

The background of the slide is a photograph of surgeons in an operating room. Two surgeons in the foreground are wearing blue scrubs, blue bouffant caps, and surgical masks. They are looking down at a patient who is lying on the operating table, covered with blue drapes. The scene is brightly lit by overhead surgical lights.

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Silicon Valley Bank

Healthcare Investments and Exits

Biopharma | HealthTech | Dx/Tools | Device

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Healthcare Fundraising and Investments

US and Europe

Investors Double Down on Venture Healthcare Promise

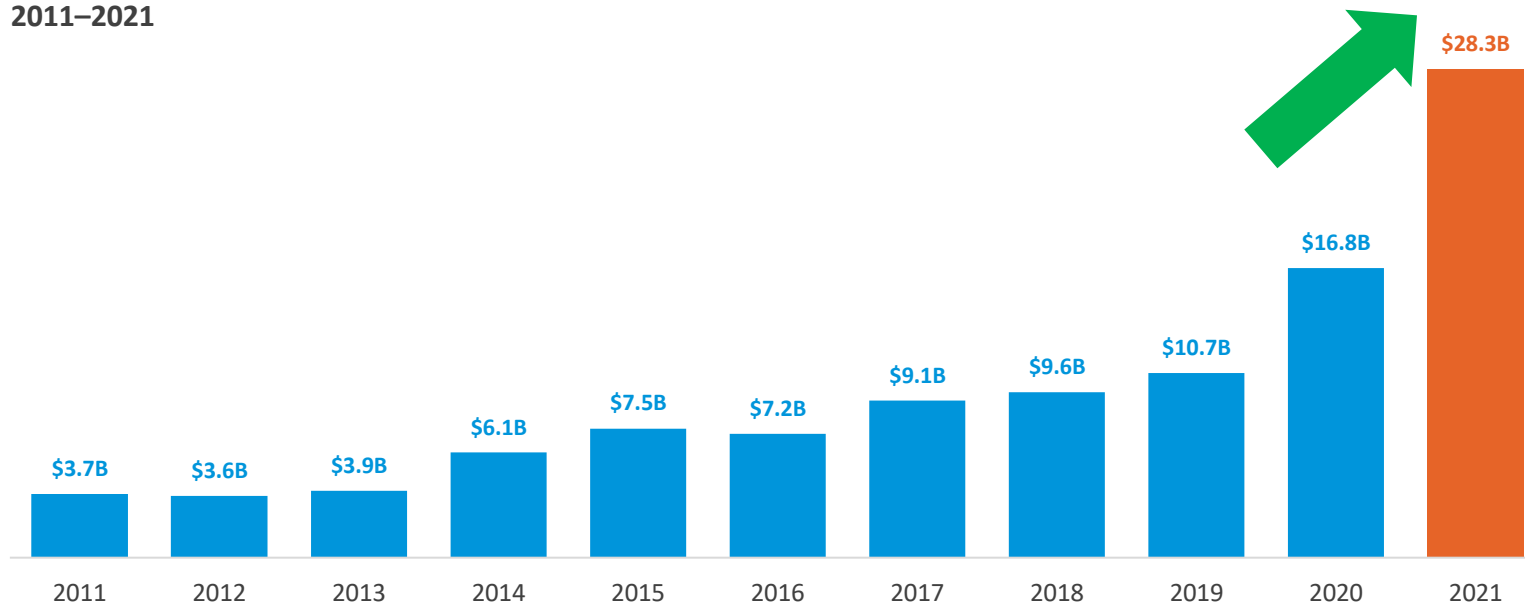
The rapid pace of investment, coupled with the increasingly quick turnaround from first venture investment to exit over the past five years, has propelled firms to deploy capital faster than ever before. These firms have benefited from great mark-ups after mezz rounds to increase TVPI¹ and have used IPOs and M&A proceeds to smash through 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.

Flagship Pioneering, Arch Venture and OrbiMed all closed \$1B+ healthcare-only funds in 2021. A number of firms with significant allocations to healthcare closed multiple strategic or opportunity funds in 2021, including Abingworth Management, Bessemer Venture Partners, Define Ventures, Foresite Capital Management, HLM Venture Partners, Khosla Ventures, Lux Capital, Venrock and Versant Ventures.

In 2022, we anticipate US venture fundraising will drop to about \$16B, as most healthcare firms have recently raised new funds and will likely slow their investment pace.

US Healthcare Venture Capital Fundraising 2011–2021



Notable Funds² Closed in 2021 with Allocations to Venture Healthcare



Note: 1) TVPI is defined as the ratio of the current value of fund investments plus distributions to date to the total amount of capital invested to date. 2) Notable funds based on largest estimated allocation to venture healthcare. US Healthcare Venture Capital Fundraising defined as an approximation of healthcare investment dollars to be invested by firms that historically invest in +50% US companies.

Source: PitchBook and SVB proprietary data.

Investment Peaks in Record Q2; Biopharma Declines in 2H

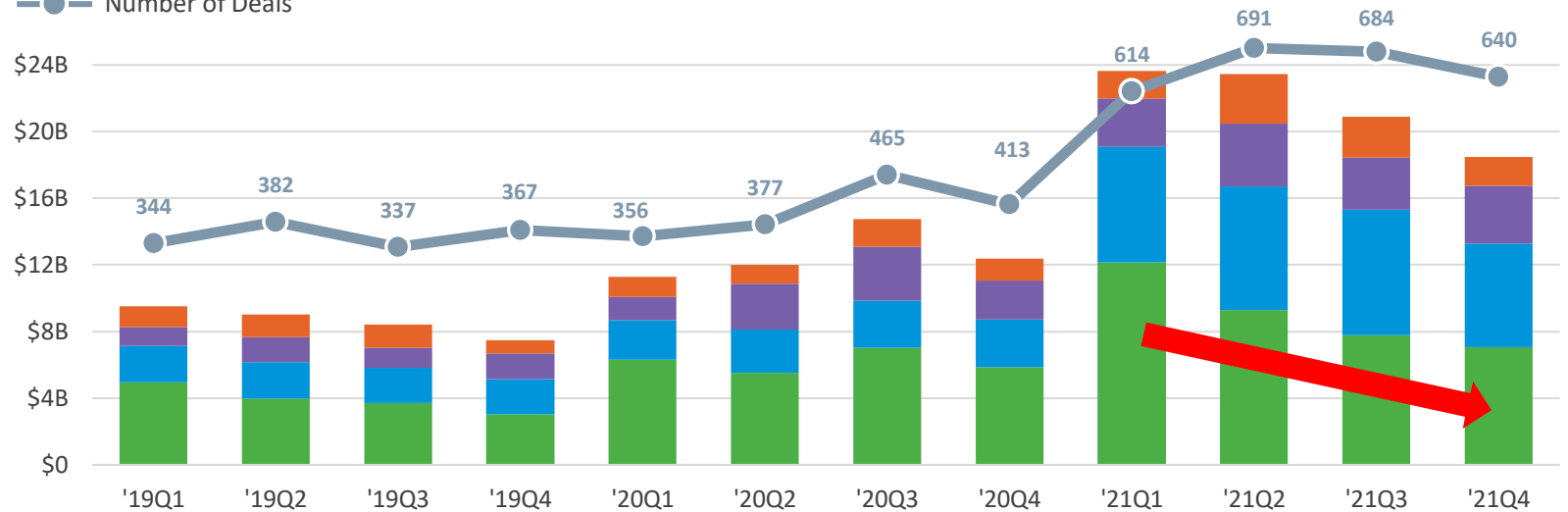
Overall healthcare investment has more than doubled every two years since 2017, from \$16B to \$34B to \$86B in 2021. All four sectors showed record investment this year, with healthtech up 157% compared to 2020. Device, led by a 3x increase in European investment, was up 53%.

Q1 2021 set a new quarterly record for investment, then Q2 eclipsed that record. Biopharma and healthtech led the charge, accounting for 46% and 31% of total investment in the first half, respectively. Biopharma was driven by the open IPO window, which was met with an increase in large pre-IPO mezzanine rounds, especially in Q1. In healthtech, the global pandemic drove a surge of investment into alternative care solutions and provider operations companies.

However, in 2H 2021 we observed a decrease in investment. Biopharma saw the most precipitous drop. 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 (LIPO¹ deals), 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

—●— Number of Deals



Sectors (\$M)	2019			2020			2021		
	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

Note: 1) The LIPO (Likely to IPO) List tracks Top 15 Crossover funded private mezzanine deals (\$40M+) as a proxy for IPO sentiment and pipeline.
 2) HealthTech deals that overlap with other sectors are not included in healthtech totals on this slide but are included in healthtech-specific analyses on pages 12-15.
 With overlap, healthtech investments for 2021 total \$40B. Financing data include private financings by venture-backed companies in the US and Europe.
 Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.

Series A Growth Led by Anti-Infective, Neuro and Platform

Seed/series A deals and dollars were up significantly overall, though flat in Europe. While later-stage biopharma investment decreased significantly in 2H 2021, early-stage activity remained strong throughout the year. Seed deal sizes increased substantially in 2021, blurring the line between seed and series A. Recent seed deals regularly total \$10-20M, often backed by institutional investors.

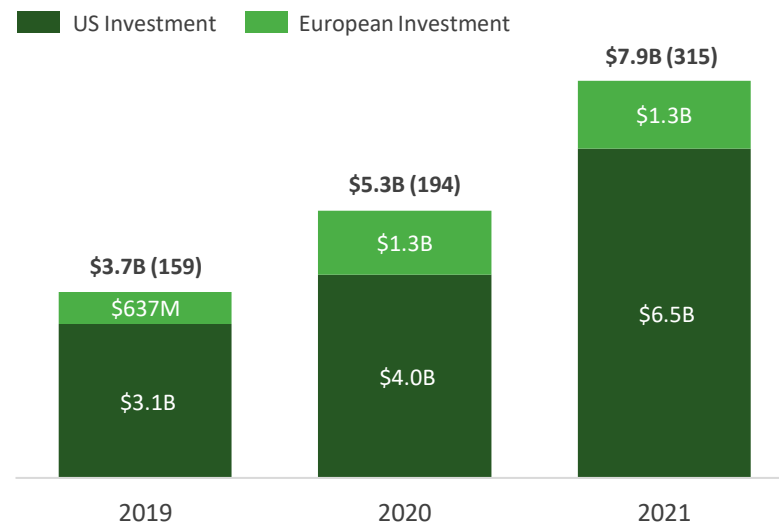
In terms of dollars, platform companies led seed/series A biopharma for the second year in a row. Since 2019, we saw a huge 6.8x increase in neurology dollars and a 4x increase in anti-infective (driven by a 2.9x increase from 2020 to 2021). By contrast, orphan/rare dollars dropped by 57% compared to 2019.

CAR-T cell therapy and CRISPR deals garner interest. We also noted numerous early-stage internal innovation “hub and spoke” deals where the underlying technology was leveraged into separately-funded companies.

There were 14 \$50M+ seed/series A investments in computational biology companies in 2021, up from four in 2019 and seven in 2020. This was led by huge deals from Neumora (\$400M), Odyssey Therapeutics (\$218M), Treeline (\$212M), and Eikon (\$148M).

The \$30M+ deals saw the largest jump in pre-money valuation, up 52% from a median of \$27M in 2020 to \$41M in 2021. However, we did notice valuations cool down in Q4 as crossover activity slowed. We counted 18 \$40M+ seed/series A deals funded by top 15 crossover investors in 1H 2021, but only six in 2H 2021.

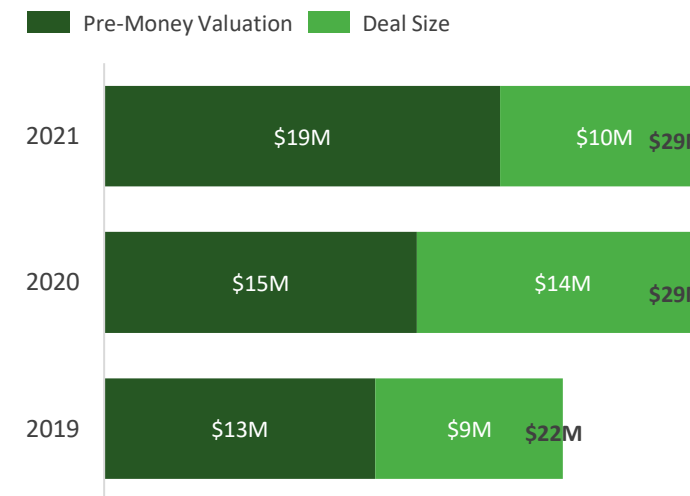
Seed/Series A¹ Dollars and (Deals) US and Europe



Seed/Series A Dollars and Deals by Top Indications

Indications	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
Platform	\$846M	30	\$1.4B	44	\$2.8B	80
Oncology	\$926M	33	\$1.3B	51	\$1.9B	72
Neurology	\$146M	20	\$850M	28	\$1.0B	45
Anti-Infective	\$101M	9	\$139M	8	\$409M	23
Orphan/Rare	\$727M	12	\$518M	19	\$312M	14
Auto-Immune	\$143M	6	\$241M	6	\$291M	8

Median Seed/Series A Post-Money Valuations US and Europe



Largest 2021 Seed/Series A Deals



Company went public



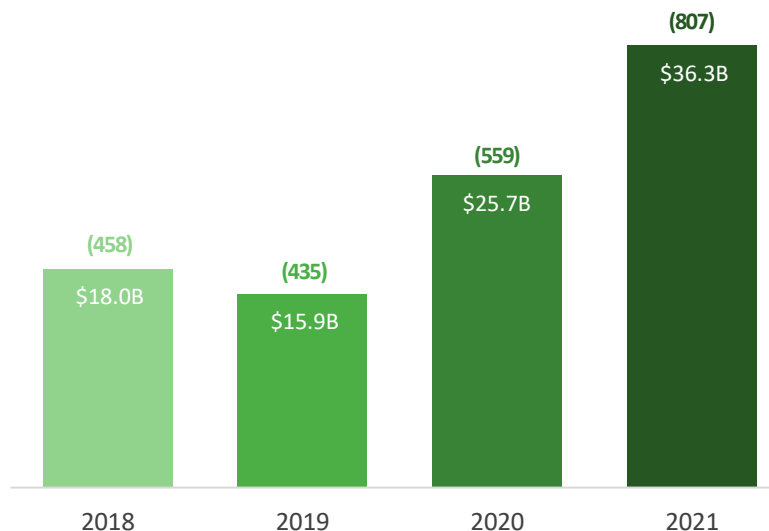
Record Funding Trails Off in 2H as LIPO Activity Wanes

In 2021, there were 21 \$200M+ biopharma financings, doubling that in 2020 and totaling \$6.8B. Five of these deals closed in Q4, even as total investment dollars decreased in that quarter. This year, we saw the most growth in investment for platform (up 1.9x in deals and 1.8x in dollars from 2020) and auto-immune deals (up 2x in deals and 2.8x in dollars from 2020).

