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Press release

Basilea provides updates on efficacy data with derazantinib in bile duct cancer and on ongoing clinical programs in urothelial and gastric cancer

- **An updated analysis shows further improvement of progression-free survival, disease control rate and objective response rate in the cohort of FGFR2 gene fusion-positive patients with bile duct cancer (iCCA) in FIDES-01 study**
- **Pursuing intensified dose regimen in FIDES-02 urothelial cancer study and FIDES-03 gastric cancer study**

Basel, Switzerland, May 31, 2021

Basilea Pharmaceutica Ltd. (SIX: BSLN) today reported updated response data from cohort 1 of the FIDES-01 study. The cohort is assessing the anti-tumor efficacy of the orally administered fibroblast growth factor receptor (FGFR) inhibitor, derazantinib, in patients with FGFR2 gene fusion-positive intrahepatic cholangiocarcinoma (iCCA), a form of bile duct cancer.[1] The positive efficacy data further substantiate the clinical proof-of-concept of derazantinib as monotherapy in iCCA.

FIDES-01: ICCA

Topline results for cohort 1 of the FIDES-01 study were presented in early February 2021.[2] An updated analysis based on a data cut-off in April 2021 has now been completed and shows that the objective response rate (ORR) increased from 20.4% to 21.4%, the disease control rate (DCR) from 72.8% to 74.8% and the median progression-free survival (PFS) from 6.6 to 7.8 months, further supporting the clinically relevant efficacy for derazantinib monotherapy in this indication.

Dr. Marc Engelhardt, Chief Medical Officer, said: “We are very pleased with the more mature results from the first fully enrolled patient cohort of the FIDES-01 study. The progression-free survival of 7.8 months is in the upper range reported for this endpoint with FGFR-inhibitors in this patient population. Derazantinib also continues to show a well-manageable safety profile, with low rates of retinal side effects, stomatitis, hand-foot syndrome and nail toxicity. Overall, these results underscore the favorable benefit to risk profile of derazantinib as a monotherapy in bile duct cancer.”

He added: “We are also making good progress in cohort 2 of the study, which is enrolling iCCA patients with FGFR2 gene mutations or amplifications. We have achieved about 50% of target enrolment and are aiming to report topline results in the first half of 2022. If the encouraging results from the recently reported interim results are confirmed upon completion of the study,

this will further strengthen the evidence of a differentiated efficacy and safety profile for derazantinib in bile duct cancer."

FIDES-02: Urothelial cancer

Basilea had decided to explore an intensified dose regimen in several cohorts with derazantinib monotherapy and combination therapy in the FIDES-02 study in patients with urothelial cancer.[3] Based on interim efficacy data from the ongoing cohort of FGFR-inhibitor naive patients in a second-line or later setting receiving derazantinib monotherapy at a dose of 300 mg per day, this cohort will not be further expanded and Basilea will focus patient enrolment on the intensified dose regimen of 400 mg per day, with the goal to maximize efficacy in this patient population. The approach is based on the available clinical data and supported by pharmacology data.

Dr. Engelhardt commented: "Derazantinib monotherapy at a dose of 300 mg per day has shown to be efficacious and safe in patients with iCCA, and has also provided signs of clinical benefit in the ongoing FIDES-02 urothelial cancer study. The unmet medical need in advanced urothelial cancer remains high. At the same time new standard-of-care treatment options are evolving and the benchmarks of anticancer efficacy for new treatments are increasing. Derazantinib dose levels above 300 mg per day have previously been studied and we believe that the intensified dose regimen of 400 mg per day could provide additional overall clinical benefit in advanced urothelial cancer."

FIDES-03: Gastric cancer

Dr. Engelhardt added: "We believe that patients with advanced gastric cancer may also benefit from an intensified dose regimen of derazantinib. We will therefore amend the FIDES-03 study to explore a dose of 400 mg per day going forward."

Future data readouts

Basilea continues to expect the first interim efficacy results from the FIDES-02 urothelial cancer study, in patients at a dose of 300 mg per day, refractory to prior FGFR-inhibitor treatment, in both monotherapy and in combination with atezolizumab, in the second half of 2021.

Initial results from cohorts utilizing the intensified dose regimen of derazantinib 400 mg per day are expected in the first half of 2022. For FIDES-02 in urothelial cancer, this will include interim efficacy data as monotherapy, in a second- and post-second-line setting, as well as atezolizumab combination data in the first-line treatment of cisplatin-ineligible patients. For FIDES-03 in gastric cancer, this will include interim efficacy data with derazantinib in monotherapy and the recommended phase 2 dose (RP2D) of derazantinib combined with ramucirumab and paclitaxel.

