ECKUITY

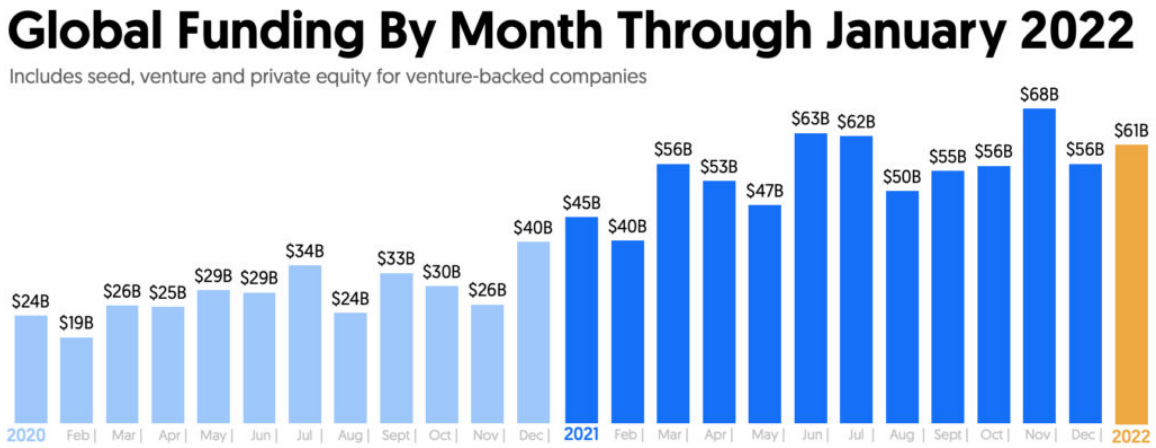
INVESTING IN EARLY-STAGE HEALTHCARE

Commercialization is key

March 2022

So you invested in a promising early-stage healthcare company?

Despite the tumult, global funding to private companies last month clocked in at $61 billion, the fourth month above the $60 billion mark in the last 12 months. Close to $3 billion was invested globally at seed last month. Startup investors spent another $18 billion at early stage and just over $40 billion at the later stage and technology-growth stage, according to Crunchbase data.



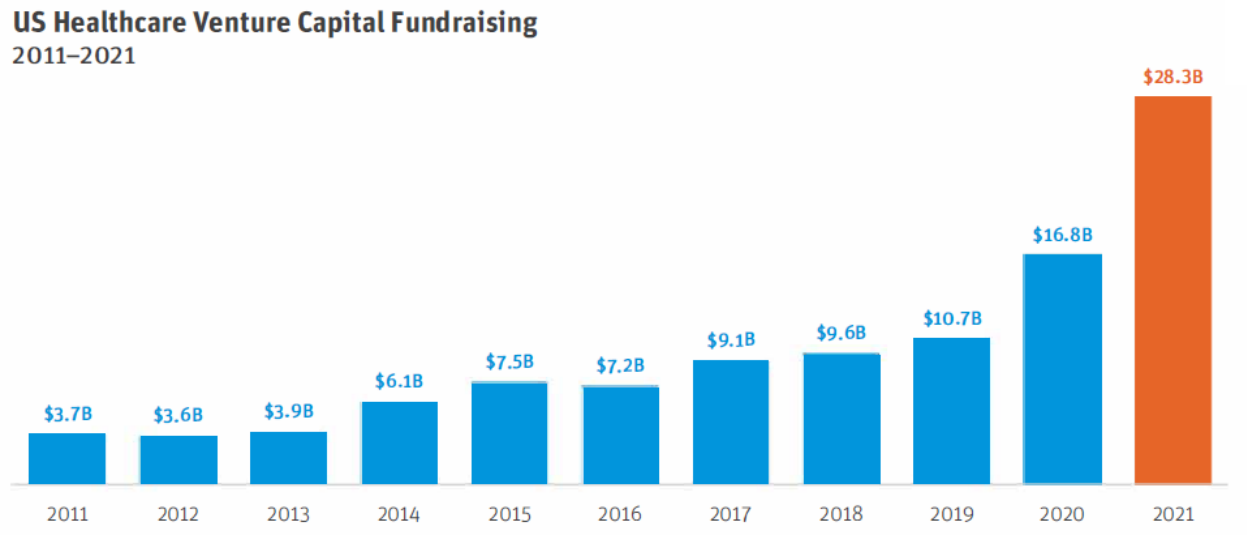
Source: Crunchbase

In sync with global private investments, Healthcare funding also set new records again. Venture fundraising hit new heights, driven by lofty step-ups in valuation and fast M&A and IPO activity. New venture funds allocated to healthcare (biopharma, healthtech, dx/tools and device) almost doubled 2020's record, providing a large pool of focused capital to support new investments in the venture healthcare ecosystem over the next few years.

Investment into companies exceeded $86B, beating 2020's record by more than 30%. Ql and Q2 set new records in succession, but Q3 and Q4 exhibited a slowdown in investment activity. Every sector hit new record highs, punctuated by a 157% increase in healthtech investment compared to 2020, according to SVB.

