

Trends in Healthcare Investments and Exits 2019

Record Investments and Fundraising Continue

ANNUAL REPORT 2019

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2018 Highlights: Investments

US and Europe* See Record Investments and Deal Values

- US healthcare venture fundraising reached a record \$9.6B, continuing a four-year upward trend.
- Venture investments increased 50 percent over 2017, setting a record.
- Biopharma dollar volume doubled that of 2017 and was 4x device and Dx/Tools volume in 2018.
- Biopharma Series A dollars increased 35 percent, led by oncology and platform companies, which accounted for more than half of all deals and dollars.
- With nearly twice the number of 2017 deals, Top 15 Crossover Investors restocked biopharma IPO pipelines by funding 60 private companies.
- Device investment grew 40 percent, and Series A dollars rose more than 30 percent to \$903M.
- Surgical robotics investment surged, closing a number of larger, later-stage device financings.
- Tech investors continued to dominate new Dx/Tools investments, making up seven of the top 10 active investors.
- Six private Dx/Tools companies were valued at more than \$1B in the last two years the largest number of any sector.



2018 Highlights: Exits

Record Upfront Payments, Rebounding Sectors

- 2018 was a banner year for biopharma IPO and M&A exits, hitting a record total deal value of \$49B.
- Biopharma IPOs reached a five-year high in pre-money valuations and dollars raised, and private M&A posted a 5x median upfront multiple and a median time to exit of just over three years.
- A record 18 \$1B+ venture-backed biopharma IPOs and M&A deals were completed in 2018.
- For the first time, venture-backed device M&A total upfront payments eclipsed all other sectors, reaching \$3.5B.
- Boston Scientific bought seven venture-backed companies, propelling device sector upfront payments to a six-year high median of \$190M.
- Device IPOs doubled over 2017, marking a five-year high for median pre-money valuation and dollars raised.
- Device De Novo 510(k) pathway deals had very successful exits with median upfront and total deal values far exceeding those of traditional 510(k) and PMA deals.
- After a single IPO in 2017 (and no M&A), Dx/Tools came back strong with 10 acquisitions and two successful IPOs.



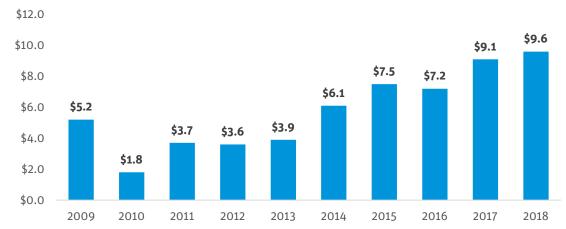


Healthcare Investments and Fundraising: Healthcare Sectors Continue Record Highs



US Venture Fundraising Continues to Break Records US Healthcare Venture Fundraising*, 2009–2018

A Healthcare Venture Capital (VC) \$ Fundraised (\$ BILLIONS)



B \$ Invested by Round Size 2017–2018



[A] US healthcare venture fundraising raised a record \$9.6B, continuing a four-year upward trend. Capital was dominated by large life science funds like Foresite, Versant, SV Health Investors (through its Dementia Fund) and Abingworth and joined by new fund spinoffs like Westlake Village, Samsara, Biomatics and 1315 Capital. In addition, generalists like Venrock, Norwest, General Catalyst and Sequoia Capital were joined by new entrants Lightspeed, 8VC, Charles River Ventures and Felicis Ventures.

[B] Quick biopharma exits and high IPO markups drove accelerated healthcare fundraising. A swell in biopharma deals and round sizes over the last two years highlights the continued appetite for venture funding in the sector.

A healthy pipeline of exciting private companies, excellent biopharma and device exit numbers and high-performing IPOs in the Dx/Tools sector mean continued robust venture fundraising through 2019. However, it will be at a pace more in line with 2016/2017 numbers at about \$8B.



*SVB calculates only the dollars allocated to healthcare by venture funds investing primarily in the US. Source: PitchBook and SVB proprietary data.

2018 Healthcare Investments Surpass 2017 by > 50% Biopharma, Device and Dx/Tools Investments and Deals, 2017–2018, US and Europe



Two-year data demonstrated record venture-backed investments in 2018 in the US and Europe. Biopharma hit full-year 2017 numbers by midyear, leading the way with multiple large mezzanine pre-IPO rounds that leveraged robust valuations and available public market dollars. Biopharma companies received about four times the investment of the other two sectors. We observed investment slowing in Q4 2018. With unsettled stock markets discouraging private crossover investment, and potential intervention from the Committee on Foreign Investment in the United States (CFIUS) moderating Chinese investment, we anticipate venture financing to lessen slightly in 2019.

Based on available VC and crossover investor activity in private deals, 2019 could show \$16B-\$18B in total investment. Device and Dx/tools sectors are expected to remain stable with biopharma investment decreasing from 2018 highs to closely match 2017 levels.



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Biopharma Series A Deals Smash Record Series A* Biopharma Investments, 2016–2018, US and Europe

A Series A Deals

124	135	143
2,612	\$2,665	\$4,166
31%	34%	24%
	2,612	2,612 \$2,665

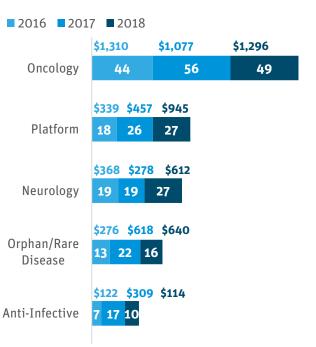
Europe Deals**	2017	2018
Number of Investments	70	42
Total Series A Funding (\$M)	\$867	\$658
Corporate Investments (%)	29%	19%

2018 Series A % by Indication, US and Europe

Indication	2018 Series A \$	2018 Total \$	2018 % Series A
Oncology	\$1,296M	\$4,873M	27%
Platform	\$945M	\$3,571M	26%
Neurology	\$612M	\$1,378M	44%
Orphan/Rare Disease	\$640M	\$1,645M	39%
Anti-Infective	\$114M	\$1,124M	10%
All Biopharma	\$4,825M	\$16,230M	30%

B Series A by Indication – US and Europe

Deal Counts (Dollars \$M Invested)



[A] US Series A funding increased 44% with oncology and platform making up almost half. Europe, however, saw a significant overall decline.

[B] Platform and neuro sectors doubled invested capital and completed more deals. Neuro hit a three-year high in dollars and deals covering a broad spectrum of central nervous system (CNS) disorders with a focus on pain. Orphan/rare had fewer Series A deals with investments barely exceeding 2017. This sluggish deal activity contrasts with the indication's historically successful IPO path.

[C] With respect to 2018 total investment, new Series A dollars dropped from 42% to 30% as investors raised large mezzanine Series B rounds ahead of IPOs. However, autoimmune Series A investments increased from 37% to 77% in 2018, led by a \$280M Series A investment in Viela Bio.

