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Phase 3 Studies of Pfizer's Novel Antibiotic Combination Offer New Treatment Hope for Patients with Multidrug-Resistant Infections and Limited Treatment Options

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- *Data support that antibiotic aztreonam -avibactam (ATM-AVI) is effective and well-tolerated in treating infections caused by Gram-negative bacteria, with a similar safety profile to aztreonam alone*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced positive results from the Phase 3 program comprising the REVISIT (NCT03329092) and ASSEMBLE (NCT03580044) studies evaluating the efficacy, safety, and tolerability of the novel investigational antibiotic combination aztreonam-avibactam (ATM-AVI) in treating serious bacterial infections due to Gram-negative bacteria, including metallo-?-lactamase (MBL)-producing multidrug-resistant pathogens for which there are limited or no treatment options. Data support that ATM-AVI is effective and well-tolerated, with no new safety findings and a similar safety profile to aztreonam alone.

"We believe these data demonstrate that ATM-AVI, if approved, could be an important treatment option for patients with life-threatening bacterial infections that are resistant to almost all currently available antibiotics," said James Rusnak, Senior Vice President and Chief Development Officer, Internal Medicine, Anti-Infectives and Hospital, Pfizer. "We are committed to meeting this critical need and helping to address the global health threat of antimicrobial resistance."

The REVISIT study compared ATM-AVI ± metronidazole (MTZ) with meropenem (MER) ± colistin (COL)for the treatment of complicated intra-abdominal infections (cIAI), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP). Key results include:

- For patients with cIAI, cure rate in the intention to treat (ITT) analysis set was 76.4% (95% confidence interval (CI) [70.3, 81.8]) for the ATM-AVI ± MTZ treatment arm vs 74.0% (95% CI [65.0, 81.7]) for the MER ± COL treatment arm, with a treatment difference of 2.4% (95% CI [-12.4, 19.1]). In the clinically evaluable (CE) analysis set, cure rate was 85.1% (95% CI [79.2, 89.9]) for ATM-AVI ± MTZ versus 79.5% (95% CI [69.9, 87.1]) for MER ± COL.
- For patients with HAP/VAP, cure rate in the ITT analysis set was 45.9% (95% CI [34.9, 57.3]) for ATM-AVI ± MTZ versus 41.7% (95% CI [26.7, 57.9]) for MER ± COL, with a treatment difference of 4.3% (95% CI [-25.6, 32.2]). In the CE analysis set, cure rate was 46.7% (95% CI [32.7, 61.1]) for ATM-AVI ± MTZ vs 54.5% (95% CI [34.3, 73.7]) for MER ± COL.
- All-cause 28-day mortality rates were 4/208 (1.9%) for ATM-AVI ± MTZ versus 3/104 (2.9%) for MER ± COL in cIAI, and 8/74 (10.8%) for ATM-AVI ± MTZ versus 7/36 (19.4%) for MER ± COL in HAP/VAP.
- ATM-AVI ± MTZ was well-tolerated, with an overall observed pattern of treatment-emergent adverse events (TEAEs) in line with that described for aztreonam alone. The incidence of serious adverse events

(SAEs) was similar between treatment groups (53 [19.3%] patients in the ATM-AVI ± MTZ group and 25 [18.2%] patients in the MER ± COL group). No patient treated with ATM-AVI ± MTZ experienced a treatment-related SAE.

These results are further supported by the ASSEMBLE study, which found that 5/12 (41.7%) of the ATM-AVI ± MTZ patients with infections due to confirmed MBL-producing Gram-negative bacteria were cured at TOC versus 0/3 (0%) of those on best available therapy (BAT). ATM-AVI patients experienced TEAEs that were in line with those of aztreonam alone. No patient treated with ATM-AVI experienced a treatment-related SAE.

Antimicrobial resistance (AMR), particularly in Gram-negative bacteria, is widely recognized as one of the biggest threats to global health and developing new treatments for infections caused by these bacteria has been highlighted as a critical area of need by the World Health Organization (WHO).[1] An estimated 1.27 million deaths globally were caused by bacterial AMR in 2019 alone.[2] Without solutions, a continued rise of AMR could make routine medical procedures too risky to perform.[3]

“These clinical findings show that ATM-AVI, if approved, could help provide coverage against Gram-negative bacteria without compromising on efficacy or safety,” said Yehuda Carmeli, Head, National Institute for Antibiotic Resistance and Infection Control, Tel Aviv Medical Center, Tel Aviv, Israel. “These data are particularly promising given the complexities of managing cIAI and HAP/VAP infections in these hospitalized, critically ill patients, and the challenges of real-world patient recruitment within this population.”

