# Entasis Publishes Data Highlighting the Potent and Differentiated Activity of ETX2514 Combinations against Drug Resistant Gram-negative Bacteria Including Acinetobacter and Pseudomonas

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*Report in Nature Microbiology Describes Entasis' Rational Design of a Next-generation Beta-Lactamase Inhibitor with an Expanded Spectrum of Beta-Lactamase Activity*

**WALTHAM, Mass. – June 30, 2017** – Entasis Therapeutics, a leader in the discovery and development of breakthrough anti-infective products, published a report in Nature Microbiology (DOI: 10.1038/nmicrobiol.2017.104) in which Entasis scientists describe the rational design and expanded spectrum activity of ETX2514 against Class A, C, and a broad spectrum of Class D beta-lactamases, important targets in the treatment of resistant bacteria.

"With the ever-growing number and diversity of beta-lactamases, novel beta-lactamase inhibitors (BLI) with an expanded spectrum of activity are urgently needed," said Ruben Tommasi, Ph.D., CSO at Entasis. "Our proprietary discovery platform was successfully used to discover ETX2514, which achieves unprecedented potency against an expanded spectrum of beta-lactamases beyond the capabilities of BLIs marketed today."

The report includes the results of in vitro and preclinical in vivo studies, which demonstrate the ability of ETX2514 to restore antimicrobial activity in combination with multiple beta-lactams against Gram-negative, multi-drug resistant (MDR) pathogens. ETX2514 exhibited particularly promising activity in combination with sulbactam against Acinetobacter baumannii, including hard-to-treat carbapenem-resistant and colistin-resistant strains, and with imipenem against carbapenem-resistant Enterobacteriaceae (CRE) and Pseudomonas aeruginosa. The ability of ETX2514 to be administered concurrently with sulbactam and/or imipenem is currently being investigated in a Phase 1 clinical trial.

"More than half of A. baumannii isolates are multi-drug resistant or extensively drug resistant, and resistance in A. baumannii and P. aeruginosa to even the last-resort agents, such as colistin, is on the rise," said Andrew Shorr, M.D., M.P.H., Director of Pulmonary and Critical Care, Washington Hospital Center. "We urgently need new agents targeting these difficult to treat infections. I look forward to seeing the results of ETX2514's Phase 1 study later this year."

MDR infections are a serious threat to public health. The increasing diversity of beta-lactamases, enzymes produced by Gram-negative bacteria that inactivate beta-lactam antibiotics, a class of antibiotics that has been a therapeutic mainstay for decades, are among the most important drivers of antibiotic resistance. Beta-lactamases are classified into four classes (A, B, C and D). BLIs recently launched or in late-stage development inhibit many class A and C beta-lactamases, but only a few are active and even those only inhibit a limited spectrum of class D enzymes. A. baumannii infections are particularly challenging to treat due to the wide variety of class D beta-lactamases expressed by this organism. ETX2514, because of its broad coverage of class D beta-lactamases, has the potential to help address the unmet medical need of MDR A. baumannii. The World Health Organization ranked carbapenem-resistant A. baumannii first in their global priority list of MDR pathogens currently threatening human health.

**About ETX2514**

ETX2514 is a potent and broad spectrum inhibitor of class A, C, and D beta-lactamases. ETX2514 restores the *in vitro* activity of multiple beta-lactams against Gram-negative, multi-drug resistant (MDR) pathogens. Entasis Therapeutics is developing ETX2514SUL, the combination of ETX2514 and sulbactam, for the treatment of severe *A. baumannii* infections. *A. baumannii* is a Gram-negative bacterium that causes severe infections which are associated with high mortality rates. *A. baumannii* infections are frequently multi-drug resistant and there is an urgent need to identify new safe and effective agents to treat affected patients. Sulbactam is a generic beta-lactam which has intrinsic activity against *A. baumannii* but suffers from widespread beta-lactamase-mediated resistance. In preclinical studies, ETX2514 restores sulbactam's antimicrobial activity against *A. baumannii.*ETX2514 is currently in Phase 1 clinical trials.

**About Entasis Therapeutics Inc.**

Entasis Therapeutics is developing a portfolio of innovative cures for serious drug-resistant bacterial infections, a global health crisis affecting the lives of millions of patients. Entasis' anti-infective discovery platform has produced a pipeline of meaningfully differentiated programs which target serious bacterial infections,including ETX2514SUL (targeting infections caused by *Acinetobacter baumannii* infections), ETX0282CPDP (targeting Enterobacteriaceae infections), and zoliflodacin (targeting the treatment of *Neisseria gonorrhoeae* infections). www.entasistx.com

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