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Mid-Year 2018 Highlights: Investments
Pioneering Innovations, Drug Development Create Investor Excitement

• At mid-year, U.S. healthcare venture fundraising reached $4.5 billion, and is on pace to closely match the 2017 record of $9.1 billion.

• Investments in VC-backed biopharma continued to surge, while device remained stable. Dx/Tools investing decreased. Full-year 2018 investment in venture life science companies likely will reach a new high, surpassing the record $17.3 billion invested in 2017.

• Biopharma Series A investments are exploding, and by mid-year reached $2.6 billion – compared to the full-year total of $2.3 billion in 2017.

• By indication, investor interest is driving biopharma platform companies to levels similar to oncology, and orphan/rare deals are making a comeback.

• Underscoring robust pre-IPO biopharma valuations, step-ups from Series A to B have seen 2x to 3x increases in the past 18 months.

• Non-invasive monitoring and imaging companies are driving investments in Series A device companies.

• While device pre-money valuations also have seen large step-ups from Series A to B, Series D valuations are flat or down rounds.

• Investment in Dx/Tools overall is lagging in 2018, dragged down by a large drop in Dx Tests deals.

• On the bright side, R&D Tools saw 20 deals from the most active investors by mid-year, representing 60% of all dollars invested in Dx/Tools in 1H 2018.

• Investments in synthetic biology building blocks, including computational design, CRISPR editing, DNA/RNA synthesis and organism engineering tools, have climbed in 2017 and 2018.

• These companies are revolutionizing the field of synthetic biology with hardware and biochemical advances in DNA/RNA synthesis.
Mid-Year 2018 Highlights: Exits
Biopharma IPOs Are Poised to Blow Past 2017 Numbers

- 75 VC-backed biopharma unicorns have reached valuations of $1 billion or higher since 2013 – either through acquisition or in the public markets. This year is shaping up to be another strong year. These biopharma exits are creating the momentum for strong fundraising and investment.
- In 1H 2018, 30 biopharma companies went public – compared to 31 IPOs for all of 2017.
- Biopharma M&A is slowing, as larger rounds and higher valuations make early-stage M&A less appealing.
- Instead, companies looking to go public are replenishing the biopharma IPO queue. This is fueled by large pre-money IPO valuations driven by continued top crossover investor activity.
- Device M&A is stable, but the IPO market is favoring neuro-focused companies, with three IPOs in 1H 2018.
- PMA/De Novo pathway companies continue to achieve better M&A values, higher multiples and faster times to exit than 510(k) companies.
- However, over the last two years, 510(k) device values and multiples have increased.
- Dx/Tools M&A activity is increasing, but these deals have lower upfront values and longer times to exit.
- There are many later-stage Dx/Tools companies that are shaping up as acquisition candidates, with 25 still-private companies valued at $150 million or higher.
Healthcare Investments and Fundraising: Biopharma Advancements Drive Investor Activity
U.S. HC Venture Fundraising Stays on Torrid Pace
U.S. Healthcare Venture Fundraising*, 2009 – 2018

HC VC $ Fundraised
($ BILLIONS)

Fundraising is on pace to match the 2017 total of $9.1B – counter to our early 2018 prediction that the annual total would decline. A confluence of events is driving investment and fundraising to new levels. Rapid technological advances, leading to clinical breakthroughs, are benefiting patients and investors alike. In this environment, quick exits are underpinning an explosion of activity, particularly in biopharma, attracting new pools of capital and giant investments by traditional and non-traditional investors, including tech investors.

With the entry of artificial intelligence (AI) and machine learning (ML), these tech investors see huge opportunities in drug development and the tools required to help identify cures for a range of diseases.

The biopharma IPO window is rewarding investors with quick valuation step-ups (many companies had IPOs within two to three years of Series A). This path to liquidity is translating into renewed excitement by limited partners who are eager to keep the investment cycle going by supporting larger venture fundraises at a faster pace.

