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# Achieve Life Sciences Announces Completion of Maximum Tolerated Dose Study

SEATTLE and VANCOUVER, British Columbia, Sept. 30, 2019 /PRNewswire/ -- Achieve Life Sciences, Inc. (Nasdaq: ACHV), a clinical-stage pharmaceutical company committed to the global development and commercialization of cytisinicline for smoking cessation, today announced completion of their maximum tolerated dose (MTD) study. The results indicate a lack of dose-limiting toxicity as defined by protocol criteria even at the highest 30 mg single, oral dose of cytisinicline evaluated in the study.

This study, initiated in March 2019, is required by the FDA as part of a New Drug Application (NDA) for marketing approval in the United States. It was designed to determine dose-limiting adverse events (AEs) and to define the maximum tolerated dose for a single, oral dose of cytisinicline.

An independent Data Safety Monitoring Committee (DSMC) composed of the Study Investigator and two independent physicians evaluated all safety outcomes before each dose escalation. Stopping criteria for further dose escalation was defined as the occurrence of severe or serious AEs or any other safety information considered as a concern.

The starting dose was 6 mg, which increased in 3 mg increments up to 21 mg. When the MTD was not reached at 21 mg, the study was amended to evaluate doses up to 30 mg. At this dose, the stopping criteria of serious or severe AEs were still not met, but the DSMC recommended stopping the study. The results will be reviewed with the FDA to determine if further escalation beyond 30 mg will be required.

"Cytisinicline continues to demonstrate an impressive safety profile, as seen in this study and in our recently announced Phase 2b ORCA-1 trial in smokers," stated Dr. Cindy Jacobs, Chief Medical Officer of Achieve. "Side effects are often a key limitation to existing smoking cessation treatments and we believe cytisinicline continues to offer an improved tolerability profile, compared to currently available medications."

The MTD has not been previously defined for cytisinicline. These results do not impact the intended 3 mg, 3 times daily dosing planned for future Phase 3 cytisinicline clinical trials, but rather demonstrate the lack of dose-limiting toxicity at doses up to 10 times higher than the planned 3 mg dose.

Additional information on cytisinicline can be found at www.achievelifesciences.com and www.orcaprogram.com

**About Cytisinicline**

Tobacco use is currently the leading cause of preventable death and is responsible for nearly seven million deaths annually worldwide[1]. It is estimated that 28.7% of cancer deaths in the U.S. are attributable to cigarette smoking[2]. Achieve's focus is to address the global smoking health 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.

As an approved, branded product in Central and Eastern Europe for more than two decades, it is estimated that over 20 million people have used cytisinicline to help combat nicotine addiction.

**About Cytisinicline MTD Study**

The MTD study was a single-center, randomized, placebo-controlled, single dose-escalation, Phase 1 clinical study in adult smokers. The starting dose was 6 mg, which increased in 3 mg increments up to 21 mg. Following the absence of dose-limiting adverse events at 21 mg, the study was amended to evaluate doses up to 30 mg of cytisinicline, as the highest dose level of cytisinicline to be evaluated.

An independent Data Safety Monitoring Committee (DSMC) composed of the Study Investigator and two independent physicians having expertise in treating smoking cessation evaluated all safety outcomes before each dose escalation. Stopping criteria for further dose escalation was defined as any one of the following occurring: severe or serious adverse events or any other safety information considered as a concern. Pharmacokinetic parameters were also assessed at each dose level.

While the stopping criteria of serious or severe adverse events were not met at the 30 mg dose, the DSMC indicated the frequency of gastrointestinal symptoms were approaching a maximum tolerated dose. Additionally, by the final dosing cohort, the pharmacokinetic results showed a progressive reduction in any increase in the maximum blood concentrations ($C_{max}$) levels, with evidence that the $C_{max}$ was approaching, or had reached, a plateau.

**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 planned cytisinicline clinical development activities, the timing of clinical development activities related to cytisinicline, the potential market size for cytisinicline and the potential benefits 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 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; 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 law.

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[1]World Health Organization. WHO Report on the Global Tobacco Epidemic, 2017. Geneva: World Health Organization, 2017

[2] Annals of Epidemiology , Volume 25 , Issue 3 , 179 - 182.e1

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