The robust post-IPO performance from 2019 and 2020 worsened for the IPO class of 2021, which has negatively impacted LIPO¹ activity. Since Q1 2021, we saw fewer LIPO deals each quarter, while the number of still private mezz-funded companies continued to grow. When crossover investors engaged in due diligence for private deals in Q3/4 2021, they were more focused on clinical-stage rather than pre-clinical companies. We will likely see a resurgence of series C financing rounds next year when mezz-funded Series B companies need to raise more private capital and the public market becomes more discerning. It will be interesting to see if later-stage VC and opportunity funds can bridge the gap left by reduced crossover investment.

Biopharma computational biology companies raised large, highly-valued rounds in 2021, including three of the top eight (Insitro, ATAI and Generate Biomedicines). Of the highest valued companies to close a private financing in 2021, ATAI, Adagio and InstilBio completed IPOs. However, at the end of 2021 ATAI and Adagio were trading at around half of their last private post-money value.

Total Dollars and (Deals) US and Europe



LIPO Deal Activity in Biopharma

Cumulative LIPO Deals from 2019					
Quarter	LIPO Deals	Median Deal Size (\$M)	Median Pre-Money (\$M)	Currently Private	Currently Public
Q1 19	16	\$66	\$136	7	9
Q2 19	13	\$82	\$160	11	18
Q3 19	11	\$102	\$125	12	28
Q4 19	11	\$85	\$100	15	36
Q1 20	18	\$108	\$245	18	51
Q2 20	22	\$86	\$150	26	65
Q3 20	33	\$92	\$140	39	85
Q4 20	21	\$87	\$140	49	96
Q1 21	48	\$100	\$184	71	122
Q2 21	35	\$105	\$200	101	127
Q3 21	29	\$90	\$169	128	129
Q4 21	16	\$102	\$172	144	129

Biopharma Deals and (Dollars) by Top Indications US and Europe

Indications	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
Platform	\$3.1B	79	\$6.4B	99	\$11.4B	187
Oncology	\$5.9B	122	\$7.4B	153	\$10.7B	224
Neurology	\$784M	49	\$2.3B	68	\$3.5B	98
Auto-Immune	\$445M	12	\$616M	15	\$1.7B	30
Anti-Infective	\$856M	23	\$1.2B	37	\$1.7B	47
Orphan/Rare	\$2.0B	41	\$2.1B	41	\$1.2B	38

2021 Highest Valued Private Companies²

Insitro ³	Platform	\$2,500M post
atai	Neurology	\$2,000M post
Cambrian	Platform	\$1,850M post
laronde	Anti-Infective	\$1,735M post
EQx	Platform	\$1,590M post
Rakuten Medical	Platform	\$1,575M post
Generate:Biomedicines ³	Oncology	\$1,566M post
InstilBio	Platform	\$1,450M post
prime medicine	Oncology	\$1,290M post
prime medicine	Platform	\$1,200M post

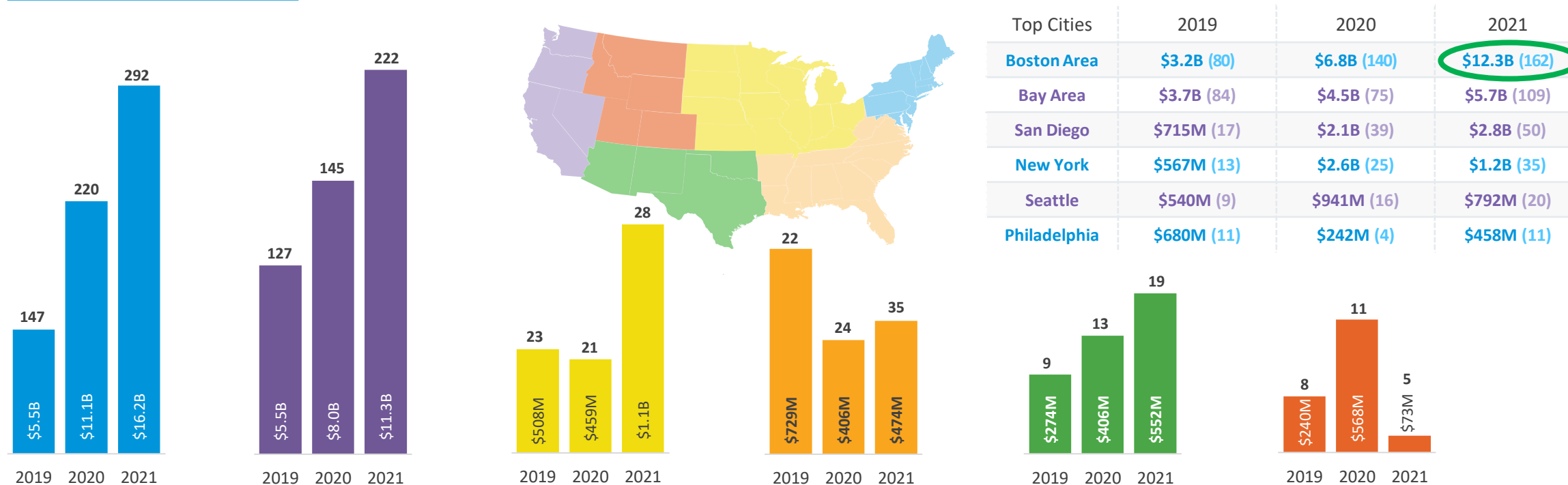
Company has since gone public

Note: 1) The LIPO (Likely to IPO) list tracks Top 15 Crossover-funded private mezzanine deals (\$40M+) as a proxy for IPO sentiment and pipeline.

2) Only includes private post-money values from publicly disclosed 2021 financings in PitchBook. 3) These companies overlap with the healthcare sector and is included in both sets of sector-specific analyses. Financing data include private financings by venture-backed companies in the US and Europe. Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.



US Biopharma Investment by Region



Notable Private Financings, US 2021



Pandemic Drives Surge in VC Activity and Mega-Rounds

The onset of the pandemic in 2020 thrust healthtech into the spotlight. The sudden demand for digital health solutions created opportunities for venture-backed healthtech companies with new technologies and engagement models. Investors certainly noticed this trend, as dollars hit a record high of \$40B in 2021, more than double 2020 and nearly 4x the average annual investment from 2018-2019 (\$11B). With another year of substantial growth and investment, buoyed by a growth in exits, healthtech is firing on all cylinders.

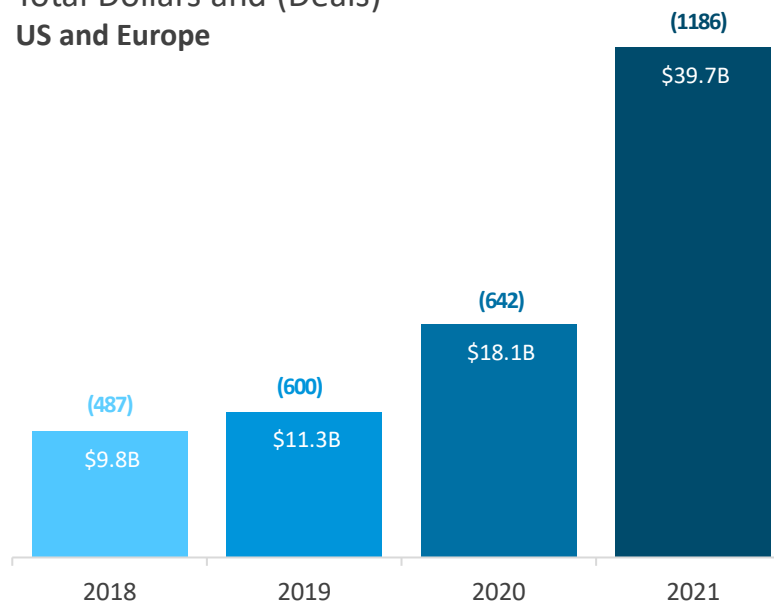
Private equity, asset managers and late-stage venture capital investors are deploying huge amounts of capital into healthtech faster than ever before, raising valuations and disrupting the traditional venture model.

The majority of 2021 funding (60%) came from 105 mega-rounds¹. Mega-rounds are up substantially from 2019 (17 deals, 30% of funding dollars) and 2020 (43 deals, 41%). This investment has resulted in a 4.7x increase in the number of **new unicorns in 2021 (42) vs 2020 (9)**.

Alternative Care (AC) companies continued to lead healthtech investment, receiving 38% of dollars this year and showing a 3x increase over 2020. We expect investor focus on AC to continue into 2022 as the healthcare industry faces mounting pressure from patients to swiftly adopt AC solutions.

Highly-valued private healthtech deals (including Color which also overlaps with dx/tools) have hit new heights, as the top eight deals are higher than the highest private valuation of 2020 (Bright Health, \$4B valuation).

Total Dollars and (Deals)
US and Europe



Notable 2021 Deals



Deals and Dollars by Top Subsectors
US and Europe

Subsectors	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
Alternative Care	\$3.1B	153	\$5.0B	173	\$14.9B	332
Provider Operations	\$3.1B	242	\$4.3B	229	\$9.6B	450
Clinical Trial Enablement	\$1.7B	83	\$5.4B	107	\$8.6B	176
Wellness & Education	\$867M	62	\$1.2B	76	\$2.3B	136
Insurance	\$1.2B	6	\$945M	12	\$1.7B	10
Healthcare Navigation	\$808M	28	\$754M	23	\$1.6B	55
































2021 Highest Valued Private Companies²

DevotedHealth	Insurance	\$12,700M post
Hinge Health	Alternative Care	\$6,200M post
Benchling ³	Clinical Trial Enablement	\$6,100M post
CITYBLOCK	Alternative Care	\$5,700M post
ro	Alternative Care	\$5,000M post
Cerebral	Alternative Care	\$4,800M post
color ³	Provider Operations	\$4,600M post
lyra	Alternative Care	\$4,600M post

Note: 1) Mega-round is a private round greater than or equal to \$100M. 2) Only includes private post-money values from publicly disclosed 2021 financings in PitchBook. Financing data include private financings by venture-backed companies in the US and Europe. 3) These companies overlap with the biopharma, dx/tools or device sectors and are included in both sets of sector-specific analyses. Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook, SVB proprietary data and [SVB HealthTech Report](#).

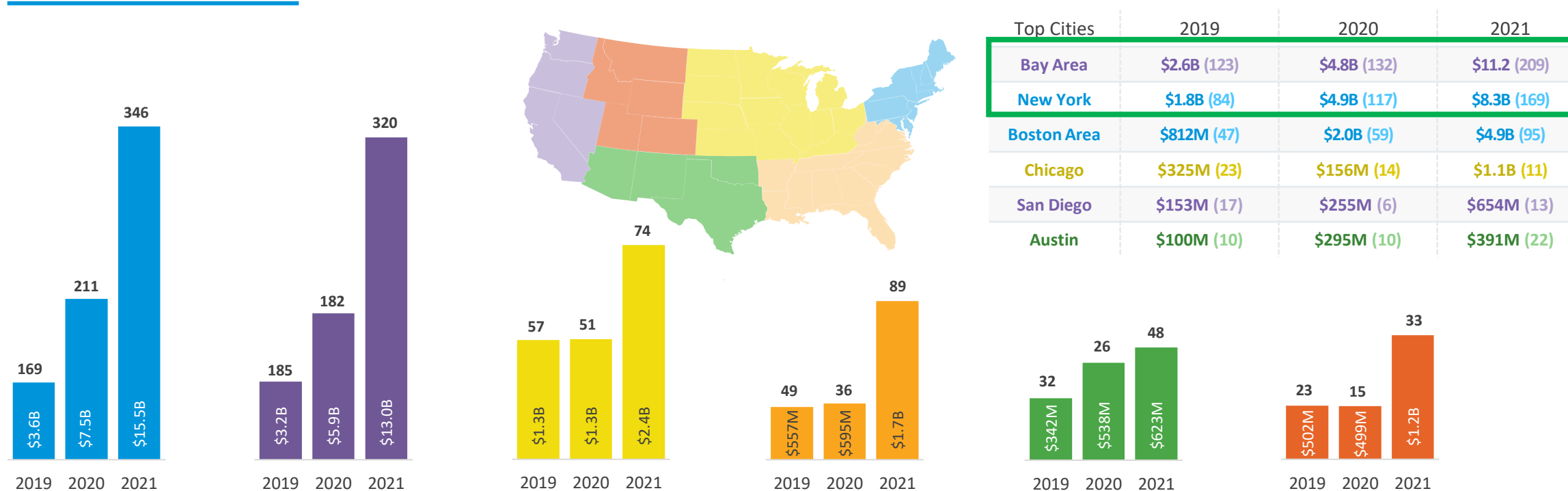
Most Active¹ New HealthTech Investors

US and Europe (2020-2021)

Venture Activity Overall		Late Stage/Crossover Activity Overall		Alternative Care		Provider Operations		Clinical Trial Enablement	
28	Gaingels 	29	TIGERGLOBA	12	TIGERGLOBA	9	TIGERGLOBA	12	
24	GENERAL CATALYST 	19		12	Gaingels 	9	GENERAL CATALYST 	9	
20	andreessen horowitz	15	 SoftBank	9	GENERAL CATALYST 	9	DEERFIELD	7	Janus Henderson INVESTORS
17		15	DEERFIELD	8		8		6	T.RowePrice®
15		13	BlackRock®	8		8	Gaingels 	6	Section 32
14	Quiet	Corporate Activity Overall		7		7	 UnityPoint Health	6	BlackRock®
13	8VC	19		7	OPERATOR	6		5	
13	DEFINE VENTURES 	18		7		6	 KAISER PERMANENTE®	5	
12	OAK HC/FT	10	 KAISER PERMANENTE®	7	MORNINGSIDE	6	PLUGANDPLAY	5	
12		9		7		6		5	andreessen horowitz ²



US HealthTech Investment by Region



Notable Private Financings, US 2021



Series A Funding Trails Other Sectors but Deal Numbers Up

Total dx/tools investment hit a record in 2021, surpassing the capital invested in device by \$4B. However, while early-stage investment in dx/tools was up in 2021, dollars continued to lag the other three sectors for the second year in a row. Surprisingly, seed/series A deal count was up significantly, doubling the deal pace of the last two years.