Large Series A deal amounts in 2018 (including 26 over \$50M) suggest potential dynamic IPO activity continuing in 2019.



*Series A Investments includes all private, first-round investments from institutional or corporate venture investment, and all first-round investments equal to or greater than \$2M, regardless of investor. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18. **SVB's European data set begins in 2017. Source: PitchBook and SVB proprietary data.

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Biopharma Fueled by Venture – Corporates Step Back Most Active New Investors* in Biopharma, 2017–2018

NUMBER OF DEALS



Corporate biopharma participation in venturebacked deals declined in 2018 due to increased competition for Series A and Series B deals. Multiple venture firms are co-leading large Series A deals, and corporates found fewer opportunities to join. Crossovers squeezed out corporates in Series B deals, as they aim to dominate mezzanine rounds with big checks, large valuation step-ups and strategic IPO support.

Top 15 Crossover Investors focused on later-stage deals. Firms with 3+ later-stage deals by indication included RA Capital (orphan/rare, oncology and neurology), Deerfield (oncology, neurology and platform), Perceptive Advisors (orphan/rare, oncology), Rock Springs (orphan/rare), Redmile Group (oncology), and EcoR1 Capital (oncology).

Six of the top 20 most active firms had 9+ new Series A deals: Firms with 3+ deals by indication include OrbiMed (oncology, orphan/rare), Novo Holdings (oncology, orphan/rare), ARCH Venture Partners (platform, neurology), Johnson & Johnson Innovation (neurology, oncology and platform), NEA (orphan/rare), Abbvie (oncology, neurology) and Novartis (orphan/rare).



*Most Active New Investors calculated as new (first-time) investments into companies in 2017–2018. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18. Alexandria investments typically average \$2M per deal, AREE, Inc. Earnings 9/30/18. Source: PitchBook and SVB proprietary data.

Large Mezzanine Investments Break Records Biopharma Deals by Indication, 2017–2018, US and Europe

NUMBER OF DEALS | \$ MILLIONS 2018 Deals over \$200M CASTLE CREEK PHARMA ■ 2017 ■ 2018 moderna Allogene gossamerbic IR 102 \$2,812 Oncology 117 \$4.873 celularity VIELABIO HARMONY BIONT-C \$1.045 42 Platform 2018 Deals \$125M-\$200M 62 \$3,571 ■ COMPASS **TCR²** bridgebio moderna Orchard therapeutics 31 \$503 Neurology 51 \$1.378 TMUNITY **Rakuten** Aspyrian ATRECA 37 \$1,178 Orphan/ 2018 Deals \$100M-\$125M Rare Disease \$1.645 34 Allogene Orchard therapeutics RubiusTherapeutics Constellati \$641 28 () Stealth SKYHAWK Mirum Pharmaceuticals Anti-Infective 🔴 Kaleido generation bio 33 \$1,124 2018 Deals \$80M-\$100M KSO MORPHIC Mi EVELO artios 4DMT **enterome** \$8,467 Total 340 Fulcrum ST€ KE ANSUNS • Galecto Biopharma TERNS Beam 418 \$16.230 7 Therapeutics Next@ure xeris IDEA A SUTRO **IT ERUM** DACT sutrevax

Biopharma investment in 2018 almost doubled to just over \$16B, with 51 deals of \$80M or more, triple that of 2017. Oncology had 16 of the \$80M+ deals, all but one were Series B+, with a median post-money valuation of \$280M. Orphan/Rare had reduced deals but continued to receive crossover investment. Top 15 Crossovers funded 11 of the 18 deals with a median post-money valuation of \$180M. We anticipate continued IPO activity in these sectors.

As CFIUS may limit the flow of Chinese investment into the US, investment could slow. Chinese investors were a significant part of the ecosystem, as they participated directly in syndicates that invested over \$4.5B in the US in 2018, up 50% from 2017. European deal activity could pick up as Chinese investors may focus investment outside the US.



Platform companies have technologies with multiple or non-specified indications. Early Stage defined as Series A & B; Late Stage defined as Series C and later. Dates of financing rounds subject to change based on add-on investments. Financing data includes private financings by venture-backed companies in the US and Europe. 2018 financing data through 12/15/18. Source: PitchBook and SVB proprietary data.

Platform and Oncology Sectors Drive Highest Value Highest-Valued Private Biotech Companies, 2017–2018

Platform Companies



This list is composed of the highest-valued private companies over the last two years, all with post-money valuations of \$400M or more*.

While Series A valuations remained stable in 2018, laterstage deals saw increases in median deal size (\$30M to \$40M) and valuation (\$88M to \$126M).

These deals yielded lots of big step-ups. 2018 saw 56 financings with post-money values over \$150M, doubling 2017's numbers.

Of the three private companies reaching valuations over \$1B, only Moderna went public. Rani Therapeutics became a unicorn with only \$123M in total equity while Intarcia raised a substantial \$615M round at a valuation of \$4B+.

Six of 19 companies listed here went public. Five have a current market cap of \$1B+**, including Armo, which went public and was subsequently acquired for \$1.6B.

Green text: Company subsequently went public



*Only includes post-money values reported by PitchBook. Dates of financing rounds subject to change based on add-on investments. **2018 financing and market cap data through 12/15/18. Source: PitchBook and SVB proprietary data.

Massachusetts and California Continue to Lead Biopharma Investments by Geography, 2018, US and Europe

Top Biopharma Regions for All Investments and Series A





Series A Investments includes all private, first-round investments from institutional or corporate venture investment, and all first-round investments equal to or greater than \$2M, regardless of investor. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18. Financing data includes private financings by venture-backed companies in the US and Europe. Source: PitchBook and SVB proprietary data.

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US and Europe Series A Dollars Surge Series A* Device Investments, 2016–2018, US and Europe

A Series A Deals

US Deals	2016	2017	2018
Number of Investments	57	57	73
Total Series A Funding (\$M)	\$314	\$446	\$646
Corporate Investments (%)	12%	19%	8%
Median Round Size (\$M)	\$4	\$4	\$7

Europe Deals**	2017	2018
Number of Investments	25	20
Total Series A Funding (\$M)	\$192	\$257
Corporate Investments (%)	8%	5%
Median Round Size (\$M)	\$4	\$6

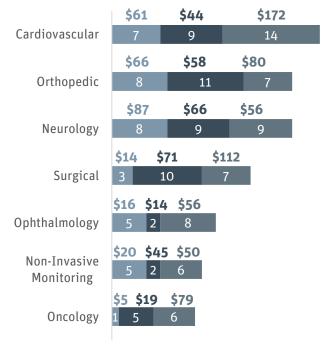
C Investment Analysis

Cardiovascular Series A deals centered around assist devices and mitral valve repair, while oncology investments focused on tumor visualization technologies and precision treatment through drug delivery and specialized equipment. Ophthalmology deals highlighted new processes for surgical treatment through targeted drugs and equipment for direct patient use.

