

PathMaker Neurosystems Inc.

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www.pmneuro.com



Industry: Medtech

- Lead product: First disease-modifying neuromodulation device to slow ALS disease progression
- Second product: First non-invasive neuromodulation device for treatment of muscle spasticity

Management Team

- Nader Yaghoubi, MD, PhD
Co-Founder and CEO
- Jerry Jennings, BSEE
Chief Technology Officer
- Jake Maslow, JD
Executive VP and Chief IP Officer
- Sheila Hemeon-Heyer, JD
VP Regulatory and Clinical Affairs



Board of Directors

- R. John Fletcher, MBA
Chairman, Board of Directors;
- John Donoghue, Ph.D.
Formerly Founding Director, Wyss Center for Neuroengineering



Scientific Advisory Board

- Zaghoul Ahmed, PhD
Scientific Founder; Chairman, Dept. of Physical Therapy, CUNY/CSI
- Emilio Bizzi, MD, PhD
Institute Professor, MIT
- Bechir Jarraya, MD, PhD
Neurosurgeon, Foch Hospital
- Ole Isaacson, MD, PhD
Professor, Harvard Medical School

Intellectual Property

- MyoRegulator platform under patent protection in 38 countries
- 5 registered trademarks
- Freedom-to-operate (FTO) confirmed

Funding to Date

- \$10.0M in non-dilutive capital and \$2.4M in seed/investor funding raised to date

Key Risks Retired to Date

- Strong safety profile established
- Robust ALS pre-clinical package
- ALS Early Feasibility Study completed
- ALS CALM study funded by US DoD
- Leading ALS centers engaged
- Confirmed regulatory pathways
- FDA “Breakthrough Device” designation
- Strong IP position

Fundraising Objective

- \$15M Series B equity financing
- Use of funds: completion of two ALS clinical trials, pivotal RCT designed, ALS device engineering completed, market access work initiated

Contacts:

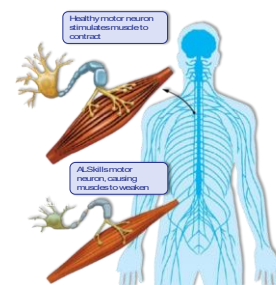
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PathMaker Neurosystems Inc.
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Executive Summary:

- PathMaker Neurosystems is a clinical-stage neuromodulation company developing a breakthrough non-invasive therapy for the treatment of patients with ALS (amyotrophic lateral sclerosis, Lou Gehrig’s disease) and other serious neurological disorders.
- PathMaker’s vision is to make ALS a livable disease using non-invasive neuromodulation.
- Our proprietary multi-site direct current stimulation technology (Multi-Site DCS) is able to non-invasively restore neural circuits damaged by ALS and other serious neurological disorders by normalizing pathway overactivity and reducing protein aggregation in motor neurons. Through this approach, we can slow down ALS disease progression and potentially reverse the disease process by bringing motor neurons back to a “healthier” state.
- We have developed a robust pre-clinical data package in the SOD1 and TDP-43 mouse models of ALS, and have won several awards in the ALS field.
- PathMaker’s investigational-use MyoRegulator® device, which implements our Multi-Site DCS technology, has now been taken into two clinical trials for ALS. Our first clinical trial in ALS has been successfully completed, and our second, larger clinical trial in ALS is now underway.

Market Opportunity/Unmet Need:

- ALS is a progressive neurodegenerative disease that affects motor neurons in spinal cord and brain. ALS causes muscle weakness, paralysis, spasticity and eventual death, typically within 2-3 years of diagnosis. ALS affects over 30,000 people in the US, and approximately 450,000 patients worldwide.
- Annually, 6,000 new cases of ALS in the US. Military veterans have ~20% increased ALS incidence.
- Motor neuron hyperexcitability and protein aggregation are hallmarks of the ALS disease process. The gradual accumulation of misfolded/aggregated proteins in the cytoplasmic compartment of motor neurons leads to toxic loss of function, toxic gain of function and prion-like disease propagation along the neural axis.
- There are currently only two FDA-approved small molecule drugs and one FDA-approved anti-sense oligo (ASO) for the treatment of ALS, all having limited effectiveness.
- As such, there is tremendous unmet medical need in the ALS field, and we are working to urgently bring an entirely new treatment modality to this unrelenting and terrible disease.
- The MyoRegulator® device is a safe, non-invasive, painless and cost-effective therapy for ALS. It represents the first non-pharmacological approach for treating ALS, and there is nothing comparable to this product either on the market or under development.
- We expect our non-invasive neuromodulation device to provide a novel treatment modality that will increase survival, motor function and QOL for those stricken with ALS.



Products, Pipeline & Competitive Advantage:

- PathMaker’s MyoRegulator® device is currently being utilized in two ALS clinical trials, and has been shown at leading ALS conferences to clinicians and people living with ALS.
- The MyoRegulator® device has FDA “Breakthrough Device” designation, is on the De Novo regulatory pathway, and clinical trials are considered by FDA as Non-Significant Risk (NSR). Regulatory clearance (FDA) is expected after completion of our pivotal RCT, followed by EU CE Mark.
- We have discovered the molecular mechanisms by which our Multi-Site DCS technology works. We published the first direct link between hyperexcitability and overexpression of a specific neuronal co-transporter (NKCC1) found on spinal cord motor neurons which is responsible for maintaining chloride gradient (Mekhael 2019). We found that Multi-Site DCS treatment suppresses NKCC1 levels and reduces motor neuron hyperexcitability.
- Our pre-clinical data package in SOD1 and TDP-43 models of ALS shows we can non-invasively reduce motor neuron protein aggregates, leading to improved motor function, increased motor neuron survival and increased lifespan.
- We expect our Multi-Site DCS platform to be a game-changer for ALS and potentially other neurodegenerative disorders linked to neuronal protein aggregation. We have completed an ALS Early Feasibility Study, supported by MDA, and have launched a second, larger clinical trial in ALS, which is being supported by the United States Department of Defense CDMRP ALSRP program.
- Our next-generation MyoRegulator® ALS system is being developed to enable at-home therapy.

PathMaker’s MyoRegulator® device



Recent Milestones & Achievements:

- \$4.9M NIH grant awarded in February 2018 to support MyoRegulator® development in US
- PathMaker was awarded France’s top prize for Innovation across technology sectors in July 2019
- \$371K NIH grant awarded in September 2021 to apply our technology to ALS
- Awarded the \$250K CERF Medical Electronics Prize in ALS in February 2022
- Awarded \$600K funding in Jan 2023 by Muscular Dystrophy Association (MDA) to launch ALS trial
- One of five companies in MA selected in June 2023 by MassVentures for \$200K of START funding
- Positive readout on EU pivotal trial of MyoRegulator® in post-stroke spasticity
- \$2.16M grant from U.S. Department of Defense ALSRP program to support second ALS trial