PitchBook

The Biotech Company Lifecycle

Examining the role of venture in biotech investment

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Credits & contact

Research
JOSHUA CHAO, Ph.D., Analyst, VC
joshua.chao@pitchbook.com

Data
VAN LE Lead Data Analyst
ALEX WARFEL Data Analyst

Design
CAROLINE SUTTIE

Contact PitchBook

RESEARCH
reports@pitchbook.com

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Key takeaways

- **Key differences exist when comparing the company lifecycle of biotech versus tech startups**. Heuristics of popular startup-building frameworks, such as the "lean startup" methodology, do not directly translate to building and operating a biotech startup.
- **Biotech startups are long-term endeavors with short-term financing needs, and VC's unique position makes it the ideal asset class to fund these risky ventures.** Long drug-development cycles align with the illiquid nature and timeline of VC investments, as biotech companies typically need multiple rounds of follow-on financing to advance through clinical trials. This permits VCs to invest at multiple points in the company lifecycle. Furthermore, the risk-return profile of biotech startups tends to align with VCs looking for moonshots with the potential to return the entire fund or more.
- **Metrics commonly used to assess the health and growth of an industry illustrate how biotech startups are unique from tech and software startups.** Biotech startups have been quicker than tech startups to access VC financing in the past few years, and they tend to come back for new financings rounds earlier than their tech counterparts. In addition, the median time since founding to IPO for biotech startups sits at 5.8 years, compared to 9.9 years for tech startups, indicating that VC-backed biotech companies are taking advantage of the healthy biotech IPO market

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Introduction

The success of high-growth tech companies has led to a rising focus on entrepreneurship and innovation, centered on software and digital products. These companies have laid the groundwork for many company-building frameworks—including the ever-popular "lean startup" methodology and "blitzscaling" techniques—that have become codified in academic curricula and corporate strategies across the world. Yet, for biotech & pharma startups with therapeutic products aimed at treating disease, these company building frameworks rarely translate.

Many heuristics of the "lean startup" methodology popular with tech companies lack direct translations when building and operating a biotech startup. The development of a minimum viable product (MVP)—namely, a pipeline drug—requires several years of research & development (R&D) efforts. In addition, testing this product on end users becomes significantly more difficult due to the challenges surrounding clinical trials and regulatory hurdles.

There is also a decoupling between the end user and payer when it comes to the biotech & pharma sector. Reimbursement and health insurance considerations add a layer of complexity when forecasting drug revenues. While tech investors expect to see future revenue models and growth plans when hearing a pitch, biotech investors heavily deemphasize the importance of business models given that revenue generation often spans a seven- to 10-year goal and the success of the drug inevitably ensures monetization.

If there are early signs of promise in a drug's development lifecycle, investors will also likely see some sort of liquidity event (for example, an acquisition or licensing deal) before the drug actually hits the market, so forecasting drug sales to estimate future cash flows becomes less relevant than for many other industries. Many biotech investors care largely about one thing—the drug's underlying technology and its biological mechanism of action. The ability for a drug to successfully treat an unmet/undermet medical need bears great weight in an investor's due-diligence process.

In our previous analyst note "Betting on Biotech," we examined how the business model of large-cap biopharma incumbents has evolved to carve out an opportunity for investors and VC-backed biotech startups. In this note, we discuss key differences between tech versus biotech company lifecycles. We also examine VC's unique position to fund these high-risk startups and how the nature of VC investment aligns with the needs of the biotech sector.

1: *The Four Steps to the Epiphany: Successful Strategies for Products That Win*, K&S Ranch Consulting, Steve Blank, 2005.
2: *The Startup Owner's Manual: The Step-by-Step Guide for Building a Great Company,* K&S Ranch Consulting, Steve Blank and Bob Dorf, 2012.
3: *The Lean Startup: How Today's Entrepreneurs Use Continuous Innovation to Create Radically Successful Businesses,* Eric Ries, Crown Business, 2011.
4: *Disciplined Entrepreneurship: 24 Steps to a Successful Startup,* Wiley, Bill Aulet, 2015.