B Series A by Indication – US and Europe

Deal Counts (Dollars \$M Invested)

2016 2017 2018



[A] Device Series A deal sizes increased in 2018, with the median US deal size nearly doubling. Even though the number of European deals declined, total dollars increased. Corporate Series A activity dropped significantly but remained strong in later-stage deals.
 [B] Cardiovascular, oncology, ophthalmology and non-invasive monitoring all saw an increase in Series A deals and dollars in 2018, with cardiovascular and oncology also leading M&A activity.

[C] Ophthalmology and surgical indications had an increase in dollars invested in Series A, boosted by a surge in robotics investment.



*Series A Investments includes all first-round investments from institutional or corporate venture investment in the US and Europe, and all firstround investments equal to or greater than \$2M, regardless of investor. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18.

**SVB's European data set begins in 2017. Source: PitchBook and SVB proprietary data.

Traditional VCs Dominate Device Investments Most Active New Investors* in Device, 2017–2018

NUMBER OF DEALS



Tech Ventures, Shangbay Capital, JJDC, Broadview Ventures and BrilliMedical International each had 3+ Series A deals.

Keiretsu Forum, FundRx,

Emergent Medical Partners, SV

Others with 3+ Series B or later deals included Endeavor Vision, Boston Scientific, Gilde Healthcare, NEA, Lightstone Ventures, Baxter, Perceptive Advisors, Richard King Mellon Foundation and Revelation Partners. Endeavor Vision, NEA and Perceptive also invested in multiple \$25M+ rounds.

With 3+ deals, Visionary Venture Fund focused on ophthalmology, NEA on vascular, Perceptive on uro/gyn and Boston Scientific on cardiovascular. International firms IdInvest Partners and Investiere Venture Capital focused on deals in France and Switzerland, respectively.



*Most Active New Investors calculated as new (first-time) investments into companies in 2017–2018. 2018 financing data through 12/15/18. Dates of financing rounds subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.

Investors Target Later-Stage Cardiovascular, Neuro Device Investments, 2017 and 2018

NUMBER OF DEALS | \$ MILLIONS



In the last two years, 78% of investment went to later-stage deals (Series B+), with many raising commercialization rounds post FDA approval.

Companies like HeartFlow, Neochord and Whiteswell raised big rounds with crossover investors, increasing cardiovascular deals and dollars. Fresh off a number of IPOs in neurology, \$50M+ later-stage deals were closed by Impel Neuropharma, Relievant Medsystems and Stimwave.

While uro/gyn missed the cut for top active indications, it received significant investment with \$40M+ deals in Procept BioRobotics, Renovia and AEGEA Medical.



Financing data includes private financings by venture-backed companies in US and Europe. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18. Source: PitchBook and SVB proprietary data.

Crossovers Led Big Deals in Device Sector Highest-Valued Private Device Companies, 2017–2018



This list is composed of the highest-valued private companies over the last two years, all with post-money valuations of \$150M or more*.

Top 15 Crossover Investors moved from biopharma to later-stage medical device rounds. Perceptive Advisors, Viking Global, Wellington and Fidelity were new investors in four of the six highestvalued rounds.

Ophthalmology and neurology each had four deals valued over \$150M. Neurology deals were Series D or later, and six of the eight deals were commercial stage.

Surgical robotics received significant investment and high valuations. Procept BioRobotics and Auris raised large rounds in 2018. Verb Surgical received sizable investment as well.

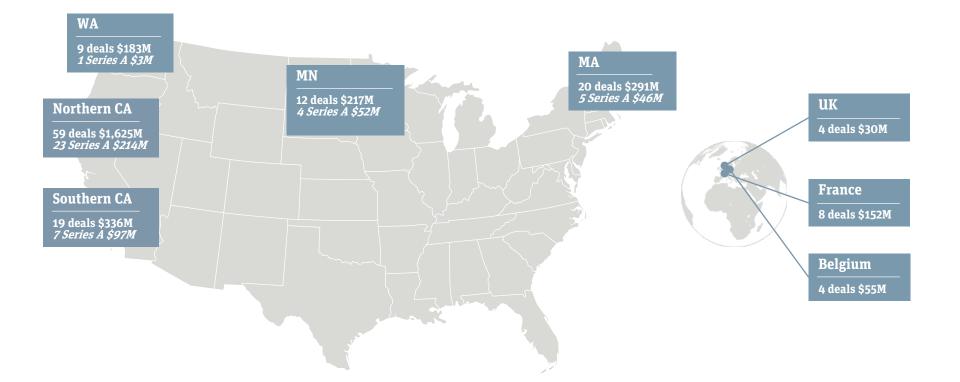
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*Only includes post-money values reported by PitchBook. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18.

Source: PitchBook and SVB proprietary data.

California Continues to Dominate Device Deals Device Investments by Geography, 2018, US and Europe

Top Medical Device Regions for All Investments and Series A





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Dx/Tools Attract Fewer Series A Deals and Dollars Series A* Dx/Tools Investments, 2016–2018, US and Europe

Series A Deals

US Deals	2016	2017	2018
Number of Investments	54	70	64
Total Series A Funding (\$M)	\$549	\$845	\$621
Corporate Investments (%)	20%	21%	19%
Median Round Size (\$M)	\$5	\$6	\$6

Europe Deals**	2017	2018
Number of Investments	33	17
Total Series A Funding (\$M)	\$211	\$88
Corporate Investments (%)	0%	29%
Median Round Size (\$M)	\$3	\$4

C % of Series A by Indication

Indication	2018 Series A \$	2018 Total \$	2018 % Series A
R&D Tools	\$267M	\$2,400M	11%
Dx Tests	\$176M	\$1,276M	14%
Dx Tools & Analytics	\$230M	\$1,111M	21%
All Dx/Tools	\$709M	\$4,824M	15%

B Series A by Indication – US and Europe Deal Counts (Dollars \$M Invested)

Dear counte (Donare gri investea)					
■ 2016 ■ 2017 ■ 2018					
\$192			\$551		\$267
R&D Tools	29		60		37
	\$306	\$151	\$176		
Dx Tests 20		25	17		
Dx Tools & \$58 \$354 \$230					
Analytics	8 20	26	5		

2018 Deals Over \$20M



[A] US and European Dx/Tools deals dropped while investments slowed 40% from 2017, reducing the Dx/Tools Series A pipeline. Following multiple large Series A investments over the past two years, it is not surprising to see a slowdown in early-stage investment as investors wait for things to play out. As a result, most investments (85%) went to later-stage companies.

