

A multi-channel pipette is shown dispensing a red liquid into a 96-well plate. The pipette has eight channels, and the liquid is being dispensed into the first row of wells. The background is dark, and the pipette and plate are illuminated with a blue light.

Year in Review



2019
2020
2021
2022
2023
2024

Neuroscience has the potential to be in the '20s what oncology has been in the last decade

-Bill Anderson – CEO, Roche Pharmaceuticals

This quote has always been powerful to me and exemplifies AxoSim's mission to **Empower Advancements in Human Neuroscience**. Until now, pharma has not had tools capable of human translation. This past year we have seen our largest year of growth and technology adoption, both across our large biopharma partners and from increased collaboration with emerging biotech companies. Our platforms are empowering change.

In 2022 we accelerated our efforts across applications in neuroprotection and neuroregeneration, giving our partners unprecedented abilities to develop more effective treatments with a better chance of clinical success using our BrainSim® and NerveSim® platforms.

Every client and partner we work with looks to AxoSim for solutions to support better neuroscience drug discovery and ultimately better patient outcomes.

For those suffering from neurodegenerative diseases like neuropathy, pain, MS, ALS, or Alzheimer's, a new drug represents hope. This is our mission.

Another milestone was the growth of our team to 32 members and counting. AxoSim's team is talented, driven, and dedicated to affecting change in the lives of patients. We have the right technology, at the right time, with the right people leading the way.

I hope you enjoy our 2022 Annual Report. This document highlights our progress from 2022 and showcases our strategies and goals moving into 2023. As always, I thank you for your continued support.

Lowry Curley, PhD
Co-Founder and CEO



“Our team is talented, driven, and dedicated”

AxoSim's Mission

Empowering Advancements in Human Neuroscience

AxoSim's Core Values

- Quality, Integrity and Reliability
- Nurturing a Collaborative Environment
- Dedication to personal and company development
- Excellence in Innovation

AxoSim's Future

To become the company most known for enabling pharmaceutical companies to cure neurodegenerative diseases. In 10 years, all of the top pharma companies will be using our technology to research cures to the most devastating neurodegenerative diseases. In 5 years, we will have been instrumental in providing breakthrough cures for those diseases.

AxoSim Board of Directors

Benjamin Cappiello

J. Lowry Curley, PhD

Mike Katz

Dale Pfof, PhD

Dave Weiner, MD

Joe Truhe (Board Observer)

AxoSim Leadership

J. Lowry Curley, PhD, Chief Executive Officer

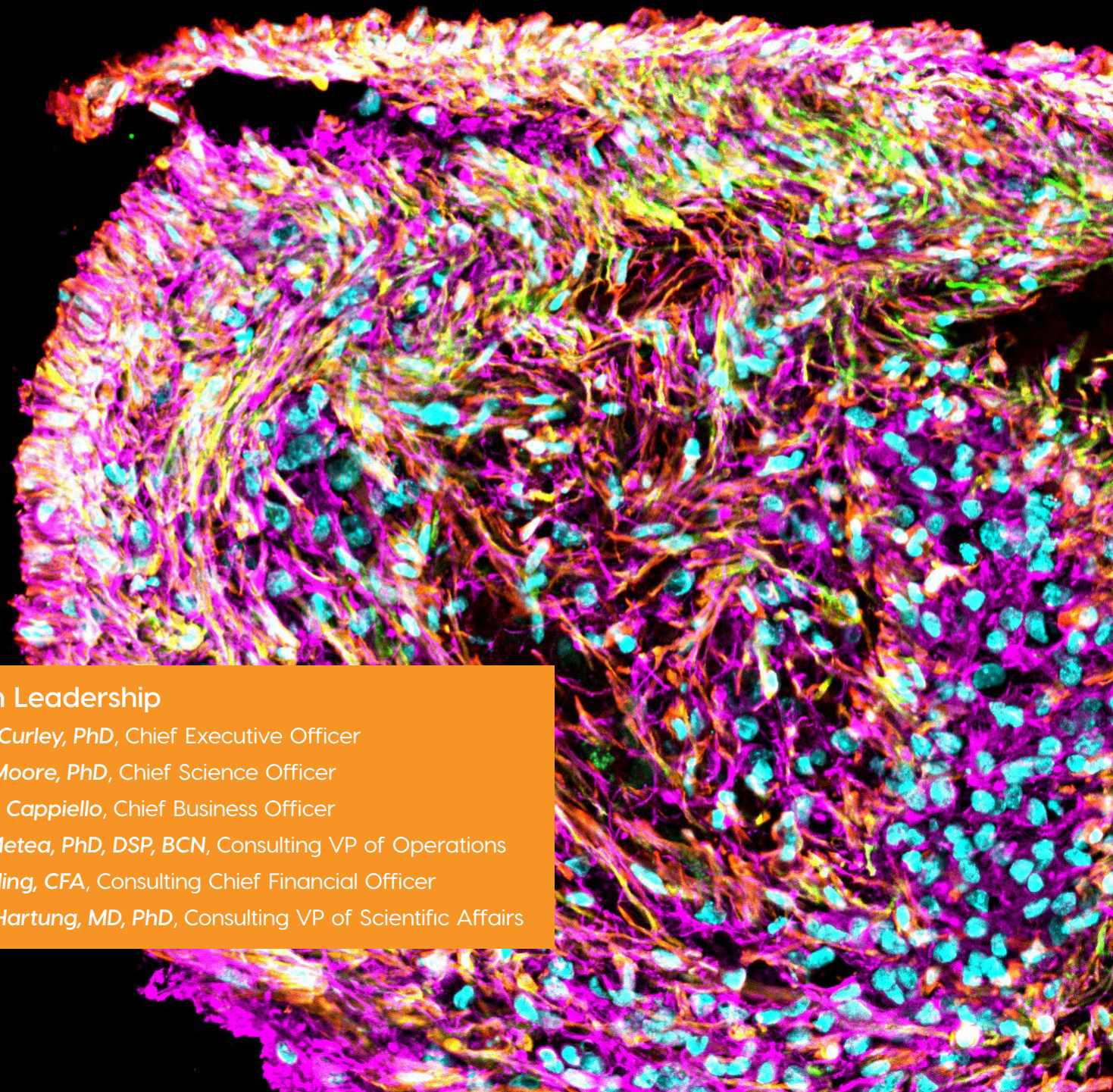
Michael Moore, PhD, Chief Science Officer

