Melinta Therapeutics and Venatorx Pharmaceuticals Announce Licensing Agreement to Commercialize Cefepime-Taniborbactam in the U.S.

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PARSIPPANY, N.J. & MALVERN, Pa.--(BUSINESS WIRE)--Melinta Therapeutics LLC (“Melinta”) and Venatorx Pharmaceuticals, Inc. (“Venatorx”), today announced that they have entered into a 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.

The partnership follows Venatorx’s submission of a New Drug Application (NDA) for cefepime-taniborbactam for the treatment of cUTI including pyelonephritis, in adults. Venatorx has been assigned a Prescription Drug User Fee Act (PDUFA) target action date for February 22, 2024. The U.S. Food and Drug Administration (FDA) granted cefepime-taniborbactam Qualified Infectious Disease Product (QIDP) and Fast Track designations for both the cUTI and HABP/VABP indications.

Cefepime-taniborbactam was developed to address the need for new, novel antibiotics to battle increasing gram-negative resistance, which is especially critical for high-risk patients. Due to its broad spectrum of in vitro activity against key, common pathogens with established and rapidly increasing mechanisms of carbapenem resistance, such as serine- and metallo-beta-lactamases, and the positive results demonstrated in the CERTAIN-1, cUTI study, cefepime-taniborbactam, if approved, will address a critical unmet need. CERTAIN-1 was a randomized, double-blind, active-controlled Phase 3 trial comparing cefepime-taniborbactam to meropenem in hospitalized adults with cUTI including acute pyelonephritis (AP). Cefepime-taniborbactam has also demonstrated in vitro activity against CDC Urgent and Serious Threat Pathogens multidrug-resistant *Pseudomonas aeruginosa*, carbapenem-resistant Enterobacterales, and Extended Spectrum Beta-lactamase-producing (ESBL) Enterobacterales.

“The addition of cefepime-taniborbactam accelerates our long-term growth strategy, and if approved, would expand and complement our existing portfolio, and provide clinicians with another option in the fight against the growing crisis of antimicrobial resistance,” said Christine Ann Miller, President and Chief Executive Officer, Melinta Therapeutics. “Importantly, this partnership supports Melinta’s mission of providing innovative therapies to people impacted by acute and life-threatening illnesses.” Miller added, “While building upon our demonstrated ability to commercialize products in the hospital market, our partnership will also provide a strong foundation for getting this important medicine into the hands of healthcare providers, and ultimately to patients across the U.S.”

“The progression of cefepime-taniborbactam from invention through clinical trials to FDA review is a source of enormous pride to the Venatorx team. With its U.S. commercial infrastructure and significant experience in commercializing antibiotics, Melinta is ideally positioned to bring this agent to patients in the U.S.,” said Christopher J. Burns, Ph.D., Chief Executive Officer of Venatorx. “This partnership will allow Venatorx to continue advancing all of the R&D and Regulatory elements of its infectious diseases portfolio including its U.S. Government contractual commitments.”

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 number 360G-Wellcome-101999/Z/13/Z, and continues with federal funds from the Biomedical Advanced Research and Development Authority, Administration for Strategic Preparedness and Response, Department of Health and Human Services 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 People's Republic of China, Macau, Hong Kong, Taiwan, South Korea, and select countries in Southeast Asia (the "Territory").

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 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 Venatorx Pharmaceuticals, Inc.

Venatorx is a private, pre-commercial pharmaceutical company focused on improving health outcomes for patients with difficult-to-treat drug resistant gram-negative bacterial infections and viral infections. Venatorx's lead asset, cefepime-taniborbactam, is an investigational antibiotic that completed a Phase 3 study (NCT03840148) in adults with complicated urinary tract infections (cUTI), including pyelonephritis and is under FDA review with a PDUFA action date of February 22, 2024. In October 2022, BARDA awarded a contract of up to $318M to Venatorx for development and procurement of cefepime-taniborbactam for the treatment of melioidosis and multidrug-resistant infections. As part of its broader pipeline, Venatorx is also developing an oral antibacterial, ceftibuten-ledaborbactam etzadroxil, that will advance directly to a global Phase 3 cUTI clinical trial under a recently announced third BARDA contract. For the license transaction cited herein, TD Cowen served as financial advisor to Venatorx. For more information about Venatorx and its anti-infectives portfolio, please visit www.venatorx.com.

About Cefepime-Taniborbactam

Cefepime-taniborbactam is an investigational intravenous (IV) beta-lactam/beta-lactamase inhibitor (BL/BLI) antibiotic combination being developed for the treatment of complicated urinary tract

infections (cUTIs), including pyelonephritis, and hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP). Cefepime-taniborbactam was accepted for review by the U.S. FDA for cUTI, including pyelonephritis with a PDUFA date of February 22, 2024.

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, is being studied as a potential treatment option for patients with serious bacterial infections caused by antibiotic resistant gram-negative bacteria, most notably Extended Spectrum Beta-lactamase (ESBL)-expressing Enterobacterales, carbapenem-resistant Enterobacterales (CRE), and multidrug-resistant (MDR) *Pseudomonas aeruginosa* (MDR-PA), which can include carbapenem-resistant *P. aeruginosa* (CRPA).

Cefepime-taniborbactam has been granted Qualified Infectious Disease Product (QIDP) and Fast Track designations by the U.S. Food and Drug Administration (FDA). Fast Track designation is designed to facilitate the development, and to expedite the review of drugs to treat serious conditions that do not have sufficient treatment options. QIDP designation provides certain incentives for the development of new antibiotics, including priority review, as well as a five-year regulatory exclusivity extension. QIDP was authorized under the Generating Antibiotic Incentives Now (GAIN) Act of 2012, as part of the FDA Safety and Innovation Act, to underscore the urgency in development of new antibiotics.