[B] In the Dx Tools and Analytics subsector, there were a significant number of artificial intelligence/machine learning (AI/ML) investments, but dollars decreased here as well. We finally observed tech and life science investors invest together in this subsector with Series A investments in Glympse Bio and Luna DNA.



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Tech Investors Continue to Lead Dx/Tools Deals Most Active New Investors* in Dx/Tools, 2017–2018



Corporate Investors

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*Most Active New Investors calculated as new (first-time) investments into companies in 2017–2018. 2018 financing data through 12/15/18.

Dates of financing rounds subject to change based on add-on investments.

Alexandria investments typically average \$2M per deal, AREE, Inc. Earnings 9/30/18. Source: PitchBook and SVB proprietary data. Tech investors made up seven of the top 10 active investors. Tech corporates GV and Baidu were also active.

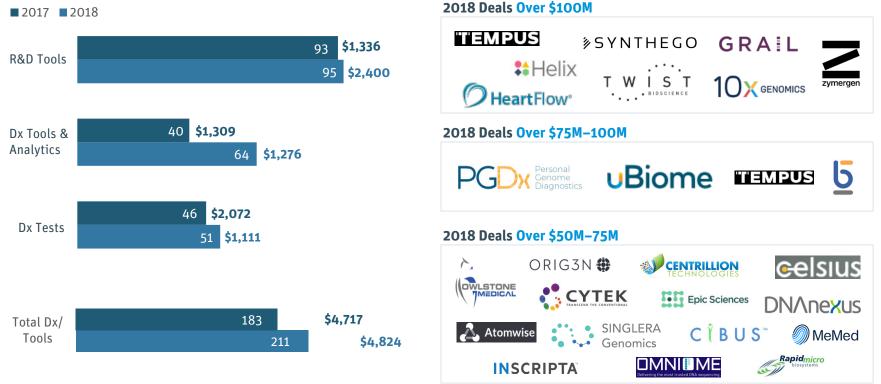
Top investors with 3+ Series A investments were: Keiretsu Forum (Dx Tests, R&D Tools [R&D]), Alexandria Venture Investments (R&D), 8VC (R&D), AME Cloud Ventures (R&D), Alumni Ventures (Dx Tools and Analytics [Analytics]), Data Collective (R&D), ARCH Venture Partners (Analytics), Civilization Ventures (R&D), Genoa Ventures (R&D) and Refactor Capital (R&D).

The top investors with 3+ Series B or later investments were: Charles River Ventures (Analytics), Illumina Ventures (R&D), GV (Analytics), Foresite Capital (R&D, Analytics), Baidu (R&D), Khosla Ventures (Analytics, Dx Tests), Northpond Ventures (R&D, Analytics) and OS Fund (R&D).

These investors funded fewer Dx Tests deals, as many of these companies raised their next round from nontraditional investors.

Investments in Dx/Tools Steady Dx/Tools by Subsector, 2017–2018, US and Europe

NUMBER OF DEALS | \$ MILLIONS



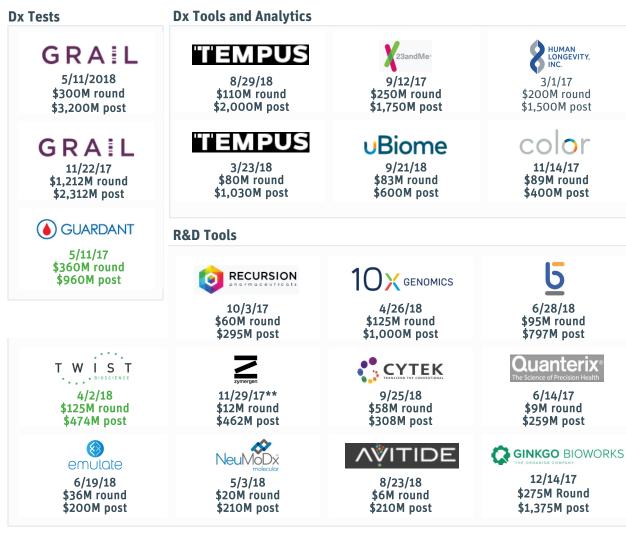
Stable investment in Dx/Tools continued in 2018, with nontraditional investors leading later-stage deals.

Twenty-five \$50M+ deals made up the majority of sector financing. Multiple private equity (PE) and asset managers participated in large rounds for venture-backed investments, including deals for Grail, Zymergen, Tempus, 10x, Synthego and Twist Bioscience. Dx Tests showed stable deal numbers with decreased investment. This could be attributed in part to the \$900M difference between Grail's \$1.2B Series B in 2017 and its \$300M Series C in 2018.



Financing data includes private financings by venture-backed companies in US and Europe. 2018 financing data through 12/15/18. Dates of financing rounds subject to change based on add-on investments. Source: PitchBook and SVB proprietary data.

Dx/Tools Attract High-Value Private Dollars Dx/Tools Post-Money by Indication, 2017–2018



This list is composed of the highest-valued private companies over the last two years, all with post-money valuations of \$200M or more*.

Dx/Tools had six deals with private valuations over \$1B double the number of private Biopharma unicorns. However, Dx/Tools trailed biopharma in 2018 M&As (10 versus 14) and IPOs (two versus 54).

The two IPOs on this list have since traded up in the public market.

A number of profiled companies have unique platform technologies and service models, which could set them up as potential 2019 IPO candidates.

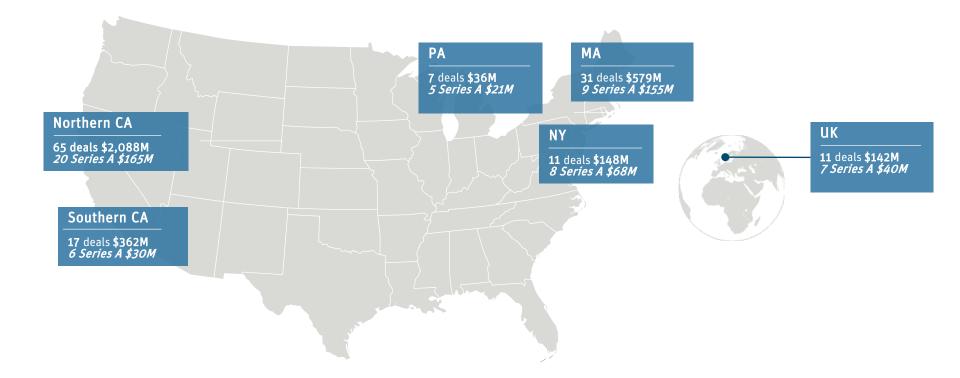
Green text: Company subsequently went public



*Only includes post-money values reported by PitchBook. Dates of financing rounds subject to change based on add-on investments. 2018 financing data through 12/15/18. **Zymergen's new \$400M financing on 12/13/18 did not disclose valuation. Source: PitchBook and SVB proprietary data.

