Agile Therapeutics Provides Clinical Update on Twirla and Status of Pipeline Evaluation

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FDA Agrees to Extended Milestones for Long-Term Twirla® Safety Study

New Publication Supports Eventual Pursuit of AG200-15 Extended Regimen Development Program

PRINCETON, N.J., Feb. 01, 2023 (GLOBE NEWSWIRE) -- Agile Therapeutics, Inc. (Nasdaq: AGRX), a women's healthcare company, today provided an update on the Twirla® post-marketing studies and status of its ongoing evaluation of the Company's pipeline.

Twirla Post-Marketing Studies

As part of Twirla's approval, the United States Food and Drug Administration (FDA) required the Company to conduct a long-term prospective, multi-center clinical post-marketing requirement study (PMR) comparing the risks of venous thromboembolism (VTE) and arterial thromboembolism (ATE) in new users of Twirla to new users of combined hormonal contraceptives (CHCs) and Ortho Evra generic patches. In January 2023, the FDA agreed with the Company's proposal to address this PMR using electronic health records (EHR) and insurance claims from a large database from multiple healthcare systems. The FDA also agreed to extend the study timelines. Under these new milestones, interim safety data reporting to the FDA is due in November 2029, and the final PMR study report is scheduled to be submitted to the FDA in November 2035.

"We are pleased that our close collaboration with the FDA resulted in agreement on an appropriate and feasible study design to collect important VTE and ATE data for Twirla, CHCs, and Ortho Evra generics" said Paul Korner, MD, MBA, FACOG, Agile Therapeutics' Chief Medical Officer.

Upon Twirla's approval, Agile also agreed to an FDA-requested post-marketing commitment study to assess the residual drug content and strength of Twirla (PMC). The final PMC study report was submitted to the FDA in June 2022, and the Company continues to discuss the results with the FDA.

Status of Pipeline Evaluation

As previously disclosed, all work on Agile's pipeline has been halted since 2021 as the Company concentrates its efforts the commercialization of Twirla. Commercializing Twirla remains the Company's primary focus into 2023; however, the Company has continued to evaluate the potential eventual advancement of the AG200-15 Extended Regimen and the progestin-only patch.

"Our primary focus since the launch of Twirla has been the commercial growth of Twirla. We believe, however, that we have potential value in our pipeline and have been evaluating how to prioritize the eventual development of our product candidates. While we do not currently expect to invest significant funds in our pipeline in 2023 as we continue to focus on maintaining capital efficiency and keeping tight control on our operating expenses, we have been using creative approaches to advance the evaluation of our pipeline and prepare for a time when we can move forward," stated, Al Altomari, Chairman and Chief Executive Officer of Agile Therapeutics.

As part of its evaluation of the AG200-15 Extended Regimen, Agile performed an analysis with a simulated pharmacokinetic (PK) model that was used to predict the systemic levonorgestrel (LNG) and ethinyl estradiol (EE) exposure of Twirla (AG200-15) if used for twelve (12) consecutive weeks.[1] Data from a previously published clinical phase 1, open-label, randomized clinical trial[2] was used for the PK model simulation, which included 36 healthy individuals who used a standard Twirla regimen for three consecutive weeks. The 12-week Extended Regimen provided similar systemic hormonal exposure as that seen by week 3 in the approved 28-day regimen. The results of the analysis were published on December 27, 2022 and are available electronically in the online journal, PLOS ONE.

Prior to halting development work, in the fourth quarter of 2021 Agile also had completed formulation selection and conducted early pre-clinical work of its novel progestin-only transdermal system. The progestin-only patch uses the same Skinfusion® patch technology and manufacturing processes as Twirla.

Dr. Korner stated, "we believe the modeling data in the new publication are encouraging for the eventual development of the potential AG200-15 Extended Regimen concept, currently in development, and support our expectation that the Extended Regimen will perform similarly to the approved product." He continued, "we are also excited about our progestin-only patch, and believe it would be an attractive option for many women seeking effective, non-daily contraception without estrogen exposure. We continue to explore our plan to develop this program and are considering all of our potential pathways, including a co-development and co-funding partnership to advance this program into the clinic."

