

PRESS RELEASE

Basilea announces presentation of interim phase 1/2a clinical data with anticancer drug candidate BAL101553 at ASCO meeting

Basel, Switzerland, June 6, 2017 – Basilea Pharmaceutica Ltd. (SIX: BSLN) announced today that updates were presented on the ongoing clinical phase 1/2a program with its anticancer drug candidate BAL101553, a novel tumor checkpoint controller, at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago on June 2-6, 2017.

“We are pleased with the progress in our phase 1/2a clinical program evaluating BAL101553 in patients with advanced solid tumors and glioblastoma,” said Prof. Achim Kaufhold, Chief Medical Officer of Basilea. “Daily oral administration provides an improved therapeutic window over a weekly 2-hour infusion, the previously evaluated regimen. We look forward this year to completing the dose-escalation in our clinical studies exploring daily oral dosing and weekly 48-hour continuous infusion in patients with solid tumors.”

In a previously conducted phase 1/2a study with weekly 2-hour intravenous (i.v.) infusion of BAL101553, dose-limiting vascular effects were observed.¹ These appeared to be related to the maximum plasma concentration (C_{max}), while non-clinical models indicated that the antiproliferative effect of the drug candidate is driven by total exposure (area under the curve, AUC). Therefore, Basilea initiated two clinical phase 1/2a studies to explore different dosing regimens to maximize the AUC and minimize the C_{max} . The overview and design of these ongoing studies as well as first interim data were presented at the ASCO meeting.

In an open-label phase 1/2a study, Basilea is exploring once-daily oral dosing of BAL101553 in adult patients with advanced solid tumors who failed standard therapy. In the cohorts completed so far, there was a dose-proportional up to five-fold higher weekly exposure at reduced maximum plasma concentrations compared with 2-hour weekly infusion. Oral BAL101553 had no effect on blood pressure and the vascular toxicity observed with the 2-hour i.v. regimen was not seen when using oral daily dosing. Of the 19 patients evaluated so far, eight had stable disease as best objective response. The determination of the maximum tolerated dose (MTD) is expected to be achieved in 2017.

Given the absence of vascular toxicity of oral BAL101553 and based on promising antitumor activity of BAL101553 in preclinical models of brain cancer,^{2,3,4} the study with once-daily oral BAL101553 was amended in late 2016 to enroll adult patients with recurrent or progressive glioblastoma after prior radiotherapy with or without chemotherapy. Phase 1 dose-escalation is currently ongoing to determine the MTD, characterize dose-limiting toxicities and assess the pharmacokinetic (PK), pharmacodynamics (PD) and antitumor properties of oral BAL101553 in this patient population. Two cohorts have been completed without dose-limiting toxicities. Glioblastoma is the most common primary brain tumor and one of the most lethal types of cancer.

In another phase 1/2a clinical study, Basilea is exploring weekly 48-hour continuous infusion of BAL101553 as an alternative high exposure/low maximum concentration dosing regimen. This study is conducted with adult patients with advanced solid tumors. Two dose cohorts have been completed so far without observation of vascular toxicity. The study continues with expected completion of dose-escalation towards the end of 2017.