Northern California Still Front Runner in Dx/Tools Dx/Tools Investments by Geography, 2018, US and Europe

Top Dx/Tools Regions for All Investments and Series A





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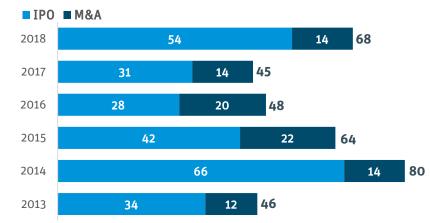


Healthcare M&As and IPOs: **Record IPOs, M&A Exits and Deal Values**



Biopharma M&A Steady, IPOs Up VC-backed Biopharma Big Exits & IPOs, 2013–2018

A Number of Exits by Year



[A] Biopharma total deal value more than doubled in 2018. Public IPO market caps contributed 70% to this number, setting a record total deal exit value of \$49B+. This was punctuated by the \$7B+ IPO by Moderna in December.

Fifty-four IPOs yielded five-year highs in both pre-money valuations and dollars raised.

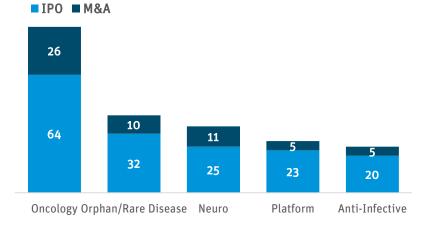
[B] M&A activity was steady, with four private acquisitions valued at over \$1B.

[C] Oncology continues to dominate biopharma exits, while platform and anti-infective IPOs increased.

B Exit Values by Year



C **Top Exits by Indication** 2013–2018

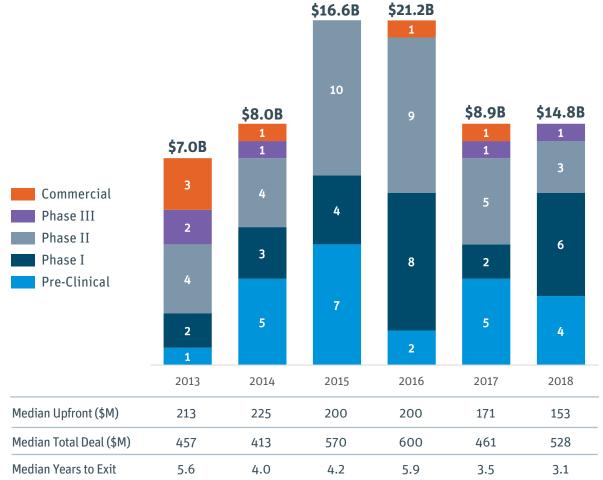




M&A defined as private, venture-backed M&A with upfront payments of at least \$75M. IPO defined as private, venture-backed IPO raising at least \$25M in proceeds. Market cap at IPO used to estimate value of public companies. Source: PitchBook, press releases and SVB proprietary data.

Early-Stage Deals Deliver Strong Biopharma M&A VC-Backed Biopharma Big Exit M&A by Stage*, 2013–2018





M&A defined as private, venture-backed M&A with upfront payments of at least \$75M. Upfront multiple is M&A payment received at deal close divided by venture investment. *Stage defined as last completed clinical trial in most advanced asset.

Attractive IPO valuations have pushed many companies to spurn early M&A, raise large crossover rounds, and pursue IPOs. Our data indicates a bifurcated exit pathway – raise large dollars and go public or use smaller dollars and pursue an early M&A.

Ten of 14 M&A deals were pre-clinical or phase I companies. These deals had a median time-to-exit of just 2.9 years, as acquirers added early-stage technologies to their pipelines. Smaller dollars invested (with a median of \$17M) and very early clinical data produced smaller deal sizes at exit. Still, these exits delivered strong median upfront multiples of 5.4x and total deal multiples of 22x.

Venture-backed oncology M&A fell into two groups: big pharma single-asset spinouts and immuno-oncology companies with multiple assets. The only late-stage oncology exit (Impact) produced a \$1B upfront payment. Pre-clinical and phase I exits were smaller (\$100M-200M upfront) but came through with a remarkable median upfront multiple of 8.5x.

After relatively small venture investments, two of three orphan/rare M&A deals (Agilis at \$100M upfront and Celenex at \$200M) were bought by Amicus and PTC (formerly venture-backed and now public acquirers). Syntimmune raised more funding and was acquired in a strategic expansion by Alexion for \$400M upfront.

BMS and Celgene each bought 4 venture-backed companies since 2015, plus Juno. With a very active, diverse biopharma acquirer group, we believe the potential merger will not have a significant impact on venture M&A in 2019.



Source: PitchBook, press releases and SVB proprietary data.

Dynamic Biopharma IPO Scene Driven by Crossovers VC-backed IPOs by Pre-Money Valuation and Dollars Raised, 2013–2018



2018 biopharma public market was hot, as IPOs nearly doubled their 2017 numbers with a record \$325M median pre-money valuation.

Private crossover-led rounds continued as IPO precursors. Of the 2018 IPOs, 69% included Top-15 Crossovers as private investors, with median financing (at the last private round) of \$64M and a median 1.3x valuation step-up. We have noted that IPOs with these crossovers have the best and most stable access to capital going forward in the public market. Top 15 Crossovers continued to back venture deals, funding 60 unique companies in 2018 and almost doubling 2017's activity. This indicates their optimistic IPO view.

Biopharma IPO activity is expected to continue in 2019 as crossovers replenished pipelines in 2018, but likely at a reduced rate.

2018 IPOs By Top Indications

Indication	Number of Deals	% Early Stage	Median Last Round Size	Median Step-Up at IPO*
Oncology	16	63%	\$80M	1.2x
Platform	14	50%	\$65M	1.0x
Orphan/Rare	7	57%	\$61M	1.5x



IPO defined as private, venture-backed IPO raising at least \$25M in proceeds.

*Pre-money IPO valuation divided by last round post-money valuation. Private valuations sourced through PitchBook.

Source: PitchBook, press releases and SVB proprietary data.

Unicorns* Flourished in 2018 \$1B+ VC-Backed M&A and Current IPO Public Values, 2013–2018



2018 IPOs used strong valuations and compelling clinical data to fuel speedy growth to unicorn status, resulting in the most unicorns of any IPO class of the last six years. M&A was split between private and public with Armo Biosciences going public and then being bought five months later for \$1.6B.

Overall, the number of \$1B+ public companies increased by three in the second half of 2018 (notwithstanding an underperforming December). We did observe some downward movement from previous years with four companies from the IPO class of 2014, and two each from IPO classes 2016 and 2017 dropping off the list.

