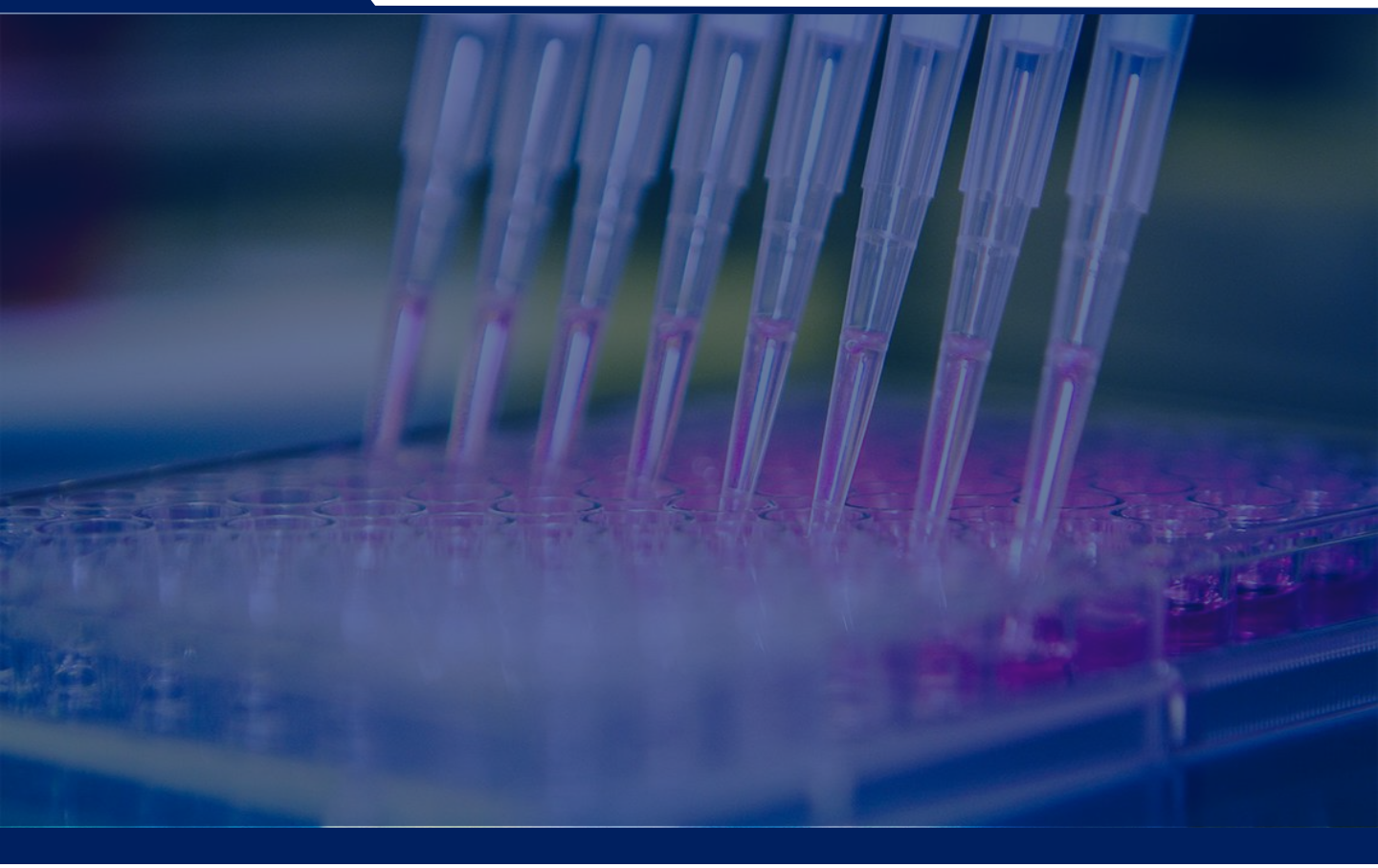

Biotechnology Industry Report

THE GENES OF A STRONG MARKET

Biotech has been utilized for thousands of years. It's laid the foundation for industries such as agriculture, healthcare and pharmaceuticals. Biotech has arguably been an underinvested/underappreciated industry and is now considered more mature, which signifies less risk, driving appetite for IPOs, M&As, licensing agreements, joint ventures and more. The industry has seen impressive growth in recent years, primarily due to the endless search of treatment to COVID-19, which received tremendous government and public attention. This has shone a fresh light on biotechnology and helps increase demand for biotechnology tools.

