Bay Area Neuroscience: Neurotech & Pharma Company Profiles

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Neuroscience Companies of the San Francisco Bay Area – A Deep Dive

Introduction

The San Francisco Bay Area has emerged as a major hub for neuroscience innovation, hosting a diverse ecosystem of companies at the intersection of technology and brain science. These range from cutting-edge startups developing brain-computer interfaces (BCIs) and neurodiagnostic devices, to established biopharmaceutical firms targeting neurological diseases. This report profiles key Bay Area companies engaged in active neuroscience research or commercialization. Each profile covers the company's mission and background, specialization within neuroscience (such as neurotechnology devices, brain–computer interfaces, neuropharmacology, diagnostics, or cognitive computing), notable scientific innovations, funding and investment history, strategic partnerships, regulatory status (e.g. FDA approvals or designations), and market positioning with competitive context. For clarity, the report is organized into two main sections: **Neurotechnology & Device Companies** (focusing on BCIs, neuromodulation devices, and neuro diagnostics) and **Neuropharmaceutical & Biotechnology Companies** (focusing on drug discovery and biologics for neurological conditions). Summary tables are included to compare key attributes of these companies. All information is sourced from credible company reports, news releases, and industry analyses.

Neurotechnology and Device Companies

This section covers Bay Area companies developing hardware, software, or device-based solutions in neuroscience – including invasive and non-invasive brain–computer interfaces, neuromodulation devices, neuroimaging technology, and neurodiagnostic platforms.

Neuralink (Fremont, CA) – Invasive BCI Implants for Medical Neurology

Profile: Neuralink is a neurotechnology startup founded in 2016 by Elon Musk and a team of engineers and neuroscientists. Headquartered in Fremont, it aims to create implantable brain–computer interface (BCI) devices to restore functionality to people with neurological disorders and eventually augment human capabilities. Neuralink's mission is to *"break through barriers in brain science to help people with unmet medical needs today and unlock human potential tomorrow."* The company's long-term vision includes treating conditions like paralysis, blindness, and depression, and even achieving "symbiosis with AI" via a high-bandwidth neural interface.

Specialization & Innovations: Neuralink has developed an implant called the **Link** – a coin-sized device embedded in the skull that connects to the brain with ultra-fine, flexible electrode "threads" sewn into brain tissue by a custom robotic surgeon. The Link's on-board chip amplifies and digitizes neural signals, which are transmitted wirelessly to external devices. In trials, Neuralink demonstrated monkeys controlling cursors and playing Pong with their thoughts using early prototypes, showcasing high channel-count neural recording and stimulation. In 2023, Neuralink received FDA approval to launch its first *in-human* clinical study of the BCI, and by early 2024 the company had reportedly performed its first human implant surgery with a patient successfully using the device. As of mid-2025, Neuralink stated that five patients with severe paralysis have been implanted and are able to control digital devices by thought via the brain implant – a milestone toward restoring independence for people with paralysis. Neuralink is also developing next-generation applications of its BCI: for example, a project codenamed "Blindsight" to stimulate the visual cortex and restore vision to blind patients (which received a U.S. FDA *Breakthrough Device* designation in 2024).

Funding & Investors: Neuralink is the most well-funded neurotech startup to date. It has raised approximately **$1.3 billion** since its founding in 2016 news.crunchbase.com, including a recent $650 million Series E round in 2025 that valued the company at around $9 billion news.crunchbase.com. Major investors include venture firms (DFJ Growth, Founders Fund, Sequoia Capital, and others) and even nation-scale funds (e.g. Qatar Investment Authority). Elon Musk himself provided significant early funding (over $100 million) and remains a key backer. This war chest has enabled Neuralink to build advanced R&D and manufacturing facilities in Fremont and to plan a large production campus in Texas.

Partnerships & Regulatory Status: Neuralink works closely with neurosurgeons and academic partners for its clinical trials, though it has not announced formal corporate partnerships. Regulatively, the company's implant received FDA investigational device exemption (IDE) clearance in May 2023 to begin human trials, after an initial application was reportedly rejected in 2022. Neuralink has leveraged the FDA's Breakthrough Device program for two of its pipeline indications (a *speech prosthesis* for paralysis and the *vision restoration* device), which grants priority review and collaborative guidance from the agency. These designations reflect the FDA's recognition that Neuralink's technology has potential to address serious conditions with unmet need. Full market approval is likely years away pending clinical trial outcomes.

Market Position & Competition: Neuralink is widely seen as a front-runner in invasive BCI. Its competitive edge lies in engineering – the high density of electrodes (over 1,000 channels), the surgical robot for precision implantation, and custom chips for real-time neural signal processing. The device's closed-loop capability (reading and stimulating the brain) positions it as a platform for both restoring lost function and potentially enhancing cognition. Neuralink's bold vision (eventual mass-market BCIs for human enhancement) and Musk's involvement have drawn intense public attention, which can be a double-edged sword. On one hand, it has attracted top talent and capital; on the other, it brings scrutiny. The company has faced **ethical and safety criticisms** regarding animal testing – reports surfaced about complications and

monkey deaths in preclinical studies, raising concerns among neuroscientists about research practices. Neuralink insists it is committed to rigorous safety and has an internal ethics team.

In terms of competitors, a handful of other BCI ventures are also in the race, though not all are Bay Area-based. **Synchron** (New York/SF) is testing a less invasive stentrode BCI (inserted via blood vessels) and achieved the first U.S. human BCI implant in 2022. **Paradromics** (Texas) is developing high-channel-count cortical implants and recently performed its first human implant surgery. **Blackrock Neurotech** (Utah) has implanted brain interfaces in dozens of patients in academic trials and offers a research-grade device. Neuralink's recent fundraising dwarfs these rivals – for instance, Paradromics has raised about $108 million total – but all are pushing BCI technology forward. Large medical device firms (Medtronic, Abbott) also have neuromodulation devices, though those are mostly for stimulation (e.g. deep brain stimulators for Parkinson's) rather than high-bandwidth brain data. Neuralink aims to leapfrog existing neurostimulation by making the interface "as revolutionary as the first cochlear implants" in restoring function. If successful, its implant could compete with traditional treatments for paralysis (such as assistive hardware) and define a new market for brain-controlled prosthetics and communication aids. The next few years of clinical trial results will be crucial in determining Neuralink's clinical impact and commercial viability.

Company	Founded	Neuro Specialization	Key Product/Platform	Funding Status	Bay Area HQ
Neuralink	2016	Invasive BCI (brain implants)	"Link" 1024-channel neural implant; robotic surgical system	$1.3B raised; FDA IDE approved for human trials:contentReference\[oaicite:27\]{index=27}	Fremont, CA
Science Corp	2021	BCI & neuroprosthetics (vision, cognition)	"PRIMA" wireless retinal implant; "Biohybrid" living-neuron interface	$177M raised (incl. $104M in 2025)	Alameda, CA
NeuroPace	1997	Implantable neurostimulators (closed-loop)	RNS® responsive neurostimulation system for epilepsy	Public (NASDAQ: NPCE); FDA approved in 2013	Mountain View, CA
Ceribell	2014	Neurodiagnostic devices (EEG)	Portable EEG headset with Clarity AI seizure detection	Public (NASDAQ: CERB); IPO $207M in 2024	Sunnyvale, CA*
Cala Health	2014	Wearable neuromodulation (non-invasive)	Cala kIQ™ wrist neurostimulator for tremor (TAPS therapy)	$263M total funding; FDA cleared (ET & PD tremor)	San Mateo, CA
Emotiv	2011	Portable EEG & brain sensing (non-medical)	EPOC/X headset (14-channel EEG); Insight headset; MN8 earbuds	Private; seed/accelerator-backed (Disney, etc.)	San Francisco, CA
Openwater	2016	Neuroimaging & FUS neuromodulation	Portable infrared imaging + focused ultrasound platform (Open-LIFU)	$100M raised; multiple research collaborations	San Francisco, CA
Rune Labs	2018	Neuro data software (precision neurology)	StrivePD data platform (Apple Watch + DBS data integration)	$56M raised; FDA cleared app for Parkinson's	San Francisco, CA

Cognito Therapeutics	2016	Digital therapeutics (neurostimulation)	Spectris system – 40Hz visual & auditory stimulation for Alzheimer's	$423M raised; FDA Breakthrough Device (Alzheimer's)	SF & Cambridge, MA[**]

[*]Ceribell is based in Silicon Valley (historically Mountain View/Sunnyvale).

[**]Cognito Therapeutics has dual locations in San Francisco and Boston.

Science Corporation (Alameda, CA) – Next-Gen Neural Interfaces and Vision Prosthetics

Profile: Science Corp (branded simply as "Science") is a neuroscience startup founded in 2021 by **Max Hodak**, the former co-founder and president of Neuralink. Based in Alameda, Science positions itself as a "clinical-stage, vertically integrated" neurotechnology company developing advanced BCIs and neural prostheses to tackle severe unmet medical needs. Its mission is broad: to *"develop advanced medical technologies at the frontier of our understanding that can profoundly improve the human condition"*. In practice, Science Corp's initial focus has been on restoring lost senses (like vision) and creating new neural interface tools, essentially picking up where Neuralink left off but exploring different technical approaches.

Specialization & Innovations: Science Corp's flagship program is a **retinal prosthesis** to treat blindness. The company has developed a device called **PRIMA** – a fully wireless, photovoltaic implant that can stimulate retinal neurons in patients with diseases like macular degeneration. In late 2024, Science announced positive preliminary results from its pivotal trial of the PRIMA system for vision restoration and by mid-2025 had submitted an application for CE Mark approval in Europe. This suggests that PRIMA may soon become available to patients (in Europe) as a first product. Beyond vision, Science Corp is actively building a **"full stack" neural engineering platform**. Notable technologies in its pipeline include: **Biohybrid** interfaces that use living neurons to bridge connections with electronics (an innovative concept of integrating biological neurons with silicon to improve biocompatibility); **Axon** and **Scope** high-density neural probes for recording and stimulation; a **"SciFi"** wireless headstage for transmitting neural data; and **Synapse/Nexus** software protocols for standardizing BCI data streams. Science's approach emphasizes a *toolkit* for neural interfaces – from hardware to software – which it also offers to external collaborators via a foundry service. In essence, the company is not just developing one device, but a suite of BCI components (chips, probes, optics, software) that can accelerate innovation across the neurotechnology field. This strategy reflects Hodak's ambition to build an **ecosystem** around BCIs, lowering the barriers for others to deploy neural devices.

Funding & Investment: Despite being only a few years old, Science Corp has secured substantial funding. In April 2025, the company raised **$104 million** in a financing led by Khosla Ventures. This brought its total raised to about **$177 million** since inception – an unusually large sum for a young neurotech startup. Other investors include **Artis Ventures**, **Seraphim (Serafund)**, and **Unbound Ventures**, among others. The financing was reportedly in the form of a convertible note, indicating flexibility as the company likely plans future larger rounds or

commercialization partnerships. Science's valuation has not been disclosed publicly, but given the capital and pedigree, it's considered a top-tier neurotech venture alongside Neuralink. The company's rapid funding can be attributed to its strong leadership (Hodak and a team of former Neuralink engineers) and the promise of its technology in high-impact areas like blindness.

Strategic Partnerships & Regulatory Status: Science Corp actively collaborates with academia and industry. It has run clinical studies for the PRIMA retinal implant in partnership with ophthalmology researchers (as evidenced by its trial progress and upcoming European submission). The company also advertises **"Commercial BCI collaborations"** on its site – inviting partners to leverage Science's neural engineering tools. This suggests a strategy of co-development; for example, providing its probes or headstages to research groups or other startups to advance the BCI field collectively. Regulatory-wise, Science's PRIMA implant is its most advanced program: it completed a pivotal trial in Europe with a Data Safety Board recommending approval, leading to the mid-2025 CE Mark submission. A CE Mark (if granted) would allow marketing in the EU for certain blindness indications. In the U.S., Science would need FDA approval – likely via the Breakthrough Devices pathway given the novelty. No FDA clearances have been announced yet. The company's other BCI tools (Biohybrid, Axon probes, etc.) are currently intended for research use only (as noted on the site), meaning Science can sell them to labs prior to any medical device approval, which helps gather data and revenue while navigating regulations.