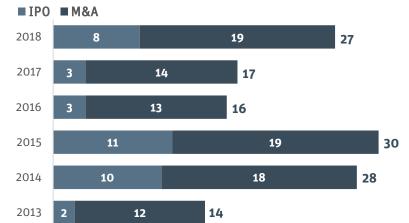


*Unicorn defined as a venture-backed company since 2013 that achieved an M&A with \$1B+ total deal value or is a public company (IPO since 2013) valued at \$1B+ as of 12/15/18.

Source: PitchBook, press releases and SVB proprietary data.

Device M&A Activity Rallies over Last Two Years VC-Backed Device Big Exits & IPOs, 2013–2018

A Number of Exits by Year



[A] Led by an active Q3 with nine M&As and two IPOs, device exits rallied following a flat performance in 2016 and 2017, logging 27 M&A and IPO exits in 2018.

[B] For the first time, total venture-backed device M&A upfront payments eclipsed other sectors with \$3.6B.

[C] There was a better public appetite for device, evidenced by eight IPOs. These were led by four neuro-focused companies: Inspire and Axonics (implantables) and Neuronetics and Electrocore (non-invasive therapies).

B Exit Values by Year

\$ BILLIONS



M&A defined as private, venture-backed M&A with upfront payments of at least \$50M. IPO defined as private, venture-backed IPO raising at least \$25M in proceeds. Market cap at IPO used to estimate value of public companies. Source: PitchBook, press releases and SVB proprietary data.

C Device IPO Activity

Year	Number of IPOs	Median Pre-Money Value	Median \$ Raised
2018	8	\$217M	\$86M
2017	3	\$59M	\$26M
2016	3	\$164M	\$75M
2015	11	\$156M	\$77M

Strong Values/Multiples Supercharge Device Deals VC-Backed Device Big Exit M&A by Stage*, 2013–2018

Number of Big Exits



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M&A defined as private, venture-backed M&A with upfront payments of at least \$50M. Upfront multiple is M&A payment received at deal close divided by venture investment. *Stage defined as last completed clinical trial in most advanced asset. Source: PitchBook, press releases and SVB proprietary data. At \$190M, 2018 had the largest median upfront device payment since 2013 and a healthy 4.3x multiple on capital invested.

Four oncology M&As took center stage in 2018, focused on guidance/marking systems (Cianna, Focal), protection (Augmenix), and a cell collection device (nVision). All four deals were commercial stage, with median upfront value of \$143M and a 7.5x multiple.

Cardiovascular and orthopedics also had four exits, followed by vascular with three and noninvasive monitoring with two.

Boston Scientific led M&A, acquiring seven venture-backed companies in 2018. Boston also announced it will buy BTG (a large public company). We will monitor Boston's activity, as big acquisitions like this historically have led to reduced M&A, as evidenced by Medtronic and Abbott (prolific acquirers in years past) remaining on the sidelines following large mergers. Medtronic's acquisition of a small public company in 2018 (Mazor) could portend this giant's return to venture M&A.

We are optimistic that 2019 M&A activity will be robust, as new acquirers Teleflex and LivaNova and stalwarts like J&J continue to be active. New acquirers (like Penumbra, Massimo, Avanos and Siemens Healthineers) could emerge as they look to add to product lines and stock their R&D pipeline.

De Novo Exit Values Shine

VC-Backed Device M&A by Pathway, 2015–2018

2015–2018	Stage at Exit	Median Invested (\$M)	Median Upfront (\$M)	Median Upfront Multiple	Median Total Deal (\$M)	Median Total Deal Multiple	Median Time to Exit (Years)
510(k) M&As 34 Exits	32 1 1	\$46	\$110	3.0x	\$128	3.6x	8.9
De Novo 51O(k) M&As 4 Exits	4	\$46	\$360	4.6x	\$435	6.1x	8.8
PMA M&As 26 Exits	3 10 13	\$39	\$215	4.0X	\$320	6.6x	6.1
Biopharma M&As 70 Exits	31 39	\$35	\$198	4.5x	\$557	12.5x	4.2
	FDA-Approved CE Mark Only Development Stage > Phase I ≤ Phase I						

While all 2018 510(k) exits had FDA clearances and revenue ramps, four of six PMA deals were acquired prior to FDA approval: two at development stage and two holding CE marks. 510(k) exit values typically are smaller than PMA and De Novo exits, but we did see 2018 median upfront deal sizes grow to \$135M with a 4x median multiple.

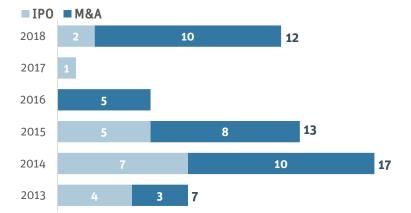
2017 saw one De Novo 510(k) company exit, and 2018 tripled that number. All the deals were US commercial, having raised capital for further commercialization and revenue ramp-up. Longer exit times make these M&As similar to 510(k) deals, however. De Novo deals showed very successful outcomes with median upfront and total deal value numbers exceeding those of 510(k) and PMA.



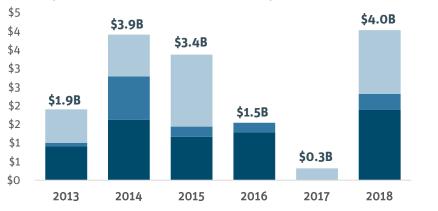
M&A defined as private, venture-backed M&A with upfront payments of at least \$50M. 510(k) is an FDA classification that provides clearance to market typically without clinical trials. De Novo 510(k) is a classification that provides approval to market but typically requires clinical trials. PMA is a classification that provides approval to market but typically requires pivotal clinical trials to collect safety and effectiveness data. Source: PitchBook, press releases and SVB proprietary data.

Dx/Tools Come Back in 2018 VC-Backed Dx/Tools Big Exits & IPOs, 2013–2018

A Number of Exits by Year



B Exit Values by Year \$ BILLIONS



■ M&A Upfront ■ M&A Milestones ■ IPO Market Cap

[A] Dx/Tools activity increased from one to 12 total exits in 2018. Deal value set a six-year record, led by \$1.9B in upfront M&A payments.

[B] Two successful late-year IPOs contributed \$1.7B in IPO market cap (close to 50% of total deal value) and could jump-start IPO interest in the sector.

Guardant Health (a liquid biopsy company that helps determine cancer treatment and is also developing an early cancer detection test), raised \$500M+ in private funding. The company then raised \$230M+ in an IPO with a market cap of \$1.6B and 1.5x step-up from its last private round. Guardant opened trading up over 40% and has continued to perform well, more than doubling its initial market cap*.

