

EDITORIAL: Future of Neuromodulation Therapies

March 2022



The field of neuromodulation is currently undergoing a renaissance of new technological development. Profound improvements in the care of chronic pain patients may appear in the very near future.

New and emerging nerve-target locations, as well as high-frequency and patterned stimulation methodologies, both driven by the need for customized therapy, are paving the way to better clinical outcomes. As we await the future, artificial intelligence, neural sensing, novel target-specific stimulation patterns, and revolutionary approaches combining multiple neuromodulation therapies are likely to alter both the prescribing and usage patterns of physicians and patients, respectively. Moreover, the increasing demand for alternatives to opioid-based pain therapies will continue to drive the need for advanced clinical research.

As these new technological approaches continue to advance, the rigor of clinical research must keep pace. The demon-

stration of long-term efficacy to patients, physicians, and payers is essential. The majority of clinical trials conducted in neuromodulation lack true sham control arms or more specifically active sham control arms. The lack of clinical rigor can lead to the approval of devices that fail to deliver durable pain relief over time and sustained improvement in quality-of-life. Well-validated outcomes would potentially help avoid therapeutic fatigue, which is the primary reason most neuromodulation device are explanted. These explants add economic costs to the healthcare system, to be sure, but they also exact a heavy toll on patients, who must undergo multiple surgeries over a short period of time. In order to eliminate therapeutic fatigue, while advancing the rigor of clinical research, the creation of new software-driven systems must become a priority. Having hardware platforms capable of delivering multiple evidence-based therapeutic modalities through advanced software design will be a signal benefit to patients. In concert with this change, various biomarkers may become increasingly important components of the treat-

ment algorithm; identifying these substances may lead to a better understanding of how to individualize neuromodulation therapy, reduce - or potentially eliminate - opioid use, and, not incidentally, better grasp why therapies fail over time.

Lastly, we need to conduct the basic research that will yield a better understanding of the physiological mechanisms of action of these therapies. Doing so will enable drug and device developers to improve upon existing technologies and drive discovery in areas not yet explored. If these promising research approaches are adopted, we are optimistic that novel neuromodulation therapies may deliver long-term durable impact and move physicians from a palliative treatment paradigm to one offering a curative alternative to opioid drugs.

David Veino

Chief Operating Officer Neuros Medical

RECENT NEWS



Oct'21 Amolyt Pharma announced positive results from its Phase 1 clinical trial of AZP-3601, a potential treatment for hypoparathyroidism, at the American Society for Bone and Mineral Research 2021 annual meeting. The findings demonstrated that repeat administration of AZP-3601 to healthy volunteers induced a rapid, dose-dependent increase in serum calcium levels that was sustained and stable over the treatment period. AZP-3601 was generally well tolerated and raised no safety concerns.

www.amolytpharma.com



Feb'22 Magnolia Medical, inventors of Steripath®, the only FDA 510(k)-cleared device platform for reducing blood-culture contamination for sepsis testing, announced a USD46m growth-equity financing. RTW and Sectoral Asset Management were co-leaders of the funding, with significant participation by new investor Janus Henderson Investors. All existing major investors, including HealthQuest Capital, Evidity Health Capital, and SightLine Partners also participated. Concurrent with the financing, Marc-Andre Marcotte, CFA, a partner at Sectoral and Ovid Amadi, PhD, a senior analyst at RTW, have joined the Board of Directors.

www.magnolia-medical.com



Nov'21 Prilenia raised USD43m in an oversubscribed Series B financing. The funding was led by new investor Sands Capital, along with Forbion and Morningstar. Amplitude Ventures also joined the round as a new investor, while current investors Sectoral Asset Management, Talisman, and the ALS Investment Fund also participated. In parallel, the company announced the completion of patient enrollment ahead of schedule in its Huntington's disease Phase 3 clinical trial. Prilenia is on track to obtain top-line results in Q1 2023.

www.prilenia.com



Nov'21 Turnstone Biologics entered a multi-year research collaboration with Moffitt Cancer Center for the pre-clinical development of investigational tumor-infiltrating lymphocyte (TIL) therapies. The partnership will evaluate new clinical candidates using Turnstone's next-generation selected TIL approach in multiple solid tumor types. Moffitt also will in addition to IND submission of Turnstone's lead TIL program, TIDAL-01. In return, Turnstone will provide financial support for research and development at Moffitt over the multi-year collaboration.

www.turnstonebio.com

COMPANY FOCUS: Garuda Therapeutics

Q&A with
DHVANIT SHAH, PH.D.
Founder, President, & CEO



What is the mission of Garuda Therapeutics?

