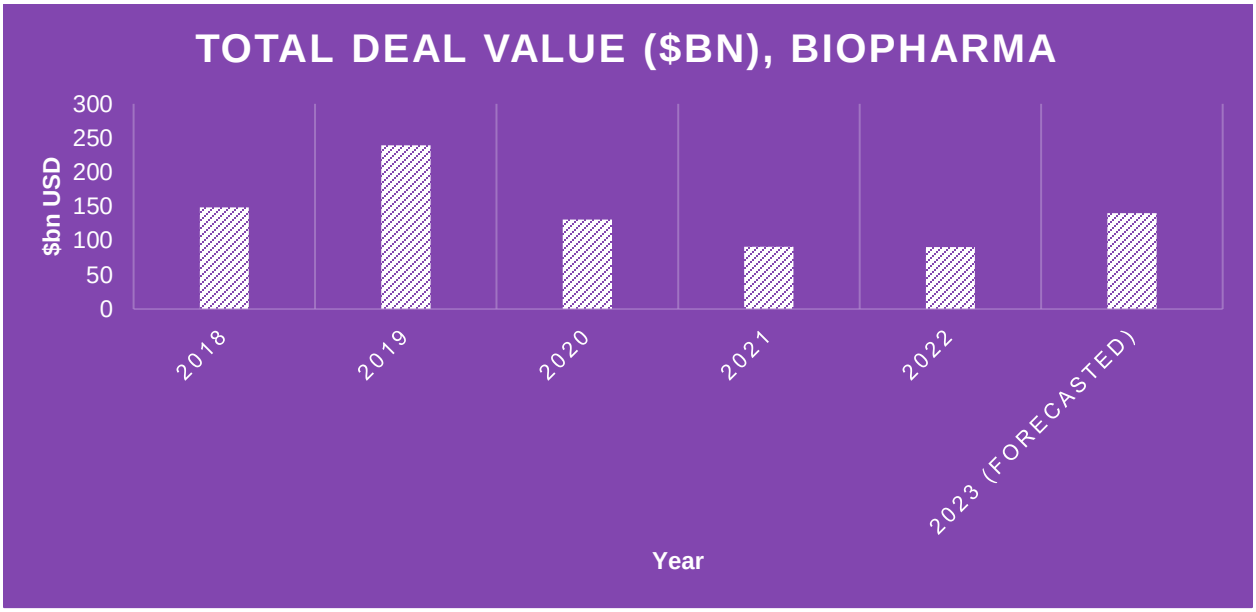
Read on for a breakdown of the anticipated headwinds, tailwinds, and potential opportunities within 2023's deals landscape.

Key takeaways

- The launch of biosimilars and generics due to pending patent expirations, as well as the enaction of the impending provisions of the IRA, may accelerate M&A activity.
- However, inflation and the current lack of funds in the biotechnology market, as well as differences in target valuation between deal stakeholders, may mitigate deal efforts.
- The gene and cell therapy spaces will continue to be therapeutic modality targets to backfill pipelines given recent clinical advances and products that have come to market, especially in oncology and rare disease. However, small target patient populations, prohibitively high price tags, and development and commercialization complexities may continue to inhibit deal activity within these treatment modalities.

Note: This report contains information from numerous sources that Amplity Health believes to be reliable but for which accuracy cannot be guaranteed. The reader assumes all responsibility for how they use this information.

Exhibit 1: Total M&A Deal Value in Biopharma, 2018-2023[1]



DEAL DRIVERS

Patent expirations on top-selling drugs

The near-term expected market flooding of biosimilars and generics will make significant cuts into product revenues, motivating companies to look externally to mitigate expected losses.

As of 2023, 5 of the top 10 best-selling drugs in the US, outside of COVID-19 vaccines, will see their first patents expire by 2026 and will face biosimilar/generic competition (Exhibit 2). Most significantly, Humira[2] will face biosimilar competition this year from Amgen, who has launched their biosimilar at 2 price points: (1) a significantly lower price (55% below) and (2) a slightly discounted price, but with large rebates compared to Humira.[3] As of 2021, Humira made up about 40% of AbbVie's yearly revenue in the US, and with the launch of the Amgen biosimilar as well as 7 others anticipated, AbbVie will likely see their revenue share fall. Altogether, we expect the crowding of these biosimilar and generic markets will result in:

- Financial losses on revenue-driving brand-name drugs
- A trend toward more innovative biosimilar pricing strategies to entice potential customers which we expect will entice companies to backfill pipelines through M&A or even enter de-risked licensing deals.

