Sulbactam-Durlobactam Unanimously Recommended for Approval by FDA Advisory Committee

April 17, 2023

- *New Drug Application (NDA) for sulbactam-durlobactam for the treatment of adults with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible strains of Acinetobacter baumannii-calcoaceticus complex (Acinetobacter), is currently under Priority Review by the FDA with a PDUFA target action date of May 29, 2023*

BURLINGAME, Calif.--(BUSINESS WIRE)--Apr. 17, 2023-- Innoviva, Inc. (Nasdaq: INVA) (Innoviva), a diversified holding company with a portfolio of royalties and other healthcare assets, today announced that the U.S. Food and Drug Administration's (FDA) Antimicrobial Drugs Advisory Committee (AMDAC) unanimously voted 12-0 in support of approval based on a favorable benefit-risk assessment of sulbactam-durlobactam for the treatment of adults with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible strains of *Acinetobacter baumannii-calcoaceticus* complex (*Acinetobacter*). The sulbactam-durlobactam New Drug Application (NDA), filed by Entasis Therapeutics Inc., a wholly owned subsidiary of Innoviva, was accepted and granted Priority Review by the FDA in November 2022, with a Prescription Drug User Fee Act (PDUFA) target action date of May 29, 2023.

"The Committee's unanimous recommendation in favor of sulbactam-durlobactam, the first pathogen-targeted therapy for *Acinetobacter*, moves us closer to potentially addressing the urgent need for new treatment options for patients with serious and life-threatening infections caused by this pathogen," said David Altarac, MD, Chief Medical Officer, Entasis Therapeutics, a wholly owned subsidary of Innoviva. "We appreciate the Committee's thoughtful deliberation and strong vote of confidence, and look forward to working with the FDA as it completes its review."

The Committee based its recommendation on the totality of scientific evidence, including results from the landmark Phase 3 trial evaluating the safety and efficacy of sulbactam-durlobactam versus colistin in patients with infections caused by *Acinetobacter*. In the trial, sulbactam-durlobactam demonstrated statistical non-inferiority versus colistin for the primary endpoint of 28-day all-cause mortality in patients with carbapenem-resistant *Acinetobacter* infections and a significant difference in clinical cure rates. Sulbactam-durlobactam also exhibited a favorable safety profile with a statistically significant lower incidence of nephrotoxicity as measured by modified Risk–Injury–Failure–Loss and End-stage kidney disease (RIFLE) criteria. The FDA will take the Committee's recommendation into consideration when it makes a final determination.

Infections caused by drug-resistant *Acinetobacter* are serious and life-threatening conditions associated with high morbidity and mortality[1] and long, expensive hospital stays. *Acinetobacter* is resistant to penicillins and has also acquired resistance genes for almost all antibiotics used to treat Gram-negative bacteria, including fluoroquinolones, aminoglycosides, cephalosporins, and carbapenems.

The Centers for Disease Control and Prevention (CDC) has identified carbapenem-resistant micro-organisms as an urgent threat[2]. Globally, *Acinetobacter baumannii* was among the top six leading pathogens for deaths associated with resistance in 2019[3]. Carbpenem-resistant *Acinetobacter* is considered a Priority 1 pathogen by the World Health Organization (WHO)[4].

About *Acinetobacter*

Members of the *Acinetobacter baumannii-calcoaceticus* complex (*Acinetobacter*) are Gram-negative, opportunistic human pathogens that predominantly infect critically ill patients often resulting in severe pneumonia and bloodstream infections. They can also infect other body sites, such as the urinary tract and the skin. *Acinetobacter* is considered a global threat in the healthcare setting due in part to its ability to acquire multidrug resistance. Based on current carbapenem resistance rates, we estimate there are more than 300,000 hospital-treated carbapenem-resistant *Acinetobacter* infections each year globally[5] for which significant morbidity and mortality exists due to limited treatment options.

