Basilea Pharmaceutica Ltd.
Grenzacherstrasse 487 | PO Box | 4005 Basel | Switzerland
basilea.com

Press release

Basilea reports positive topline results from phase 2 study FIDES-01 for derazantinib in FGFR2 gene fusion-positive patients with bile duct cancer (iCCA)

- **Clinical proof of concept achieved for derazantinib monotherapy in FGFR2 gene fusion-positive iCCA**
- **20.4% objective response rate and 6.6 months median progression-free survival consistent with previously published interim results**
- **Safety and tolerability profile confirmed**

Basel, Switzerland, February 10, 2021

Basilea Pharmaceutica Ltd. (SIX: BSLN) announced today topline results from cohort 1 of the phase 2 study FIDES-01, which is assessing the anti-tumor efficacy of the orally administered fibroblast growth factor receptor (FGFR) inhibitor, derazantinib, in patients with inoperable or advanced intrahepatic cholangiocarcinoma (iCCA), a form of bile duct cancer, and confirmed FGFR2 gene fusions.[1] Patient enrolment into cohort 1 was completed in July 2020. Enrolment into cohort 2 of FIDES-01 is ongoing, assessing the activity of derazantinib in iCCA patients with FGFR2 gene mutations or amplifications.

In total, 103 patients with iCCA and FGFR2 gene fusions who had received at least one prior chemotherapy regimen were enrolled in the intent-to-treat population in cohort 1. The objective response rate (ORR) is 20.4% based on 21 patients with a confirmed partial response. ORR is the pre-defined primary efficacy endpoint for cohort 1 and has been assessed through an independent central radiology review. The disease control rate (DCR), reflecting the proportion of patients with a partial response or with stable disease, was 72.8%. The median progression-free survival (PFS) in patients was 6.6 months. The results are not yet fully mature, as 12 patients are still ongoing, including 3 patients with a partial response. Consistent with previous data, derazantinib has shown a well manageable safety profile. The most common drug-related adverse events reported for once-daily oral 300 mg derazantinib were hyperphosphatemia (elevated phosphate levels in the blood), asthenia (weakness)/fatigue, increased liver enzymes, nausea, dry mouth, dry eye, diarrhea and dysgeusia (distorted taste). The percentage of patients experiencing drug-related adverse events of nail toxicities was low (6%) and events of retinopathy, stomatitis or hand-foot syndrome were each reported in only 1% of patients.

Dr. Marc Engelhardt, Chief Medical Officer, said: “We are very pleased that the positive topline results from the first cohort of the FIDES-01 study provide the clinical proof of concept for derazantinib as monotherapy in its first indication, although the data are not fully mature yet and a number of patients are still continuing their treatment. The efficacy results shown with

derazantinib are consistent with the efficacy seen with FGFR inhibitors as a class in FGFR2 gene fusion-positive iCCA patients, and the safety and tolerability data strengthen the evidence for derazantinib's potential differentiation versus other FGFR inhibitors."

He continued: "We expect the publication of a number of interim and topline results across the entire FIDES clinical program throughout 2021 and 2022. Based on its unique kinase inhibition profile, derazantinib has potential for enhanced activity in combination therapy. We are therefore particularly interested to see the first efficacy data on the combination of derazantinib with other anti-cancer agents in our urothelial and gastric cancer studies, which may allow us to further strengthen the evidence for its differentiation versus other FGFR inhibitors both from the efficacy and safety perspective. The upcoming data read-outs across different patient populations and indications both as monotherapy and combination therapy will also help us determine the optimal overall regulatory strategy for derazantinib."

About derazantinib

Derazantinib is an investigational orally administered small-molecule FGFR inhibitor with strong activity against FGFR1, 2, and 3.[2] 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.[3] In these cancers, FGFR genetic aberrations are found in a range of 5% to 30%.[4] Derazantinib also inhibits the colony-stimulating-factor-1-receptor kinase (CSF1R).[2, 5] 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.[6] 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.[7, 8] Derazantinib has demonstrated antitumor activity and a manageable safety profile in a previous biomarker-driven phase 1/2 study in iCCA patients,[9] 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.[10] 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.[11] Basilea 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.[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.[13]

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 infectious diseases. 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.