Exhibit 2: Notable Patent Expirations Through 2026

Product	Company	Treatment Type	Patent Expiration	# of Biosimilars/Generics Approved	Percent of Company U.S Revenue (FY2021)[4]	Rank (Total U.S Revenue)[5]
Humira	AbbVie	Anti-inflammatory	2023	7	39.80%	#1
Revlimid	BMS	Oncology	2025-2026[6]	1	29.70%	#4
Stelara	J&J	Anti-inflammatory	2023	1 (BLA approved)	26.50%	#6
Eylea	Regeneron/ Bayer	Opthamology/ Oncology	2025-2026	0 (U.S rights purchased 1/2023)	36%	#7
Xarelto	J&J/Bayer	Heart disease	2024	0	10.90%	#10

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The enactment of the IRA will see significantly one-sided federal regulation over drug pricing, which will likely require a new external investment strategy for many affected manufacturers.

Additionally, the enaction of the IRA may lead to increased 2023 deal velocity, although negotiated Part D drug prices will not go into effect until 2026 at the earliest. Ultimately, this will give manufacturers around 2 years to prepare for potential revenue hits from anticipated decreased drug prices. We expect that CMS will be very aggressive in the negotiations on these drug prices with little room for biopharma to intervene, making it even more imperative that biopharma companies explore alternative ways to grow revenue, perhaps through deals involving targets that may be IRA-ineligible, but still provide strong cash flow.

Companies may consider targeting products that are ineligible or are more durable against the anticipated price negotiations under the IRA, such as:

- Single-indication orphan drugs
- Human whole-blood products, and/or plasma or plasma-derived products
- Reference products for biosimilars and generics
    - Price reductions via the IRA could be more detrimental to revenue than lost market share through patent expiry. (If the IRA were launched in 2018, CMS would have saved "$5.9 billion [74%] on adalimumab [Humira].")[7]
- Biologics over small molecules, which have 4 extra years of protection

Other investment areas may include small biotechnology companies, such as the purchasing of minority stakes in companies with a product that produces >80% of their business, as these products may fall under the "small biotech drug" criteria of the IRA. Finally, increased deals in international markets will be something to watch out for as well, given the impact of the IRA on the pharmaceutical industry in the US. To preserve their bottom line and expand their international presence, companies may look to push R&D and commercialization of their products out of the US and into other nations with strong market demand, low development costs, and significant expertise, such as China and India.

DEAL RISKS AND MITIGATING FACTORS

Inflation and the current state of the biotech market

With borrowing power high and cash reserves low, biopharma companies may choose to cut out M&A from their 2023 investment strategies.

After a market boom at the beginning of the pandemic, biotech has suffered from a bear market amid rapidly accelerating inflation. Commercialization and talent retainment expenses have significantly risen over the last year, given 2022's 6.5% rate of inflation and a competitive talent pool driven by a low unemployment rate of 3.5% reported at the end of the year. Additionally, borrowing power has decreased amid efforts to curb inflation. The federal interest rate increased from 1.6% in January of 2022 to 4.6% in January of 2023,[9] which has made it more expensive for companies to exercise loans for business purposes. On top of this, leverage has become more expensive as well, dampening investor buying power and mitigating deal volume. Amid a rising cost of goods (specifically reagents, development materials, and clinical trials), a diminished level of borrowing potential, and an increased cost of amplifying investments through leverage, the availability of additional funds that could be used for new deal opportunities has decreased in both large pharma and small biotech. Although the demand from potential sellers is there, only a select few potential buyers can exercise excess cash for deal-making.

