April 27, 2022

Achieve Life Sciences Announces Successful, Statistically Significant Smoking Cessation Results in Phase 3 ORCA-2 Clinical Trial of Cytisinicline in Adult Smokers

Clinically robust and statistically significant results in primary and secondary endpoints for both 6- and 12-week cytisinicline treatment compared to placebo

Primary endpoints demonstrated 6-8x increased odds of smoking abstinence with cytisinicline compared to placebo

Cytisinicline was well tolerated with single-digit rates of adverse events observed

Management to host conference call today, April 27th at 8:30AM EST

SEATTLE and VANCOUVER, British Columbia, April 27, 2022 (GLOBE NEWSWIRE) -- Achieve Life Sciences, Inc. (NASDAQ: ACHV), today announced positive topline results from the Phase 3 ORCA-2 trial of cytisinicline. ORCA-2 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 in 810 adult smokers (randomized 1:1:1). Subjects were monitored for smoking abstinence for 24 weeks post randomization and received standard behavioral support for the duration of the trial.

The primary endpoints for ORCA-2 were biochemically verified continuous abstinence measured during the last 4 weeks of treatment. Both the 6- and 12-week cytisinicline treatments demonstrated significantly better quit rates than placebo with odds ratios of 8.0 and 6.3, respectively.

- Subjects who received 12 weeks of cytisinicline treatment had 6.3 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 abstinence rate during weeks 9-12

was 32.6% for cytisinicline compared to 7.0% for placebo.

- Subjects who received 6 weeks of cytisinicline treatment had 8 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 abstinence rate during weeks 3-6 was 25.3% for cytisinicline compared to 4.4% for placebo.

ORCA-2 participants were an average age of 54 years, smoked on average 20 cigarettes per day at baseline, and had a median smoking history of 38 years with 4 prior quit attempts.

“Cytisinicline demonstrated impressive efficacy for smoking cessation compared to placebo in this trial, the first large randomized clinical trial conducted in a U.S. population,” said Dr. Nancy Rigotti, Professor of Medicine at Harvard Medical School, and Principal Investigator of ORCA-2. “The trial is also notable as the first one to test the long-term efficacy of a new cytisinicline dosing schedule that has not previously been tested in a large population.”

The secondary endpoints measured continuous abstinence after treatment out to 24 weeks. Both the 6- and 12-week secondary endpoints demonstrated significantly better quit rates for cytisinicline treated subjects than placebo. The continuous abstinence rate from week 9 to 24 was 21.1% for the 12-week cytisinicline arm compared to 4.8% for placebo, with an odds ratio of 5.3 ($p<0.0001$). The continuous abstinence rate from week 3 to 24 was 8.9% for the 6-week cytisinicline arm compared to 2.6% for placebo, with an odds ratio of 3.7 ($p=0.0016$).

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: (4.8%, 8.6%, 9.6%)
- Abnormal dreams: (3.0%, 8.2%, 7.8%)
- Headaches (8.1%, 6.7%, 7.8%)
- Nausea (7.4%, 5.9%, 5.6%)

“These strongly positive results are extremely encouraging, and we are thrilled for the successful quitters, whom after decades of smoking and multiple attempts, were finally able to kick the habit thanks to cytisinicline and the ORCA-2 trial,” commented John Bencich, CEO of Achieve Life Sciences. “These data confirm that cytisinicline, if approved by the FDA, has the potential to become the first new agent approved in nearly two decades and an important treatment option for smoking cessation, which is much needed given the limitations, particularly the significant side effects associated with existing agents. We would like to thank the investigators, healthcare providers, and subjects whose commitment and efforts to ORCA-2 made this trial a success.”

In connection with the positive ORCA-2 trial results, the Company has also received approval from Silicon Valley Bank to access the remaining capital available under its $25.0 million debt facility put in place in December 2021. Per the terms of the agreement, the remaining $10.0 million of commitments are being made available to the Company through April 30, 2023. Amounts drawn under the remaining commitments will incur interest at the greater of 3.50% and the WSJ prime rate, and will be subject to interest only payments through April 30, 2024, and then amortize fully over the following 24 months. No amounts have been drawn at close and the Company will have the discretion to make draws under the facility through April 30, 2023. Additional terms of the agreement can be found within the company’s Form 8-K filing issued on April 27, 2022.

Additional information on cytisinicline and the ORCA program, including the ongoing Phase 3 ORCA-3 trial, can be found at www.achievelifesciences.com and www.orca-3.com.

Conference Call Details
Achieve will host a conference call at 8:30 a.m. Eastern time today, Wednesday, April 27, 2022. To access the webcast, log on to the investor relations page of the Achieve website at https://ir.achievelifesciences.com/news-events/ir-calendar. Alternatively, access to the live conference call is available by dialing (877) 472-9809 (U.S. & Canada) or (629) 228-0791 (International) and referencing conference 2558687. A webcast replay will be available approximately two hours after the call and will be archived on the website for 90 days.

About ORCA-2
The Phase 3 ORCA-2 trial evaluated the efficacy and safety of cytisinicline as a treatment for smoking cessation in 810 adult smokers at 17 clinical trial locations in the United States. Smokers were randomized to one-of-three treatment arms to receive either placebo or 3 mg cytisinicline taken three times daily for a period of either 6 or 12 weeks. Subjects were monitored for smoking abstinence for 24 weeks post randomization and received standard behavioral support for the duration of the trial. ORCA-2 is the first randomized Phase 3 clinical trial to show a smoking cessation benefit and potential for a new FDA-approved treatment option in nearly two decades.

About Achieve and 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] Achieve's focus is to address the global smoking health and nicotine addiction epidemic through the development and commercialization of cytisinicline.

Cytisinicline is a plant-based alkaloid with a high binding affinity to the nicotinic acetylcholine receptor. It is believed to aid in smoking cessation by interacting with nicotine receptors in the brain by reducing the severity of nicotine withdrawal symptoms and by reducing the reward and satisfaction associated with smoking.

Cytisinicline is an investigational product candidate being developed for treatment of nicotine addiction and has not been approved by the Food and Drug Administration for any indication in the United States. For more information on cytisinicline and Achieve visit www.achievelifesciences.com.

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, the development and effectiveness of new treatments, and the intention to submit cytisinicline to the FDA for approval. 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 the Russian military action in Ukraine; risks related to the impact on our business of the COVID-19 pandemic or similar public health crises 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] World Health Organization. WHO Report on the Global Tobacco Epidemic, 2019. Geneva: World Health Organization, 2017.

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

A video accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/73205edb-b9f7-4299-b087-d35df52e88fb

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