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Press Release

Basilea reports preclinical data on oncology drug candidates BAL0891, derazantinib and lisavanbulin at AACR Annual Meeting

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Basilea Pharmaceutica Ltd. (SIX: BSLN), a commercial-stage biopharmaceutical company committed to meeting the needs of patients with infectious diseases and cancer, reported today that promising preclinical data on the anti-cancer activity of its three oncology drug candidates, BAL0891, derazantinib and lisavanbulin, have been presented at the Annual Meeting of the American Association for Cancer Research (AACR) that took place April 8-13, 2022, in New Orleans, USA.

BAL0891 is a potential first-in-class mitotic checkpoint inhibitor (MCI) that drives aberrant tumor cell division leading to tumor cell death. A first poster showed in-vitro data on the activity of BAL0891 against its targets, threonine tyrosine kinase (TTK) and polo-like-kinase 1 (PLK1). The activity of BAL0891 led to a faster disruption of the mitotic spindle assembly check point (SAC) than TTK- and PLK1-specific inhibitors alone. This was associated with a broad anti-cancer effect across diverse tumor cell lines, including those derived from breast, gastric and colorectal cancer. Data presented on a second poster confirmed the good tolerability and potent single-agent anti-cancer activity of BAL0891 across a panel of patient-derived xenograft (PDX) in-vivo models of triple-negative breast cancer. Complete tumor regressions were observed in a significant number of PDX models and support the further development of BAL0891 for the potential treatment of human cancer. The data on both posters were generated in collaboration with the Dutch precision medicine company, NTRC B.V., from which Basilea in-licensed the drug candidate.

Dr. Laurenz Kellenberger, Chief Scientific Officer of Basilea, said: “The data presented at the AACR Annual Meeting confirm the differentiated profiles of our drug candidates. For BAL0891, the in-vitro an in-vivo data provide additional support for the novel mode of action of our compound and its potent single-agent activity. We are particularly pleased that BAL0891 shows convincing activity in models of human triple-negative breast cancer, a difficult-to-treat cancer with a high medical need.”

Further in-vitro and in-vivo data was also presented for derazantinib, a fibroblast growth factor receptor (FGFR) inhibitor, confirming similar sensitivity of FGFR1-3 and colony stimulating factor 1 receptor (CSF1R) to derazantinib. CSF1R plays an important role in the anti-tumor immune response to PD-L1 checkpoint inhibitors used for cancer therapy. In-vivo tumor models with high CSF1R levels were partially sensitive to derazantinib, but not to another FGFR inhibitor

with no activity against CSF1R. The importance of the additional CSF1R inhibition was highlighted by data that showed a synergistic effect of the combination of derazantinib with a PD-L1 antibody in an immunologically competent breast cancer model. As compared to the single agents, this combination increased efficacy against the primary tumor, and liver and lung metastases. The combination also led to a more pronounced activation of the immune microenvironment in the primary tumor.

Finally, preclinical data were presented on avanbulin, the active moiety of Basilea's tumor checkpoint controller lisavanbulin. In-vitro, avanbulin treatment was associated with high anti-tumor activity in models of diffuse large B cell lymphoma (DLBCL), supporting a potential application of lisavanbulin for the treatment of lymphoma patients. These data were generated in collaboration with Prof. Bertoni (Institute of Oncology Research, USI, Bellinzona, Switzerland).

