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Achieve Life Sciences Announces Publication of Cytisinicline Vaping Cessation Trial Results in JAMA Internal Medicine

Phase 2 ORCA-V1 trial showed treatment with cytisinicline more than doubled odds of quitting e-cigarettes compared with placebo

Cytisinicline treatment well tolerated with no serious adverse events reported and excellent compliance to study treatment

Achieve expects to conduct an End-of-Phase 2 Meeting with the FDA later this year to discuss Phase 3 trial plans

SEATTLE and VANCOUVER, British Columbia, May 06, 2024 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a late-stage pharmaceutical company committed to the global development and commercialization of cytisinicline for smoking cessation and nicotine dependence, today announced publication of the ORCA-V1 trial results in the *Journal of the American Medical Association* (JAMA) *Internal Medicine*. ORCA-V1 evaluated the efficacy and safety of 3 mg cytisinicline dosed three times daily for 12 weeks compared to placebo in 160 non-smoking adults who used e-cigarettes or nicotine vapes and wanted to quit e-cigarettes. All participants received behavioral support for vaping cessation.

As reported today, the ORCA-V1 trial demonstrated that biochemically confirmed continuous vaping abstinence during the last 4 weeks of treatment, the primary outcome measure, was significantly higher for cytisinicline treatment compared to placebo. For cytisinicline treatment compared to placebo, 31.8% versus 15.1% of participants were abstinent during weeks 9 to 12, and participants receiving cytisinicline treatment had 2.6 times higher odds, or likelihood, to have quit vaping (odds ratio (OR) 2.64 [95% CI, 1.06-7.10]; P=.04)

A consistent trend in favor of cytisinicline was found across the secondary endpoints, evaluating abstinence during and beyond end of treatment. During the 12-week study treatment, the past seven-day prevalence of vaping abstinence at each week was

consistently higher in the cytisinicline group than the placebo group. Similarly, the mean biochemical cotinine levels were consistently lower in the cytisinicline group than the placebo group at each weekly visit during study treatment. Including a four-week follow-up after treatment ended, continuous abstinence from weeks 9 to 16 remained higher in the cytisinicline group than the placebo group at 23.4% versus 13.2%, respectively (OR, 2.0; [95% CI, 0.82-5.32]).

"Many people who use e-cigarettes want to quit but find it difficult due to nicotine dependence. They need help to stop vaping, yet no FDA-approved medication is currently available to help them do so," said Dr. Nancy Rigotti, Director, Tobacco Research and Treatment Center Massachusetts General Hospital, Professor of Medicine at Harvard Medical School, and Principal Investigator of ORCA-V1. "Cytisinicline has been shown in clinical trials to be effective and safe to help adults stop smoking cigarettes. The results of this study indicate that it might also help people to quit vaping."

Study drug compliance was high; 72.7% and 66.0% of participants treated with cytisinicline and placebo, respectively, took >90% of study drug doses. Cytisinicline was well tolerated and no serious adverse events were reported. Similar rates of adverse events were observed between treatment arms (50.9% in the cytisinicline arm versus 54.7% in the placebo arm). The most frequent (>5%) treatment-emergent adverse events for cytisinicline subjects were sleep disturbances, anxiety, headache, fatigue, and upper respiratory tract infection and for placebo subjects were nausea, COVID-19, headache, anxiety and upper respiratory tract infection. Higher rates of headache and nausea were reported by participants treated with placebo.

“As we’ve seen now in multiple clinical trials, the safety and tolerability profile of cytisinicline is very compelling and we believe it will be a key driver of compliance when approved for use,” commented Cindy Jacobs, MD, PhD, President and Chief Medical Officer at Achieve. “Many people who attempt to quit nicotine struggle with withdrawal symptoms and cravings, making it difficult to maintain abstinence. Current treatments can have high rates of headaches and nausea, and we are simply not seeing that with cytisinicline, giving us confidence that cytisinicline’s profile will help more people, who want to quit, succeed in doing so.”

