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Achieve Life Sciences Reports Statistically Significant Smoking Cessation Benefit for Cytisinicline in Second, Confirmatory Phase 3 Clinical Trial

ORCA-3 demonstrated statistically significant topline results in primary and secondary smoking cessation endpoints for both 6- and 12-week cytisinicline treatment durations compared to placebo

Cytisinicline demonstrated 6x increase in odds of continuous smoking abstinence at 6 months

Cytisinicline treatment well tolerated with low rates of adverse events reported

Management to host conference call today, May 23 at 8:30AM EDT

SEATTLE and VANCOUVER, British Columbia, May 23, 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 announced positive topline results from the Phase 3 ORCA-3 trial of cytisinicline. Consistent with the previously reported Phase 3 ORCA-2 study, ORCA-3 showed a statistically significant benefit in helping people to quit smoking compared to placebo, with low rates of adverse events.

ORCA-3 was designed to evaluate the efficacy and safety of 3mg cytisinicline dosed 3 times daily for a period of 6 weeks or 12 weeks compared to placebo. ORCA-3 randomized 792 adult smokers at 20 clinical trial sites in the United States. All participants received standard behavioral support for the duration of the trial. The primary endpoint for ORCA-3 was biochemically verified smoking cessation measured during the last 4 weeks of treatment. Subjects were monitored for smoking cessation for 24 weeks post randomization.

Both the 6- and 12-week cytisinicline treatment durations demonstrated statistically significant smoking cessation on both the primary and secondary efficacy analyses compared to placebo.

12-Week Cytisinicline Efficacy Results

- Primary Endpoint: Subjects who received 12 weeks of cytisinicline treatment had 4.4 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p<0.0001$). The smoking cessation rate during weeks 9 through 12 was 30.3% for cytisinicline compared to 9.4% for placebo.
- Secondary Endpoint: The continuous smoking cessation rate from week 9 to week 24 was 20.5% for the 12-week cytisinicline arm compared to 4.2% for placebo, with an odds ratio of 5.79 ($p<0.0001$).

6-Week Cytisinicline Efficacy Results

- Primary Endpoint: Subjects who received 6 weeks of cytisinicline treatment had 2.85 times higher odds, or likelihood, to have quit smoking during the last 4 weeks of treatment compared to subjects who received placebo ($p=0.0008$). The smoking cessation rate during weeks 3 through 6 was 14.8% for cytisinicline compared to 6% for placebo.
- Secondary Endpoint: The continuous smoking cessation rate from week 3 to week 24 was 6.8% for the 6-week cytisinicline arm compared to 1.1% for placebo, with an odds ratio of 6.25 ($p=0.0006$).

ORCA-3 subjects had an average age of 53 years, smoked a median of 20 cigarettes per day at baseline, and had a median smoking history of 36 years with 4 prior quit attempts.

Similar to ORCA-2 findings, cytisinicline was well-tolerated with no treatment-related serious adverse events reported. The most commonly reported (>5% overall) adverse events for placebo, 6-week cytisinicline, and 12-week cytisinicline were:

- Insomnia: (7.6%, 11.0%, 11.9%)
- Abnormal dreams: (5.7%, 9.1%, 7.7%)
- Nausea (7.3%, 9.5%, 6.9%)
- Headache (6.1%, 7.6%, 8.5%)

“The ORCA-3 study findings add to a large body of evidence showing that cytisinicline appears to be a very well-tolerated and effective treatment compared to behavioral support alone for people who are dependent on cigarettes and want to quit,” said Dr. Omer Abid, Board Certified Addiction Medicine Physician & Medical Director of Insight Behavioral Health, Principal Investigator at Insight Research Institute, and ORCA-3 Investigator. “Cytisinicline gives hope for future smoking cessation success, given that there are limited available treatments, and many have tolerability limitations that lead to lack of compliance or adoption.”

The health consequences of smoking are widely known, yet the use of combustible nicotine cigarettes continues to be a global health issue. There are an estimated 28.3 million adults in the United States, and more than 1 billion people globally that currently smoke. Smoking remains the leading cause of preventable death and disease and claims the lives of an estimated 8 million people worldwide each year. If approved, cytisinicline could be the first new prescription treatment in nearly 20 years to help the millions of people who smoke to overcome nicotine dependence.

“Following the success of our previous clinical trials, and years of research, we are thrilled with the results from this second and confirmatory Phase 3 study of cytisinicline. With more than 2,000 clinical trial participants in our ORCA program to date, we are confident that cytisinicline has the potential to help the millions of people who are battling nicotine dependence,” said John Bencich, Chief Executive Officer of Achieve Life Sciences. “We would like to extend our gratitude to the ORCA-3 trial participants, the healthcare providers, and to everyone who continues to support Achieve’s mission of helping people live better and healthier lives. We are excited about the future and continuing our work with regulators with the aim of bringing cytisinicline to market.”

Conference Call Details
Achieve will host a conference call at 8:30 AM EDT today, Tuesday, May 23, 2023. To access the webcast and the accompanying data presentation, visit 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 13739070. A webcast replay will be available approximately two hours after the call and will be archived on the website for 90 days.

Further information on cytisinicline and Achieve Life Sciences can be found at www.achievelifesciences.com.

About ORCA-3
The Phase 3 ORCA-3 trial evaluated 792 adults who smoked cigarettes on a daily basis at 20 clinical trial locations in the United States. The trial was initiated in January 2022 and completed enrollment in September 2022, with topline results reported in May 2023. ORCA-3 participants received 3mg cytisinicline dosed 3 times daily for either 6 or 12 weeks and were monitored through 24 weeks post randomization. The trial was blinded, placebo-controlled, and all subjects received behavioral support for the duration of the trial. The primary endpoint was biochemically verified continuous abstinence during the last four weeks of treatment. Secondary outcome measures assessed continued abstinence rates through 6 months from the start of study treatment.

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 11 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, and the development and effectiveness of new treatments. 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 macroeconomic conditions, including inflation, rising interest rates, instability in the global banking sector, and public health crises, such as the COVID-19 pandemic 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, Jamal A, et al. Tobacco Product Use Among Adults — United States, 2021. MMWR Morb Mortal Wkly Rep 2023;72:475–483.

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Source: Achieve Life Sciences