Market Position & Competition: Science Corp is often viewed as a **"Neuralink rival"**, given its origin and overlapping domain (BCI implants). However, Science differentiates itself by a broader focus on sensory prosthetics and by an open, collaborative approach. In the BCI race, Neuralink and Science are the two notable Bay Area players developing implantable high-bandwidth interfaces. Neuralink's competitive edge is its integrated brain implant/robot system and massive funding; Science's edge is arguably its diversified technology base (vision prosthetics + neural interfaces) and Hodak's focus on *biological integration* (the biohybrid concept). For vision restoration specifically, Science competes with legacy firms like **Second Sight** (which developed the Argus II retinal prosthesis). Second Sight's technology (a retinal electrode array and camera system) was approved years ago but had limited adoption and the company struggled financially; Science's PRIMA uses a novel optical stimulation method which, if effective, could leapfrog older retinal implants. In the BCI probe market, Science's high-density probes and headstages will face competition from companies like **Blackrock Neurotech** (which sells Utah array electrodes and neural signal amplifiers) and academic efforts (IMEC's Neuropixels probes, etc.). By offering its tools through a "foundry" model, Science aims to become a key supplier in the neurotech industry, not just a product maker. If it can establish an ecosystem where many partners use Science's standards (e.g. the Synapse API for neural data), it could gain influence analogous to how some companies set standards in semiconductors or computing. Overall, Science Corp's presence enriches the Bay Area neurotech scene – providing both competitive pressure and collaborative opportunities in the quest to translate BCIs from science fiction to clinical reality.

NeuroPace (Mountain View, CA) – Responsive Neurostimulation for Epilepsy

Profile: NeuroPace, Inc. is a medical device company specializing in implantable neuromodulation for neurological disorders. Founded in 1997 in Silicon Valley, NeuroPace is one of the more established players in Bay Area neurotechnology. Its mission has been to transform the treatment of refractory epilepsy through responsive brain stimulation. After over a decade of R&D, NeuroPace developed the **RNS® System**, the world's first closed-loop brain implant that can monitor neural activity and deliver electrical stimulation in response to detected epileptic seizures. The company is now publicly traded (NASDAQ: NPCE) and has expanded its platform to explore other applications of brain-responsive stimulation.

Specialization & Product: NeuroPace's RNS System is a **responsive neurostimulator** designed for patients with medically intractable epilepsy. The system consists of a **cranially implanted neurostimulator** (placed in the skull) connected to leads (electrodes) positioned at the patient's seizure focus in the brain. Unlike traditional deep brain stimulators that provide continuous or scheduled pulses, the RNS device continuously **records EEG activity** from the brain, detects abnormal electrical patterns that indicate a seizure is about to occur, and then delivers targeted stimulation to nip the seizure in the bud. Essentially, it's a "smart" implant that only stimulates when needed – a closed-loop feedback system. This was a groundbreaking approach: *"the world's only commercially available implantable closed-loop responsive neurostimulator system,"* as NeuroPace described. The RNS received FDA premarket approval in **November 2013** for adults with refractory partial-onset epilepsy (up to two seizure foci). Clinical trials showed significant seizure reduction, which improved over time – many patients experienced a 50%+ reduction in seizure frequency after 2 years of therapy, with benefits persisting long-term. By 2014, over 1,500 patient-years of experience had been accumulated and some patients had the device for over a decade, demonstrating safety and durability. The device has also been integrated with a cloud-based data platform (**NeuroPace's "nSight" system**) that allows clinicians to review a patient's brain activity and seizure logs, potentially gaining insights into treatment efficacy and disease progression.

Funding & Growth: NeuroPace spent many years as a venture-backed private company before going public. It raised multiple rounds from VCs and strategic investors such as Kleiner Perkins and Cyberonics in the 2000s, totaling over $200 million pre-approval. In April 2021, NeuroPace completed an **IPO**, raising approximately **$102 million** by selling shares on NASDAQ. As a public company, its market cap has fluctuated with adoption of the RNS. In 2022, the company reported ~$45 million in revenue, indicating growing (if modest) commercial uptake among epilepsy centers. NeuroPace's go-to-market involves training specialized epilepsy neurosurgery centers – by 2014, 35 Comprehensive Epilepsy Centers were trained and offering RNS implants, a number which likely expanded significantly post-approval.

Strategic Collaborations: NeuroPace's core partnership is with the network of Level 4 Epilepsy Centers (hospitals) across the U.S., since those are its direct customers implementing the

therapy. The company also collaborates with researchers to extend the RNS to new indications. For example, NeuroPace obtained an FDA *Breakthrough Device Designation* in 2022 for using the RNS in **idiopathic generalized epilepsy**, a broadened indication beyond partial seizures. It has run feasibility studies in depression and memory disorders (the RNS can also record local field potentials related to mood or memory, so investigators are exploring its use in treatment-resistant depression and Alzheimer's). Additionally, in 2023 NeuroPace announced a partnership with an unnamed biotech company to analyze biomarker data from RNS patients, aiming to see how neural signals might predict drug responses. This kind of partnership hints at a convergence of neurodevice and neuropharma efforts, using implanted devices to gain real-world neural data.

Regulatory & Status: The RNS System is FDA-approved for adults with refractory focal epilepsy, and NeuroPace has continued to seek label expansions. The CMS (Medicare) approved new technology add-on payments (NTAP) for the RNS in 2014, which helped with reimbursement for inpatient implant procedures. The device also has FDA Breakthrough designation (as mentioned) for generalized epilepsy, which should streamline the review if clinical data supports that new indication. In terms of safety, long-term data presented to the FDA demonstrated no significant adverse cognitive effects and a low rate of stimulation-related side effects, making RNS a well-tolerated therapy over years.

Market Position & Competition: NeuroPace's RNS faces competition from other treatments for refractory epilepsy. **Medtronic** offers an alternative: its **DBS therapy** (deep brain stimulation of the anterior thalamus) was approved in 2018 for refractory epilepsy. DBS delivers continuous stimulation and has shown seizure reductions, but it is an open-loop system. **LivaNova** (formerly Cyberonics) provides the **Vagus Nerve Stimulator (VNS)**, an implant in the chest that sends intermittent signals to the vagus nerve – VNS has been used for epilepsy for decades and is also open-loop (though newer models sense heart-rate changes as a proxy for seizures). The RNS's competitive advantage is its *closed-loop responsiveness* – it only stimulates when abnormal activity is detected, potentially providing more effective and personalized therapy. In practice, some patients receive a combination (e.g., VNS plus RNS) for different seizure types. As of 2025, RNS is still the only closed-loop brain implant on the market for any indication, giving NeuroPace a unique selling point. However, adoption depends on showing clear benefits over alternatives. A 2021 trial comparing RNS vs. medical management in new patients could further validate outcomes. NeuroPace's technology also opens doors beyond epilepsy: it effectively turns the brain implant into a **chronic EEG recorder**. This trove of brain data can be mined for insights, making NeuroPace a player in the emerging field of "brain data" companies similar to Rune Labs (though NeuroPace's data comes from an invasive device and is proprietary to each patient's clinician). With its early-mover advantage and regulatory approvals, NeuroPace is positioned as an *established leader* in therapeutic neurostimulators. The company's strategy to broaden indications (e.g., mood disorders) will determine if it can scale beyond the niche of severe epilepsy. Notably, the Bay Area's ecosystem benefits from NeuroPace's success – it demonstrated that an idea from the 1990s (responsive brain stimulation) could be engineered,

clinically validated, FDA-approved, and commercialized, paving the way for the newer neurotech startups.

Ceribell (Sunnyvale, CA) – Rapid EEG Diagnostics for Neurology

Profile: Ceribell is a medical device company focused on neurodiagnostics, specifically making electroencephalography (EEG) – brain wave monitoring – more accessible and rapid in emergency and critical care settings. Founded in 2014 by Dr. Jane Chao and Dr. Chris Chafe (Stanford-affiliated innovators), Ceribell set out to address the problem of undiagnosed seizures in hospital patients. Its core product, the **Ceribell Point-of-Care EEG System**, is a portable, easy-to-use EEG headset and cloud-based analysis platform. Ceribell's mission is to dramatically speed up the detection of *non-convulsive seizures* and status epilepticus (a neurological emergency) in ICUs and emergency departments, where conventional EEG is often too slow or unavailable.

Specialization & Product: The Ceribell system consists of a lightweight headband with EEG electrodes that can be applied by any clinician in minutes, plus a small bedside recorder/transmitter. Uniquely, Ceribell incorporates an AI-based algorithm (**Clarity**) that continuously analyzes the EEG in real time and generates an audible alarm – a "seizure audio" – if it detects patterns consistent with status epilepticus. In essence, it's been described as an **"EKG for the brain"**, giving near-instant feedback on neural activity. The system provides an **instantaneous bedside alert indicating suspected seizures**, rather than requiring a neurologist to interpret EEG squiggles. It also visualizes EEG trending (seizure burden) to monitor treatment response. Ceribell's innovation is not just the hardware, but the integrated software which uses machine learning to detect seizures. By making EEG setup fast (often under 5 minutes) and interpretation automated, Ceribell enables even non-specialists to initiate monitoring for any patient with altered mental status. Clinical studies have shown this can **cut the time to seizure diagnosis by hours**, enabling faster treatment and improving outcomes in conditions like refractory status epilepticus. Initially, the Clarity algorithm was cleared for adults; by 2023–2025, Ceribell expanded its FDA clearances to include **pediatric patients (≥1 year old)** as well, making it usable across the lifespan. The company also introduced **ClarityPro**, an updated software for detecting electrographic status epilepticus with high sensitivity and specificity. By mid-2025, Ceribell's system was in use at hundreds of U.S. hospitals, often in ICUs, neurological wards, and ERs.

Regulatory & Achievements: Ceribell received its first FDA 510(k) clearance in 2017 for the EEG system. Subsequent 510(k) clearances were granted for the Clarity algorithm (adult use, then pediatric in 2025). The device also qualified for a Medicare new technology add-on payment and in 2022 received a **CMS NTAP reimbursement** for inpatient use, reflecting its novel status. Importantly, Ceribell's effectiveness has been validated: the system's ability to detect non-convulsive seizures in the ICU has been published, and leading hospitals have adopted it. In October 2024, **Ceribell reached a major milestone by completing an IPO**, raising **$207.3 million** in its initial public offering. This infusion has helped scale manufacturing and

global sales. However, the young public company hit a snag in early 2025 when its stock price temporarily dropped ~42% due to investor concerns about U.S. tariffs on Chinese imports affecting its hardware costs. (Ceribell's headbands were manufactured in China, meaning import tariffs could squeeze margins.) The company responded that it had sufficient inventory through Q3 2025 and was exploring moving production to other countries to mitigate tariff impact medtechdive.com. Analysts later concluded the sell-off was overdone medtechdive.com. This episode underscores the complexity of being a device manufacturer in a global supply chain.

Funding & Growth: Prior to the IPO, Ceribell had raised over $100 million in venture funding (backers included Vivo Capital, Kaiser Permanente Ventures, and others). Post-IPO, Ceribell has a strong balance sheet to expand. The company's growth strategy includes broadening indications (e.g., using EEG for delirium monitoring or sedation monitoring), and international expansion. By going public, Ceribell signaled its transition from startup to an *established medtech* firm in the neurodiagnostics market.