The results from cohort 1 of FIDES-01 and the interim results from the 300 mg per day monotherapy cohort in FGFR-inhibitor naive patients in a second-line or later setting of FIDES-02 will be published upon completion of the cohorts at future scientific conferences.

About derazantinib

Derazantinib is an investigational orally administered small-molecule FGFR inhibitor with strong activity against FGFR1, 2, and 3.[4] FGFR kinases are key drivers of cell proliferation, differentiation and migration. FGFR genetic aberrations, e.g. gene fusions, mutations or amplifications, have been identified as potentially important therapeutic targets for various cancers, including intrahepatic cholangiocarcinoma (iCCA), urothelial, breast, gastric and lung cancers.[5] In these cancers, FGFR genetic aberrations are found in a range of 5% to 30%.[6] Derazantinib also inhibits the colony-stimulating-factor-1-receptor kinase (CSF1R).[4, 7] CSF1R-mediated signaling is important for the maintenance of tumor-promoting macrophages and therefore has been identified as a potential target for anti-cancer drugs.[8] Pre-clinical data has shown that tumor macrophage depletion through CSF1R blockade renders tumors more responsive to T-cell checkpoint immunotherapy, including approaches targeting PD-L1/PD-1.[9, 10] Derazantinib has demonstrated antitumor activity and a manageable safety profile in a previous biomarker-driven phase 1/2 study in iCCA patients,[11] and has received U.S. and EU orphan drug designation for iCCA. Basilea is currently conducting three clinical studies with derazantinib. The first study, FIDES-01, is a phase 2 study in patients with inoperable or advanced iCCA. It comprises one cohort of patients with FGFR2 gene fusions and another cohort of patients with mutations or amplifications.[1] The second study, FIDES-02, is a phase 1/2 study evaluating derazantinib alone and in combination with Roche's PD-L1 checkpoint inhibitor, atezolizumab, in patients with advanced urothelial cancer, including metastatic, or recurrent surgically unresectable disease, expressing FGFR genetic aberrations.[12] The third study, FIDES-03, is a phase 1/2 study evaluating derazantinib alone and in combination with Lilly's anti-VEGFR2 antibody ramucirumab and paclitaxel, or with Roche's PD-L1 checkpoint inhibitor atezolizumab, in patients with advanced gastric cancer with FGFR genetic aberrations.[13] Basilea has in-licensed derazantinib from ArQule Inc., a wholly-owned subsidiary of Merck & Co., Inc., Kenilworth, N.J., U.S.A.

About intrahepatic cholangiocarcinoma

Intrahepatic cholangiocarcinoma (iCCA) is a cancer originating from the biliary system. The age-adjusted incidence rate of iCCA in the United States has been increasing over the past decade and is currently estimated to be approximately 1.2 per 100,000.[14] Patients are often diagnosed with advanced or metastatic disease that cannot be surgically removed. Current first-line standard of care is the chemotherapy combination of gemcitabine and platinum-derived agents. The prognosis for patients with advanced disease is poor, with a median survival of less than one year.[15]

About urothelial cancer

These cancers start in the urothelial cells that line the inside of the bladder. 80,000 new cases of bladder cancer have been estimated in the U.S. for 2017. Up to 20% of patients will have muscle-invasive disease and present with or will later develop metastases.[16] FGFR gene aberrations occur in about 15-20% of advanced urothelial cancers.[17, 18] For patients with advanced urothelial cancer, outcomes can be poor due to the often rapid progression of the tumor and the lack of efficacious treatments, especially in relapsed or refractory disease.

About gastric cancer

Gastric cancer is the fifth most common cancer worldwide and the third most lethal cancer type.[19] Median survival rarely exceeds twelve months and the five-year-survival is less than 10%.[20] Basilea estimates that there are approximately 190,000 new cases of gastric cancer per year in total across the EU top 5 countries, Japan and the U.S. FGFR genetic aberrations have been observed in about 10% of gastric cancers.[21]

About Basilea

Basilea is a commercial-stage biopharmaceutical company founded in 2000 and headquartered in Switzerland. We are committed to discovering, developing and commercializing innovative drugs to meet the medical needs of patients with cancer and infectious diseases. We have successfully launched two hospital brands, Cresemba for the treatment of invasive fungal infections and Zevtera for the treatment of severe bacterial infections. We are conducting clinical studies with two targeted drug candidates for the treatment of a range of cancers and have a number of preclinical assets in both cancer and infectious diseases in our portfolio. Basilea is listed on the SIX Swiss Exchange (SIX: BSLN). Please visit basilea.com.

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This press release can be downloaded from www.basilea.com.

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