Akelos is an **innovative research-based biotechnology company** that was partially funded by the National Institutes of Health (NIH) with **a non-opioid drug candidate already in pre-clinical development for the treatment of neuropathic pain**. The company's development efforts are focused on the HCN1 ion channel present in primary sensory neurons, and increased HCN channel function in these cells is a key driver in the development of neuropathic pain. There are approximately 20 million people in the US living with chronic neuropathic pain who desperately need safe and effective pain relief; currently available medications are simply not sufficient.[1-4]. The company is led by Dr. Steven Fox, an entrepreneur, who previously founded Enamelon, a public oral care company, and has been awarded the **Ernst & Young's Entrepreneur of the Year and Medal of Freedom by members of the United States Senate** for his previous scientific work.

In 2019, the research team at Weill Cornell Medicine, led by Dr. Peter Goldstein, a scientific co-founder of Akelos, received a $1.7M grant from the NIH in support of this work. In Fall of 2022, the **NIH awarded a $3.69M multi-year grant** to Akelos in further support of these efforts. These highly competitive research grants demonstrate NIH's recognition of the importance of this work and the pressing need to develop a non-opioid, non-addictive, medication for the treatment of neuropathic pain.

Research by Weill Cornell Medicine scientists has resulted in intellectual property covering novel compounds and methods of treating pain using these compounds. This IP consists of a patent family, filed in the US, Europe, Japan, China, Canada and Australia, all derived from PCT International Patent Application, PCT/US2019/038493, filed on June 27, 2019. Patents have been issued or allowed in the US, China, Japan and Australia and we expect allowances everywhere we filed. The claims cover Akelos' lead compound, AKE-1018, other related compounds, and their use to treat pain.

Since our founding of the company, we have assembled an **outstanding executive team and Scientific Advisory Board with renowned academic and business leaders** to support our research team at Weill Cornell**.** These include:

- **Peter Goldstein, MD** – Chair of Scientific Advisory Board & Scientific Co-Founder
- **Cyrus Arman, PhD, MBA** – Former Director, Corporate Strategy; Global Director & Head of Competitive Strategy, Amgen; Senior VP, Business Operations; President & Principal Executive Officer, CytoDyn

- **Charles Berde, MD, PhD** – Senior Associate in Perioperative Anesthesia & Pain Medicine, Dept. of Anesthesia, Critical Care & Pain Medicine (Boston Children's Hosp), co-founder Pain Treatment Service at Boston Children's Hospital, Professor of Anaesthesia (Pediatrics), Harvard Medical School
- **Senator Thomas Daschle** - Former Senate Majority Leader
- **Scott L. Dax, MS, PhD,** Research and development champion and former Analgesics Research Team Lead at Johnson & Johnson
- **Michael Levitt, PhD** – Robert W. & Vivian K. Cahill Professor of Cancer Research, Stanford Medicine; Nobel Laureate (Chemistry, 2013)
- **Darryle Schoepp, PhD** – Former VP Neuroscience Research and Early Clinical Development, Eli Lilly; Senior VP & Neuroscience Head, Merck
- **Gareth Tibbs, PhD** – Senior Research Associate, Weill Cornell Medical College (and scientific co-founder, Akelos)
- **Dianna Willis, PhD** - Associate Director, Burke Neurological Institute (BNI), Lab Director, Laboratory for Axonal & RNA Biology (BNI), Co-Director, Center for Pain & Sensory Recovery (BNI)
- **Peter Hutt, JD** – FDA Counsel, Former Chief Counsel, Food and Drug Administration
- **Robert Benson, PhD** – Former leader at the National Institutes of Health and Harvard University

We have an opportunity to change modern medicine and have already made strides to do so. As recently demonstrated by Drs. Gareth Tibbs, Dianna Willis, and Peter Goldstein in their recently published article in the *British Journal of Anaesthesia* (Tibbs *et al*. 2023), our **lead molecule, AKE-1018, provided safe and effective pain relief following peripheral nerve injury**.[5] In rats, pain relief was observed within 24 hours of the first oral dose, and once daily dosing over the next seven days provided significant additional pain relief. AKE-1018 had an **excellent safety profile**: at 10x an effective dose, there were **no adverse cardiovascular effects** (no change in heart rate or blood pressure)**, no adverse motor effects** (no change in muscle strength or coordination), and **no evidence of either sedation or abuse potential**. The *in vivo* effects correlated with *in vitro* inhibition of the HCN1 ion channel. Critically, AKE-1018 was designed to not cross the blood-brain barrier; this was confirmed in both *in silico* molecular modeling and *in vivo* pharmacodynamic studies, highlighting a peripheral mechanism of action.[5]

Furthermore, research teams from Weill Cornell Medicine, the University of Miami, and Linköping University in Sweden, reported **identifying the binding site** for the alkylphenol

general anesthetic 2,6-diisopropylphenol (also known as **propofol)** on the human **HCN1 (hHCN1) ion channel**. These findings, recently published in *Nature*, reinforce the proposed mechanism of action and support ongoing efforts to identify next-generation pharmacophores.[6]

Akelos continues to evaluate its proprietary series of HCN1 inverse agonists, including lead compound AKE-1018, for formal Development including IND Enablement. The latest data indicates that AKE-1018 and the chemical series possess favorable drug-like properties.

The NIH grant was important, but did not provide all the financing needed to allow us to meet our goal of submitting an Investigational New Drug (IND) application to the Food and Drug Administration for first-in-human studies of AKE-1018**.** With your help, Akelos will be that much closer to providing life-changing care and potentially dominating a US$13 billion/yr. market.[7]


1. National Institute of Health Fact Sheet, 2022
2. Smith et al. JAMA, 2013.
3. Rao et al. Cancer, 2007
4. Hange et al. Neurology Research International, 2022
5. Tibbs et al. British Journal of Anaesthesia, 2023
6. Kim, E.D., Wu, X., Lee, S. et al. Propofol rescues voltage-dependent gating of HCN1 channel epilepsy mutants. Nature 632, 451–459 (2024).
7. Allied Market Research, December 2023