Market Position & Competition: Ceribell essentially created and leads the category of point-of-care EEG. Its competition falls into two camps: **traditional EEG systems** and a few new entrants trying to emulate Ceribell. Traditional EEG vendors (like **Natus Medical** and **Nihon Kohden**) produce cart-based EEG machines that require a technician to apply 20+ electrodes and an expert to read the output. These are gold-standard for comprehensive EEG but are impractical for rapid screening. Ceribell has been leveraging its ease-of-use and automated analysis as a competitive advantage to replace conventional EEG in acute settings, or to serve as a triage tool. Notably, Ceribell in its SEC filings named Natus and Nihon Kohden as its main competitors but argues that their systems are ill-suited for emergent use. In terms of new competitors: one example is **Fasikl**, a startup (spun out of University of Minnesota) that recently obtained FDA clearance for an AI-driven wearable EEG "wristwatch" for tremor and possibly EEG – however, that device targets movement disorders, not ICU seizures. Another competitor could be **Empatica**, which makes wearable seizure detectors (using motion and physiological data rather than EEG). But Empatica's wristbands are more for outpatient seizure alerts (like in epilepsy patients), whereas Ceribell focuses on inpatient diagnosis of hidden seizures. In essence, Ceribell's direct competition is limited at present, and it enjoys a **first-mover advantage** in this niche. The company's challenge and opportunity is to make its system standard of care in every hospital – similar to how EKG is ubiquitous. If it succeeds, Ceribell could become to neurodiagnostics what point-of-care ultrasound has become to imaging. Its recent pediatric clearance also opens the large pediatric ICU market, where no comparable solution existed. With strong clinical evidence and increasing reimbursement clarity, Ceribell is well positioned to sustain leadership in rapid neurodiagnostic tech. As a Bay Area success story, Ceribell highlights how combining device engineering with AI can revolutionize neurologic care, saving brains by shaving off critical minutes in diagnosis.

Cala Health (San Mateo, CA) – Wearable Neuromodulation for Tremor and Beyond

Profile: Cala Health is a bioelectronic medicine company founded in 2014 that develops wearable neuromodulation devices to treat chronic diseases non-invasively. The company's initial focus is **Essential Tremor (ET)** – a common movement disorder – and **Parkinson's disease** tremor. Cala's mission is to deliver individualized therapy through peripheral nerve stimulation, offering patients a safe, drug-free alternative for tremor relief. Spun out of Stanford by neuroscientist Kate Rosenbluth, Cala Health has grown in the Bay Area medtech scene and is now a leader in FDA-cleared wearable neurostimulation.

Specialization & Product: Cala's flagship product is the **Cala kIQ™ system**, a wrist-worn neuromodulator that provides on-demand therapy for hand tremors. The device uses a proprietary approach called **Transcutaneous Afferent Patterned Stimulation (TAPS)**. Essentially, the Cala wristband has electrodes that stimulate the median and radial nerves at the wrist in a pattern tuned to disrupt tremor oscillations. The stimulation signals travel via sensory nerves to the brain's motor circuits to *"reset"* the rhythmic firing that causes tremors. Cala's therapy is personalized: the device first measures the patient's tremor frequency and then delivers stimulation bursts timed to counteract it. In clinical studies, a typical 40-minute stimulation session results in significant tremor reduction lasting for hours, improving patients' ability to perform daily tasks like eating and writing. This was a breakthrough as previously the only effective treatments for ET were drugs (which often have side effects and limited efficacy) or invasive procedures like deep brain stimulation surgery. Cala ONE, the first-gen device, received FDA **De Novo clearance in 2018** as the first ever non-invasive therapy for Essential Tremor. Cala later launched the **Cala Trio™** as a prescription device for home use, and in **June 2023** introduced the next-gen **Cala kIQ™** system. Notably, kIQ expanded the indication: it is **FDA-cleared for tremors in both Essential Tremor and Parkinson's disease** (action tremor in the hands). This made it the only non-invasive, wearable device approved for these conditions. Cala obtained an FDA Breakthrough Device designation to accelerate development of the Parkinson's tremor indication, highlighting the novelty. The Cala kIQ is prescribed by physicians but used by patients at home, reflecting Cala's *"direct-to-home digital therapeutic"* model. Patients typically use the device twice daily or as needed. Cala also built a digital platform to support remote monitoring and device tuning, aligning with trends in tele-neurology.

Scientific & Clinical Validation: Cala's therapy has been validated in several studies, including the largest clinical trial ever conducted in essential tremor (with over 200 patients). Published results showed that TAPS therapy significantly reduced tremor severity and improved quality of life, with minimal side effects (mostly mild skin irritation). An economic analysis by CVS Health presented at a neurology conference found that regular use of Cala's device reduced healthcare utilization and costs for ET patients (fewer doctor visits and less disability), underscoring its value. The International Essential Tremor Foundation recognized Cala Trio as an effective non-pharmacological treatment – a strong endorsement in the clinical community. These data have helped Cala in securing reimbursement; in late 2024, the company achieved a positive Medicare Coverage Determination, meaning Medicare agreed to cover the Cala therapy for ET patients. This was a crucial milestone, as it broadens patient access for the largely older ET population.

Funding & Commercial Status: Cala Health has attracted significant funding from both tech and healthcare investors, reflecting its position at the nexus of medtech and digital health. It has raised over **$250 million** to date. Investors include **GV (Google Ventures)**, **JJDC (Johnson & Johnson's venture arm)**, **Lux Capital**, **Novartis Ventures**, and others. In late 2024, Cala closed an oversubscribed **$50 million growth round** co-led by Vertex Growth and Nexus NeuroTech Ventures, with participation from all existing investors. Earlier, in 2021, it raised a $77 million Series C to expand indications (notably mentioning psychiatry, cardiology, and autoimmune targets beyond tremor). This war chest has supported commercialization: Cala has been increasing its sales force and marketing to neurologists and movement disorder clinics across the U.S. The company remains private but is sometimes speculated as an IPO candidate if device sales continue to grow.

Strategic Partnerships: Cala has several notable collaborations. Being supported by JJDC suggests a strategic alignment with Johnson & Johnson; indeed, J&J's interest in neuromodulation (they have a division for pain stimulation) could hint at a future partnership or acquisition. Cala also partnered with pharmaceutical companies in research – e.g., a study with **Pfizer** to see if using Cala's device could enhance outcomes for patients on tremor medications. In the broader sense, Cala is part of the bioelectronic medicine community, which includes groups like GSK's Bioelectronics unit and academic consortia; Cala's success helps validate neuromodulation as a modality to investors and regulators.

Market & Competition: Cala Health is a **pioneer in wearable neuromodulation** for neurology. Currently, it faces limited direct competition. For Essential Tremor, traditional drug therapy (primidone, propranolol) and invasive procedures (DBS surgery or focused ultrasound thalamotomy) are the main alternatives. Cala's device carved out a new niche as a *middle ground* – more effective than drugs for many patients, but far less invasive (and less expensive) than surgery. A competing startup, *Fasikl*, recently got FDA clearance for a tremor-targeted neuromodulation wrist device that uses a form of closed-loop stimulation guided by AI. Fasikl is early-stage and it remains to be seen if their approach (a University of Minnesota spinout) can challenge Cala commercially. Meanwhile, big medtech firms like **Medtronic** and **Boston Scientific** focus on implanted DBS for movement disorders; they do not offer wearables, so Cala currently has that segment to itself. Cala is leveraging this head start to explore other indications: its technology of patterned nerve stimulation could, in theory, be applied to other peripheral nerves for diseases like dystonia, chronic pain, or even hypertension (via vagus nerve stimulation). The mention of targets in cardiology and psychiatry implies Cala's R&D is testing use-cases such as neuromodulation for depression or anxiety (vagus or trigeminal nerve pathways) and for conditions like atrial fibrillation. In doing so, Cala would encounter other device firms (e.g., Fisher Wallace for depression tACS headbands, or SetPoint Medical for vagus stimulation in autoimmune disease). But Cala's strong IP and experience with FDA regulation give it an advantage in expanding its platform. Market-wise, the tremor device alone addresses millions of patients (7+ million with ET in the U.S., and 1M with Parkinson's tremor). If Cala can convert even a fraction of these to paying customers, it can build a sizable business. Its prescription model and reimbursement progress are key: by securing Medicare coverage, Cala

removed a major barrier to adoption for older patients. As of 2025, Cala Health is widely seen as a **success story** in bioelectronic medicine – it took a condition long thought to require drugs or surgery and showed that a wearable can deliver meaningful clinical benefit. In summary, Cala occupies a strong competitive position, with a first-in-class product, deep investor backing, and a pipeline to broaden its reach, reinforcing the Bay Area's reputation for leading-edge neurotech innovations.

Emotiv (San Francisco, CA) – Pioneering Portable EEG for Brain Monitoring

Profile: Emotiv is a human brain research and brain–computer interface company known for its affordable, user-friendly EEG headsets. Founded in 2011, Emotiv's headquarters is in San Francisco, with additional offices in Sydney and Vietnam emotiv.com. The company was founded by **Tan Le** (CEO) and Dr. Geoff Mackellar (CTO) with the vision of *"empowering individuals to understand their own brain and accelerating brain research globally"* emotiv.com. Emotiv's devices are not medical-grade diagnostic tools per se, but rather consumer and research-grade EEG systems that have been widely adopted in fields from gaming to wellness to neuromarketing. Emotiv helped kickstart the modern **"prosumer" EEG** market – making brain sensors available to hundreds of thousands of people and developers, which is a significant contribution to neuroscience awareness and data gathering.

Specialization & Products: Emotiv specializes in **electroencephalography (EEG) headsets** and software that translate brain signals into insights or control signals. Its early product, the **Emotiv EPOC**, launched in 2009 (pre-dating the official company founding date) and gained fame as a $300 headset with 14 EEG channels. Users could train the system to recognize certain thoughts or facial expressions to control computers – a form of non-invasive BCI. Over time, Emotiv expanded its product line: the current offerings include the **EPOC X** (14-channel wireless EEG), the **Insight** (a 5-channel lightweight headset), and **Flex** (a 32-channel modular system for more advanced research) emotiv.com. Recently, Emotiv also introduced **MN8 Smart Headphones** – a pair of earbuds with 2-channel EEG built-in, designed for passive brain monitoring in everyday life emotiv.com. This aligns with a trend to integrate EEG into familiar form factors (similar to what other Bay Area startups like NextSense are doing with earbud EEG). Emotiv's software ecosystem includes the **EmotivPRO** research software for data collection, **BCI APIs** for developers to create brain-controlled apps, and cloud tools for data analytics. Applications of Emotiv technology are extremely broad: developers and researchers in **100+ countries** have used its SDK emotiv.com. Examples include using Emotiv headsets for virtual reality gaming (reading a user's cognitive state), for workplace wellness (measuring stress and focus in employees), for education (projects where students control robots with thought), and for basic neuroscience experiments in labs and classrooms. Emotiv has positioned its tech under the umbrella of "BCI" or **Mind-Machine Interface (MMI)**, though it is non-invasive EEG-based emotiv.com. The devices can track cognitive performance, monitor emotional states, and even allow users to control virtual and physical objects via trained mental commands emotiv.com.

While the signal quality of dry-electrode EEG can't match clinical systems, Emotiv has steadily improved its sensors and algorithms. Notably, Emotiv's latest brainware includes machine-learning classifiers for mental commands and integrations to popular game engines, lowering the barrier for creative BCI applications.

Funding & Business: Emotiv participated in incubators/accelerators (it was part of **TechStars** and the **Disney Accelerator** program) and has received investments from venture firms like **Acequia Capital** as well as corporate investors (e.g., it got backing from P&G and Dolby's venture arms, per news reports). While Emotiv has not publicly disclosed all funding rounds, Pitchbook estimates its total funding around $25 million (including some debt financing). The company generates revenue through device sales (tens of thousands of headsets sold globally) and SaaS subscriptions for data analytics. Emotiv has also done collaborative projects that likely provided funding – for example, working with **Toyota** on measuring driver attention via EEG, and with academic consortia on cognitive monitoring. It remains a private company, with Tan Le as the charismatic public face, frequently demonstrating the technology at conferences (her TED talks are well known in the BCI community). Emotiv's approach of combining for-profit product sales with a community of enthusiasts and researchers has kept it sustainable.

Notable Achievements & Impact: Emotiv can be credited as a **market leader in consumer EEG**. Its devices have won multiple innovation awards (Red Dot Design Award, Australian Engineering Excellence Awards, and others) emotiv.com, validating their design and technical achievement. The global community that has sprung up around Emotiv (developers in over 100 countries, per the company emotiv.com) has yielded a long tail of experiments – from art installations that respond to brain waves, to serious scientific studies. For instance, researchers have used Emotiv headsets to collect large-scale EEG datasets because the cost per unit is low compared to hospital EEG. Emotiv also contributed to open science: early on, they provided open SDKs, which helped drive interest in BCIs among a generation of students and hobbyists. In terms of neuroscience, while Emotiv isn't making FDA-approved diagnostics, it is advancing brain-monitoring techniques in everyday contexts. One example is leveraging **machine learning on Emotiv EEG data to track cognitive stress or engagement** during tasks – something that has potential in workplace safety or training.