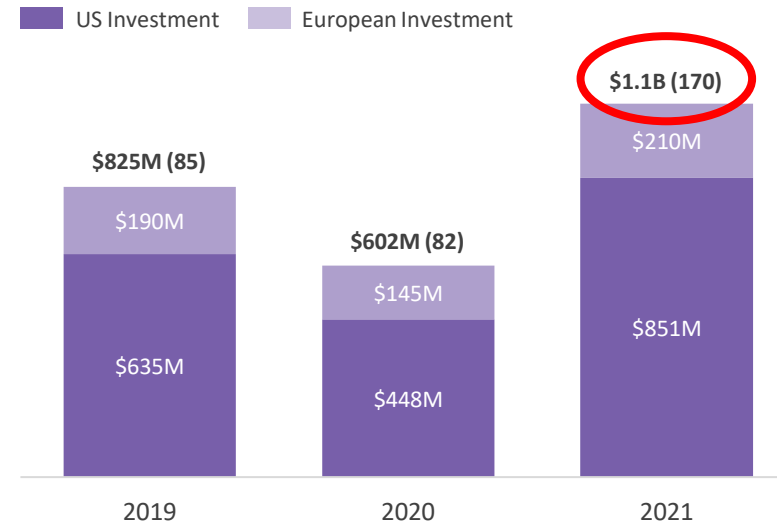
The UK continues to be a hotbed for seed/series A dx/tools activity this year (20 deals), matching Massachusetts and just lagging behind Northern California (26).

The pandemic continued to drive consumer demand for home testing. As a result, dx tests deal activity spiked in 2021, with a heightened focus on platform technologies, but also oncology (11), anti-infective (9) and urology/gynecology (5).

R&D Tools recorded four \$20M+ financings and three of the top four largest early-stage deals. We continue to see significant seed/series A activity in computational biology companies (Beacon Biosignals, Sequare, One Biosciences and ImmunelD) and synthetic biology (Slingshot).

Dx Analytics, which leverages artificial intelligence/machine learning algorithms to help clinicians determine the best treatment, experienced more deal activity in 2021, with the largest focus on oncology (12 deals). Dx Analytics also had the highest median pre-money valuation (\$12M) of the three subsectors.

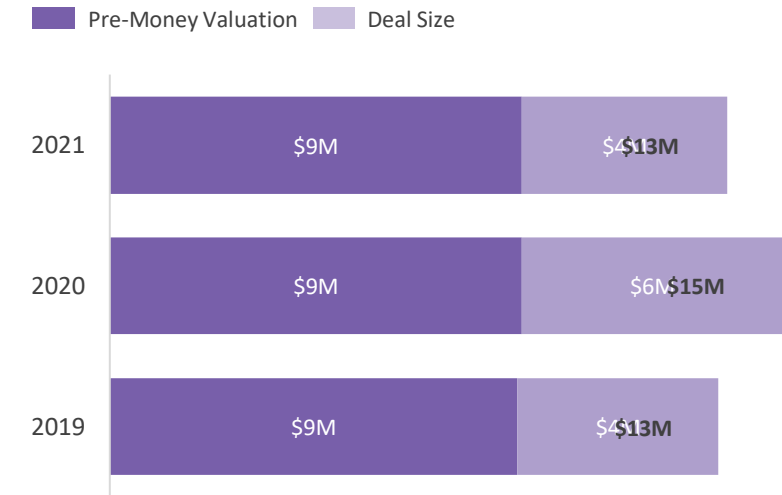
Seed/Series A¹ Dollars and (Deals) US and Europe



Seed/Series A Dollars and Deals by Subsectors

Subsectors	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
R&D Tools	\$201M	39	\$247M	34	\$492M	79
Dx Analytics	\$267M	23	\$179M	20	\$286M	45
Dx Tests	\$357M	23	\$176M	28	\$283M	46

Median Seed/Series A Post-Money Valuations US and Europe



Largest 2021 Seed/Series A Deals



Note: 1) Seed/series A includes first-time investments from institutional or corporate venture investment in the US and Europe and any first-round investments equal to or greater than \$2M, regardless of investor. 2) This company overlaps with the healthtech sector and is included in both sets of sector-specific analyses.

Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.

R&D Tools Investment Leads Record Late-Stage Activity

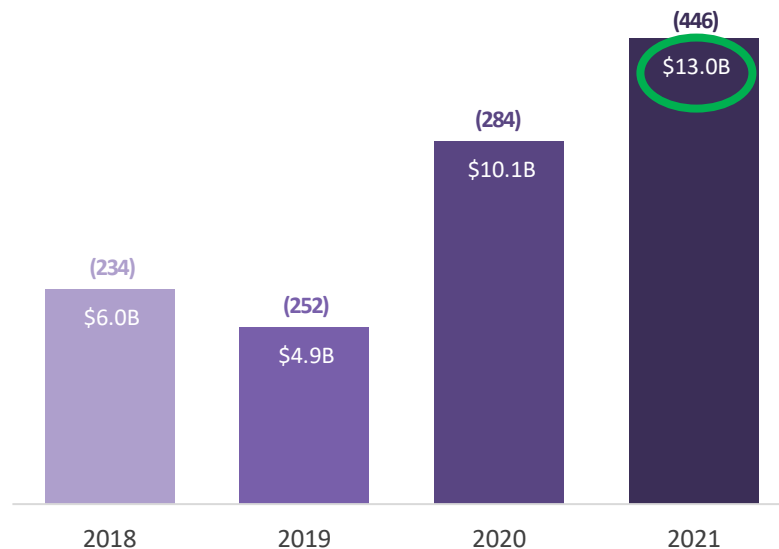
Dx/Tools investment reached new heights in 2021, more than doubling the dollar totals from 2018 and 2019. For the dx tests subsector, deal activity was up, but growth in investment dollars lagged slightly behind the other two subsectors.

There were 40 \$100M+ financings in 2021, more than tripling 2020's activity. Twelve of these financings yielded \$1B+ valuations.

Despite the uneven IPO performance in 2021, investors remained bullish on exciting later-stage technologies in the second half. The most active investors in \$50M+ deals in 2H 2021 included SoftBank Investment Advisors, Catalio Capital Management and Morningside Group (three deals each) and Coatue Management, Sherpa Venture Capital, Koch Disruptive Technologies, Wellington Management, D1 Capital Partners and Perceptive Advisors (two deals each). However, as a caution we have seen anecdotal evidence that valuations compressed late in Q4.

While IPO performance was down, there were positive examples of highly-valued private companies that went public. Oxford Nanopore, an R&D tools company focused on sequencing and molecular analysis, had the third highest-valued financing in 2021. This company went public in Q3 and was trading at more than 2x its last private valuation at the end of 2021.

Total Dollars and (Deals) US and Europe



Notable 2021 Deals



Deals and Dollars by Subsectors US and Europe

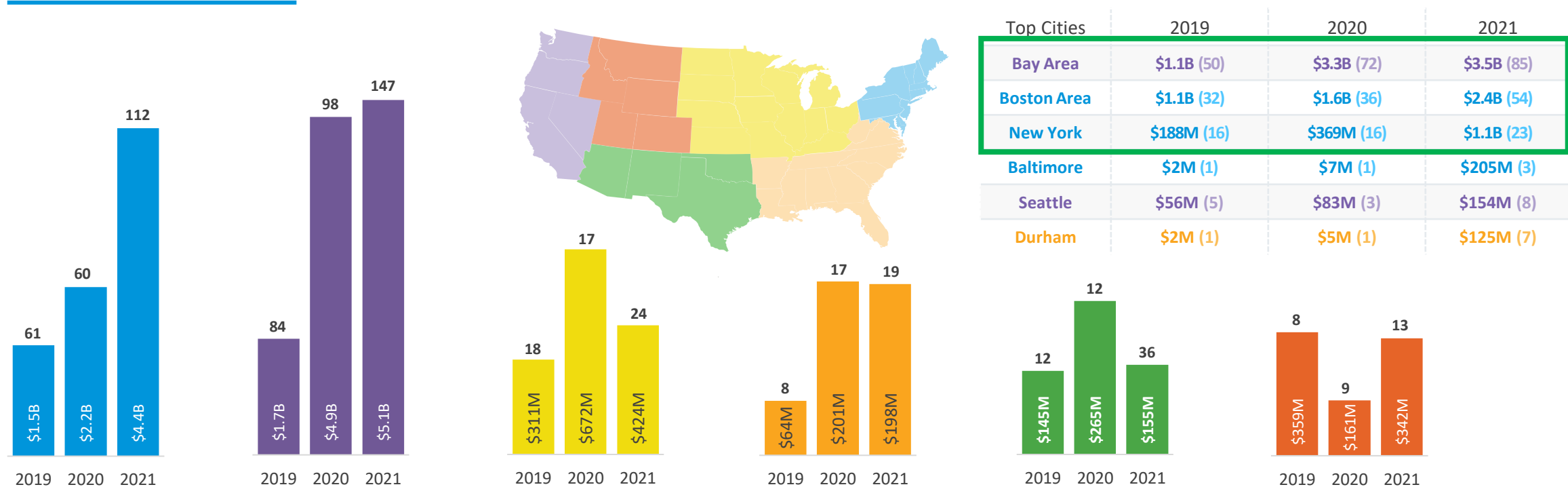
	2019		2020		2021	
Subsectors	Dollars	Deals	Dollars	Deals	Dollars	Deals
R&D Tools	\$1.9B	101	\$4.8B	121	\$6.5B	195
Dx Tests	\$1.4B	72	\$3.0B	80	\$3.4B	133
Dx Analytics	\$1.6B	79	\$2.3B	83	\$3.1B	118

2021 Highest Valued Private Companies²

RESILIENCE	R&D Tools	\$5,656M post
color ¹	Dx Tests	\$4,600M post
NANOPORE	R&D Tools	\$3,274M post
XtaIPi ¹	R&D Tools	\$2,006M post
Element Biosciences ¹	R&D Tools	\$1,606M post
freenome ¹	Dx Tests	\$1,400M post
INSCRIPTA ¹	R&D Tools	\$1,300M post
elemey ¹	Dx Tests	\$1,150M post

Company has since gone public

US Dx/Tools Investment by Region



Notable Private Financings, US 2021



Early Device Dollars Spike, Led by Tech-Enabled Services

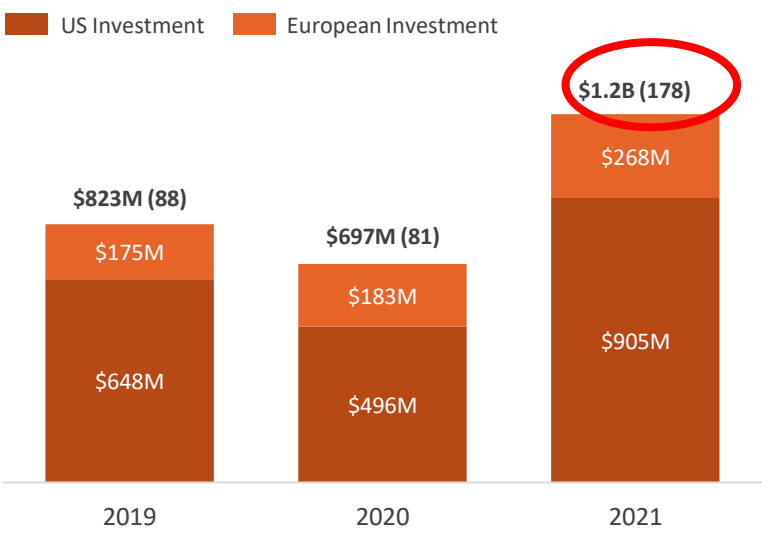
Early-stage device investment eclipsed \$1B for the first time ever. This increase was led by non-invasive monitoring (NIM) investment, which was up 92% over 2020. The need to monitor patients outside the hospital has become paramount during the COVID-19 pandemic, ushering in more investment in tech-enabled service models (NIM, imaging). We have already seen multiple M&A in NIM this year, including Preventice Solutions and Bardy Dx. While these two NIM exits were in the cardiovascular space, seed/series A activity in NIM exploded across multiple areas, led by neurology (10 deals), cardiovascular (nine), respiratory (five) and metabolic (three) companies.

The imaging subsector also drew significant early-stage investment as hospitals looked to optimize procedure efficiency in their most profitable surgical areas. We also noted a surge of investment in platform technologies in 2021, with the largest deals focused on organ preservation (Bridge to Life, Advitos) and aging treatments (Aviv Scientific).

Even in the face of declining elective procedures, two of the largest series A deals were dermatology companies focused on aesthetics, Revelle Aesthetics and Cartessa Aesthetics. Surprisingly, cardiovascular had only one of the 10 largest financings (Galaxy Medical). While neurology was not represented in the largest 10 deals, we did see continued early-stage investment into brain/computer interface technologies (INBRAIN Neuroelectronics, Precision Neuroscience and Blackrock Neurotech).

European investment activity centered on NIM (17) and ophthalmology (four) companies, accounting for close to half the deal activity in each indication.

