

## PRESS RELEASE

# Basilea announces that European Commission approves isavuconazole (CRESEMBA®) as a treatment for invasive aspergillosis and mucormycosis in the European Union

- **Basilea's second anti-infective product approved in Europe, providing potential commercial synergy with Zevtera® (ceftobiprole)**

*Basel, Switzerland, October 16, 2015* – Basilea Pharmaceutica Ltd. (SIX: BSLN) announced today that the European Commission has approved the antifungal isavuconazole for the treatment of adult patients with invasive aspergillosis and for the treatment of adult patients with mucormycosis for whom amphotericin B is inappropriate. Invasive aspergillosis and mucormycosis are life-threatening fungal infections often occurring in patients with cancer and other immunocompromised patients. Isavuconazole will be marketed in Europe under the trade name CRESEMBA®.

Ronald Scott, Basilea's Chief Executive Officer, said: "The European approval of CRESEMBA for the treatment of invasive aspergillosis and mucormycosis is a key milestone for Basilea. It provides us with the unique opportunity to launch CRESEMBA as our second hospital anti-infective in Europe and offers an important new therapeutic option to healthcare professionals and their patients suffering from these life-threatening fungal infections."

David Veitch, Basilea's Chief Commercial Officer added: "CRESEMBA and our broad-spectrum antibiotic Zevtera both target serious hospital infections. There is a significant overlap of the prescribing physicians for both brands, thus providing a substantial commercial synergy in Europe."

The European Commission followed the positive opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency recommending the approval of isavuconazole. The marketing authorization for isavuconazole will be valid in all 28 European Union (EU) member states, as well as in Iceland, Liechtenstein and Norway.

### Progress update on programs

With the approval of **CRESEMBA®** (isavuconazole) in Europe, Basilea expects to initiate a commercial launch of the drug in major European countries in early 2016.

**Zevtera® or Mabelio®** (ceftobiprole medocartil) is currently approved in 13 European countries<sup>1</sup> and Canada and has been launched in Germany, France, Italy and the United Kingdom. A launch in Switzerland is planned for the fourth quarter of 2015 or early 2016, and launches in other countries through distributors or licensors. In the United States, ceftobiprole was designated as a Qualified Infectious Disease Product (QIDP) for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI). Ceftobiprole is not approved in the United States. Basilea is currently determining the phase 3 regulatory and development path for ceftobiprole in the United States. The company plans to have discussions with the U.S. Food and Drug Administration (FDA) about the design of a clinical phase 3 program. Basilea believes that two cross-supportive phase 3 studies in CABP and ABSSSI, if successful, may be sufficient to obtain U.S. regulatory approval for both indications. Basilea

may also initiate a phase 3 study in bacteremia (blood stream infections) caused by *Staphylococcus aureus*, an area of high medical need.

An inhalable formulation of the antibiotic **BAL30072** with activity against many clinically relevant multidrug-resistant Gram-negative bacteria is being developed and currently advanced into preclinical studies under an agreement with the iABC consortium (inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis) for the potential treatment of chronic lung infections, the main cause of disease and mortality in patients with bronchiectasis and cystic fibrosis.

Basilea's tumor checkpoint controller **BAL101553** is being investigated in two separate phase 1/2a studies with an oral and an intravenous formulation in adult patients with advanced solid tumors. Initial topline data for the intravenous phase 2a study are expected by the end of 2015, and topline data for the phase 1 portion of the oral study are expected in 2016.

**BAL3833** is an orally available anti-cancer product candidate, a panRAF kinase inhibitor that has progressed into a phase 1/2a study enrolling patients with advanced solid tumors.

### About the isavuconazole studies

The approval of CRESEMBA® is based on results from the isavuconazole development program. The safety and efficacy profile of isavuconazole in adult patients with invasive aspergillosis was demonstrated based on data from two phase 3 clinical studies: SECURE, a randomized, double-blind, active-control study in 516 patients (intent-to-treat population, ITT) with invasive aspergillosis, and VITAL, an open-label non-comparative 146-patient study (ITT) of isavuconazole in the treatment of invasive aspergillosis patients with renal impairment, or invasive fungal disease (IFD) caused by rare molds, yeasts or dimorphic fungi, including invasive mucormycosis.