Key trends in the industry: Growing R&D, increasing healthcare expenditures, advancements in artificial intelligence (AI) and big data, to name a few.

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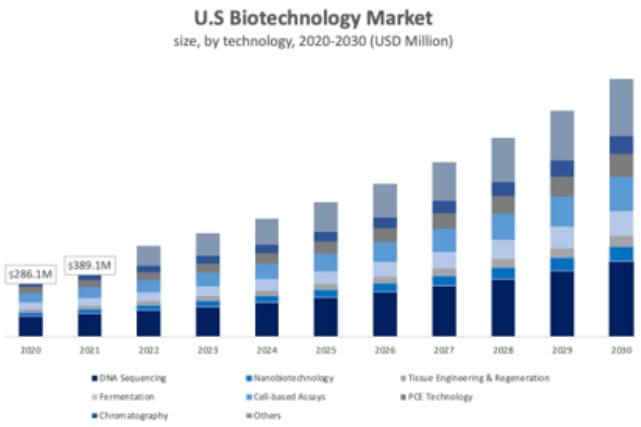
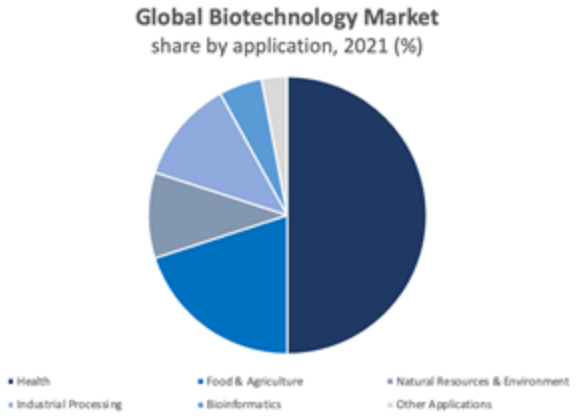
Introduction

The global biotechnology market size was estimated at USD 1,023.92 billion in 2021 and is expected to grow at a compound annual growth rate (CAGR) of 13.9% from 2022 to 2030.

North America accounted for the largest share of 44.20% in 2021. The regional market is witnessing growth due to several factors, such as the presence of key players, extensive R&D activities, and high healthcare expenditure. The rise in prevalence of chronic diseases and rising adoption of personalized medicine applications for the treatment of life-threatening disorders is expected to positively impact the market growth in the region.





The health application segment accounted for the largest share in 2021 at more than 50.00% and is expected to be the leading segment throughout the forecast period. The segment growth is in part fueled by significant advancements in the fields of Artificial Intelligence (AI), machine learning, and big data, which are expected to increase penetration of bioinformatics applications, especially in industries, such as food and beverages.

The global major manufacturers of Biochemistry Analysers include Thermo Fisher Scientific, Abbott, HORIBA, Siemens Healthcare, Xylem Analytics, Agappe Diagnostics, RMS, MicroLab Instruments and Labindia Instruments. etc.

Key Players

The three main types of biotechnology are medical, agricultural, and industrial, and they are referred to as "red", "green", and "white" biotechnology respectively. Other types of biotechnology are a combination of these three main fields. Medical biotechnology is used to better the health or reduce the suffering of humans or other creatures. Agriculture biotechnology is focused on genetically modifying plants for the purpose of increasing production or introducing desirable characteristics. Industrial biotechnology utilizes the use of plants, marine organisms, microorganisms, algae, and fungi to produce things like chemicals and energy for industrial applications. Three main players in biotechnology by market share are Johnson & Johnson, Eli Lilly, and Roche.

#1 Johnson & Johnson

Johnson & Johnson is an American multinational corporation that develops medical devices, pharmaceuticals, and consumer packaged goods. The company has competitive advantages due to its massive size, scale, and intellectual property library.

#2 Eli Lilly

Eli Lilly and Company is a pharmaceutical company with offices in 18 countries. Its products are sold in approximately 125 countries. Lilly's achievements include being the first company to mass-produce the polio vaccine developed by Jonas Salk, and insulin.

