New England Journal of Medicine Publishes Positive Results of Cefepime-Taniborbactam from Phase 3 CERTAIN-1 Study of Patients with Complicated Urinary Tract Infection

Cefepime-Taniborbactam Superior to Meropenem for the Composite Efficacy Endpoint

Composite Efficacy Sustained at Late Follow-up Visit

Safety Profile Consistent with Meropenem

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MALVERN, Pa. & PARSIPPANY, N.J. & FLORENCE, Italy--(BUSINESS WIRE)--Venatorx Pharmaceuticals, Melinta Therapeutics LLC (“Melinta”), and Menarini Group today announced that The New England Journal of Medicine (NEJM) published the results of the CERTAIN-1 Phase 3 clinical study of the investigational agent cefepime-taniborbactam for the treatment of adult patients with complicated urinary tract infections (cUTI) and acute pyelonephritis (AP), including those with bacteremia. The results showed that cefepime-taniborbactam was superior to meropenem for the treatment of complicated UTI that included acute pyelonephritis, with a similar safety profile to meropenem.

“Gram-negative infections such as cUTI have become increasingly difficult to treat due to acquired bacterial resistance to multiple classes of antibiotics. Cefepime-taniborbactam has the potential to treat a broad range of patients with cUTI due to suspected or confirmed multidrug-resistant (MDR) pathogens including Enterobacterales and *Pseudomonas aeruginosa*,” said Paul C. McGovern, MD, Senior Vice President at Venatorx and co-author of the publication. “This Phase 3 study is the culmination of a long journey of discovery and development, and we look forward to progressing this agent through the next regulatory stages so that the drug may reach patients world-wide as expeditiously as possible.”

Christine Ann Miller, President and Chief Executive Officer of Melinta Therapeutics added, “We are pleased to see these results published in the New England Journal of Medicine. We look forward to leveraging our experience in marketing infectious disease products and our established commercial infrastructure, especially within the hospital and acute care settings, to make cefepime-taniborbactam available to physicians and their patients with complicated urinary tract infections if approved.”

“*E.coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* are largely involved in cUTI Gram-negative pathogens infections reaching nearly 75% in Europe. We believe that the NEJM published CERTAIN-1 Phase 3 data indicating cefepime-taniborbactam's superiority on the composite endpoint of microbiological and clinical response alongside its comparable safety profile versus meropenem provides useful insight as to its expected contribution, upon approval by relevant regulatory authorities, in the treatment of hospitalized patients with cUTI starting in Europe,” said Najy Alsayed, Global Therapeutic Area Head-Infectious Diseases at Menarini Group.

About CERTAIN-1

CERTAIN-1 was a randomized, multicenter, double-blind, active-controlled, non-inferiority study of hospitalized patients (N=661) with complicated urinary tract infections (cUTI), including acute pyelonephritis (AP), comparing cefepime-taniborbactam (2.5 g every 8 hours) to meropenem (1 g every 8 hours). The primary endpoint was the composite microbiologic and clinical response at the Test of Cure (TOC) visit (Day 19-23) in the microbiological intention-to-treat (microITT) population. The non-inferiority margin was -15% and there was a prespecified superiority analysis if non-inferiority was concluded.

Efficacy Data

Cefepime-taniborbactam met the prospectively defined non-inferiority primary endpoint of composite microbiologic and clinical response versus meropenem at the TOC visit (70.6% response rate for cefepime-taniborbactam versus 58.0% for meropenem). The prespecified superiority analysis at the TOC visit demonstrated that cefepime-taniborbactam was statistically superior to meropenem for the composite endpoint (response rate difference: 12.6% [95% confidence interval (CI): 3.1, 22.2]; p=0.009) and for the microbiologic endpoint (response rate difference: 11.7% [CI: 2.9, 21.0]); the clinical endpoint response rate difference was 4.5% [CI: -2.6, 12.6]. At the Late Follow-up (LFU) visit (Day 28-35), cefepime-taniborbactam demonstrated sustained statistical superiority to meropenem for the composite endpoint (63.8% response rate for cefepime-taniborbactam versus 51.7% for meropenem (response rate difference: 12.1% [CI: 2.2, 21.9]) and for the clinical response endpoint (response rate difference: 9.9% [CI: 1.5, 18.8); the microbiologic endpoint response rate difference was 7.7% [CI: -1.6, 17.3]. Additionally, cefepime-taniborbactam maintained a numerical advantage to meropenem against resistant pathogens: cefepime-resistant (71% response rate for cefepime-taniborbactam versus 53% for meropenem), ESBL-producing (71% response rate for cefepime-taniborbactam versus 55% for meropenem) and MDR (68% response rate for cefepime-taniborbactam versus 60% for meropenem).

