Trends in Neuro Device Investing

Advances in Neurology Drive New Activity

MARCH 2018
Neuro Devices: A Highly Active Area in Medtech

Neuro devices are medical devices used to diagnose and treat neurological diseases as well as non-neuro diseases in which the therapeutic effect is mediated through the nervous system. ¹

The report’s purpose is to highlight some of the leading private companies and investors in the space, the diseases they are targeting and the technologies they are developing.

Note that this report is limited to private financings ² of $1M+ between 2016 and 2017 and excludes structural treatments for pain (e.g., spinal fusion), in vitro diagnostics, regenerative medicine, non-medical solutions and joint ventures between large public companies.

Investment activity is being fueled by:
- Significant unmet needs in neurological and psychiatric diseases
- Rapidly expanding knowledge of the nervous system and its broader influence on physiology
- The need to perform more timely interventions that mitigate the effects of diseases such as stroke

Report Highlights:
- Financings increased by over 40 percent and invested equity grew by over 50 percent from 2016 to 2017.
- Significant early-stage investment took place, with 16 Seed and Series A financings raising more than $10M each, spanning all relevant disease areas.
- Nervous system diseases, including pain, movement disorders and epilepsy, among others, represented the largest disease focus for neuro devices, capturing 40 to 45 percent of financings in 2016 and 2017.
- Neuromodulation, or the direct stimulation of the nervous system, represented nearly 70 percent of the total invested equity in neuro devices.

¹ Relevant disease areas have been selected and grouped according to ICD-10.
² The sample includes 107 financings and 94 companies.
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Trends in Neuro Device Investing 2018
Neuro Device Financings by Disease Focus
Private Company Investment Exceeds $1B in 2017

Neuro device companies raising rounds in 2016 and 2017 are grouped by lead program/device according to disease focus.

Venture Investment in Neuro Devices: 2016–2017

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Invested Equity 1</th>
<th>Financing Count by Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric</td>
<td>$204M</td>
<td>6 (2016) 7 (2017)</td>
</tr>
</tbody>
</table>

$10M+ Rounds: Nervous System 2

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>2016 Invested Equity</th>
<th>2017 Invested Equity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>$962M</td>
<td>$1,152M</td>
</tr>
<tr>
<td>Paralysis/Rehabilitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td>$962M</td>
<td>$1,152M</td>
</tr>
<tr>
<td>Brain Tumors 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Movement Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td>$373M</td>
<td>$163M</td>
</tr>
<tr>
<td>Neurocognitive</td>
<td>$373M</td>
<td>$163M</td>
</tr>
</tbody>
</table>

Companies focused on treating nervous system diseases represented 40 to 45 percent of financings in both 2016 and 2017. Invested equity in the same category increased from 45 percent in 2016 to 55 percent of the total invested equity in 2017.

2. Stimwave (Pain), Invicta Medical (Sleep), Synergia Medical (Epilepsy), raised a $50M Series C, a $21M Series B and a $10M Series A round respectively in early 2018.
3. Brain tumors have been grouped into nervous system diseases; ICD-10 classifies neoplasms of the eye, brain and central nervous system separately.
4. Research/Platform includes companies that have not disclosed a clinical indication.

Sources: Pitchbook, CB Insights, SVB analysis
Sixteen Seed and Series A financings spanning all disease areas were $10M+ rounds, with the majority of these companies receiving their first venture capital (VC) investment. Four were research/platform companies, developing foundational technologies that will propel the next generation of neuro devices.

1. Total invested equity in all series.
2. Neurovascular does not include embolic protection technologies.
3. Non-neuro includes technologies that treat non-neurological diseases/disorders in which the therapeutic effect is mediated through the nervous system.

Sources: PitchBook, CB Insights, SVB analysis
Neuro Device Financings by Modality
**Investment Increases for All Modalities**

Software-Based and imaging & monitoring neuro devices begin to attract VC attention.

