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Venatorx Pharmaceuticals Announces Positive Results for Phase 3 Clinical Trial (CERTAIN-1) of Cefepime-Taniborbactam for Treatment of cUTI

Cefepime-taniborbactam met the primary noninferiority efficacy endpoint and demonstrated statistical superiority to meropenem
Cefepime-taniborbactam was well-tolerated with similar safety profile to meropenem
NDA on track to be submitted in the fourth quarter 2022

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MALVERN, Pa.--(BUSINESS WIRE)--Venatorx Pharmaceuticals today announced positive results from its pivotal Phase 3 study evaluating cefepime-taniborbactam, an investigational new drug, as a potential treatment for adult patients with complicated urinary tract infections (cUTI), including acute pyelonephritis.

Cefepime, a fourth-generation cephalosporin, is a widely used beta-lactam (BL) antibiotic with more than two decades of proven safety and clinical utility against susceptible gram-negative and gram-positive bacteria. **Taniborbactam** is a beta-lactamase inhibitor (BLI) that, in combination with cefepime, may offer a potential treatment option for patients with serious bacterial infections caused by difficult-to-treat drug resistant gram-negative bacteria, most notably carbapenem-resistant Enterobacterales (CRE) and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). Many of these organisms are also multidrug-resistant (MDR), further limiting treatment options. Cefepime-taniborbactam has been granted Qualified Infectious Disease Product (QIDP) and Fast Track designation by the U.S. Food and Drug Administration (FDA).

CERTAIN-1 (Cefepime Rescue with Taniborbactam in cUTI) was a global, randomized, double-blind, active-controlled non-inferiority Phase 3 study evaluating the efficacy, safety, and tolerability of cefepime-taniborbactam compared to meropenem in adults with cUTI, including acute pyelonephritis. The trial enrolled 661 adult patients who were randomized 2:1 to receive cefepime-taniborbactam 2.5g q8h or meropenem 1g q8h for 7 days (up to 14 days for patients with bacteremia). The primary efficacy endpoint evaluated the composite clinical and microbiologic response (i.e., bacterial eradication) at the Test of Cure (TOC) visit (Day 19-23) in the microbiological intent-to-treat (microITT) population as specified by FDA and European Medicines Agency guidance.

Cefepime-taniborbactam met the primary efficacy endpoint of statistical noninferiority (NI) to meropenem in the microITT population at TOC with composite microbiologic and clinical success occurring in 70.0% of cefepime-taniborbactam treated patients and 58.0% of meropenem treated patients (treatment difference 11.9; 95% confidence interval (CI), 2.4, 21.6). A prespecified superiority test following confirmation of NI demonstrated the statistical superiority of cefepime-taniborbactam for the composite endpoint at TOC. The superiority of cefepime-taniborbactam was sustained for the composite microbiologic and clinical response at the Late-Follow-Up (Day 28-35) visit.

Rates of treatment-emergent adverse events (TEAEs) were 35.5% for cefepime-taniborbactam and 29.0% for meropenem. Serious TEAEs occurred in 2.0% and 1.8% of cefepime-taniborbactam and meropenem treated patients, respectively. Treatment discontinuations due to TEAEs occurred in 3.0% of cefepime-taniborbactam patients and 0.9% of meropenem treated patients. There was one death in the cefepime-taniborbactam treatment group, which was unrelated to study treatment as assessed by the investigator.

Complete CERTAIN-1 study results will be presented at an upcoming scientific meeting.

“These data demonstrate that cefepime-taniborbactam may represent a significant improvement over the standard of care and could support global health efforts to combat antibiotic-resistant infections,” said Christopher J. Burns, Ph.D., President and CEO of Venatorx. “Cefepime-taniborbactam, if approved by the FDA, may offer a new treatment option for patients with infections caused by highly resistant bacteria, even those resistant to widely used carbapenem antibiotics. We want to thank the patients who enrolled in the trial, the clinical investigators who participated in the study, as well as our employees and partners for their steadfast support and determination to bring a lifesaving medicine to patients around the world. We plan to submit a New Drug Application with the FDA for cefepime-taniborbactam for the treatment of cUTI in adult patients later this year.”