Full results from the studies will be submitted for scientific publication. Data from the REVISIT and ASSEMBLE studies are expected to form the basis for planned regulatory filings in the European Union, United Kingdom, China, and the U.S. in the second half of 2023. Pfizer holds the global rights to commercialize ATM-AVI outside of the U.S. and Canada, where the rights are held by its development partner AbbVie.

These studies were sponsored by Pfizer and funded in whole or part with federal funds from the U.S. Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under OTA number HHSO100201500029C. The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement 115620, resources of which are composed of financial contribution from the European Union Seventh Framework Programme (FP7/2007-2013) and EFPIA companies in kind contribution. Additional information about the studies can be found at www.clinicaltrials.gov under the identifiers NCT03329092 and NCT03580044.

About the Aztreonam-Avibactam (ATM-AVI) Phase 3 Development Program

The Phase 3 development program for ATM-AVI is comprised of two studies: REVISIT and ASSEMBLE. These studies were not designed for inferential testing of efficacy, but do provide randomized, assessor-blinded descriptive efficacy data and contribute to the safety database. This streamlined development approach for ATM-AVI has been confirmed by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA).

REVISIT is a Phase 3, prospective, randomized, multicenter, open label, central assessor blinded, parallel group comparative study conducted with 422 hospitalized adult patients across 81 locations in 20 countries. The study was to determine the efficacy, safety, and tolerability of ATM-AVI ± MTZ versus MER ± COL in the treatment of hospitalized adults with cIAI or nosocomial pneumonia including HAP and VAP, in regions with endemic or emerging carbapenem resistance, and where MBL-producing multidrug-resistant pathogens are suspected.

ASSEMBLE is a Phase 3, prospective, randomized, multicenter, open-label, parallel group comparator study conducted with 15 adult patients across 12 locations in 9 countries. The study was to determine the efficacy,

safety, and tolerability of ATM-AVI versus BAT in the treatment of hospitalized adults with infections confirmed due to MBL-producing Gram-negative bacteria.

About Aztreonam-Avibactam (ATM-AVI)

Aztreonam-avibactam (ATM-AVI) is an investigational treatment for infections caused by Gram-negative bacteria with limited treatment options.[4,5,6] It combines aztreonam, a monobactam ?-lactam, with avibactam, a recent broad-spectrum ?-lactamase inhibitor.[5,6] Metallo-?-lactamases (MBLs) are a class of ?-lactamase enzymes which are not inhibited by current ?-lactamase inhibitors and hydrolyze nearly all ?-lactam antibiotics, the exception being monobactams such as aztreonam. However, monobactams are degraded by other ?-lactamases that are frequently co-produced with MBLs, limiting the clinical usefulness of aztreonam monotherapy.

The combination of aztreonam with avibactam restores aztreonam's activity against bacteria that co-produce MBLs and other ?-lactamases and, if approved, could offer a much-needed safe and effective treatment option against multidrug-resistant Gram-negative bacteria.[5]

ATM-AVI is being jointly developed with AbbVie. Pfizer holds the global rights to commercialize this investigative therapy outside of the U.S. and Canada, where the rights are held by AbbVie. Development of ATM-AVI is also supported by public-private partnerships between Pfizer and the Biomedical Advanced Research and Development Authority (BARDA), and between Pfizer and the European Union's Innovative Medicines Initiative (IMI) – a partnership between the European Union and the European pharmaceutical industry, under a project called COMBACTE-CARE (Combating Bacterial Resistance in Europe – Carbapenem Resistance). The COMBACTE-CARE consortium is a unique public-private collaboration that unites the knowledge and capabilities of leading drug resistant bacterial infection experts and is supported by the COMBACTE clinical and laboratory networks.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 170 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News,LinkedIn, YouTube and like us on Facebook at www.facebook.com/Pfizer/

Disclosure Notice

The information contained in this release is as of June 1, 2023. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about an investigational antibiotic, aztreonam-avibactam (ATM-AVI), and planned regulatory filings, including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and

development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed in any jurisdictions for ATM-AVI; whether and when regulatory authorities in any such jurisdictions where applications may be filed or pending may approve such applications, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy, and, if approved, whether ATM-AVI will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of ATM-AVI; the impact of COVID-19 on our business, operations and financial results;and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2022 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results," as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com

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