Methodology and timeline of tech startups

Many systematic frameworks for building startups have been developed, including Steve Blank's "customer development" methodology,[1,2] Eric Ries' "lean startup" methodology,[3] and Bill Aulet's "disciplined entrepreneurship" toolbox,[4] to name a few. These widely used methodologies typically follow this formula:

1. Identify a gap in the market that is ripe for disruption
2. Determine end-user pain point(s) through customer discovery
3. Develop a minimum viable product (MVP) to address pain point(s)
4. Obtain customer validation and feedback through beta testing
5. Iterate on value proposition to optimize product-market fit
6. Distribute golden master version of product and begin growing user base
7. Use end-user feedback to continuously improve product
8. Ramp up, scale, and achieve escape velocity

Key factors such as product-market fit and value proposition, along with metrics such as customer acquisition costs (CAC), lifetime value (LTV), and daily/monthly active users (DAU/MAUs), are the lifeblood of tech startups and the criteria upon which investors rely to determine investment potential. Tech startups utilize the bulk of their capital to achieve scale and quickly establish a foothold in the market. By running lean on low capital expenditures and taking advantage of the advent of cloud services and other digital advances, tech startups have been able to proliferate at breakneck speeds over the last several years.

Methodology and timeline of biotech startups

When it comes to building a biotech startup, the company lifecycle rarely follows the tech framework mentioned above. While parallels may exist between tech and biotech companies, there are several key differences. First, biotech startups typically produce a drug (if not multiple drugs), which makes them subject to stringent testing conditions before the drug can be approved and marketed. This requires significant academic and scientific labor to identify drug compounds or platform technologies, and many more years to determine the drug's safety and efficacy profiles.

Unique aspects of biotech startups:

1. *Drug products are subject to stringent clinical testing before obtaining market approval.*
2. *Significant capital and nontrivial marginal costs are needed to develop drug pipeline.*
3. *Lack of beta testers and initial customers makes iterating and pivoting difficult.*
4. *FDA approval is a significant hurdle for drugs in order to hit the market.*
5. *Revenue sales are largely dependent on reimbursement policies.*
6. *First-mover advantage plays an outsized role for a drug's total addressable market (TAM).*

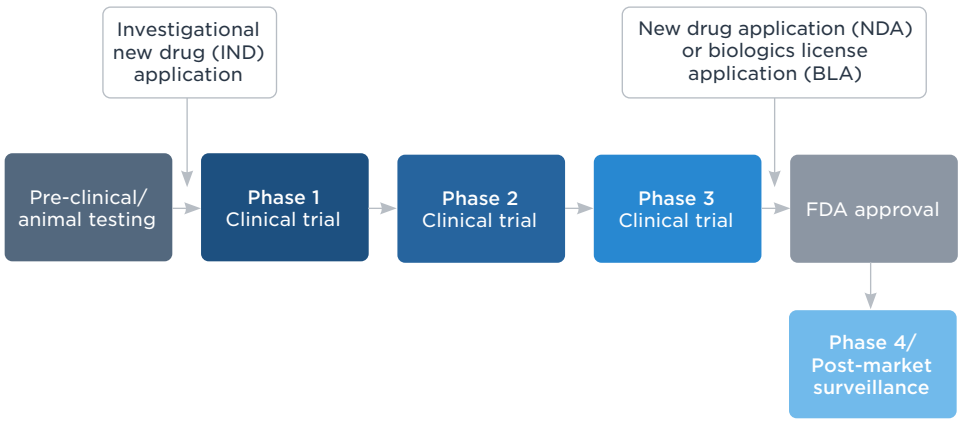
Second, the capital required to develop a startup's drug pipeline is magnitudes greater than what most tech startups spend. The marginal costs associated with developing new software and adding new lines of code pales in comparison to the incremental costs of lab equipment, staffing, and consumables. Third, without feedback from beta testers and initial customers, biotech companies struggle to quickly iterate on a drug product and pivoting a drug compound into a new trial is arduous due to the level of pre-clinical data required by regulators.

Fourth, the go-to-market strategy for biotech companies is bound by the US Food & Drug Administration (FDA) as companies require regulatory approval for their drug products. Fifth, revenue streams are dependent on reimbursement policies from private health insurance providers and government-based programs such as Medicare and Medicaid.

Lastly, first-mover advantage plays an outsized role for a drug's total addressable market (TAM) due to protection from patents and exclusivity periods and slow competition from copycats. Econometric analysis has shown that first-to-market drugs almost never lose their market dominance to minimally differentiated competitors during the patent timeline, and that subsequent drugs show a significant dependence on order of entry, promotional spending, and time delay from launch of the previous entrant when attempting to capture market share.[5]

FDA checkpoints serve as major binary events for biotech startups. Typically, once a drug compound has been identified and pre-clinical/ animal testing has shown early signs of efficacy, companies will file an Investigational New Drug (IND) application with the FDA. This application contains clinical trial protocols and, upon approval, allows the company to progress into human clinical trials and begin patient recruitment. As we detailed in a previous analyst note, average clinical trial costs can range from $4 million for a Phase 1 trial to $20 million for a Phase 3 trial.

