Executive Summary

Mission & Vision:
AXONIS Therapeutics is advancing breakthrough drug discoveries to develop first-in-class therapeutics for neurological disorders, to make a real difference for patients, their families, and the global healthcare system.

Company Overview:
Operational since 2020, AXONIS is a seed-stage therapeutics company based in Tufts LaunchPad BioLabs, Boston, MA, and has assembled a team of entrepreneurs, drug developers, scientists and advocates to pursue our mission: Drs. Joanna Stanicka (CEO), Corey Goodman (Executive Chairman), Shane Hegarty (CSO), along with scientific advisors including Drs. Lisa McKerracher, Oswald Steward, Zhigang He, Yves De Koninck, Clifford Woolf and James Guest. AXONIS has raised $15.5M seed funding and $5.5M in state and federal non-dilutive funding to date. The recent seed round of financing was led by Alexandria Venture Investments with participation by EOS BioInnovation, BoxOne Ventures and Civilization Ventures and two leading spinal cord injury non-profit foundations, Christopher & Dana Reeve Foundation and Spinal Research UK, joined by AXONIS' Founders and angel investors. Most notably, awards received by AXONIS include $2.2M from NIH SBIR and $1.8M from DoD SCIRP for development of KCC2 neuromodulators to treat spinal cord injury (SCI). AXONIS is currently preparing for Series A in mid-2023 to fund Phase 1/2 clinical trials.

Technology Overview:
Disease-modifying therapeutics for central nervous system (CNS) disorders are an urgent, unmet and growing need, especially as more people are living longer. The majority of CNS disorders converge on three central pathological problems: (1) neuron degeneration; (2) excitation/inhibition (E/I) imbalance; and (3) failure of regeneration. Common, adult-onset neurological disorders share one or more of these issues. AXONIS is progressing a pipeline of neuron-reviving therapeutics which enable an intrinsic ability of CNS neurons to: (1) resist degeneration; (2) restore E/I balance; and (3) regenerate. This novel pipeline is based on 3 independent, unprecedented *in vivo* phenotypic screens in mouse models of neurological disorders: (1) Genome-wide AAV-CRISPR screen for neuroprotection in a mouse model of CNS degeneration; (2) Screen of neuromodulatory drug-like compounds for restoration of stepping ability in paralyzed mice; and (3) Genetic screen *in vivo* for neuron regeneration after CNS injury.

Asset 1: Small molecule KCC2 enhancer to restore E/I balance in neurological disorders
For restoration of E/I balance in neuron circuits, AXONIS is developing small molecule enhancers of KCC2, a CNS-specific potassium/chloride co-transporter that enables neuronal responses to synaptic GABA/glycine-mediated inhibition. In many neurological disorders and after neurotraumas, KCC2 is downregulated leading to E/I imbalance within CNS neuronal circuits. AXONIS' lead program is advancing a first-in-class oral KCC2 enhancer drug with multi-model therapeutic action that improves mobility, and alleviates chronic pain and spasticity, in animal models of SCI. A KCC2 enhancer drug represents a pipeline within a product as KCC2 mutations are often found in E/I disorders, for example, epilepsy and neurodevelopmental disorders. The therapeutic benefits of KCC2 enhancement have also been shown in animal models of chronic pain, epilepsy, Rett syndrome and traumatic brain injury. In addition, AXONIS' KCC2 enhancers do not have sedative effects, like other drugs on the market. AXONIS is now at the lead selection stage and will nominate the development candidate by early-2023.

Asset 2: Undisclosed targets to enable CNS neurons to resist degeneration and regenerate
For neuroprotection in neurodegenerative disorders, AXONIS' early-stage stealth program is focusing on silencing a degenerative signaling complex to treat neurodegenerative disorders and CNS injuries. AXONIS' CEO and CSO led an *in vivo* AAV-CRISPR screen of >2,000 individual genes (tested one-by-one) in a mouse neurodegeneration model. Deletion of the novel target, or its binding partner, prevented CNS neuron degeneration in this model. Small molecule drugs for targets are in development.