In the SECURE study, isavuconazole was non-inferior to voriconazole based on the primary endpoint of all-cause mortality at Day 42 in the intent-to-treat population. All-cause mortality through Day 42 was 18.6% in the isavuconazole treatment group and 20.2% in the voriconazole treatment group.<sup>2</sup>

In the SECURE study, similar rates of non-fatal adverse events were observed for isavuconazole and the comparator, voriconazole. Further, the percentage of study drug-related adverse events in invasive aspergillosis patients was 42% for isavuconazole and 60% for voriconazole. In addition, the percentage of treatment-emergent adverse events in the system organ classes of hepatobiliary was 9% for isavuconazole versus 16% for voriconazole; skin was 33% for isavuconazole versus 42% for voriconazole; and eye was 15% for isavuconazole versus 27% for voriconazole.<sup>2</sup>

The safety and efficacy profile of isavuconazole in patients with mucormycosis was demonstrated based on data from the VITAL study, which included a subpopulation of 37 patients with proven or probable mucormycosis, of whom 21 received isavuconazole as primary treatment for their infection. All-cause mortality at Day 42 was 38% which is similar to mortality rates reported in literature for the treatment of mucormycosis. In this trial the rate of overall response against mucormycosis at the end of therapy was 31%, with an additional 29% exhibiting a stable response. For patients receiving isavuconazole as primary therapy, this number was 32%, with an additional 32% having stable disease. The efficacy of isavuconazole for the treatment of mucormycosis has not been evaluated in concurrent, controlled clinical trials.

The most frequent adverse events for patients treated with isavuconazole in clinical phase 3 studies were nausea (26%), vomiting (25%), diarrhea (22%), headache (17%), elevated liver chemistry tests (17%), hypokalemia (14%), constipation (13%), dyspnea (12%), cough (12%), peripheral edema (11%), and back pain (10%).

## About invasive aspergillosis and mucormycosis

Invasive aspergillosis and mucormycosis are life-threatening fungal infections that often affect immunocompromised patients, such as patients with cancer. Invasive aspergillosis is known for high morbidity and mortality. Mucormycosis (also known as zygomycosis) is a rapidly progressing and life-threatening invasive fungal infection, known for high morbidity and mortality.

## About isavuconazole

Isavuconazole is an intravenous and oral azole antifungal and the active agent of the prodrug isavuconazonium sulfate. The drug is being co-developed with Astellas Pharma Inc. under an agreement granting Astellas a license to commercialize isavuconazole in the U.S.; Basilea holds full rights to commercialize isavuconazole in markets outside the United States. On March 6, 2015, the United States Food and Drug Administration (FDA) approved Astellas' New Drug Application (NDA) for the use of isavuconazonium sulfate for patients 18 years of age and older in the treatment of invasive aspergillosis and invasive mucormycosis. Astellas markets the drug as CRESEMBA® in the United States.

## About Basilea

Basilea Pharmaceutica Ltd. is a biopharmaceutical company developing products that address increasing resistance and non-response to current treatment options in the therapeutic areas of bacterial infections, fungal infections and cancer. The company uses the integrated research, development and commercial operations of its subsidiary Basilea Pharmaceutica International Ltd. to discover, develop and commercialize innovative pharmaceutical products to meet the medical needs of patients with serious and potentially life-threatening conditions. Basilea Pharmaceutica Ltd. is headquartered in Basel, Switzerland and listed on the SIX Swiss Exchange (SIX: BSLN). Additional information can be found at Basilea's website [www.basilea.com](http://www.basilea.com).

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This press release can be downloaded from [www.basilea.com](http://www.basilea.com).

## References

- 1 Ceftobiprole (European trade name Zevtera® or Mabelio®, depending on the country) has received national licenses in 13 European countries for the treatment of adult patients with community- and hospital-acquired pneumonia (CAP, HAP), excluding ventilator-associated pneumonia (VAP): Austria, Belgium, Denmark, Finland, France, Germany, Italy, Luxembourg, Norway, Spain, Sweden, Switzerland and the United Kingdom.

- 2 A. J. Ullmann et al. A comparison of the safety profiles of isavuconazole vs voriconazole in the phase 3 SECURE study in patients with invasive mould infections. European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) 2015, ePoster EP018;  
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