PRESS RELEASE

Basilea reports presentation of data on clinical oncology programs BAL101553 and BAL3833 at ASCO meeting

- **Clinical data reported from completed phase 1/2a study of BAL101553, with once-weekly 2-hour infusion showing signals of clinical activity**
- **Design of ongoing phase 1/2a study with once-daily oral BAL101553 presented, with four dose cohorts completed**
- **Design of ongoing BAL3833 oral phase 1 study presented, with four dose cohorts completed**

Basel, Switzerland, June 9, 2016 – Basilea Pharmaceutica Ltd. (SIX: BSLN) announced today that the final clinical data from the first-in-human phase 1/2a study with the intravenous (i.v.) form of its tumor checkpoint controller BAL101553 were presented at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago, USA, on June 3-7, 2016. The study showed signals of clinical activity at doses associated with a promising safety profile. In addition, the design of a phase 1/2a study with the oral formulation of BAL101553 given once daily as well as the design of the first-in-human phase 1 study with the oral panRAF/SRC kinase inhibitor BAL3833 were presented. Dose-escalation in these studies is currently ongoing.

In the open-label phase 1/2a study, i.v. BAL101553 was administered over two hours on days 1, 8 and 15 of 28-day treatment cycles to patients with advanced solid tumors who failed standard therapy or for whom no effective standard therapy was available. Based on preclinical data and the evaluation of a range of biomarkers, patients with colorectal cancer, non-small cell lung cancer, pancreatic, ovarian, gastric and triple negative breast cancer were included in the phase 2a part of the study.

Across the entire study, out of the 59 patients who were evaluable for efficacy, 39 patients received 30 mg/m^2 as starting dose or after adjustment. Of these 39 patients, one long-lasting partial response of more than two years and one prolonged stable disease of six months were observed in two patients with ampullary (pancreaticobiliary) cancers. Nine additional patients presented stable disease lasting between two and eight months. Overall, the drug was well-tolerated in the 15-30 mg/m^2 dose groups; these patients were on treatment longer and showed more signals of clinical activity than patients treated at higher doses of 45-80 mg/m^2. This may be related to different tumor vascular effects at low versus high BAL101553 doses.

The recommended Phase 2 dose for BAL101553 when given as a 2-hour infusion once per week was therefore determined to be 30 mg/m^2. Dose-limiting adverse effects at higher dosages included transient and reversible grade 2 to grade 3 gait disturbance, which occurred together with transient grade 1 to grade 2 peripheral sensory neuropathy, and asymptomatic and reversible myocardial ischemia. These adverse effects appeared to be primarily related to the peak drug plasma concentration (C_{max}), while preclinical data[1] indicate that the anti-proliferative effects are driven by total drug exposure (area under the curve, AUC). This suggests that there may be a possibility to further widen the therapeutic window of BAL101553 through alternative dosing regimens, such as using daily oral dosing. After completion of four dose cohorts, no dose-limiting toxicities have been observed in the ongoing oral study.

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BAL1011553 posters at ASCO Annual Meeting 2016

- *Phase 1/2a trial of intravenous BAL101553, a novel tumor checkpoint controller (TCC), in advanced solid tumors – J. Lopez, T. R. J. Evans, E. R. Plummer, N. Diamantis, H. M. Shaw, I. H. Zubairi, N. R Md Haris, J. MacDonald, A. Greystoke, R. L. Roux, N. Tunariu, L. R. Molife, A. L. Hannah, S. Anderson, H. A Lane, M. Maurer, A. Schmitt-Hoffmann, F. Bachmann, M. F. Engelhardt, R. S. Kristeleit; Abstract 2525, Poster Board #225*
- *A Phase 1 study to assess the safety, pharmacokinetics (PK), pharmacodynamics (PD) and antitumor activities of daily oral BAL101553, a novel tumor checkpoint controller (TCC) in adult patients with advanced solid tumors – R. S. Kristeleit, T. R. J. Evans, J. Lopez, S. Slater, M. D'Arcangelo, Y. Drew, S. Adeleke, J. Brown, D. Crawford, N. Diamantis, P. Gougis, A. Tzankov, A. L. Hannah, S. Anderson, H. A Lane, A. Schmitt-Hoffmann, M. Maurer, F. Bachmann, M. F. Engelhardt, E. R. Plummer; Abstract TPS2594, Poster Board #292b*

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In addition, the design of the ongoing first-in-human open-label multi-center phase 1 study with the oral panRAF/SRC kinase inhibitor BAL3833, also known as CCT3833, in patients with advanced solid tumors including metastatic melanoma, was presented at ASCO.

