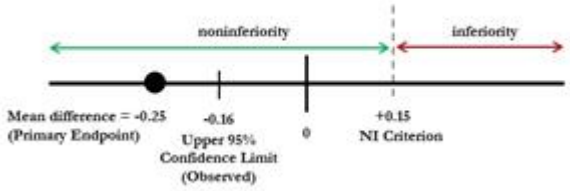
Agile Therapeutics, Inc. Announces that Twirla® Meets Primary Endpoint in Comparative Wear Study and Demonstrates Non-Inferior Adhesion to Xulane®

February 11, 2019

Company now focused on completing plan to resubmit NDA in first half of 2019



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PRINCETON, N.J., Feb. 11, 2019 (GLOBE NEWSWIRE) -- Agile Therapeutics, Inc., (Nasdaq: AGRX), a women's healthcare company, today announced topline results from a comparative wear study testing the adhesion of Twirla® compared to that of Xulane® (the "comparative wear study"), the generic version of the previously marketed Ortho Evra® contraceptive patch, a product the U.S. Food and Drug Administration ("FDA") considers to have acceptable adhesion. In the study, Twirla met its primary endpoint and demonstrated non-inferior adhesion to Xulane.

The Company conducted the comparative wear study as part of its plan to implement the recommendations of the FDA's Office of New Drugs ("OND") that were delivered to the Company in OND's formal dispute resolution decision letter. OND recommended that the Company complete a comparative wear study as part of a potential path forward for seeking regulatory approval of the Twirla NDA.

The comparative wear study design follows the 2018 ANDA Guidance for Assessment of Adhesion entitled *Assessing Adhesion With Transdermal and Topical Delivery Systems for ANDAs*. The study was a randomized, open-label, crossover adhesion study in healthy women aged 18 to 35 years with a Body Mass Index of less than 35 kg/m^2. Subjects were randomized to wear either Twirla or Xulane for the first week and then switched to the patch not initially worn for the second week. Eighty-three subjects were randomized; 79 subjects completed the study, and 77 subjects were included in the Per Protocol population used in the primary analysis. Investigators assessed patch adhesion for each day of wear and assigned the patch a daily score ranging from 0 (essentially no patch lift off skin) to 4 (complete patch detachment).

The primary endpoint for the study was the mean difference in adhesion scores between Twirla and Xulane. As agreed upon at the December 2018 Type A meeting with the FDA's Division of Bone, Reproductive, and Urologic Products ("DBRUP"), Twirla was to be considered statistically non-inferior to Xulane if the upper 95% confidence limit of the mean difference was less than +0.15. The study met this non-inferiority criterion by demonstrating a mean difference of -0.25 and upper 95% confidence limit of -0.16. **(See Table 1).**

Table 1. Primary endpoint: mean adhesion scores for Twirla and Xulane

	Twirla		*Xulane*		*Difference (Twirla – Xulane)*		
	N	*Mean (SD)*	*N*	*Mean (SD)*	*Mean (SD)*	*One-sided upper 95% CL*	*Non-inferiority criterion met*
Adhesion score in the Per Protocol population	77	0.14 (0.28)	77	0.39 (0.40)	-0.25 (0.23)	-0.16	Yes

Table 1 shows the results for the primary endpoint: the mean difference in adhesion scores between Twirla and Xulane. The mean difference in Twirla minus Xulane is -0.25. The mean adhesion score for Xulane is higher than the mean score for Twirla, producing a negative mean difference. The upper bound of the 95% confidence limit for the mean difference is -0.16, thus Twirla met the non-inferiority criterion of +0.15. **(See Figure 1).**

Figure 1. Non-inferiority (NI) scale

A graphic accompanying this announcement is available at http://www.globenewswire.com/NewsRoom/AttachmentNg/eb520acd-e1fe-4038-8798-fce04909d5c0.

No complete detachments of Twirla or Xulane occurred during the trial. The final study report, when complete, will contain additional analyses

pertaining to secondary endpoints and safety data.

