

Press release

Basilea reports data from poster presentations at ESMO Virtual Congress 2020

- **Gene expression data may explain differences in clinical adverse event profiles of FGFR inhibitors**
- **Antitumor activity of derazantinib in preclinical cancer models with FGFR aberrations supports planned gastric cancer study**
- **Full results from the completed phase 1 study in patients with brain cancer underscores the potential for lisavanbulin to be developed in a targeted patient population using end-binding protein 1 (EB1) as a patient selection criterion**

Basel, Switzerland, September 22, 2020

Basilea Pharmaceutica Ltd. (SIX: BSLN) today reports on several e-posters with new preclinical and clinical data on its fibroblast growth factor receptor (FGFR) inhibitor derazantinib and its tumor checkpoint controller, lisavanbulin, presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2020, which took place from 19-21 September, 2020.

A preclinical study showed that treatment-specific gene expression patterns in tumor models may help elucidating the biological processes driving differences in the clinical adverse event profiles of FGFR inhibitors. Moreover, the results from this study may explain low rates of adverse events reported with derazantinib for retinal events, mucositis and nail toxicities.

Results from a series of preclinical efficacy models of breast, colorectal, head & neck, lung, ovarian and gastric cancer with confirmed FGFR1-3 genetic aberrations, showed that FGFR2-fusion-positive gastric cancer models were particularly sensitive to treatment with derazantinib. In addition, gastric and lung cancer models showed the strongest correlation of FGFR1-3 expression versus the anticancer activity of derazantinib. The results support the planned clinical investigation of derazantinib in gastric cancer as its next indication.

Full results from a phase 1 study with once-daily oral lisavanbulin in adult patients with recurrent glioblastoma (GBM), or high-grade glioma, showed an overall clinical benefit rate of 44% at six months at daily doses of 25-30 mg. There was an exceptional long-lasting response in a patient, whose tumor tissue was positive for end-binding protein 1 (EB1), a previously identified response predictive biomarker for lisavanbulin in preclinical studies. A phase 2 expansion study will be initiated shortly, which will use EB1-positivity as a patient selection criterion.¹ Lisavanbulin is dosed at the recommended phase 2 dose of 25 mg/day in this phase 2 study in patients with recurrent GBM. The prevalence of EB1-positivity in GBM is estimated at 2-5%.

Dr. Marc Engelhardt, Chief Medical Officer, said: “The results presented at ESMO support our differentiation strategy for derazantinib, which is based on its unique kinase inhibition profile and its clinical safety profile. They also provide the preclinical rationale for our decision to initiate a clinical study of derazantinib alone and in combination with other therapies in patients with advanced gastric cancer. The full results from the completed phase 1 study with lisavanbulin underscore its potential to be developed in a targeted patient population. Our initial focus will be on glioblastoma. We may decide to explore other tumor types upon achieving clinical validation of EB1 as a response-predictive biomarker in glioblastoma.”

The following e-posters were presented at ESMO Virtual Congress 2020:

Presentation #	Title
1960P	Differential induction of gene expression may explain differences in reported adverse event profiles between the FGFR-inhibitors derazantinib and erdafitinib: an analysis in safety relevant normal tissues from urothelial cancer (UC) patient-derived mouse xenograft (PDX) models.
541P	Derazantinib (DZB), an oral Fibroblast Growth Factor Receptor inhibitor (FGFRi), shows promising activity in PDX-tumor models with aberrations in FGFR1-3
382P	The potential utility of end-binding protein 1 (EB1) as response-predictive biomarker for lisavanbulin: Final results from a phase 1 study of lisavanbulin (BAL101553) in adult patients with recurrent glioblastoma (GBM)

For further information, please visit <https://www.esmo.org/meetings/esmo-virtual-congress-2020>

About derazantinib

Derazantinib is an investigational orally administered small-molecule FGFR kinase 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 Preclinical 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 previous

clinical studies, including a 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 two clinical studies with derazantinib. The first study, FIDES-01, is a registrational 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.¹⁰ 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®)¹¹ in patients with advanced urothelial cancer, including metastatic, or recurrent surgically unresectable disease, expressing FGFR genetic aberrations.¹²

Basilea in-licensed derazantinib from ArQule Inc, a wholly-owned subsidiary of Merck & Co., Inc., Kenilworth, N.J., U.S.A.

About lisavanbulin (BAL101553)

Basilea's oncology drug candidate lisavanbulin (BAL101553, the prodrug of BAL27862)¹³ is being developed as a potential therapy for diverse cancers.^{1, 14, 15} In preclinical studies, lisavanbulin demonstrated in-vitro and in-vivo activity against diverse treatment-resistant cancer models, including tumors refractory to conventional approved therapeutics and radiotherapy.^{16, 17, 18} Lisavanbulin efficiently distributes to the brain, with anticancer activity in glioblastoma models.^{19, 20, 21} In preclinical studies, end-binding protein 1 (EB1) was identified as a potential response-predictive biomarker in glioblastoma models.²¹ The active moiety BAL27862 binds to the colchicine site of tubulin, with distinct effects on microtubule organization,²² resulting in the activation of the "spindle assembly checkpoint" which promotes tumor cell death.²³

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.

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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. Derazantinib and its uses are investigational and have not been approved by a regulatory authority for any use. Efficacy and safety have not been established. The information presented should not be construed as a recommendation for use. The relevance of findings in nonclinical/preclinical studies to humans is currently being evaluated.

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

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