AiCuris Announces Milestone Achievements Further Validating its Pipeline of Anti-viral Solutions for Immuno-compromised Patients

- PREVYMIS® (letermovir) gains approval in Japan for prevention of cytomegalovirus disease in adult patients with a solid organ transplant (SOT) triggering next milestone payment of EUR €7.5 million from partner MSD
- Comprehensive pharmacokinetic data package for Phase 3 lead candidate pritelivir published in *Clinical Pharmacology in Drug Development*
- Company receives clinical trial approval to initiate Phase 1 study with AIC468 in healthy volunteers; AIC468 is designed to treat BKV-associated nephropathy and graft loss in kidney transplant patients

Wuppertal, Germany, July 17, 2024 - AiCuris Anti-infective Cures AG, announced today multiple milestone achievements for letermovir (marketed by MSD as PREVYMIS®) and across its pipeline of anti-viral therapeutics serving the growing population of people whose immune systems are impacted due to disease or immunosuppressive therapies. These achievements recognize AiCuris' rapid progress in developing a clinical pipeline of precise therapies to effectively treat infections in a population for whom an otherwise manageable infection, can mean life or death.

"Our mission is to make a difference for people with weakened immune systems, by giving them options in preventing or treating infections that are life-threatening for them. The expanded approval of PREVYMIS® in Japan highlights its unique drug profile in diverse transplant settings where CMV infections pose a significant risk to adult patients on immunosuppressive therapies. Combined with the existing approvals in the U.S. and Europe, it provides further validation for the outstanding drug development capabilities of the AiCuris team and the benefit PREVYMIS® can provide for immunocompromised patients," said **Larry Edwards, CEO of AiCuris.** "It is our goal to achieve the same level of success for patients with our two follow-on pipeline programs pritelivir, which is close to pivotal Phase 3 read-out, and AIC468's first-in-human study starting in the near-term."

PREVYMIS® Update

In May, PREVYMIS® (letermovir) achieved approval in Japan for the use in adult patients receiving solid organ transplants (SOT). This significant milestone represents the first pan transplant indication approval for PREVYMIS®, a first-in-class antiviral agent commercialized by our partner MSD (tradename of Merck & Co., Inc., Rahway, N.J., USA) for the prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant and prophylaxis of CMV in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]). PREVYMIS® is marketed in over 60 countries. Following this achievement, AiCuris will receive a milestone payment of EUR €7.5 million from MSD.

Pipeline Updates

AiCuris published pharmacokinetic data for its lead candidate pritelivir (AIC316), an innovative therapeutic candidate targeting HSV replication, in May 2024. Pritelivir is currently being evaluated in a Phase 3 trial for the treatment of acyclovir-resistant HSV infections in immunocompromised patients. The study expects to complete patient enrollment in 1H 2025. The study titled "Evaluation of the Clinical Drug-Drug Interaction Potential of Pritelivir on Transporters and CYP450 Enzymes Using a Cocktail Approach" was recently published in the journal *Clinical Pharmacology in Drug Development* and provides data on the drug-drug interaction profile of pritelivir. The results demonstrated that pritelivir has a low risk of drug-drug interaction, as there was no effect on intestinal uptake and efflux transporters. These findings are crucial for ensuring the safety and efficacy of pritelivir as a treatment option for patients with resistant HSV infections, who are often receiving a range of additional treatments.

In addition, AiCuris' third pipeline candidate AIC468 is rapidly nearing the clinic after the regulatory approval of its clinical trial application by the German national authority. AIC468, an antisense RNA therapeutic candidate, is designed to treat BK virus (BKV) infection, which can lead to BKV-associated nephropathy, increasing the risk of chronic kidney failure or graft loss. AIC468 will be investigated in a first-in-human Phase 1 trial in healthy volunteers starting in Q3 of 2024. Up to 88 healthy individuals are expected to be enrolled in multiple single and multi-ascending dose cohorts with the objective to investigate safety and tolerability of AIC468. AIC468 specifically inhibits BKV replication, addressing the critical need to target the virus directly. By not compromising ongoing immunosuppressive treatments - the current standard of care – it helps to reduce the risk of graft loss. Preclinical studies have shown AIC468's mechanism of action effectively inhibits BKV replication in human kidney cells and achieved efficacious concentrations in kidney tissues *in vivo*. Additionally, a favorable pharmacokinetic and safety profile as well as a broad therapeutic window could be demonstrated preclinically warranting the start of clinical development.