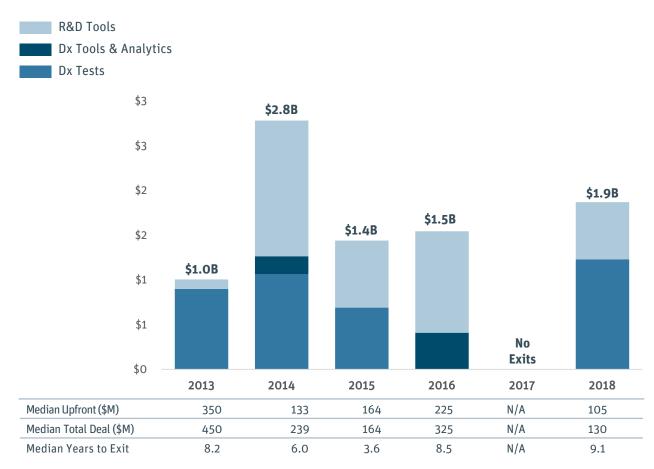
Twist Bioscience, an R&D Tools company with over \$250M in private funding, raised \$86M in an IPO at a modest discount to the last private round. The company offers precise DNA manufacturing at scale. Its initial IPO market cap was \$372M, which has since risen almost 50%.



M&A defined as private, venture-backed M&A with upfront payments of at least \$50M. IPO defined as private, venture-backed IPO raising at least \$25M in proceeds. Market cap at IPO used to estimate value of public companies. *Market Cap as of 12/15/18. Source: PitchBook, press releases and SVB proprietary data.

Dx/Tools Activity Strong, Yet Dollars Trail VC-Backed Dx/Tools Big Exit M&A, 2013–2018

Number of Big Exits



2018 Dx/Tools M&A activity was tremendous; still median upfront investment and total deal size significantly trailed other sectors. Nine of 10 deals were at a commercial stage and acquired by traditional lab instrument, research and diagnostic companies. We are surprised to see no new acquirers, especially tech players, emerge.

M&A was divided between Dx Tests (four deals) and R&D Tools (six deals). Three of the four Dx Tests companies were commercial.

Dx Tests exits STAT-Dx and Counsyl are building technology applicable to multiple diseases, and Astute and Exosome are focused on diseasespecific diagnostics capabilities.

The majority of R&D Tools companies were focused on sequencing technologies. Agilent, seeking to bolster their drug discovery efforts, was the only acquirer with multiple deals when they bought LaserGen and Acea.



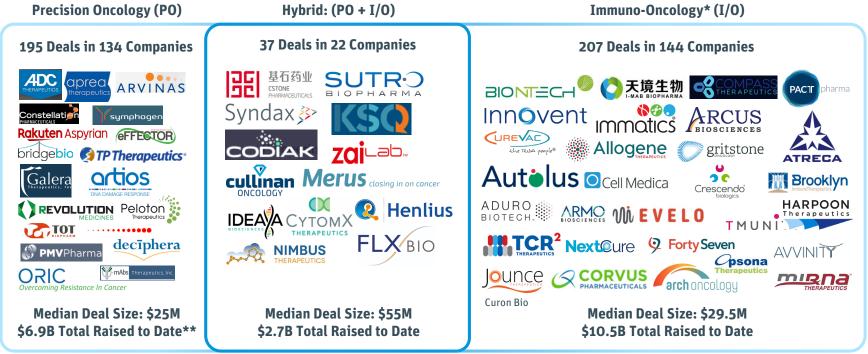


Biopharma Deep Dive: Oncology Investments and Exits



Hybrid Companies Find Largest Deals, Step-Ups Private Venture-Backed Oncology Financings, 2015–2018

Oncology financings can be categorized into precision, immuno, and hybrid (which contain both types).



Logos: Companies with \$100M+ Raised to Date

Oncology dominated biopharma funding over the last four years, raising over \$20B.

I/O funded a similar number of companies as PO, but deal size was 50% greater. Hybrid, which typically has a broader pipeline of both PO and I/O assets, had the largest median deal size. This funding is likely to help with multiple clinical trials.

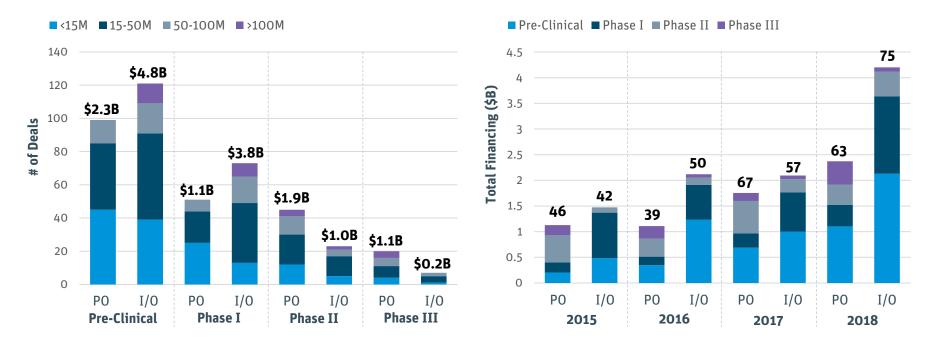
Companies with hybrid pipelines saw a phenomenal 2.9x median step-up valuation from Series A (PO: 1.7x, I/O: 1.4x).



*I/O companies have the following modalities: cell therapy, oncolytic viruses, checkpoint inhibitors, immunostimulation. PO defined as all other oncology modalities.
**Includes financing raised prior to 2015
Sources: PitchBook and SVB proprietary data.

Pre-Clinical Companies Dominate Funding Private Venture-Backed Oncology Financings, 2015–2018

Financing in I/O* has consistently outpaced PO by clinical stage through the years



I/O deals comprised 15 of 22 companies that raised \$100M+ rounds, with more than 50% completed in 2018. While these deals typically are preludes to an IPO, only five of the 22 have gone public to date. China companies are especially active, with seven of these 22 companies based in China and six \$100M+ deals closed in 2018, including CStone Pharmaceuticals, Curon Biopharmaceutical, Henlius, I-Mab Biopharma, Innovent Biologics and TOT Biopharma.

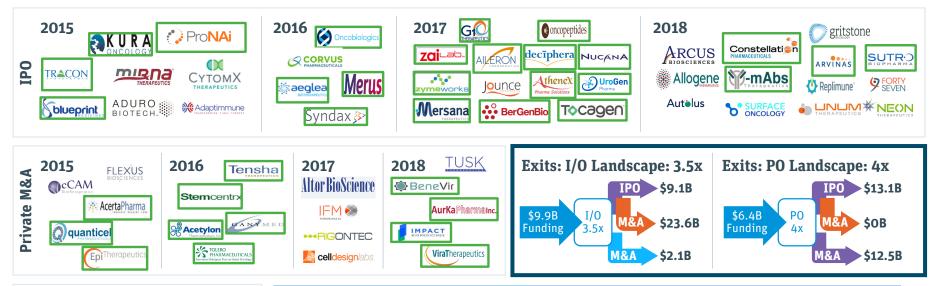
2018 showed a period-high in financing amount and volume. The majority of deals have been early stage, with \$7.1B invested into preclinical companies. With so many companies pursuing early-stage clinical trials, a potential issue will be patient enrollment.



