Regenacy Pharmaceuticals
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Regenacy is poised to deliver the first treatment for peripheral neuropathy

Unlike standard analgesics, the company's lead compound ricolinostat is a disease-modifying therapy that reverses nerve damage and reduces pain, numbness, and muscle weakness resulting from diabetes, chemotherapy, and Charcot–Marie–Tooth disease.

Peripheral neuropathy affects nerves outside of the brain and spinal cord. Dysfunction of these nerves can cause spontaneous, inappropriate signals or loss of signals, leading to symptoms such as pain and numbness. This condition affects more than half of all diabetic adults, approximately 500,000 chemotherapy-treated patients, and an estimated one million individuals with an inherited degenerative nerve condition called Charcot–Marie–Tooth disease type 2 (CMT2). Peripheral neuropathy can cause severe disability and increases the risk of limb amputation, which significantly diminishes quality of life, but currently there is no approved treatment.

Regenacy Pharmaceuticals is developing a novel, disease-modifying approach to treating peripheral neuropathies that goes beyond pain and symptom management to restore peripheral nerve function. The company's lead compound ricolinostat is an oral, selective inhibitor of the microtubule-modifying enzyme histone deacetylase 6 (HDAC6). With first-in-class potential, ricolinostat is currently positioned to enter a phase 2 clinical trial for diabetic neuropathic pain.

"Temporary, symptomatic treatments for neuropathic pain are poorly tolerated, minimally effective and addictive," said Regenacy's vice president of research and development Matthew Jarpe. "Unlike approved medicines, ricolinostat is well tolerated, non-addictive, and has potential to achieve lasting relief of all neuropathy symptoms rather than transient relief of some symptoms."

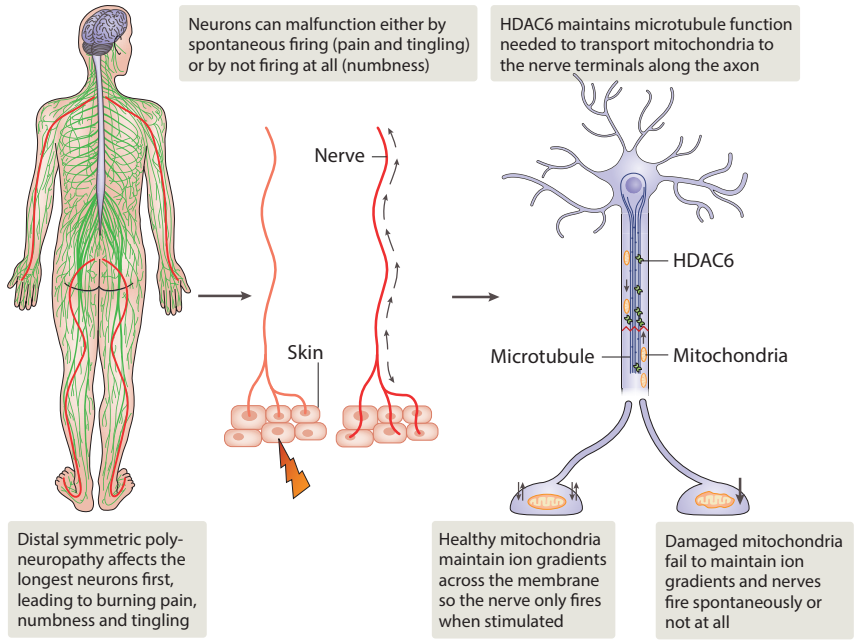

Fig. 1 | Mitochondrial transport by histone deacetylase 6 (HDAC6). HDAC6 is a key regulator of fast axonal transport, which is impaired in distal symmetric polyneuropathy. The slowing of transport in the longest nerves leads to dysfunction of the nerve terminals, causing pain symptoms, numbness and tingling. These appear in a 'stocking and glove' pattern in patients with diabetes, inherited neuropathy or in patients undergoing chemotherapy.

Restoring nerve function

Neurons conducting signals to and from the spinal cord into the feet and hands are the longest cells in the body. These neurons rely on an internal microtubule transport network to supply energy and nutrients to maintain nerve ends in the skin and muscles. When this transport is disrupted by disease nerve cells can malfunction and send random signals, resulting in pain, tingling, muscle spasms, or no signal at all, leading to numbness or paralysis. These are the symptoms of peripheral neuropathy that can result from diabetes, chemotherapy, and mutations.

Intracellular transport is regulated by HDAC6—a microtubule-associated deacetylase that plays a significant role in axonal functioning in the nervous system. Inhibition of HDAC6 is a novel approach to restoring nerve function for the treatment of peripheral neuropathies by re-establishing the transport function of microtubules (**Fig. 1**). Phase 1 and 2 clinical trials in 250 cancer patients demonstrated ricolinostat's excellent safety and tolerability profile, particularly when contrasted with the high toxicity of currently marketed, nonspecific pan-HDAC inhibitors such as vorinostat and panobinostat.

Moreover, preclinical studies in multiple models of genetic and induced forms of peripheral neuropathy provide compelling evidence that HDAC6 inhibition normalizes the function of damaged peripheral nerves. In animal models of chemotherapy-induced neuropathy, ricolinostat reduces pain and numbness, restores nerve function, promotes nerves to grow back into the skin, and exerts long-lasting effects that persist for days after the end of dosing, suggesting a disease-modifying capability. Similar effects are seen in models of diabetic neuropathy and CMT2. "We plan to explore the efficacy of ricolinostat in diabetic peripheral neuropathy patients first," Jarpe said. "Later we will expand into chemotherapy induced neuropathy and CMT2."

Expanding horizons

Currently, Regenacy is seeking additional partnerships to develop its portfolio of HDAC inhibitors. Recently, the company announced a collaboration with the Charcot–Marie–Tooth Association, a non-profit organization serving the hereditary neuropathy patient community, to validate the role of HDAC6 in multiple forms of CMT2 and evaluate the efficacy of ricolinostat in animal models to support the initiation of clinical trials.

"We are thrilled to have such a substantial collaboration to broaden our programs for ricolinostat into inherited forms of neuropathy where there is a tremendous unmet need," Jarpe said. "This and future alliances will position us to deliver a superior, first-in-class treatment for peripheral neuropathies, which affect many millions of people worldwide."

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