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Lohocla Research Announces FDA Clearance of Investigational New Drug Application for Nezavist, a Novel Molecule for Treating Addiction and Craving

Focusing on non-addictive treatments for chronic pain and addiction, Lohocla Research Corporation gets the go-ahead for first-in-human trials of their first-in-class therapeutic for alcohol use disorder.

Aurora, Colorado, 13 March 2024 – **Lohocla Research Corporation** today announced that the U.S. Food and Drug Administration (FDA) has cleared its IND application, enabling the company to proceed with Phase 1 and 2 trials for **Nezavist**. Nezavist is Lohocla's first-in-class, non-addicting small molecule for treating Alcohol Use Disorder (AUD) and craving.[i] Lohocla will begin first-in-human trials in the fourth quarter of 2024. Acknowledging the promise of this new drug, the National Institutes of Health (NIH) National Institute on Alcohol Abuse and Alcoholism (NIAAA) has committed substantial funding to researching the safety and effectiveness of this innovative, rationally designed molecule.

Company founder and CEO Dr. Boris Tabakoff said, "Nezavist has been designed to break the cycle of the biological processes that underlie craving, which leads abstinent individuals to relapse. We foresee Nezavist serving as an important tool for alcohol-dependent individuals in their battle to quit drinking and maintain sobriety,"

About Alcohol Use Disorder

According to the NIAAA, AUD is a "chronic, relapsing brain disease characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences." As of 2019, AUD affected 14.1 million adults[i] and 623,000 adolescents in the US, and data from 2010 estimate an economic burden of $249 billion in the US.[ii] Globally, alcohol misuse was the fifth leading risk factor for premature death and disability in 2010.

The research of Lohocla scientists has contributed critical information to the understanding of the mechanisms by which alcohol affects behavior as well as the changes caused in the brain by chronic alcohol ingestion that results in alcohol addiction. When you consume alcohol, it acts in the brain to potentiate the actions of the GABA system and inhibit the actions of the glutamate (NMDA) system. The brain is, however, a malleable organ that acts to adapt to the chronic presence of alcohol and, under such conditions, decreases the function of the GABA system and increases the function of the glutamate (NMDA) system to counter the action of ethanol. Such changes may help the individual

function while drinking but, when the individual tries to stay sober, the altered brain function produces hyperexcitability, anxiety, depression, and craving to return to drinking

About **Nezavist**

GABA and NMDA systems notwithstanding, current research has demonstrated that a more holistic mechanism is responsible for human and other animal alcohol drinking behavior. Recent work shows that alcohol's actions in the gut may be the initial site that instigates the biological changes that lead to AUD.

The gut is the area of the body having the greatest concentration of immune cells as well as hormones controlling intake of caloric substances. The immune- and hormonal-systems of the gut communicate with the brain thereby affecting behavior. This gut-brain communication can occur by two paths: 1. by chemical signals traveling through the blood stream or 2. by signals carried along the vagus nerve, which creates a neuronal bridge between the gut and the brain. It has been proposed that ingested ethanol activates the immune system in the gut and inflammatory signals travel to the brain via the blood stream. Over time, these signals produce inflammation in brain tissue by activating cells called microglia. The inflammation in the brain leads to changes in brain chemistry that result in craving for alcohol leading to relapse in individuals trying to abstain.

Nezavist has been designed to break this cycle and reduce craving and relapse. Nezavist acts on the vagus nerve at the gut level to create neural signals that counter the inflammation caused in the gut and the brain by the chronic consumption of alcohol. Nezavist changes the pattern of vagal nerve signaling to the brain and vagal signals have been shown to suppress the microglial inflammatory state, thus reducing the craving for alcohol, supporting the maintenance of healthy brain tissue and aiding abstinence.

About Lohocla Research

At Lohocla Research Corporation, we work towards one goal: developing pharmaceutical innovations that improve people's lives. Understanding the challenges of chronic pain and addiction, we focus on transforming the lives of patients suffering from these conditions. Built upon a rationally designed, proprietary molecular platform, we have developed a first-of-its-kind molecule that selectively modulates a discrete set of receptors involved in the chronic pain signaling pathway in overactive peripheral nerves as well as a pioneering drug for the treatment of alcohol use disorder, addiction, and craving.

Phonetic pronunciation: low-HOE-kluh

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[i] https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder

[ii] https://www.cdc.gov/alcohol/features/excessive-drinking.html