Lynparza approved in EU for the treatment of germline BRCA-mutated HER2-negative advanced breast cancer

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AstraZeneca and MSD's Lynparza reduced the risk of disease progression or death by 42% vs. chemotherapy in Phase III OlympiAD trial

First PARP inhibitor approved in the EU for patients with this difficult-to-treat disease and third EU approval for Lynparza

AstraZeneca and MSD Inc., Kenilworth, N.J., US (MSD: known as Merck & Co., Inc. inside the US and Canada) today announced the European Commission has approved *Lynparza* (olaparib) as a monotherapy for the treatment of adult patients with germline *BRCA*1/2-mutations (g*BRCA*m), and who have human epidermal growth factor receptor 2 (HER2)-negative locally-advanced or metastatic breast cancer.

Under the licensed indication, patients should have previously been treated with an anthracycline and a taxane in the (neo)adjuvant or metastatic setting unless they were unsuitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should also have progressed on or after prior endocrine therapy, or be considered unsuitable for endocrine therapy.

Dave Fredrickson, Executive Vice President, Oncology, said: "With this approval, *Lynparza* provides patients throughout the EU with a targeted and oral chemotherapy-free treatment option for a difficult-to-treat cancer. It also reinforces the importance of testing for biomarkers including *BRCA*, hormone receptor and HER2 expression, helping physicians to make the most informed treatment decisions for patients."

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: "In the OlympiAD trial, which supported this approval, *Lynparza* demonstrated a meaningful improvement in progression-free survival compared to chemotherapy in patients with germline *BRCA*-mutated metastatic breast cancer. We look forward to making this new option available across the EU, where we hope it will improve outcomes for many patients."

The approval was based on data from the randomised, open-label, Phase III OlympiAD trial which tested *Lynparza* vs. physician's choice of chemotherapy (capecitabine, eribulin, or vinorelbine). In the trial, *Lynparza*provided patients with a statistically-significant median progression-free survival improvement of 2.8 months (7.0 months for *Lynparza* vs. 4.2 months for chemotherapy). Patients taking *Lynparza* experienced an objective response rate (ORR) of 52%, which was double the ORR for those in the chemotherapy arm (23%).

This is the third indication for *Lynparza* in the EU, and AstraZeneca and MSD are working together to deliver *Lynparza* as quickly as possible to more patients across multiple settings. *Lynparza* has a broad clinical development programme, including the ongoing Phase III OlympiA which is testing *Lynparza* as an adjuvant treatment in patients with g*BRCA*m HER2-negative breast cancer.

About OlympiAD

OlympiAD was a global, randomised, open-label, multi-centre Phase III trial of 302 patients, assessing the efficacy and safety of *Lynparza* tablets (300mg twice daily) compared to the physician's choice of chemotherapy (capecitabine, eribulin or vinorelbine); 205 patients were randomised to receive *Lynparza*and 97 patients were randomised to receive chemotherapy. Patients in the OlympiAD trial had germline *BRCA*1- and/or *BRCA*2-mutated, HER2-negative (HR-positive or triple negative) breast cancer and received *Lynparza* for treatment in the metastatic setting.

Prior to enrolment, all patients were treated with an anthracycline (unless it was contraindicated) and a taxane chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with metastatic breast cancer (71% of patients) had received no more than two previous chemotherapy treatments for metastatic disease. Patients with HR-positive breast cancer had received at least one endocrine (hormonal) therapy (in the adjuvant or metastatic setting) and had disease progression during therapy, unless they had disease for which endocrine therapy was considered inappropriate. Previous treatment with platinum chemotherapy in the neoadjuvant, adjuvant or metastatic setting was allowed (28% of patients).

The most common adverse reactions (≥20%) in the OlympiAD trial of patients who received *Lynparza* were nausea (58%), anaemia (40%), fatigue (including asthenia) (37%), vomiting (30%), neutropenia (27%), respiratory tract infection (27%), leukopenia (25%), diarrhoea (21%) and headache (20%). The percentage of patients who discontinued treatment in the *Lynparza* arm was 5% vs. 8% in the chemotherapy arm.