Benjamin Cappiello, Chief Business Officer

Monica Metea, PhD, DSP, BCN, Consulting VP of Operations

Greg Kading, CFA, Consulting Chief Financial Officer

Thomas Hartung, MD, PhD, Consulting VP of Scientific Affairs



Scientist Name: **Corey Rountree, PhD**

Scientist Title: **Lead Scientist**

Area of Expertise: **Electrophysiology, data analysis, and engineering**

No other platform can measure these human relevant translational metrics.

Tell us about the NerveSim® Platform and what it means for neuroscience drug discovery?

The NerveSim® Platform has been designed from the ground up to be a drug discovery system for neuroscience. It is a custom 24-well tissue culture plate that has embedded electrode arrays (EEAs) in each well to permit electrical stimulation and recording. We combine peripheral neurons and support cells (rodent or human derived) into a spheroid and place it at one end of channel on top of the EEA in each well. Over the course of about 4-6 weeks, the neurons form a nerve-like bundle over the EEA that we can then dose with drugs to measure the effects using electrophysiology, top-down imaging, cell viability, transcriptomics and/or proteomics. With this new

tool, we can measure over 12 endpoints spanning the spontaneous and stimulus-evoked electrophysiology of our NerveSim® cultures, which are the same tools used clinically to diagnose neurodegenerative diseases and conditions. No other platform can measure these human relevant translational metrics, and in combination with multiplexing of the other readouts, we can leverage unprecedented fundamentally enabling biology.



“This tech is going to completely change the industry.”

What are the product development goals for 2023?