Drug approval process in the US



Source: PitchBook

5: "Forecasting Market Share in the US Pharmaceutical Market." Nature Reviews Drug Discovery, Stephanie A. Regnier and David B. Ridley, 2015.

If a drug meets its primary endpoints as it progresses through trials, companies will eventually submit a New Drug Application (NDA) or Biologics License Application (BLA) to the FDA. At this stage, the drug sponsor formally proposes that the FDA approve the drug for sale and marketing based on the clinical trial data. A study of 106 drug assets has shown that the average time from NDA/BLA application to FDA approval is roughly 16 months (around 1.3 years).[6]

All these checkpoints affect a biotech company's ability to raise additional capital—be it to fund other clinical trials or to further build out their R&D programs. Investors use these checkpoints to determine the short- and long-term probability of success (POS) and likelihood of approval (LOA) of a drug asset. Indeed, keen investors heavily rely on medical conferences, clinical trial readouts, and the FDA's Prescription Drug User Fee Act (PDUFA) calendar to determine how these catalysts influence a biotech company's valuation.

Ultimately, investors weigh two key pieces of information when determining an accurate valuation: how the drug's mechanism-of-action will perform against standard-of-care and the drug's revenue potential down the road. Depending on the company's stage in the lifecycle, investors place different weights on these two points. For early-stage biotechs, investors focus on technical due diligence and derisking scientific or clinical barriers. For late-stage biotechs, investors emphasize manufacturing, reimbursement, and marketing concerns and build discounted cash flow models (DCFs) to forecast revenues. Particularly if there are no approved drugs in that specific market and the company is still private, public comps or fundamentals cannot be used. When it comes to building a biotech company, myriad pathways exist given drug development and clinical complexities; however, most companies tend to follow one of the two approaches detailed below.

Drug-centric approach (bottom-up)

This approach first identifies a drug candidate/ technology with novel IP to commercialize, and then focuses on searching for a clinical target to treat with said drug.

The first approach is a bottom-up approach, or a drug-centric approach. This is perhaps the approach that many fledgling biotech startups take, particularly when they are spun out of an academic institution. The drug-centric approach first identifies a drug candidate/technology with novel IP to commercialize, and then focuses on searching for a clinical target to treat with said drug. By targeting multiple diseases and drug targets, this approach focuses on the drug product as a platform to treat a breadth of potential diseases.

6: "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs." Journal of Health Economics, Joseph A. DiMasi, et al., 2016.

This approach first identifies a specific clinical indication or shortcoming within the current realm of patient treatment, and then focuses of searching for drug candidates to fill the gap.

Biodesign methodology: *A process used for medical device innovation in which entrepreneurs identify, invent, and implement new medical technologies through iterative processes of clinical immersion and device design and strategy.*

Venture-creation model: *A process used by some venture capital firms to build first-in-class biotechnology companies through an internal creation engine and a network of entrepreneurs-in-residence.*

Disease-centric approach (top-down)

The second approach is a top-down methodology, or a disease-centric approach. Similar to the Biodesign methodology[7] for medical device innovation and the "venture creation" model[8] within biotechnology innovation, the disease-centric approach first identifies a specific clinical indication or shortcoming within the current realm of patient treatment, and then focuses on searching for drug candidates to fill the gap. This approach tends to be more open-ended and abstract than the drug-centric approach because there are fewer constraints around drug IP when first starting with a clinical problem. Some biotech startups pursue a hybrid of both approaches, but generally, most companies fall into one camp or the other.

Biotech versus tech comparison

	Biotech startups	Tech startups
Risks	Scientific and technical risks around drug development	Market and execution risks
Customer	Decoupling of end-user (patient) and payee due to reimbursement policies	End-user (individual or enterprise) pays for the product
Intellectual property (IP)	Rely on patents and market exclusivity periods for protection	Patents tend to provide less protection than biotech
Fundraising	Larger seed and early-stage rounds needed to prove drug efficacy	Smaller early-stage rounds with larger late-stage rounds to achieve scale and capture market share
Primary capital spend	Drug research & development (R&D) programs	Human capital and headcount (i.e. engineering, sales, etc.) and external marketing & advertising
Go-to-market strategies	Significant regulatory hurdles with FDA and other regulatory agencies	Rapid scaling, high-growth mentality to capture market share
Revenue generation	Typically pre-revenue for the entirety of time under VC backing	Generating revenue early on in the company lifecycle

Source: PitchBook

7: *Biodesign: The Process of Innovating Medical Technologies*, Cambridge University Press, Paul G. Yock, et al., 2019.
8: "New Venture Creation in Biotechnology," *The Business of Healthcare Innovation*, Jason Rhodes, edited by Lawton Robert Burns, 3rd ed., Cambridge University Press, Cambridge, 2020.

