March 26, 2026

Achieve Life Sciences Announces Publication in Nicotine & Tobacco Research Linking Cytisinicline's Receptor Selectivity to Low Nausea Rates and Favorable Tolerability

Preclinical findings show cytisinicline's minimal 5-HT3 serotonin receptor binding offers insight into observed low nausea rates in smoking and vaping cessation trials

SEATTLE and VANCOUVER, British Columbia, March 26, 2026 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a late-stage specialty pharmaceutical company focused on the global development and commercialization of cytisinicline as a treatment of nicotine dependence, today announced the publication of a manuscript in *Nicotine & Tobacco Research* describing the receptor selectivity profile of cytisinicline. This study provides mechanistic characterization of cytisinicline's receptor selectivity profile, which informs understanding of its favorable tolerability.

There have been no new FDA-approved treatments for smoking cessation in 20 years, and there are currently no FDA-approved treatments for vaping cessation. Of the approximately 25 million U.S. adults who smoke and the nearly 18 million U.S. adults who vape, more than half want to quit.[1] Research shows only 10% of people who try to quit smoking each year are successful, signaling the need for more treatment options.[2]

The *Nicotine & Tobacco Research* publication, entitled "Receptor Selectivity of Cytisinicline: Minimal 5-HT3 Binding May Explain Lower Incidence of Nausea in Smoking Cessation Therapy," demonstrates that cytisinicline binds to the nicotinic receptor, which is believed to reduce nicotine cravings and support smoking cessation, while showing it has minimal interaction with the serotonin receptor known to trigger nausea. This may be appealing for people who are trying to quit smoking but have struggled with tolerability in past quit attempts.[3-5]

Key Findings:

- **Strong binding:** Cytisinicline demonstrated strong binding at the α4β2 nicotinic receptor, displacing nearly all (99%) of the comparison compound in laboratory testing. This high level of receptor engagement suggests cytisinicline effectively targets the mechanism associated with smoking cessation.
- **Minimal 5-HT3 receptor displacement:** At the same concentration, cytisinicline showed minimal displacement (-8%) at the 5-HT3 receptor, indicating negligible binding under assay conditions. This minimal interaction is significant as activation of the 5-HT3 receptor is known to induce nausea, which helps explain cytisinicline's tolerability profile observed in clinical trials.

“These findings from our preclinical program provide additional insights regarding cytisinicline’s pharmacologic profile and support observations from clinical studies,” said Mark Rubinstein, MD, Chief Medical Officer of Achieve Life Sciences. "Namely, these results may lend further biological basis for why cytisinicline has such low rates of adverse events like nausea, which is thought to be linked to binding at the 5-HT3 receptor.”

The data in this publication complement late-breaking voluntary survey data from ORCA-OL that were recently presented at the Society for Research on Nicotine & Tobacco (SRNT) 2026 Annual Meeting. The open-label, long-term exposure safety study of cytisinicline followed participants for up to one year of treatment. In the voluntary post-trial survey of cytisinicline use, participants self-reported high quit and reduction rates of nicotine use, driven by fewer cravings, and few or manageable side effects. Together, these data contribute to a more complete understanding of cytisinicline’s potential impact on the lives of people who smoke as they strive to quit nicotine.

Nicotine dependence remains a leading cause of preventable death, claiming nearly half a million lives annually in the United States alone.[6-7] Despite the availability of smoking cessation pharmacotherapies, poor tolerability and side effects remain significant barriers to effective treatment.

About Achieve Life Sciences, Inc.
Achieve Life Sciences, Inc. is a late-stage specialty pharmaceutical company focused on the global development and commercialization of cytisinicline as a treatment of nicotine dependence. In September 2025, the company announced that its New Drug Application, submitted to the U.S. Food and Drug Administration (FDA) in June 2025, had been accepted for review. The FDA has assigned a Prescription Drug User Fee Act (PDUFA) date of June 20, 2026. The NDA is for cytisinicline to be used as a treatment of nicotine dependence for smoking cessation in adults, based on two successfully completed Phase 3 studies and its open-label safety study. Additionally, the company has completed a Phase 2 study with cytisinicline in vaping cessation and conducted a successful end-of-Phase 2 meeting with the FDA for a future vaping indication.

About Cytisinicline
There are approximately 25 million adults in the United States 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. [6-7] 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.[7]

In addition, there are nearly 18 million adults in the United States who use e-cigarettes, also known as vaping.[1] In 2024, approximately 1.6 million middle and high school students in the United States reported using e-cigarettes.[8] There are no FDA-approved treatments indicated specifically as an aid to nicotine e-cigarette cessation. FDA has awarded the Commissioner's National Priority Voucher for e-cigarette or vaping cessation and 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 as a treatment of nicotine dependence for smoking cessation and has not been approved by the FDA 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 Achieve makes 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 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 law.

Achieve Contact
Nicole Jones
VP, Strategic Communications and Stakeholder Relations
ir@achievelifesciences.com
425-686-1510

References

1. National Center for Health Statistics. *National Health Interview Survey, 2023 and 2024*. 2026 (https://www.cdc.gov/nchs/nhis.htm).
2. 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.
3. Miller AD, Nonaka S. Mechanisms of vomiting induced by serotonin-3 receptor agonists in the cat: effect of vagotomy, splanchnicectomy or area postrema lesion. *J Pharmacol Exp Ther.* 1992;260:509-517.
4. Aubin HJ, Bobak A, Britton JR, *et al.* Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. *Thorax.* 2008;63:717-724.

5. Machu TK. Therapeutics of 5-HT3 receptor antagonists: current uses and future directions. *Pharmacol Ther.* 2011;130:338-347.
6. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2019. Geneva: World Health Organization, 2017.
7. U.S. Department of Health and Human Services. The Health Consequences of Smoking – 50 Years of Progress. A Report of the Surgeon General, 2014.
8. 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.

ACHIEVE
LIFE SCIENCES

Source: Achieve Life Sciences