About Gram-Negative Infections and Antimicrobial Resistance (AMR)

In a recent report on AMR, the U.S. Centers for Disease Control and Prevention (CDC) reported rates of resistance have increased significantly in the U.S. among bacterial pathogens including those commonly causing cUTI, pyelonephritis, and bacteremia. The CDC also 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.[1]

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, patients with bacteremia (urosepsis) due to CR pathogens had a significantly higher rate of mortality than those with carbapenem susceptible pathogens.[2]

Gram-negative bacteria have multiple AMR mechanisms that continue to adapt in response to increases in antibiotic usage. Carbapenems are broad-spectrum antibiotics that have been widely used to treat infections caused by multidrug-resistant gram-negative bacteria, including Enterobacterales. With the increased global use of carbapenems, CRE have emerged, which have limited treatment options and are associated with increased morbidity and mortality. Resistance to carbapenems among Enterobacterales is primarily achieved by production of carbapenemases, which are enzymes capable of hydrolyzing carbapenem antibiotics and most other beta-lactams and fall into two distinct families: serine beta-lactamases and metallo-beta-lactamases (MBLs). K*lebsiella pneumoniae* carbapenemase (KPC), a class-A serine beta-lactamase, is one of the most prevalent carbapenemases, and New Delhi MBL (NDM) and Verona Integron-encoded MBL (VIM) are common variants of MBLs identified in gram-negative infections due to Enterobacterales and *P. aeruginosa.* According to an IHMA surveillance study in 2018-2019 and a JMI U.S. Surveillance

study from 2021, MBLs were the most commonly identified carbapenem resistance mechanism globally among Enterobacterales isolates, with ~16 to 18% of U.S. CRE isolates carrying MBLs.[3,4]

While CRPA is also increasing in some geographies due to emergence of MBLs, MDR-PA, which may exhibit resistance to carbapenems, represents an increasing challenge for clinicians and their patients in the U.S. and globally due to the paucity of treatment options for this primarily hospital-associated pathogen. Especially outside the U.S., CRPA may carry carbapenemases including MBLs (i.e., VIM); however, non-carbapenemase resistance mechanisms (i.e., efflux pumps, porins) also contribute to the growing global resistance of MDR-PA and CRPA.[5]

If AMR infections continue on this trajectory, it has been projected that an estimated 10 million people will die per year of resistant infections by 2050—a number that surpasses the projected annual number of deaths (8.2 million) caused by cancer—and the cumulative cost to the global economy could be as high as U.S. $100 trillion.[6] In the U.S., estimates have reached as high as U.S. $20 billion in excess direct healthcare costs, with an additional U.S. $35 billion associated with lost productivity.[7] 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 U.S. $3.4 trillion by 2030, a figure on par with losses attributable to the 2008 global financial crisis.[8]

The Infectious Disease Society of America (IDSA) maintains updated guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections online at https://www.idsociety.org/practice-guideline/amr-guidance/.[9] For those patients who do not respond to current treatment, new antibiotic therapies are needed to combat AMR.

About Complicated Urinary Tract Infections

Complicated UTIs, which include 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 infections like cUTI and can result in substantial morbidity and mortality. [1] Annually in U.S., it is estimated that more than 3 million cUTI patients will be diagnosed and require antibiotic therapy leading to over $6 billion in annualized 30-day costs.[10]

References

[1] Antibiotic Resistance Threats in the United States 2019, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

[2] Shields et al. Burden of illness in U.S. hospitals due to carbapenem-resistant gram-negative urinary tract infections in patients with or without bacteremia. BMC Infectious Diseases (2021) 21:572.

[3] Estabrook et al. Epidemiology of Resistance Determinants Identified in Meropenem-Nonsusceptible Enterobacterales Collected as Part of a Global Surveillance Study, 2018 to 2019. Antimicrobial Agents and Chemotherapy; May 2023, Vol. 67, Issue 5

[4] Castanheira et al. Increase in the Occurrence of Carbapenem-Resistant Enterobacterales in United States Hospitals from 2019 to 2021 and Activity of Novel Beta-Lactams/Beta-Lactamase Inhibitor Combinations Against these Isolates, 2022 ID Week Abstract #664. Open Forum Infectious Diseases, Volume 9, Issue Supplement_2, December 2022, ofac492.716

[5] Jean S-S, Harnod D and Hsueh P-R (2022) Global Threat of Carbapenem Resistant Gram-Negative Bacteria. Front. Cell. Infect.Microbiol.12:823684. doi:10.3389/fcimb.2022.823684[6] O'Neill, J. 'Tackling Drug-Resistant Infections Globally: Final Report and Recommendations'. Review on Antimicrobial Resistance. May 2016.

[6] O'Neill, J. 'Tackling Drug-Resistant Infections Globally: Final Report and Recommendations'. Review on Antimicrobial Resistance. May 2016.

[7] Antibiotic Resistance Threats in the United States 2013, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

[8] World Bank. Final Report Drug Resistant Infections: A Threat to Our Economic Future. Mar 2017.

[9] Infectious Disease Society of America maintains updated guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections posted online at https://www.idsociety.org/practice-guideline/amr-guidance/ accessed November 2023.

[10] Carreno et al. Longitudinal, nationwide, cohort study to assess incidence, outcomes, and costs associated with complicated urinary tract infection. *Open Forum Infectious Diseases*. 8 October 2019

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