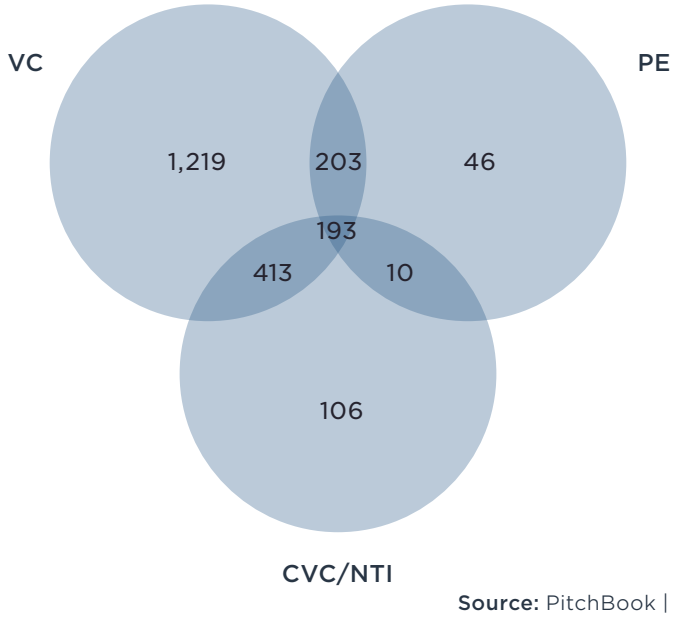
Why venture capital?

Biotech startups are long-term endeavors with short-term financing needs. These companies share traits with most companies that pursue VC funding, namely, a long pathway to profitability, high burn rates and capital intensity, and the potential for asymmetric returns. Long drug-development cycles align with the illiquid nature and timeline of VC investments, as biotech companies typically need multiple rounds of follow-on financing to advance through clinical trials. This permits VCs to invest at multiple points in the company lifecycle, uniquely positioning venture as the ideal asset class to fund these risky biotech startups.

Many inherent risks surrounding drug development exist. Biotech startups are notoriously plagued with high failure rates—90% of clinical programs ultimately fail to receive FDA approval[9] and 92% of biopharmaceutical companies are unprofitable at any given time.[10] This risk profile tends to align with VCs looking for moonshots with the potential to return the entire fund or more.

Biotech entrepreneurs are hard-pressed to find asset managers outside of venture willing to fund financings round of this size and risk. LPs that contribute to specialist funds understand the nature of early-stage biotech investing and recognize that the asymmetric returns of these companies outweigh many of the risks surrounding lengthy illiquidity. As such, the VC asset class matches the risk profile and financing size that biotech startups

Biotech & pharma deals (#) by investor participation from 2017 to 2020*



Source: PitchBook | **Geography:** US
*As of September 24, 2020

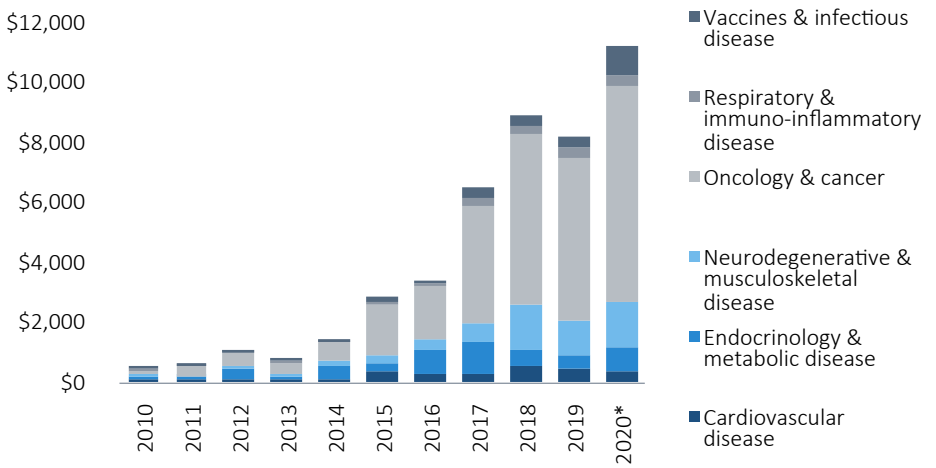
9: "Clinical Development Success Rates 2006–2015", Biotechnology Innovation Organization (BIO) Industry Analysis, 2016.
10: "The Biotechnology Ecosystem: By the Numbers," Biotechnology Innovation Organization (BIO), Infographic, 2017.

tend to look for. Our data indicates that VC investors dominate the majority of biotech & pharma deals, consistently participating in 65%-70% of financings.

