SK 13174
Halting Neurodegeneration by Restoring Mitophagy

AcureX

Indication	Neurodegenerative and movement disorders, including Parkinson's disease
Type of technology (platform, cell/gene thrapy, SM, device etc)	Drug discovery platform and biomarker, which led to the validation of two distinct targets and the development of two small molecule CNS drugs to these targets
Executive Summary (2-3 sentences)	Acurex's approach and founding intellectual property is based on a Stanford University breakthrough discovery that identified dysfunctional Miro1-mediated mitophagy as an early and key driver of pathology in neurodegenerative disease. With exclusive rights to this intellectual property, Acurex has built an industrialized drug discovery platform that enables the identification of druggable targets responsible for mitophagy defects. Out of these proprietary insights Acurex has developed two therapeutic drug programs and a biomarker for Parkinson's disease. Acurex is advancing small molecule drugs to these two targets into the clinic for CNS diseases, with the lead program expected to enter humans in 2024
Unmet Need, MOA, Approach (3-4 sentences)	Neurodegeneration represents a significant and growing unmet medical need across the world. A large body of evidence supports that mitophagy, the normal process by which cells dispose of dysfunctional mitochondria, plays an important and early role in the pathogenesis of neurodegenerative diseases including Parkinson's disease and Frontal Temporal Dementia. Acurex has leveraged it's proprietary insights to develop small molecule drugs to restore mitophagy, provide clinical benefit for patients and slow the progression of neurodegeneration. Further, Acurex's blood-based drug-responsive biomarker will enable longitudinal studies to better understand PD and diagnose patients at the earliest possible time, significantly increasing the chance of improving the quality of life of PD patients
Keywords (~10)	Parkinson's disease, Frontal Temporal Dementia, Essential Tremor, Precision Biomarker, Mitophagy, Mitochondria, Precision Medicine, Small Molecule, Drug Discovery Platform
What do you want to do with this asset (licening/partnering, funding (how much), clinical tiral etc)	Acurex is persuing both partnering and Series A funding opportunities to fund the continued development of its therapeutic and biomarker programs and conduct first in human clinical trials for it's lead therapeutic program

Milestones Achieved

- Acurex has secured over $18M in private and grant seed funding including funds from Stanford University, the Silverstein Foundation, the Michael J. Fox Foundation and the NIH
- Acurex has developed three oral, small molecule therapeutics, a clinical biomarker program and a drug discovery platform in under three years
- Acurex drugs prevent and restore damage in three key aspects of Parkinson's disease: dysfunctional mitophagy, formation of toxic pS129-alpha-synuclein and axon retraction, at nM potency
- Demonstrated, with our peripheral biomarker of PD pathology, that a PD patient with the LRRK2 G2019S mutation has a mitophagy defect that can be corrected ex-vivo with AcureX drugs
- Begun an IRB-approved clinical biomarker study, with the head of UCSF's movement disorder clinic, Dr. Jill Ostrem, chairing this trial's DSMB
- Acurex's lead therapeutic program will begin IND-enabling studies in Q4 2023

Value Proposition

Value Proposition:

- Acurex's mitophagy biomarker will bring precision medicine to the CNS field and enable early value inflection in Ph1b/2a clinical trials
- Targets identified by Acurex address fundamental drivers of Parkinson's disease in both genetic and sporadic patients. When approved, Acurex's therapeutics will address significant unmet needs in neurology, the final frontier of medicine
- Neurodegenerative diseases are increasing worldwide and will represent the largest cost burden on the US healthcare system in 10 years. Parkinson's disease therapeutic drugs which do not slow progression or adequately address symptoms represent a global market size of $5B
- Acurex's insights and assets can unlock valuable opportunities in other therapeutic areas where mitophagy is a driver of disease

Key Publications

Bharat, V. & Wang, X. Precision Neurology for Parkinson's Disease: Coupling Miro1-Based Diagnosis with Drug Discovery. Mov. Disord. mds.28194 (2020)

Functional Impairment in Miro Degradation and Mitophagy Is a Shared Feature in Familial and Sporadic Parkinson's Disease. Cell Stem Cell. 19: 709–724 (2016)

Shaltouki, A., Hsieh, C.-H. H., Kim, M. J. & Wang, X. Alpha-synuclein delays mitophagy and targeting Miro rescues neuron loss in Parkinson's models. Acta Neuropathol. 136, 607–620 (2018)

Hsieh, C.-H. et al. Miro1 Marks Parkinson's Disease Subset and Miro1 Reducer Rescues Neuron Loss in Parkinson's Models. Cell Metab. 1131–1140 (2019)

Nguyen, D., Bharat, V., Conradson, D. M., Nandakishore, P. & Wang, X. Miro1 Impairment in a Parkinson's At-Risk Cohort. Front. Mol. Neurosci. 14, 1–8 (2021)

Li L, Conradson DM, Bharat V, Kim MJ, Hsieh C, et al. A mitochondrial membrane-bridging machinery mediates signal transduction of intramitochondrial oxidation. Nat Metab. 3: 1242–1258. (2021)

IP Status (patent #)

Acurex has granted and filed patents covering composition of matter and method of treatment and use

Team Member Details

Acurex was co-founded by a team comprised of seasoned drug developer William Shrader, Ph.D., Stanford Professor Xinnan Wang, MD, Ph.D. and successful life-science entrepreneurs Lev and Galina Leytes. In addition, leaders in Parkinson's disease research, drug development, and business constitute Acurex's board and advisory team. With an experienced team and a strong IP portfolio, Acurex is recognized as the leading expert in its field