# LYNPARZA APPROVED BY THE US FDA

## LYNPARZA™ approved by the US FOOD AND DRUG ADMINISTRATION FOR THE TREATMENT OF ADVANCED OVARIAN CANCER IN PATIENTS WITH GERMLINE BRCA-MUTATIONS

AstraZeneca today announced that the US Food and Drug Administration (FDA) has approved LYNPARZA™ (olaparib) capsules (400mg twice daily) as the first monotherapy for patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) advanced ovarian cancer, who have been treated with three or more prior lines of chemotherapy. Olaparib has been approved under the FDA's Accelerated Approval programme, based on existing objective response rate and duration of response data. Continued approval for this indication is contingent upon verification of clinical benefit in ongoing confirmatory Phase III trials.

Olaparib is a poly ADP-ribose polymerase (PARP) inhibitor that exploits tumour DNA repair pathway deficiencies to preferentially kill cancer cells. It is the first PARP inhibitor to be approved for patients with germline *BRCA*-mutated advanced ovarian cancer, as detected by an FDA approved companion diagnostic test, BRACAnalysis CDx™.

Dr. Briggs Morrison, Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca, said "LYNPARZA is an excellent example of how advances in the understanding of cancer biology can be used to develop the next generation of targeted medicines. It is a much-needed new therapeutic option for patients with germline *BRCA*-mutated advanced ovarian cancer. Today's approval also marks the first of what we hope will be a number of indications in which this medicine has the potential to improve the lives of cancer patients."

AstraZeneca filed a US regulatory submission for olaparib in February 2014, based on data from a Phase II maintenance study1 of olaparib compared to placebo in platinum-sensitive relapsed high grade serous ovarian cancer patients. Following the FDA Oncologic Drugs Advisory Committee recommendation on 25 June 2014 and in response to an FDA request for additional data, AstraZeneca submitted a major amendment to the olaparib New Drug Application on 24 July 2014. The FDA approval is therefore based on efficacy data from a single-arm, open-label, Phase II study2 of olaparib in patients with deleterious or suspected deleterious germline *BRCA*-mutated advanced cancers, as well as safety data from several other olaparib studies, including the placebo-controlled study.

The efficacy of olaparib is based on analysis of 137 patients with measurable, germline *BRCA* mutated advanced ovarian cancer treated with three or more prior lines of chemotherapy. The trial results demonstrated an overall response rate of 34% (95% Confidence Interval: 26%, 42%). The median response duration was 7.9 months (95% Confidence Interval: 5.6, 9.6 months). The most common adverse events associated with olaparib monotherapy to date have been generally mild to moderate and have included nausea, vomiting, fatigue and anaemia.

Dr. Ursula Matulonis, Associate Professor of Medicine, Harvard Medical School and Director of the Gynaecological Oncology Programme at the Dana-Farber Cancer Institute, Boston said: "Ovarian cancer is diagnosed in nearly 22,000 women per year. The long-term survival rate in patients with advanced ovarian cancer is 10% to 30%. The FDA approval of LYNPARZA is a significant milestone for our patients as currently there are only limited treatment options available to women with ovarian cancer who carry the *BRCA* mutation."

A full review of data from either of two ongoing studies under the SOLO Phase III clinical programme will be required for the accelerated approval of olaparib in *BRCA*-mutated advanced ovarian cancer to be converted to a full approval: SOLO2 is evaluating olaparib compared to placebo as a maintenance therapy and SOLO3 is evaluating olaparib compared to standard chemotherapy for relapsed disease. Data from the SOLO2 study is expected in 2015 and data from SOLO3 is expected in 2019.

The FDA's approval follows the announcement on 18 December of the approval of olaparib in the European Union, as the first therapy for the maintenance treatment of adult patients with platinum-sensitive relapsed *BRCA*-mutated serous ovarian cancer.

1 Ledermann J et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by *BRCA* status in a randomised phase 2 trial. *Lancet Oncology*. 2014. http://dx.doi.org/10.1016/S1470-2045(14)70228-1

2 Kaufman B, Shapira-Frommer R, Schmultzler RK et al. Olaparib Monotherapy in Patients With Advanced Cancer and a Germline *BRCA*1/2 Mutation. *Journal of Clinical Oncology 2014*. http://jco.ascopubs.org/content/early/2014/10/30/JCO.2014.56.2728

### About ovarian cancer

Ovarian cancer is the fifth leading cause of cancer death among women in the United States, mainly because it is often diagnosed late and has an extremely poor prognosis. For the 61% of ovarian cancer patients whose cancer has metastasised by the time of diagnosis, the five-year survival rate is only 27%.

Up to 15% of women with ovarian cancer have a *BRCA* mutation, which is the most common cause of homologous repair deficiency. In *BRCA*-mutated tumour cells, homologous recombination is defective and DNA double-strand break repair is forced to occur via error-prone pathways, which can lead to genomic instability and cell death.

### About LYNPARZA™ (olaparib)

Olaparib is an innovative, first-in-class oral poly ADP-ribose polymerase (PARP) inhibitor that exploits tumour DNA repair pathways deficiencies to preferentially kill cancer cells. This mode of action gives olaparib the potential for activity in a range of tumour types with DNA repair deficiencies.

Concurrent with the approval of olaparib, the FDA has approved the BRACAnalysis CDx™ (Myriad Genetic Laboratories) for the qualitative detection and classification of variants in the BRCA1 and BRCA2 genes.

**About the Phase III SOLO programme**

AstraZeneca initiated the Phase III SOLO programme in September 2013. The programme consists of three studies:

· SOLO1: designed to evaluate olaparib as a maintenance monotherapy for ovarian cancer in patients who have a germline *BRCA* mutation and who demonstrated a complete or partial response following first-line platinum-based chemotherapy

· SOLO2: designed to evaluate olaparib as a maintenance monotherapy for relapsed ovarian cancer in patients who have a germline *BRCA* mutation and who demonstrated a complete or partial response following platinum-based chemotherapy

· SOLO3: designed to evaluate olaparib versus non-platinum chemotherapy as third-line or later treatment for relapsed ovarian cancer in patients who have a germline *BRCA* mutation

For further information, please visit: www.ovariancancertrials.com

In addition to ovarian cancer, AstraZeneca is committed to investigating the potential of olaparib in multiple tumour types, with Phase III studies in adjuvant and metastatic *BRCA*-mutated breast cancers, *BRCA*-mutated pancreatic cancer and second line gastric cancer underway.

**About AstraZeneca**

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. 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

**CONTACTS**

**Media Enquiries**

Esra Erkal-Paler +44 20 7604 8030 (UK/Global)

Vanessa Rhodes +44 20 7604 8037 (UK/Global)

Ayesha Bharmal +44 20 7604 8034 (UK/Global)

Jacob Lund +46 8 553 260 20 (Sweden)

Michele Meixell + 1 302 885 6351 (US)

**Investor Enquiries**

Thomas Kudsk Larsen +44 20 7604 8199 mob: +44 7818 524185

Karl Hård +44 20 7604 8123 mob: +44 7789 654364

Eugenia Litz +44 20 7604 8233 mob: +44 7884 735627

Christer Gruvris +44 20 7604 8126 mob: +44 7827 836825

19 December 2014

-ENDS-