#3 Roche

Roche is a Swiss multinational healthcare company that operates worldwide under two divisions: Pharmaceuticals and Diagnostics. Roche is the leading provider of cancer treatments globally.

Sectors Within Biotechnology

Agriculture: The utilization of genetic engineering to increase the efficiency of agricultural outputs through a reduction of input or an increasing output with no greater input. Solutions could include pest-resistant crops, reduced water dependence for Arid land, yield-increases, etc.. Companies operating in this sector include AgBiome, Atomwise, Innatrix, ZestBio, Rothamsted Research, Pheronym.

Nutrition: The application of biotechnology in nutrition involves upgrading traditional food processing based on fermentation. Biotechnology can also help to eliminate toxic components, either by genetic engineering or through food processing. Production of glucose from starch, production of high fructose syrup and vitamin C, conversion of lactose to galactose and glucose are examples of large-scale applications.

Environment: Environmental biotechnology optimizes the use of nature, to produce renewable energy, food, and nutrients in a synergistic integrated cycle of profit-making processes where the waste of each process becomes the feedback for another process. This has paved the way for efficient environmental conservation strategies against global warming and climate change.

Marine: Marine biotechnology is a field where marine organisms and their compounds are identified, extracted, isolated, characterized and used for applications in various sectors to benefit society, ranging from food/feed to pharmaceutical and biomedical industries.

Health & Medicine: Biotech in health and medicine facilitates quicker and more accurate diagnostic tests, therapies with fewer side effects and new and safer vaccines. This is achieved through development of new diagnostic tools and machines, which expand the capabilities of medical professionals while also reducing costs. BioNTech SE is an example of health & medicine company, developing immunotherapies.

Industrial: Industrial biotechnology is one of the most promising new approaches to pollution prevention, resource conservation, and cost reduction. Also, since many of its products do not require the lengthy review times that drug products must undergo, it's a quicker, easier pathway to the market. Industrial biotechnology companies use many specialized techniques to find and improve nature's enzymes.

***Bioinformatics*:** A scientific subdiscipline that applies tools of computation to capture, analyze and aid in the interpretation of biological data. This field is often employed to handle and derive insights from complex and extremely large datasets with many projects complemented by the use of supercomputers. Bioinformatics is used in both academic-related research and applied research and can go as far as predicting drug resistance for example.

Ethics and Laws: While biotechnology is a thriving field full of innovation, there are still ethical implications in nearly every aspect of the field. Examples include human participation in new medication tests, environmental interference, etc.

THE GENES OF A STRONG MARKET

Key Trends

Aging Population **-** Life expectancy for the US is constantly increasing resulting from medical advancements and therefore have caused more age-related illnesses. Increasing age means an increase in demand for breakthrough and inexpensive medical products, especially as the public sector seeks to reduce the cost of treatment through curative + preventative treatments

R&D Expenditure **-** Over 17% of all the revenue generated by the industry is funneled into R&D, as biotech is one of the most active fields when it comes to research. R&D spend incentivizes new developments, of drugs, disease-resistant crops, etc. which boosts revenue generation resultantly. R&D expenditure may be difficult to finance due to increasing costs of debt, but cash-flush firms will continue successfully.

Patent Cliff **–** Lots of patent expirations will occur over the next coming years, which in-turn can sharply effect revenue and profitability due to the increased competition from generic drug makers. There's an expected $180B in revenue expected to be lost from the top Pharmaceutical companies during 2023 to 2028 consequently (66% of BMS's revenue comes from products with patent expirations during the decade).

Overall Environment **-** Politics, fiscal, & monetary policy plays a massive role in the ability of operators to be approved for the projects in the pipeline. Bootstrapping businesses isn't an option due to the large capital requirements, so an accommodative credit environment is important for the progress of a project. Under certain political rulings, the rate of project approvals by the FDA can increase or decrease accordingly.

The Product Development Process

1. ***Preliminary Research:*** This involves researchers trying to discover new drugs through new insights, tests, new technologies, etc. These tasks are completed in the most cost-effective manner.