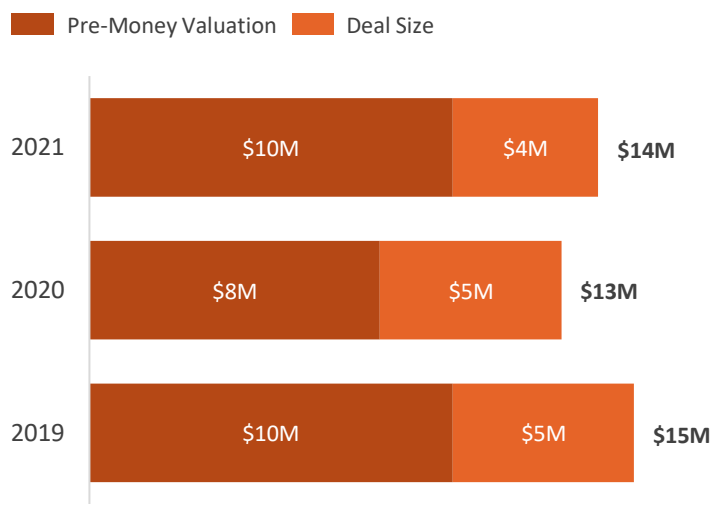
Seed/Series A¹ Dollars and (Deals) US and Europe



Seed/Series A Dollars and Deals by Top Indications

Indications	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
Non-Invasive Monitoring	\$99M	12	\$130M	15	\$250M	46
Platform	\$0M	0	\$11M	3	\$119M	9
Imaging	\$149M	12	\$76M	8	\$108M	17
Dermatology	\$9M	2	\$2M	1	\$100M	8
Vascular	\$16M	3	\$49M	8	\$89M	8
Neurology	\$100M	12	\$148M	8	\$77M	10
Cardiovascular	\$46M	8	\$98M	7	\$76M	13

Median Seed/Series A Post-Money Valuations US and Europe



Largest 2021 Seed/Series A Deals



Note: 1) Seed/series A includes first-time investments from institutional or corporate venture investment in the US and Europe and any first-round investments equal to or greater than \$2M, regardless of investor. 2) This company overlaps with the healthtech sector and is included in both sets of sector-specific analyses. Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.

Device Investment Surge Led by Large, Later-Stage Rounds

Device investment scaled to new heights in 2021, far ahead of 2020 investment and almost doubling the investment pace of 2018 and 2019. Device investment peaked at \$3B in Q2 then declined slightly in Q3 and Q4. The top five financings, totaling \$1.5B, all clustered in June and July.

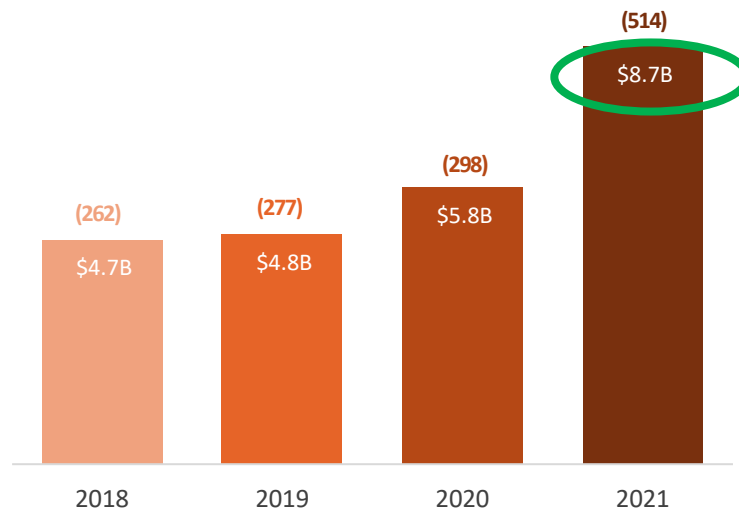
Technology-enabled services (NIM, imaging) continued to attract the lion's share of investment in device. However, as a caution for this indication, we have noticed some supply-chain issues for commercial-stage NIM companies that might impact their revenue trajectories into 2022.

Neurology and cardiovascular activity was also up significantly. The seven largest cardiovascular deals (with a median post-money value of \$150M) and six of the seven largest neurology deals (with a median post-money of \$183M) were all series C or later financings, setting the stage for these companies to ramp revenue and explore potential exit discussions.

It is interesting to note that half of the highest valued private device companies on this list have not yet reached the revenue stage. For these early-stage companies, execution risk is still a large part of their story, and access to the public market may be impacted by the poor IPO performance we experienced in 2021.

Based on broad public market trends, crossovers will likely be less active in late-stage device deals in 2022. Venture investors remain interested with freshly raised capital, though likely more valuation-sensitive than the crossovers.

Total Dollars and (Deals) US and Europe



Notable 2021 Deals



Deals and Dollars by Top Indications US and Europe

Indications	2019		2020		2021	
	Dollars	Deals	Dollars	Deals	Dollars	Deals
Imaging	\$563M	29	\$605M	33	\$1.2B	56
Non-Invasive Monitoring	\$425M	32	\$620M	34	\$924M	94
Neurology	\$295M	26	\$590M	25	\$856M	40
Cardiovascular	\$447M	24	\$744M	29	\$691M	38
Drug Delivery	\$153M	15	\$268M	23	\$647M	38
Vascular	\$393M	19	\$346M	22	\$534M	29

2021 Highest Valued Private Companies²

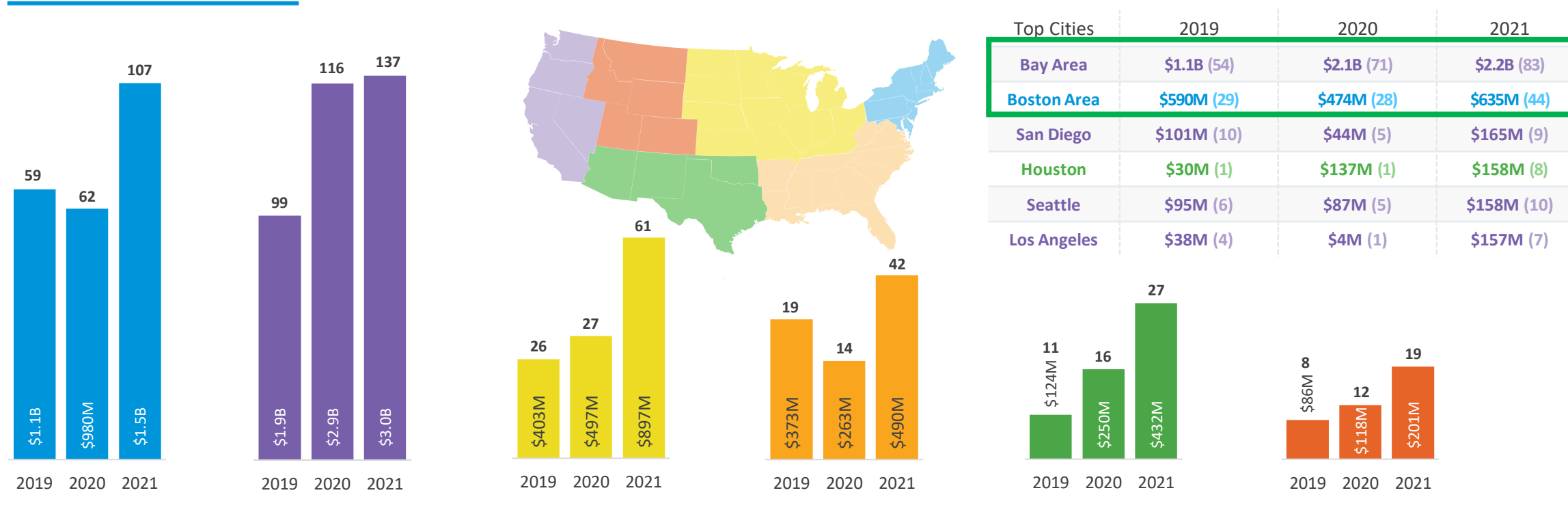
	Surgical	\$3,000M post
	Neurology	\$2,105M post
	Vascular	\$1,260M post
	NIM	\$900M post
	Urology/Gynecology	\$885M post
	Metabolic	\$870M post
	Imaging	\$645M post
	Orthopedic	\$538M post

Company has since gone public

Note: 1) These companies overlap with the healthtech sector and are included in both sets of sector-specific analyses. 2) Only includes private post-money values from publicly disclosed 2021 financings in PitchBook. Financing data include private financings by venture-backed companies in the US and Europe. Dates of financing rounds are subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.



US Device Investment by Region



Notable Private Financings, US 2021



Deep Dive: Computational Bio Analysis



Comp Bio: A New Paradigm of Drug Discovery & Development

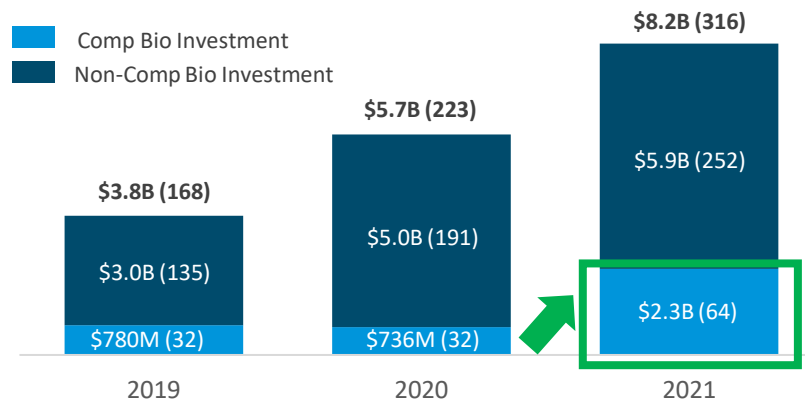
A growing number of companies are leveraging massive biological datasets to develop algorithms that offer deeper insights into disease and fundamentally change the drug discovery and development process. This field, computational biology (comp bio), gained traction through accelerators and incubators that created a structured space to collaborate and experiment with data management and analysis in healthcare. Venture investor activity in this area has accelerated dramatically over the past three years.

To qualify as a comp bio company in this analysis, per review of their website, the company must (1) focus on drug discovery or development (biopharma/R&D tools), (2) apply novel computational tools to gain biological or chemical insights, (3) have the ability or potential for platform creation and (4) have a team with computational experience.

Comp bio companies accounted for 129 (18%) of 707 total biopharma and R&D tools companies that raised their first seed/series A round since 2019¹. Investment into comp bio deals spiked this year, nearly doubling the combined dollars raised in 2019 and 2020. In Massachusetts and NorCal, where we've seen the most comp bio activity over the past three years, seed/series A dollars spiked 3x from 2020 to 2021. Notably, we also saw eight deals in the UK this year, after none in 2020.

Of these 129 comp bio companies, 89 (69%) incorporate machine learning or artificial intelligence algorithms into their technology, most often applied for genomic analysis to inform the discovery of small molecule therapeutics.

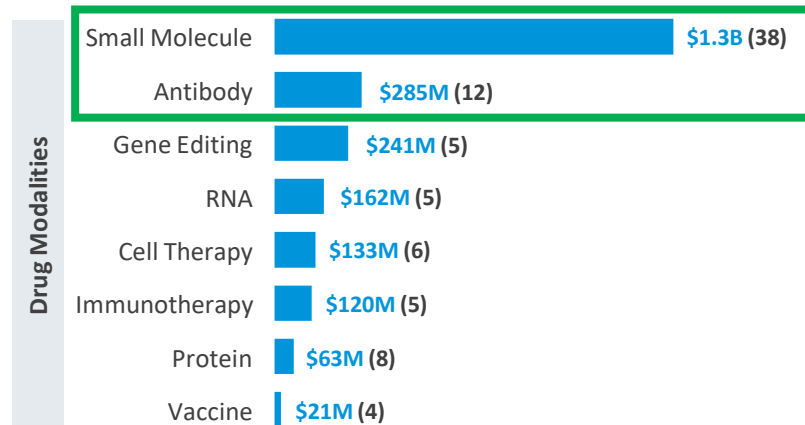
Overall Biopharma/R&D Tool (707 Seed/Series A¹ Deals): Investment by Year US and Europe



"There will be more progress in discovering new medicines in the next ten years than the last one hundred. Software-driven innovation is transforming how drugs are developed, and will soon make the term computational biology redundant."

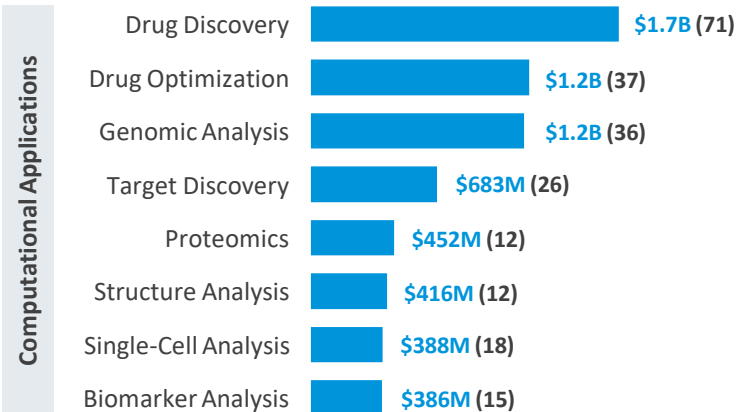
-John Noonan, Managing Partner LifeForce Capital

Comp Bio (129 Seed/Series A Deals): Top Modalities and Applications² US and Europe, 2019-2021



Comp Bio (129 Seed/Series A Deals): Investment by Region US and Europe

Top Regions	2019	2020	2021
Massachusetts	\$224M (8)	\$366M (11)	\$1.1B (18)
NorCal	\$386M (10)	\$104M (3)	\$317M (6)
United Kingdom	\$33M (1)	\$0M (0)	\$135M (8)
New York	\$6M (1)	\$32M (3)	\$125M (5)
SoCal	\$51M (2)	\$60M (3)	\$104M (4)



Comp Bio: Early-Stage Investment Leaders

We landscaped a subset of 70 smaller early-stage deals (\$2.5M-\$10M each) that have helped to push the field forward since 2019. Since their first seed/series A deal, 16 (23%) of the companies in this subset have already raised a follow-on financing.

Upon review of these companies' websites, we categorized the deals based on whether the company publicly stated that they were creating their own portfolio of therapeutics (biopharma) or developing technologies to enable drug discovery and development (R&D tools). We have seen many R&D tools companies begin to develop or license assets over time, so we predict that a number of these current R&D tools companies will later pivot to the biopharma sector.

We listed a snapshot of investors who are leaders in the early-stage comp bio space. While not an exhaustive list, these investors have a core investment thesis in comp bio, actively invest in this space and typically lead or anchor seed/series A rounds.

To identify promising early-stage companies, these investors often look for a novel computational approach, differentiated data, and a strong founding team. Most of the firms that are comfortable with underwriting this risk in seed/series A deals have expertise in both life science and technology, enabling them to provide critical resources including top talent, exposure to partners and access to new investors.