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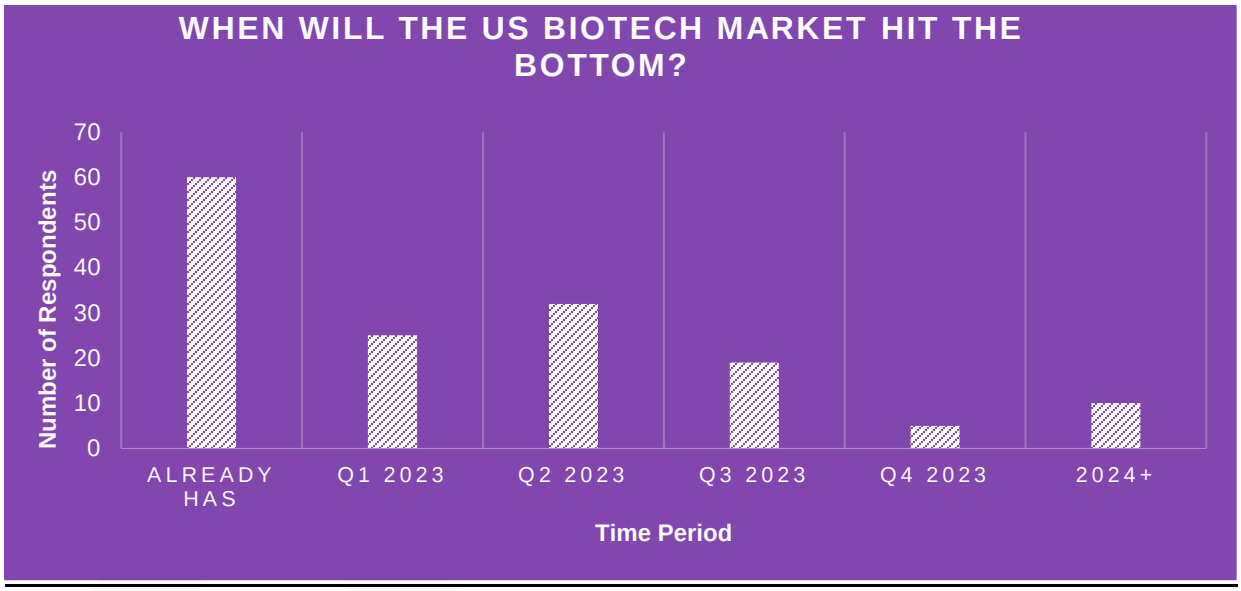
However, all are not immune from the squeeze of this market: Pfizer, the developer of the high-selling Comirnaty COVID-19 vaccine, recently announced large cuts to its R&D staff in an effort to open up cash to revamp its R&D pipeline.[10]

Although many market stakeholders expect that the biotechnology market has already hit its bottom according to an EvaluatePharma study from November 2022, a strong contingent still believes the bottom has yet to occur.

Exhibit 3: EvaluatePharma Study, November 2022, Showing Biotech KOL Market Expectations[11]



(Exhibit 3). With inflation still increasing, it is likely that this will still be a factor mitigating potential deals throughout the year.

Misalignment between buyers and sellers

The pace of M&A may be slow as buyers struggle to negotiate fair market value buyouts with sellers.

Misalignment in expectations on M&A target value between buyers and sellers may also hinder deal execution. Buyers are looking for valuable assets, placing a premium on clinical validation and wanting a “diamond in the rough” technology with potential for high ROI. Sellers, on the other hand, are placing their sale-price premium on both preclinical data and their historical valuation. Despite being in what we may describe as a “buyer’s market,” where potential sellers are desperate for cash flow, we are still finding that buyers and sellers struggle to agree on fair value. Buyers have been significantly adjusting their offers based on incoming clinical data as well, which has led to dramatic fluctuations in total deal value. For example, Amgen’s final purchase price of Cincor this year was ~40% lower than their initial offer due to failed clinical data that emerged during negotiations.[12]