VC financings in the biotech sector has grown considerably in the last decade. As many of the industry incumbents have trimmed R&D budgets and shied away from high-risk pre-clinical programs, VC investors have the opportunity to fund cutting-edge biotech programs. Many GPs and LPs alike view healthcare and biotechnology as the next frontier of scientific discovery and are making increasingly larger bets on promising startups.

As new innovations in science continue to spring up, VC deal activity in clinical subsectors such as oncology and neurodegenerative & musculoskeletal diseases has skyrocketed, reaching $7.2 billion and $1.5 billion year-to-date (YTD, as of September 24, 2020), respectively. Given the pervasiveness of the COVID-19 pandemic, VC financings for companies focusing on vaccines and infectious disease in 2020 have reached an all-time high of $1.0 billion YTD. While this is not an exhaustive list of all clinical subsectors within the biotech & pharma sector, these areas represent some of the largest unmet medical needs and investors are doubling down on promising biotech & pharma startups developing drugs to tackle these challenges.

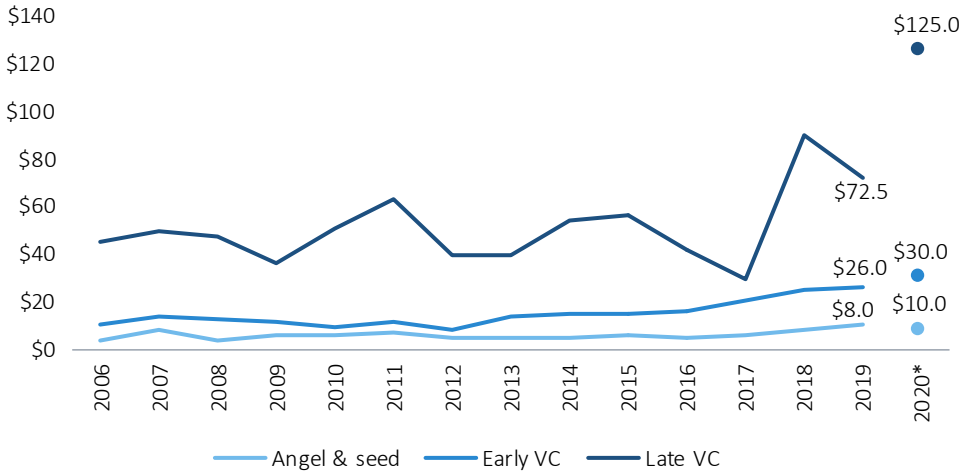
VC deals ($M) by clinical subsector



Source: PitchBook | **Geography:** US
*As of September 24, 2020

Valuations in the biotech & pharma sector are also elevated in 2020, as VCs are always looking for the next generation of transformative biotechs. Pre-money valuations for biotech companies have remained robust over the last several years with early-stage and late-stage medians at $30.0 million and $125.0 million, respectively, through 2020 YTD. Because of this, biotech companies have been able to command strong valuations as VCs compete for deals. The supply constraint of high-potential biotechs, countered with the flood of demand from capital allocators, has led to an extremely competitive financing environment. This, along with robust exit opportunities in the equities market, has driven the upward move in valuations in recent years.