*I/O companies have the following modalities: cell therapy, oncolytic viruses, checkpoint inhibitors, immunostimulation. PO defined as all other modalities. For this slide, Hybrid companies are categorized into PO or I/O based on most advanced asset. Sources: PitchBook and SVB proprietary data.

Oncology Exits Show 3x+ Multiple vs. Investment Private Venture-Backed Oncology Exits, 2015–2018

I/O* excels in public M&A while PO performs strongly in private M&A.





I/O and PO venture-backed exits (either current public market cap or upfront payments in an M&A) both achieved great multiples versus private dollars invested from 2015 to 2018. I/O showed a 3.5x on dollars invested and PO was 4x, signaling that even with significant investment investors can find good returns.

IPO data since 2015 shows that I/O and PO companies go public at different clinical stages. Thirteen out of 15 I/O IPOs were early-stage (pre-clinical or phase I), while 16 out of 25 PO IPOs were later-stage (phase II and later).

Returns were dominated by a few big M&A deals. PO returns were driven by two large private M&A deals, with monster upfront payments from Stemcentrx (\$5.8B) and Acerta Pharma (\$4B). I/O retur<u>ns were led by public market</u> M&A with huge deals from Kite Pharma (\$12B) and Juno Therapeutics (\$9B). While exit values look promising, the sheer number of companies financed since 2015 translates into an uphill battle to achieve one of these amazing exits. Still, we expect more of these exits in the coming years from a very promising class of venture investments.

Green boxes denote PO companies

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*I/O companies have the following modalities: cell therapy, oncolytic viruses, checkpoint inhibitors, immunostimulation. PO defined as all other modalities. Funding values are total deal sizes from 2015 to 2018, IPO values are total market cap at 12/15/18; M&A values are total upfront payments. For this slide, Hybrid companies are categorized into PO or I/O based on most advanced asset. Sources: PitchBook and SVB proprietary data.

2019 Outlook

- We anticipate total investment into life science to continue at a healthy pace, reaching about \$8B, with established funds likely to be joined by new spinout funds anchored by established investors. In addition, tech firms may raise life science–only sister funds.
- Top 15 Crossover investment in venture-backed companies could soften by 25 percent or more, leading to biopharma investments decreasing to more closely match 2017 numbers.
- The biotech IPO pipeline is strong, but market uncertainty could drag IPOs down to 30 to 35 deals and moderately reduce pre-money valuations and dollars raised. As a result, we expect an increase in private biopharma M&As.
- Device investments are expected to be stable with additional growth in Series A. A strong performing group of later-stage, venture-backed companies shows promise for up to eight device IPO opportunities in 2019. We don't expect much change in device M&A activity from 2018.
- Dx/Tools Series A deals will likely climb in 2019, although overall investment dollars could lag following multiple larger 2017 and 2018 financings. Tech acquirers will likely scoop up a few Dx Tests and Dx Tools and Analytics companies, which could spur an uptick in M&A deal value. Also, we anticipate there could be two to four IPOs of revenue-generating R&D Tools companies.



Glossary

Big Exits

Big Exits defined as a private, venture-backed merger and acquisition in which the upfront payment is \$75 million or more for biopharma deals and \$50 million or more for device and Dx/Tools deals.

Initial Public Offering

IPO defined as a venture-backed company raising IPO proceeds of \$25 million or more.

Deal Descriptions

Structured Deal defined as a pay-for-performance acquisition where some of the deal value is paid upfront when the deal closes, but also contains additional value based on milestones that must be achieved.

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

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 any 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

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

Series A

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.

Device Regulatory Definitions

Non-approved defined as a device product that has no regulatory clearance or approval for its product.

CE Mark Only 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.

510(k) defined as an FDA classification that provides clearance to market typically without clinical trials.

De Novo 510(k) defined as an FDA classification that provides approval to market but typical requires clinical trials.

PMA defined as an FDA classification that provides approval to market but typically requires pivotal clinical trials to collect safety and effectiveness data.

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

Indication Definitions

Neurology (neuro) defined as CNS, pain and psychology companies, as well as neuro implant technologies.

Non-Invasive Monitoring defined as medical data collection through sensors and other technology.

Dx Tests defined as proprietary Yes/No diagnostic tests.

Dx Tools and Analytics defined as actionable data analytics to help determine/direct treatment.

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

Top 15 Crossover Investor

Top 15 Crossover Investor defined as a public-minded investor who strategically invests in private companies. The top 15 list includes: Casdin Capital, Cormorant Asset Management, Deerfield Management, EcoR1 Capital, Fidelity Investments, Foresite Capital Management, Perceptive Advisors, RA Capital Management, Redmile Group, Rock Springs Capital, Softbank, T. Rowe Price, Viking Global Investors, Wellington Management and Woodford Investment Management.



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Thomas Joyce Senior Associate Silicon Valley Bank tjoyce@svb.com As a Managing Director, Jonathan Norris spearheads strategic relationships with many healthcare VC firms. In addition, he helps SVB Capital through sourcing and advising on limited partnership allocations and direct investments.

Jonathan speaks at major investor and industry conferences and authors widely cited analyses of healthcare VC trends. He has 18+ 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.

Andrew is a Senior Manager in San Francisco focused on early-stage biopharma companies. He manages SVB's thought-leadership team.

Before joining SVB, Andrew was a Management Consultant at ZS Associates, where he focused on forecasting, pipeline strategy and market research for pharmaceutical and biotech companies. He holds a B.A. in chemistry from Carleton College in Northfield, Minnesota, and a Ph.D. in chemistry from the University of California, Berkeley.

As a Healthcare Consultant, Ritish Patnaik helped develop SVB's Deep Dives of the Dx/tools, synthetic biology and oncology biopharma subsectors. He also helped analyze data sets, generate slides and put together takeaways for investment trends presented in this report.

Ritish is pursuing a Ph.D. in bioengineering at Stanford University where he is using bioinformatics and magnetics to create a liver cancer liquid biopsy test. He is a co-founder of Luso Labs, a startup that brings affordable cervical cancer screening worldwide. Ritish earned a B.S. in Biomedical Engineering at Columbia University and an M.S. in management science and engineering from Stanford University.

Thomas Joyce is a Life Science Senior Associate based in Boston, where he focused on diagnostics and tools.

Joyce was previously a Senior Associate in SVB's commercial bank, focused on financial analysis, portfolio management, business development and underwriting of complex credit transactions. Prior to SVB, Joyce was responsible for originating and analyzing private equity transactions for KamylonCapital, a principal investment firm. Joyce earned a bachelor's degree in finance with a minor in economics from Suffolk University's honors program, graduating summa cum laude and as a member of the Beta Gamma Sigma Honors Society.



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