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Achieve Life Sciences Announces Critical Milestone Successfully Reached in ORCA-OL Cytisinicline Clinical Trial Required for NDA Submission

Over 300 Participants Have Completed Cumulative Six Months of Cytisinicline Treatment in the ORCA-OL Trial, Completing the Long-Term Exposure Requirement for NDA Submission

ORCA-OL Long-Term Exposure Timelines Remain on Track with No Safety Concerns Identified

Planned Cytisinicline NDA Submission on Target for Q2 2025

SEATTLE and VANCOUVER, British Columbia, Jan. 07, 2025 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a late-stage pharmaceutical company focused on the global development and commercialization of cytisinicline for smoking cessation as a treatment for nicotine dependence, today announced that its ongoing ORCA-OL clinical trial, designed to evaluate the long-term safety exposure of cytisinicline, has reached the goal of at least 300 participants completing six months of cumulative cytisinicline treatment. The U.S. Food and Drug Administration (FDA) requested six-month safety exposure data to be included in the company's planned New Drug Application (NDA). Further, based on ongoing Data Safety Monitoring Committee (DSMC) review, no safety concerns have been identified, and the study continues to proceed as planned with no modifications. Achieve remains on track for the planned NDA submission, expected to occur in the second quarter of 2025.

"Achieving this critical milestone for the NDA submission clearly advances our mission to bring treatment to people who struggle with nicotine dependence," stated Cindy Jacobs, Ph.D., M.D., President and Chief Medical Officer of Achieve. "We are deeply grateful to the clinical sites and participants for their continued commitment and dedication in helping bring a new therapy for nicotine dependence forward, one which aims to help address a persistent public health challenge."

In late 2023 pre-NDA discussions, the FDA expressed its support for an NDA submission based on sufficient data from the two completed randomized, controlled Phase 3 trials,

ORCA-2 and ORCA-3, to assess efficacy for cytisinicline six-week and 12-week treatment durations. The FDA also requested cytisinicline exposure data out to six months and one year to evaluate adequate longer-term safety risks, given that smoking cessation drugs are intended for chronic, repeated, or intermittent use, as patients may relapse and require repeated treatments. The FDA agreed to having the six-month cumulative exposure safety data submitted in the NDA submission and the one-year cumulative exposure safety data submitted later, prior to potential NDA approval.

“The completion of the cumulative six-month treatment reflects the dedication of our team and study participants, bringing us closer to our goal of potentially becoming the first new FDA-approved smoking cessation treatment in nearly two decades,” said Rick Stewart, Chief Executive Officer of Achieve. “As we move forward, our team remains focused on fulfilling all NDA-related requirements and ensuring cytisinicline reaches those who need it most.”

To date, Achieve has successfully completed two Phase 3 clinical trials of cytisinicline in more than 1,600 subjects who either smoke cigarettes or vape nicotine e-cigarettes and have the desire to quit. The ORCA-OL clinical trial continues to evaluate longer-term safety exposure of the novel 3 mg cytisinicline three times a day dosing regimen in individuals who want to end their nicotine dependence.

About ORCA-OL Trial
ORCA-OL is an open-label trial designed to evaluate the long-term exposure of 3 mg cytisinicline treatment dosed three times daily in adults 18 years of age or older who want to quit smoking or vaping and is being conducted at 29 clinical sites across the United States. The trial results are expected to meet the FDA's requirement for safety data from at least 300 participants treated with cytisinicline over a cumulative six-month period for the NDA submission. Additionally, data on at least 100 subjects treated for a cumulative one-year period will be provided prior to potential product approval.

About Achieve Life Sciences, Inc.
Achieve Life Sciences is a specialty pharmaceutical company committed to addressing the global smoking health and nicotine addiction epidemic through the development and commercialization of cytisinicline. The company has successfully completed two Phase 3 studies with cytisinicline for smoking cessation and one Phase 2 study with cytisinicline in vaping cessation. The company has fully enrolled its ongoing open-label safety study with cytisinicline and plans to submit its new drug application for smoking cessation in Q2 2025. Achieve has conducted a successful end-of-Phase 2 meeting with the FDA for the vaping indication and expects to initiate its single Phase 3 clinical study in vaping later in 2025.

About 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 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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