### Venture Investment in Neuro Devices: 2016–2017

<table>
<thead>
<tr>
<th>Modality</th>
<th>Software-Based</th>
<th>Imaging &amp; Monitoring Device</th>
<th>Therapeutic Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financing Count by Series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Series D+</td>
<td>Series B–C</td>
<td>Seed–Series A</td>
</tr>
<tr>
<td>2016</td>
<td>2</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>2017</td>
<td>6</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Invested Equity $^2$</td>
<td>$178M</td>
<td>$149M</td>
<td>$528M</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>$105M</td>
<td>$119M</td>
<td>$963M</td>
</tr>
<tr>
<td>Venture Age (Median) $^3$</td>
<td>1.0 Years</td>
<td>1.3 Years</td>
<td>3.7 Years</td>
</tr>
</tbody>
</table>

Software-based solutions are dominated by early-series rounds and total invested equity is overwhelmingly driven by a few high performers. Furthermore, VC involvement in this modality is relatively recent.

Financings increased modestly for imaging and monitoring devices but invested equity more than doubled when excluding MindMaze’s $100M 2016 round. Surprisingly, despite this increase in invested equity, the distribution shifted to earlier rounds.

Therapeutic devices are a more mature category with more than half of the invested equity going to later-series rounds. That’s not to say that early financing activity is anemic; Kernel, GTX medical and Neuralink raised over $167M combined in 2016 and 2017.

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1. Software-based does not include solutions whose function is primarily to connect patient and care provider.
2. Total invested equity in all series; 2016 software-based and imaging & monitoring device financings both include MindMaze’s $100M Series A round.
3. Time from first VC investment to latest round.

Sources: PitchBook, CB Insights, SVB analysis
A Deeper Dive into Modalities
Big Pharma Backs Software-Based Solutions

Financings in software-based solutions are dominated by a few companies that are defining the category.

Venture Investment in Software-Based Solutions: 2016–2017

<table>
<thead>
<tr>
<th>Round Group by Size</th>
<th>Invested Equity ¹</th>
<th>Financing Count by Stage ²</th>
<th>Development Stage</th>
<th>Commercial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less Than $10M</td>
<td>$34M</td>
<td>5</td>
<td>$2M 0 Yrs.</td>
<td>$4M 1.5 Yrs.</td>
</tr>
<tr>
<td>$10M+</td>
<td>$248M</td>
<td>4</td>
<td>$26M 1.6 Yrs.</td>
<td>$24M 3.3 Yrs.</td>
</tr>
</tbody>
</table>

Leading developers of software-based solutions are raising very large professionally led rounds in both development and commercial stages. These investments are focused on validating the modality’s ability to treat neurological and psychiatric diseases.

Despite the relatively low safety risk of these technologies, leading companies are conducting extensive clinical trials and seeking approved/cleared indications to achieve general acceptance of their therapeutic benefit.

With significant unmet needs in neurological and psychiatric diseases, combined with a short time to market, this new therapeutic approach should continue to attract the attention of high-profile investors and big pharma.

$10M+ Rounds

- mindstrong *(Series A: $14M)*
- akili *(Series B: $42M)*
- mindmaze *(Series A: $100M)*
- PEAR *(Series A: $20M)*
- cognoa *(Series A: $12M)*
- Neurotrack *(Series A: $10M)*

Active Tech Investors

AME CLOUD VENTURES
TEMASEK
Kapor

Active Life Sciences Investors

ARBORETUM
AMGEN
ABV
FORESITE CAPITAL
M. VENTURES

1. Total invested equity in all stages.
2. For sample sizes less than 5, round size and venture age figures represent means; MindMaze has not been included in the round size statistic.
3. Pear Therapeutics raised a development stage round in 2016 and a commercial round in 2017.

Sources: PitchBook, CB Insights, SVB analysis
Early Rounds Boost Imaging & Monitoring

Six Series A rounds account for over half of the total invested equity in imaging & monitoring.

Venture Investment in Imaging & Monitoring Devices: 2016–2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Invested Equity</th>
<th>Financing Count by Stage</th>
<th>Development Stage</th>
<th>FDA Cleared/Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>$149M</td>
<td>9</td>
<td></td>
<td>$8M 0 Yrs. 1</td>
</tr>
<tr>
<td>2017</td>
<td>$119M</td>
<td>5</td>
<td>$6M 0 Yrs. 6</td>
<td>$16M 2.2 Yrs.</td>
</tr>
</tbody>
</table>

Despite ongoing reimbursement challenges facing nontherapeutic medical devices, a handful of imaging and monitoring device companies are raising healthy rounds.