2. ***Preclinical Testing:*** At this point, the company must show that their product is safe and understand the effects of what happens when the drug enters the body. A lot of the research comes from modelling and animal trials before they can move onto people.

3. ***Clinical Research:*** After receiving approval to begin clinical trials, the goal is to make sure it's safe to use with humans, then increase the number of participants to understand optimal dosages, etc. then tries to find whether it was effective or not.

4. ***FDA Review:*** It's at this point the company will file its New Drug Application (NDA) to the FDA and they will determine whether the product is safe to go to market. If declined, businesses have a chance to reapply after applying feedback. This whole process is a rigorous one since it will introduce the public to the new drug.

5. ***Post-Market Safety Monitoring:*** The drug will continue to be monitored once entering the market since there's no feasible way, despite the rigor in approval, to know how the drug effects the masses without it being in action. They will monitor problems and act as deemed necessary.

Source(s): IBISWorld, FDA, PwC, EY, Businesswire, Company Filings

The FDA Approval Process

Investigated New Drug (IND) Analysis

After everything is completed on the sponsors end regarding drug development, preclinical research, etc. they must submit an IND application to the FDA based on the results of the initial testing which includes the drug composition, manufacturing, and the plan for testing the drug on people. The FDA will review the application to determine whether the proposed tests won't place people at unreasonable risk of harm and confirms that participants are consenting, fully informed, and protected as human subjects in the trial.

Phase:	Clinical Studies & Trials
#1	When beginning the first phase of clinical trials, there usually on 20-80 volunteers being used, as the emphasis here is on safety. They use the small sample size to determine what the drugs most frequent side effects are and, often, how the drug is metabolized and excreted.
#2	The focus on this phase in the trial is on effectiveness, through the collection of preliminary data on whether the drug works in people who have the disease or condition in question. There's usually 100's of people in this and in controlled trials, placebo's may be used to derive further conclusions.
#3	This is traditionally the final phase of clinical trials, with 1000's of participants being used to gather data regarding safety and effectiveness. The sample size allows studies to be done on the effects of the drug on participants under a variety of conditions and provide comprehensive, insightful results.

New Drug Application (NDA) Review

The FDA will meet with the drug sponsor prior to the submission of the NDA and at this point, the sponsor will formally make the request for the NDA to be approved. The point of this NDA is to give the sponsor the greenlight to market the drug in the US and this application will include all the animal, human and drug related data for the regulatory body to dig deeper into. The FDA has 60 days to determine whether the NDA should be filed for further review and if they decide to file it, a dedicated team will be assigned to the sponsors drug to evaluate the research themselves, along with the drug labelling and manufacturing sights.

Post-Approval Risk Assessment

The FDA will continue to keep a close eye on the product after it enters the market and will receive continuous updates from the sponsor on safety, with certain online resources allowing physicians and patients to document adverse effects for the FDA to observe.

Source(s): FDA website

Value-Adding Activities

Basic Research - Research done for the purpose of expanding knowledge that is done solely for knowledge's sake completed most often by academia, research institutes, etc.

Applied Research - Research that is done for the purpose of creating practical solutions for very specific problems, done often by R&D segments of a business or specialized firms.

Integration & Development - Focuses on integrating research depending on a firm's capabilities and the develops solutions related to the market the firms are hoping to target.

Production & Manufacturing - This is regarding the manufacturing activities for solutions to produce for the intended market in a sustainable and economic fashion.

Marketing & Sales - After safety-related activities have been completed, distributing the solutions to the target market through licensing, selling rights, or selling the product itself along with marketing is pursued to achieve profitability for the firm to continue operations.

Testing & Validation - The process of making sure solutions are performing as intended and safe for consumption through validation by the dedicated regulatory bodies.

Services - Within this activity, services can encompass nearly everything listed above or can be related to the ongoing sale of solutions including consultations to more specialized offerings like gene therapy, which inserts genes into a subject's cells to treat diseases.

AXSOME THERAPEUTICS

Axsome Therapeutics does most of the activities listed above, albeit with respect to less basic research since they're not an academically oriented institute. However, they do more applied research since as a firm, they need to prioritize profit generation.

They are a Biopharmaceutical company that is developing and delivering novel therapies for the management of central nervous system disorders, They're current pending approval from the FDA for a couple projects in their pipeline and since acquiring a business focused on sleep-related medication, have made their first commercial sale with the products.