Comp Bio (70 Seed/Series A¹ Deals): Landscape of \$2.5M-\$10M Subset US and Europe

Raised at least one follow-on deal

	2019	2020	2021
Biopharma			
Average pre-money	\$11.8M (n=8) ²	\$12.0M (n=1)	\$14.0M (n=7)
Average deal size	\$5.3M (n=10)	\$4.2M (n=6)	\$4.7M (n=15)
R&D Tools			
Average pre-money	\$9.6M (n=11)	\$8.0M (n=4)	\$11.9M (n=7)
Average deal size	\$5.0M (n=12)	\$5.7M (n=9)	\$5.4M (n=18)

Early-Stage Comp Bio Focused Investors

8VC	ARCH VENTURE PARTNERS	ARTIS VENTURES	BE Bio	FORESITE CAPITAL	LIFEFORCE CAPITAL
LU+	Northpond Ventures	OBVIOUS		venrock	

Comp Bio: Building Value in Follow-On Deals and Exits

For comp bio companies that already raised both a seed/series A and another follow-on deal in the past three years, the step-ups² have been impressive, with a median step-up of 2.1x. Traditional life sciences investors and crossovers joined many of these follow-on deals, indicating that they believe comp bio will play an integral role in the future of drug discovery and development.

To unlock this investor set, companies must often validate their platform through partnerships, which are key to (1) demonstrate interest from pharma, (2) leverage revenue/milestones to defray costs and (3) pique M&A interest. This year, for instance, Outpace Bio (biopharma) raised a \$30M series A round and partnered with Lyell to commercialize a cancer immunotherapy. Other companies like A-Alpha Bio (R&D tools) applied their platform technology to help pharma partners accelerate their drug pipeline.

Of the 52 biopharma and R&D tools IPOs valued at \$1B+ since 2019, 13 (25%) were comp bio companies. These IPOs have performed tremendously, increasing total market cap by 3.7x and showing a median post-IPO performance of +54%. This growth was led by BioNTech (a key contributor to the COVID-19 response), 10x Genomics and Kymera. There were significantly fewer big M&A deals, as acquirers focused on targeting therapeutic assets with definitive clinical data rather than comp bio platforms. One notable exception was Vividion, which was acquired by Bayer this year for \$1.5B upfront and up to \$500M in milestones.

Comp Bio (22 Seed/Series A¹ Follow-On Deals): Step-Ups² US and Europe, 2019-2021

	1-2.4x	2.5-5x	13x+
Biopharma			
R&D Tools			
Most Active New Investors in Follow-On Deals			

Comp Bio: Largest IPOs by IPO Market Cap US and Europe, 2019-2021

	NAS:ABCL	NAS:SANA	NAS:TXG	NAS:BNTX	NAS:RXRX	NAS:EXAI	NAS:ADPT	NAS:ATAI	NAS:RLAY	NAS:KYMR
SVB Subsector	R&D Tools	Biopharma	R&D Tools	Biopharma	Biopharma	R&D Tools	R&D Tools	Biopharma	Biopharma	Biopharma
IPO Price (Date)	\$20.00 (12/11/20)	\$25.00 (2/4/21)	\$39.00 (9/13/19)	\$15.00 (10/10/19)	\$18.00 (4/16/21)	\$22.00 (10/1/21)	\$20.00 (6/27/19)	\$15.00 (6/18/21)	\$20.00 (7/16/20)	\$20.00 (8/21/20)
Market Cap at IPO	\$4.6B	\$4.4B	\$3.7B	\$3.4B	\$2.7B	\$2.4B	\$2.2B	\$2.1B	\$1.3B	\$863M
Price 12/31/21	\$14.30	\$15.48	\$148.96	\$257.80	\$17.13	\$19.76	\$28.06	\$7.63	\$30.71	\$63.49
Price +/-	-29%	-38%	+282%	+1619%	-5%	-10%	+40%	-49%	+54%	+217%
Market Cap 12/31/21	\$4.0B	\$2.8B	\$16.6B	\$62.3B	\$2.9B	\$2.4B	\$4.0B	\$1.2B	\$3.3B	\$3.3B

Comp Bio (All Deal Stages): 2021 Top Post-Money Values (US and Europe)

	Step-Up From Last Round ³	Most Recent Deal Size	Post-Money Valuation
insitro	3.4x	\$400M	\$2.5B
XtalPi	--	\$400M	\$2.0B
atai	5.0x	\$157M	\$2.0B
Generate: Biomedicines	15.3x	\$370M	\$1.5B
immunai	--	\$274M	\$1.4B
OWKIN	4.9x	\$180M	\$1.3B
Exscientia	2.8x	\$228M	\$1.1B
Neumora	--	\$100M	\$800M
TESSERA THERAPEUTICS	13.8x	\$230M	\$780M
vividion	1.5x	\$135M	\$585M

Company went public

Company was acquired

Healthcare M&A and IPO Activity Global



IPOs Set Record, Performance Lags

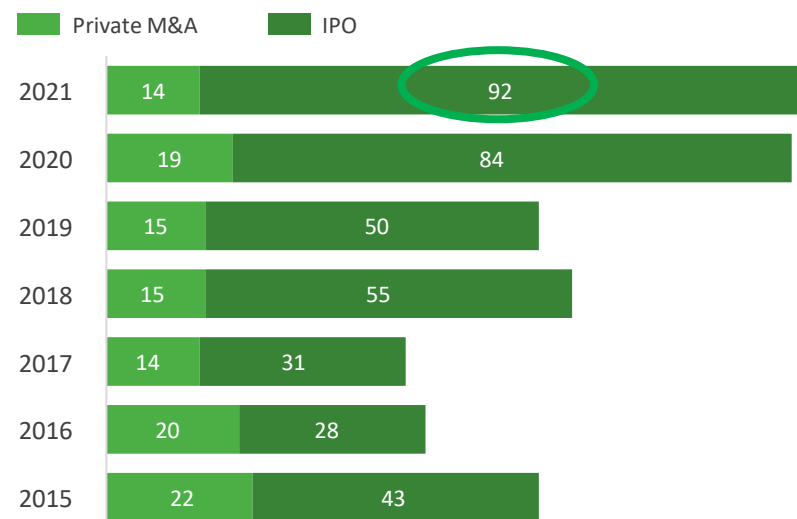
There were a record number of IPOs in 2021, but post-IPO performance was significantly down vs the previous two years. For the class of 2021, the average post-IPO performance was -21%, with only three companies trading above +100%.

By comparison, the average post-IPO performance for the class of 2020 was +100% at the end of 2020. However, this class also suffered during 2021 and was up just +12% at year end. The class of 2020 still had 11 companies with post-IPO performance over +100% at 2021 year end, including five early-stage companies (two pre-clinical and three phase I at IPO). However, as a sign of the current times, the bottom 11 performers (-68% performance and below) also contained five early-stage companies.

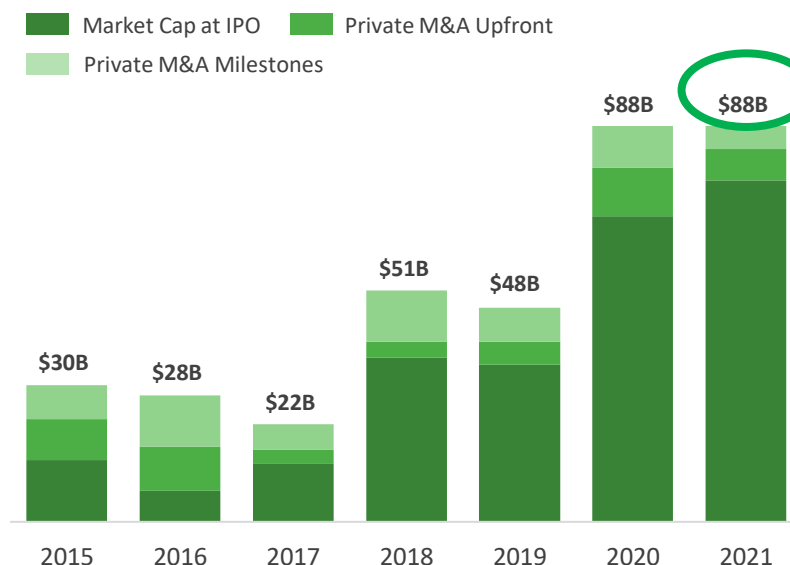
Private M&A activity in 2021 dropped to the lowest level we have seen since 2013. This downward trend is directly related to the open IPO window over the past five years, as most early-stage companies have embraced mezzanine rounds and then IPOs (at very good valuations) rather than early-stage exits. Many healthcare venture firms also raised later-stage opportunity funds which influenced companies to spurn early M&A.

While private M&A was down, we believe venture M&A is still quite viable with strong activity in pre-clinical deals. In addition, numerous venture-backed companies have also recently gone public and then were acquired, such as Translate Bio (\$3.2B), Viela Bio (\$3B), Pandion (\$1.9B) and Constellation (\$1.7B).










A) Biopharma Private M&A Deals and IPOs by Year



B) Biopharma Exit Values by Year



C) 2021 Largest IPOs by IPO Market Cap

								
	NAS: SANA	NAS: LYEL	NAS: RXRX	SEHK:2171	NAS: ATAI	SEHK:2137	NAS:TIL	NAS: ERAS
SVB Indication	Platform	Oncology	Platform	Oncology	Central Nervous System (CNS)	Anti-Infective	Oncology	Oncology
IPO Price (Date)	\$25.00 (2/4/21)	\$17.00 (6/17/21)	\$18.00 (4/16/21)	\$4.21 (6/17/21)	\$15.00 (6/18/21)	\$2.85 (7/13/21)	\$20.00 (3/19/21)	\$16.00 (7/16/21)
Market Cap at IPO	\$4.4B	\$4.1B	\$2.7B	\$2.4B	\$2.1B	\$2.0B	\$2.0B	\$1.9B
Price 12/31/21	\$15.48	\$7.74	\$17.13	\$3.53	\$7.63	\$4.22	\$17.11	\$15.58
Price +/-	-38%	-54%	-5%	-16%	-49%	+48%	-14%	-3%
Market Cap 12/31/21	\$2.8B	\$1.9B	\$2.9B	\$2.0B	\$1.2B	\$3.0B	\$2.2B	\$1.9B

Note: 1) This company overlaps with the healthtech sector and is included in both sets of sector-specific analyses. M&A defined as all private, global, venture-backed M&A deals with upfront payments of at least \$75M. IPO defined as all private, global, venture-backed IPOs raising at least \$25M in proceeds. Market cap at IPO used to estimate value of public companies. Public market performance metrics calculated as of 12/31/21. Source: PitchBook, Capital IQ and SVB proprietary data.



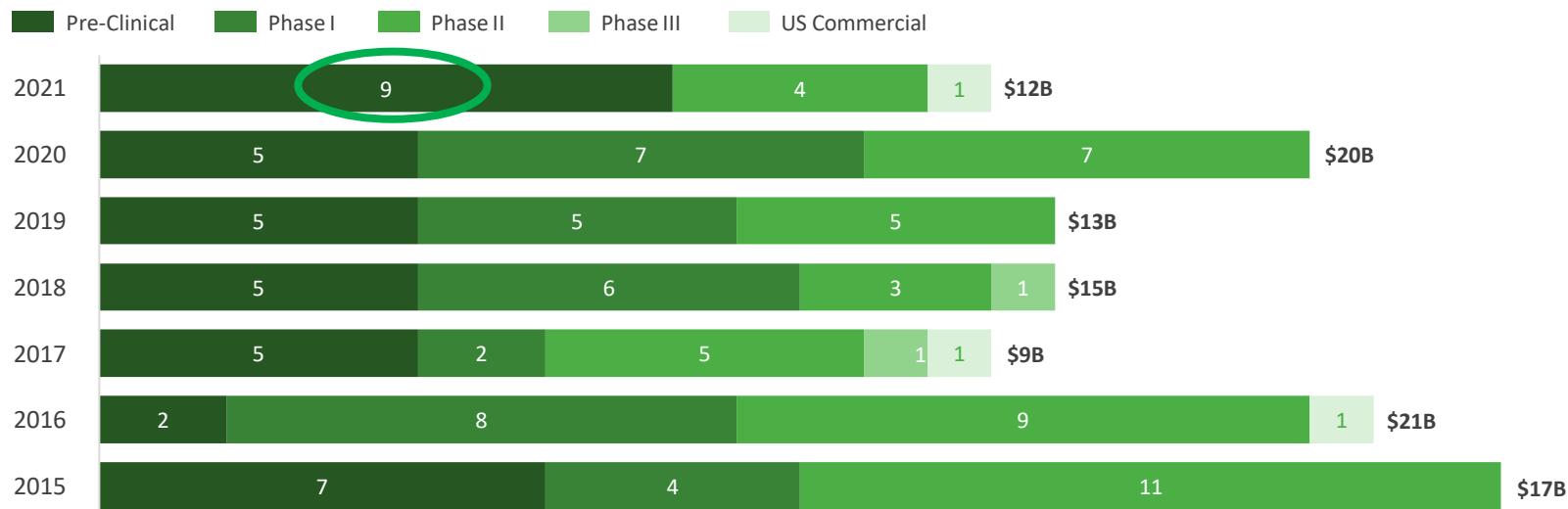
Private M&A Activity Down; Pre-Clinical Deals Reward VCs

Early-stage pre-clinical and phase I deals continued to dominate private M&A in 2021. The number of pre-clinical deals (nine) jumped to set a new yearly record.

These pre-clinical deals had a median \$31M in venture capital invested and exited in a median 5.2 years from the close of series A. The median upfront deal value was \$350M, with an additional \$358M in milestones. The median multiple on investment for the upfront payment (upfront payment divided by total capital invested) was an impressive 5.6x. Of the nine deals, three were acquired for \$1B+ in total deal value in 2021: Vividion Therapeutics (by Bayer), Teneobio (by Amgen) and Amunix (by Sanofi).

Big pharma has lots of cash, so we expect M&A to be robust in 2022, although the activity will likely be dominated by large acquirers that are hunting for recently public companies trading at depressed valuations. Many of these IPOs were pre-clinical or phase I at IPO (131 of 280 total since 2018), with current market caps significantly off their previous highs. These companies may be open to M&A as an attractive alternative to raising more equity. It will be harder to convince private companies and investors of mezz-funded deals to acquiesce to M&A at reduced values that do not match venture-type returns. However, we still believe that there is a large subset of higher-valued private early-stage companies to fill big pharma's need for pipeline assets and platform technologies.