Safety Data

Cefepime-taniborbactam demonstrated a safety profile consistent with meropenem. Treatment-emergent adverse events occurred in 35.5% and 29.0% of cefepime-taniborbactam and meropenem treated patients respectively. Serious adverse events occurred in 2.0% of cefepime-taniborbactam patients and 1.8% of meropenem treated patients. The most frequently reported treatment-emergent adverse events were headache (6.1% with cefepime-taniborbactam versus 3.7% for meropenem), diarrhea (4.1% versus 2.3%), and constipation (3.2% versus 1.4%). Three percent of patients treated with cefepime-taniborbactam discontinued therapy due to a treatment-emergent adverse event versus 0.9% of patients treated with meropenem. The safety data for cefepime-taniborbactam was consistent with the historical safety data for cefepime.

About Cefepime-Taniborbactam

Cefepime-taniborbactam is an investigational agent that is a combination of cefepime, a fourth-generation cephalosporin, and the novel beta-lactamase inhibitor (BLI), taniborbactam, that exhibits broad coverage of both serine- and metallo-beta-lactamases. In combination with cefepime, taniborbactam is under development as a new treatment option for patients with serious bacterial

infections caused by difficult-to-treat drug resistant gram-negative pathogens, including carbapenem-resistant Enterobacterales (CRE) and carbapenem-resistant or multidrug-resistant *Pseudomonas aeruginosa* (CRPA/MDR-PA).

Funding Partners and Collaborators for Cefepime-Taniborbactam

This project has been funded in part 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 has continued with federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority, under contract numbers HHSO100201900007C and 75A50122C00080.

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 the GARDP Foundation (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.

In November 2023, Venatorx and Melinta entered into an exclusive License Agreement to facilitate a strategic partnership in the U.S. to commercialize cefepime-taniborbactam, a beta-lactam / beta-lactamase inhibitor (BL/BLI) combination antibiotic being developed for the treatment of complicated urinary tract infections (cUTI) and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) in adults.

In December 2023, Venatorx entered into an agreement with Menarini Group, who acquired the exclusive rights to commercialize, upon approval of relevant health authorities, cefepime-taniborbactam in 96 countries in Europe, Latin America, Middle East, Turkey and North Africa and the Commonwealth of Independent States (CIS).

About Venatorx Pharmaceuticals

Venatorx is a private, late-stage clinical 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 (cUTI), including pyelonephritis. In October 2022, BARDA awarded a contract of up to $318M for development and procurement of cefepime-taniborbactam for the treatment of melioidosis and multi-drug resistant infections. Cefepime-taniborbactam is currently under review by the FDA for the treatment of cUTI, including acute pyelonephritis. Venatorx is also developing an oral antibacterial, ceftibuten-ledaborbactam (formerly known as VNRX-7145), for the treatment of cUTI, including pyelonephritis, caused by certain bacteria in adult patients with limited treatment options; this product is completing Phase 1 and will advance directly to a global Phase 3 cUTI clinical trial.. For more information about Venatorx and its anti-infectives portfolio, please visit www.venatorx.com.

About Melinta Therapeutics LLC

Melinta Therapeutics is a biopharmaceutical company dedicated to providing innovative therapies to

people impacted by acute and life-threatening illnesses. We focus our expanding portfolio on serving patients with an unmet need because that's how we make the most meaningful impact. At Melinta, we're visionaries dedicated to innovation while staying grounded in what matters most: patients. Our portfolio currently includes seven commercial-stage products: BAXDELA® (delafloxacin), KIMYRSA® (oritavancin), MINOCIN® (minocycline) for Injection, ORBACTIV® (oritavancin), REZZAYO® (rezafungin for injection), TOPROL-XL® (metoprolol succinate) and VABOMERE® (meropenem and vaborbactam). For more information about Melinta Therapeutics, our commitment to patients, and to learn about our portfolio of therapies, visit www.melinta.com.

About Menarini Group
The Menarini Group is a leading international pharmaceutical and diagnostics company, with a turnover of over $4.4 billion and over 17,000 employees. Menarini is focused on therapeutic areas with high unmet needs with products for cardiology, oncology, pneumology, gastroenterology, infectious diseases, diabetology, inflammation, and analgesia. With 18 production sites and 9 Research and Development centers, Menarini's products are available in 140 countries worldwide. For further information, please visit www.menarini.com.

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