Lynparza positive in metastatic BRCA breast cancer

This announcement contains inside information

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LYNPARZA MEETS PRIMARY ENDPOINT IN PHASE III TRIAL IN BRCA-MUTATED METASTATIC BREAST CANCER

Lynparza provided a statistically-significant improvement in progression-free survival compared to chemotherapy

First positive randomised trial to evaluate the efficacy and safety of a PARP inhibitor beyond ovarian cancer

AstraZeneca today announced positive results from its Phase III OLYMPIAD trial comparing *Lynparza* (olaparib) tablets (300mg twice daily) to physician's choice of a standard of care chemotherapy in the treatment of patients with HER2-negative metastatic breast cancer harbouring germline BRCA1 or BRCA2 mutations. Patients treated with *Lynparza* showed a statistically-significant and clinically-meaningful improvement in progression-free survival (PFS) compared with those who received chemotherapy (capecitabine, vinorelbine or eribulin).

Sean Bohen, Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca, said: "These results are positive news for patients with BRCA-mutated metastatic breast cancer, a disease with a high unmet need, and are the first positive Phase III data for a PARP inhibitor beyond ovarian cancer. This is highly encouraging for the development of our broad portfolio which aims to treat multiple cancers by targeting DNA damage response pathways."

Initial findings from the OLYMPIAD study indicate that the safety profile of *Lynparza* was consistent with previous studies.

A full evaluation of the OLYMPIAD data is ongoing and the results will be submitted for presentation at a forthcoming medical meeting. AstraZeneca will be working with regulatory authorities to make *Lynparza* available to patients with this type of breast cancer.

About Metastatic Breast Cancer

Approximately one in eight women are diagnosed with breast cancer. Of these patients, approximately one-third are either diagnosed with or progress to the metastatic stage of the disease.[i] Despite treatment options increasing during the past three decades there is currently no cure for patients diagnosed with metastatic breast cancer. Thus, the primary aim of treatment is to slow progression of the disease for as long as possible, improving or at least maintaining a patient's quality of life.

About OLYMPIAD

OLYMPIAD is a randomised, multi-center Phase III trial assessing the efficacy and safety of *Lynparza* (300 mg twice daily) to 'physician's choice' chemotherapy (capecitabine, vinorelbine, eribulin) in 302 patients with HER2-negative metastatic breast cancer with germline BRCA1 or BRCA2 mutations, which are predicted or suspected to be deleterious. The international study was conducted in 19 countries from across Europe, Asia, North America and South America.

The primary endpoint of the trial was progression-free survival (PFS) as measured by a Blinded Independent Central Review (BICR). Secondary endpoints include overall survival (OS), time to second progression or death (PFS2), objective response rate (ORR), and effect on health-related quality of life (HRQoL).

About Germline BRCA mutations

BRCA1 and BRCA2 are human genes that produce proteins responsible for repairing damaged DNA and play an important role maintaining the genetic stability of cells. When either of these genes is mutated, or altered, such that its protein product either is not made or does not function correctly, DNA damage may not be repaired properly. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer.[ii]

Specific inherited mutations in BRCA1 and BRCA2 increase the risk of female breast and ovarian cancers, and they have been associated with increased risks of several additional types of cancer. Together, BRCA1 and BRCA2 mutations account for about 20 to 25 percent of hereditary breast cancers[iii] and about 5 to 10 percent of all breast cancers[iv]. In addition, mutations in BRCA1 and BRCA2 account for around 15 percent of ovarian cancers overall[v]. Breast and ovarian cancers associated with BRCA1 and BRCA2 mutations tend to develop at younger ages than their nonhereditary counterparts.

About *Lynparza*

Lynparza (olaparib) is an innovative, first-in-class oral poly ADP-ribose polymerase (PARP)

inhibitor that may exploit tumour DNA damage response (DDR) pathway deficiencies to

preferentially kill cancer cells. *Lynparza* is the foundation of AstraZeneca's industry-leading portfolio of compounds targeting DNA damage response (DDR) mechanisms in cancer cells.

Lynparza is currently approved by regulatory health authorities in the EU for use as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy. It is also approved in the US as monotherapy in patients with deleterious or suspected deleterious germline BRCA-mutated (as detected by an FDA-

test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

Lynparza is currently being investigated in another separate non-metastatic breast cancer Phase III study called OLYMPIA. This study is still

open and recruiting patients internationally.

About AstraZeneca in Oncology AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that have the potential to transform patients' lives and the Company's future. With at least 6 new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advancing Oncology as one of AstraZeneca's six Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms -- immuno-oncology, the genetic drivers of cancer and resistance, DNA damage response and antibody drug conjugates -- and by championing the development of personalised combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca.com and follow us on Twitter @AstraZeneca.

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[i] Dr Joyce O'Shaughnessy; Extending Survival with Chemotherapy in MBC" The Oncologist 2005:10

[ii] NCI website - BRCA Fact-sheet … https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet Last accessed January 2017

[iii] Easton DF. How many more breast cancer predisposition genes are there? Breast Cancer Research 1999; 1(1):14-17.

[iv] Campeau PM, Foulkes WD, Tischkowitz MD. Hereditary breast cancer: New genetic developments, new therapeutic avenues. Human Genetics 2008; 124(1):31-42.

[v] Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. Cancer 2005; 104(12):2807-16.