About sulbactam-durlobactam

Sulbactam-durlobactam is an intravenous, or IV, investigational drug that is a combination of sulbactam, a beta-lactam antibacterial, and durlobactam, a beta-lactamase inhibitor, being developed for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia caused by susceptible strains of *Acinetobacter baumannii-calcoaceticus* complex *(Acinetobacter)*. Sulbactam-durlobactam has been designated a Qualified Infectious Disease Product by the FDA, a designation that aims to spur development of new antibiotics for serious and life-threatening infections. In November 2022, the FDA accepted the New Drug Application (NDA) for sulbactam-durlobactam for Priority Review and set a Prescription Drug User Fee Act (PDUFA) target date of May 29, 2023.

About Innoviva

Innoviva is a diversified holding company with a portfolio of royalties and other healthcare assets. Innoviva's royalty portfolio includes respiratory assets partnered with Glaxo Group Limited GSK), including RELVAR®/BREO® ELLIPTA® (fluticasone furoate/vilanterol, FF/VI) and ANORO® ELLIPTA® (umeclidinium bromide/vilanterol, UMEC/VI). Under the Long-Acting Beta2 Agonist (LABA) Collaboration Agreement, Innoviva is entitled to receive royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. Innoviva's other healthcare assets include infectious disease and critical-care assets stemming from acquisitions of Entasis Therapeutics Inc., including its lead asset sulbactam-durlobactam, and La Jolla Pharmaceutical Company, including GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock,

and XERAVA® (eravacycline), for the treatment of complicated intra-abdominal infections in adults.

ANORO®, RELVAR® and BREO® are trademarks of the GSK group of companies.

Forward Looking Statements

This press release contains certain “forward-looking” statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives, and future events. Innoviva intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. The words “anticipate”, “expect”, “goal”, “intend”, “objective”, “opportunity”, “plan”, “potential”, “target” and similar expressions are intended to identify such forward-looking statements. Such forward-looking statements involve substantial risks, uncertainties, and assumptions. These statements are based on the current estimates and assumptions of the management of Innoviva as of the date of this press release and are subject to known and unknown risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Innoviva to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: expected cost savings; lower than expected future royalty revenue from respiratory products partnered with GSK; the commercialization of RELVAR®/BREO® ELLIPTA®, ANORO® ELLIPTA® and, formerly, TRELEGY® ELLIPTA® in the jurisdictions in which these products have been approved; the strategies, plans and objectives of Innoviva (including Innoviva’s growth strategy and corporate development initiatives beyond the existing respiratory portfolio); the timing, manner, and amount of potential capital returns to shareholders; the status and timing of clinical studies, data analysis and communication of results; the potential benefits and mechanisms of action of product candidates; expectations for product candidates through development and commercialization; the timing of regulatory approval of product candidates; and projections of revenue, expenses and other financial items; the impact of the novel coronavirus (COVID-19). Other risks affecting Innoviva are described under the headings “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” contained in Innoviva’s Annual Report on Form 10-K for the year ended December 31, 2022 and Quarterly Reports on Form 10-Q, which are on file with the Securities and Exchange Commission (SEC) and available on the SEC’s website at www.sec.gov. Past performance is not necessarily indicative of future results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. The information in this press release is provided only as of the date hereof, and Innoviva assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

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[1] Tala, B., Jad, A., Claude, A., Jihad, I., Chantal, L., Rakan, N.,& Eid, A. (2017). Risk Factors, Clinical Presentation, and Outcome of *Acinetobacter baumannii* Bacteremia. Front. Cell. Infect. Microbiol., 04 May 2017, Sec. Molecular Bacterial Pathogenesis Volume 7 – 2017: https://doi.org/10.3389/fcimb.2017.00156

[2] Centers for Disease Control and Prevention, “Carbapenem-resistant *Acinetobacter baumannii* (CRAB): An urgent public health threat in United States healthcare facilities,” August 2021: https://arpsp.cdc.gov/story/cra-urgent-public-health-threat

[3] Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022; 399(10325):629-655. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

[4] World Health Organization, “WHO publishes list of bacteria for which new antibiotics are urgently needed,” February 27, 2017: https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

[5] Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022; 399(10325):629-655. Supplementary Material. Supplementary appendix. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

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