EXELIXIS®

Exelixis focuses as well on similar tasks in a different field. The company has been focused on the development of their pipeline projects and making sure they progress in their go-to-market goal.

They've recently began their first-in-human phase 1 study for XL114, which focuses on non-Hodgkins Lymphoma. They've also focused on Business Development through the signing of agreements with BioInvent and Ryvu Therapeutics to expand their capabilities and portfolio. They've seen immense growth in commercial activities since last quarter.

M&A Activity - Consolidation Continues

With pharmaceutical companies coming up on a slew of patent expirations, they're looking to grow market share through inorganic means thanks to hefty cash reserves (especially ones with COVID-19 treatments in inventory). Despite that and a deteriorating macro environment, strong operators have continued making deals within the space.

Most major industry players consequently took part in the M&A activity that defined the past half decade, and these same players are expected to continue this trend to make up for what was lost during this most recent economic downturn. Capitalizing on the R&D efforts of other businesses has helped provide those acquired excess capital to continue funding these project, along with greater access to resources. The deal also provides the acquirer profit retention and diversified revenue streams.

This restricted capital access from the macro environment is giving large pharma and biotech companies a chance to use their reserves to purchase early-stage assets at depressed valuations and get more pipeline projects initiated. There will also be strategic deals taking place to unlock value as quickly as possible, such as dealing with talent attrition, or digital capabilities to reduce CapEX spend, etc. Companies with promising pipeline projects will be sought after since future income generated from these projects is subjective and can help influence acquisition value.

Relevant Transactions

Pfizer Inc. Acquisition of Biohaven Pharmaceutical Holding Company Ltd.

The deal was announced on May 10th, 2022, with Pfizer expected to have a total consideration of $12.2B all-cash at a 33% premium. The transaction provides Pfizer ownership of Biohaven's CGRP programs including Rimegpant (NURTEC® ODT) which was approved in the US for acute treatment of migraine issues, Zavegepant which is on track for US approval & five other preclinical CGRP assets. This provides Pfizer a new revenue stream as NURTEC is currently the #1 prescribed migraine medication in the US within its class.

Bristol-Myers Squibb Company Acquisition of Turning Point Therapeutics Inc.

The acquisition took place on June 3rd, with BMS acquiring all outstanding shares of Turning Point for $76 per share with cash, making the total consideration amount $4.1B. The focus of the transaction is to expand BMS' core therapeutics offerings. Turning Point's lead asset, repotrectinib, which is considered a potential best-in-class therapy for certain lung cancers and tumors is expected to be approved by the FDA by the end of 2023. BMS expects repotrectinib to be approved in the second half of 2023 and become a standard of care for patients. BMS will also explore Turning Points pipeline assets to help bring the projects to fruition and protect themselves against future revenue loss from patent expirations.

Government Risk

While companies in every other industry are valued based on their expected profitability compared with cash flows and other potential investments, biotech is typically expected to lose money in the short- and medium-term, attaining profitability only a long time into the future. And that future is subject to a substantial amount of risk, which are risks from government and corporate relationship.

Poor government regulation and support put a drag on the value creation of the biotechnology industry, especially consisting of discovery R&D, preclinical research, and clinical trial stage.
Without proper regulation, biotech would lose the transparency, predictability it should have, which would devastate investors as they have already put in a lot of money. If they lose confidence in the products, the company, or even the industry, liquidity will fundamentally shift to other areas.

Lacking proper innovation support, the industry would be significantly affected by the Matthew Effect. Those big pharmaceutical companies can market drugs to fund their cash flow and can be shored up by investors more since they have more exposure to the market.

Corporation Relation Risk

Secondly, vulnerable corporate relations limit the synergy and efficacy of the bioeconomy once able to achieve. Namely, corporate relations contain relations with investors and other biotech companies.

Healthy relationship maintained with investors would reduce the development risk. As we talked above, biotech industry is an industry that needs to return to the capital market again and again to raise money to fund the next state of their development. As investors nowadays usually expect biotech companies to raise money after the announcement of positive Phase 2 or Phase 3 clinical data, clear and convincing development life-cycle involving value-creation life-cycles is essential in develop a landscape conductive to sequential capital raises.