Garuda Therapeutics seeks to create a medical world that eliminates the dependency on donor or patient cells for blood stem-cell transplants. Our proprietary technology for generating off-the-shelf, self-renewing blood stem cells is poised to provide patients with rapid and broad access to consistent, durable, human leukocyte antigen (HLA)-compatible and transgene-free blood stem-cell therapies. Like bone-marrow transplants, our technology could provide potentially curative therapies for more than 70 diseases.

Manufacturing a cell-based product could be challenging. What is your plan for success?

Garuda is developing a pipeline, which includes therapeutic indications in hematologic malignancies, sickle-cell disease, β -thalassemia and bone-marrow-failure diseases, among others. We have recruited industry leaders to our manufacturing advisory board, and we are developing robust manufacturing technologies. Because the potential of our breakthrough platform technology is immense, we are also working to ensure our manufacturing infrastructure is robust, and we have the capacity to avoid delays in delivering these potentially life-changing cellular therapeutics to patients.

Launching new companies can be daunting. Tell us about your experience in Cambridge, MA?

In 2015, talented team members in my Harvard laboratory not only discovered how hematopoietic stem cells (HSCs) are born in Mother Nature, but we also were able to recreate these findings to make brand new human HSCs from an unlimited source of induced pluripotent stem cells. Given the significance of the discovery and the transformative potential of its application for human health, I began working to make our discovery available publically in the most responsible and meaningful way for all current and future stakeholders. After going through the MassConnect program and meeting with various venture capital groups, I joined with co-founders Kiran Reddy, David Scadden, and Sean Morrison to build Garuda from the ground up. In this journey, we have been fortunate to have the support of experts in blood stem-cell and bone-marrow transplants, as well as that of people with expertise in bringing transformative medicines to patients. Last year, we were delighted to announce our USD72m Series A financing, supported by marquee investors, including Sectoral, and move one step closer to bringing this potentially lifesaving treatment to patients.

Sectoral invested in Garuda Therapeutics'
Series A financing in September 2021.

ABOUT PRIVATE INVESTMENTS AT SECTORAL

Founded in 2000, Sectoral Asset Management Inc. is one of industry-leading specialists in managing global investment portfolios in the healthcare sector. Sectoral's first private equity investments were made by allocating assets from our small-cap funds. Since then, we have built on our early successes, backing innovative private companies, and launched the first dedicated fund to private companies in 2015. Investment focus is maintained on late-stage development for drugs and medical technologies addressing significant markets and having high potential for approval. We leverage Sectoral's established healthcare expertise and capabilities across public- and private-company investments to capture meaningful value creation for our investors.

INVESTMENT TEAM



Michael Sjöström, CFA
Senior Partner
Co-founded Sectoral in 2000



Marc-André Marcotte, CFA
Partner
Joined Sectoral in 2006



Stefan Larson, Ph.D.
Partner
Joined Sectoral in 2018



Alain Gilbert
Venture Partner
Sectoral advisor since 2015



Howard Riback, CPA, CA
Director
Joined Sectoral in 2015



François Beaubien, Ph.D., CFA
Principal
Joined Sectoral in 2014



Gabriel Douville, MBA
Principal
Joined Sectoral in 2021



Catherine Poulin-Filion
Senior Associate
Joined Sectoral in 2018

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Former Senior Vice President at Medtronic



David Veino
Industry Partner
Neuros Medical
Chief Operating Officer



Robert Wasserman, M.D.
Industry Partner
Inspirna, Inc.
Chief Medical Officer

VISIT US AT

sectoral.com/PE

OR

CONTACT US AT

PE@SECTORAL.COM

1010 Sherbrooke St. West, Suite 1610, Montreal, QC, Canada H3A 2R7

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