About advanced breast cancer

Advanced/metastatic breast cancer refers to Stage III and IV breast cancer. Stage III disease may also be referred to as locally-advanced breast cancer, while metastatic disease is the most-advanced stage of breast cancer (Stage IV) and occurs when cancer cells have spread beyond the initial tumour site to other organs of the body outside the breast. Since there is no cure for the disease, the goal of current treatment is to delay disease worsening or death.

In 2018, there were an estimated 2.1 million new cases of breast cancer worldwide - one in four cancer cases among women (24.2%). In Europe the estimated 5-year prevalence of breast cancer in 2018 was 2,054,887 cases.1 Approximately 30% of women who are diagnosed with early breast cancer will go on to develop advanced disease.

About BRCA

Breast cancer susceptibility genes 1/2 *(BRCA*1 and *BRCA*2) 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, and cells become unstable. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer.

About *Lynparza*

Lynparza (olaparib) is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response in cells/tumours harbouring a deficiency in homologous recombination repair (HRR), such as mutations in *BRCA*1 and/or *BRCA*2. Inhibition of PARP with *Lynparza* leads to the trapping of PARP bound to DNA single-strand breaks, stalling of replication forks, their collapse and the generation of DNA double-strand breaks and cancer cell death. *Lynparza* is being tested in a range of tumour types with defects and dependencies in the DDR.

Lynparza, which is being jointly developed and commercialised by AstraZeneca and MSD, is approved for multiple indications in advanced ovarian cancer and metastatic breast cancer and has been used in over 20,000 patients worldwide. On 26 February 2019, AstraZeneca and MSD announced that *Lynparza* became the first PARP inhibitor to demonstrate benefit in g*BRCA*m metastatic pancreatic cancer in the Phase III POLO trial.

Lynparza has the broadest and most advanced clinical trial development programme of any PARP inhibitor, and AstraZeneca and MSD are working together to understand how it may affect multiple PARP-dependent tumours as a monotherapy and in combination across multiple cancer types. *Lynparza* is the foundation of AstraZeneca's industry-leading portfolio of potential new medicines targeting DDR mechanisms in cancer cells.

About the AstraZeneca and MSD strategic oncology collaboration

In July 2017, AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the United States and Canada, announced a global strategic oncology collaboration to co-develop and co-commercialise *Lynparza*, the world's first PARP inhibitor and potential new medicine selumetinib, a MEK inhibitor, for multiple cancer types. Working together, the companies will develop *Lynparza* and selumetinib in combination with other potential new medicines and as a monotherapy. Independently, the companies will develop *Lynparza* and selumetinib in combination with their respective PD-L1 and PD-1 medicines.

About AstraZeneca in Oncology

AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly-growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance Oncology as one of AstraZeneca's four 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, Tumour Drivers 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 therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visitastrazeneca.com and follow us on Twitter @AstraZeneca.

Media Relations

Gonzalo Viña		+44 203 749 5916
Rob Skelding	Oncology	+44 203 749 5821
Rebecca Einhorn	Oncology	+1 301 518 4122
Matt Kent	BioPharma	+44 203 749 5906
Jennifer Hursit	Other	+44 203 749 5762
Christina Malmberg Hägerstrand	Sweden	+46 8 552 53 106
Michele Meixell	US	+1 302 885 2677

Investor Relations

Thomas Kudsk Larsen		+44 203 749 5712
Henry Wheeler	Oncology	+44 203 749 5797
Christer Gruvris	BioPharma (cardiovascular, metabolism)	+44 203 749 5711
Nick Stone	BioPharma (respiratory, renal)	+44 203 749 5716
Josie Afolabi	Other medicines	+44 203 749 5631
Craig Marks	Finance, fixed income	+44 7881 615 764
Jennifer Kretzmann	Corporate access, retail investors	+44 203 749 5824
US toll-free		+1 866 381 72 77

Adrian Kemp

Company Secretary

AstraZeneca PLC

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