Over 65 percent of the invested equity in 2016 came from MindMaze’s $100M Series A round. When excluding that round, the majority of the increase from 2016 to 2017 was driven by four Series A rounds (Ceribell, Alzeca Biosciences, Neural Analytics, and Bioserenity).

On average, imaging & monitoring companies are gaining regulatory clearance/approval in one to two years after receiving their first VC investment, and total invested equity prior to commercialization tends to be less than $10M.

Disease Focus by Form Factor

1. Total invested equity in all stages.
   Sources: PitchBook, CB Insights, SVB analysis

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Neuromodulation Dominates Therapeutic Devices

Neuromodulation technologies represent over 70 percent of financings in therapeutic neuro devices and nearly 90 percent of the invested equity.


<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Therapeutic Modality</th>
<th>Neuromodulation</th>
<th>Psychiatric</th>
<th>Non-Neuro</th>
<th>Nervous System</th>
<th>Neurovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System</td>
<td>Research/ Platform</td>
<td>NeuroStar</td>
<td>CVRx</td>
<td>insightEC</td>
<td>NeuroPace</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>Respicardia</td>
<td>electroCore®</td>
<td>Neosync</td>
<td>relevant</td>
<td>INSIGHTEC</td>
<td>Respicardia</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>beluda MEDICAL</td>
<td>GTX Medical</td>
<td>NeuroSigma</td>
<td>MONTERIS</td>
<td>Respicardia</td>
<td>beluda MEDICAL</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>spinnovation</td>
<td>SPR</td>
<td>NeuroSigma</td>
<td>MONTERIS</td>
<td>beluda MEDICAL</td>
<td>spinnovation</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>Nyxoah</td>
<td>neuralink</td>
<td>Neosync</td>
<td>monteris</td>
<td>spinnovation</td>
<td>Nyxoah</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>aleva</td>
<td>synchron</td>
<td>kernel</td>
<td>metacognition</td>
<td>monteris</td>
<td>aleva</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>AUTONOMIC TECHNOLOGIES®</td>
<td>inspire</td>
<td>inspire</td>
<td>metametrics</td>
<td>monteris</td>
<td>AUTONOMIC TECHNOLOGIES®</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td>MicroTransponder</td>
<td>Theragen</td>
<td>inspire</td>
<td>NICO corporation</td>
<td>monteris</td>
<td>MicroTransponder</td>
<td>INSIGHTEC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

26 5 4 14 3 1 3 18

1. Numbers represent the total number of financings in each group.
2. Surgical tools includes devices used during a therapeutic procedure that are not left in the patient.
3. Structural repair includes implants who’s therapeutic effect is achieved by occluding, opening, or otherwise supporting tissue.
Sources: PitchBook, CB Insights, SVB analysis

Trends in Neuro Device Investing 2018
Neuromodulation Draws Broad Investor Interest

Development cycles in neuromodulation can exceed 10 years, putting pressure on later-series rounds.

Venture Investment in Neuromodulation Devices: 2016–2017

<table>
<thead>
<tr>
<th>Form Factor</th>
<th>Invested Equity</th>
<th>Financing Count by Stage</th>
<th>Development Stage</th>
<th>FDA Cleared/Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive</td>
<td>$902M</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$18M</td>
<td>2.4 Yrs.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>$36M</td>
<td>10.3 Yrs.</td>
</tr>
<tr>
<td>Noninvasive</td>
<td>$383M</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$5M</td>
<td>0.7 Yrs.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>$15M</td>
<td>10.6 Yrs.</td>
</tr>
</tbody>
</table>

More mature neuromodulation companies have historically been highly capital intensive and characterized by long development cycles. Nonetheless, this category continues to receive attention from high profile VCs and medical device corporates.

Interestingly, FDA cleared/approved noninvasive and invasive companies have a similar venture age even though the noninvasive companies have been on the market for a lot longer on average (8.5 years for noninvasive versus 3.9 years for invasive).

This confirms the challenges faced by first-generation noninvasive technologies, but recent VC interest in early-stage noninvasive companies such as Cala Health, Invicta Medical, and NeuraLace holds promise for the category.