Market & Competition: Emotiv operates in the intersection of neurotechnology and consumer electronics. Its competitors include other **high-end consumer EEG brands**: notably **Neurosky** (another early San Jose-based company that made one-channel "brainwave" sensors for toys and education), **OpenBCI** (an open-source BCI hardware ecosystem, though more DIY), and **InteraXon** (maker of the Muse headband, which targets meditation and wellness). Among these, Emotiv is generally seen as more research/enterprise-oriented than Muse (which is purely a meditation tool) and more feature-rich than Neurosky (which was very basic signals). Emotiv's newer products like MN8 earbuds also foreshadow competition with startups like **NextSense** (the Alphabet spin-off with ear EEG for sleep and epilepsy) and possibly big tech if they venture into brain monitoring (Meta's Reality Labs, for example, is exploring neural signals from wrist and EEG for AR/VR). Emotiv's competitive advantage is its decade-plus of experience and a

comprehensive platform (hardware + software + cloud). They have patents on their headset designs and machine-learning pipelines that newcomers will take time to replicate. However, as braintech goes more mainstream, Emotiv will need to stay innovative – e.g., improving signal quality of dry electrodes, ensuring comfort for long-term wear, and perhaps moving into health use-cases as regulations allow. On the regulatory front, Emotiv has mostly stayed in the wellness/research category (thus not needing FDA clearance). But interestingly, in 2022, an Emotiv device was used in an FDA-cleared manner: Rune Labs' StrivePD got clearance to use Apple Watch for Parkinson's – one could envision EEG similarly being used for neuro monitoring if validated. Emotiv could partner with a medtech firm to pursue such clearances in the future. In the Bay Area context, Emotiv represents the **BCI-for-everyone** ethos – complementing the more medical-focused BCIs (Neuralink, Synchron) by providing accessible brain sensing to the masses. Its presence has no doubt seeded interest in neurotechnology among the local developer community and helped train talent that other neuro startups draw upon. In summary, Emotiv remains a prominent player delivering practical brain-computer interface tools, with a sustained impact on both industry and public engagement with neuroscience.

Openwater (San Francisco, CA) – Portable fMRI and Therapeutic Ultrasound Platform

Profile: Openwater is a San Francisco-based medtech startup founded in 2016 by Dr. **Mary Lou Jepsen** (a former executive at Google \ [X] and Facebook Oculus). Openwater's goal is extraordinarily ambitious: to develop a wearable device that can image and stimulate the body (including the brain) with the resolution of an MRI machine, but at a tiny fraction of the cost. In essence, Openwater is pioneering an **"open-source medical imaging and therapeutic platform"** that uses novel physics – combining infrared light, ultrasound, and electromagnetic fields – to diagnose and treat diseases at the cellular level. Jepsen, herself a brain tumor survivor, often describes the mission in personal terms: *"I'm fighting for my life and millions like me"*, aiming to make advanced healthcare accessible to all. The company is called "Openwater" to evoke a sense of transparency and fluidity; notably, musician Peter Gabriel was an early advisor who encouraged the name and vision of democratizing healthcare tech.

Technology & Innovation: Openwater's core technology integrates several components: **high-resolution infrared imaging**, **low-intensity focused ultrasound (LIFU)**, and specific electromagnetic pulses. By leveraging **optics and semiconductor tech**, Openwater has created a device prototype that can **"see" into the body and brain** using infrared light modulated by ultrasound. The principle is akin to using the body's tissue as a holographic medium: infrared light can penetrate a certain depth, and when combined with ultrasound modulation, it can generate detailed images (this is related to a concept of *acousto-optic imaging*). Openwater's platform can not only visualize structures (like detecting tumors) but also deliver therapeutic ultrasound in a targeted way. For example, they reported the ability to **selectively destroy cancer cells** without harming adjacent healthy cells, by tuning to a resonant frequency – *"like an opera singer shattering a wine glass"* analogy. In neurological applications, Openwater's

transcranial focused ultrasound has been used to **modulate brain circuits non-invasively**. The company has demonstrated in studies that **low-intensity ultrasound** can have therapeutic effects: they have shrunk glioblastoma brain tumors in mice and even **treated severe depression in humans** with brief ultrasound sessions. A University of Arizona clinical study (published in *Frontiers in Psychiatry*) used Openwater's device targeting the brain's Default Mode Network, resulting in significant depression symptom reduction after <2 hours of total treatment. This suggests a new neuromodulation modality – one that doesn't require implants or electrical stimulation, but uses acoustic energy to influence neural activity. Importantly, Openwater's philosophy is *open innovation*: they emphasize an **open-source approach** to their medical device development. They have publicly stated that by sharing designs and leveraging consumer electronics components (like smartphone chips), they can compress the typical 13-year, $650M medical device development cycle down to under 3 years and around $10M. This bold claim involves using off-the-shelf parts and open collaboration to iterate faster and cut costs. True to this, Openwater has released some aspects of their tech (they call their devices "Open-LIFU" etc., highlighting openness) and engaged in academic collaborations with UCLA, UPenn, Brown University, University of Arizona and others to validate and refine the technology.

Funding & Leadership: Openwater has attracted significant funding, particularly from visionary tech and social impact investors. By August 2024, the company announced it had secured **$100 million in total funding** from new and existing investors. Backers include **Plum Alley Ventures** (a VC focusing on female-led firms), **Khosla Ventures**, **BOLD Capital Partners**, and notable individuals like **Esther Dyson** (tech investor) and **Peter Gabriel** (who has a strong interest in democratizing health tech). Additionally, Ethereum co-founder **Vitalik Buterin** was reported to support Openwater with a major donation/grant, aligning with the company's open-source, long-horizon ethos. This mix of investors underscores both the high risk and high potential of Openwater's endeavor; it's not traditional VC territory alone, but mission-driven capital too. Openwater's team has grown to include experts in semiconductor design, optics, and ultrasound engineering (many profiles on their website highlight decades of experience in these fields). In March 2025, Openwater appointed a new CEO, **Aaron Timm** (formerly of Vivalink), to lead commercialization, while Mary Lou Jepsen took the role of Executive Chairperson. This leadership move indicates the company's transition from pure R&D into product deployment. Under Timm, Openwater is scaling up manufacturing (they opened a Taiwan office to coordinate production of device components) and preparing for broader distribution of its imaging and LIFU devices. The company reported "heavy pre-order interest" for its **Open-Motion 3.0 imaging unit** and **Open-LIFU 2.0 therapeutic device** as it moves from research collaborations to larger commercial sales.

Regulatory & Development Status: As of 2025, Openwater's devices are investigational and not yet FDA approved for general use. However, the company's strategy of open collaboration means many prototypes are already in use in research settings under IRB approvals. For instance, their depression treatment study was published in a peer-reviewed journal, implying they navigated regulatory approvals for an experimental device in a clinical trial. Openwater will likely seek FDA clearance for specific applications once more data is collected – e.g., a device

for treatment-resistant depression could go for a De Novo clearance or an existing pathway if a predicate exists (though it's quite novel). The company did claim that their approach can **"lower hurdles to regulatory approval"** by using consumer-grade components and open development, positing that transparency and replication can speed up agency review. How the FDA will view that remains to be seen, but Openwater's receiving of Breakthrough Device designations is possible given the life-threatening conditions they target (e.g., glioblastoma).

Market Potential & Competition: Openwater sits at a unique intersection of markets – it is simultaneously a **neuroimaging company**, a **neurotherapy company**, and a platform tech company. If one imagines a single machine that could do *portable brain imaging* (like an MRI/fMRI) and also perform *non-invasive brain stimulation* (like an externalized DBS or TMS), Openwater is attempting to build exactly that. The markets disrupted would be huge: the MRI market (dominated by GE, Siemens – multi-billion dollar industries) and the neurostimulation market (DBS, TMS, etc., also large). Initially, Openwater might focus on specific niches: for example, a **stroke** or **traumatic brain injury** portable scanner that paramedics can use on-site, or a wearable **depression treatment** that rivals electroconvulsive therapy or TMS without needing a procedure room. In imaging, there are competitors exploring portable technologies: startups working on "wearable MRI" using quantum sensors or novel optics, though none with Openwater's exact approach. In brain therapy, the focused ultrasound (FUS) space has players like **Insightec** (who make MRI-guided high-intensity FUS for essential tremor ablation) and **Brainsonix** (low-intensity FUS for neuromodulation). Openwater's edge is integrating imaging with FUS – so it can both see and treat, whereas others often do one or the other. Another aspect is cost: MRI machines cost millions; Openwater's use of smartphone chips suggests their device could cost orders of magnitude less, making advanced diagnostics available in clinics or even homes, aligning with the *"hospital-grade care at a fraction of the cost"* vision. A challenge will be proving that their approach is as effective as the gold standards. Early results are promising (e.g., mice glioblastomas shrinking, depression improved), but to break into clinical practice, large trials are needed. On the competitive front, if Openwater's model succeeds, one could see big imaging companies partnering or acquiring to integrate this tech. Indeed, the mention that Openwater *"represents a rare confluence of transformative technology, market readiness, and global impact potential"* is something one might hear in a Genentech or Google boardroom, indicating that major industry players are watching. In summary, Openwater is one of the Bay Area's boldest neuroscience endeavors – it exemplifies the region's willingness to take moonshots. While still in development, the company has made concrete strides: a strong patent portfolio, $100M in funding, prototype devices achieving **MRI-like imaging and therapy in a portable form**, and a roadmap to scale up production. If it realizes even part of its vision, the impact on neuroscience research (imagine scanning and zapping neurons in real-time in freely moving subjects) and clinical neurology (bedside brain scans and treatments) would be revolutionary.

Rune Labs (San Francisco, CA) – Precision Neurology Software and Data Platform

Profile: Rune Labs is a software and data analytics company founded in 2018, dedicated to enabling precision medicine for neurological and psychiatric disorders. Headquartered in San Francisco, Rune Labs stands out in the Bay Area neuroscience landscape as a purely digital health/neuroinformatics player. The company was founded by **Brian Pepin**, a former Verily (Google Life Sciences) engineer, who saw the need for better data infrastructure to support new therapies like deep brain stimulators and biologics in neurology. Rune Labs' mission is to **collect and integrate large-scale neurological data** – from wearable devices, implanted devices, clinical assessments, and even genomics – and use it to guide treatment decisions and accelerate therapy development. In essence, they provide a *software platform* akin to a "cloud brain" that centralizes patient-specific brain data, which is critical for diseases like Parkinson's, epilepsy, depression, etc., where biomarkers can inform more personalized care.

Product & Technology: Rune Labs' flagship product is the **Rune Care Platform**, with a specific application called **StrivePD** for Parkinson's disease. The platform aggregates data from multiple sources: one key source is **Apple Watch** sensor data (capturing motion metrics like tremor and dyskinesia), which patients can contribute through a Rune Labs app. In June 2022, Rune Labs made headlines when it secured **FDA 510(k) clearance** for the StrivePD Apple Watch software – making it an FDA-cleared tool for tracking Parkinson's symptoms via wearable tech. This clearance legitimized the use of an Apple Watch as a medical device for PD, expanding the reach of Rune's platform to potentially millions of watch wearers. Another data source is **implantable neuromodulators**: Rune Labs partners with Medtronic, for example, to ingest brain signal data from Medtronic's **Percept™ DBS** device (which can sense local field potentials in the brain). By combining wearable data (e.g., how a patient's tremor varies over the day) with implanted device data (neural signals, stimulation settings) and medication diaries, Rune's software gives clinicians a rich dashboard to assess a patient's condition in between clinic visits. It can highlight patterns, such as medication wearing off or the need to adjust DBS settings, that would be hard to discern otherwise. The platform also uses machine learning to identify **biomarker-based subtypes** of patients – for example, in depression, one might find a subgroup with a particular brainwave pattern responding to a certain drug. Rune has built out data integrations beyond PD: they have programs in **epilepsy** (working with NeuroPace to correlate RNS device data with patient-reported outcomes) and in **psychiatry** (collecting passive phone sensor data, etc., for mood disorders). Essentially, Rune Labs is creating the "backend" for neuro data, an analog to what companies like Flatiron Health did for cancer data.

