

## 2021 Annual Letter to Neuropathix, Inc. Shareholders

April 6, 2022

**Dear Shareholders,**

I believe it is important to give a good measure of gratitude to start a letter to shareholders. All of us at Neuropathix are very grateful to all our existing and new shareholders who have stood by us and continued to add to their ownership in Neuropathix. We continue to believe our technology is highly advanced, cutting edge and has the potential to be a positive disruption on the healthcare system by addressing one of the largest unmet need areas of chronic neuropathic pain.

Before I address some of the advancements and recently completed milestones in our clinical research, I want to take a moment to highlight the support we continue to experience from our shareholders, long-term investors, and the medical community as a whole. In 2021, Neuropathix broadened its shareholder base sustainably and we estimate that more than half of our shareholders hold mid-to-large positions within our company. We believe this illustrates a truly grass roots organic shareholder base from when we started trading in December 2019 to present day. In fact, I am pleased to say that one of our largest and long-time investors stepped up to the plate and reinforced their belief in our technology by making an additional investment via a recently completed private placement for Neuropathix. These additional funds will support and leverage the NIH grant currently in place, enabling us further runway in the advancement and completion of our pre-clinical research regarding CIPN. We remain steadfast in our commitment and mission of the advancement of our novel life sciences technology towards the resolution of two of the most prominent crises facing the world today – chronic pain and addiction.

To demonstrate the importance and timeliness of our technology, the February 2018 Biotechnology Innovation Organization (“BIO”) journal report, “The State of Innovation in Highly Prevalent Chronic Diseases – Volume II: Pain and Addiction Therapeutics”, by David Thomas, CFA and Chad Wessel is telling. Significant key take-aways outlined in this report include these headshaking facts: *“Chronic pain affects as many as 100 million people in the U.S. alone,”* and *“Total economic and direct healthcare costs for treating pain in the U.S. have been estimated to be as high as \$635 billion annually, higher than the costs for cancer, Alzheimer’s, or cardiovascular disease.”*

The BIO report also states that, *“There have been only two novel chemical entities FDA approved to treat pain in the past decade,”* and that *“Private company investment, as measured by venture capital into U.S. companies with lead stage*

*programs in pain is 3.6% of total drug development funding.* The report's key findings concluded with the statement that "*Venture investment for addiction drug R&D is nearly non-existent.*" The two groups - pain and addiction are most certainly concomitant and most certainly ignored.

We are focused on providing a solution for these difficult problems. Research in pain treatment has been historically focused on the central nervous system and has been evaluated for efficacy in the clinic using subjective techniques. In the past, this led to poor outcomes and missing clinical endpoints. Lack of verifiable biomarkers and the inability to assess pain had caused many to walk away from drug discovery and stalled further advancement in pain treatments. Additionally, companies that were involved in the manufacture and sale of opioids to treat pain have been reluctant to find solutions given the crisis the opioid epidemic has caused. This creates an opportunity for Neuropathix. Specifically to look at resolving the problem of chronic pain from a new perspective. And we are not alone. We have partnered with the National Institutes of Health and specifically the HEAL Initiative (Help to End Addiction Long Term).

I thank God for the National Institutes of Health and the establishment of the HEAL Initiative in 2017. The HEAL Initiative, which stands for Help to End Addiction Long-term, was established to tackle the scourge, misuse, and abuse of opioids in our society, is designed to find non-opioid solutions to deal with chronic pain and reduce the potential for opioid addiction and overdose.

On September 28, 2021, we received a notice of award for a \$2.97 million non-dilutive grant from National Institutes of Health, National Institutes of Neurological Disorders and Stroke ("NIH-NINDS") for the Development of KLS-13019 for Neuropathic Pain. This grant award from NIH is a major milestone for our company. Our award was based on review by three of the top review scientists at NIH-NINDS who gave us an exceptional and rare perfect score of 20. This impact score is a testament to the novelty and advancement in our scientific discovery, as validated by renowned scientists working at the highest level of the federal scientific community. I am delighted to share that it further positions us as on track for investigational new drug (IND) enabling studies, and on our way towards the clinic.

Reflecting back on the data from the 2018 BIO report, there is currently no FDA approved pharmaceutical solution for the treatment of chemotherapy induced peripheral neuropathy (CIPN). Opioids are still used off-label and as a first choice to deal with the current problem. Many of us know someone that fought cancer and the negative effects of the chemotherapy regimens. Chemotherapy is trouble enough on its own, but it is necessary in many cases in the fight against, and to beat cancer. As opioids are prescribed to ameliorate the problem of neuropathic pain, the side effects often times result in the patient refusing to take opioids and

is left with the neuropathic pain associated with the chemotherapy. In such cases, at this juncture, patients stop the chemotherapy regimen altogether.

