BioAxone BioSciences Inc.
www.bioaxonebio.com

# Transforming treatments for neurotrauma and neurovascular disorders

**BioAxone is developing a suite of game-changing treatments for spinal cord injury, neurovascular diseases, and eye disorders by targeting Rho/Rho kinase signaling pathways involved in a variety of pathological processes.**

BioAxone is a clinical-stage biopharmaceutical company focused on unmet needs in central nervous system disease and ophthalmology. The privately held Massachusetts-based company, founded in 2011, is leveraging decades of pioneering research to identify and develop a pipeline of therapeutic drugs that are based on a deep understanding of axon regeneration and neuronal signaling pathways and are designed to transform the lives of patients afflicted with neurotrauma or neurovascular disorders.

BioAxone's broad pipeline of drugs targets different points in Rho/Rho kinase (ROCK) signaling and related pathways, which play key roles in serious conditions such as spinal cord injury, stroke, cerebral cavernous malformations (CCMs), and glaucoma (**Fig. 1**). BioAxone has developed a suite of selective ROCK2 inhibitors that avoid off-target effects on ROCK1 or protein kinase A and therefore may have a better safety profile than other types of ROCK inhibitors in development.

The company's lead drug VX-210, which was licensed to Vertex Pharmaceuticals in 2014, is in a phase 2b/3 SPRING clinical trial that is currently actively recruiting subjects with acute traumatic cervical spinal cord injury (NCT02669849). This first-in-class biologic drug inhibits the small GTPase Rho, which is a key signaling molecule that affects regeneration and repair after spinal cord injury.

In addition to VX-210, BioAxone is developing ROCK2 inhibitors as second-generation drugs to treat spinal cord injury. These ROCK2 inhibitors are being evaluated for their potential to extend the window of treatment after spinal cord injury to promote axon regeneration, heal the broken blood–brain barrier, and promote functional recovery during active rehabilitation. "There has been much focus on neuroprotection and regeneration with ROCK inhibitors," said BioAxone's CEO, Lisa McKerracher. "But their ability to repair blood–brain barrier disruption has not been well appreciated for treatment of acute SCI."

BioAxone is also developing innovative therapies designed to overcome older axons' diminished capacity for regeneration. For example, a novel RNA interference technology called BA-434 transiently silences PTEN expression to promote axon regrowth, potentially improving the ability of the central nervous system to recover after injury by helping neurons create new adaptive circuitry.

"Despite the serious nature of spinal cord injury and potential for therapeutic benefit, there are no drugs on the market to repair neuronal damage and reduce paralysis after spinal cord injury," McKerracher said. "The first approved drug for spinal cord injury will change the field forever by trailblazing a clinical path, and significantly impact patients' quality of life."

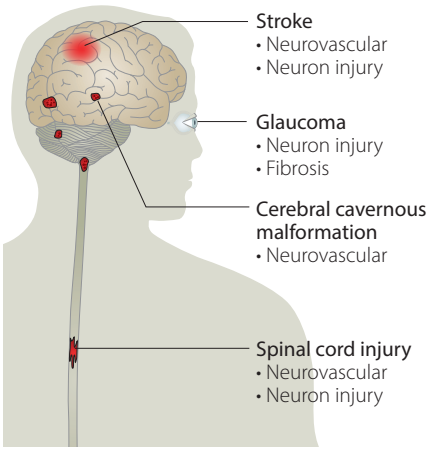


**Figure 1: BioAxone's drug target areas.** Key sites of neurovascular and neuron injury along the Rho/Rho kinase (ROCK) signaling and related pathways.

## Nexus pathway in neurovascular disease

Beyond spinal cord injury, the ROCK signaling pathway is disrupted in a variety of pathological processes. For example, ROCK is hyperactive in brain capillary endothelial cells in patients with CCM and other neurovascular disorders. CCM is a serious genetic disease in which endothelial cells form cavernous lesions that leak and may cause seizure, hemorrhagic stroke, and neurological deficits. Currently, there are no drugs that prevent or reverse the formation of CCM lesions, and the only treatment able to target the underlying cause of symptoms is brain surgery, which may not successfully remove multiple lesions and can cause additional neurotrauma.

To address this need, BioAxone is developing a ROCK2 inhibitor called BA-1049, which is the only new chemical entity that targets the cause of CCM. This game-changing drug repairs the endothelial cell defect to reduce the permeability of the blood–brain barrier. Preclinical studies have shown that BA-1049 restores the barrier function of endothelial cells, reverses hyperactivation of ROCK, and reduces lesion genesis. In CCM transgenic mice, BA-1049 reduces the leakiness of lesions, prevents the growth and formation of lesions, and slows disease progression. BA-1049 is expected to be ready for investigational new drug (IND) status in 2018.

"Because the blood–brain barrier is defective in many neurodegenerative diseases, success with BA-1049 for the treatment of CCM will have relevance to other neurological diseases such as stroke, where it could potentially be used to prevent reperfusion injury and perhaps also edema," McKerracher said.

## Preventing blindness and advancing clinical programs

ROCK inhibitors could also offer a more effective therapy for glaucoma, the second leading cause of blindness in the United States. Glaucoma is a slowly progressing neurodegenerative disease in which high intraocular pressure leads to optic nerve injury. Current drugs do not treat some forms of glaucoma, and compliance is low because of side effects such as red eye.

To overcome these limitations, BioAxone is developing BA-1076 and BA-2057 as two 'better-than-class' ROCK2 inhibitors for the treatment of glaucoma. In preclinical models, these novel compounds effectively penetrate the retina, reduce fibrosis to prevent increases in intraocular pressure, and prevent the death of retinal ganglion cells, while avoiding side effects such as red eye. Unlike existing therapies, these two compounds have the potential to reverse disease progression in glaucoma. Moreover, ROCK2 inhibitors could be relevant to the treatment of age-related macular degeneration and diabetic neuropathy. BA-1076 is expected to be IND-ready in 2019.

Currently, BioAxone is seeking licensing partners to advance the clinical development of its ROCK2 inhibitors for CCM, stroke, and ophthalmological conditions such as glaucoma and age-related macular degeneration. There is also potential to explore ROCK2 inhibitors for the treatment of gastrointestinal disorders. "BioAxone has proven success in substantial strategic collaborations with academic labs and with other biotech companies," McKerracher said. "By forming new partnerships with world-class biopharmaceutical companies, we will fulfill our commitment to accelerating breakthrough therapies to patients."

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