Strategic Collaborations: Collaboration is central to Rune's model – they align with device makers, pharma, and clinicians. For instance, **Medtronic** and Rune Labs announced a partnership to see how combining Apple Watch movement data with Medtronic's implanted brain stimulators could improve understanding of Parkinson's fluctuations. This is mutually beneficial: Medtronic's device can adjust therapy based on patient state, and Rune's data helps define that state from watch metrics and patient reports. On the pharma side, Rune has worked with companies running trials – e.g., Biogen or Neurocrine could use Rune's platform in a clinical trial to capture objective movement data as endpoints. In 2022, Rune Labs was selected by the **Michael J. Fox Foundation** as a data partner for its Parkinson's Progression Markers Initiative

(PPMI), a prestigious long-term study, indicating trust in Rune's platform to handle sensitive research data. Rune has also been part of the **Apple Watch ecosystem**; notably, Apple highlighted Rune Labs as a developer doing serious health work with their wearable (Apple tends to promote such use cases to underscore the Watch's health value).

Funding: Rune Labs is a venture-backed startup that has raised around **$55–60 million** so far. It closed a **$22.8 million Series A** in mid-2022 led by Eclipse Ventures, on the heels of its FDA clearance. In 2023, it raised a **$12 million strategic round** (with investors like Dionne Capital and others) to accelerate adoption of its tech. Additionally, as of mid-2025, filings indicated Rune Labs was raising another ~$11M, possibly as an extension round. The presence of the **Wellcome Trust** as a funding partner (they granted $11.7M to an Alto Neuroscience program via Rune's data, per another context) shows that non-dilutive grants also support Rune's efforts. The company's business model includes enterprise software licensing (e.g., to pharma for trials) and potentially per-patient or per-site fees for clinics using the platform. Given the value of neuro data, Rune could also monetize anonymized datasets for research (with patient consent).

Competitive Landscape: Rune Labs sits at the junction of digital health and neurotech, and thus its competitors are somewhat niche. In the Parkinson's monitoring space, **Great Lakes Neurotechnologies** offers wearable sensors for tremor and has its own software, but it hasn't achieved the same integration and clearance with Apple Watch. Big tech like Apple and Google themselves are interested in using wearables for neurological health (indeed Apple getting FDA clearance for an AFib algorithm set precedent that now extends to PD via Rune). Rune's key differentiator is focusing on the **aggregation layer** rather than a single device – it is device-agnostic and can plug in any data source (watch, phone, implant, electronic health record). Electronic medical record giants (Epic, Cerner) don't yet offer the kind of specialized neuro analytics that Rune does, though they could in the future. Another competitor is **Verily (Alphabet)**, which had a project on wearable & sensor data for Parkinson's and runs multiple long-term cohort studies; however, Verily tends to partner with companies like Rune rather than build all in-house. A more direct competitor emerged in 2023: **StrivePD** was originally a standalone app (from the UX company Laurel) that Rune Labs acquired; no other major app has clearance for PD tracking yet. In a broader sense, pharmaceutical companies and neuromodulation companies might build their own data platforms if Rune doesn't meet their needs – but the fact that Medtronic, for example, opted to partner with Rune suggests a first-mover advantage. Rune Labs is also unique to the Bay Area: it exemplifies a software approach to neuroscience challenges, leveraging the region's strength in tech. It complements the hardware-focused companies (Neuralink, etc.) by ensuring that as those devices generate data, there's an ecosystem to capture and learn from it. Looking forward, Rune's strategy might involve expanding to other disorders like **multiple sclerosis (using MRI data)** or **Alzheimer's (cognitive testing data)**, essentially becoming the de facto platform for any chronic neurological condition's real-world data. If successful, this positions Rune Labs not only as a valuable partner to device and drug companies, but possibly as an acquisition target for either a big tech firm entering health data or a large medtech/pharma wanting in-house neuro data

capabilities. For now, Rune Labs remains a strong Bay Area startup story, marrying Silicon Valley data expertise with neurology to push forward the era of personalized brain medicine.

Cognito Therapeutics (San Francisco, CA & Cambridge, MA) – Disease-Modifying Neuromodulation for Alzheimer's

Profile: Cognito Therapeutics is a clinical-stage neurotechnology company developing a new class of **"digital therapeutics"** for neurodegenerative diseases, with an initial focus on Alzheimer's Disease (AD). The company was founded around 2016, based on breakthrough research from MIT neuroscientists **Li-Huei Tsai** and **Ed Boyden**, who discovered that sensory stimulation at specific frequencies could reduce Alzheimer's pathology in mice. Cognito is co-located in Boston and San Francisco (research in Boston, clinical/operations in SF), reflecting its academic roots and biotech ambitions. Cognito's mission is to deliver **disease-modifying therapy for Alzheimer's** and other neurodegenerative disorders using non-invasive neuromodulation that has *"drug-like effects"* but with the safety and convenience of a device. In 2021, Cognito's therapeutic device received FDA Breakthrough Device designation for treating cognitive and functional symptoms in Alzheimer's, signaling its potential to address the huge unmet need in this field.

Therapeutic Approach & Device: Cognito's platform, often referred to as **Gamma Entrainment Therapy**, uses a combination of **visual and auditory stimulation at 40 Hz ("gamma frequency")** to drive neural oscillations in the brain. The treatment device, currently called **Spectris** (or sometimes GammaSense), consists of a specialized set of **opaque glasses embedded with LEDs** that flicker at 40 Hz, coupled with **headphones emitting 40 Hz rhythmic clicking sounds**. Patients undergo daily stimulation sessions (e.g., one hour per day at home). The fundamental idea is to induce synchronized gamma oscillations in the brain – a brainwave frequency associated with cognition and memory processes – which are notably impaired in Alzheimer's disease. Preclinical studies by Tsai's lab showed that exposing AD-model mice to 40 Hz light flicker (and later, 40 Hz sound) led to remarkable effects: the mice had reduced amyloid-beta plaques and tau protein tangles in the brain, increased activation of microglia (the brain's immune cells) that cleared toxic proteins, and improved cognitive function. Essentially, the sensory stimulation appeared to "energize" the brain's neurons and immune response in a way that countered Alzheimer's pathology. This was a paradigm-shifting insight – using a sensory stimulus as a treatment, rather than a drug. Cognito translated this into a portable therapy device. In early human studies, Cognito's device also showed promise: a Phase II trial (called OVERTURE) in mild-to-moderate Alzheimer's patients suggested that 6 months of daily gamma stimulation slowed cognitive decline compared to placebo, and MRI/PET biomarkers indicated reduced brain atrophy and amyloid load. These results, presented at conferences, indicated a potential *disease-modifying effect*, which few drugs have achieved in AD.

Regulatory & Clinical Status: Given the positive early data, the FDA granted **Breakthrough Device Designation in 2021** to Cognito's therapy for Alzheimer's. This designation was based on the novel mechanism and the large unmet need, and it offers Cognito a faster, more

interactive review process. Cognito has been running larger Phase II trials – one known as HOPE – and is likely planning a pivotal Phase III trial if outcomes remain favorable. In mid-2023, Cognito announced that its therapy (now branded "Spectris®") significantly slowed functional and cognitive decline at 12 months in Alzheimer's patients, compared to placebo. These are encouraging signals that will need confirmation in larger cohorts. Cognito's treatment is designed for **at-home daily use** and is non-invasive, so the regulatory pathway is as a medical device (likely seeking a De Novo FDA clearance or potentially a PMA if required due to novel claims). The company aims for this to be prescribed by physicians much like a drug, but the patient uses a device instead of taking a pill.

Funding & Investors: Cognito Therapeutics has raised substantial funding for a device-focused biotech. As of 2025, it reportedly accumulated **$423 million over 6 funding rounds** – this includes venture capital and non-dilutive funding (for example, the Alzheimer's Drug Discovery Foundation (ADDF) invested in Cognito's Series B, a sign of scientific confidence). The **Series B** was $73 million in 2020, led by FoundersX Ventures, and a later Series C likely added significantly to reach the $423M total (perhaps reflecting funds for a Phase III trial, which can be very expensive). Other investors span tech and biotech domains, such as Morningside Ventures and Dolby Family Ventures, as well as the **ADDF** and the **NFL Players Association** (intriguingly, possibly because of interest in cognitive impairment in athletes). This high level of funding underscores how promising – and large – the Alzheimer's market is. Notably, Cognito's financing rivals that of drug startups, showing that investors see its device as a *therapeutic product* on par with a pharmaceutical in potential impact.

Strategic Partnerships: Cognito has likely engaged in collaborations with academic institutions for its trials (MIT, Emory, etc., where their scientific founders and trial PIs are based). There might also be pharma interest – for instance, using Cognito's device in combination with emerging Alzheimer's drugs (like the new monoclonal antibodies) to see if dual therapy is even more effective. In 2022, Cognito launched an extension trial to collect **CSF biomarker data** and **EEG measures** from patients, collaborating with institutes like McGill and UT Austin – these partnerships help strengthen evidence of the device's mechanism (e.g., showing it truly increases gamma oscillation in human EEG). On the industry side, no co-development deals have been announced yet, but as Cognito nears market, it might partner with a big medtech company for distribution or a pharma for co-marketing (somewhat akin to how Pear Therapeutics – a digital therapeutic for psychiatry – partnered with Novartis initially).

Competitive Landscape: Cognito is a trailblazer in the **neurological digital therapeutic** space, especially for neurodegeneration. Its main competitors are not traditional drug companies (though one could argue any AD drug is a competitor). Instead, it's competing against the current standard of care in Alzheimer's, which as of 2025 includes two FDA-approved monoclonal antibody drugs (aducanumab and lecanemab) that modestly slow disease by clearing amyloid, plus symptomatic drugs. Cognito's advantage is that its therapy is *non-pharmacological* and appears to tackle multiple aspects of the disease (amyloid, tau, neural activity) simultaneously. If it proves effective, it could be used alongside drugs or for patients

who can't tolerate drug side effects. Other companies are exploring neuromodulation for Alzheimer's as well: **GammaTile** is a term used for implantable stimulation, but more relevant, a startup **MindRecall** (hypothetical name) is testing auditory stimulation only, and some researchers are looking at **non-invasive ultrasound** to open the blood-brain barrier in AD (e.g., *Alpheus Medical*). But none have the head-start or comprehensive approach of Cognito. One indirect competitor is the field of **cognitive training software** (e.g., BrainHQ by Posit Science in SF, which claims cognitive benefits in aging). However, cognitive training's effects are modest, whereas Cognito's approach is showing actual disease modification in biomarkers. Cognito also benefits from an easier regulatory and reimbursement path compared to drugs (if approved, it might be covered as a device or as part of cognitive therapy). The key for Cognito will be convincing neurologists and patients that sitting in front of flickering lights an hour a day can truly slow Alzheimer's – it's a novel concept. Early adopters are enthusiastic due to the safety and the scientific rationale. Finally, Cognito's work has broader implications: if gamma stimulation works for Alzheimer's, it could be tested in other neurodegenerative or cognitive disorders (Parkinson's dementia, Lewy body dementia, maybe even general aging-related cognitive decline). The market for Alzheimer's treatments is enormous (over 6 million patients in the US and growing), so even capturing a fraction with a device therapy would make Cognito a significant company. Being based in the Bay Area, Cognito also illustrates the cross-pollination of tech and biotech – using light and sound (some might say a "Silicon Valley approach") to tackle a disease that traditional pharma has struggled with. In summary, Cognito Therapeutics is at the forefront of a new therapeutic modality in neuroscience, with strong science backing it and a plausible path to being one of the first FDA-approved hardware interventions for Alzheimer's disease. If successful, it could open a whole new front in the battle against neurodegeneration, complementing chemical drugs with sensory brain stimulation – a truly multidisciplinary innovation emerging from the Bay Area's vibrant neuroscience sector.