About Agile Therapeutics, Inc.
Agile Therapeutics is a women's healthcare company dedicated to fulfilling the unmet health needs of today's women. Our product and product candidates are designed to provide women with contraceptive options that offer freedom from taking a daily pill, without committing to a longer-acting method. Our initial product, Twirla®, (levonorgestrel and ethinyl estradiol) transdermal system, is a non-daily prescription contraceptive. Twirla is based on our proprietary transdermal patch technology, called Skinfusion®, which is designed to allow drug delivery through the skin. For more information, please visit the company website at **www.agiletherapeutics.com**. The Company may occasionally disseminate material, nonpublic information on the Company's website, Twitter account (@agilether), and LinkedIn account.

About Twirla®

Twirla (levonorgestrel and ethinyl estradiol) transdermal system is a once-weekly combined hormonal contraceptive (CHC) patch that contains the active ingredients levonorgestrel (LNG), a type of progestin, and ethinyl estradiol (EE), a type of estrogen. Twirla is indicated for use as a method of contraception by women of reproductive potential with a body mass index (BMI) < 30 kg/m^2 for whom a combined hormonal contraceptive is appropriate. Healthcare providers (HCPs) are encouraged to consider Twirla's reduced efficacy in women with a BMI ≥ 25 to <30 kg/m^2 before prescribing. Twirla is contraindicated in women with a BMI ≥ 30 kg/m^2. Twirla is also contraindicated in women over 35 years old who smoke.

Cigarette smoking increases the risk of serious cardiovascular events from CHC use. Twirla is designed to be applied once weekly for three weeks, followed by a week without a patch.

Forward-Looking Statements

Certain information contained in this press release includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We may in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties, including our expectations regarding the performance of our pipeline candidates in the clinical setting, statements regarding our ongoing and planned manufacturing and commercialization of Twirla®, the attractiveness of our pipeline candidates to potential investors, the potential regulatory approval of our pipeline candidates, our ability to meet the timelines agreed to with the FDA for our PMR study, the outcome of our discussions with FDA regarding the results of our PMC study, our future plans with respect to additional commercial products, our ability to become cash flow positive, our prospects for future financing arrangements, and our financial condition, growth and strategies. Any or all of the forward-looking statements may turn out to be wrong or be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. These forward-looking statements are subject to risks and uncertainties including risks related to our ability to resume development of our pipeline products, including potentially finding interested partners to co-fund product development, our ability to successfully complete our PMR study, our ability to gain regulatory approval of our pipeline candidates and the labeling under any approval we obtain, regulatory and legislative developments in the United States and foreign countries, our ability to obtain and maintain intellectual property protection for Twirla and our product candidates, the effects of the ongoing COVID-19 pandemic on our commercialization efforts, clinical trials, supply chain, operations and the operations of third parties we rely on for services such as manufacturing, marketing support and sales support, as well as on our potential customer base, our ability to regain compliance with the listing requirements of the Nasdaq Capital Market and the other risks set forth in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. For all these reasons, actual results and developments could be materially different from those expressed in or implied by our forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this press release. We undertake no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

1. Stanczyk FZ, Archer DF, Lohmer LR, Pirone J, Previtera M, Korner P. Extended regimen of a levonorgestrel/ethinyl estradiol transdermal delivery system: predicted serum hormone levels using a population pharmacokinetic model. *PLOS ONE*. Published online December 27, 2022. https://doi.org/10.1371/journal.pone.0279640.

2. Archer DF, Stanczyk FZ, Rubin A, Foegh M. Ethinyl estradiol and levonorgestrel pharmacokinetics with a low-dose transdermal contraceptive delivery system, AG200-15: a randomized controlled trial. Contraception 2012; 85:595–601.

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