About Gram-Negative Infections and Antimicrobial Resistance (AMR)

According to the U.S. Centers for Disease Control and Prevention (CDC), rates of resistance for certain gram-negative bacteria have increased significantly in the U.S. and are common causes of cUTI, acute pyelonephritis, and bacteremia. In a recent report on AMR, the CDC cited that there are more than 2.8 million AMR infections annually in the U.S. which are directly related to more than 35,000 deaths.[i] Between 2014 and 2019, an analysis of U.S. UTI patients determined that 4.4% of cases were carbapenem resistant (CR) and 24.5% of U.S. UTI patients were bacteremic with 1.7% of cases caused by a CR pathogen. Patients with CR infections had a significantly longer hospital length of stay (LOS), were less likely to be discharged home, had a higher readmission rate, and had greater LOS-associated charges than patients with carbapenem-susceptible infections. Additionally, bacteremic (urosepsis) CR patients had a significantly higher rate of mortality than those with carbapenem susceptible bacteremia.[ii]

If AMR infections continue on this trajectory, it is estimated that there will be 10 million deaths per year by 2050—a number that surpasses the projected number of deaths (8.2 million) caused by cancer—and the cumulative cost to the global economy could be as high as US$100 trillion.[iii] In the U.S., estimates have reached as high as US$20 billion in excess direct healthcare costs, with an additional US$35 billion associated with lost productivity.[iv] By 2050, the world is at risk of losing up to 3.8% of its annual gross domestic product with an annual shortfall of up to US$3.4 trillion by 2030, a figure on par with losses attributable to the 2008 global financial crisis.[v] For those patients who do not respond to current treatment, new antibiotic therapies are needed to combat AMR.

About Complicated Urinary Tract Infections (cUTIs)

cUTIs, which include acute pyelonephritis, are defined as urinary tract infections ascending from the bladder accompanied by local and systemic signs and symptoms, including fever, chills, malaise, flank pain, back pain, and/or costovertebral angle pain or tenderness, that usually occur in the presence of a functional or anatomical abnormality of the urinary tract or in the presence of catheterization. Bacteremia can arise secondary to acute systemic infections like cUTI and can result in substantial morbidity and mortality.[i] Annually, it is estimated that more than 3 million cUTI patients would be diagnosed and require antibiotic therapy leading to over $6 billion in annualized 30-day costs.[vi]

Funding Partners and Collaborators for Cefepime-Taniborbactam

Development of cefepime-taniborbactam began with federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract number HHSN272201300019C, and Wellcome Trust under Award No. 360G-Wellcome-101999/Z/13/Z, and continues with federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, under contract number HHSO100201900007C.

In September 2018, Venatorx entered into an exclusive license agreement with Everest Medicines to support the development, registration and commercialization of cefepime-taniborbactam in Greater China, South Korea, and select countries in Southeast Asia. Everest will be solely responsible for the commercialization of cefepime-taniborbactam in its territory and Venatorx will be eligible to receive royalties on net sales.

In April 2020, Venatorx and GARDP announced a collaboration to accelerate the development of, and access to, cefepime-taniborbactam for adult and pediatric populations. Venatorx has granted GARDP exclusive rights to distribute and sub-distribute cefepime-taniborbactam, once it is approved for clinical use, in low- and lower-middle-income countries.

About Venatorx Pharmaceuticals, Inc.

Venatorx is a private, clinical-stage pharmaceutical company focused on improving health outcomes for patients with multidrug-resistant bacterial infections and hard-to-treat viral infections. Venatorx's lead program, cefepime-taniborbactam, is a clinical-stage antibiotic that completed a Phase 3 study in adults with complicated urinary tract infections. Based on positive results from the CERTAIN-1 Phase 3 clinical trial, the Company expects to submit a New Drug Application with the U.S. Food and Drug Administration for cefepime-taniborbactam in the fourth quarter 2022. Venatorx also has an oral antibacterial clinical-stage program, ceftibuten/VNRX-7145, that is in Phase 1. For more information about Venatorx and its anti-infectives portfolio, please visit www.venatorx.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical development of Venatorx Pharmaceuticals' product candidates.

References

[i] Antibiotic Resistance Threats in the United States 2019, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.
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[iv] Antibiotic Resistance Threats in the United States 2013, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.
[v] World Bank. Final Report Drug Resistant Infections: A Threat to Our Economic Future. Mar 2017.
[vi] Carreno et al. Longitudinal, nationwide, cohort study to assess incidence, outcomes, and costs associated with complicated urinary tract infection. *Open Forum Infectious Diseases.*

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