*SVB calculates only the dollars allocated to healthcare by U.S. venture funds or funds investing primarily in the U.S.
Source: PitchBook and SVB proprietary data.
Biopharma Series A Deals Set Blazing Pace
U.S. Series A Biopharma Investments, 2016 – 1H 2018

Series A Deals

<table>
<thead>
<tr>
<th></th>
<th>2016*</th>
<th>2017*</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Investments</td>
<td>122</td>
<td>128</td>
<td>77</td>
</tr>
<tr>
<td>Total Series A Funding ($M)</td>
<td>$2,299</td>
<td>$2,259</td>
<td>$2,632</td>
</tr>
<tr>
<td>Corporate Investments (%)</td>
<td>26%</td>
<td>31%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Series A by Indication

- **Oncology**: 36, 32, 19 - $2,362M
- **Platform**: 18, 19, 17 - $1,395M
- **Orphan/Rare Disease**: 14, 12, 11 - $987M
- **Neuro**: 16, 12, 6 - $650M
- **Anti-Infective**: 5, 9, 3 - $281M

2017 Median Series A Funding by Quarter ($M)

- 2017Q1: $19.1
- 2017Q2: $6.9
- 2017Q3: $5.9
- 2017Q4: $11.0

2018 Median Series A Funding by Quarter ($M)

- 2018Q1: $8.0
- 2018Q2: $32.5

By mid-year, biopharma Series A investments reached $2.6B, already surpassing the full-year 2017 total. The activity was punctuated by a total of $1.8B invested in 15 big-money deals. Four deals each raised $250M+ (Allogene, Harmony, Viela and Cellularity), and an additional 11 deals each raised $50M+. Series A investment is on pace to reach 150 deals in 2018. Tech, angel and incubator/accelerator investors drove Q1 deal-making. Large venture healthcare syndicates (with corporates) led Q2 activity in fewer deals, driving up the Q2 2018 median deal value to more than $30M.

Venture and Crossovers Lead Biopharma Activity
Most Active New Investors* in Biopharma, 2017 – 1H 2018

# OF DEALS

26
20
17
15
13
12
11
10
9
8
7

New investors joining the most active list include 5AM, 6 Dimensions, HBM, Third Rock, Versant and crossovers RA Capital and Rock Springs.

By indication, the most active investors in platform companies were Arch, Orbimed and Third Rock (4+ deals each), in oncology were 6 Dimensions, Celgene, GV, Orbimed, Osage, Versant and Vivo (4+ deals each) and in orphan/rare were 5AM, Orbimed and RA Capital (3+ deals each).

*Most Active New Investors in biopharma defined as Top 60 venture and corporate investors based on new investments in 2016–2017. Financing data through 6/15/18. Platform companies have technologies with multiple or non specified indications. Source: PitchBook and SVB proprietary data.
Oncology and Platform Deals Capture Most Interest

Most Active New Investments* in Biopharma by Indication, 2017 – 1H 2018

| # DEALS | $ MILLIONS |
|----------------------------------------|
| **Early Stage** | **Late Stage** | **Undesignated** |
|--------------------------------------------------|
| Oncology | 44 | 7 | 4 | $2,486M |
| Platform | 30 | 3 | 1 | $2,276M |
| Orphan/Rare Disease | 18 | 3 | 1 | $907M |
| Neuro | 13 | 3 | 6 | $999M |
| Anti-Infective | 9 | 3 | 1 | $639M |
| Auto-Immune | 5 | 5 | 2 | $648M |
| Metabolic | 8 | 2 | | $286M |

Underscoring the recent influx of capital over the past two years from the most active investors, every top indication in 1H 2018 other than oncology has already surpassed investment levels for full-year 2016.

Waves of new biopharma investment are pushing funding for platform companies to levels similar to oncology and driving a comeback for orphan/rare drugs.

*Most Active New Investments in biopharma defined as Top 60 venture and corporate investors based on new investments in 2016–2017. 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. Financing data through 6/15/18. Source: PitchBook and SVB proprietary data.
Robust IPOs Lead to Soaring Private Valuations
Series A/B Deals, Size and Valuation by Most Active Investors*, 2013 – 1H 2018

Median Round Size by Series

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A</td>
<td>14.3</td>
<td>22.8</td>
<td>22.0</td>
<td>28.7</td>
<td>28.6</td>
<td>46.0</td>
</tr>
<tr>
<td>Series B</td>
<td>25.5</td>
<td>28.5</td>
<td>42.2</td>
<td>44.9</td>
<td>44.0</td>
<td>58.0</td>
</tr>
</tbody>
</table>

Round sizes by the most active investors have exploded in 1H 2018. This has been led by top 15 crossover investors, who have shifted from later stage (Series C/D) to earlier stage (Series A/B) with the expectation of quick IPOs. For IPOs involving top 15 crossover investors, it took a median 7.5 months from their last private financing to go public.

Median 2-Year Series A to Series B Step-ups

<table>
<thead>
<tr>
<th>Year</th>
<th>2014-2016</th>
<th>2015-2017</th>
<th>2016-1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A - Series B</td>
<td>0.8</td>
<td>3.2</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Higher pre-money IPO valuations are leading to larger step-ups from Series A to B, allowing companies to raise more money and increase valuations. Series A to B valuation step-ups have soared to 3.2x in 2017 and 2.3x in 1H 2018.

