Entasis Therapeutics Announces Zoliflodacin Phase 2 Results Published in The New England Journal of Medicine

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Zoliflodacin Was Well-Tolerated and Successfully Treated Substantially All Uncomplicated Gonorrhea Cases

Phase 3 clinical trial, in partnership with GARDP, to begin in 2019

WALTHAM, Mass., Nov. 07, 2018 (GLOBE NEWSWIRE) -- Entasis Therapeutics (NASDAQ: ETTX), a clinical-stage biopharmaceutical company focused on the discovery and development of novel antibacterial products, announced that *The New England journal of Medicine* (NEJM) published results from a Phase 2 clinical trial evaluating the safety and efficacy of zoliflodacin in patients with uncomplicated gonorrhea. Zoliflodacin represents a new type of oral antibiotic that inhibits DNA synthesis in a manner different from currently approved classes of antibiotic drugs. The clinical trial was sponsored by The National Institute of Allergy and Infectious Disease (NIAID), part of the U.S. National Institutes of Health (NIH).

Gonorrhea is a common sexually transmitted disease (STD) that affects both men and women, particularly young people ages 15 to 24 years. Gonorrhea is the second most commonly reported notifiable disease in the United States. In 2017, more than 550,000 cases of gonorrhea were reported in the United States. If untreated, gonorrhea infection can lead to pelvic inflammatory disease, ectopic pregnancy, infertility, and an increased risk of HIV infection. Pregnant women can pass the infection to their babies, who can become blind or develop life-threatening infections as a result.

Gonorrhea is caused by the bacterium *Neisseria gonorrhoeae*, which has progressively developed resistance to each of the antimicrobials used to treat it. As a result, in 2015, the U.S. Centers for Disease Control and Prevention revised gonorrhea treatment guidelines to recommend dual therapy with injectable ceftriaxone and oral azithromycin to reduce the emergence of resistance to ceftriaxone.

“The rate of reported gonorrhea cases in the United States has increased 75 percent since the historic low in 2009, and antibiotic resistance has considerably reduced the number of treatment options for this disease,” said NIAID Director Anthony S. Fauci, M.D. “These research findings published today suggest that zoliflodacin has the potential to be a useful and easy-to-administer oral antibiotic for treating gonorrhea.”

The study took place from November 2014 through December 2015 and was a multi-center, randomized, open-label study that enrolled 179 participants (167 men, and 12 non-pregnant women) between the ages of 18 to 55 with either symptoms of uncomplicated urogenital gonorrhea, untreated urogenital gonorrhea or sexual contact with someone with gonorrhea within 14 days before enrollment. Participants were randomly selected to receive either a single 2- or 3-gram dose of oral zoliflodacin or a 500 milligram (mg) dose of injectable ceftriaxone. Among the 117 per-protocol participants who were evaluated six days after treatment, 98 percent (48 of 49 participants) of those who received the 2-gram zoliflodacin dose, 100 percent (47 of 47 participants) of those who received the 3-gram dose, and all (21 of 21) of the participants in the ceftriaxone group were considered cured of their urogenital gonorrhea based on culture results.

Zoliflodacin cured all rectal gonorrheal infections (5 of 5 participants who received the 2-gram dose; 7 of 7 participants who received the 3-gram dose) as did ceftriaxone (3 of 3 participants). In treating patients with gonorrhea infections of the throat (pharyngeal), 50 percent of volunteers who received the 2-gram dose (4 of 8 participants) and 82 percent of those who received the 3-gram dose (9 of 11 participants) were cured. All of the participants (4 of 4) in the ceftriaxone group achieved a cure. Zoliflodacin was generally well-tolerated with transient gastrointestinal upset the most commonly reported adverse effect. Microbiological evaluation of post-treatment clinical isolates did not show any resistance to zoliflodacin.

“We are grateful for the work done by the NIAID and pleased to have data on zoliflodacin published in the New England Journal of Medicine,” stated Manos Perros, President and Chief Executive Officer of Entasis Therapeutics. “The results highlighted in the NEJM’s publication provide support for the therapeutic potential of zoliflodacin in gonococcal infections and we look forward to advancing our Phase 3 clinical trial.”

Zoliflodacin has received Fast Track designation and qualified infectious disease product (QIDP) designation by the U.S. Food and Drug Administration (FDA) for development solely as oral treatment for gonococcal infections. Entasis, in partnership with GARDP, will begin Phase 3 testing of zoliflodacin in the Netherlands, South Africa, Thailand and the United States next year.

About Zoliflodacin

Zoliflodacin is a novel oral antibiotic for the treatment of uncomplicated gonorrhea and the first of a novel class of molecules to be developed for this indication. Uncomplicated gonorrhea is becoming increasingly difficult to treat as the *Neisseria gonorrhoeae* bacterium has developed resistance to successive classes of antibiotics. There are currently few oral treatment options, and the Centers for Disease Control and Prevention (CDC) has designated *N. gonorrhoeae* an urgent public health threat that requires aggressive action. *N. gonorrhoeae* has developed resistance to all classes of antimicrobials previously recommended for treatment of uncomplicated gonorrhea. As a result, the CDC treatment guidelines require dual therapy with injectable ceftriaxone and oral azithromycin.

Uncomplicated gonorrhea infections carry high morbidity, enhance transmission of other sexually transmitted diseases and are highly stigmatized. Published studies have demonstrated the potent *in vitro* activity of zoliflodacin against *N. gonorrhoeae*, including isolates resistant to fluoroquinolones and extended spectrum cephalosporins. Zoliflodacin received Fast Track designation and qualified infectious disease product (QIDP) designation by the U.S. Food and Drug Administration (FDA).

About Entasis

Entasis Therapeutics is developing a portfolio of innovative product candidates to treat serious Gram-negative multi-drug resistant bacterial infections. Entasis’ anti-infective discovery platform has produced a pipeline of meaningfully differentiated programs which target serious bacterial infections, including ETX2514SUL (targeting *Acinetobacter baumannii* infections), zoliflodacin (targeting *Neisseria gonorrhoeae*), ETX0282CPDP (targeting

Enterobacteriaceae infections), and non-Beta-lactam PBP inhibitors or NBPs (targeting Gram-negative infections). www.entasistx.com

About the National Institutes of Health (NIH)
NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

About The National Institute of Allergy and Infectious Diseases (NIAID)
The NIAID conducts and supports research—at NIH, throughout the United States, and worldwide—to study the causes of infectious and immune-mediated diseases, and to develop better means of preventing, diagnosing and treating these illnesses. News releases, fact sheets and other NIAID-related materials are available on the NIAID website.

About GARDP
GARDP is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavoring to ensure their sustainable access. Initiated by the World Health Organization (WHO) and the Drugs for Neglected Disease *initiative* (DND*i*), GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage research and development of new antimicrobial agents and diagnostics. GARDP is currently hosted by DNDi. www.gardp.org

Forward-Looking Statements
This press release includes certain disclosures which contain "forward-looking statements," including, without limitation, statements regarding potential attributes and benefits of zoliflodacin and Entasis' expectations regarding a planned Phase 3 trial. Forward-looking statements are based on Entasis' current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, unexpected safety or efficacy data observed during preclinical or clinical trials, clinical trial site activation or enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, failure of the Company's collaborators to support or advance collaborations or product candidates and unexpected litigation or other disputes. Many of these factors are beyond Entasis' control. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the final prospectus related to Entasis' initial public offering filed with the Securities and Exchange Commission. Forward-looking statements contained in this announcement are made as of this date, and except as required by law, Entasis assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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