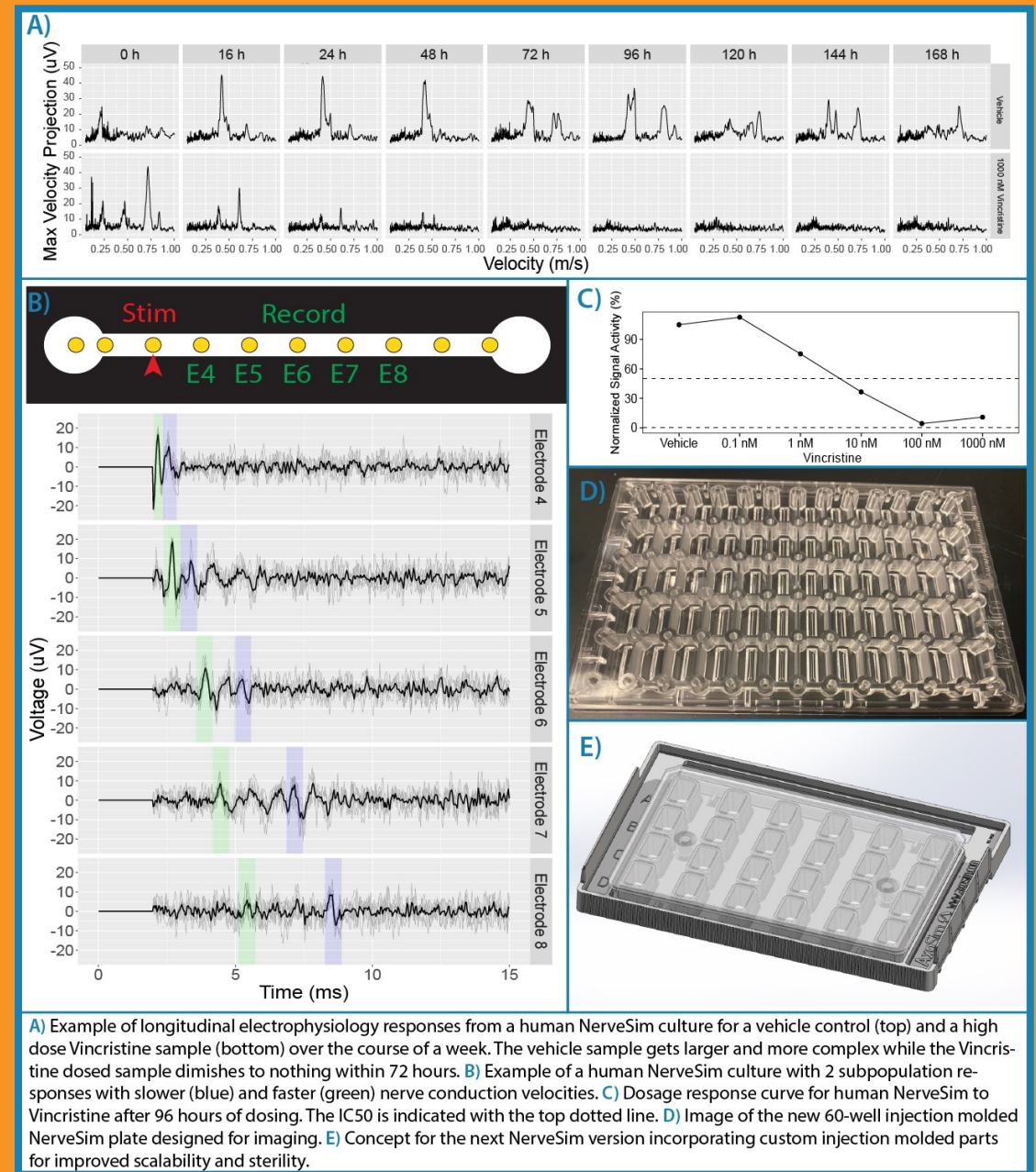
We have a number of product development goals for 2023:

1) Transition to the new version of the NerveSim® platform(3.0) using injection molded parts to improve scalability and sterility in Q1-Q2 2023.

2) Test out our design applying current-based stimulation over time on a larger scale, which has been shown in literature to significantly improve neurite outgrowth and myelination. From our internal studies, we anticipate that this will also increase electrophysiological responses over time as well.

3) Testing of different methods to keep cultures in close proximity to the electrodes using different hydrogels, different channel materials, and/or periodic electrical stimulation.

4) Test out a new electrophysiology measurement system that has the potential to further increase throughput by 4-16X while also allowing for additional clinically-relevant metrics.



A) Example of longitudinal electrophysiology responses from a human NerveSim culture for a vehicle control (top) and a high dose Vincristine sample (bottom) over the course of a week. The vehicle sample gets larger and more complex while the Vincristine dosed sample diminishes to nothing within 72 hours. **B)** Example of a human NerveSim culture with 2 subpopulation responses with slower (blue) and faster (green) nerve conduction velocities. **C)** Dosage response curve for human NerveSim to Vincristine after 96 hours of dosing. The IC50 is indicated with the top dotted line. **D)** Image of the new 60-well injection molded NerveSim plate designed for imaging. **E)** Concept for the next NerveSim version incorporating custom injection molded parts for improved scalability and sterility.



“I’m eager to progress the BrainSim tech study.”