*Most Active Biopharma Investors by Indication defined as Top 42 venture and corporate investors calculated as new (first-time) investments into companies. Crossover investors defined as public-minded investors who opportunistically invest in private deals. Numbers denote median values. Financing data through 6/15/18. Source: PitchBook and SVB proprietary data.
Non-Invasive Monitoring Drives Device Series A
U.S. Series A Device Investments, 2016 – 1H 2018

Series A Deals

<table>
<thead>
<tr>
<th></th>
<th>2016*</th>
<th>2017*</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Investments</td>
<td>60</td>
<td>59</td>
<td>37</td>
</tr>
<tr>
<td>Total Series A Funding ($M)</td>
<td>$284</td>
<td>$333</td>
<td>$232</td>
</tr>
<tr>
<td>Corporate Investments (%)</td>
<td>12%</td>
<td>21%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Series A by Indication

- **Non-Invasive Monitoring**: $120M
  - 2016: 4, 2017: 11, 2018: 7
- **Orthopedic**: $78M
  - 2016: 6, 2017: 8, 2018: 2
- **Neuro**: $86M
  - 2016: 5, 2017: 7, 2018: 2
- **Cardiovascular**: $79M
  - 2016: 5, 2017: 3, 2018: 4
- **Imaging**: $45M
  - 2016: 3, 2017: 4, 2018: 5
- **Ophthalmology**: $29M
  - 2016: 7, 2017: 2, 2018: 1

Series A Corporate Investors: 2017 – 1H 2018

- **HC Insurers/Providers**
  - Partners Healthcare
  - Innovation BlueCross BlueShield
  - Wellmark
  - MGH
  - Ascension Ventures

- **Medical Device**
  - MicroPort
  - Intuitive Surgical

- **Digital/Wellness/NIM**
  - Bose Ventures
  - Kofa
  - Merck Ventures

- **Biopharma**
  - Senju

Device Series A in 1H 2018 is slightly ahead of the 2017 pace, measured by deals and dollars. Hospital digitization technologies offered by non-invasive monitoring and imaging companies are driving 1H 2018 Series A activity. However, neuro-focused companies lagged. Since 2017, health insurers/providers and Chinese companies have led corporate investments in Series A device. J&J is the only traditional corporate to do a Series A deal since 2017, completing 3 early-stage investments.

Traditional Venture Investors Support Device
Most Active New Investors* in Device 2017 – 1H 2018

# OF DEALS

- KEIRETSU
- F O R U M
- FundRx
- Emergent Medical Partners
- SV TECH Ventures
- Boston Scientific
- Johnson & Johnson
- KCK
- Aperture Venture Partners, LLC
- Innogest
- NEA
- OrbiMed
- SightLine Partners

New Enterprise Associates and Aperture Venture Partners join the most active new investor list. Early-stage groups like Keiretsu and FundRx are aggregating angel interest when approaching device investments. Corporate investor activity has declined. The most active corporate investors, J&J and Boston Scientific, are also major acquirers.

**Device Investing Stays Consistent**

**Most Active Device Investors by Indication*, 2017 – 1H 2018**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Early Stage</th>
<th>Late Stage</th>
<th>Undesignated</th>
<th>Total Deals</th>
<th>Total Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>10</td>
<td>$338M</td>
</tr>
<tr>
<td>Neuro</td>
<td>4</td>
<td>3</td>
<td></td>
<td>7</td>
<td>$182M</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>5</td>
<td>2</td>
<td></td>
<td>7</td>
<td>$149M</td>
</tr>
<tr>
<td>Surgical</td>
<td>3</td>
<td>4</td>
<td></td>
<td>7</td>
<td>$76M</td>
</tr>
<tr>
<td>Metabolic</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>$219M</td>
</tr>
<tr>
<td>Vascular</td>
<td>4</td>
<td>1</td>
<td></td>
<td>5</td>
<td>$84M</td>
</tr>
<tr>
<td>Non-invasive</td>
<td>2</td>
<td>2</td>
<td></td>
<td>4</td>
<td>$100M</td>
</tr>
<tr>
<td>Monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENT</td>
<td>1</td>
<td>2</td>
<td></td>
<td>3</td>
<td>$200M</td>
</tr>
<tr>
<td>Aesthetics/Dermatology</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>$73M</td>
</tr>
</tbody>
</table>

*Most Active Device Investors defined as Top 35 venture and corporate investors calculated as new investments into companies in 2016 – 2017.

