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Achieve Life Sciences to Advance First Vaping Cessation Therapy After Successful End-of-Phase 2 Meeting with FDA

Milestone Reinforces the Potential for Cytisinicline as a First-in-Class Treatment for Vaping Cessation

SEATTLE and VANCOUVER, British Columbia, Dec. 03, 2024 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a late-stage pharmaceutical company focused on the development and commercialization of cytisinicline for nicotine dependence, announced today the successful outcome of its End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA). This meeting represents a key milestone in advancing cytisinicline's development as a potential first-in-class treatment for nicotine e-cigarette or vaping cessation. Achieve obtained FDA agreement on the proposed single Phase 3 study design for cytisinicline treatment in vaping cessation and on the additional requirements for submitting a supplemental new drug application (sNDA) to expand cytisinicline for the treatment for vaping cessation.

The End-of-Phase 2 meeting resulted in alignment with the FDA on the proposed Phase 3 study design, including the inclusion/exclusion criteria, primary and secondary efficacy objectives, definition of vaping abstinence with biochemical verification, and other overall study assessments. The FDA agreed that one well-controlled Phase 3 trial (ORCA-V2), in addition to Achieve's completed Phase 2 ORCA-V1 trial, would be acceptable for a vaping cessation indication as an sNDA. Additionally, the FDA agreed that the company's safety exposure data from the ongoing ORCA-OL study would be adequate for the vaping cessation label expansion.

There are 11 million adults in the United States who use e-cigarettes, most of whom are 18 to 24 years old and have never smoked. Notably, about 60% of vape users want to quit, and there is currently no approved treatment.

“The success of our End-of-Phase 2 meeting reaffirms the clinical development strategy for cytisinicline and its potential as a groundbreaking therapy for nicotine dependence,” stated Cindy Jacobs, M.D., Ph.D., President and Chief Medical Officer of Achieve. “The FDA’s Breakthrough Therapy designation, granted earlier this year, has expedited and enhanced our interactions with the FDA thereby enabling us to receive timely feedback and accelerate the program’s timeline. We are steadfast on addressing the critical unmet need in vaping cessation and pioneering a path toward the first approved treatment for this growing public health challenge.”

The Phase 3 ORCA-V2 trial will assess the efficacy and safety of cytisinicline for nicotine e-cigarette cessation, building on the previous Phase 2 vaping cessation trial as well as the Phase 3 smoking cessation clinical trials with cytisinicline. The trial population and design are similarly aligned with Achieve’s successful Phase 2 ORCA-V1 trial. Achieve is currently targeting ORCA-V2 to initiate in the third quarter of 2025.

Key study design highlights include:

- **Study Population:** Adults 18 years of age or older who are dependent on nicotine e-cigarettes and who have failed at least one previous attempt to stop vaping nicotine.
- **Study Design:** ORCA-V2 will evaluate the efficacy and safety of 3 mg cytisinicline dosed three times daily (TID) for 12 weeks compared to placebo in approximately 800 adults who use e-cigarettes or nicotine vapes and do not currently smoke cigarettes. All participants will receive behavioral support for nicotine cessation and will be assessed throughout the 24-week trial duration.
- **Study Objectives:** The primary objective for ORCA-V2 mirrors the Phase 2 ORCA-V1 trial objective and will be weekly vaping abstinence with biochemical confirmation, measured during the last four weeks of treatment, weeks 9 to 12. The secondary objective will evaluate continuous vaping cessation from weeks 9 to 24. Safety, adherence to study treatment, and other patient-reported outcomes on vaping urges and craving symptoms will also be collected.

Rick Stewart, Chief Executive Officer of Achieve, commented, “Advancing our Phase 3 program for cytisinicline in vaping cessation marks a significant milestone. We remain confident in our ambition to revolutionize the category and provide a much-needed solution for quitting nicotine e-cigarettes and will continue to work closely with the FDA as the program advances.”

To date, Achieve has successfully completed two Phase 3 clinical trials of cytisinicline in more than 1,600 subjects who smoke combustible cigarettes and one Phase 2 clinical trial for adults who vape nicotine e-cigarettes and desire to quit. It completed enrollment of the ORCA-OL clinical trial, evaluating long-term safety exposure of the novel 3 mg cytisinicline TID dosing regimen in individuals who smoke cigarettes or vape nicotine, and expects to file its NDA submission for smoking cessation in the second quarter of 2025.

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 3 mg 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 approximately 29 million adults 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.[4] In 2024, approximately 1.6 million middle and high school students in the United States reported using e-cigarettes.[5] There are no FDA-approved treatments indicated specifically as an aid to nicotine e-cigarette cessation. Cytisinicline has been granted Breakthrough Therapy designation to address this critical need.

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 nicotine craving 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 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, the development and effectiveness of new treatments, and the successful commercialization of cytisinicline. 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 and commercialization of cytisinicline; the risk that cytisinicline will not receive regulatory approval or be successfully commercialized; the risk that new developments in the smoking and vaping cessation landscapes 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, volatile interest rates, 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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References

[1]VanFrank B, Malarcher A, Cornelius ME, Schecter A, Jamal A, Tynan M. Adult Smoking Cessation — United States, 2022. MMWR Morb Mortal Wkly Rep 2024;73:633–641.

[2]World Health Organization. WHO Report on the Global Tobacco Epidemic, 2019. Geneva: World Health Organization, 2017.

[3]U.S. Department of Health and Human Services. The Health Consequences of Smoking – 50 Years of Progress. A Report of the Surgeon General, 2014.

[4]Cornelius ME, Loretan CG, Jamal A, et al. Tobacco Product Use Among Adults – United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483.

[5]Jamal A, Park-Lee E, Birdsey J, et al. Tobacco Product Use Among Middle and High School Students — National Youth Tobacco Survey, United States, 2024. MMWR Morb Mortal Wkly Rep 2024;73:917–924

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