Median pre-money valuations ($M) for biotech & pharma by stage



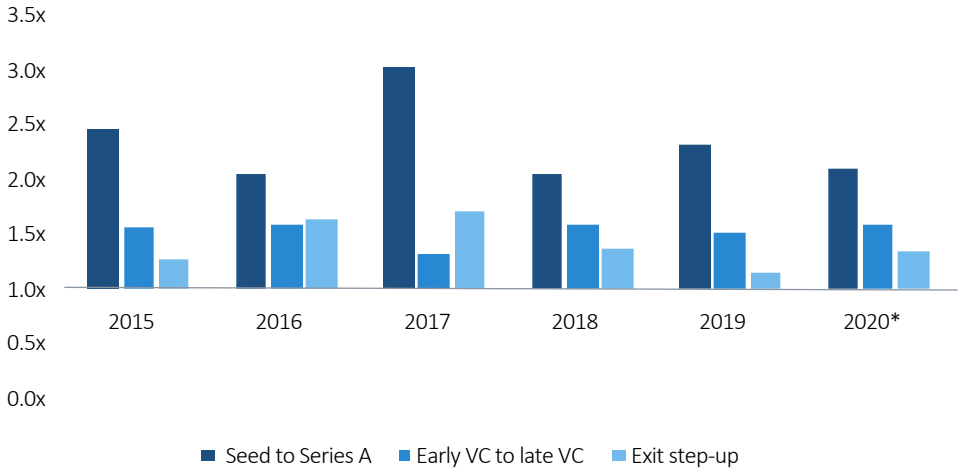
Source: PitchBook | **Geography:** US
*As of September 24, 2020
Note: Low angel & seed counts for 2006-2013 and 2020.

As touched on earlier, we attribute much of the strength in valuations and exits for biotech companies to the strength of a drug's IP and patent exclusivity. Whereas fast-followers and copycats pose significant risks for tech companies, biotech companies rely on strong patent protection to provide the moat they need to get a drug to market. Once companies file a patent application, they begin a 20-year exclusivity countdown on that drug.

Considering the number of years that go into R&D and clinical testing, along with the high costs associated with developing new drugs, biotech companies rely on patents—essentially government-granted monopolies—to protect them as they accelerate their drug to market to generate revenue. As such, investors looking to back a specific drug technology (CRISPR/Cas9 or kinase inhibitors, for example) for a specific disease target (such as non-small-cell lung carcinoma (NSCLC), non-alcoholic steatohepatitis (NASH), and so on) have a relatively limited number of companies to choose from because of the constraints on specific innovation due to patent competition.

Step-up multiples within biotech & pharma deals tend to be strongest going from seed to Series A financings, with medians hovering above 2.0x for the last seven years. Seed financings are usually used to test the lead drug candidate or platform technology in robust pre-clinical animal models. This serves as a checkpoint for startups before progressing toward the extensive (and expensive) process of human clinical trials. Series A financings are then raised to help startups progress into first-in-human trials. This robust step-up is due in part to the value attributed to derisking a drug candidate at the pre-clinical stage and also in part to the large infusions of capital needed to conduct Phase 1 clinical trials while maintaining R&D programs.

Step-up multiples for biotech & pharma VC deals by stage



Source: PitchBook | **Geography:** US
*As of September 24, 2020
Note: Low data counts for certain datasets.

Performance comparison of biotech versus tech startups

The ability to maintain a strong cash runway is the lifeblood of biotech companies. Venture financings play a crucial role in a company's ability to progress along the company lifecycle. In this section, we compare biotech and tech startups and look at three key metrics: the time since founding to first VC financing, the time between financing rounds, and the time since founding to exit.

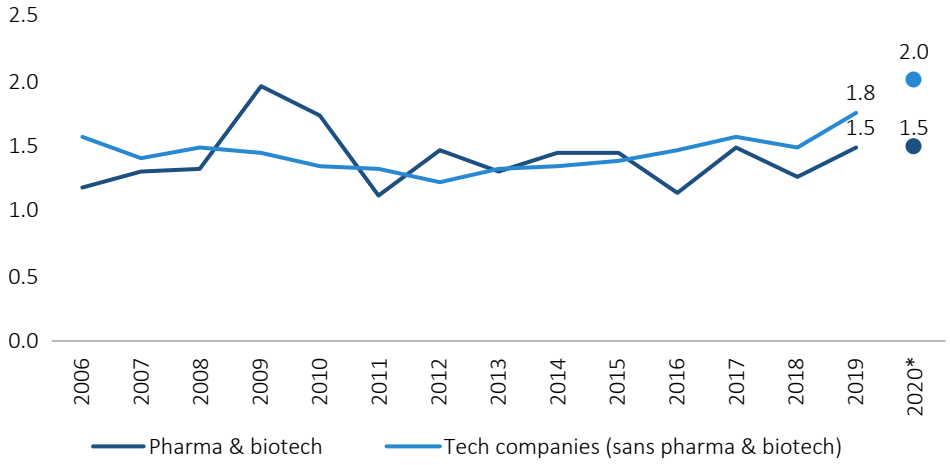
Time since founding to first VC financing

The median time since founding to first VC financing in 2020 is 1.5 years for biotech & pharma startups and 2.0 years for tech startups (excluding companies co-tagged as biotech & pharma). To note, the median time for tech startups has exceeded that of biotech startups in each of the last five years. This indicates that tech startups have been able to bootstrap their finances for longer before having to raise institutional capital. As server and cloud computing costs have dropped in response to stiff competition between AWS, Google Cloud, and Microsoft Azure, entrepreneurs have kickstarted tech companies with minimal infrastructure costs.