“We believe that the topline data from our comparative wear study provide important insights into the adhesion performance of Twirla that we can share with the FDA to support that Twirla demonstrates adequate *in vivo* adhesion. While the results from the study will need to be reviewed by the FDA as part of our planned NDA resubmission, we are very pleased with the results,” said Dr. Elizabeth Garner, Senior Vice-President and Chief Medical Officer of Agile. “We greatly appreciate the hard work and dedication from our clinical team and wish to thank the research professionals and staff at TKL Research, and most importantly, the women who participated in the trial.”

The Company plans to include the results of the comparative wear study along with additional information relating to the manufacture of Twirla in its response to the Complete Response Letter (“CRL”) it received in December 2017. The FDA has previously informed the Company that in connection with its review of the Twirla NDA, the FDA plans to bring the safety and efficacy of Twirla to an Advisory Committee. The Company also expects that the FDA will conduct a pre-approval inspection of the Company’s third-party manufacturer’s facility, which must be successfully completed prior to approval.

“We believe that the topline results from the comparative wear study enable us to respond to the *in vivo* adhesion questions raised by the FDA in the December 2017 CRL and in subsequent communications,” said Al Altomari, Chairman and Chief Executive Office of Agile. Mr. Altomari continued, “We are now focused on completing our plan to resubmit our Twirla NDA in the first half of 2019, which we believe will position us to receive a PDUFA date before the end of the year.”

About Twirla® (AG200-15)
Twirla (levonorgestrel/ethinyl estradiol transdermal system) or AG200-15 is an investigational low-dose, once-weekly contraceptive patch. AG200-15 is a combined hormonal contraceptive (“CHC”) patch that contains the active ingredients ethinyl estradiol (EE), a type of estrogen and levonorgestrel (“LNG”), a type of progestin. Twirla is designed to be applied once weekly for three weeks, followed by a week without a patch. The Company has completed its Phase 3 clinical trials of Twirla and is pursuing regulatory approval in the U.S. Agile received a complete response letter (“CRL”) from the FDA in December 2017 relating to the New Drug Application (“NDA”) for Twirla. In the CRL, the FDA informed the Company that the product could not be approved in its present form due to deficiencies related to, among other things, the *in vivo* adhesion properties of Twirla and their potential relationship to the Company’s Phase 3 clinical trial results. With the successful completion of the comparative wear study, the Company plans to resubmit the Twirla NDA in the first half of 2019.

About Agile Therapeutics, Inc.
Agile Therapeutics is a forward-thinking women's healthcare company dedicated to fulfilling the unmet health needs of today's women. Our 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 lead product candidate, Twirla® (levonorgestrel/ethinyl estradiol transdermal system), also known as AG200-15, is an investigational low-dose, 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.

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Xulane® is a registered trademark of Mylan N.V., and Ortho Evra® is a registered trademark of Johnson & Johnson.

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, related to our regulatory submissions. 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 statements regarding our belief that a reformulation of Twirla may not be necessary. 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 manage costs and execute on our operational and budget plans, the FDA requiring us to reformulate Twirla, our ability to develop a reformulation that will address the FDA’s concerns, including showing bioequivalence, if necessary, that the results of the comparative wear study do not support a conclusion by the FDA that Twirla has demonstrated adequate adhesion, the potential that we may be required to conduct an additional Phase 3 trial, the likelihood that we will require additional correspondence with the FDA prior to the resubmission of our NDA, our third-party manufacturer’s ability to successfully complete a pre-approval inspection, our ability to resubmit and the timing of our resubmission of the NDA for Twirla, FDA acceptance and approval of the resubmitted NDA, or whether other issues will arise that will negatively impact acceptance, review, and approval of Twirla by the FDA, including a determination by the Advisory Committee that Twirla should not be approved, our ability to address the deficiencies identified by the FDA in the CRL issued in December 2017 and in subsequent communications with the FDA, the fact that our existing cash and cash equivalents may not be sufficient to fund the completion of the development and regulatory review process for Twirla, our ability to raise capital when needed to complete the development and regulatory review process for Twirla, and unforeseen market factors or events in our clinical and manufacturing development plans 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.

SOURCE: Agile Therapeutics, Inc.

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