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Achieve Life Sciences Announces Positive Outcome of Second Data Safety Monitoring Committee Review for the ORCA-OL Clinical Trial

No Safety Concerns Identified by DSMC in the ORCA-OL Long-Term Exposure Trial

Achieve Reiterates Planned Cytisinicline NDA Submission in Q2 2025

SEATTLE and VANCOUVER, British Columbia, Feb. 10, 2025 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a late-stage specialty pharmaceutical company focused on the global development and commercialization of cytisinicline for smoking cessation and nicotine dependence, today announced that the Data Safety Monitoring Committee (DSMC) has recently completed its second independent review of the ongoing ORCA-OL trial, evaluating long-term exposure of the novel 3 mg cytisinicline treatment dosing regimen in individuals who smoke cigarettes or vape nicotine.

Following this second comprehensive review of available safety data, the DSMC stated that it did not identify any unexpected treatment-related adverse events and that the participants' adherence to their cytisinicline medication was excellent. Overall safety data remains consistent with previous findings. The DSMC concluded the study may continue as planned without any modifications.

"The positive outcome of the DSMC's second review continues to confirm the previous findings from our Phase 2 and Phase 3 trials regarding the overall safety of cytisinicline," said Cindy Jacobs, PhD, MD, President and Chief Medical Officer of Achieve. "This reinforces our confidence in the cytisinicline safety profile from the ORCA-OL trial and the broader ORCA program, moving us closer to filing our cytisinicline New Drug Application or NDA."

In October 2024, Achieve announced the completion of the ORCA-OL trial enrollment, with 479 participants enrolled across 29 clinical trial sites in the United States. All participating sites and individuals were previously involved in Achieve's ORCA "Ongoing Research of Cytisinicline for Addiction" program, which focused on smoking and e-cigarette cessation. In

January 2025, Achieve announced that the ongoing ORCA-OL clinical trial had reached its goal of at least 300 participants completing six months of cumulative cytisinicline treatment, which was an important milestone for proceeding with the company's planned NDA filing.

Rick Stewart, Chief Executive Officer of Achieve, added, "Achieve remains on track with our expected NDA submission next quarter for cytisinicline as a treatment of nicotine dependence for smoking cessation. We believe it will be the first new prescription treatment in nearly 20 years to provide physicians and smokers with an important new tool to stop smoking. Achieve remains focused on and committed to addressing the public health crisis of nicotine dependence."

The ORCA-OL clinical trial is designed to satisfy the U.S. Food and Drug Administration's (FDA) long-term exposure safety data requirements for cytisinicline's potential approval. The FDA requested six-month safety exposure data from at least 300 participants who have been treated with cytisinicline to be included in the company's planned NDA, with one-year cumulative exposure safety data from a minimum of 100 participants treated with cytisinicline submitted during the NDA review period, prior to potential NDA approval.

To date, Achieve has successfully completed two Phase 3 clinical trials of cytisinicline in more than 1,600 subjects who smoke 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 late-stage specialty pharmaceutical company committed to addressing the global smoking health and nicotine dependence 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 also conducted a successful end-of-Phase 2 meeting with the FDA for a future vaping indication.

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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