Early Stage defined as Series A & B; Late Stage defined as Series C and later.

Financing data through 6/15/18.

Source: PitchBook and SVB proprietary data.

While active investor activity by indication is closely mirroring previous years, non-invasive monitoring (which has received a lot of early stage Series A interest) and drug delivery investment have not scaled as expected.

Three neuro IPOs and a pair of uro/gyn M&A deals may spur additional interest in those areas.
Device Round Sizes Increase as Later-Round Valuations Drop
Median Round Size and Valuations (Pre/Post) by Series, 2013 – 1H 2018

Median Round Size ($M) by Series 2013 – 1H 2018

<table>
<thead>
<tr>
<th>Series</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A</td>
<td>4.3</td>
<td>5.0</td>
<td>6.3</td>
<td>6.6</td>
<td>5.7</td>
<td>8.3</td>
</tr>
<tr>
<td>Series B</td>
<td>6.5</td>
<td>8.2</td>
<td>10.3</td>
<td>10.0</td>
<td>8.0</td>
<td>14.4</td>
</tr>
<tr>
<td>Series C</td>
<td>10.0</td>
<td>8.0</td>
<td>15.3</td>
<td>17.9</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>Series D</td>
<td>16.0</td>
<td>11.0</td>
<td>15.0</td>
<td>22.2</td>
<td>20.0</td>
<td>20.0</td>
</tr>
</tbody>
</table>

Median 2-Year Series/Series Step-ups 2013 – 1H 2018

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Series A - Series B</td>
<td>1.7</td>
<td>1.7</td>
<td>1.4</td>
<td>2.0</td>
</tr>
<tr>
<td>Series B - Series C</td>
<td>2.2</td>
<td>0.8</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Series C - Series D</td>
<td>0.6</td>
<td>1.1</td>
<td>1.2</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Device round sizes have increased for Series A-C, up 2x in 1H 2018 over 2013.
Series A to B valuation step-ups have recently reached as high as 2x. But Series C to D valuations are flat or down rounds, as later-stage investors may be bargain hunting with limited capital. This hampers returns for early-stage investors.

Medical device companies funded between 2013 and 1H 2018.
Source: PitchBook and SVB proprietary data as of 5/31/18
Dx/Tools Series A Activity Declines from Record 2017
U.S. Series A Dx/Tools Investments, 2016 – 1H 2018

Series A Deals

<table>
<thead>
<tr>
<th></th>
<th>2016*</th>
<th>2017*</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Investments</td>
<td>54</td>
<td>73</td>
<td>27</td>
</tr>
<tr>
<td>Total Series A Funding ($M)</td>
<td>$481</td>
<td>$548</td>
<td>$224</td>
</tr>
<tr>
<td>Corporate Investments (%)</td>
<td>21%</td>
<td>20%</td>
<td>17%</td>
</tr>
</tbody>
</table>

$5M+ Investments in 1H 2018

- **Streamlined Dx Tests**
  - Ultivue
  - ALVEC
- **NGS-Enabling Tools**
  - Archer
  - Roswell Genomics
- **Oncology-Focused**
  - NuProbe
  - SageMedic
- **Neuro-Focused**
  - NeuCyte
- **3D Tissue Bioprinter**
  - OxSyBio

Dx/Tools Series A funding and deals decreased in 1H 2018 after a strong 2017.

Dx Analytics companies had fewer deals but raised larger rounds in 1H 2018 with a median deal size of $18M.

AI/ML dominated $10M+ Series A deals in 2017 (7/13), but only had one deal at $5M+ (PAIGE.AI) in 1H 2018.

Dx Tests are yes/no tests. Dx Analytics provide more information for diagnosis/treatment. R&D tools advance researchers’ capabilities.
Financing data through 6/15/18.
Source: PitchBook and SVB proprietary data.
New Tech Investors Join Most Active Dx/Tools List

Most Active New Investors* in Dx/Tools, 2017 – 1H 2018

# OF DEALS

8

Khosla Ventures

6

Data Collective

5

Foresite Capital, Tencent

4

Alumni Ventures Group, Andreessen Horowitz

Corporate Investor

The list of tech-focused investors active in Dx/Tools is impressive: Andreessen Horowitz and Alumni Ventures Group in 1H 2018 joined return investors AME Cloud Ventures, Data Collective, Google Ventures, Khosla Ventures and Tencent. We anticipate new tech-focused venture and corporate investors to become more active as opportunities to leverage software-based big data solutions emerge.