Posters on Basilea's oncology candidates presented at AACR Annual Meeting 2022

Abstract #	Authors/title
5646	E. Zanini, N. Forster-Gross, F. Bachmann, N. Willemsen-Seegers, J. De Man, G. J. R. Zaman, R. C. Buijsman, A. Groner, M. Roceri, K. Burger, P. McSheehy, L Kellenberger, H. A. Lane BAL0891: A novel, small molecule, dual TTK/PLK1 mitotic checkpoint inhibitor (MCI) that drives aberrant tumor cell division
5645	H. A. Lane, F. Bachmann, E. Zanini, P. McSheehy, K. Litherland, N. Forster-Gross, L. Bury, D. Vu-Pham, J. de Man, W. E. van Riel, G. J. R. Zaman, R. C. Buijsman, L. Kellenberger BAL0891: A novel dual TTK/PLK1 mitotic checkpoint inhibitor (MCI) that drives aberrant tumor cell division resulting in potent anti-cancer activity
5501	M. El Shemerly, L. Kellenberger, E. Zanini, H. Lane, P. McSheehy Derazantinib, an FGFR1-3 inhibitor, inhibits CSF1R in macrophages and tumor cell lines and synergizes with a PDL1-antibody in an FGFR-driven murine syngeneic model
2575 / 14	F. Spriano, L. Aresu, L. Cascione, A. J. Arribas, N. Forster-Gross, F. Bachmann, H. Lane, F. Bertoni Avanbulin, the active moiety of the tumor checkpoint controller lisavanbulin (BAL101553) has anti-lymphoma activity

For further information please visit https://www.aacr.org/meeting/aacr-annual-meeting-2022/.

About BAL0891

BAL0891 is a first-in-class mitotic checkpoint inhibitor (MCI) that pushes cells through mitosis without adequate time for correct chromosome alignment and segregation. This results in aberrant tumor cell division leading to tumor cell death. The compound is a unique dual inhibitor of threonine tyrosine kinase (TTK) and polo-like kinase 1 (PLK1). Both kinases collaborate in activating the mitotic spindle assembly checkpoint (SAC), a cell division mechanism regulating correct chromosome alignment and segregation. The dual action of BAL0891 leads to a rapid disruption of the SAC driving cells through mitosis before the chromosomes are properly aligned, leading to premature cell division and tumor cell death. BAL0891 has shown anti-proliferative activity across diverse tumor cell lines in vitro and single agent efficacy in in-vivo models of solid human cancers. Basilea has in-licensed BAL0891 from Dutch precision medicine company NTRC B.V.

About derazantinib

Derazantinib is an investigational orally administered small-molecule FGFR inhibitor with strong activity against FGFR1, 2, and 3.[1] 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.[2] In these cancers, FGFR genetic aberrations are found in a range of 5% to 30%.[3] Derazantinib also inhibits the colony-stimulating-factor-1-receptor kinase (CSF1R).[1, 4] 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.[5] 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.[6, 7] Derazantinib has demonstrated antitumor activity and a manageable safety profile in a previous biomarker-driven phase 1/2 study in iCCA patients,[8] 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.[9] 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 has 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)[12] is currently being developed as a potential therapy for glioblastoma.[13, 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] In preclinical studies, end-binding protein 1 (EB1) was identified as a potential response-predictive biomarker in glioblastoma models and strong EB1-positivity was shown in about 5% of tissue samples from glioblastoma patients.[21, 22] The strongest expression of EB1 in non-glioblastoma tumors was detected in tissue samples from medulloblastomas and neuroblastomas, which are cancers that occur predominantly in the pediatric population. EB1-positive staining was also found in tissue samples from metastatic melanoma (skin cancer). Other tumors expressing slightly lower levels of EB1 staining include non-small cell lung cancer, colorectal cancer and triple-negative breast cancer.[24] The active moiety BAL27862 binds to the colchicine site of tubulin, with distinct effects on microtubule organization,[23] resulting in the activation of the "spindle assembly checkpoint" which promotes tumor cell death.[24]

About Basilea

Basilea is a commercial-stage biopharmaceutical company founded in 2000 and headquartered in Switzerland. We are committed to discovering, developing and commercializing innovative drugs to meet the needs of patients with bacterial and fungal infections and cancer. We have successfully launched two hospital brands, Cresemba for the treatment of invasive fungal infections and Zevtera for the treatment of severe bacterial infections. We are conducting clinical studies with two targeted drug candidates for the treatment of a range of cancers and have several preclinical assets in both anti-infectives and cancer in our portfolio. Basilea is listed on the SIX Swiss Exchange (SIX: BSLN). Please visit basilea.com.

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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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