Biopharma Private M&A Deals by Stage¹



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

2021 Notable M&A Deals

			Platform	
			Cardiovascular	
			Neurology	
				Oncology
			Uro/Gyn	



Since 2018 Early-Stage IPOs Fare Better Than Later-Stage

IPO median pre-money valuations hit a record high in 2020 (\$500M) then dropped in 1H 2021 (\$478M). From there, we saw a continued downward trend in Q3 (\$412M) and Q4 (\$378M). Post-IPO performance for the class of 2021 IPOs averaged -21% at year end.

The top 10 post-IPO performers in the class of 2021 averaged +75% and were split across clinical stages, with two pre-clinical (Verve Therapeutics and Dice Molecules), three phase I (Prometheus Biosciences, Arecor and Icosovax), three phase II (Vera Therapeutics, Rani Therapeutics and Imago Biosciences) and two commercial (San Nuo Technology and Brie Biosciences). These deals had a median step-up of 1.4x from venture to mezz and 1.3x from mezz to pre-money IPO.

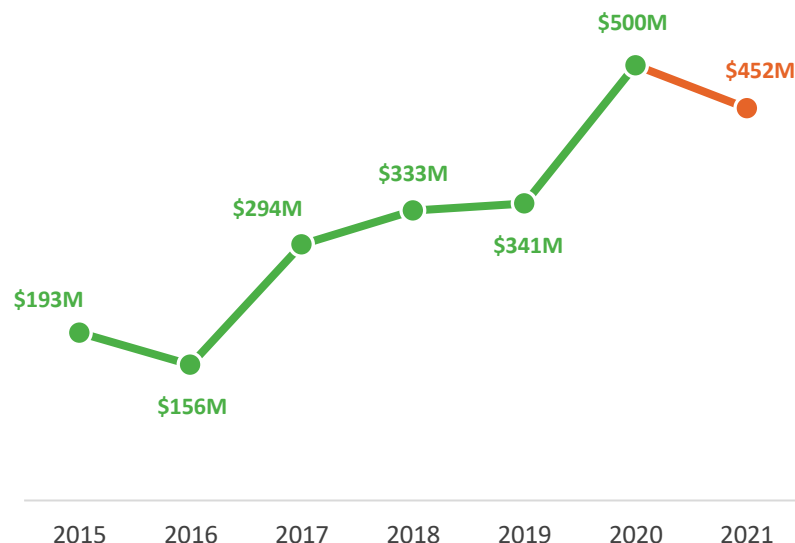
Oncology-focused deals continued to dominate the number of IPOs, accounting for 43 of the 93 IPOs in 2021 (average post-IPO performance of -32%), followed by 10 platform companies (-9%), seven orphan/rare (-34%), six anti-infective (the best-performing indication at -5%) and eight neurology deals (-30%).

Since 2018, early-stage IPOs (pre-clinical and phase I) appeared to have better post-IPO performance than later-stage deals (phase II to commercial). However, the large difference between average and median performance for these early-stage IPOs indicate that a few huge winners were responsible for driving the performance up. These early-stage deals also received better step-ups from venture to mezz to pre-money IPO valuations. We think that early-stage IPOs will continue to be part of the IPO mix in 2022, offering lucrative returns for early investors even if IPO performance is muted.

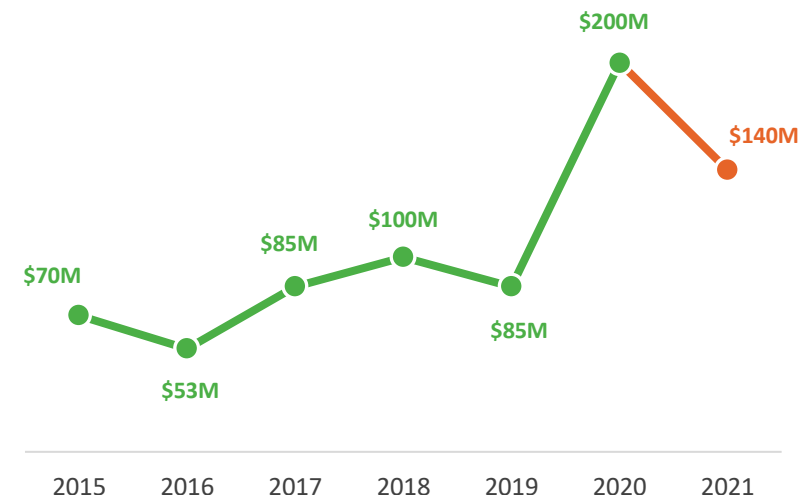


Note: 1) Step-Up defined as the valuation change from the last round post-money value to the next round pre-money value) Public market performance metrics calculated as of 12/31/21. IPO defined as all private, global, venture-backed IPOs raising at least \$25M in proceeds. Source: PitchBook, Capital IQ and SVB proprietary data.

IPO Median Pre-Money Valuations



IPO Median Proceeds



Valuation Step-Ups¹ and Performance² in Biopharma IPOs

	2018 IPOs		2019 IPOs		2020 IPOs		1H 2021 IPOs		2H 2021 IPOs	
	Early-Stage	Later-Stage	Early-Stage	Later-Stage	Early-Stage	Later-Stage	Early-Stage	Later-Stage	Early-Stage	Later-Stage
Median Venture to Mezz Step-Up ¹	1.8x	1.5x	2.0x	2.1x	1.8x	1.9x	1.7x	1.4x	2.1x	1.9x
Median Mezz to Pre-Money IPO Step-Up	1.5x	1.2x	1.0x	1.2x	1.4x	1.3x	1.5x	1.5x	1.3x	1.1x
Average Post-IPO performance	86%	38%	41%	106%	22%	122%	-16%	-30%	-11%	-11%
Median Post-IPO Performance	-23%	-56%	11%	-17%	-11%	-14%	-26%	-43%	-18%	-27%



HealthTech Exits Marked by Hefty Market Caps

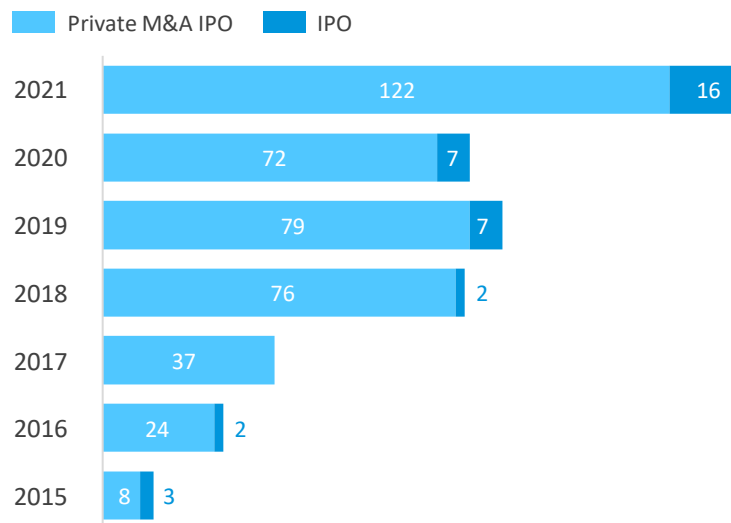
HealthTech's IPO window remained open despite the pandemic, with seven IPOs in 2020 and a record 16 in 2021. Insurance companies Oscar Health (\$1.4B in proceeds with a market cap of \$7.9B) and Bright Health (\$924M in proceeds with a market cap of \$11B) completed the two largest IPOs of 2021. These IPOs helped propel healthtech exit values to \$46B, more than doubling the record performance of 2019 and beating 2020 exit values by more than 3x.

However, the class of 2021's performance remains largely negative, with an average post-IPO performance of -28%. Oscar Health (-80%) and Bright Health (-81%) are both down substantially. The aggressive valuation premiums we have seen in the healthtech private market have not translated to the public market. The notable exception is provider operations company Doximity, which went public at the third largest healthcare market cap (\$4.6B) and is now up +93% at year end 2021. Immuneering is the only other IPO to be trading higher than its IPO price.

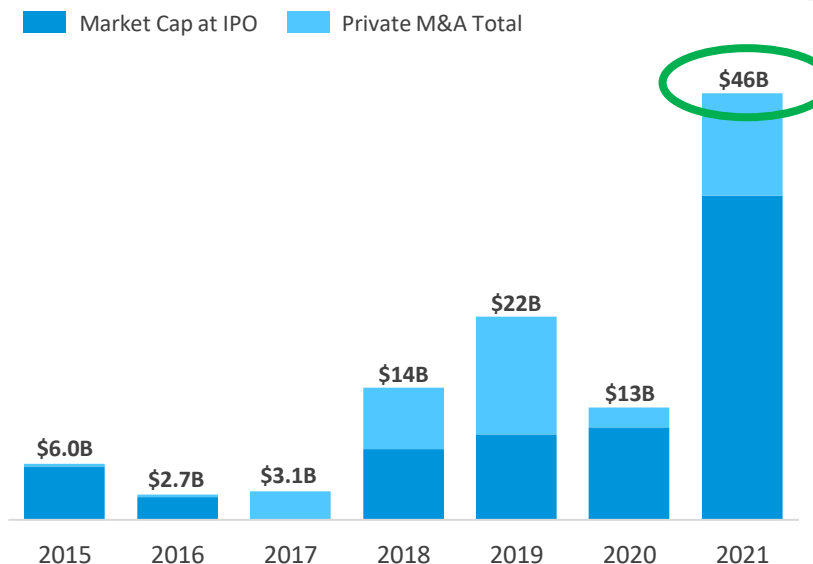
On the private M&A side, increased consolidation of point solutions healthcare companies drove increased activity, almost doubling acquisitions in 2020.

We have seen private companies, many of which are venture funded, become acquirers. Flush with cash from large rounds raised in 2020 and 2021, these private healthtech companies have accelerated M&A in 2021 to expand both vertically and horizontally, by integrating point solutions in their product offerings and scaling commercial growth and revenue.










HealthTech Private M&A Deals and IPOs by Year



HealthTech Exit Values by Year



2021 Largest IPOs by IPO Market Cap

									
	NYSE:BHG	NYSE:OSCR	NYSE:DOCS	NAS:ALHC	NAS:HLTH	NAS:SOPH	SEHK:2251	TSE:CARE	NAS:IMRX
SVB Subsector	Insurance	Insurance	Provider Operations	Insurance	Alternative Care	Provider Operations	Provider Operations	Alternative Care	Clinical Trial Enablement
IPO Price (Date)	\$18.00 (6/24/21)	\$39.00 (3/3/21)	\$26.00 (6/24/21)	\$18.00 (3/26/21)	\$16.00 (9/24/21)	\$18.00 (7/23/21)	\$9.65 (11/5/21)	\$9.62 (3/30/21)	\$15.00 (7/30/21)
Price 12/31/21	\$3.44	\$7.86	\$50.13	\$14.06	\$13.41	\$14.10	\$4.92	\$5.76	\$16.17
Price +/-	-81%	-80%	+93%	-22%	-22%	-22%	-49%	-40%	+8%
Market Cap 12/31/21	\$2.2B	\$1.6B	\$9.2B	\$2.6B	\$2.0B	\$900M	\$526M	\$379M	\$426M

Note: 1) These companies overlap with dx/tools or biopharma sectors and are included in both sets of sector-specific analyses. M&A defined as all private, venture-backed M&A deals with no upfront limitations, globally. IPO defined as all private, venture-backed IPOs raising at least \$25M in proceeds, globally. Market cap at IPO used to estimate value of public companies. Public market performance metrics calculated as of 12/31/21.

Source: PitchBook, Capital IQ, SVB proprietary data and [SVB HealthTech Report](#).

Uptick in M&A Driven by Expansion to Platform Solutions

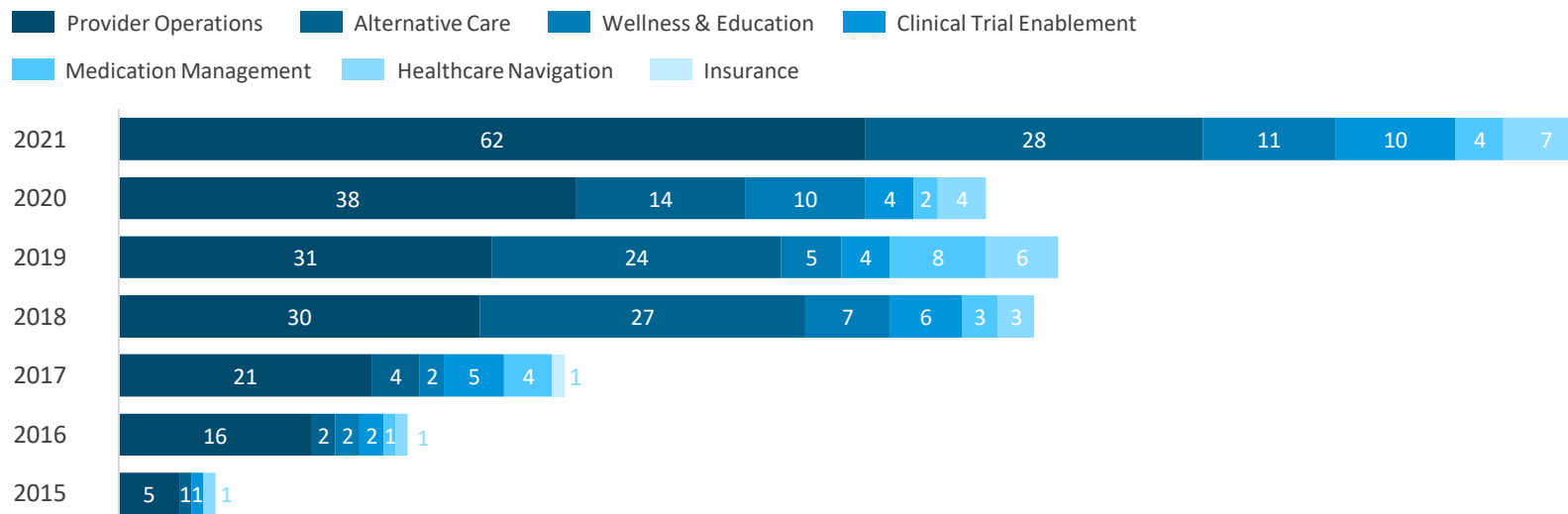
With 122 M&A deals this year, 2021 shot past 2019's record of 76. While deal volume increased, acquisition prices were slightly down; median deal size was \$63M, down from 2020 (\$84M) but ahead of 2019 (\$40M). The majority of acquirers were healthcare companies, and we noted acquisitions by PE firms have declined in 2021.

