



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 LabCentral, Cambridge, MA, and has assembled a team of entrepreneurs, drug developers, scientists and advocates to pursue our mission: Joanna Stanicka (CEO), Corey Goodman (Executive Chairman), Shane Hegarty (CSO), along with scientific advisors including Lisa McKerracher, Oswald Steward, Zhigang He, and Yves De Koninck. AXONIS has raised \$9M seed funding to date. The second seed round of financing was led by Alexandria Venture Investments with participation by R3 Bio, BoxOne Ventures and Civilization Ventures and two leading spinal cord injury non-profit foundations, Christopher & Dana Reeve Foundation and Spinal Research UK, joined by our Founders and angel investors. We are preparing for Series A in late 2022 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disorders: (1) Genome-wide AAV-CRISPR screen for neuroprotection in a mouse model of CNS neurodegeneration (*Unpublished*); (2) Screen of neuromodulatory drug-like compounds for restoration of stepping ability in paralyzed mice (*Cell*); and (3) Genetic screen of tumor suppressors by *in vivo* knockout for neuron regeneration after CNS injury (*Science*).

Assets 1/2: Small molecule KCC2 enhancer and AAV-KCC2 – the key to restore E/I balance.

For restoration of E/I balance in neuron circuits, we are developing small molecule enhancers of KCC2, a CNS-specific potassium/chloride co-transporter that enables neuronal responses to synaptic GABA/glycine-mediated inhibition. After CNS injury (e.g., spinal cord injury (SCI)), KCC2 is downregulated leading to E/I imbalance within the spared neuronal circuits. Our 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 autism spectrum disorder. 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, our 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 mid-2022.

Assets 3/4: Undisclosed targets to enable CNS neurons to resist degeneration and regenerate

For neuroprotection in neurodegenerative disorders, our new early-stage stealth program is focusing on silencing a degenerative signaling complex to treat neurodegenerative disorders and CNS injuries. The CEO and CSO co-led an *in vivo* AAV-CRISPR screen of >2,000 individual genes (tested one-by-one) in the mouse optic nerve crush (ONC) model. Deletion of our novel target, or its binding partner, prevented CNS neuron degeneration in this model. For neuroregeneration, we received non-dilutive grant funding for the development of a neuron-specific AAV-shRNA that targets PTEN, or our new proprietary regenerative target genes from the AAV-CRISPR screen, within adult neurons to induce CNS axon regeneration.