*Most Active Dx/Tools Investors calculated based on new (first-time) investments into companies from 2017 to 1H 2018. Financing data through 6/15/18.
Source: PitchBook and SVB proprietary data.
Dx/Tools saw $801M in investments by the most active investors in 1H 2018, compared to $2.8B invested in full-year 2017.

Dx Analytics funding dropped to $322M with a focus on early-stage (seed and Series A/B). Dx Tests financing fell off the cliff from 2017, with just $52M in investments in 1H 2018; four big-money deals (including GRAIL and Guardant) pushed up investment totals in 2017.

On the bright side, R&D Tools soared to 20 deals, with investments totaling $427M. That represents more than half of 1H 2018 Dx/Tools funding. 34% of R&D Tools investments were in tools that accelerate synthetic biology research, as detailed in the following slides.

*Most Active Dx/Tools Investors calculated based on new investments into companies from 2017 to 1H 2018. Dx Tests are yes/no tests. Dx Analytics provide more information for diagnosis/treatment. R&D tools advance researchers’ capabilities. Financing data through 6/15/18.

Source: PitchBook and SVB proprietary data.
Large-scale synthetic biology is being simplified by innovations like CRISPR gene editing and machine learning. A new flood of therapeutics investment built around genome engineering is leveraging these groundbreaking technologies.

This analysis focuses on companies making these tools that do not have a clinical or agricultural/industrial product pipeline.

Buoyed by $100M+ investments in Zymergen, Twist Bioscience and Gingko Bioworks, sector financing has grown since 2015. While most investment has been in organism engineering, nucleic acid synthesis has dominated 1H 2018.

Computational design technologies provide data-backed suggestions for optimizing experiments and new molecules. CRISPR editing technologies simplify gene modifications.

DNA/RNA synthesis technologies create DNA/RNA. Organism engineering technologies introduce DNA/RNA or editing tools into cells or organisms.

Financing data through 6/15/18.

Source: PitchBook, press releases and SVB proprietary data.
SVB Deep Dive: Innovation in DNA/RNA Synthesis
Companies with Venture-Backed Deals, Total Raised to Date

<table>
<thead>
<tr>
<th>TOTAL RAISED TO DATE</th>
<th>HARDWARE ADVANCES</th>
<th>BIOCHEMICAL ADVANCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; $50M</td>
<td>TWIST BIOSCIENCE</td>
<td>greenlight BIOSCIENCES</td>
</tr>
<tr>
<td></td>
<td>High-Throughput, Silicon Platform that Reduces the Needed Volumes for DNA Synthesis Reactions</td>
<td>Utilizes Reusable Enzymes from Dead Cells to Produce RNA</td>
</tr>
<tr>
<td>$5–50M</td>
<td>evonetix</td>
<td>DNA SCRIPT</td>
</tr>
<tr>
<td></td>
<td>Pairs High-Throughput Silicon Platform with Error Detection and Annealing for Checking DNA Quality</td>
<td>Template-Free DNA Synthesis through Proprietary Enzymes</td>
</tr>
<tr>
<td>&lt; $5M</td>
<td>Synthomics</td>
<td>MOLECULAR ASSEMBLIES</td>
</tr>
<tr>
<td></td>
<td>Developing a Microfluidic, Automated System to Bring DNA Synthesis into the Lab</td>
<td>Template-Free DNA Synthesis through Proprietary Enzymes</td>
</tr>
</tbody>
</table>

Semiconductor-based technology popularized by Twist Bioscience has now made high-throughput DNA/RNA synthesis possible. Evonetix builds upon this platform by integrating multiple reaction sites on the chip surface to error-check the synthesized DNA, and Synthomics aims to bring synthesis capabilities into labs by automating the entire process in a microfluidics-based device. Greenlight Biosciences, DNA Script and Molecular Assemblies utilize biocompatible enzymes to avoid error-prone synthesis steps. Integrating this enzymatic approach into recent hardware advances is ushering in a new era of synthetic biology research.
Healthcare Exits and IPOs: Biopharma IPOs Surge while M&A Slows
Investors Find Blessing in 75 Biopharma Unicorns*

$B+ M&A Unicorns by Year: 19 Private/10 Public

Public Unicorns by IPO Vintage: 46 Deals

The hot biopharma sector has created a blessing of 75 unicorns between 2013 and 1H 2018. Half of private M&A unicorns were pre-clinical or Phase I (10/19), while all of the public M&A unicorns were Phase III (9) or commercial (1).

Not all biopharma companies are build-to-sell. In fact, 61% of unicorns (46/75) have gone public and become stand-alone high-value companies. Of the 46 public unicorns, top 15 crossover investors participated in 31 of these deals prior to the IPO.