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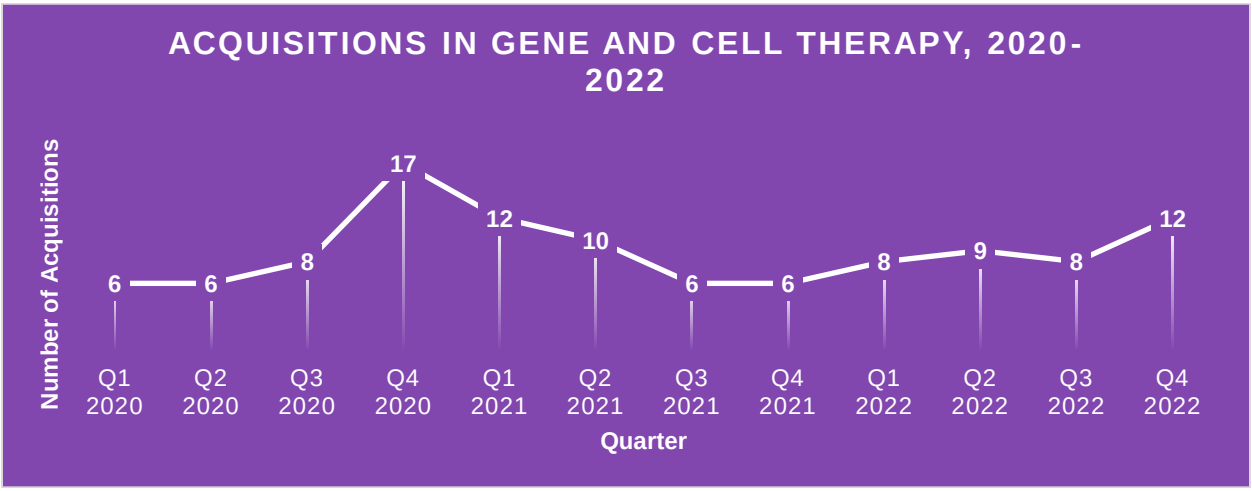
POTENTIAL TARGET THERAPEUTIC MODALITIES

Gene and cell therapies present significant opportunity for future investment areas, given their promising clinical data and growing pipeline popularity.

As has been the case for the last few years, oncology-targeted and immunology-focused products will continue to remain popular investment areas given unmet need and the clinical advances that have been made in these spaces. We expect to see the continued emergence of gene and cell therapies in the marketplace, especially for rare disease and oncology indications. According to Endpoints News, only 30 gene and cell therapies have been approved by the FDA, but that number will grow over the coming years as there are currently about 2,500 active INDs (Investigational New Drug applications) for these therapies (~1,300 in gene therapy, ~1,200 in cell therapy).[12] Gene and cell therapy acquisitions are rebounding in the marketplace as well, with 12 reported last quarter, a 2-year high (Exhibit 4).[13]

Exhibit 4: Gene and Cell Therapy Acquisitions, 2020-2022[13]



Gene Therapy

Gene therapies have exploded in the R&D space over the past decade and will expand as an M&A stalwart as they continue to demonstrate clinical value.

RNA-Based Therapy

The emergence of mRNA-based gene therapies has accelerated in the wake of the COVID-19 pandemic as Pfizer/BioNTech as well as Moderna have proved that these therapeutic modalities can be highly effective in the treatment of disease. We are currently seeing a renaissance in the mRNA-based cancer vaccine space, an area which was relatively unproven before the pandemic. Recently, Moderna and Merck released promising phase 2b data in melanoma patients using their mRNA-based neoantigen personalized vaccine in combination with checkpoint inhibitors, cutting risk of recurrence or death by 44% versus checkpoint inhibitor therapy alone.[14] The mRNA space is certainly a space to look at with cautious optimism, as it has proven itself in infectious disease through COVID-19 vaccines and is beginning to prove itself in oncology. As an early pioneer in the space, mRNA-based technologies have provided the RNA therapy blueprint for potential success in solid tumor indications and have made other nucleic acid–based therapies such as siRNA-based therapies and ASO-based therapies seem more promising. In the siRNA space, Alnylam has led the way with multiple on-market products