BAL101553 posters at ASCO 2017

- Phase 1/2a trial of daily oral BAL101553, a novel tumor checkpoint controller (TCC), in advanced solid tumors – R. S. Kristeleit, T. R. J. Evans, A. H. Ingles Garces, S. Slater, Y. Drew, M.-J. Devlin, N. R. Md Haris, N. Diamantis, J. MacDonald, F. Bachmann, A. L. Hannah, S. Anderson, H. A. Lane, A. Schmitt-Hoffmann, P. McKernan, M. F. Engelhardt, A. Greystoke, R. Miller, E. R. Plummer, J. S. Lopez; abstract 2532
- 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 progressive or recurrent glioblastoma (GBM) or high-grade glioma – A. H. Ingles Garces, E. R. Plummer, J. S. Lopez, R. S. Kristeleit, J. MacDonald, L. Sweeting, M.-J. Devlin, Y. Drew, A. L. Hannah, N. Aceto, S. Anderson, H. A. Lane, P. Larger, M. Maurer, P. McKernan, M. F. Engelhardt, A. Greystoke, N. Coleman, T. R. J. Evans, P. J. Mulholland; abstract TPS2601
- A phase 1 study to assess the safety, pharmacokinetics (PK), pharmacodynamics (PD) and antitumor activities of BAL101553, a novel tumor checkpoint controller (TCC), administered as 48-hour infusion in adult patients with advanced solid tumors – M. Joerger, A. Stathis, I. Metaxas, D. Hess, A. G. Omlin, G. Mayer, S. Gaggetta, S. Anderson, M. G. Pasqualotto, F. Hutter, N. Levy, S. Stuedeli, M. Landau-Salzberg, P. McKernan, H. A. Lane, P. Larger, R. Scheerlinck, M. F. Engelhardt, R. Von Moos, C. Sessa; abstract TPS2602

For further information please visit <https://am.asco.org/>.

About BAL101553

Basilea's small molecule oncology drug candidate BAL101553 (the prodrug of BAL27862)⁵ is being developed as a potential therapy for diverse cancers. BAL101553 is currently undergoing clinical phase 1/2a evaluation in patients with advanced solid tumors or glioblastoma (brain cancer). 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.^{6,7,8} BAL101553 efficiently distributes to the brain, with anticancer activity in glioblastoma models.^{2,3,4} The active moiety BAL27862 binds the colchicine site of tubulin with distinct effects on microtubule organization,⁹ resulting in the activation of the "spindle assembly checkpoint" which promotes tumor cell death.¹⁰

About Basilea

Basilea Pharmaceutica Ltd. is a biopharmaceutical company developing products that address the medical problem of 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 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.

References

- 1 J. Lopez et al. Phase 1/2a trial of intravenous BAL101553, a novel tumor checkpoint controller (TCC), in advanced solid tumors. *Journal of Clinical Oncology* 2016 (34), suppl., abstract 2525
- 2 R. Bergès et al. The novel tubulin-binding checkpoint activator BAL101553 inhibits EB1-dependent migration and invasion and promotes differentiation of glioblastoma stem-like cells. *Molecular Cancer Therapeutics* 2016 (15), 2740-2749
- 3 A. Schmitt-Hoffmann et al. BAL27862: a unique microtubule-targeted agent with a potential for the treatment of human brain tumors. AACR-NCI-EORTC symposium 2009, abstract C233; *Molecular Cancer Therapeutics* 2009, 8 (12 Supplement)
- 4 A. C. Mladek et al. The novel tubulin-binding 'tumor checkpoint controller' BAL101553 has anti-cancer activity alone and in combination treatments across a panel of GBM patient-derived xenografts. American Association for Cancer Research (AACR) annual meeting 2016, abstract 4781
- 5 J. Pohlmann et al. BAL101553: An optimized prodrug of the microtubule destabilizer BAL27862 with superior antitumor activity. American Association for Cancer Research (AACR) annual meeting 2011, abstract 1347; *Cancer Research* 2011, 71 (8 Supplement)
- 6 A. Broggini-Tenzer et al. The novel microtubule-destabilizing drug BAL101553 (prodrug of BAL27862) sensitizes a treatment refractory tumor model to ionizing radiation. EORTC-NCI-AACR symposium 2014, abstract 202
- 7 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
- 8 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
- 9 A. E. Prota et al. The novel microtubule-destabilizing drug BAL27862 binds to the colchicine site of tubulin with distinct effects on microtubule organization. *Journal of Molecular Biology* 2014 (426), 1848-1860
- 10 F. Bachmann et al. BAL101553 (prodrug of BAL27862): the spindle assembly checkpoint is required for anticancer activity. American Association for Cancer Research (AACR) annual meeting 2015, abstract 3789