*Unicorn defined as venture-backed company since 2013 that achieved an M&A with $B+ total deal value or is a public company (IPO since 2013) valued at $B+ as of 6/15/18.
Source: PitchBook, press releases and SVB proprietary data.
As is typical in a hot IPO market, M&A activity slowed significantly in 1H 2018. By mid-year, 30 biopharma IPOs had priced – compared to 31 for all of 2017.

The biopharma IPO queue is substantial, and 2H 2018 activity will likely push the full year total to between 40 and 45 – far surpassing our early 2018 prediction of 28 to 32.

Though the number of deals declined, total M&A deal value in 1H 2018 already has blown past the total for full-year 2017. However, huge milestones drive these deals: 3 involve potential earn-outs of $900M or higher.

Oncology led the 1H 2018 M&A/IPO exit pack (10), followed by platform (7), orphan/rare (4) and aesthetics/dermatology (4). Aesthetics/dermatology is a surprise because of its relatively small investment levels.
Smaller Early-Stage Deals Dominate Biopharma M&A
VC-backed Biopharma Big Exit M&A by Stage* 2013 – 1H 2018

# of Big Exits

While overall M&A activity is down, 1H 2018 saw 4 early-stage exits – which signals that pre-clinical/Phase I deals may hit the typical annual total of 7 to 11 exits.

The 1H 2018 median milestone earn-out of $900M is nearly double the median from 2015 to 2017.

Smaller early-stage deals, with median investment of $17M, are providing quick times to exit of 3.1 years. They are also yielding a 7x median upfront multiple on invested capital, making the deals attractive to investors.

To exit at an early stage, companies typically need to show a minimum 3x to investors. However, early-stage investment rounds are shifting to $50M and higher, and with the median M&A upfront value at $123M, a 3x return is out of reach. Instead, these companies are heading to the public markets with pre-money IPO valuations far exceeding the private upfront M&A value, providing a hefty step-up from the last private round and generating large IPO proceeds to continue asset development.

<table>
<thead>
<tr>
<th>Year</th>
<th>Commercial</th>
<th>Phase III</th>
<th>Phase II</th>
<th>Phase I</th>
<th>Pre-Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>2014</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2015</td>
<td>10</td>
<td>4</td>
<td>7</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>2016</td>
<td>9</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2017</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1H 2018</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

**Median Upfront (M)**

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>213</td>
<td>225</td>
<td>200</td>
<td>200</td>
<td>171</td>
<td>123</td>
</tr>
</tbody>
</table>

**Median Total Deal (M)**

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>457</td>
<td>413</td>
<td>570</td>
<td>600</td>
<td>461</td>
<td>1040</td>
</tr>
</tbody>
</table>

**Median Years to Exit**

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>5.6</td>
<td>4.0</td>
<td>4.2</td>
<td>5.9</td>
<td>3.5</td>
<td>3.1</td>
</tr>
</tbody>
</table>

*Stage defined as last completed clinical trial in most advanced asset.
Source: PitchBook, press releases and SVB proprietary data.
Half of H1 2018 IPOs raised at least $100M, spurred on by pre-money IPO valuations hitting cycle-highs. The median step-up from last round private money to pre-money IPO was 1.2x. About half of the IPOs were pre-clinical/Phase I (14/30).

Top 15 crossover investors remain major players, as an impressive 21 of 30 IPOs included at least one top 15 crossover investor in the private syndicate. These IPOs had a higher median pre-money value ($341M) and better step-up from last round private money (1.3x). Historically, these IPOs perform better in the public markets.

<table>
<thead>
<tr>
<th>IPOs Raised $100M+</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of IPOs Raised $100M+</td>
<td>24%</td>
<td>18%</td>
<td>31%</td>
<td>4%</td>
<td>39%</td>
<td>57%</td>
</tr>
</tbody>
</table>

*Pre-money IPO valuation divided by venture capital invested. Private valuations sourced through PitchBook.
Source: PitchBook, press releases and SVB proprietary data.
### Device M&A Activity Stable but IPO Window Cracks Open

**VC-backed Device Big Exits & IPOs, 2013 – 2017**

#### # of Exits by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>M&amp;A</th>
<th>IPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1H 2018</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2017</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>2016</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>2015</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>2014</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>2013</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

The slow start to the year is typical for device, and activity should increase in 2H 2018. J&J and Boston Scientific continue acquiring venture-backed companies, but Medtronic and Abbott remain quiet after huge public acquisitions in 2015 and 2017. Further consolidation among large device companies could hurt M&A exits.

