Two Recent Publications on Pritelivir Confirm the Potency of the Novel AiCuris Anti-Herpes Simplex Virus Drug

- Clinical data published in the peer-reviewed "Journal of Infectious Diseases" showed no evidence of resistance in HSV-2 sequences obtained from genital swabs collected during a phase II trial
- Pritelivir clinical phase II data were used for the development of a mathematical model to optimize dose selection for clinical trials published in the renowned journal "Science Translational Medicine"

Wuppertal, Germany, June 23, 2016 - AiCuris Anti-infective Cures GmbH, a leading company in the discovery and development of drugs against infectious diseases, announced today the publication of results assessing molecular signals of drug resistance over 28 days of therapy; this was a secondary objective from a recent phase II dose finding study with pritelivir. The peer-reviewed article titled: "No evidence of resistance of HSV-2 to pritelivir following four weeks of daily therapy" was prepared in collaboration with Dr. Paul Edlefsen and colleagues at the Fred Hutchinson Cancer Research Center and University of Washington, Seattle, Washington, USA, and will be published in the July issue of "The Journal of Infectious Diseases".

Pritelivir belongs to a new class of antiviral compounds, the helicase-primase inhibitors, being developed to treat herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) infections. Oral pritelivir has successfully completed a phase II clinical trial in 156 participants with genital HSV-2 infections showing reduced viral shedding and genital lesions. The mentioned peer-reviewed article reports the results of a secondary objective of this clinical study. It specifically assesses the emergence of mutations consistent with helicase-primase inhibitor resistance in people receiving pritelivir for daily treatment of genital HSV-2 infections, even at suboptimal doses.

Importantly, no changes in HSV-2 sequence occurred during treatment in the individual patients and no emergence of resistance mediating mutations was observed. Overall, only few mutations relative to the consensus sequence were found and these observed variations were considered to be reflective of pre-existing HSV-2 diversity among the trial participants.

Link to published article:
http://jid.oxfordjournals.org/content/early/2016/04/07/infdis.jiw129.abstract

"The prevalence of HSV-2 infections in the general population ranges from 10% to 60% worldwide. HSV-2 infections can lead to genital herpes, which typically causes painful ulcers. Infections can also be unrecognized, meaning that infected individuals, with or without symptoms, can shed HSV and so can infect sexual partners," **said Dr. Holger Zimmermann, CEO of AiCuris**. "These publications show, once again, that pritelivir is proving to be an exceptional approach to herpes treatment. With its novel mode of action and no evidence of resistance to pritelivir, we are confident that this small molecule therapy could become an important option to treat HSV infections," he added.

Using data from the same clinical phase II dose finding trial, the renowned journal "Science Translational Medicine" published an article in February 2016 titled "Mathematical modeling of herpes simplex virus-2 suppression with pritelivir predicts trial outcomes." In this article, again in collaboration with the Fred Hutchinson Cancer Research Center as well as with ICPD (Institute for Clinical Pharmacodynamics, Latham, New York, USA), Dr. Joshua Schiffer *et al*. introduced a mathematical model to optimize dose

selection for clinical trials by combining for the first time population pharmacokinetics with a previously established model of viral pathogenesis in genital HSV infection to simulate the efficacy of a compound.

The mathematical simulation was able to model viral shedding kinetics in the five treatment groups and thus to predict the trial outcome. Moreover, it confirmed that based on its innovative mode of action and its long half-live, pritelivir can effectively and dose-dependently decrease viral replication by decreasing shedding episode frequency, duration, and viral load. In addition, the model indicates that besides inhibiting replication in epithelial cells, pritelivir seems also to inhibit the virus directly in the neuron.

Link to published article: http://stm.sciencemag.org/content/8/324/324ra15.

About Pritelivir

Pritelivir is an innovative, highly active and specific inhibitor of herpes simplex virus (HSV). As a compound derived from a novel chemical class (thiazolylamides), pritelivir is active against both types of herpes simplex virus (HSV-1 and HSV-2) causing labial and genital herpes, respectively, and retains activity against viruses which have become resistant to marketed drugs. Pritelivir has a mode of action that is distinct from other antiviral agents currently in use for treating HSV infections (i.e., the nucleoside analogues acyclovir and its prodrug valacyclovir as well as famciclovir, the prodrug of penciclovir). Whereas nucleoside analogs terminate ongoing DNA chain elongation through inhibition of viral DNA polymerase, pritelivir prevents *de novo* synthesis of virus DNA through inhibition of the helicase-primase complex. In addition, it does not require activation within an HSV infected cell by viral thymidine kinase and is therefore also protective to uninfected cells.

Currently the company runs two clinical development programs with pritelivir. The most advanced program, **pritelivir (oral),** showed superiority against standard treatment valacyclovir in a clinical phase II trial in patients with genital HSV-2 infection. **Pritelivir (topical),** designed for the treatment of recurrent labial herpes (mainly HSV-1), just entered phase I clinical testing.

About HSV

Herpes simplex viruses (HSV) are widespread in the human population (seroprevalence up to 100%, depending on geographic area and subpopulation), and are divided into herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2). Infections lead to lifelong persistence of the virus, with frequent and sometimes painful recurrences. While HSV-1 predominantly causes oral lesions (cold sores), HSV-2 manifests in the genital region and is mainly sexually transmitted. In immunocompromised patients, HSV can lead to serious complications. In the immune competent, the negative stigma associated with genital herpes and visible facial lesions might cause psychological distress.

About AiCuris Anti-infective Cures GmbH

AiCuris was founded in 2006 as a spin-off from Bayer and focuses on the discovery and development of drugs against infectious diseases. Majority investor is the SANTO Holding. The company is developing drugs for the treatment of viruses such as human cytomegalovirus (HCMV), herpes simplex virus (HSV), hepatitis B virus (HBV), and adenoviruses. In the field of antibacterials, AiCuris is concentrating on the search for innovative treatment options for life-threatening (multi)resistant hospital-treated pathogens. In 2012, AiCuris signed a license agreement with Merck & Co (MSD) which attracted significant attention being one of the largest agreements of this kind in the European biotech industry. The agreement covers the development of novel drug candidates against HCMV. Letermovir, the most advanced compound, is currently in phase III clinical trials in patients undergoing bone marrow transplantation.

Contact:

AiCuris Anti-infective Cures GmbH
Katja Woestenhemke
Friedrich-Ebert-Str. 475/Geb. 302
42117 Wuppertal

Phone +49 202 317 63 0
Fax +49 202 317 63 1601
Email business@aicuris.com
Web www.aicuris.com

Media Relations
MC Services AG
Anne Hennecke
Kaiser-Friedrich-Ring 5
40545 Düsseldorf

Phone +49 211 529 252 22
Fax +49 211 529 252 29
Email anne.hennecke@mc-services.eu
Web www.mc-services.eu