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Achieve Life Sciences Announces Positive Phase 2 ORCA-V1 Trial Results Showing Statistically Significant Vaping Cessation Benefit for Participants Treated with Cytisinicline

First Randomized, Placebo-Controlled Clinical Study to Report Successful E-Cigarette Cessation Benefit with Pharmacological Treatment

Study Supports Potential Broad Utilization of Cytisinicline for Treatment of Nicotine Dependence

Management to Host Conference Call Today, April 20, 2023, at 8:30 AM EDT

SEATTLE and VANCOUVER, British Columbia, April 20, 2023 (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 reported positive topline results from its Phase 2 ORCA-V1 trial. ORCA-V1 evaluated the efficacy and safety of 3mg cytisinicline dosed three times daily for 12 weeks compared to placebo in 160 adults who use e-cigarettes or nicotine vapes and who do not currently smoke cigarettes. All participants received behavioral support for nicotine cessation.

The primary endpoint for ORCA-V1 was biochemically verified continuous abstinence from nicotine e-cigarette use, measured during the last 4 weeks of treatment. Subjects who received 12 weeks of cytisinicline treatment had 2.6 times higher odds, or likelihood, to have quit vaping during the last 4 weeks of treatment compared to subjects who received placebo (p=0.035). The vaping cessation rate during weeks 9-12 was 31.8% for cytisinicline compared to 15.1% for placebo. A benefit in favor of cytisinicline was consistently observed across the secondary endpoints. Additionally, a cessation benefit was observed for cytisinicline across clinical trial sites and participant demographics such as age, gender, race, or whether they had smoked cigarettes in the past.

“These groundbreaking results from ORCA-V1 reaffirm our confidence that cytisinicline could be a safe and effective option to treat nicotine dependence,” said Dr. Cindy Jacobs, Chief Medical Officer and President at Achieve Life Sciences. “We believe that cytisinicline has the potential to become the first treatment for nicotine vaping cessation, offering new hope to those who want to quit e-cigarettes.”

Cytisinicline was well tolerated and no serious adverse events were reported. Similar rates of adverse events (AE’s) were observed between treatment arms (54.7% in the placebo arm vs. 50.9% in the cytisinicline arm). The most commonly reported (>5%) AEs in the placebo arm were anxiety, headache, upper respiratory tract infection, nausea, and COVID-19 infection. In the cytisinicline arm, >5% AEs reported were sleep disturbances, anxiety, headache, fatigue, and upper respiratory tract infection.

ORCA-V1 participants had an average age of 34 years and were engaged in current daily use of nicotine-containing e-cigarettes. Approximately half of the participants had previously tried to quit vaping by self-attempt methods. Subjects were stratified based on past smoking history. Approximately 72% were former smokers of combustible cigarettes, while 28% had not smoked cigarettes. Efficacy results were similar for both groups. ORCA-V1 was supported by the National Institute on Drug Abuse of the National Institutes of Health.

“This new study suggests cytisinicline, which has previously helped people to quit smoking cigarettes, may also help adults to stop using e-cigarettes, another nicotine-containing product,” said Dr. Nancy Rigotti, Professor of Medicine at Harvard Medical School, and Principal Investigator of ORCA-V1.

Tobacco use continues to be a major health concern, with an estimated 47 million adults in the United States using tobacco in some form in 2020, including an estimated 9 million adults who used e-cigarettes to vape nicotine. Many individuals have become dependent on nicotine and want to quit but have difficulty in doing so. No FDA-approved treatments have been specifically evaluated in this population and the ORCA-V1 trial is the first randomized, placebo-controlled clinical study to demonstrate successful e-cigarette cessation.

In addition to the results of this study, Achieve Life Sciences plans to announce topline results in the second quarter of 2023 from the Phase 3 ORCA-3 trial for cytisinicline as a new smoking cessation treatment in people who want to quit daily cigarette smoking but have not been able to do so using other available treatments.

For more information on cytisinicline and Achieve visit www.achievelifesciences.com.

Conference Call Details
Achieve will host a conference call at 8:30 AM EDT today, Thursday, April 20, 2023. To access the webcast, log on to the investor relations page of the Achieve website at http://ir.achievelifesciences.com/events-and-webcasts. Alternatively, access to the live conference call is available by dialing (877) 269-7756 (U.S. & Canada) or (201) 689-7817 (International) and referencing conference ID 13738334. A webcast replay will be available approximately two hours after the call and will be archived on the website for 90 days.

The research and clinical study discussed in this press release is supported by the National Institute on Drug Abuse of the National Institutes of Health (NIH) under Award Number 4R44DA054784-02. The content is the sole responsibility of the authors and does not necessarily represent the official views of the NIH.

About ORCA-V1
The Phase 2 ORCA-V1 trial evaluated 160 adults who used e-cigarettes on a daily basis at 5 clinical trial locations in the United States. The trial was initiated in June 2022 and completed enrollment in approximately 4 months, with topline results reported in April 2023. 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 by the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (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. 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.[1,2] 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.[2]

In addition, there are over 9 million adults in the United States who use e-cigarettes, also known as vaping.[3] In 2022, approximately 2.5 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.

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, data results and commercialization activities, the potential market size for cytisinicline, the potential benefits, 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, the development and effectiveness of new treatments, and the intention to submit cytisinicline to the FDA for approval. 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 the Russian military action in Ukraine; risks related to the impact on our business of the COVID-19 pandemic or similar public health crises 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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[3]Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco Product Use Among Adults — United States, 2020. MMWR Morb Mortal Wkly Rep 2022;71:397–405.

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