

EMERGING COMPANY PROFILE

FLEX: FLEXING MUSCLE

BY CATHERINE SHAFFER, SENIOR WRITER

Flex Pharma Inc. is developing an ion channel activator that could be the first therapeutic approved to treat nighttime leg cramps, and muscle cramps and spasticity associated with diseases like multiple sclerosis and spinal spasticity.

The sixth start-up of biotech entrepreneur Christoph Westphal, Flex is launching with \$38 million in cash, clinical data showing proof of concept, and filed applications for method of use patents covering natural products that activate the transient receptor potential vanilloid 1 (TRPV1; VR1) and transient receptor potential A1 (TrpA1) ion channels.

According to Chairman and CEO Westphal, about 15 million U.S. patients per year visit a doctor seeking a solution for nocturnal leg cramps. Quinine was used off label, but FDA issued a safety warning in 2010 noting that the malaria drug can cause life-threatening hematological complications like severe bleeding.

Co-founders Bruce Bean and Roderick MacKinnon took an offbeat path to drug discovery, looking at how pickle juice — used by athletes for exercise-induced muscle cramps — might work. The pair guessed its modest activity might be due to an effect on TRPV1 and TrpA1, because pickle juice contains protons and they knew that protons are weak activators of TRPV1 and TrpA1.

Bean is a professor of neurophysiology at [Harvard University](#), and MacKinnon is a professor of molecular neurobiology and biophysiology at [The Rockefeller University](#).

According to Westphal, Bean and MacKinnon also theorized that quinine's effect on muscle cramps is due to activation of TRPV1 and TrpA1.

“Research in the last 10 years or so has shown that the causes of muscle cramping are in the nerves that control the muscles themselves.

FLEX PHARMA INC.

Boston, Mass.

Technology: TRP ion channel activation

Disease focus: Neurology

Clinical status: Not disclosed

Founded: 2014 by Christoph Westphal, Bruce Bean and Roderick MacKinnon

University collaborators: None

Corporate partners: None

Number of employees: 10

Funds raised: \$38 million

Investors: Longwood Fund LP, Bessemer Venture Partners, EcoR1 Capital, Jennison Associates, Alexandria Equities LLC, CD-Venture GmbH, Lightstone Ventures, City Hill Ventures LLC, Kraft Group and individual investors

CEO: Christoph Westphal

Patents: None issued

The nerves in the spinal cord experience hyperexcitability in a way they normally would not, so it is actually not the muscle, but the nerve that is producing the muscle cramping,” MacKinnon told BioCentury.

More specifically, Flex's founders believe cramping is caused by excessive firing of alpha motor neurons in the spinal cord, and that stimulating sensory neurons of the mouth, esophagus and stomach via TRPV1 and TrpA1 ion channels enhances the inhibition of spinal circuits that regulate alpha motor neurons.

The company has human data showing that FLEX 767, a combination of capsaicin, gingerol and cinnamaldehyde, can relieve muscle cramps.

Inducing muscle cramping in healthy volunteers through repeated electrical stimulation of the toe muscle, Flex ran two randomized, blinded, placebo-controlled crossover studies, FLEX-001 and FLEX-002. Both studies showed a treatment effect beginning as early as 15

minutes and lasting 6 hours. The product was well tolerated with no serious adverse events.

Flex plans to begin three trials in 1H15. The randomized, blinded, placebo-controlled studies will be carried out in the U.K. and Australia in patients with nocturnal leg cramps (40 patients at 6-8 sites), spasticity (20 patients at 4 sites), and cervical dystonia (10 patients at 4 sites). The company did not disclose what phase the studies will be.

Flex also plans to develop the therapy in neuromuscular diseases like MS, amyotrophic lateral sclerosis (ALS) and spinal spasticity. The only available treatment for muscle cramping in those conditions is intrathecal baclofen, which has side effects including loose muscles, headache, nausea and withdrawal symptoms including high fevers and muscle rigidity.

Westphal said he expects the regulatory pathway will be uncomplicated. “Regulatory authorities around the world have addressed cramping and spasms in MS and spinal spasticity. There is a clear path forward,” he said.

He said the company's cash should last for more than three years. “We don't have a big burn. We're fortunate that we can move into trials that are not overwhelmingly expensive,” Westphal said. “Every patient or every individual can be their own control.”

Flex is also looking into developing a consumer product based on the same ingredients; however, Westphal said the consumer product opportunity is a “minor effort” compared to FLEX 767. [bc](#)

COMPANIES AND INSTITUTIONS MENTIONED

Flex Pharma Inc., Boston, Mass.

Harvard University, Cambridge, Mass.

The Rockefeller University, New York, N.Y.