PRESS RELEASE

Basilea reports at ESMO meeting that drug candidate derazantinib showed clinical benefit in intrahepatic cholangiocarcinoma (iCCA) patients with various FGFR2 genetic aberrations

Basel, Switzerland, September 30, 2019 – Basilea Pharmaceutica Ltd. (SIX: BSLN) reported today that a post-hoc analysis of efficacy data from a previously completed phase 1/2 study with its oncology drug candidate derazantinib in patients with intrahepatic cholangiocarcinoma (iCCA) was presented at the Annual Congress of the European Society for Medical Oncology (ESMO) in Barcelona, Spain, on September 29, 2019. The analysis shows that derazantinib provided clinically meaningful anti-tumor activity, not only in iCCA patients with FGFR2 gene fusions, but also in iCCA patients with FGFR2 gene mutations and amplifications.

Dr. Marc Engelhardt, Basilea's Chief Medical Officer, said: "The data presented at ESMO indicate that derazantinib may provide clinical benefit in a broader iCCA population, including patients with FGFR2 gene mutations and amplifications as well as FGFR2 gene fusions. We have therefore recently extended our ongoing phase 2 registrational study with a cohort enrolling patients with FGFR2 gene mutations and amplifications, in addition to the ongoing cohort of patients with FGFR2 gene fusions. Activity of derazantinib in patients with FGFR2 gene mutations and amplifications could be an important differentiation factor in this indication and would address an important unmet medical need."

The post-hoc analysis is based on data from 44 patients with locally advanced, inoperable or metastatic iCCA with either FGFR2 gene fusions, mutations or amplifications, or no FGFR2 genetic aberrations at all, who received once-daily oral derazantinib in a previously completed non-comparative phase 1/2 study.[1] The analysis shows that the disease control rates (DCRs), comprising all patients with partial response and stable disease as best responses to treatment, were similar across the groups of iCCA patients with the different FGFR2 genetic aberrations.

DCRs were 67% for patients with FGFR2 gene mutations or amplifications compared to 83% for patients with FGFR2 gene fusions. Median duration of disease control and median progression-free survival were also similar at 8.6 months vs. 8.1 months and 6.7 months vs. 5.7 months, respectively. Overall, clinical meaningful response, defined as partial responses and stable diseases lasting more than six months, was achieved in 50% of the iCCA patients with FGFR2 gene mutations or amplifications compared to 45% in the FGFR2 gene fusions group. ICCA patients without any FGFR2 genetic aberration did not respond to treatment with derazantinib, which is consistent with previous reports.

The safety profile of derazantinib was consistent across all patient groups. The analysis suggests that the iCCA patient populations that may benefit from derazantinib could be expanded to FGFR2 gene mutations and amplifications. Previously, FGFR2 gene fusions had been identified as oncogenic drivers in iCCA and as susceptible for treatment with derazantinib. Based on these results, Basilea recently extended its ongoing phase 2 registrational study in iCCA with a cohort enrolling patients with FGFR2 gene mutations and amplifications.[2]

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Derazantinib abstract at the 2019 ESMO Annual Congress

- Efficacy of derazantinib (DZB) in patients (pts) with intrahepatic cholangiocarcinoma (iCCA) expressing *FGFR2*-fusion or *FGFR2* mutations/amplifications – Michele Droz Dit Busset, Stephan Braun, Bassel F. El-Rayes, William Proctor Harris, Nevena Damjanov, Gianluca Masi, Lorena Rimassa, Sherri Bhoori, Monica Niger, Nicola Personeni, Fadi S. Braiteh, Sara Lonardi, Marc Engelhardt, Mikael Saulay, Brian E. Schwartz, Walid Labib Shaib, Vincenzo Mazzaferro, Kyriakos P. Papadopoulos; abstract 3879. ClinicalTrials.gov identifier: NCT01752920

For further information, please visit https://www.esmo.org/Conferences/ESMO-Congress-2019.

About derazantinib

Derazantinib (formerly ARQ 087) is an investigational orally administered small-molecule panFGFR kinase inhibitor with strong activity against FGFR1, 2, and 3.[3] 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.[4] In these cancers, FGFR genetic aberrations are found in a range of 5% to 30%.[5]
In iCCA, the estimated prevalence of FGFR2 gene fusions is 13-22%.[6, 7] FGFR2 gene mutations and amplifications are less frequent and account for about 10% of FGFR2 genetic aberrations in iCCA.[7]
Derazantinib also inhibits the colony-stimulating-factor-1-receptor kinase (CSF1R).[3] 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]
Basilea in-licensed derazantinib from ArQule Inc. in April 2018. Derazantinib has demonstrated antitumor activity and a manageable safety profile in previous clinical studies, including a biomarker-driven phase 1/2 study in iCCA patients,[1] and has received U.S. and EU orphan drug designation for iCCA. Basilea is currently conducting two clinical studies with derazantinib. The first study, FIDES-01, is a registrational phase 2 study in patients with iCCA with FGFR2 gene fusions or mutations and amplifications.[2] The second study, FIDES-02, is a phase 1/2 study evaluating derazantinib alone and in combination with Roche's PD-L1-blocking immune-checkpoint inhibitor atezolizumab (Tecentriq®) in patients with advanced urothelial cancer, including metastatic, or recurrent surgically unresectable disease, expressing FGFR genetic aberrations.[11]

About intrahepatic cholangiocarcinoma (ICCA)

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.[12] 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 with chemotherapy.[13] There is no proven effective treatment for patients who progress on first-line chemotherapy, thus there is a high unmet medical need.[14]

About Basilea

Basilea Pharmaceutica Ltd. is a commercial stage biopharmaceutical company, focused on the development of products that address the medical challenges in the therapeutic areas of oncology and anti-infectives. With two commercialized drugs, the company is committed to discovering, developing and commercializing innovative pharmaceutical products to meet the medical needs of patients with serious and 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.

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

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