Entasis Therapeutics Introduces ETX0462, a First-in-Class Candidate, Targeting Multidrug-Resistant Gram-Negative and Biothreat Pathogens

July 1, 2021

WALTHAM, Mass., July 01, 2021 (GLOBE NEWSWIRE) -- Entasis Therapeutics Holdings Inc. (NASDAQ: ETTX), a clinical-stage biopharmaceutical company focused on the discovery and development of novel antibacterial products, today announced the presentation of preclinical data on ETX0462, a novel, first-in-class, diazabicyclooctane with antimicrobial activity against multidrug-resistant (MDR) Gram-negative and biothreat pathogens, at the 2021 World Microbe Forum. ETX0462 potentially represents the first new antibiotic class in 35 years to treat MDR Gram-negative and biothreat infections.

At the World Microbe Forum, Entasis scientists presented their approach to the discovery of ETX0462 that incorporated Structure-Porin Permeation Relationships and Structure-Based Drug Design to identify key principles for penicillin-binding protein (PBP) inhibition and corresponding antimicrobial activity against contemporary MDR Gram-negative and biothreat isolates, including *P. aeruginosa, K. pneumoniae, S. maltophilia, E. coli, B. anthracis, Y. pestis, F. tularensis and Burkholderia* spp. Entasis scientists further demonstrated that the activity of ETX0462 was unaffected by all four Ambler classes of β-lactamases and has a low propensity for resistance emergence due to its ability to permeate bacterial cells through multiple porins and inhibit several PBPs.

“ETX0462 is the latest product candidate to emerge from our discovery platform and the first example of a novel class of agents targeting the established mechanism of β-lactam antibiotics without being susceptible to the most common β-lactam resistance mechanism, β-lactamases,” commented Ruben Tommasi, Chief Scientific Officer at Entasis. “We look forward to continuing our successful collaboration with CARB-X as we progress ETX0462 towards the clinic.”

In *in vivo* studies, ETX0462 exhibited robust bactericidal activity reaching >3-log drop in bacterial count vs. initial inoculum in a neutropenic murine lung model against clinical isolates of *P. aeruginosa*. Similar *in vivo* efficacy was also demonstrated for the biothreat pathogens *Y. pestis* and *B. pseudomallei*. Entasis also shared that the PK/PD index of ETX0462 is driven by % Time > MIC and a ~60% target for 1-log bactericidal activity. Entasis demonstrated that ETX0462 was well tolerated in a rat 14-day GLP toxicology study reaching the limit dose of 2,000 mg/kg.

Additional details of the ETX0462 data presented can be found on the Entasis Presentations webpage.

About Entasis Therapeutics Inc.
Entasis is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel antibacterial products to treat serious infections caused by multidrug-resistant Gram-negative bacteria. Entasis’ pathogen-targeted design platform has produced a pipeline of product candidates, including SUL-DUR (targeting *Acinetobacter baumannii* infections), zoliflodacin (targeting *Neisseria gonorrhoeae* infections), ETX0282CPDP (targeting Enterobacterales infections) and ETX0462 (targeting *Pseudomonas* infections). For more information, visit www.entasistx.com.

About ETX0462
ETX0462 is a novel, first-in-class, diazabicyclooctane with antimicrobial activity against multidrug-resistant (MDR) Gram-negative and biothreat pathogens including, *P. aeruginosa, K. pneumoniae, S. maltophilia, E. coli, B. anthracis, Y. pestis, F. tularensis and Burkholderia spp*. Similar to β-lactam antibiotics, ETX0462 inhibits penicillin-binding proteins which are essential for bacterial cell wall biosynthesis, however, unlike β-lactam antibiotics, ETX0462 is unaffected by β-lactamase mediated resistance. ETX0462 is supported by CARB-X.

Company Contact	**Investor Contact**
Kyle Dow	Bruce Mackle
Entasis Therapeutics	LifeSci Advisors
(781) 810-0114	(929) 469-3859
kyle.dow@entasistx.com	bmackle@lifesciadvisors.com

Source: Entasis Therapeutics Holdings Inc.