Lynparza Phase III PROfound trial in HRR*

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***Lynparza* Phase III PROfound trial in HRR* mutation-selected metastatic castration-resistant prostate cancer met primary endpoint**

AstraZeneca and MSD's Lynparza met the primary endpoint of significantly increasing the time patients selected for BRCA1/2 or ATM mutations live without radiographic disease progression vs. standard of care treatment

Only PARP inhibitor with positive Phase III results in four different cancer types (ovarian, breast, pancreatic and prostate)

AstraZeneca and MSD Inc., Kenilworth, N.J., US (MSD: known as Merck & Co., Inc. inside the US and Canada) today announced positive results from the Phase III PROfound trial of *Lynparza* (olaparib) in men with metastatic castration-resistant prostate cancer (mCRPC) who have a *homologous recombination repair gene mutation (HRRm) and have progressed on prior treatment with new hormonal anticancer treatments (e.g. enzalutamide and abiraterone).

Results from the trial showed a statistically-significant and clinically-meaningful improvement in the primary endpoint of radiographic progression-free survival (rPFS) with *Lynparza* vs. enzalutamide or abiraterone in men with mCRPC selected for BRCA1/2 or ATM gene mutations, a subpopulation of HRR gene mutations. The safety and tolerability profile of *Lynparza* was generally consistent with previous trials.

José Baselga, Executive Vice President, Oncology R&D, said: "For men with metastatic castration-resistant prostate cancer the disease remains deadly, especially in those who have failed on a new hormonal anticancer treatment. This trial is the only positive Phase III trial of any PARP inhibitor in metastatic castration-resistant prostate cancer, where the need for new, effective therapies is high. The PROfound trial also demonstrates the potential value of genomic testing in this at-risk patient population. We look forward to discussing these results with global health authorities soon."

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: "Metastatic castration-resistant prostate cancer is a deadly disease and represents an area of critical unmet medical need. The Phase III PROfound trial is another example of MSD and AstraZeneca's shared commitment to improving long-term outcomes for people living with cancer. These results represent the potential for a new, oral targeted treatment option for this patient population."

AstraZeneca and MSD plan to present the full data from the trial at a forthcoming medical meeting. The companies are also exploring additional trials in prostate cancer, including the ongoing Phase III PROpel trial, testing *Lynparza* as a 1st-line therapy in mCRPC, in combination with abiraterone.

About PROfound

PROfound is a prospective, multicentre, randomised, open-label, Phase III trial testing the efficacy and safety of *Lynparza* versus enzalutamide or abiraterone in patients with mCRPC who have progressed on prior treatment with new hormonal anticancer treatments and have a qualifying tumour mutation in one of 15 genes involved in the HRR pathway, including among them BRCA1/2, ATM and CDK12.

About metastatic castration-resistant prostate cancer

Prostate cancer is the second-most common cancer in men, with an estimated 1.3 million new cases diagnosed worldwide in 2018 and is associated with a significant mortality rate.1Development of prostate cancer is often driven by male sex hormones called androgens, including testosterone.2mCRPC occurs when prostate cancer grows and spreads to other parts of the body despite the use of androgen-deprivation therapy to block the action of male sex hormones.2 Approximately 10-20% of men with advanced prostate cancer will develop CRPC within five years, and at least 84% of these will have metastases at the time of CRPC diagnosis.3Of men with no metastases at CRPC diagnosis, 33% are likely to develop metastases within two years.3 Despite an increase in the number of available therapies for men with mCRPC, five-year survival remains low.3

About *Lynparza*

Lynparza (olaparib) is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response (DDR) in cells/tumours harbouring a deficiency in homologous recombination repair (HRR), such as mutations in BRCA1 and/or BRCA2. 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 PARP-dependent tumour types with defects and dependencies in the DDR pathway.

Lynparza is currently approved in 64 countries, including those in the EU, for the maintenance treatment of platinum-sensitive relapsed ovarian cancer regardless of BRCA status. It is approved in the US, EU, Japan and several other countries as 1st-line maintenance treatment of BRCAm advanced ovarian cancer following response to platinum-based chemotherapy. It is also approved in 40 countries, including the US and Japan, for germline BRCAm HER2-negative metastatic breast cancer previously treated with chemotherapy; in the EU this includes locally advanced breast cancer. Regulatory reviews are underway in other jurisdictions for ovarian, breast and pancreatic cancers.

Lynparza, which is being jointly developed and commercialised by AstraZeneca and MSD, is approved for advanced ovarian cancer and metastatic breast cancer and has been used in over 25,000 patients worldwide. *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.

In January 2016, AstraZeneca announced that *Lynparza* was granted Breakthrough Therapy Designation by the US Food and Drug Administration (FDA) for the monotherapy treatment of BRCA1/2- or ATM gene-mutated mCRPC in patients who have received a prior taxane-based chemotherapy and at least one newer hormonal agent (abiraterone or enzalutamide), based on the positive results of the TOPARP-A

Phase II trial.

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 monotherapies. 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, CVRM and Respiratory. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit astrazeneca.com and follow us on Twitter @AstraZeneca.

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