The rapid pace of investment, coupled with the increasingly quick turnaround from first venture investment to exit over the past five years, has propelled firms to deploy capital faster than ever before. These firms have benefited from great mark-ups after mezz rounds to increase TVPI and have used IPOs and M&A proceeds to smash though J-curves and return capital at a record pace.
The frothy market has led firms to increase their fund size and also raise stand-alone opportunity funds to double down on perceived portfolio winners. All this momentum has turned 2021 into the largest healthcare fundraising year ever, surpassing 2020's record of

$16.8B and nearly tripling the capital available just two years ago. There is now a very large supply of investor capital to support venture companies over the next few years.



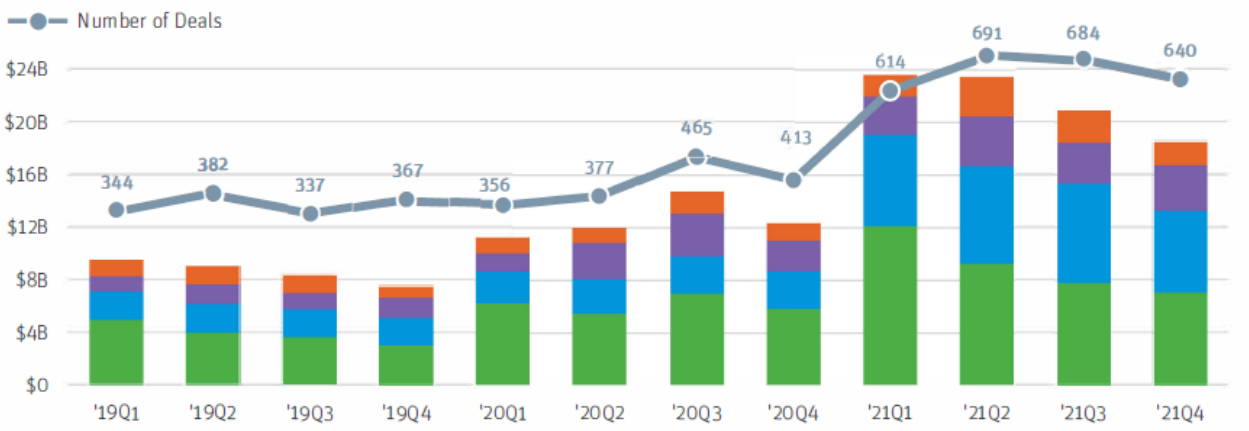
Source: Pitch Book and SVB

Wait... not so fast

While the overall healthcare investment has more than doubled every two years since 2017, from $168 to $348 to $868 in 2021; in 2H 2021 we observed a decrease in investment. Biopharma saw the most precipitous drop.

According to SVB, following a 24% decrease from Q1 to Q2, we noted another 17% from Q2 to Q3 and 9% from Q3 to Q4. Poor performance of biopharma IPOs in 1H led to fewer IPOs in 2H and caused more crossover-funded companies to remain private. This discouraged crossover investors from investing in additional private pre-IPO mezzanine rounds, which reduced biopharma investment numbers. Interestingly, though IPOs saw similar poor performance in healthtech, this sector showed fairly consistent investment dollars in 2H.

VC Dollars and Deals by Healthcare Sectors
US and Europe



	2019			2020			2021		
Sectors ($M)	US	Europe	Total	US	Europe	Total	US	Europe	Total
Biopharma	12,790	3,101	15,891	21,060	4,604	25,664	29,747	6,582	36,329
HealthTech[2]	7,142	1,431	8,573	9,616	1,357	10,973	25,602	2,579	28,181
Dx/Tools	4,036	905	4,940	8,430	1,675	10,105	10,617	2,414	13,031
Device	3,895	896	4,790	4,982	773	5,755	6,451	2,341	8,792
Total	27,863	6,332	34,196	44,088	8,409	52,497	72,417	13,916	86,333

Source: Pitch Book and SVB

Commercialization is Key

It is not uncommon to witness exuberance when the entire world is optimistic and similarly, it is commonplace to run to safe havens when central banks globally sing the same tune about rising interest rates. But venture investing is a (relatively) long-term business. It is important to understand the key exit drivers for your investment which go far beyond valuation and "current" market dynamics. And exit is not TVPI but DPI, which remains elusive for many investors because when the markets change, people wonder what happened to the great science and wonderful founders that they backed and why aren't big M&A buyers lining up their doors!

The exit for most venture investments is through either an IPO or a sale. The former is highly dependent on macroeconomics which is largely beyond our control. Not only is it driven by interest rates, but also by geopolitical dynamics, unforeseen six-sigma events like the current pandemic or any number of variables that are unfathomable, and importantly, uncontrollable. That leaves a strategic sale as the only other viable option for most exits. This latter option can have a few alternative features including a licensing deal, milestone-based payments, or indication-specific structures.