1. Total invested equity in all stages.
2. Most Active Investors have invested in at least two neuromodulation companies from the sample in this report.
3. Action Potential Venture Capital is GSK’s independently managed VC fund focused specifically on bioelectronics.

Sources: PitchBook, CB Insights, SVB analysis
Pre-Money Valuations\(^1\) in Neuromodulation

Healthy step-ups are common for early and mid-series rounds; however, as with medical devices in general, step-ups become far more difficult at later-series rounds in the absence of solid commercial traction.

<table>
<thead>
<tr>
<th>Series</th>
<th>Median Pre-Money(^2)</th>
<th>Total # of financings by series(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seed–Series A</td>
<td>$11M</td>
<td>$11</td>
</tr>
<tr>
<td>Series B</td>
<td>$26M</td>
<td>$26</td>
</tr>
<tr>
<td>Series C</td>
<td>$42M</td>
<td>$42</td>
</tr>
<tr>
<td>Series D+</td>
<td>$80M</td>
<td>$80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>Round Size (Median)</th>
<th>Prior Invested Equity (Median)</th>
<th>Venture Age (Median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seed–Series A</td>
<td>$7M</td>
<td>$0M</td>
<td>0 Yrs.</td>
</tr>
<tr>
<td>Series B</td>
<td>$20M</td>
<td>$10M</td>
<td>1.9 Yrs.</td>
</tr>
<tr>
<td>Series C</td>
<td>$34M</td>
<td>$29M</td>
<td>5.0 Yrs.</td>
</tr>
<tr>
<td>Series D+</td>
<td>$25M</td>
<td>$95M</td>
<td>10.3 Yrs.</td>
</tr>
</tbody>
</table>

1. Pre-money valuation data is based on SVB proprietary data and publicly available information and represents slightly more than half of the publicly disclosed financings that have occurred in 2016 and 2017.
2. Pre-money statistics: N=28 financings, 27 companies.
3. For sample sizes less than 5, pre-money valuations, round size, prior invested equity, and venture age figures represent means.

Sources: PitchBook, CB Insights, SVB analysis
Enabling Tech Sets the Stage for Future Growth

Development of foundational technologies may lead to dramatic performance improvements and new applications for neuro devices.

Novel Reading Technologies

**Paradromics**
(Seed: $2M)

**INSCOPIX**
(Series A: $10M)

Novel Neural Interfaces & Materials

**WISE**
(Series B: $7M)

**synchron**
(Series A: $10M)

Novel Powering Technologies

**neuspera**
(Series A: $9M)

Closed Loop Systems

**kernel**
(Series A: $100M)

**NEURALINK**
(Series A: $27M)

**NeuroLutions**
(Series A: $5M)

**GTX medical**
(Series A: $40M)

**bajuda MEDICAL**
(Series D: $39M)

**NEUROPACE**
(Recap: $74M)

**inspire**
(Series F: $13M)

“Future bioelectronic medicines will contain closed-loop feedback, advanced signal processing, and novel wireless powering to enable a new class of therapies that compete with earlier-line drugs and open entirely new markets. Minimally invasive devices with the ability to titrate dosing automatically and resolve the compliance challenges of drugs are becoming a reality.”

Juan-Pablo Mas & Imran Eba,
Action Potential Venture Capital

"Bioelectronics represents a new and exciting era in medicine, in which we will be addressing brain disease not via a small molecule or biologic, but via a targeted electrical signal. Closed loop systems that allow for high bandwidth interfacing of the cortex with the outside world (and vice-versa) will be of significant medical utility, and radically improve patients lives.”

Dr. Enke Bashllari,
Arkitekt Ventures

1. Includes significant funding from DARPA.

Note: Paradromics, Inscopix, Wise, Synchron, Kernel and Neuralink represent the six research/platform companies in the set.

Sources: PitchBook, CB Insights, SVB analysis
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About Silicon Valley Bank
For more than 35 years, Silicon Valley Bank has helped innovative companies and their investors move bold ideas forward, fast. SVB provides targeted financial services and expertise through its offices in innovation centers around the world. With commercial, international and private banking services, SVB helps address the unique needs of innovators.