



FDA Approves AEMCOLO™ (rifamycin), the First Antibiotic Approved for the Treatment of Travelers' Diarrhea in Over a Decade

San Diego – November 19, 2018 –Aries Pharmaceuticals, Inc. (a Cosmo Pharmaceuticals N.V. Company) announced today that the U.S. Food and Drug Administration (FDA) has approved AEMCOLO (rifamycin) 194mg delayed-release tablets, a new minimally-absorbed antibiotic that is delivered to the colon, for the treatment of adult patients with Travelers' Diarrhea caused by non-invasive strains of *Escherichia coli*. In October 2017, the FDA granted Qualified Infectious Disease Product (QIDP) and Fast Track designations for AEMCOLO. With the QDIP designation, intended for antibacterial drugs that treat serious or life-threatening infections, AEMCOLO will have marketing exclusivity through 2028. AEMCOLO will be available in pharmacies in the first quarter of 2019.

Travelers' Diarrhea is the most common and predictable travel-related illness with bacteria accounting for up to 80-90% of cases, the most common of which is enterotoxigenic *Escherichia coli* (*E. coli*). "Travelers' diarrhea can be highly disruptive and cause significant discomfort for patients, and in some cases, it can progress to more serious conditions if not treated effectively. The recent approval of AEMCOLO is an important step for Aries as we continue to grow our portfolio to address important unmet needs in the GI community", said Tom Joyce, CEO of Aries Pharmaceuticals.

AEMCOLO was approved based on data from two randomized, multi-center, controlled Phase 3 clinical trials. In both trials AEMCOLO was dosed at 388mg twice daily for three days. AEMCOLO demonstrated superiority to placebo ($p = 0.0008$) and non-inferiority to Ciprofloxacin ($p=0.0033$ for non-inferiority) for the primary endpoint (time to last unformed stool). The most common adverse reactions that occurred in at least 2% of AEMCOLO-treated patients in these clinical trials were constipation and headache (3.5% and 3.3%, respectively).

Herbert L. DuPont, MD, Professor of Infectious Diseases at The University of Texas-Houston School of Public Health and primary investigator said, "given the potential seriousness of Travelers' Diarrhea and growing resistance to antibiotics that have been in widespread use since the early '90s, it's important to have new options for treatment. Because AEMCOLO is a minimally absorbed, colon-targeted antibiotic, it will be an important new option for patients." Dr. DuPont, the founding President of the International Society of Travel Medicine, has studied Travelers' Diarrhea on four continents for more than 30 years and has been important in establishing the principles of travel medicine.

About AEMCOLO

AEMCOLO (rifamycin) is an orally administered, minimally absorbed antibiotic approved for the treatment of Travelers' Diarrhea caused by non-invasive strains of *Escherichia coli* in adults. AEMCOLO is the first antibiotic engineered with Cosmo Pharmaceuticals' Multi Matrix Technology (MMX®) which allows for the delayed-release to the colon. Rifamycin using MMX® technology is also being studied for Irritable Bowel Syndrome with diarrhea (IBS-D) (NCT03099785) and uncomplicated diverticulitis (NCT01847664).

INDICATION

AEMCOLO is indicated for the treatment of travelers' diarrhea caused by non-invasive strains of *Escherichia coli* in adults.

Limitations of Use

AEMCOLO is not indicated in patients with diarrhea complicated by fever or bloody stool or due to pathogens other than noninvasive strains of *Escherichia coli*.

IMPORTANT SAFETY INFORMATION

- AEMCOLO is contraindicated in patients with a known hypersensitivity to rifamycin, any of the other rifamycin class antimicrobial agents, or any of the components in AEMCOLO.
- AEMCOLO was not shown to be effective in patients with diarrhea complicated by fever and/or bloody stool or diarrhea due to pathogens other than noninvasive strains of *E.coli* and is not recommended for use in such patients.
 - Discontinue use if diarrhea gets worse or persists more than 48 hours, and consider alternative antibacterial therapy.
- Consider CDAD in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.
- Prescribing AEMCOLO in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- Discontinuation of AEMCOLO due to adverse reactions occurred in 1% of patients. The most frequent adverse reactions were abdominal pain (0.5%) and pyrexia (0.3%).
- The common adverse reactions that occurred in at least 2% of AEMCOLO-treated patients in the clinical trials were constipation 3.5% and headache 3.3%.

Full Prescribing Information for AEMCOLO is available at www.ariespharma.com.

About Aries Pharmaceuticals, Inc.

Aries Pharmaceuticals, Inc. (Aries) is a specialty pharmaceutical company commercializing best-in-class gastroenterology products for the United States market with a focus on products utilized in endoscopy and for the treatment of specific gastrointestinal diseases. The company's initial portfolio of four products, two of which are still in development, are licensed from Cosmo Pharmaceuticals N.V. to Aries Ltd. Aries is the US Commercial and Medical Affairs arm of Aries Ltd., a wholly owned subsidiary of Cosmo Pharmaceuticals N.V. For further information on Aries, please visit the company's website: www.ariespharma.com.

About Cosmo Pharmaceuticals

Cosmo is a specialty pharmaceutical company that aims to become a global leader in the field of optimized therapies for selected Gastrointestinal Disorders and Endoscopic Procedures. The Company's proprietary clinical development pipeline specifically addresses innovative treatments for IBD, such as Ulcerative Colitis and Crohn's Disease, and Colon Infections. In addition, the Company has developed a medical device for polyp and adenoma excision and is has completed clinical trials of Methylene Blue MMX[®], a diagnostic drug for the detection of colon cancer as well as new chemical entities that are being developed by the associate company Cassiopea S.p.A. for the topical treatment of skin diseases. Cosmo's MMX products that have reached the market are Lialda[®]/Mezavant[®]/Mesavancol[®], a treatment for IBD that is licensed globally to Giuliani and Shire Limited and Uceris[®], the first glucocorticosteroid indicated for the induction of remission in active, mild to moderate Ulcerative Colitis, licensed in US to Santarus/Salix/Valeant and in the Rest of the World to Ferring as Cortiment[®]. Cosmo's proprietary MMX technology is at the core of the Company's product pipeline and was developed from its expertise in formulating and manufacturing gastrointestinal drugs for international clients at its GMP (Good

Manufacturing Practice) facilities in Lainate, Italy. The technology is designed to deliver active ingredients in a targeted manner in the colon. For further information on Cosmo, please visit the Company's website: www.cosmopharma.com.

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