The primary burn for tech startups is people costs, but many startups give more equity in lieu of cash, preserving runway and making the most of bootstrapped capital. Serial tech entrepreneurs can also use payouts from previous ventures to finance the startup before seeking venture funding. Biotech companies do not have that luxury given high cash burn and the need for capital to run R&D labs and fuel drug development. Commercial lab space prices have continued to climb in top-tier life sciences markets, according to our previous analyst note. They are also less able to lean on equity stakes in compensation packages given the high failure rate of biotech

startups. While many can survive off NIH commercialization grants and Small Business Innovation Research (SBIR) grants for some time, VC financing is really the only viable long-term, risk-aligned option that provides adequate capital.

Median time (years) since founding to first VC financing by sector



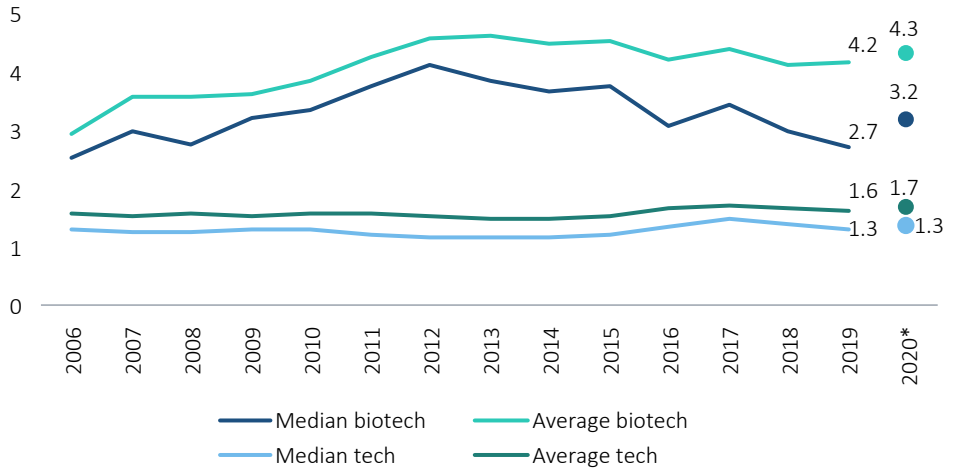
Source: PitchBook | **Geography:** US
*As of September 24, 2020

Time between rounds

The median and average time between financing rounds for biotech startups in 2020 sits at 3.2 and 4.3 years, respectively, compared to the median and average time between rounds for tech startups at 1.3 and 1.7 years, respectively. This stark difference indicates that tech startups return to their private backers more quickly than biotech startups. The steep ramp-up on engineering and sales & marketing functions often seen with the "growth at all costs" mentality of tech startups makes returning for follow-on financing rounds quite advantageous. Tech startups cannot rely on patents and market exclusivities to protect them from competition and, as such, these companies must scale at breakneck speeds to quickly penetrate the market and establish network effects.

New trends and developments in tech require a winner-take-all mentality, whereas in biotech, companies are rarely approaching the same problem from the same angle as someone else, so there is less direct competition. This is possible because the sheer breadth of the biotech landscape and the constraints on specific innovation due to patent competition forces companies to tackle less-crowded disease markets. Drug-development cycles at biotech startups are also longer than product-development lifecycles at tech companies, which also plays a role in the disparity in time between financing rounds. Metrics such as the pre-clinical data needed for next infusion of capital are a more time-intensive barrier than showing daily active users, customer retention, and platform stickiness. In addition, biotech companies cannot "supercharge" drug development the same way that tech startups can supercharge growth when they see evidence of traction.