The three device IPOs in 1H 2018 equal full-year 2017 activity. Neuro-focused IPOs by Inspire Medical Systems, electroCore and Neuronetics have performed well and could lead to a few more IPOs by revenue-generating device companies in 2H 2018.

#### Exit Values by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>$ BILLIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>$2.8B</td>
</tr>
<tr>
<td>2014</td>
<td>$6.4B</td>
</tr>
<tr>
<td>2015</td>
<td>$7.6B</td>
</tr>
<tr>
<td>2016</td>
<td>$4.9B</td>
</tr>
<tr>
<td>2017</td>
<td>$4.9B</td>
</tr>
<tr>
<td>1H 2018</td>
<td>$2.6B</td>
</tr>
</tbody>
</table>

The slow start to the year is typical for device, and activity should increase in 2H 2018. J&J and Boston Scientific continue acquiring venture-backed companies, but Medtronic and Abbott remain quiet after huge public acquisitions in 2015 and 2017. Further consolidation among large device companies could hurt M&A exits.

The three device IPOs in 1H 2018 equal full-year 2017 activity. Neuro-focused IPOs by Inspire Medical Systems, electroCore and Neuronetics have performed well and could lead to a few more IPOs by revenue-generating device companies in 2H 2018.

#### Top Exits by Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>M&amp;A</th>
<th>IPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Vascular Access</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Surgical</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Neuro</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

Source: PitchBook, press releases and SVB proprietary data.
Device M&A Upfront Deal Values Dip
VC-backed Device Big Exit M&A by Stage 2013 – 1H 2018

By indication, 1H 2018 M&A exits were cardiovascular (2), uro/gyn (2), orthopedic (1) and non-invasive monitoring (1). Cardiovascular has remained strong for the last 5 years.

Building on a two-year trend, 4 of 6 device deals had milestone earn-outs.

The sole PMA/De Novo acquisition was for a non-approved device and the four 510(k) acquisitions had FDA approvals.
## PMA/De Novo Deals Exit Pre-FDA Approval

**VC-backed Device M&A by Pathway, 2015 – 1H 2018**

<table>
<thead>
<tr>
<th>2015 – 1H 2018</th>
<th>Stage at Exit</th>
<th>Median Invested ($M)</th>
<th>Median Upfront ($M)</th>
<th>Median Upfront Multiple</th>
<th>Median Total Deal ($M)</th>
<th>Median Total Deal Multiple</th>
<th>Median Time to Exit (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>510(k) M&amp;As</strong>&lt;br&gt;29 Exits</td>
<td>27</td>
<td>$46</td>
<td>$110</td>
<td>3.1x</td>
<td>$135</td>
<td>3.6x</td>
<td>9.1</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PMA/De Novo</strong>&lt;br&gt;510(k) M&amp;As&lt;br&gt;22 Exits</td>
<td>2</td>
<td>$45</td>
<td>$225</td>
<td>4.0x</td>
<td>$353</td>
<td>6.8x</td>
<td>5.5</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Biopharma M&amp;As</strong>&lt;br&gt;60 Exits</td>
<td>32</td>
<td>$37</td>
<td>$200</td>
<td>4.4x</td>
<td>$578</td>
<td>12.5x</td>
<td>4.2</td>
</tr>
<tr>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **FDA-Approved**
- **CE Mark Only**
- **Development Stage**
- **≥ Phase I**
- **< Phase I**

Device M&A continues the trend of early-stage PMA/De Novo exits and commercial-stage 510(k) exits.

The median upfront deal value of 510(k) companies has increased and the total deal value has more than doubled from 2015 – 2016 to 2017 – 1H 2018. This has resulted in higher deal value multiples, with upfront multiples increasing from 2.2x to 3.5x.

### 510(k) Big Exits (29 Deals)<br>2015 – 1H 2018

<table>
<thead>
<tr>
<th>2015 – 2016</th>
<th>2017 – 1H 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 Deals</td>
<td>11 Deals</td>
</tr>
<tr>
<td>Median Upfront Value ($M)</td>
<td>$105M</td>
</tr>
<tr>
<td>Median Upfront Deal Multiple</td>
<td>2.2X</td>
</tr>
<tr>
<td>Median Total Deal Value ($M)</td>
<td>$110M</td>
</tr>
<tr>
<td>Median Total Deal Multiple</td>
<td>2.6X</td>
</tr>
</tbody>
</table>

Source: PitchBook, press releases and SVB proprietary data.
Despite experiencing a large 1H 2018 bump in M&A activity and with immense private capital invested, Dx/Tools M&A deals were smaller with long times to exit.