While there were no \$1B+ venture-backed private M&A in 2020, we saw three big transactions in 2021, all in the alternative care space: Ginger (virtual care) was acquired by Headspace for \$3.0B, MDLive (virtual care) by Cigna for \$2.0B and Iora Health (hybrid care) by One Medical for \$1.4B. Another \$1B+ transaction, while not an M&A but worth noting, was the Grand Rounds and Doctor on Demand all-stock merger.

Provider operations continued to dominate the M&A space in deal activity with larger M&A deals such as PatienCo, OODA Health, Citizen and VisitPay. However, alternative care saw the largest uptick in deal activity this year (2x 2020's pace) with the three \$1B+ deals noted above and other sizable M&A such as PlushCare, Contessa and Access Physicians.

The uptick in M&A this year is further evidence of companies shifting to either a more vertical integrated strategy to capture more of a patient's continuum of care or a horizontal strategy to provide platform solutions to broader consumer bases. We expect this high volume of private M&A to continue in 2022 as companies look to enhance their platforms.

HealthTech Private M&A Deals by Subsectors



HealthTech M&A Deal Median Values by Year

Year	Total Deal	Years to Exit
2021	\$63M	5.0
2020	\$84M	6.2
2019	\$40M	5.8
2018	\$100M	4.9
2017	\$41M	3.6
2016	\$10M	4.2
2015	\$70M	4.3

2021 Notable M&A Deals

PlushCare iorahealth current health	Alternative Care
ginger MDLIVE Modern Fertility	
Genuity ¹ 4G Clinical zebiAT ¹	Clinical Trial Enablement
Healthify dottori.it Tango health	Healthcare Navigation
BardyDX ¹ nanox ¹ PATIENTCO visitpay ciitizen ooda health	Provider Operations



Dx/Tools Exit Activity Catches Fire; IPO Performance Down

There was record M&A and IPO activity in 2021. IPOs tripled and M&A doubled 2020 records.

The median pre-money value and dollars raised for 2021 IPOs was \$582M and \$131M, doubling 2019 medians but falling behind 2020 medians of \$929M and \$178M.

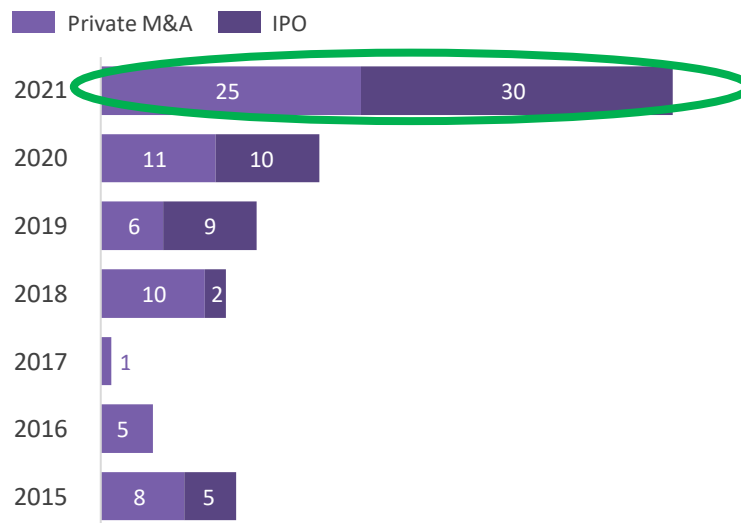
However, IPO performance in 2021 was mixed, with average post-IPO performance just breaking positive at +3%. R&D Tools deals performed much better than dx tests. The 17 R&D tools IPOs were up an average of +25% from their IPO, while the 10 dx tests companies were down -26%.

Most of the positive IPO performance was outside of the US, including the two biggest IPOs by market cap, Oxford Nanopore Technologies and Vazyme Biotech. At year end, 14 US-based companies traded down an average of -36% from their IPO prices. Only one of the 14 was in positive territory (Alpha Teknova) while three were down more than 50% (Zymergen, Talis Biomedical and Sera Prognostics). On the other hand, the nine China IPOs in 2021 shined, showing an average performance increase of +78%.

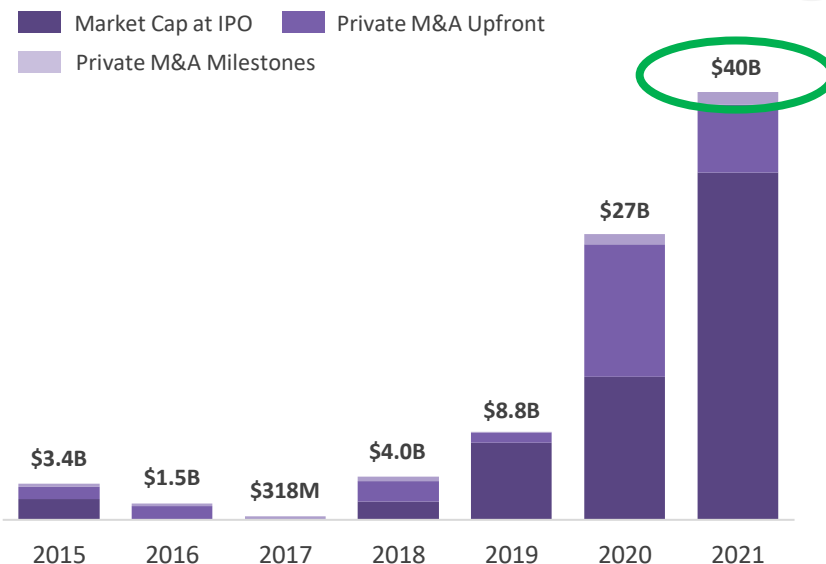
Previous IPOs show mixed performance during 2021, with the class of 2019 (+139% after one year) still strong at +198%. Five deals were still trading over +100% from their IPO price, including 10X Genomics and Castle Biosciences. The IPO class of 2020 (+110% after one year) was down substantially to -13% at 2021 year end, with only Shrodinger over +100%.

M&A was strong in 2021, with nine deals garnering \$300M+ upfront payments (vs six in 2020 and two in 2019).










Dx/Tools Private M&A Deals & IPOs by Year



Dx/Tools Exit Values by Year



2021 Largest IPOs by IPO Market Cap

											
	LSE:ONT	SHSE:688105	NAS:ZY	NAS:EXAI	NAS:HLTH	NAS:CTKB	SEHK:6606	NAS:ABSI	NAS:OMIC	SEHK:2251	
SVB Subsector	R&D Tools	R&D Tools	R&D Tools	R&D Tools	Dx Tests	R&D Tools	Dx Tests	R&D Tools	R&D Tools	Dx Tests	
IPO Price (Date)	\$5.63 (8/23/21)	\$8.63 (11/15/21)	\$31.00 (4/22/21)	\$22.00 (10/1/21)	\$16.00 (9/24/21)	\$17.00 (7/23/21)	\$3.43 (2/17/21)	\$16.00 (7/22/21)	\$22.00 (5/27/21)	\$9.64 (11/5/21)	
Market Cap at IPO	\$4.6B	\$3.4B	\$3.0B	\$2.4B	\$2.3B	\$2.2B	\$1.5B	\$1.5B	\$1.4B	\$1.0B	
Price 12/31/21	\$9.45	\$16.68	\$6.69	\$19.76	\$13.41	\$16.32	\$2.83	\$8.20	\$11.56	\$4.92	
Price +/-	+68%	+93%	-78%	-10%	-16%	-4%	-17%	-49%	-47%	-49%	
Market Cap 12/31/21	\$7.8B	\$6.7B	\$685M	\$2.4B	\$2.0B	\$2.2B	\$1.2B	\$759M	\$833M	\$526M	

Note: 1) These companies overlap with the healthtech sector and are included in both sets of sector-specific analyses. M&A defined as all private, venture-backed M&A deals with at least \$50M upfront, globally. IPO defined as all private, venture-backed IPOs raising at least \$25M in proceeds, globally. Market cap at IPO used to estimate value of public companies. Public market performance metrics calculated as of 12/31/21.

Source: PitchBook, Capital IQ, SVB proprietary data.

Dx/Tools Deal Multiples Up; Mid-Cap Activity Grows

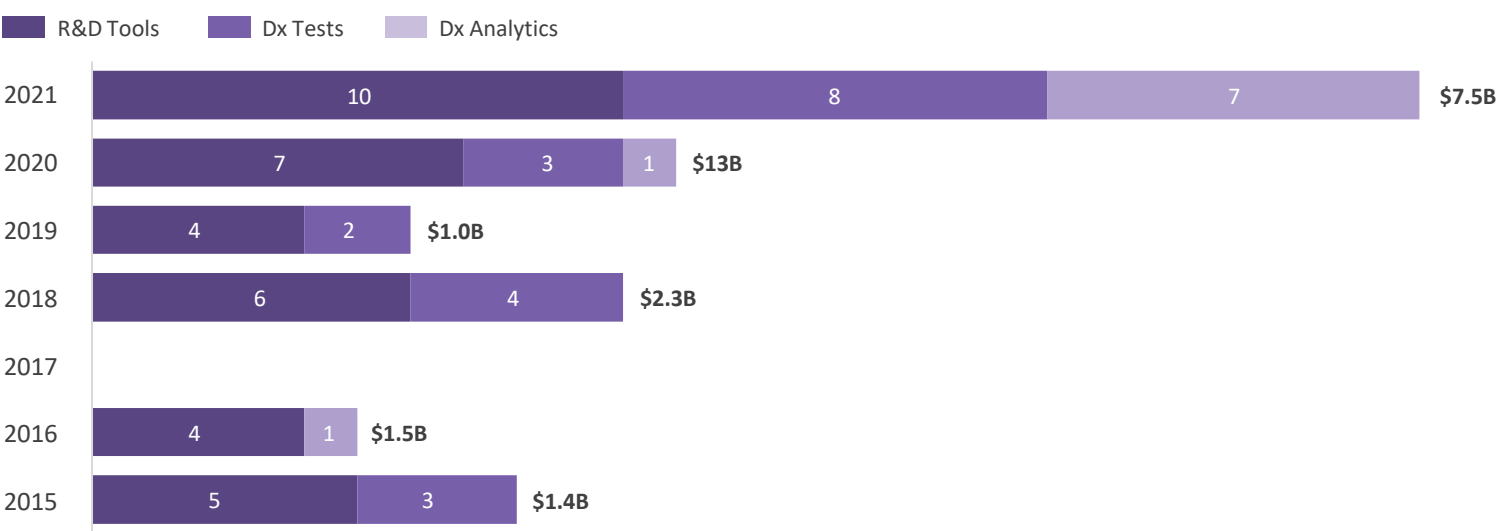
M&A activity exploded in 2021. While median deal values were down vs 2020, the median upfront deal multiple (upfront payment divided by total invested capital) was the highest we have seen. The median multiple was a paltry 1.3x in 2018, growing to 3.2x in 2019, 4.3x in 2020 and 5.3x in 2021. This growth is impressive considering that 18 of the 20 deals were already commercial-stage, and recent IPO comps have been down. Of the three subsectors, dx tests had the highest median upfront value (\$310M), followed by R&D tools (\$222M) and dx analytics (\$62M).

In 2021 we noted recently public biopharma companies buying R&D tools companies to help expand their technology or offerings, with acquisitions of Guide (by Beam) and ZebAI (by Relay). We also saw well-funded private venture-backed companies pick up dx/tools companies. R&D Tools company Exscientia acquired Allcyte (dx analytics) to expand drug discovery capabilities, and well-funded healthcare company Ro acquired Modern Fertility (dx tests) to expand its women’s health vertical.

Two dx tests acquirers picked up dx analytics companies in 1H: HaliDx (by Veracyte) and Trapelo Health (by NeoGenomics). These acquirers struck again in 2H, each picking up a dx tests company: Decipher Biosciences (by Veracyte) and Inivata (by NeoGenomics).

Hologic completed two dx tests acquisitions in 2021, Biotheranostics and Diagenode, as well as two medical device deals.

Dx/Tools Private M&A Deals by Indications



Dx/Tools M&A Deal Median Values by Year

Year	Upfront	Total Deal	Years to Exit
2021	\$225M	\$270M	5.9
2020	\$350M	\$350M	5.4
2019	\$68M	\$83M	5.3
2018	\$126M	\$161M	9.1
2017	—	—	—
2016	\$225M	\$325M	8.5
2015	\$164M	\$164M	3.6

2021 Notable M&A Deals

allcyte: ¹	zebra ¹	Cardiologs ¹	<div>Dx Analytics</div> <div>Dx Tests</div> <div>R&D Tools</div>
trapelo ¹	halio dx	PerGen	
Asuragen ¹	BIO THERANOSTICS	DECIPHER BIOSCIENCES	
Inivata	MESA BIOTECH	PGDx	
UNCHAINED LABS	OMNIOME	AVITIDE	
zebiAI ¹	Guide THERAPEUTICS	PRECISION NANOSYSTEMS	

Note: 1) These companies overlap with the healthcare sector and are included in both sets of sector-specific analyses. M&A defined as all private, venture-backed M&A deals with at least \$50M upfront, globally. Source: PitchBook and SVB proprietary data.

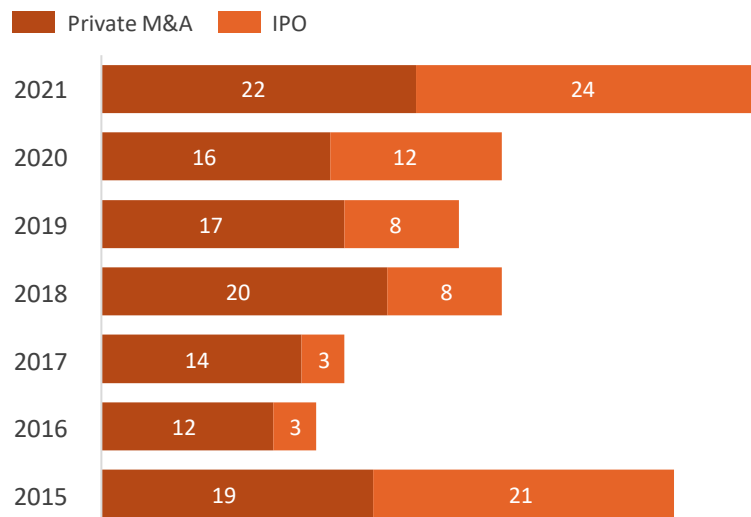
IPOs Doubled, M&A Value Up as Exit Values Soared

2021 yielded record device IPO and M&A activity, beating 2015's previous high-water marks. The median upfront value for M&A also reached a six-year high. Device exit value, mainly fueled by IPO market caps, doubled 2020's record.