"AiCuris is driving innovation in antiviral therapies with our pipeline candidates pritelivir and AIC468. The recent publication on pritelivir underscores its potential as a breakthrough treatment for acyclovir-resistant HSV infections for immunocompromised patients," **said Larry Edwards**. "Additionally, achieving Phase 1 approval for AIC468 marks a significant milestone in our efforts to address BK virus infections, showcasing promising preclinical efficacy data. We look forward to the upcoming data from these programs which will be important steppingstones in developing novel therapies for immunocompromised people."

About Prevymis®

PREVYMIS® (letermovir), developed by AiCuris and marketed by MSD, is indicated for prophylaxis of CMV infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant and prophylaxis of CMV in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]. The drug is marketed in more than 60 countries outside the U.S., including in the E.U., Canada, Japan and China, and has received approval for prevention of CMV infections in adult solid organ transplant (SOT) recipients in Japan in 2024. The recent approval for SOT in Japan is supported by robust clinical trials demonstrating its efficacy and safety in preventing CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative).

About Pritelivir

Pritelivir, a novel helicase-primase inhibitor developed by AiCuris, targets both HSV-1 and HSV-2. These viruses are responsible for genital, oral or disseminated infections with increasing severity and resistance development in immunocompromised people. Unlike traditional antivirals, pritelivir blocks viral DNA synthesis by inhibiting the helicase-primase complex, a mechanism distinct from nucleoside analogues like acyclovir. Earlier Phase 1 and Phase 2 trials in immune competent and immune compromised individuals showed a favorable safety profile and an improved clinical efficacy compared with standard of care treatments like valaciclovir and Foscarnet (including resistant or intolerant infections). Recognized with Breakthrough Therapy designation by the FDA for immunocompromised patients, pritelivir is currently advancing through a pivotal Phase 3 trial. The results of this trial will serve as a basis for filing for marketing authorization in 2026.

About AIC468

AIC468 is a pioneering RNA-based therapy designed to treat BK virus (BKV) reactivation in kidney transplant patients. BKV infections prove to be a significant clinical challenge, particularly for kidney transplant recipients, as they can lead to BKV-associated nephropathy, resulting in chronic kidney failure or graft loss. To date, there are no approved antiviral treatments for BKV; the only option is to reduce immunosuppression therapy, increasing the risk of graft rejection. AIC468 is an antisense oligonucleotide that targets viral replication within infected cells by inhibiting the splicing of mRNA coding for the BKV master regulator large T-antigen. This innovative approach has demonstrated favorable pharmacokinetics and significant inhibition of BKV replication in preclinical studies. AiCuris expects to initiate the first human trial for AIC468 in Q3 of 2024, aiming to provide a much-needed therapeutic option for kidney transplant patients at risk of BKV reactivation.

About Herpes Simplex Virus

Herpes Simplex Virus (HSV) includes two types, HSV-1 and HSV-2, both of which cause lifelong infections. HSV-1 typically leads to oral herpes, resulting in cold sores around the mouth, while HSV-2 is commonly associated with genital herpes. These viruses can cause recurrent painful blisters and sores, and in severe cases, complications such as encephalitis, disseminated disease and neonatal herpes. HSV infections are widespread globally, with a significant impact on public health, especially immunocompromised patients, due to their high prevalence, more severe and more frequent manifestations and increased potential for drug resistance.

About BK Virus

BK virus (BKV) is a polyomavirus that commonly infects the urinary tract. While it remains latent in most healthy individuals, it can reactivate in immunocompromised patients, such as those undergoing organ transplantation. Reactivation of BKV can lead to serious complications, including BK virus-associated nephropathy (BKVN), which can cause kidney dysfunction and graft loss in transplant recipients. Managing BKV infections is essential in immunocompromised patients to prevent significant morbidity and improve transplant outcomes.

About AiCuris

AiCuris is meeting the needs of the growing population of immunocompromised people who require precise therapies to effectively treat infection. Our flagship product, PREVYMIS®, marketed by our partner MSD, prevents CMV in a defined group of transplant recipients. Our pivotal Phase 3 candidate pritelivir aims to address recurrent and resistant HSV infections in a broad population of patients with weakened immune systems. For immunocompromised people, an otherwise manageable infection can mean life or death. AiCuris, with its expertise and growing pipeline, is committed to providing therapeutic solutions for them now and in the future.

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