The prevalence of e-cigarette use by adults in the United States continues to rise. It is estimated that 4.5% among all adults in the United States and 11% among adults aged 18-24 used e-cigarettes in 2021. While adults who switch from smoking combustible cigarettes to using nicotine e-cigarettes reduce their tobacco-related health risks, e-cigarettes products are not harmless and sustain nicotine dependence. In surveys, more than half of adults who vape nicotine plan to quit. Cytisinicline, if approved, could be the first prescription drug to help people who are ready to address their addiction to e-cigarettes. Achieve plans to conduct an End-of-Phase 2 Meeting with the FDA later this year to discuss future clinical trial requirements to pursue an indication for vaping cessation.

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About ORCA-V1
The Phase 2 ORCA-V1 trial evaluated 160 adults who used e-cigarettes on a daily basis at five clinical trial locations in the United States. ORCA-V1 participants were randomized to

receive 3mg cytisinicline three times daily or placebo for 12 weeks in combination with standard cessation behavioral support. The dose and administration of cytisinicline in the ORCA-V1 study is identical to that used in the Phase 3 registrational trials for smoking cessation. ORCA-V1 was supported in part by the National Institute on Drug Abuse (NIDA) of the NIH through grant funding which was awarded in two phases totaling $2.8 million.

About Achieve and Cytisinicline

Achieve's focus is to address the global smoking health and nicotine addiction epidemic through the development and commercialization of cytisinicline. There are an estimated 28 million adults in the United States alone who smoke combustible cigarettes.[1] Tobacco use is currently the leading cause of preventable death that is responsible for more than eight million deaths worldwide and nearly half a million deaths in the United States annually.[2,3] More than 87% of lung cancer deaths, 61% of all pulmonary disease deaths, and 32% of all deaths from coronary heart disease are attributable to smoking and exposure to secondhand smoke.[3]

In addition, there are over 11 million adults in the United States who use e-cigarettes, also known as vaping.[1] In 2023, approximately 2.1 million middle and high school students in the United States reported using e-cigarettes.[4] Currently, there are no FDA-approved treatments indicated specifically as an aid to nicotine e-cigarette cessation.

Cytisinicline is a plant-based alkaloid with a high binding affinity to the nicotinic acetylcholine receptor. It is believed to aid in treating nicotine addiction for smoking and e-cigarette cessation by interacting with nicotine receptors in the brain, reducing the severity of withdrawal symptoms, and reducing the reward and satisfaction associated with nicotine products. Cytisinicline is an investigational product candidate being developed for the treatment of nicotine addiction and has not been approved by the Food and Drug Administration for any indication in the United States. For more information on cytisinicline and Achieve visit www.achievelifesciences.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the timing and nature of cytisinicline clinical development and regulatory review and approval, data results and commercialization activities, the potential market size for cytisinicline, the potential benefits, efficacy, safety and tolerability of cytisinicline, the ability to discover and develop new uses for cytisinicline, including but not limited to as an e-cigarette cessation product, and the development and effectiveness of new treatments. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Achieve may not actually achieve its plans or product development goals in a timely manner, if at all, or otherwise carry out its intentions or meet its expectations or projections disclosed in these forward-looking statements. These statements are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described in the forward-looking statements, including, among others, the risk that cytisinicline may not demonstrate the hypothesized or expected benefits; the risk that Achieve may not be able to obtain additional financing to fund the development of cytisinicline; the risk that cytisinicline will not receive regulatory approval or be successfully commercialized; the risk that new developments in the smoking cessation landscape require changes in business strategy or clinical development plans; the risk that Achieve's intellectual property may not be adequately protected; general business and economic

conditions; risks related to the impact on our business of macroeconomic and geopolitical conditions, including inflation, rising interest rates, increased volatility in the debt and equity markets, actual or perceived instability in the global banking system, global health crises and pandemics and geopolitical conflict and the other factors described in the risk factors set forth in Achieve's filings with the Securities and Exchange Commission from time to time, including Achieve's Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q. Achieve undertakes no obligation to update the forward-looking statements contained herein or to reflect events or circumstances occurring after the date hereof, other than as may be required by applicable.

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Source: Achieve Life Sciences