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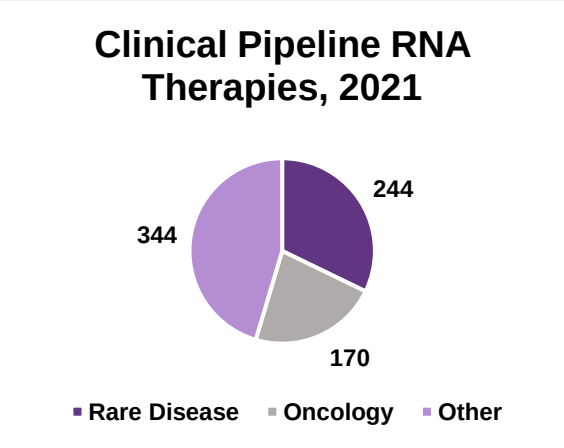
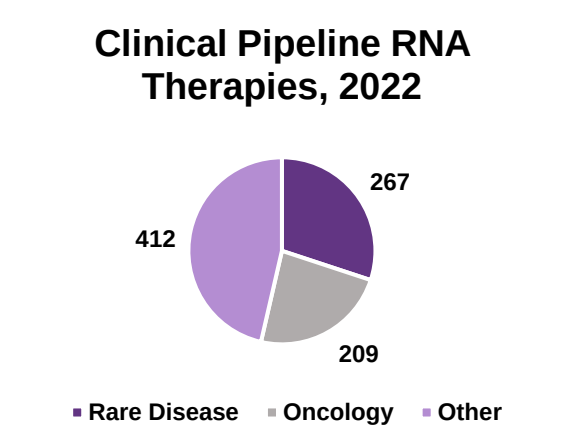
and promising clinical data through their RNAi technology. In addition, some of the strongest positioned players with significant capital access are the companies who developed the mRNA COVID-19 vaccines, given the substantial revenues they drove in over the last few years. As a result, we anticipate this could be an area of expansion in the marketplace, either among the top-tier players in the mRNA space who hope to add to their portfolios, or among potential new players who see the promise of the technology. Exhibit 5 highlights the expansion in RNA therapeutics among pipeline products, as the total number of RNA therapies in the US clinical pipeline increased by about 17% from 2021 to 2022.[13]

Exhibit 5: RNA Therapies, Preapproval, 2021-2022





CRISPR Therapy

CRISPR is an additional gene therapy technology that has seen positive clinical data and could be a target for potential deals as it enters the market. Analysts are expecting the first CRISPR-based therapy to be approved by the FDA this year, with CRISPR Therapeutics and Vertex Pharmaceuticals submitting a Biologics License Application for their first CRISPR therapy by the end of Q1 of this year.[15] Venture capital has been particularly interested in the space as well, with over $1.3 billion invested in gene editing in 2021, and CRISPR technologies accounting for roughly 60% of this share.[15] CRISPR has experienced traction outside of the oncology space, specifically in sickle cell disease, but is a technology worth watching regarding potential deals given its relative clinical success.

Viral Vector Therapy

The use of genetically engineered viral vectors, such as lentiviral vectors and adeno-associated viral vectors (AAV Vectors), could also prove to be a potentially popular area for deals this year. These technologies use viral vectors to insert genetic material into cells, which are then replicated inside the cell and help produce proteins to aid in disease treatment. The lentiviral therapy area did see some success in 2022 as the FDA approved its first 2 lentiviral therapies (both by bluebird bio) for the treatment of specific rare diseases.[16] Though these products have been quite transformative, they also come with prohibitively high price points alongside their high clinical efficacy. Given these factors, they may also be an attractive target for companies looking to work value-based agreements into their portfolios.

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Cell Therapy

Like gene therapies, cell therapies have revolutionized healthcare and will continue to be an attractive M&A target.

Like gene therapy, cell therapy could also be a strong area for deals. Autologous and allogeneic stem cell transplants in the clinic have proven to be highly efficacious in treating hematologic malignancies. Additionally, CAR-T therapy, a type of gene and cell therapy which has emerged over the last decade, despite complex infrastructure requirements and a high price, has proven to be quite effective in treating hematologic malignancies. Although the CAR-T space could be a fruitful investment area, oncology companies looking to add cell therapies to their R&D product portfolio might consider antigen-specific/TCR-based T-cell transfer therapies or tumor infiltrating lymphocyte (TIL)-based therapies. Antigen-specific/TCR-engineered therapies involve the extraction of T cells from a sick patient's blood, rapidly expanding them ex vivo,[17] priming them to target tumor antigens of interest (or re-engineering their TCRs to target these specific tumor antigens), and reintroducing the cells to the body. TIL therapies, on the other hand, operate similarly except lymphocytes are extracted directly from the tumor, rapidly expanded ex vivo,[17] engineered with certain attributes, and reintroduced to the body to fight the tumor. Early clinical data have shown some promise in solid tumor studies, especially in melanoma, and in hematologic tumor studies. Additionally, from a financial perspective, these therapies may be able to avoid the pricing provisions under the IRA, as they are sourced through blood and may be able to achieve single-indication orphan drug designation. Although these therapies come with high manufacturing costs and complex production processes, they could be an impactful investment by companies looking to make a splash in the cell therapy space and potentially avoid price provisions of the IRA.