Many high-value companies remain private. Of 28 companies with $150M post-money valuations since 2015, only 3 have exited: Assurex, Astute and Natera.

Tech companies continue to expand into healthcare through Dx/Tools investments: Google, Fitbit, Microsoft and Nikon were new corporate investors in 1H 2018 deals. Looking ahead, tech acquisitions of Dx Analytics companies are likely in the next two years as tech companies expand their healthcare footprint and move from investment to acquisition.

---

*IPO/Exit Multiples*
2013 – 1H 2018

<table>
<thead>
<tr>
<th>Year</th>
<th>IPO</th>
<th>M&amp;A</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>2014</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>2015</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>2016</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>2017</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>1H 2018</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

---

*Exit multiple calculated as upfront deal value divided by private invested capital.
Dx Tests are yes/no tests. Dx Analytics provide more information for diagnosis/treatment. R&D Tools advance researchers’ capabilities.
Source: PitchBook, press releases and SVB proprietary data.
Second Half of 2018 Outlook

• We predict full-year 2018 U.S. healthcare venture fundraising will reach $9 billion, closely matching the record $9.1 billion set in 2017.

• While the pace of biopharma investments may slow in 2H 2018, continuing large round sizes likely will propel the annual investment total to a record high.

• Biopharma M&A is likely to reach between 11 and 13 deals for the year. Most companies will push to the public markets to seek higher-value IPOs. We expect between 40 and 45 IPOs for 2018, absent unexpected market fluctuations.

• Series C and D deals will drive investment in the device sector; however, Series D valuation resets could dilute early-stage investors.

• Device M&A activity should pick up, with quick PMA/De Novo exits and improving multiples for 510(k) exits. We expect another three IPOs in 2H 2018, which would be double the 2017 number.

• Dx/Tools investment will fall short of record year 2017. Investment in 2H 2018 will continue to focus on R&D Tools companies.

• The field of synthetic biology will continue to grow as pioneering companies make hardware and biochemical advances in DNA/RNA synthesis.

• Highly valued R&D Tools and liquid biopsy companies may test the public markets in the U.S. or Hong Kong, and we expect additional Dx Tests M&A activity.
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 on deal close.

Upfront Payments defined as initial proceeds from an acquisition paid upon the close of a structured deal; it does 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.

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

Regulatory
Non-approved defined as a device company that has no regulatory 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.

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

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.

Indication Definitions
Neurology (neuro) defined as CNS, pain and psychology companies.

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

Dx Tests defined as proprietary Yes/No diagnostic tests.

Dx 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
About the Authors

Jonathan Norris  
Managing Director  
Silicon Valley Bank  
jnorris@svb.com  
@jonnysvb

As a Managing Director, Jonathan Norris spearheads strategic relationships with many healthcare venture capital 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 venture capital trends. He has 17+ years of banking experience working with healthcare companies and venture capital firms. Jonathan earned a B.S. in Business Administration from the University of California, Riverside, and a J.D. from Santa Clara University.

Andrew Olson  
Senior Manager  
SVB Strategic Advisory  
aolson@svb.com

Andrew Olson is part of SVB’s strategic advisory group where he partners with both early-stage and larger biotech companies to help them navigate the strategic investing and M&A landscape. 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.

Bill Sideris  
Senior Associate  
SVB Strategic Advisory  
bsideris@svb.com

As part of SVB’s strategic advisory group, Bill Sideris helps clients refine and execute their strategic investing and M&A strategy as they create the next generation of medical technologies. Prior to joining SVB, Bill worked as an R&D engineer at Abbott Laboratories focused on medical optics. Bill also co-founded Cardian Inc., a private medical device company developing a clinical stage cardiovascular technology for stroke prevention. Bill completed his PDEng at the Technical University of Delft in Bioproduct Design and holds both a B.S. and M.S. in Biomedical Engineering from the University of Houston.

Ritish Patnaik  
Healthcare Consultant  
rp2616@stanford.edu

As a Healthcare Consultant, Ritish Patnaik helped develop SVB’s Dx/Tools and Synthetic Biology classification schemes. He also helped analyze the datasets, generate new slides and put together takeaways for investment trends presented in this report. Ritish is pursuing a Ph.D. in Bioengineering and M.S. in Management Science and Engineering at Stanford University where he is using bioinformatics and magnetics to create a liver cancer liquid biopsy test. He is a co-founder in Luso Labs, a startup that brings affordable cervical cancer screening worldwide. Ritish earned a B.S. in Biomedical Engineering at Columbia University.
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