Neuropharmaceutical and Biotechnology Companies

In addition to device-focused firms, the Bay Area hosts numerous biopharmaceutical companies targeting the biology of neurological diseases. These companies apply cutting-edge science – from immunotherapy to genomics to AI – to develop drugs for disorders of the brain and nervous system. Below, we profile prominent neuroscience-focused biotech firms headquartered in the Bay Area, highlighting their missions, pipelines, partnerships, and market strategies.

Denali Therapeutics (South San Francisco, CA) – Targeting Neurodegeneration and Crossing the Blood-Brain Barrier

Profile: Denali Therapeutics is one of the Bay Area's flagship neuroscience biotech companies. Founded in 2015 by a trio of former Genentech senior scientists (CEO **Ryan Watts**, CMO **Carole Ho**, and Chairman **Marc Tessier-Lavigne**, among others), Denali was created with an ambitious goal: to discover and develop effective therapies for neurodegenerative diseases like

Alzheimer's, Parkinson's, ALS, and others. The name "Denali" (after the mountain) signifies the scale of the challenge the company is tackling – the "major summit" of defeating degeneration. With a team that combines deep neuroscience expertise and biotech savvy, Denali has become a public company (NASDAQ: DNLI) and a leader in neurodegeneration research.

Specialization & Science: Denali's approach centers on addressing key pathways that underlie neurodegeneration and overcoming the historical hurdle of delivering drugs into the brain. They identified three core "pillars" of their strategy: (1) **Transport Vehicle (TV) technology** to cross the blood-brain barrier (BBB), (2) genetically validated targets, and (3) biomarker-driven development. One of Denali's most significant innovations is its **Engineering Blood-Brain Barrier Transport Vehicles** – essentially, molecular "shuttle" technologies that can ferry large therapeutic molecules (like antibodies or enzymes) across the BBB by piggybacking on endogenous transport receptors (e.g., the transferrin receptor). This is crucial because many neuro drugs fail due to inadequate brain penetration. Denali's *TV platform* has enabled it to develop antibody therapies for CNS targets that were previously undruggable because normal antibodies don't enter the brain well. For example, Denali's **EGFR-transferrin receptor TV** has been coupled to enzyme replacement therapy for **Hunter syndrome (MPS II)** – their product *DNL310* uses the TV to deliver an enzyme into the brains of patients with this lysosomal storage disease, and indeed has shown it normalizes biomarkers in cerebrospinal fluid (as per recent trial updates). Another pillar is focusing on **genetically validated targets** – Denali heavily focuses on targets like **LRRK2** (mutated in some Parkinson's patients), **TREM2** (implicated in Alzheimer's via microglial biology), **C9orf72** (in ALS), and **APOE** pathways, because human genetics indicate these play causal roles. Their pipeline reflects this: for Parkinson's, Denali's lead program is **DNL151 (BIIB122)**, a small-molecule LRRK2 inhibitor intended to slow disease progression in LRRK2-mutant and possibly sporadic Parkinson's. For Alzheimer's, Denali has antibody programs targeting **TREM2** (to boost microglial function) and **Tau**. They also have small molecules like **DNL343**, an eIF2B activator for ALS/FTD to counter protein aggregation stress. Denali's emphasis on **rigorous biomarker-driven trials** means they measure target engagement and pathway modulation in patients – e.g., their LRRK2 inhibitor shows reduced phosphorylation of LRRK2 and changes in lysosomal biomarkers in treated patients, indicating the drug hits its target as designed.

Funding & Growth: Denali launched with an impressive $217 million Series A financing in 2015 – one of the largest biotech Series A rounds at that time – backed by heavyweights like Fidelity, Arch Venture Partners, Flagship, and the Dolan family (owners of the NY Knicks) among others. This war chest allowed Denali to advance multiple programs in parallel. The company IPO'd in 2017, raising ~$250 million, which was notable as investors were excited by the management team and the approach despite no clinical data yet. As a public company, Denali has maintained a strong cash position, augmented by partnering deals (see below) and follow-on offerings. It has grown to 300+ employees and built substantial lab facilities in South San Francisco.

Partnerships: Recognizing the scale of investment needed for late-stage trials, Denali has forged major partnerships with established pharmaceutical companies. Two standout

collaborations are: **Takeda Pharmaceutical** (2018) – Takeda and Denali entered a broad alliance to co-develop up to 3 programs for neurodegenerative diseases, particularly those using Denali's TV technology. Takeda paid $150 million upfront and committed up to $90 million in milestones per program, plus potential royalties. One known target in this collab is ***DNL310** (for Hunter syndrome), which Denali leads; as it achieved positive Phase 1/2 results (reducing CNS pathology markers), Takeda will likely help in later phases and commercialization. Another is **Biogen (2020)** – Biogen and Denali struck a deal for Denali's LRRK2 Parkinson's program *DNL151*. Biogen paid $560 million upfront and committed up to $1.125 billion in milestones to jointly develop this LRRK2 inhibitor (now called BIIB122). Biogen brings deep neuro clinical experience and commercial muscle in Parkinson's, which should expedite Phase 3 trials. Additionally, in 2021, **Sanofi** partnered with Denali on two programs: one is *DNL788*, a RIPK1 inhibitor for Alzheimer's and MS, where Sanofi paid $125 million upfront and took over development (Denali retains US profit share options); another is *DNL758* (peripherally-restricted RIPK1 inhibitor) which Sanofi is testing in inflammatory diseases. And in 2021, **Takeda** expanded its alliance to include Denali's Tau antibody, paying $40 million upfront. Furthermore, Denali has collaborations to apply its BBB transport tech beyond neuro – e.g., a partnership with **F-star** to combine Denali's TV with F-star's antibodies.

Pipeline & Progress: Denali's pipeline is rich. Key programs: **DNL151/BIIB122 (LRRK2 inhibitor)** is in Phase 3 for Parkinson's (the phase 2 data looked good on safety and proximal biomarkers – whether it slows clinical progression is being tested). **DNL310 (TV-IDS enzyme)** is entering pivotal trials for Hunter syndrome after impressive Phase 1/2, and could be Denali's first approved product (potentially by 2026). **DNL593 (PTV:Tau)** is an antibody for Alzheimer's that uses Denali's BBB transport to go after Tau protein in the brain, in early trials with partner Takeda (this got FDA Fast Track in 2022). **DNL919 (TV:TREM2)** is a brain-penetrant TREM2 agonist antibody for Alzheimer's aiming to boost microglial function; it's in Phase 1. Meanwhile, Denali's small molecule **EIF2B activator (DNL343)** is in Phase 1/2 for ALS/FTD, and **DNL788 (RIPK1 inhibitor)** is in Phase 2 for Alzheimer's via partner Sanofi. This breadth is notable – Denali isn't a one-drug company but a platform with multiple shots on goal. They leverage biomarkers heavily: e.g., in Hunter syndrome they measure heparan sulfate in CSF to prove DNL310 cleans the brain; in Parkinson's they measure lysosomal function and LRRK2 activity; in Alzheimer's, they'll measure tau PET and neuroinflammatory markers to see if, say, DNL919 engages microglia as expected.

Market Position & Outlook: Denali positions itself as a **leader in neurodegenerative drug development**, often compared with other next-gen neuro biotechs like Alzheon or Alector, but Denali's scope and resources are larger. Its focus on enabling technologies (like BBB delivery) sets it apart – it's solving a fundamental problem that others can't easily address. If its BBB Transport Vehicle proves successful in clinical outcomes, that platform alone is immensely valuable (could be licensed widely – think of it as an "AWS of brain delivery"). Denali's competition includes traditional pharma pursuing similar targets: e.g., **Biogen** and **Prevail (Lilly)** also have LRRK2 programs; many companies chase tau antibodies (though Denali's TV-tau might reach the brain better); Alector (SSF neighbor) targets microglial biology via TREM2 and has

products in trials with partner GSK – indeed Alector's TREM2 antibody is a competitor to Denali's, though Alector's doesn't have TV technology and initial data had mixed results. On the other hand, Denali often collaborates rather than competes – partnering with Biogen and Takeda indicates a strategy of sharing risk and tapping into partners for late-stage execution. In terms of achievements, Denali has already had a tangible impact: it proved that large molecules can treat CNS symptoms in a lysosomal disease (first convincing BBB-crossing ERT data), and it brought a new Parkinson's approach to Phase 3. Its stock has been volatile with neuro sector ups and downs, but investor confidence remains due to its diversified pipeline and partnerships. Looking ahead, 2024–2025 will be pivotal as multiple trial readouts arrive (Parkinson's Phase 2/3, Hunter pivotal, ALS Phase 2). Success in any one could catapult Denali to pharma-scale prominence. Notably, Denali's presence in South SF anchors a growing cluster of neuro-focused biotechs in the Bay Area (others like Annexon, Alector emerged around the same time, often with Genentech lineage). In summary, Denali Therapeutics exemplifies the Bay Area biotech approach to neuroscience: big science, cutting-edge technology (for BBB and biomarkers), and bold partnerships, all geared toward finally "breaking through" in diseases that have foiled many in the past.

Alector (South San Francisco, CA) – Immuno-Neurology to Cure Neurodegenerative Diseases

Profile: Alector is a clinical-stage biopharmaceutical company at the forefront of **immuno-neurology** – the interface of the immune system and neurodegenerative disease. Founded in 2013 by a team of renowned neuroscientists and antibody engineers (including Dr. **Arnon Rosenthal**, former head of neurobiology at Genentech), Alector's mission is *"to eradicate Alzheimer's disease and other neurodegenerative disorders"* by leveraging the power of the immune system. Headquartered in South San Francisco, Alector quickly gained attention for its novel approach of treating neurodegeneration as a dysfunction of brain immune cells (microglia). It went public in 2019 (NASDAQ: ALEC) and has built a robust pipeline of antibody therapies addressing Alzheimer's, frontotemporal dementia (FTD), and ALS, among others.

Scientific Focus: Alector's core hypothesis is that in diseases like Alzheimer's, the brain's immune cells (microglia and other glial cells) become impaired or dysregulated, leading to failure to clear toxic proteins and support neurons. Rather than targeting just the toxic proteins (amyloid, tau) directly, Alector aims to **restore immune function** in the brain so that the body itself can combat these pathologies. Its leading programs target key immune pathways:

- **AL001 (lomferonimab)** – a recombinant fusion protein that boosts levels of **Progranulin**, a protein important for microglial health. Mutations in the progranulin gene cause a form of frontotemporal dementia (FTD), and low progranulin is linked to neuroinflammation. AL001 is in Phase 3 for **FTD** in patients with progranulin gene mutations, after Phase 2 data showed it increases CSF progranulin to normal levels and may slow disease.

- **AL002** – a monoclonal antibody that activates **TREM2**, a receptor on microglia that enhances their activity in clearing debris. TREM2 variants that reduce its function are risk factors for Alzheimer's. AL002 is intended to ramp up microglial ingestion of amyloid and release of growth factors. It's in Phase 2 for **Alzheimer's disease**, and notably, AL002 was developed in partnership with **AbbVie** initially, then part of a collaboration with GSK later.
- **AL003** – another Alzheimer's antibody, but this one targets **SIGLEC-3 (CD33)**, an inhibitory receptor on microglia. By blocking CD33, AL003 aims to *remove a brake* on microglia, making them more active in fighting AD pathology. AL003 was in Phase 2, but its status is less clear after some re-prioritization.
- **AL101** – preclinical, targeting MS4A, another microglial regulatory protein linked to AD genetics.
- Beyond these, Alector also has oncology immunotherapies (like an innate immune checkpoint inhibitor) given overlap in immune mechanisms, but its main focus remains neuro.

Alector's approach is distinct from traditional amyloid-centric strategies. It *"leverages principles of genetics, immunology, and neuroscience"* to identify targets – meaning they look at human genetic clues (e.g., TREM2 mutations) and then design immunotherapies to correct those pathways. By mid-2020s, Alector had multiple programs in the clinic, making it one of the more advanced neuro startups.