Risks in Investing in Gene, RNA, and Cell Therapies

Complexities and high expenses in the manufacturing and administration of gene and cell therapies may dissuade potential M&A partners from investment.

There are multiple risks in investing in the gene and cell therapy space. For example, given that a strong majority of diseases treated by cell and gene therapies are in the rare disease space, target patient populations are often small. In addition, these therapies are often expensive given the complexities in drug development and delivery, lack of scale-up power, and the customization required for individual patients. As a result, therapies can be prohibitively expensive from an acquisition cost perspective. A single course of Kymriah, a highly effective CAR-T therapy for B-cell leukemia in patients under age 25, is priced at $475,000[18] while Zynteglo, bluebird bio's lentiviral therapy for the rare drug disorder beta thalassemia, sells for about ~$2.8 million per treatment.[19] These high costs may be pushed onto payers, who may be unwilling to cover a single-treatment drug with such high costs, or may be pushed onto the patient. Given these high costs and potential unwillingness to cover, price accessibility to patients remains a key concern. Treatment logistics are an additional factor that may hinder accessibility. Healthcare systems may need specialized facilities and training to administer many of these therapies, meaning many patients may need to make long trips for care if their nearest treatment centers are not qualified to administer the therapies. Also, many of these treatments target very specific genes in a patient's genome. As a result, patients may need to go through multiple series of genetic testing and counseling to determine treatment eligibility, which may be a significant burden especially for sick patients. Prospective investors in the space will need to be cautious, given the complexities in design, manufacturing, distribution, and administration of these products, and aware of key concerns regarding product accessibility.

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To mitigate these risk factors, rather than looking to purchase a drug asset, companies could consider investing in contract development and manufacturing organizations (CDMOs), which will play a larger role in the biopharma ecosystem as these therapies continue to develop and enter the market. These organizations can provide outsourced development and manufacturing of these products, and may serve as more risk-averse investment areas versus drug assets, due to:

- A strong demand for the service by biotechnology companies for highly complex manufacturing processes without the capital to bring commercialization in house
- Avoidance of payer/patient treatment price considerations and drug accessibility

Conclusion

Overall, we predict that deals in biopharma will certainly gain momentum this year but may not immediately return to prepandemic levels. Looming patent expirations of top-selling drugs, emergence of biosimilars to the market, and the beginning of the drug price negotiation provisions of the IRA will promote an uptick in M&A to backfill pipelines. However, the deals market will still be prevented from reaching its full potential due to inflation's impact on cash reserves and a product valuation misalignment between buyers and sellers. In light of this, cell and gene therapies touting significant clinical efficacy, although coming with limitations, present unique M&A opportunities for biopharma companies seeking to inject new innovation into their portfolios and will continue to be mainstays in the deals market for years to come. The biopharma market is constantly shifting, and we may see improved activity this year, but a full return to normal may not be in the cards until 2024.

Amplity Strategic Consulting

Amplity Consulting's leadership team can offer our biopharma clients an innovative perspective based on experience, deep market knowledge, and strong market data collection and modeling. We have years of experience across the deals strategy continuum and are poised to assist your team at "deals speed." Pairing our team with industry experts throughout the entire project, we deliver in-depth data-driven insights, quantitative rigor, and responsive service to all our clients. Therapeutically, we cross many areas, but have been a leader in oncology, biosimilars, cell and gene therapy, and rare diseases. Contact us to initiate a discussion on how we can help strengthen your investment decision-making.

Footnotes

[1] EvaluatePharma; 2023 forecast is based on the previous 5-year total deal value average; includes pure-play drug acquisitions
[2] US top-selling drug product in 2022 (outside of COVID vaccines)
[3] Reuters
[4] Data from company FY2021 10-K reports
[5] FiercePharma. Disregards COVID vaccines
[6] Revlimid biosimilar was launched in the US in Q2 2022, but is volume restricted through 01/2026
[7] Rome et al. (from JAMA Health Forum, published 1/27/2023)
[8] CNBC
[9] FederalReserve.gov
[10] FiercePharma
[11] EvaluatePharma; responses were from public and private investors, bankers, and other industry KOLs
[12] Endpoints News
[13] American Society for Cell and Gene Therapy
[14] Moderna Press Release: December 13, 2022
[15] Pharmaceutical Technology
[16] BioPharma Dive
[17] "out of the body"
[18] Endpoints News
[19] FierceBiotech

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