Scientist Name: **Lise Harbom, PhD**

Scientist Title: **Research Scientist II**

Area of Expertise: **BrainSim®, iPSC-derived neuron culture, 2D assays**

A powerful tool for pharmaceutical companies to test novel drugs.

BrainSim® is a powerful model of the human central nervous system (CNS). Tell us about the BrainSim® Platform and what it means for neuroscience drug discovery.

While many models, both *in vivo* and *in vitro*, exist for modeling CNS diseases, the development of induced pluripotent stem cell-(iPSC-) derived neurons enables studying these conditions in a human setting. BrainSim® begins with an iPSC-derived neural stem cell population and is differentiated over 12 weeks. Our current major goal is to combine our already successful neuronal differentiation with protocols to enhance the production of glial cell types (astrocytes and oligodendrocytes) to better mimic the *in vivo*

environment of a human brain and increase relevance for diseases and drug treatments that target these cell types. Once successful, this will be a powerful tool for pharmaceutical companies to test novel drugs on a mixed population of human brain cells. In particular, no other commercially available platform has oligodendrocyte precursor cells, oligodendrocytes or functional myelination, which are fundamental to studying diseases like multiple sclerosis (MS).

What exciting developments happened with the platform in 2022.

We are in the final stages of the 12-week culture period for our current study, in which we are growing BrainSim® using a variety of media formulations designed to enhance glial differentiation. Based on data gathered to date, feedback given by scientific advisory board members, and examples in literature, we expect to see significant increases in differentiation of at least three of our target cell types: neurons, astrocytes, oligodendrocyte precursor cells, and oligodendrocytes.

What are some obstacles AxoSim has faced with BrainSim®?

The long culture period associated with a full BrainSim® study makes it logistically difficult for large scale studies. We are already working to implement automation and scale into our workflow to increase our impact on

drug discovery.

What are the product development goals for 2023?

We will be working on additional case studies to test drugs known to enhance myelination and accelerate oligodendrocyte precursor cells. This will serve as critical data for customers, many of whom are ready to expand our partnerships with the platform.

Personally, what are you most excited about moving into 2023?

I am eagerly anticipating the results of current studies, because I believe we can demonstrate never before seen results of an *in vitro* platform to measure pharmacological responses for enhanced oligodendrocyte precursor cell differentiation and ultimately demyelination and remyelination. Oligodendrocytes are responsible for forming myelin, which is a key factor in

many debilitating neurological disorders, and to our knowledge, no other commercially available platform has demonstrated such advanced biology.

We have identified what we need to build an industry-leading drug discovery platform.

“We focused our efforts towards drug discovery partnerships.”

Our 2022 goal for the Business Development team was to begin evolving our business model from contract research services to drug discovery partnerships. At the beginning of the year, our primary focus was on chemotherapy-induced peripheral neuropathy (CIPN) and we kicked off an extensive customer discovery and outreach effort. We formally interviewed more than 30 of the top experts, and informally spoke with over 100, in the field of peripheral nerve disorders, which led to some important insights. Our key finding was the incredible amount of opportunity in pain therapeutics discovery, a field severely lacking in human-based translational platforms. We've estimated the partnering landscape for AxoSim in pain alone to be worth well over \$1B.

Most importantly, we signed two Priority Access Pilots with global leaders in pain and neuropathy therapeutics as ideal partners as we continue building our capabilities. These partnerships will empower us with large transcriptomic & proteomic analyses of ion channels/pain targets in NerveSim® human co-cultures,

leading to priceless molecular pharmacology data. In addition, we now have access to top-notch groups that are providing funding, drugs, and design input for a valuable neurodegeneration case study.

Looking forward into 2023 and beyond, it is important to heed what every single industry leader with whom we spoke said: modern drug discovery platforms need to be built with human cells. To that end, we are developing the cellular logistics for both human primary and iPSC-derived DRG cultures alongside specific injury/disease models – such as Charcot-Marie-Tooth (CMT), ALS, and Diabetic Peripheral Neuropathy – to provide multiple avenues to IND submissions alongside our partners.

Ben Cappiello
CBO



We have the right technology, at the right time, with the right people.

-Lowry Curley, PhD - CEO, AxoSim

AxoSim has a diverse team of talented individuals spanning many disciplines. We pride ourselves on collaborating to solve problems in measurable ways, both internally and externally. We're quality obsessed. We work tirelessly to help our pharmaceutical partners find the solutions they need to succeed, all while they learn to admire and respect our team, products, and solutions.

We now have over 30 team members and continue to grow through seeking the most talented and driven candidates to fill our constantly expanding needs.