Median and average time (years) between financing rounds by sector

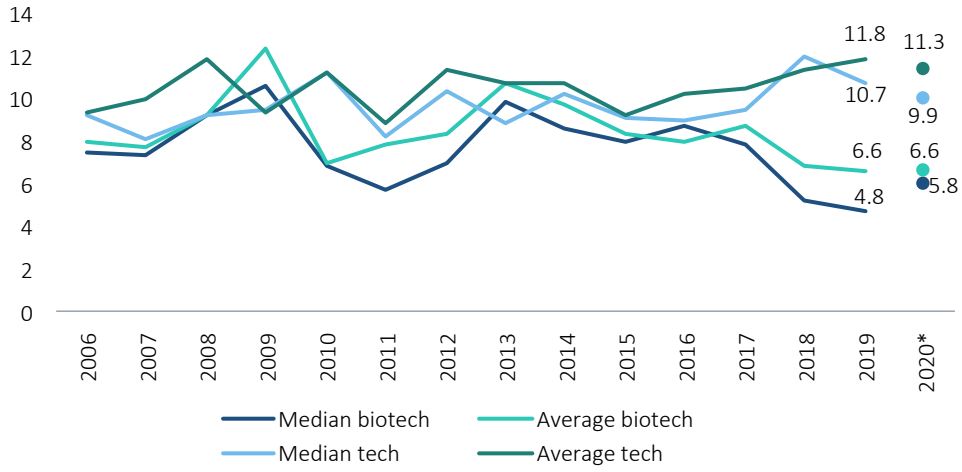


Source: PitchBook | **Geography:** US
*As of September 24, 2020

Time since founding to IPO

The median and average time since founding to IPO for biotech startups in 2020 is 5.8 and 6.6 years, respectively, whereas the median and average time between rounds for tech startups is 9.9 and 11.3 years, respectively. The median for biotech companies has dropped notably in the last few years, declining from 8.7 years in 2016 to 4.8 years in 2019 at a -18.2% YoY decline. This is due in large part to a healthy IPO market for biotech companies in the last few years, coupled with renewed interest from large-cap biopharma incumbents in startups' drug portfolios. As IPOs act as a large financing event for VC-backed biotechs rather than a traditional "exit" for early investors, companies are able to use the capital raised by issuing new shares to fund clinical trials and build out R&D programs. Biotech companies can also gauge the relative success/failure of their products in a binary manner. Negative results in pre-clinical and early-phase clinical trials are clear checkpoints of a drug's efficacy and thus indicate whether a company needs to raise IPO-level amounts of capital.

Median and average time (years) since founding to IPO by sector



Source: PitchBook | **Geography:** US
*As of September 24, 2020
Note: Low data counts for 2008.

Outlook

The landscape of VC investing has shifted significantly since the early days of venture financing within biotech. Indeed, the delineation between tech and biotech has certainly become fuzzier in the last decade as synergies and overlap between the two sectors continues to grow. New industry verticals such as AI-powered drug discovery, digital therapeutics, and lab-on-a-chip diagnostics have been born out of the combination of digital advances with biotechnological innovations.

Yet, we believe these gentle disruptions to the biotech & pharma sector will not drastically transform the company lifecycle to more closely resemble the technology sector. Key differences surrounding product-market fit, financings and capital spend, and the role of regulatory approval remain barriers that have shaped the biotech industry to what it is today.

Some lessons from tech can be carried over to the biotech sector, however. Notably, the adoption of virtual biotechs that utilize contract research organizations (CROs) and contract manufacturing organizations (CMOs) for much of the supply chain has proven beneficial to companies that want to run lean and cast a wide drug discovery net. Nonetheless, the costs saved on capital expenditures, lab space, and salaries is spent elsewhere on CROs, and makes it more difficult to nimbly change drug development processes when problems arise.

Prominent tech investors argue that drug development and the biotech company lifecycle can be radically changed by implementing key tenets of building tech startups. Y Combinator partner Jared Friedman argues that virtualization and new infrastructure has dramatically reduced the cost of doing biology.[11] Also, Andreessen Horowitz partner Jorge Conde asserts that emerging fields such as computational biology and biological engineering are changing the landscape of drug discovery by democratizing company building.[12] Yet, Atlas Venture partner Bruce Booth counters by arguing that R&D costs haven't meaningfully changed even with the advent of new technologies, and that seed-stage capital remains inadequate when considering the costs associated with drug development.[13]

Only time will tell what facets of biotech will converge or diverge with the tech industry. Our data does not currently indicate that the world of biotech is becoming more like tech, particularly when it comes to key elements of the company lifecycle. While tech advances have permeated into biotech and drug development, biotech companies, at their core, are fundamentally unique.

11: "How Biotech Startup Funding Will Change in the Next 10 Years," YCombinator, Jared Friedman, 2019.
12: "Biotech Researchers Venture into the Wild to Start Their Own Business," TechCrunch, Jorge Conde, 2019.
13: "The Creation of Biotech Startups: Evolution Not Revolution," Life Sci VC, Bruce Booth, 2019.