Disclaimer

This communication expressly or implicitly contains certain forward-looking statements, such as "believe", "assume", "expect", "forecast", "project", "may", "could", "might", "will" or similar expressions concerning Basilea Pharmaceutica Ltd. and its business, including with respect to the progress, timing and completion of research, development and clinical studies for product candidates. Such statements involve certain known and unknown risks, uncertainties and other factors, which could cause the actual results, financial condition, performance or achievements of Basilea Pharmaceutica Ltd. to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Basilea Pharmaceutica Ltd. is providing this communication as of this date and does not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.

For further information, please contact:

Peer Nils Schröder, PhD

Head of Corporate Communications & Investor Relations

Phone +41 61 606 1102

E-mail media_relations@basilea.com
investor_relations@basilea.com

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

References

1. FIDES-01: ClinicalTrials.gov identifier: NCT03230318
2. T. G. Hall, Y. Yu, S. Eathiraj et al. Preclinical activity of ARQ 087, a novel inhibitor targeting FGFR dysregulation. PLoS ONE 2016, 11 (9), e0162594
3. R. Porta, R. Borea, A. Coelho et al. FGFR a promising druggable target in cancer: Molecular biology and new drugs. Critical Reviews in Oncology/Hematology 2017 (113), 256-267
4. T. Helsten, S. Elkin, E. Arthur et al. The FGFR landscape in cancer: Analysis of 4,853 tumors by next-generation sequencing. Clinical Cancer Research 2016 (22), 259-267
5. P. McSheehy, F. Bachmann, N. Forster-Gross et al. Derazantinib (DZB): A dual FGFR/CSF1R-inhibitor active in PDX-models of urothelial cancer. Molecular Cancer Therapeutics 2019 (18), 12 supplement, pp. LB-C12
6. M. A. Cannarile, M. Weisser, W. Jacob et al. Colony-stimulating factor 1 receptor (CSF1R) inhibitors in cancer therapy. Journal for ImmunoTherapy of Cancer 2017, 5:53
7. Y. Zhu, B. L. Knolhoff, M. A. Meyer et al. CSF1/CSF1R Blockade reprograms tumor-infiltrating macrophages and improves response to T cell checkpoint immunotherapy in pancreatic cancer models. Cancer Research 2014 (74), 5057-5069
8. E. Peranzoni, J. Lemoine, L. Vimeux et al. Macrophages impede CD8 T cells from reaching tumor cells and limit the efficacy of anti–PD-1 treatment. Proceedings of the National Academy of Science of the United States of America 2018 (115), E4041-E4050
9. V. Mazzaferro, B. F. El-Rayes, M. Droz dit Busset et al. Derazantinib (ARQ 087) in advanced or inoperable FGFR2 gene fusion-positive intrahepatic cholangiocarcinoma. British Journal of Cancer 2019 (120), 165-171. ClinicalTrials.gov identifier: NCT01752920
10. FIDES-02: ClinicalTrials.gov identifier: NCT04045613
11. FIDES-03: ClinicalTrials.gov identifier: NCT04604132
12. S. K. Saha, A. X. Zhu, C. S. Fuchs et al. Forty-year trends in cholangiocarcinoma incidence in the U.S.: intrahepatic disease on the rise. The Oncologist 2016 (21), 594-599
13. A. Lamarca, D. H. Palmer, H. S. Wasa et al. ABC-06 | A randomised phase III, multi-centre, open-label study of Active Symptom Control (ASC) alone or ASC with oxaliplatin/5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced/metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy. Journal of Clinical Oncology 2019 (37), supplement, abstract 4003