News Release

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Dainippon Sumitomo Pharma Co., Ltd.

Dainippon Sumitomo Pharma announces clinical data of anti-cancer drugs BBI608 and BBI503 will be presented at the 2014 ASCO Annual Meeting

Osaka, Japan, May 15, 2014 – Dainippon Sumitomo Pharma Co., Ltd. (Head office: Osaka, Japan; President: Masayo Tada) ("DSP") announced that clinical study data on BBI608 and BBI503 will be presented in four sessions at the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago from May 30 to June 3, 2014. The abstracts are now available on the official website of ASCO (http://am.asco.org/). Outlines of the four sessions follow:

1. A phase I extension study of BBI608, a first-in-class cancer stem cell (CSC) inhibitor, in patients with advanced solid tumors.

【Scheduled Presentation at ASCO】
Abstract Number: #2546
Date and Time: Sunday, June 1, 2014, 08:00-11:45
Presentation Venue: S Hall A2
Session: General Poster Session

【Objectives of the study】
The dose escalation study of Phase I/II Clinical Study (BBI608-101 study) in patients with advanced solid tumors was conducted to determine the safety, tolerability, recommended dose, pharmacokinetics (PK) and preliminary anti-tumor activity of BBI608. The result of the dose escalation study was presented at the 2013 ASCO Annual Meeting, as announced in the DSP press release dated June 4, 2013.
BBI608-101 extension study to be presented this time evaluated safety, PK and preliminary anticancer activity of the new formulation designed for improving compliance and reducing side effects for pivotal trials. Based on its result, Phase III study (Global clinical trial: CO.23 trial) by monotherapy is now underway in patients with pretreated advanced colorectal carcinoma (CRC).

【Highlights of the abstract】
The new formulation designed for pivotal trials (DP2A) was evaluated in 24 patients. Neither significant difference in plasma exposure between the original formulation (DP1) and DP2A nor significant food effect was observed. Despite PK equivalence to DP1, nine patients received BBI608 DP2A 500 mg twice daily 4 h apart (DP2A-4h), and 15 patients received BBI608 DP2A 500 mg bid 12 h apart (DP2A-12h). DP2A-12 h had fewer gastrointestinal adverse events than DP2A-4h. In the result, the recommended dosing regimen for BBI608 in pivotal trials was determined to be about 500 mg bid q12 h. Among 15 patients receiving DP2A-12h, prolonged stable disease was observed in 2 of 7 non-CRC patients (ovarian cancer-16 weeks and anal squamous cancer-32 weeks) and among 8 CRC patients enrolled, disease control was observed in 67% evaluable for response (4/6), with progression free survival and overall survival at 17 weeks and 39 weeks, respectively.

2. A phase Ib study of the cancer stem cell inhibitor BBI608 administered with paclitaxel in patients with advanced malignancies.

【Scheduled Presentation at ASCO】
Abstract Number: #2530
Date and Time: Friday, May 30, 2014, 13:00 -16:00, Discussion: 16:30-17:45
Presentation Venue: E354b
Session: Poster Highlights Session

【Objectives of the study】
This phase I study in patients with advanced cancer was conducted to determine safety, tolerability, recommended dose and preliminary anti-cancer activity of BBI608 plus paclitaxel (BBI608-201 study).
Phase III study (Global clinical trial: BBI608-336 study) by combination therapy with paclitaxel in patients with gastric/GEJ adenocarcinoma was initiated in the U.S.

【Highlights of the abstract】
BBI608 was administered in 3 escalating dose cohorts (200 mg BID, 400 mg BID, 500 mg BID) in combination with paclitaxel in 24 patients. The BBI608 monotherapy recommended dose could be given in combination with paclitaxel in full dose. MTD was not determined. No new adverse events were observed, and the safety profile was similar to that of each agent as monotherapy. No significant pharmacokinetic interactions were observed. Disease control (CR+PR+SD) was observed in 10 of 15 evaluable patients.
Of 5 patients with refractory gastric/GEJ adenocarcinoma enrolled, 2 had PR (48% and 45% regressions), 1 had SD with 25% regression, and 2 (who failed prior taxane) had prolonged SD ≥ 24 weeks. Tumor regression or SD ≥ 16 weeks was also seen in patients with platinum-resistant ovarian cancer (1 of 2), melanoma (2 of 3), bladder CA (1 of 3) and NSCLC (1 of 1).

3. The NCIC CTG and AGITG CO.23 trial: A phase III randomized study of BBI608 plus best supportive care (BSC) versus placebo (PBO) plus BSC in patients (Pts) with pretreated advanced colorectal carcinoma (CRC).

【Scheduled Presentation at ASCO】
Abstract Number: #TPS3660
Date and Time: Saturday, May 31, 2014, 08:00-11:45
Presentation Venue: S Hall A2
Session: General Poster Session

【Objectives of the study】
This Phase III study (Global clinical trial: CO.23 trial) in patients with pretreated advanced colorectal carcinoma (CRC) is conducted in the U.S., Canada and Japan, etc. Based on the result, application for approval will be submitted.

【Highlights of the abstract】
This randomized, double-blind, PBO-controlled study will assess the efficacy and safety of

BBI608+BSC (best supportive care) vs PBO+BSC in patients with metastatic or advanced, unresectable, refractory CRC (target n=650). Primary endpoint is OS (overall survival).
(Note) Only the study plan will be presented.

4. A phase I dose escalation study of BBI503, a first-in-class cancer stemness kinase inhibitor in adult patients with advanced solid tumors.

【Scheduled Presentation at ASCO】
Abstract Number: #2527
Date and Time: Friday, May 30, 2014, 13:00-16:00, Discussion: 16:30-17:45
Presentation Venue: E354b
Session: Poster Highlights Session

【Objectives of the study】
A first-in-man phase I dose escalation study in patients with advanced solid tumors was conducted to determine safety, tolerability, recommended dose, pharmacokinetics and preliminary anti-tumor activity of BBI503 (BBI503-101 study).

【Highlights of the abstract】
Escalating doses from 10 mg to 450 mg once daily were administered to 26 patients. MTD was not reached. BBI503 was well tolerated, with mild gastrointestinal adverse events, including grade 1, 2 diarrhea, abdominal cramping, nausea, anorexia. Grade 3 diarrhea was observed in 2 subjects at 450 mg once daily. BBI503 exhibited pharmacokinetics with dose-dependent increases in plasma concentration up to 300 mg once daily. Of 20 evaluable patients, 11 (55%) had SD with a median time to progression of 16 weeks. Of those patients with SD, tumor regression and/or prolonged stable disease (≥ 16 weeks) were observed in 10.
Once daily recommended dose of BBI503 was determined to be 300 mg.

Reference information (BBI608 and BBI503):
BBI608 and BBI503 are orally-administered first-in-class anti-cancer drugs created and currently under development by Boston Biomedical, Inc., a DSP subsidiary in the U.S., and they are small-molecule compounds with a novel mechanism that blocks cancer stem cell (cancer cell with stem cell-like properties) self-renewal and induces cell death in CSC as well as other heterogeneous cancer cells. By targeting cancer stem cells in addition to heterogeneous cancer cells, efficacy is expected in the current challenges in therapy against cancer, such as treatment resistance, metastasis and recurrence.
BBI608 has been shown to inhibit the Stat3 pathways, Nanog pathways and β-catenin pathways in the pre-clinical study.
BBI503 is of a different mechanism from that of BBI608 and has been shown to inhibit multi-kinase in the pre-clinical study.

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