



Drug-Exposure Limitations of Oral Methotrexate at Doses Greater Than or Equal to 15 Mg May Be Overcome with Subcutaneous Administration

Antares Pharma Announces the Publication of a Head-to-Head, Randomized, Crossover Study of Oral versus Subcutaneous Methotrexate in Patients with Rheumatoid Arthritis

April 17, 2014 07:00 AM Eastern Daylight Time

EWING, N.J.--(BUSINESS WIRE)--Antares Pharma, Inc. (NASDAQ: ATRS) today announced that the Annals of the Rheumatic Diseases has published results from an open-label, head-to-head randomized, crossover study comparing the relative bioavailability, safety and tolerability of OTREXUP to oral methotrexate (MTX) in adult patients with rheumatoid arthritis (RA).

In this multicenter, three-way crossover study, patients greater than or equal to 18 years old with adult RA undergoing treatment with MTX for three months or more were assigned to receive one of four dose levels of OTREXUP, 10 mg, 15 mg, 20 mg, and 25 mg weekly in a random sequence of three treatments: oral, subcutaneous into the abdomen and subcutaneous into the thigh. For 24 hours after the administration of each treatment, blood samples were collected to measure drug levels and injection sites were assessed. Forty-seven patients completed the study and the results showed that the systemic availability of methotrexate following oral dosing plateaus at 15 mg and greater. Following administration of OTREXUP, the systemic availability increased proportionally at every dose, which extended the range of exposure compared to patients receiving oral therapy. No unexpected adverse events were noted for either formulation in this short term study and higher systemic MTX exposure was not associated with increases in adverse events.

“The study results show for the first time that plasma levels of oral dosed MTX are no greater for 20 mg or 25 mg doses than for 15 mg doses,” said Michael H. Schiff, M.D., Clinical Professor of Medicine in the Rheumatology Division at the University of Colorado School Of Medicine in Denver. “If a patient fails to respond to 15 mg of MTX orally, it may be more effective to switch to a subcutaneous regimen rather than continue to raise the oral dose. These findings may have implications on future prescribing habits of specialists.”

Historically, parenteral MTX use has been limited in clinical practice for several reasons including the inconvenience of weekly injections by a healthcare professional, and/or the challenges associated with teaching patients with impaired hand function, safe, sterile and precise self-injection techniques. To address these issues, an easy to use, single-use MTX auto injector (OTREXUP) was developed to optimize the clinical benefit of MTX, potentially leading to cost effective treatment outcomes.

Paul K. Wotton, Ph.D., President and Chief Executive Officer, stated, "The publication of this data by the Annals of the Rheumatic Diseases adds further validation to the value proposition of OTREXUP." He continued, "The parenteral administration of methotrexate is an accepted treatment method for extending the use to higher doses. We believe OTREXUP provides not only greater bioavailability, but more precise, hygienic and greater dosing flexibility for RA patients."

The article can be accessed using the following link: <http://ard.bmj.com/cgi/content/full/annrheumdis-2014-205228>

IMPORTANT SAFETY INFORMATION (ABBREVIATED)

Otrexup (methotrexate) injection, for subcutaneous use

Otrexup can cause serious side effects that can lead to death, including:

- **An increased risk of death from organ toxicity. Types of organ toxicity can include: gastrointestinal, bone marrow, liver, immune system, nerve, lung, kidneys and skin.**
- **Women who are pregnant are at increased risk for death of the baby and birth defects.** Women who are pregnant or who plan to become pregnant **must not take Otrexup.** Contraception should be used by both females and males while taking Otrexup. For males, pregnancy should be avoided for a minimum of 3 months after treatment with Otrexup, and for females, for at least 1 menstrual cycle after treatment.

Do not take Otrexup if you:

- Are pregnant or planning to become pregnant
- Are breastfeeding
- Have alcohol problems
- Have liver problems
- Have problems fighting infection
- Have a blood disorder
- Have an allergy to methotrexate

- **Fertility problems**
- **Certain cancers**
- **Tissue and bone problems**

Common side effects of Otrexup include: nausea, stomach pain, indigestion, mouth sores, and rash.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. For more information, go to www.Otrexup.com or call 1-855-OTREXUP (1-855-687-3987).

About Vibex Auto Injectors

The Vibex Auto Injector is a single-dose, disposable pressure assisted auto injector designed to provide a fast, safe and time-efficient method of self-injection. The Vibex system features a triggering collar that shields the needle from view. The patented retracting collar springs back and locks in place as a protective needle guard after the injection, making the device safe for general disposal. Encompassing a wide variety of sizes and designs, this technology operates by using pressure to force the drug, solution or suspension through the skin and deposit the drug into the subcutaneous tissue. Our proprietary Vibex disposable auto injector systems combine a low-energy, spring-based power source with a shielded needle designed to deliver the needed drug solution. Vibex® Auto Injectors are designed, developed and manufactured in America.

About Antares Pharma

Antares Pharma focuses on self-administered parenteral pharmaceutical products. The Company has received marketing approval from the U.S. Food and Drug Administration for OTREXUP (methotrexate) injection for the treatment of adults with severe active rheumatoid arthritis, children with active polyarticular juvenile idiopathic arthritis and adults with severe recalcitrant psoriasis. Antares Pharma is also developing VIBEX QS T for testosterone replacement therapy. The Company's technology platforms include VIBEX disposable Medi-Jet, disposable multi-use pen injectors and reusable needle-free injectors marketed as Tjet and Zomajet by Teva Pharmaceutical Industries, Ltd (Teva) and Ferring Pharmaceuticals (Ferring), respectively. Antares Pharma has a multi-product deal with Teva that includes Tev-Tropin [somatropin (rDNA origin) for injection] human growth hormone (hGH), VIBEX epinephrine and several other products. Antares Pharma's partnership with Ferring includes Zomacton hGH (somatropin) injection. In the U.S. Antares has received FDA approval for Gelnique 3% (oxybutynin) gel, a treatment for overactive bladder that is marketed by Actavis. Elestrin (estradiol gel) is FDA approved for the treatment of moderate-to-severe vasomotor symptoms associated with menopause, and is marketed in the U.S. by Meda Pharma. Antares Pharma has two facilities in the U.S. The Parenteral Products Group located in Minneapolis, Minnesota directs the manufacturing and marketing of the Company's reusable needle-free injection devices and related disposables, and develops its disposable pressure-assisted Medi-Jet and pen injector systems. The Company's corporate office and Product Development and Commercial Groups are located in Ewing, New Jersey.

Safe Harbor Statement

This press release contains forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are indicated by the words "may," "will," "plans," "intends," "believes," "expects," "anticipates," "potential," "could," "would," "should," and similar expressions. Such forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that may cause actual results to differ materially from those anticipated by the forward-looking

these and other factors that may cause actual results to differ materially from those anticipated in the forward-looking statements is contained in the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2013, and in the Company's other periodic reports and filings with the Securities and Exchange Commission. The Company cautions investors not to place undue reliance on the forward-looking statements contained in this press release. All forward-looking statements are based on information currently available to the Company on the date hereof, and the Company undertakes no obligation to revise or update these forward-looking statements to reflect events or circumstances after the date of this press release, except as required by law.

Contacts

Antares Pharma, Inc.

Jack Howarth

Vice President, Corporate Affairs

609-359-3016

jhowarth@antarespharma.com