Large-Scale Collaboration and Cooperation can significantly accelerate biotech R&D. On one hand, legally guided collaboration would benefit small companies by increasing the diffusion and accessibility of technologies and expertise. On the other, strategic alliance between companies can benefit big cooperation as small companies with a big product opportunity have huge sensations.

THE GENES OF A STRONG MARKET

COVID impact:

COVID has shifted the commercial territory within segments of biotech industry entirely. In 2021, in the 46 commercial leaders generated 86% of the industry's total revenues, an astonishing 22% of the revenue were generated solely by BioNTech and Moderna. BioNTech and Moderna are the two companies that pioneered mRNA-based vaccines against COVID-19, and they only joined the ranks of the commercial leaders in 2020.

As we see biotech stocks underperformed in 2021, it has cast more challenges to the industry.

Biotech access to capital markets via IPOs looks increasingly difficult. Since early 2021, the valuations of biotech companies have plunges, which hurt the market sentiment towards the whole industry. Smaller and earlier stage companies now face an existential path to the capital markets and access to capital in general.

Significant operation challenges have occurred because of the uncertainty in the future. For example, the supply chain disruption has intensified the competition for biotech talents; the ability to achieve scalability has challenged the established commercial models; the rising pressure for companies to demonstrate commitment in addressing ESG issues has created difficulty in R&D. The skills to navigate these complex and unprecedented challenges will be essential in the biotech C-suite.

Long-term outlook:

Despite the recent market volatility and correction in biotech, the industry remains in a position of strength as evidenced by the following reasons:

The strength of biotech R&D engine is still strong. Though vaccines will continue to dominate this space, drugs will take a growing share of the market. Even though the market sentiment is down, FDA has already approved 13 products till July, reaching the yearly average pre-pandemic. On top of the approvals, biotech has stuffed up its pipeline with over 6,000 drugs are in active development.

On the other hand, there are still robust tide of dollars in the pool waiting for future investments.

- **VC money remains strong as it follows science trend, investors continue to bet on biotech's long-term viability.** By monitoring top 15 VC firms early- and seed-stage deals, biotech is the second largest investment segment in deal value in 2022

- **M&A activities has been driven by industry specific needs.** In 2022, patent expirations and the need to access new modalities will increase the pressure on biotech to use M&A and partnerships to obtain future revenue. Big players may seize the opportunity for large-scale M&A later this year. In the interim, big pharma continues to favor de-risked, late-stage biotech assets that fit naturally into a company's strategic pipeline

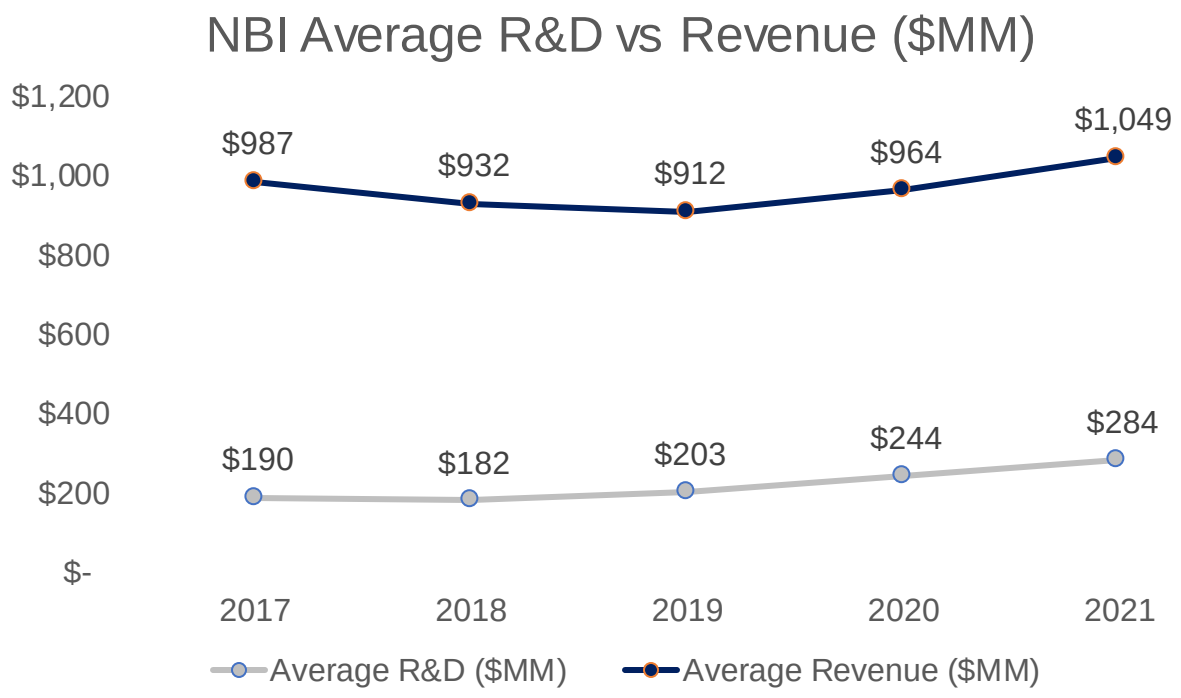
Source(s):

