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Virginia Commonwealth University Scientists Report Anti-Inflammatory Effect of Aradigm's Inhaled Liposomal Ciprofloxacin

Major Inflammation Stimulating Factor Produced During Serious Lung Infections Inhibited by Aradigm's Drug

HAYWARD, Calif.--(BUSINESS WIRE)-- Today at the annual meeting of the American Association of Pharmaceutical Scientists (AAPS) in Chicago, IL, scientists from the Virginia Commonwealth University (Richmond, VA) will report findings about the anti-inflammatory effects of Aradigm Corporation's (OTCBB:ARDM) (the "Company") inhaled ciprofloxacin in human bronchial lung cells stimulated by the lipopolysaccharide (LPS) produced by *Pseudomonas aeruginosa*.

Pseudomonas aeruginosa is one of the most significant bacterial pathogens in patients with cystic fibrosis, bronchiectasis and severe COPD. LPS produced by this organism is a key virulence-causing factor associated with the respiratory infections due to this microorganism.

Aradigm's proprietary drug, Pulmaquin™, is a mixture of a small amount of free ciprofloxacin that provides a spike of immediately available antibiotic for rapid anti-infective activity plus liposomal ciprofloxacin that provides sustained release of the antibiotic in the lung facilitating once daily dosing and improved airway tolerability.

In the experiments reported by Ruba Darweesh and Masahiro Sakagami from the Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University, liposomal ciprofloxacin and free ciprofloxacin were applied onto the monolayer of human bronchial lung cells for 24 hours. LPS from *Pseudomonas aeruginosa* was then added to stimulate the inflammatory response. At 24 and 48 hours of this stimulation, samples were taken for determination of cellular release of an important pro-inflammatory cytokine, interleukin-8 (IL-8). IL-8 release was negligible from the unstimulated negative control cells. In contrast, 10 µg/ml LPS stimulation for 24 and 48 hours caused significant 24.1 ± 9.2 and 39.5 ± 11.6 ng of IL-8 release, respectively (positive control). Despite its application 24 hours prior to the LPS stimulation, liposomal ciprofloxacin at 0.1 mg/ml still inhibited this LPS-induced IL-8 release (60.1 ± 9.8% and 45.6 ± 4.8% inhibition, respectively). Free ciprofloxacin alone also showed comparable inhibition, but was eliminated much faster from the surface of the cells.

"Chronic respiratory infections with *Pseudomonas aeruginosa* with the associated airway inflammation are the key cause of the deterioration in the quality of life and premature death of patients with cystic fibrosis and bronchiectasis. We are excited that our findings suggest that liposomal ciprofloxacin could exert both anti-pseudomonal and anti-inflammatory effects in the lungs," said Virginia Commonwealth University School of Pharmacy Associate Professor Masahiro Sakagami, the principal investigator and corresponding author of the study.

About inhaled ciprofloxacin (Pulmaquin and Lipoquin™)

Ciprofloxacin is a widely prescribed antibiotic to treat infections of the lung frequently experienced by cystic fibrosis (CF) and non-cystic fibrosis bronchiectasis (BE) patients. It is often preferred because of its broad-spectrum anti-bacterial action. The available oral and intravenous formulations of the drug are used to treat episodes of acute exacerbations of lung infections in CF patients. The Company's once-a-day novel inhaled formulations of ciprofloxacin are encapsulated in liposomes, allowing for a sustained release of the drug within the lung and improving airway tolerability. The formulations are to be used for chronic maintenance therapy as they are expected to achieve higher antibiotic concentration at the site of infection and relatively low systemic antibiotic concentrations to minimize side-effects. Lipoquin is a liposomal formulation of ciprofloxacin. Pulmaquin is a dual release formulation that is a mixture of Lipoquin with unencapsulated ciprofloxacin. Pulmaquin has been tested extensively in preclinical tests, as well as in the ORBIT-2 Phase 2b bronchiectasis study in which outstanding antimicrobial activity coupled with good safety and tolerability was found, and, most importantly, the positive impact on prevention of exacerbations compared to placebo was also observed. The Company previously reported positive results in Phase 2a studies of 22 CF patients and 36 BE patients who received Lipoquin once-a-day for 2 (CF) or 4 (BE) weeks, respectively. Additionally, Aradigm is developing these formulations as a potential medication for the prevention and treatment of high threat and bioterrorism infections, such as inhaled anthrax, tularemia and Q fever. Aradigm has been granted orphan drug designation for liposomal ciprofloxacin for cystic fibrosis in the U.S. and the E.U., and for the combination of liposomal ciprofloxacin and free ciprofloxacin for BE in the U.S.

About Aradigm

Aradigm is an emerging specialty pharmaceutical company focused on the development and commercialization of a portfolio of

drugs delivered by inhalation for the treatment of severe respiratory diseases by pulmonologists. The Company has product candidates addressing the treatment of bronchiectasis, cystic fibrosis, inhalation tularemia and anthrax infections, and smoking cessation.

More information about Aradigm can be found at www.aradigm.com.

Forward-Looking Statements

Except for the historical information contained herein, this news release contains forward-looking statements that involve risk and uncertainties, including the ability of in vitro results to predict efficacy in humans, as well as the other risks detailed from time to time in the Company's filings with the Securities and Exchange Commission (SEC), including the Company's Annual Report on Form 10-K for the year ended December 31, 2011 filed with the SEC on March 28, 2012, and the Company's Quarterly Reports on Form 10-Q.

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Source: Aradigm Corporation