And it is easy to get swayed by the media's selective focus on large, successful, or unique wins in the healthcare sector. For example, just because a biotech targeting a similar indication got acquired for a handsome amount, doesn't mean the next company targeting that same indication will also be acquired by a competing buyer, especially the buyer who missed out on the first one. There are numerous parameters which need to be carefully studied to ensure that your investment will lead to a successful exit. The most important parameter, we believe, is the ability to achieve strong commercialization. This is a function of not just the core technology, management and TAM, but also regulatory, pricing, marketing and a whole host of other aspects that need to be taken into account. We believe that once you have a strong handle on these key parameters, the likelihood of an exit increases substantially.

Let's take an area that has historically garnered significant investor and buyer interest: Oncology. It is easy to get impressed with highly promising pre-clinical data, and in some cases, clinical data. And with a management team that has done it before, what could go wrong?

A few things to note: Clinical trials in all therapeutic areas are increasing in complexity, but oncology trials are outstripping the rest of the field due to enrollment challenges, protocol deviations and a burgeoning amount of data that are adding months to their timelines.

The three phases of oncology trials each take 14 to 18 months longer, on average, than trials for other drugs, lasting almost 12 years compared to almost eight years for non-oncology trials, according to a new report by the Tufts Center for the Study of Drug Development (CSDD).

Trials of oncology drugs are more difficult to execute because they typically involve more countries and investigative sites and require more patient visits per protocol. They also generate a much higher volume of data compared to trials for other drugs — for example, 3.1 million data points per protocol in phase 2 oncology compared to 1.9 million in non-oncology. The number of investigational drugs targeting cancer has nearly quadrupled since 2000, to 1,489 trials in 2021, up from 421 two decades earlier.

Oncology drug developers are increasingly shifting toward precision medicine, embracing new molecular targets and improvements in genetic sequencing technologies. But as sponsors of cancer treatments shift their focus to precision medicine, it becomes harder to find participants that fit increasingly selective criteria. That hurdle, combined with the high number of sites and countries involved in the trials, "underscores the challenges associated with finding, competing for and enrolling patients [in oncology]," CSDD said. Success at finding eligible trial participants was far more challenging for oncology trials, especially in phase 2, where only 14 percent of participants screened were enrolled and eventually completed the trial compared to 54 percent in non-oncology trials.

Even if enrollment hurdles are overcome, by doing many activities in parallel and shortening regulatory reviews, which is increasingly the case, one still faces the hurdle of finding the right

buyer at the right price. As per Capital IQ, of the 249 healthcare (not just biopharma) M&A deals over $1 billion announced over the last five years (Jan 2017 – Jan 2022) in US and EU, only 19 were for targets with less than $25 million in revenues and more than half of those deals were done by just 4 big-pharma companies. So if we assume a similar run-rate, unless your investment is interesting enough to be bought by one of these handful of big companies, it becomes challenging to realize an exit for your limited partners. Given there were over 2,500 deals done in the healthcare sector just in 2021, it is anyone's guess how many will actually see a reasonable exit. And on top of that, if we add 2020 and 2019 vintages, the problem quickly becomes apparent.

Working backwards

The solution is to start working backwards from commercialization and understand the likelihood for a given Seed or Series A investment to be "commercializable" in a reasonable time frame, which we believe to be around 5 years. The ability to commercialize can come from either generating straight revenues, like for HealthTech or diagnostic companies, or from licensing or strategic sale or IPO for most biopharma companies.

Biopharma M&A Deal Median Values by Year

Year	Upfront	Total Deal	Years to Exit
2021	$310M	$513M	5.2
2020	$300M	$770M	4.0
2019	$250M	$600M	2.7
2018	$140M	$480M	3.1
2017	$171M	$461M	3.5
2016	$200M	$600M	5.9
2015	$200M	$570M	4.2

M&A defined as all private, venture-backed M&A deals with at least $75M upfront, globally.
Source: Pitch Book and SVB

The current public markets further prove the importance of revenue and commercialization. For the best performing healthcare companies – defined as the ones with at least 50% price increase since the pandemic, in US and EU, with over $1 billion in market cap, the median revenue growth rate was 33% and the growth rate was over 58% for the top 10. Similarly, the worst performing companies – defined as the ones with at least 50% drop in price, the median revenue growth rate was 10.6% and the growth rate was -17.5% for the worst 10.

Conclusion

The key is to focus on unmet need that is indeed unmet. Marginal improvements like 2-month OSR (overall survival rate) for cancer patients, 10% lower cost for your next hospital equipment, or your next weight-loss health app can sound interesting at the outset, but you need to ensure you have the physician buy-in or pharma buy-in for your cancer drug; you have a big MedTech company ready to deploy your equipment; and a large distribution platform willing to accept your app on their platform. And if these don't exist, you need to work harder to get them in place or have visibility on when and how you can on-board them. As a VC, if you start thinking about commercialization until after you've made the investment, then you'll need a lot more than just good luck to make these investments generate a good return.