Appendix A

Merger/Acquisition Transactions (Last 6 Months)

Announced Date	Target	Buyer/Investors	Size ($mm)
Aug-08-2022	Global Blood Therapeutics, Inc. (NasdaqGS:GBT)	Pfizer Inc. (NYSE:PFE)	5,581.03
Aug-04-2022	ChemoCentryx, Inc. (NasdaqGS:CCXI)	Amgen Inc. (NasdaqGS:AMGN)	3,944.87
Jun-03-2022	Turning Point Therapeutics, Inc. (NasdaqGS:TPTX)	Bristol-Myers Squibb Company (NYSE:BMY)	3,975.8
Jun-02-2022	Worldwide Exclusive License Rights of Libtayo	Regeneron Pharmaceuticals, Inc. (NasdaqGS:REGN)	1,100.0
May-31-2022	Affinivax, Inc.	GSK plc (LSE:GSK)	3,300.0
May-10-2022	Biohaven Pharmaceutical Holding Company Ltd. (NYSE:BHVN)	Pfizer Inc. (NYSE:PFE)	12,184.25
Mar-01-2022	Syndesi Therapeutics SA	AbbVie Inc. (NYSE:ABBV)	1,000.0
Feb-28-2022	Biosimilars Portfolio and Related Commercial and Operational Capabilities of Viatris Inc.	Biocon Biologics Limited	3,285.0
Feb-25-2022	Channel Biosciences, LLC	Biohaven Therapeutics Ltd	1,238.5

Appendix B


NBI Average R&D vs Revenue ($MM)
$1,200
$1,000
$800
$600
$400
$200
$-
$987
$932
$912
$964
$1,049
$190
$182
$203
$244
$284
2017
2018
2019
2020
2021
Average R&D ($MM)
Average Revenue ($MM)

Appendix C

Valuation Statistics Company name	Market CAP ($m)	Enterprise Value ($m)	EV/Revenue LTM (x)	EV/Revenue NTM (x)	EV/EBITDA LTM (x)	EV/EBITDA NTM (x)	P/E LTM (x)	P/E NTM (x)
Pfizer Inc.	$ 281,235	$ 288,674	2.9	3.3	6.4	6.94	9.8	8.5
Moderna Inc.	$ 66,966	$ 49,794	2.2	2.9	3.1	5.99	5.2	11.1
Novo Nordisk A/S	$ 240,551	$ 239,778	11.1	9.6	23.9	19.4	32.1	27.6
Johnson & Johnson	$ 434,603	$ 434,532	4.5	4.5	13.3	12.48	16.55	16.24
Thermo Fisher Scientific Inc.	$ 236,331	$ 264,881	6.2	6.2	20.4	23.16	37.8	26.7
Maximum	$ 434,603	$ 434,532	11.1	9.6	23.9	23.2	37.8	27.6
Minimum	$ 66,966	$ 49,794	2.2	2.9	3.1	6.0	5.2	8.5
Median	$ 240,551	$ 264,881	4.5	4.5	13.3	12.5	16.6	16.2
Average	$ 251,937	$ 255,532	5.4	5.3	13.4	13.6	20.3	18.0