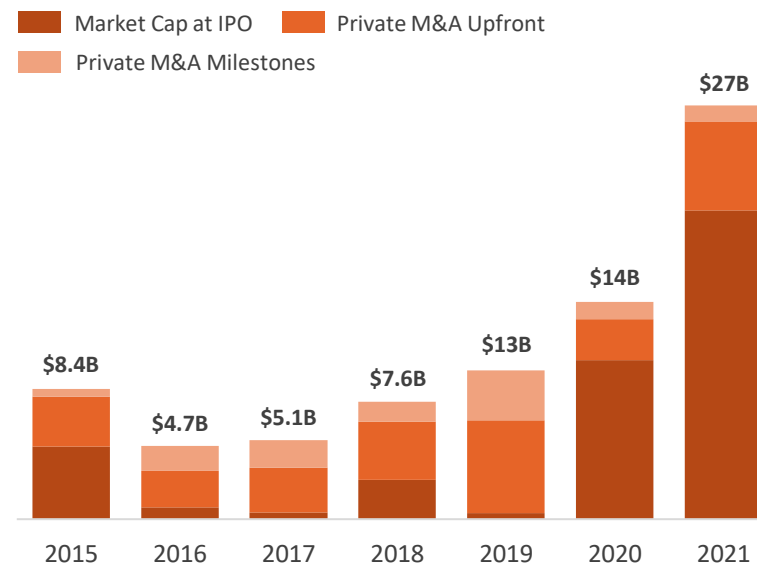
Over the previous three years, device IPOs have outperformed all other healthcare sectors, driven by 10 outsized IPOs that have shown an average post-IPO performance of +470%. Overall, these IPOs helped their IPO classes achieve impressive performance through 2021. At year end, the class of 2018 was still up an average of +197% (led by Inspire Medical Systems, Establishment Labs and Axonics Modulation Technology), and the class of 2019 was up +204% (led by Shockwave Medical and Silk Road Medical). The IPO class of 2020's performance fell more than half during this year but still reached +60% by the end of 2021 (led by Inari Medical, Outset Medical and Pulmonx).

However, the 24 IPOs in the class of 2021 treaded just above water, coming in at an average post-IPO performance of +2%. The 14 US-based IPOs fared worse, at -28%, with only Elite Body Sculpture, Paragon 28 and PROCEPT BioRobotics in positive territory. By contrast, China device IPOs excelled in the public market, up +73%, though many were more mature companies. This tough market in the US has already deterred a number of pre-IPO device companies, as many pushed off 2H 2021 IPO plans and raised additional private capital instead.










Device Private M&A Deals & IPOs by Year



Device Exit Values by Year



2021 Largest IPOs by IPO Market Cap

									
	SEHK:2160	SZSE:301087	SEHK:2190	HKG:2235	SEHK:2216	NYSE:FNA	NAS:SGHT	NAS:PRCT	SEHK:6609
SVB Indication	Cardiovascular	Platform	Vascular	Metabolic	Respiratory	Orthopedic	Ophthalmology	Surgical	Neurology
IPO Price (Date)	\$1.57 (2/3/21)	\$14.60 (10/25/21)	\$5.48 (7/5/21)	\$3.91 (10/19/21)	\$2.40 (9/13/21)	\$16.00 (10/15/21)	\$24.00 (7/15/21)	\$25.00 (9/15/21)	\$21.93 (8/20/21)
Price 12/31/21	\$0.50	\$12.42	\$3.27	\$3.64	\$1.15	\$17.69	\$17.57	\$25.01	\$13.44
Price +/-	-68%	-15%	-40%	-7%	-52%	+11%	-27%	0%	-39%
Market Cap 12/31/21	\$1.2B	\$2.0B	\$1.1B	\$6.3B	\$607M	\$1.4B	\$831M	\$1.1B	\$522M

Note: M&A defined as all private, venture-backed M&A deals with at least \$50M upfront, globally. IPO defined as all private, venture-backed IPOs raising at least \$25M in proceeds, globally. Market cap at IPO used to estimate value of public companies. Public market performance metrics calculated as of 12/31/21.

Source: PitchBook, Capital IQ, SVB proprietary data.



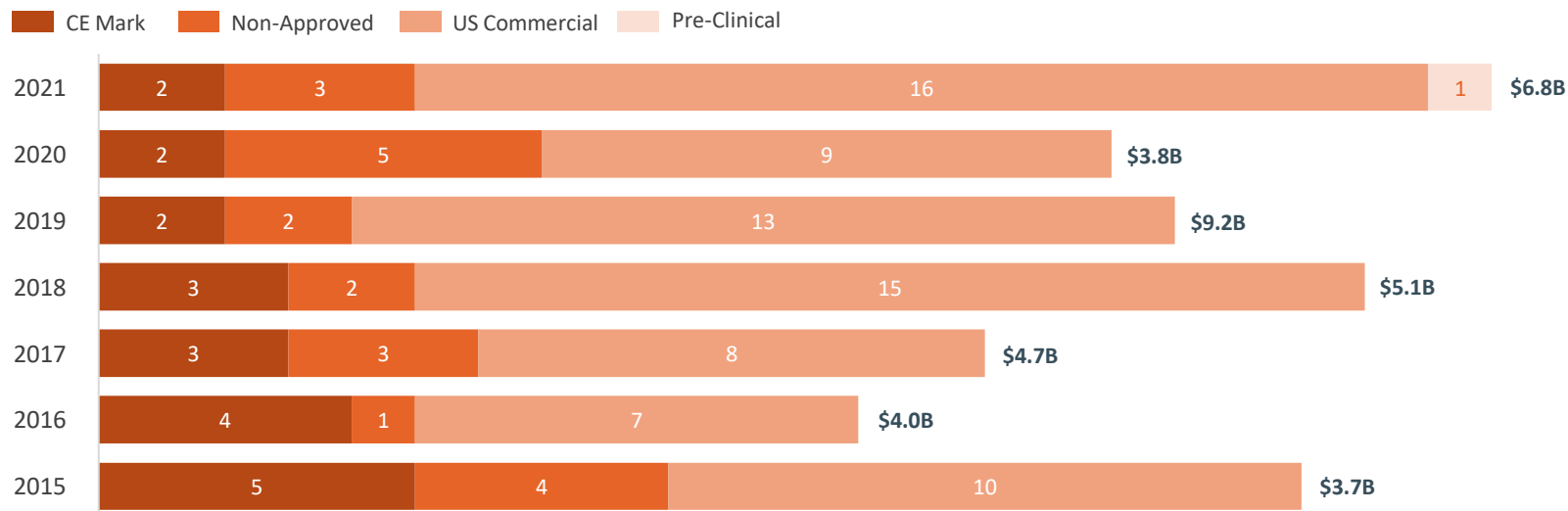
Record Number of M&A Led by Small/Mid-Cap Acquirers

M&A activity was busy in 2021, beating 2015's records for number of deals and median upfront deal value. The mix of new acquirers expanded to include multiple small and mid-cap acquirers, big company spin-offs and China-based companies. Many of the IPOs over the last five years have grown into small to mid-cap companies, and have built up investment arms of their own to fund venture-backed deals. These firms have also started to pull the trigger on technology acquisitions, forcing bigger players to buy companies earlier. This has led to a very active M&A market.

Implants and surgical tools continue to lead acquisition opportunities. However, tech-enabled services exits have become more prevalent as acquirers look to expand connected care and/or imaging solutions. We saw four tech-enabled services exits in 2021, lead by three deals in NIM (acquired by Boston Scientific, Hill-Rom and Hologic) and one in imaging (acquired by Olympus).

The majority of 510(k) pathway companies continue to need FDA clearance and revenue uptake at exit. The median upfront payment for 510(k) deals was up this year (\$160M) vs the historical median from 2015-2020 (\$105M), and the time to exit was faster. PMA pathway exits typically happen prior to commercialization, but in 2021 we saw more commercial-stage exits. Deal size also increased in 2021 to hit a median of \$275M upfront (vs \$206M), however time to exit also increased.

A) Device Private M&A Deals by Indications



B) Device M&A Deal Median Values by Year

Year	Upfront	Total Deal	Years to Exit
2021	\$223M	\$268M	5.8
2020	\$132M	\$210M	4.8
2019	\$120M	\$220M	7.9
2018	\$195M	\$223M	7.8
2017	\$131M	\$283M	7.7
2016	\$173M	\$260M	8.6
2015	\$125M	\$141M	7.0

C) 2021 Notable M&A Deals

			PMA	510(k) Pathway
preCARDIA	FARAPULSE	CARDIOVALVE		Cardiovascular
Respicardia				Neurology
SimplifyMedical	OrthoSpin	70 SURGICAL		Orthopedic
DEVORO MEDICAL	WENCLOSE	Vesper Medical		Vascular
Alydia	contura			Uro/Gyn
BardvDx ¹	Preventice SOLUTIONS ¹	somatix ¹		Non-Invasive Monitoring

Healthcare Outlook: 2022 and Beyond

Fundraising and Investments: Venture healthcare fundraising in the US will likely hit \$16B and investment into companies in the US and Europe will total about \$64B, as VCs slow down their deal pace but continue to invest from recently-closed funds.

Biopharma: LIPO deals will mirror Q4 2021 activity or decrease, leading to less investment in the sector and lower valuations for series B and later deals. We think IPO activity will be down about 50% (50+IPO), favoring companies with a differentiated but straightforward story and strong insider syndicate. M&A should pick up in 2022 but will focus more on newly-public companies already trading at a discount and private pre-clinical deals.

HealthTech: 2022 will be the year of M&A for healthtech as we anticipate massive consolidation. Investments will be healthy but not at 2021 levels. This will create many acquisition opportunities as companies look to enhance their product offerings, expand their reach to other markets or acquire for talent and/or clinicians (both of which are in short supply).

Dx/Tools: IPO valuations were high in 2021 and post-IPO performance was mixed. Some air has come out of the sector to push revenue multiples back to pre-2019 levels. We estimate another 10-15 IPOs in 2022, but at lower valuations. Private M&A will remain strong with 20+ deals in 2022. We will monitor the ability of highly-valued private companies to exit.

Device: Investment will likely decline as non-venture investors slow down mezz investing. The IPO window will remain open for big market stories with early revenue traction, leading to an estimated 10-12 IPOs in 2022. Pre-revenue companies or 510(k) deals with burgeoning revenue will find it challenging to go public.

M&A activity will stay hot, as a diverse set of acquirers compete for the top deals.

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Jonathan speaks at major investor and industry conferences about healthcare VC trends. He has 20+ years of banking experience working with healthcare companies and VC firms.

Jonathan earned a B.S. in business administration from the University of California, Riverside, and a J.D. from Santa Clara University.



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Outside of SVB, Beatriz is a Ph.D. candidate at Stanford University. She has more than seven years of experience developing new biomedical technologies, from peptide-based therapeutics to microfluidic and bioinformatics tools.

Beatriz earned a B.S. in bioengineering from the California Institute of Technology.

Glossary

Descriptions

All-In Deal defined as an acquisition where the full deal value is paid at deal close.

Series A defined as all first-round institutional or corporate venture investment, and all first-round investments equal to or greater than \$2M, regardless of investor.

Upfront Payments defined as initial proceeds from an acquisition paid upon the close of a structured deal; they do not include milestones.

Milestones to be Earned defined as proceeds from an acquisition that are paid once predetermined milestones are met.

Total Deal Value defined as the full value of the acquisition, including milestones to be earned.

Time to Exit defined as the time from the close of a company's first institutional round of financing to the exit.

Step-Up defined as the valuation change from the last round post-money value to the next round pre-money value.

Corporate Investor defined as a corporate venture and parent company investment into venture-backed companies.

Special Purpose Acquisition Company (SPAC) defined as a company with no commercial operations that is formed strictly to raise capital through an initial public offering (IPO) for the purpose of acquiring an existing company.

De-Special Purpose Acquisition Company (De-SPAC) defined as a transaction consisting of a completed merger between a private operating company and a publicly traded SPAC.

Computational Biology: To qualify as a computational biology company in this analysis, per review of their website, the company must (1) focus on drug discovery and/or development (biopharma/R&D tool), (2) apply novel computational tools to gain biological and/or chemical insights, (3) have the ability or potential for platform creation and (4) have a team with computational experience.

European Data: All European data and statistics includes data from the European Union and the United Kingdom.

Device Regulatory Definitions

Non-approved defined as a device product that has not obtained regulatory clearance or approval for its product.

CE Mark defined as a device company that has CE Mark approval but has not received FDA approval. CE Mark is a European Union designation that is typically less difficult to obtain than FDA approval, and the approval process often has a faster timeline.

US Commercial defined as a device company that has received FDA approval or clearance of its product and usually is in a commercial stage.

Indication Definitions

Neurology defined as CNS, pain and psychology companies, as well as neurology implant technologies.

Non-Invasive Monitoring (NIM) defined as medical data collection through sensors and other technology worn outside the body.

Dx Tests defined as proprietary yes/no diagnostic tests.

Dx Analytics defined as actionable data analytics to help determine treatment.

R&D Tools defined as research equipment/services for biopharma and academia.

HealthTech Subsector Definitions

Provider Operations defined as companies that provide solutions to increase the efficiency and accuracy of provider-provider, and provider-patient interactions.

Alternative Care defined as companies that provide primary or specialty care outside a hospital or private practice.

Clinical Trial Enablement defined as companies that develop solutions to accelerate drug discovery and the digitization of clinical trials.

Healthcare Navigation defined as companies that guide users to relevant providers and/or payers based on their needs.

Medication Management defined as companies that aid users in access and adherence to their prescribed medication.

Wellness & Education defined as companies that inform users of healthy lifestyle and medical best practices.

Biopharma Top 15 Crossover Investors

Biopharma Top 15 Crossover Investor defined as a public-minded investor who strategically invests in private companies. The Top 15 list includes: RA Capital, Perceptive Advisors, Deerfield Management, Redmile Group, Cormorant Asset Management, The Invus Group, Fidelity (et al.), EcoR1, Casdin Capital, Janus, Logos, Viking, Citadel, Rock Springs Capital, and Wellington Management.

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