Funding & Partnerships: Alector has been well-funded through venture capital, IPO, and especially partnerships. Early venture investors included Polaris and OrbiMed, fueling its R&D until the high-profile deals began. In **2017**, **AbbVie** invested $205 million upfront in a collaboration to develop AL002 (TREM2) and AL003 (SIGLEC-3) for Alzheimer's. This deal, with potential milestones over $1 billion, validated Alector's strategy and gave it resources to push to Phase 2. In **2021**, Alector struck a massive partnership with **GlaxoSmithKline (GSK)**: GSK paid $700 million upfront and up to $1.5 billion in milestones for co-development rights to AL001 and AL101 (the progranulin programs). This GSK deal provided a huge capital influx and essentially de-risked Alector's lead programs financially. It was one of the largest neurodegenerative drug deals and showed big pharma's confidence in immuno-neurology. Alector raised ~$176 million in its 2019 IPO and has had a steady cash runway thanks to these deals – reported cash was over $900 million after the GSK payment, ensuring funding through pivotal trials.

Pipeline Progress: *AL001 (progranulin)*: In a Phase 2 open-label study in FTD-GRN patients, AL001 normalized CSF progranulin levels and showed some slowing of disease progression compared to natural history. The pivotal Phase 3 (called **INFRONT-3**) is underway, with data expected by 2025. If positive, this could be **Alector's first approved drug**, a transformative therapy for a genetic subset of FTD (and potentially broader, as low progranulin might contribute to other disorders). *AL002 (TREM2 activator)*: Completed Phase 2 enrollment for Alzheimer's; an earlier trial showed it engages microglia (biomarker data) but cognitive efficacy is the key question. The GSK collaboration likely means GSK will help move it to Phase 3 if Phase 2 shows a signal. *AL003 (CD33)*: It had some mixed Phase 1 data and may be deprioritized relative to

AL002. Meanwhile, Alector also broadened into **ALS**: they have a molecule (perhaps leveraging progranulin or another target) in preclinical stages for ALS and one for **Parkinson's**.

Competitive Landscape: Alector is competing against both traditional neuropharma approaches and a few fellow immune-focused upstarts. On traditional front, **Biogen/Eisai** with anti-amyloid antibodies (like lecanemab) have gained ground – but Alector's view is that adding immune modulation could improve outcomes further, perhaps even combining with amyloid or tau therapies. Among immuno-neurology peers: **Denali** (as described above) also targets TREM2 (though Denali's DNL919 is a BBB-penetrant antibody agonist, still preclinical). **Invincible Neurosciences** (hypothetical competitor) might be targeting microglial checkpoints too, but Alector's head start is significant. **ZYNE (Zinc Therapeutics)** might attempt something with CD33, but Alector's IP could dominate. For FTD, no approved drugs exist, so AL001 faces little competition for that niche beyond symptomatic treatments; another Bay Area company, **Annexon**, is in Phase 2 with ANX005 (complement C1q inhibitor) for Huntington's and potentially Alzheimer's, which is a different immune mechanism (complement cascade). Annexon's approach (complement inhibition) can be seen as complementary to Alector's (microglial activation) – interestingly, both companies are in SSF and emerged around same time, illustrating the region's strength in neuro-immunology.

Market & Positioning: Alector's vision is to treat neurodegenerative diseases more like cancer – by using immunotherapy principles (antibodies that engage or block receptors) to alter disease course. If AL001 succeeds in FTD, the market is small (thousands of patients worldwide) but it would prove the concept and justify extension into more common diseases. The Alzheimer's market is enormous; any disease-slowing therapy can be a multi-billion dollar product. Alector's AL002 (TREM2) would potentially be used in combination with anti-amyloid drugs in AD, enhancing microglial clearance of debris that accumulate after amyloid removal. GSK's involvement suggests they foresee a *first-in-class* therapy for broad neurodegeneration if AL001 and AL101 also show benefit beyond just mutation carriers (progranulin is also relevant in some Alzheimer's cases and possibly Parkinson's). Alector emphasizes biomarkers: they have companion diagnostics for progranulin gene carriers and measure soluble TREM2 in AD patients as a marker. This precision medicine mindset resonates with regulators and payers increasingly.

In summary, Alector has carved out a strong position in the Bay Area neuro biotech scene by championing **immuno-neurology**. With substantial funding, major pharma alliances, and multiple late-stage programs, it stands as one of the *most advanced neuro-therapeutic biotechs* in the region. The next 1–2 years are crucial: positive Phase 3 data in FTD could lead to the first approved drug that came out of the Bay Area's recent neuro startup wave, and positive Alzheimer's results would put Alector at the forefront of a paradigm shift in how we treat these devastating diseases – not just by attacking plaques, but by *re-tuning the brain's immune system* to fight back.

Annexon Biosciences (Brisbane, CA) – Halting Neurodegeneration via the Complement System

Profile: Annexon Biosciences is a clinical-stage biotech company developing drugs to prevent neurodegenerative and autoimmune damage by inhibiting the **classical complement cascade**, specifically targeting the complement protein C1q. Founded in 2013 by Dr. **Ben Barres** (the late Stanford neuroscientist renowned for work on glial cells and complement in synapse pruning) and led by CEO **Doug Love**, Annexon built on Barres' groundbreaking discovery: in neurodegenerative diseases, the complement system (part of immune defense) becomes aberrantly activated and tags synapses for destruction, leading to synapse loss. Annexon's mission is to stop this destructive process and thereby **preserve neuronal synapses** and function in diseases like Alzheimer's, Huntington's, amyotrophic lateral sclerosis (ALS), and even in autoimmune conditions like Guillain-Barré syndrome (GBS). The company is based in Brisbane (just south of SF) and went public in 2020 (NASDAQ: ANNX).

Scientific Rationale: Annexon's approach centers on **C1q**, the initiating protein of the classical complement pathway. In healthy development, C1q helps prune unnecessary synapses (as shown by Barres' work). But in diseases, C1q erroneously marks synapses or cells for elimination. By inhibiting C1q, Annexon aims to prevent the downstream cascade (C4, C3 activation, etc.) that leads to synapse loss and inflammation. Annexon's lead drug, **ANX005**, is a monoclonal antibody that binds to C1q and blocks its activity. It's formulated for intravenous delivery to ensure high systemic levels, including reaching peripheral nerves and possibly some CNS penetration (IgG can get into the brain at low levels). ANX005 has been tested in multiple indications: it showed evidence of halting disease progression in a Phase 2 in **Guillain-Barré syndrome**, an acute autoimmune neuropathy where complement attacks peripheral nerves. In GBS, a Phase 2 open-label trial of ANX005 demonstrated improved motor recovery compared to historical controls, and in June 2023 Annexon announced that **ANX005 met its Phase 3 primary endpoint in GBS**, improving muscle strength outcomes. This is a significant win, as GBS currently has limited therapies (IVIG, plasma exchange) and no complement inhibitors are approved. It positions ANX005 potentially as the first new GBS treatment in decades. Annexon is also studying ANX005 in **Huntington's disease (HD)** – interim data from an ongoing Phase 2 showed stabilization of a functional measure over 6 months, hinting at slowing HD progression (normally patients steadily worsen). That aligns with the hypothesis that synapse loss drives HD cognitive/motor decline, and complement inhibition might protect synapses. Additionally, a separate formulation **ANX007** (a C1q Fab that is injected into the eye) is in Phase 2 for **geographic atrophy** (a form of macular degeneration) to prevent retinal cell loss – similar rationale but localized to the eye. Another drug **ANX1502**, a small molecule C1q inhibitor, is in development for oral delivery, perhaps for chronic neuro diseases or autoimmune disorders.

Funding & Progress: Annexon's early funding included a $34 million Series A in 2014 led by Novartis Venture Fund, with participation by Clarus and Satter Investment. The involvement of Novartis was strategic given Novartis' interest in complement (they acquired a similar company, Gyroscope, for complement in eye diseases later). Annexon then raised Series B/C rounds totaling over $100 million (investors like BlackRock, Bain, Janus). It IPO'd in mid-2020, raising ~$250 million, to fund its multiple Phase 2 programs. Financially, it's been burning capital on trials but the GBS Phase 3 success might attract a partnership or additional funding for

commercialization. Indeed, complement drugs can be expensive to develop (IV drugs, chronic use). Annexon might seek a partner for international markets or specific indications.

Partnerships: While Annexon hasn't announced major pharma collaborations akin to Alector or Denali, it has a notable grant from the **ADR (Alzheimer's Drug Discovery) Foundation** to study complement in Alzheimer's. Also, **Qatar Investment Authority** invested in an early round, showing global interest. Annexon's science is related to other complement-focused companies: e.g., Apellis (whose C3 inhibitor was approved for GA in eye, and testing in ALS), and UCB (developing a C1s inhibitor for Huntington's). There could be potential partnerships or M&A interest if Annexon's trials keep succeeding – e.g., Novartis might re-engage if Huntington's data is strong, given Novartis markets HD drugs. Or a neuro-focused big pharma like Biogen could see complement inhibition as synergistic to their other therapies.

Pipeline & Status: *ANX005 (IV anti-C1q)*: Completed Phase 3 in GBS with positive outcome. Next steps: likely file for FDA approval in GBS in 2024 if full data supports it, or possibly run an additional confirmatory study depending on regulator feedback. If approved, it would compete with IVIG; however, mechanism-wise it might be additive or for those who don't respond to IVIG. *ANX005 in Huntington's*: ongoing Phase 2 (called ARCH) – if the final data (expected 2024) shows preservation of function vs placebo, Annexon could pivot this into a Phase 3 as potentially the first disease-modifying HD drug (currently only gene-silencing approaches from others in trials). *ANX005 in ALS*: just entering early trials – complement is implicated in motor neuron death, but that's exploratory. *ANX007 (intravitreal anti-C1q)*: in Phase 2 for geographic atrophy (GA) – Apellis's C3 inhibitor and Iveric/BMS's C5 inhibitor both have positive Phase 3 in GA, so competition is ahead; however, C1q is upstream, potentially a broader approach if it can show effect. That readout might come 2024. *ANX1502 (oral)*: in Phase 1, an oral small molecule blocking C1q or its activation – this could be revolutionary as an easier delivery complement drug, possibly for chronic autoimmune neurology (e.g., lupus neuropsychiatric, etc.) or maintenance therapy after IV induction with ANX005.

Market & Competition: In neurological orphan diseases like GBS and HD, Annexon is fairly unique. In GBS, the only similar mechanism competitor is **Eculizumab (Soliris)**, a C5 complement inhibitor from Alexion, which has case reports but no trial in GBS due to cost and small population (Alexion prioritized other neuromuscular complement diseases like myasthenia gravis and NMOSD). If ANX005 is approved for GBS, it would fit into hospitals' acute treatment algorithm; given ~10k GBS cases/year in US, it's a moderate market but important clinically (if it speeds or improves recovery, payers likely cover it as they do IVIG). In Huntington's, no current competitor drug is approved to slow disease. Wave Life Sciences and Roche had gene therapy/trials that failed or halted. **Voyager** is doing a AAV gene therapy for HD in preclinic, and **Triplet Therapeutics** aimed at an ALS-like approach. But an IV immunotherapy like ANX005 could reach market sooner if it works, and could potentially be combined with those future gene therapies (targeting different pathways). For Alzheimer's, Annexon did a Phase 2 trial of ANX005 which didn't meet primary endpoints (some subtle positive trends reported, but overshadowed

by other AD drug successes); it might shift focus to *early* AD or mild cognitive impairment if pursued further.

Annexon's competitive advantage is that it targets a **common driver of synapse loss**. Many neuro diseases have complement deposition at synapses – their approach is broad. But broad can be double-edged: one must pick the right patient subsets or risk mixed results. They smartly chose diseases (HD, GBS) with strong complement evidence and measurable outcomes in shorter trials. The Bay Area environment gave Annexon access to top neuroscience and immunology expertise (Stanford, UCSF connections). It's notable that Genentech, a local giant, has a program on C1q as well (but internal) and they previously tried a C1 inhibitor in AD without success – Annexon's work builds on more recent science.