We believe that our lead drug candidate, KLS-13019, once proven in the clinic, can solve this problem. We also believe that KLS-13019 has the potential to be fast tracked for compassionate use after a successful FDA Phase IIa human clinical trial. We are making significant strides towards getting KLS-13019 into human clinical trials. While the steps in the process are challenging, we have great partners. Through the NIH grant we are able to continue to our relationship with Temple University to conduct further preclinical research. We have also recently contracted with Purisys and the University of Illinois. At the completion of our IND enabling studies, we believe we will be in position to file an IND and start proving the efficacy of KLS-13019. Additionally, once in the clinic, opportunities for accelerated use of KLS-13019 is a potential via the patients' right-to-try "act". Given the lack of available therapy for CIPN and the need to replace opioids as a go-to-for-all, we believe our path through the clinic can be shorter than the conventional wisdom roadmap suggests.

In addition to the \$2.97 million NIH-NINDS HEAL Initiative grant, we are also pleased to have received a forward commitment from a globally recognized life sciences fund and CRO for sum of \$1.5 million, which will commence at the onset of Phase 1a human safety trials and spread out over Phase Ib and Phase IIa trials, to advance additional safety and efficacy.

In early 2020, we completed a convertible debt financing that kept us on a path towards accomplishing our main goal of advancing our technology. The great news is that half of that debt has been retired via conversion to common stock and, the additional shares added to the public float through this financing have been instrumental in bringing forth a more fluid tradable market for our security. The cost of capital from the conversions of debt paved the way for \$2.97 million in non-dilutive NIH grant funding – leading us to the conclusion that the transaction was overall beneficial for the company.

Here are some of the company's accomplishments during 2021:

- We advanced our technology, utilizing necessary financing to enable improvements to the re-application process for NIH-NINDS for a Phase 2 STTR study grant filed in January 2021, which resulted in the granting of \$2.97 million in funding from life sciences funds and/or NIH under the HEAL Initiative ("Helping to End Addiction Long-Term").
- As a result of the NIH-NINDS grant, we are now on track towards IND enabling animal toxicity studies and commercial scale up of our lead drug candidate, KLS-13019.
- In September 2021, we obtained a forward commitment of \$1.5 million from a highly regarded and extremely successful life sciences fund and CRO.

- We advanced our chemistry yield for scale up of our lead drug candidate KLS-13019 with the engagement of Purisys, a crucial step when preparing for animal and human clinical studies.
- We advanced three new intellectual properties via global patent protection under PCT publication WO2021/097351, PCT publication WO2021/264324, and U.S. patent protection under provisional patent filing 63144471.
- We added strategic corporate advisors; key life sciences opinion leaders and clinicians to the Company's corporate and scientific advisory boards, most notably, Dr. Charles Loprinzi and Dr. Michael Ropacki.

As I write this letter to you, we are still dealing with a significant crisis of unmet need in treatment of chronic pain and addiction in this country and throughout the world.

The opioid crisis began about twenty-five years ago. It started with a new class of drugs focused on mediating receptor activity in the central nervous system that could help prevent pain. Unfortunately, these drugs, while promising, didn't make it all the way through Phase III human clinical trials at the FDA. As the clinical trials failed, this caused for an evacuation of these new concepts, and the door swung wide open for opioids as a broad solution. Is there a place for opioids? The answer is yes. However, we believe there are superior solutions, and we believe our technology can deliver those solutions without the associated risks of opioids.

Opioid related deaths are now the 8<sup>th</sup> largest cause of death in the United States, ahead of diabetes and quickly approaching Alzheimer's Disease, as a leading cause of death in the United States. We hear about it almost every day in the news. It's effecting everyday Americans and our quality of life.

2022 has already commenced as a pivotal year for NeuroPathix. Pursuant to our budget and outline of aims from our NIH-NINDS HEAL Initiative grant, we will continue to work towards scaling up our lead drug candidate KLS-13019.

Your investment in NeuroPathix goes to the heart of bringing a potentially revolutionary drug into the marketplace to treat chronic and neuropathic pain - as well as putting a charge in the fight to ending the opioid crisis. Together we are advancing new, exceptional life changing medicines to address significant unmet medical needs – and that is something to be proud of and forge on in our mission for. Our future could not be brighter!

Sincerely,

Dean Petkanas, CEO  
NeuroPathix, Inc.  
April 6, 2022