

## PRESS RELEASE

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

- Tumor checkpoint controller BAL101553 demonstrates pre-clinical activity in treatment-refractory glioblastoma models as single agent and in combination treatment
- PanRAF/SRC kinase inhibitor BAL3833 inhibits tumor growth in preclinical KRAS-driven cancer models

**Basel, Switzerland, April 21, 2016** – Basilea Pharmaceutica Ltd. (SIX: BSLN) announced today that preclinical data on the oncology drug candidates BAL101553 and BAL3833 were presented at the American Association for Cancer Research (AACR) annual meeting in New Orleans, USA, April 16-20, 2016. The tumor-checkpoint controller BAL101553 is currently in Phase 1/2a clinical development, and the panRAF/SRC kinase inhibitor BAL3833 is currently in Phase 1.

At the AACR meeting, preclinical data were presented demonstrating anti-cancer activity of BAL101553 against glioblastoma multiforme (GBM), a highly malignant form of brain cancer that has very limited treatment options and often has poor prognosis. BAL101553 efficiently penetrates the brain in preclinical models and has previously demonstrated anti-cancer activity in treatment-refractory solid tumor models alone and in combination with radiotherapy.<sup>1</sup> The data presented at the AACR were generated by the group of Prof. Jann N. Sarkaria (Mayo Clinic, Rochester) and demonstrate statistically significant single agent activity in a panel of *in vivo* GBM models after daily, oral administration, including models refractory to temozolomide (TMZ) and radiotherapy, the standard of care for newly diagnosed GBM. Moreover, using a model with reduced sensitivity to both radiotherapy and TMZ, BAL101553 combined with either radiotherapy alone or radiotherapy and TMZ together provided additional benefit, leading to statistically significant prolongation of survival as compared to the standard of care treatment regimens. These data indicate that BAL101553 alone or in combination may provide a survival extension in GBM patients, potentially offering an alternative therapeutic option in this area of high medical need. BAL101553 is currently being evaluated in phase 1/2a clinical trials with both oral and i.v. administration schedules.

In a late-breaking research session, the groups of Prof. Caroline Springer (The Institute of Cancer Research, London) and Prof. Richard Marais (Cancer Research UK Manchester Institute, University of Manchester) reported that the novel panRAF/SRC kinase inhibitor BAL3833, also known as CCT3833, has anti-cancer activity in KRAS-driven *in vitro* and *in vivo* tumor models via inhibition of the RAF and SRC family kinases. KRAS is an important driver of tumor cell growth, with high rates of KRAS mutation found in several major cancer types, including pancreatic, colorectal and non-small-cell lung cancer. BAL3833 inhibits mutant BRAF as well as the CRAF and SRC protein kinases and was initially developed to address the increasing medical need of melanoma patients who progress on current mutant BRAF pathway inhibitors. The data presented show that BAL3833 may also be effective in non-melanoma KRAS-mutant cancers, potentially providing a new therapeutic option for these patients. Orally administered BAL3833 is currently being explored in a phase 1 clinical study in patients with solid tumors, including BRAF-mutant and BRAF inhibitor-resistant melanomas.

#### **BAL1011553 poster at AACR 2016**

- *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 – Ann C. Mladek, Jenny L. Pokorny, Heidi Lane, Felix Bachmann, Mark A. Schroeder, Katrina K. Bakken, Brett L. Carlson, Paul A. Decker, Jeanette E. Eckel-Passow, Jann N. Sarkaria; Abstract 4781*

#### **BAL3833 poster at AACR 2016**

- *Therapeutic efficacy of the paradox-breaking panRAF and SRC drug CCT3833/BAL3833 in KRAS-driven cancer models – Grazia Saturno, Filipa Lopes, Maria Romina Girotti, Ion Niculescu-Duvaz, Dan Niculescu-Duvaz, Alfonso Zambon, Lawrence Davies, Louise Johnson, Natasha Preece, Amaya Viros, Malin Pedersen, Robert McLeary, Ruth Knight, Rebecca Lee, Denys Holovanchuk, Alberto Fusi, Paul Lorigan, Nathalie Dhomen, Richard Marais, Caroline Springer; Abstract LB-212*

For further information please visit [www.aacr.org](http://www.aacr.org).

#### **About BAL101553**

Basilea’s oncology drug candidate BAL101553 (the prodrug of the small-molecule BAL27862) is being developed as a potential therapy for diverse cancers, including tumor types unresponsive to standard therapeutics. BAL101553 is currently undergoing clinical evaluation in patients with advanced solid tumors as an i.v. (phase 2a) and oral (phase 1) formulation. It has shown evidence of clinical anti-tumor activity in a phase 1 study during which the maximum tolerated dose was established.<sup>2</sup> In previous pre-clinical 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.<sup>1, 3, 4</sup> BAL101553 efficiently distributes to tumors and to the brain, with cytotoxic effects in glioblastoma (brain tumor) cell lines.<sup>5</sup> The active moiety BAL27862 binds the colchicine site of tubulin with distinct effects on microtubule organization, resulting in the formation of the “spindle assembly checkpoint” which promotes tumor cell death.<sup>6</sup> Potential biomarkers are being tested in early 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, are active in diverse patient-derived models resistant to standard BRAF as well as MEK inhibitor therapies.<sup>7</sup> BAL3833 has progressed into a phase 1 study in adult patients with advanced solid tumors including BRAF-mutant and BRAF inhibitor-resistant melanomas. 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](http://www.basilea.com).

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This press release can be downloaded from [www.basilea.com](http://www.basilea.com).

## References

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- 7 M. R. Girotti et al. Paradox-breaking RAF inhibitors that also target SRC are effective in drug-resistant BRAF mutant melanoma, *Cancer Cell* 2015 (27), 85-96