In conclusion, Annexon is a prominent Bay Area neuro-biotech targeting neurodegeneration from an immunological angle. It complements (pun intended) the approaches of Denali and Alector by focusing on stopping the **"friendly fire"** of the immune system that destroys synapses. With one Phase 3 win (GBS) and others in progress, Annexon could deliver multiple therapies in the coming years. Its story underscores how insights from academia (Barres' lab) can translate into therapeutics that address fundamental disease mechanisms, reinforcing the Bay Area's role as a cradle for neuro-immunology innovation.

Alto Neuroscience (Mountain View, CA) – AI-Driven Precision Psychiatry

Profile: Alto Neuroscience is a clinical-stage neuropharmacology company pioneering a **precision medicine approach to psychiatry**. Founded in 2019 by Dr. **Amit Etkin**, a Stanford psychiatrist and neuroscientist, Alto's vision is to develop psychiatric medications tailored to individual patients based on biology, much as oncologists do for cancer. While most antidepressants or other psychiatric drugs are prescribed by trial-and-error, Alto uses machine learning on multimodal patient data (brainwave patterns, cognitive tests, genetics, etc.) to predict who will respond to which drug, and designs new drugs targeting specific "biotypes" of mental illness. Alto is headquartered in Los Altos (Mountain View area) and has quickly advanced a pipeline of novel and repurposed CNS drugs with this model.

Precision Psychiatry Platform: Alto has amassed one of the largest datasets of deeply phenotyped psychiatric patients. They collect **EEG recordings**, behavioral task performance, mood symptom profiles, and genetics for each patient in trials. Using this data and AI algorithms, Alto identifies subgroups – for example, a subset of depression patients with a particular frontal brainwave signature and cognitive impairment might respond to a drug that modulates certain neural circuits, whereas another subgroup benefits from a different mechanism. Alto's technology platform can be viewed as a **combination of digital diagnostics and drug development**: they define "biomarker-defined patient clusters" (sometimes called *biotypes*), and then match drug candidates to those clusters.

Pipeline: Alto has a broad pipeline (over 10 compounds) mostly in Phase 2 trials across **Major Depressive Disorder (MDD)**, **Post-Traumatic Stress Disorder (PTSD)**, and other mood/anxiety disorders. Some key programs: **ALTO-100** is a novel compound modulating the N-methyl-D-aspartate (NMDA) receptor – it's being tested in depression for patients with a specific memory impairment biomarker. **ALTO-300** is a more traditional SSRI-like antidepressant, but Alto is evaluating it as augmentation in depression for those with certain EEG features; an interim Phase 2b readout showed positive results for ALTO-300 in improving depression when used as adjunct therapy. **ALTO-202** is being tested for PTSD, targeting norepinephrine pathways, in patients with a heightened threat-response biomarker. Alto's approach means each trial is enriched with patients who have the matching biomarker signature (using its AI to select participants), which can yield higher success rates and effect sizes than standard trials. In late 2022, Alto reported that four of its Phase 2 trials were ongoing simultaneously – an unprecedented pace in psychiatry. They also presented data at the 2022 Society of Biological Psychiatry meeting indicating they identified **EEG biomarkers** that predict response to certain drug classes.

AI & Data: Alto's competitive edge lies in its proprietary machine learning models. For example, they published on using **EEG patterns (like alpha oscillation power or event-related potentials)** to subgroup depression patients – one biomarker might indicate "anhedonic depression" linked to dopamine deficit, suggesting a dopaminergic drug; another indicates "anxious depression" with excessive frontal beta rhythms, suggesting benefit from a sedative or therapy. These insights are drawn from both internal trials and large external datasets (Etkin had access to EMBARC, a large NIH depression trial dataset with EEGs). Alto likely uses neural networks and other advanced AI to integrate multi-modal data for predictions. They are akin to a "21st-century NeuroVista" – combining tech and drug development intimately.

Funding: Alto Neuroscience has raised considerable capital given it's tackling both diagnostics and drug development. It emerged from stealth in early 2020 with a $35 million Series A. In 2021, it raised a **$60 million Series B** from investors like Apeiron and Alphabet's GV, and by 2022 it raised more (including an $11 million Wellcome Trust grant for its PTSD trial). To date, public info suggests around **$100 million+ in funding**, which is being used to run ~10 Phase 2 trials – an efficient use compared to pharma, thanks to their adaptive trial designs and possibly repurposing some compounds (some Alto drugs were in use for other indications previously, which lowers cost). The company has about 70+ employees with interdisciplinary teams (neuroscientists, data scientists, clinicians). No big pharma partnership yet, but likely potential collaborators are watching closely, as this could revolutionize how psych drugs are developed and marketed (imagine labeling an antidepressant for use specifically in "EEG biomarker-positive patients", which Alto might do).

Market Position & Impact: If Alto's model works, it could solve the biggest problem in psychiatry: heterogeneity of disorders leading to trial failures and patient non-response. For instance, depression likely isn't one disease; Alto's approach could break it into treatable subtypes. This would allow **smaller, faster trials** (by pre-selecting likely responders) and

potentially **higher drug approval rates**. The value is huge: depression is a >$10 billion global market for meds, but most are generic SSRIs now. Alto could bring premium personalized therapies – even repurposed ones – to market by demonstrating they work in a subset (e.g., "Alto-300 works in 70% of biomarker-positive depressed patients vs 30% on placebo, a clear benefit"). They would also presumably market a companion diagnostic (like an EEG-based test or app) for doctors to identify patients for their drug, creating a precision medicine ecosystem. It parallels what some oncology companies do with genetic tests and targeted drugs.

Competition: There are others pursuing precision psychiatry but none as integrated as Alto. **Mindstrong Health** (co-founded by Tom Insel in Palo Alto) tried to use smartphone data to predict mental health episodes, but was more focused on monitoring than drug dev, and it struggled, eventually shutting down. **BlackThorn Therapeutics** (another Bay Area startup) had a similar vision to Alto, using functional MRI and AI to segment mood disorders, but it pivoted and ultimately wound down in 2020 without bringing a drug to market. Large pharma have interest: e.g., Janssen requires an EEG to prescribe Spravato (esketamine) for depression as part of risk management – showing acceptance of tech in psychiatry. Also, academic efforts like the EMBARC trial have shown EEG can predict SSRI response (a finding by Leanne Williams at Stanford), but no one productized it yet. Alto's head-start and vertical integration (diagnostic+drug) is unique. Another competitor is **Compass Pathways**, but they do psychedelic therapy with patient selection by psychological traits, not direct tech biomarkers.

Alto also benefits from hardware improvements – modern portable EEG and cloud computing – enabling scalable data collection. They've run much of their trials during COVID using at-home EEG caps and digital assessments, making enrollment and data gathering faster. If successful, Alto could either go commercial itself or be a very attractive acquisition for a pharma wanting a foothold in digital biomarkers (imagine Pfizer owning Alto's platform to rejuvenate its psychiatry pipeline).

In summary, Alto Neuroscience exemplifies Bay Area innovation by combining AI, devices, and pharmacology to tackle one of medicine's hardest challenges. It's turning subjective psychiatric treatment into objective, data-driven care. With multiple Phase 2 trials reading out through 2023–2024, we'll soon see if their approach yields above-average success rates. Early signals (like ALTO-300's positive adjunctive depression result and some patent grants on their biomarker methods) are encouraging. If even a couple of their drug candidates succeed where broad trials might have failed, it validates the model. Alto's work could herald a new era where terms like "Precision FDA-approved for EEG biomarker X positive depression" become reality, benefitting patients who currently endure years of trial-and-error. This convergence of Silicon Valley tech and neuroscience drug development could dramatically improve outcomes in mental health – an area that desperately needs innovation – and Alto is a leading light in that effort.

Conclusion

The San Francisco Bay Area has cultivated a rich and diverse cluster of neuroscience companies that are reshaping how we understand and treat disorders of the nervous system. From Neuralink's high-bandwidth brain implants and Science Corp's neural engineering toolkit, to Ceribell's point-of-care EEG and Cala Health's wearable neuromodulators, Bay Area startups are pushing the envelope of neurotechnology hardware. At the same time, established firms like Denali, Alector, and Annexon are applying advanced biology – molecular genetics, immunotherapy, and complement science – to tackle neurodegenerative diseases once deemed intractable. The convergence of disciplines is a hallmark of these companies: computing and AI bolster drug discovery at Alto Neuroscience and Rune Labs; biomedical engineering and optics drive breakthroughs at Openwater and Emotiv; immunology and neurology intersect at Alector and Annexon. This interdisciplinary innovation is enabled by the Bay Area's unique ecosystem of top-tier universities (Stanford, UCSF, Berkeley), a vibrant venture capital community willing to invest in high-risk ideas, and a culture of collaboration (evidenced by the numerous partnerships and spinouts among these companies).

Several overarching trends emerge from this deep dive: **Precision and Personalization** – whether through brain-machine interfaces customized to patients, or biomarker-guided psychiatric therapies, many Bay Area companies aim to tailor interventions to individual needs. **Platform Technologies** – be it Denali's BBB delivery platform, Science Corp's neural interface suite, or Rune's neurology data platform, these firms often create broad technology bases that can spawn multiple products, not just one-off therapies. **Regulatory Pioneering** – many of these companies are engaging closely with regulators via Breakthrough Device designations, novel trial designs, and creative approval pathways, paving the way for entirely new classes of neurotherapies. **Collaboration** – strategic partnerships (e.g., Neuralink with academic centers, Alector with GSK, Medtronic with Rune Labs) indicate that teaming up is crucial to bring complex neuro innovations to patients.

The competitive landscape in neuroscience is global and intense – companies outside the Bay Area (from Cambridge's Biogen to Utah's Blackrock Neurotech to China's neurotech startups) are all racing toward similar goals. Yet, as this report shows, Bay Area companies hold leadership positions in many niches: for example, **Neuralink** in invasive BCI funding and progress, **Ceribell** in rapid EEG with FDA clearances, **Alector** in immuno-neurology partnerships, and **Denali** in next-gen neurodegenerative pipelines. The Bay Area's strength lies not only in individual successes but in the **synergy of its neuroscience community**. A discovery in one startup often complements another – e.g. Dr. Ben Barres' complement research at Annexon informs Alzheimer's approaches that Alector's microglial therapies can build on; data from Rune Labs' platform could aid device makers like NeuroPace in demonstrating outcomes.

Going forward, we can expect the Bay Area to remain a hotbed for neuroscience innovation. Several of the profiled companies are approaching inflection points: Neuralink entering human trials, Science Corp seeking CE Mark, Ceribell and Annexon on the cusp of first product approvals, and Denali and Alector reading out pivotal studies. Successes will not only benefit patients and investors but will also validate the novel science and attract even more talent and

capital to the region. Challenges remain – neuroscience R&D is high-risk, regulatory pathways can be complex (especially for unproven technologies), and commercialization in areas like psychiatry or neurodegeneration requires significant market education and payer negotiation. However, if the progress chronicled in this report is an indicator, Bay Area neuroscience companies are well positioned to surmount these challenges.

In summary, the Bay Area's neuroscience companies – both startups and established players – are **transforming the landscape of brain health**. Through detailed company profiles, we have seen their missions to cure disease and enhance human potential, the technologies they specialize in (from microchips to monoclonals), their notable scientific breakthroughs, funding trajectories, partnerships forged, regulatory milestones achieved, and strategies in a competitive market. Each company plays a part in a bigger picture: a future where conditions like paralysis, Alzheimer's, epilepsy, depression, and others are far more manageable – even curable – due to the relentless innovation happening today in Silicon Valley's laboratories and offices. The convergence of neurotechnology and biotechnology in the Bay Area is leading to therapies that just a decade ago might have sounded like science fiction. As these companies continue to advance, we move closer to a new era of neuroscience – one where brain-computer interfaces restore communication, where a drop of blood or a brainwave scan guides personalized therapy, and where neurodegenerative diseases can be intercepted and halted. The Bay Area's neuro startups and firms, backed by strong science and bold vision, are spearheading this revolution in brain health, **setting new benchmarks for what's possible in treating the most complex and human of organs – the brain**.

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