In the study, after receiving initial single oral doses for clinical safety and pharmacokinetic analysis, patients are administered oral BAL3833 once-daily on a continuous basis over 28-day treatment cycles. In the dose-escalation part, the safety and tolerability profile of BAL3833 will be evaluated and the maximum tolerated dose (MTD) as well as the recommended phase 2 dose (RP2D) will be established. The study further includes pharmacokinetic analyses and assessments of patient blood and tumor samples for drug response biomarkers as well as exploratory patient selection biomarkers. The protocol provides that, once the MTD and RP2D are defined, there will be an expansion phase in patients with locally advanced or metastatic malignant melanoma, such as untreated BRAF-mutant melanoma, variants with progression under conventional BRAF-inhibitor therapy as well as RAS-mutant melanoma.

The study is expected to include 69 patients and is conducted in the United Kingdom at the Royal Marsden and Christie NHS Foundation Trusts in collaboration with The Institute of Cancer Research, London, and The CRUK Manchester Institute, The University of Manchester. To date, four cohorts have completed enrollment without experiencing dose-limiting toxicity.

BAL3833 poster at ASCO Annual Meeting 2016

- *A Phase 1 first-in-human trial to evaluate the safety and tolerability of CCT3833, an oral panRAF inhibitor, in patients with advanced solid tumours, including metastatic melanoma – E. J. Dean, U. Banerji, R. Girotti, I. Niculescu-Duvaz, F. Lopes, L. Davies, D. Niculescu-Duvaz, N. Dhomen, S. Ellis, Z. Ali, B. O'Carrigan, L. Carter, L. Chisholm, C. Dive, H. A. Lane, P. Lorigan, M. E. Gore, J. Larkin, R. Marais, C. Springer; Abstract TPS9597, Poster Board #199a*

For further information please visit http://am.asco.org/.

About BAL101553

Basilea's small molecule oncology drug candidate BAL101553 (the prodrug of BAL27862)[1] is being developed as a potential therapy for diverse cancers, including tumor types unresponsive to standard therapeutics. BAL101553 is currently undergoing clinical phase 1/2a evaluation in patients with advanced solid tumors as an oral dosage form. It has shown evidence of clinical anti-tumor activity in a phase 1/2a study with the intravenous (i.v.) formulation during which the maximum tolerated dose and the recommended phase 2 dose for weekly 2-hour i.v. administration were established. In preclinical studies, the drug candidate demonstrated *in-vitro* and *in-*

vivo activity against diverse treatment-resistant cancer models, including tumors refractory to conventional approved therapeutics and radiotherapy.[2, 3, 4] BAL101553 efficiently distributes to tumors and to the brain, with cytotoxic effects in glioblastoma (brain tumor) cell lines.[5] The active moiety BAL27862 binds the colchicine site of tubulin with distinct effects on microtubule organization[6], resulting in the formation of the "spindle assembly checkpoint" which promotes tumor cell death.[7] Basilea's approach to oncology includes the early evaluation of potential biomarkers, which are already being tested in phase 1/2a clinical studies in order to optimize dose selection and identify cancer patient groups more likely to respond.

About BAL3833

BAL3833 (also known as CCT3833) is an orally available small-molecule panRAF/SRC kinase inhibitor targeting cell proliferation signaling pathways that are associated with tumor growth and resistance development to current therapies. It is the lead compound of a series of kinase inhibitors in-licensed by Basilea in April 2015 under an agreement with The Institute of Cancer Research, London, Cancer Research Technology, the Wellcome Trust, and The University of Manchester. BRAF is mutated in a range of cancers including melanomas, colorectal and serous ovarian cancer. Data from preclinical studies suggest that this class of compounds, targeting the BRAF, CRAF and SRC family kinases, is active in diverse patient-derived melanoma models with intrinsic or acquired resistance to currently marketed BRAF-specific as well as MEK inhibitor therapies.[8] Moreover, activity of BAL3833 has also been demonstrated in KRAS-driven cancer models, including non-small cell lung cancer, colorectal cancer and pancreatic cancer.[9] BAL3833 has been progressed into a phase 1 study in adult patients with advanced solid tumors including metastatic melanoma. The compound originates from research at The Institute of Cancer Research and the Cancer Research UK Manchester Institute, by scientists funded by Cancer Research UK and the Wellcome Trust.

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.

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3 G. E. Duran et al. In vitro activity of the novel tubulin active agent BAL27862 in MDR1(+) and MDR1(-) human breast and ovarian cancer variants selected for resistance to taxanes. American Association for Cancer Research (AACR) annual meeting 2010, abstract 4412

4 F. Bachmann et al. BAL101553 (prodrug of BAL27862): A unique microtubule destabilizer active against drug refractory breast cancers alone and in combination with trastuzumab. American Association for Cancer Research (AACR) annual meeting 2014, abstract 831

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