NEWS RELEASE

# LYNPARZA® (olaparib) in Combination with Bevacizumab, and as a Monotherapy, Demonstrates Clinically Meaningful Survival Benefit in 1st-Line Advanced Ovarian Cancer Across Two Phase III Trials

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## Landmark 5-year follow-up of PAOLA-1 Phase III trial demonstrated LYNPARZA plus bevacizumab meaningfully extended survival with 65.5% of HRD-positive patients surviving 5 years vs. 48.4% treated with bevacizumab and placebo

## SOLO-1 Phase III trial demonstrated 67% of advanced ovarian cancer patients with BRCA mutations treated with LYNPARZA were alive at 7 years vs. 47% on placebo

WILMINGTON, Del.--(BUSINESS WIRE)-- Positive long-term follow-up results from the PAOLA-1 and SOLO-1 Phase III trials of LYNPARZA® (olaparib), jointly developed and commercialized by AstraZeneca and Merck & Co., Inc., known as MSD outside the US and Canada, with or without bevacizumab demonstrated clinically meaningful improvements in overall survival (OS). Further results showed class-leading progression-free survival (PFS) in combination with bevacizumab for homologous recombination deficiency (HRD)-positive patients, versus active comparator, bevacizumab, and as monotherapy for patients with BRCA mutations, versus placebo, respectively.

Both trials which were conducted in biomarker-selected, newly diagnosed patients with advanced ovarian cancer in the 1st-line maintenance setting also demonstrated a consistent safety profile.1,2

The results for PAOLA-1 (Abstract #LBA29) and SOLO-1 (Abstract #517O) were presented on September 9 at the

2022 European Society of Medical Oncology (ESMO) and SOLO-1 results were published in Journal of Clinical Oncology.

Ovarian cancer is one of the most common gynecologic cancers, with a poor prognosis and a high mortality rate.3 Over two thirds of patients are diagnosed with advanced disease, and approximately 50-70% of these patients die within five years.4,5 Up to one in five women with advanced ovarian cancer have a BRCA mutation, and roughly half of women have HRD-positive tumors (which includes those with a BRCA mutation).6-8

Professor Isabelle Ray-Coquard, principal investigator from the PAOLA-1 trial and the President of the Gineco group, said: "For women facing an advanced ovarian cancer diagnosis who are HRD-positive, a targeted treatment in the 1st-line maintenance setting is critical to helping them live longer. These latest results at the five-year landmark demonstrate that olaparib with bevacizumab reduces the risk of death by 38% in HRD-positive patients compared to bevacizumab alone, further reinforcing the clinically meaningful long-term survival benefit of this combination. This should be promising news for both clinicians and patients, as we see these additional data show that this combination may allow patients more time with family and loved ones. These results also highlight the importance of biomarker testing as part of a precision medicine approach to guide treatment decisions in ovarian cancer patients."

Professor Paul DiSilvestro, investigator from the SOLO-1 trial and Director of the Program in Women's Oncology at Women and Infants Hospital in Providence, Rhode Island, said: "The long-term results from SOLO-1 confirm that olaparib continues to elicit a clinically meaningful improvement in overall survival in the 1st-line maintenance setting for more than seven years. Achieving long-term survival for patients with newly diagnosed advanced ovarian cancer is critical because the first line setting offers the greatest potential to impact patient survival."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "Historically the five-year survival rate of newly diagnosed patients with advanced ovarian cancer is 30-50%. In that context, it is phenomenal to share the long-term overall survival data from both PAOLA-1 and SOLO-1, with two out of three patients still alive in these trials. We continue to believe in LYNPARZA's ability to help biomarker-selected patients with advanced ovarian cancer to achieve better outcomes."

Dr. Eliav Barr, Senior Vice President, Head of Global Clinical Development and Chief Medical Officer, Merck Research Laboratories, said: "These latest data from the PAOLA-1 and SOLO-1 trials further highlight the importance of HRD testing, including for BRCA1/2 mutations, for all newly diagnosed advanced ovarian cancer patients at the point of diagnosis. Maintenance therapy with LYNPARZA may provide certain patients with HRD-positive and/or BRCA-mutated advanced ovarian cancer the opportunity to live longer."

## Updated results from the PAOLA-1 Phase III trial

Updated results from the PAOLA-1 Phase III trial demonstrate that LYNPARZAplus bevacizumab increased median overall survival to 56.5 months versus 51.6 months with bevacizumab alone, in patients with newly diagnosed advanced ovarian cancer irrespective of HRD status. This increase was not statistically significant.

In HRD-positive patients, LYNPARZAplus bevacizumab provided a clinically meaningful improvement in overall survival, reducing the risk of death by 38% versus bevacizumab (based on a HR of 0.62; 95% CI 0.45-0.85) despite PAOLA-1 having 30% Stage IV patients. 65.5% of patients treated with LYNPARZA plus bevacizumab were still alive at five years versus 48.4% of those treated with bevacizumab alone. LYNPARZAplus bevacizumab also improved median PFS to almost four years (46.8 months) versus 17.6 months with bevacizumab plus placebo and 46.1% of patients treated with LYNPARZAplus bevacizumab remain progression free at five years versus 19.2% of patients treated with bevacizumab alone. The safety and tolerability profile of LYNPARZA in this trial was in line with that observed in prior clinical trials, with no new safety signals.

## Updated results from the SOLO-1 Phase III trial

Updated results from the SOLO-1 Phase III trial demonstrate that LYNPARZA provided a clinically meaningful improvement in overall survival (OS) versus placebo in patients with BRCA-mutated (BRCAm) newly diagnosed advanced ovarian cancer, reducing the risk of death by 45% (based on an HR of 0.55; 95% CI 0.40-0.76; nominal p=0.0004 [not statistically significant]). Median OS was still not reached with LYNPARZA versus 75.2 months with placebo. At the seven-year descriptive OS analysis, 67% of LYNPARZA patients were alive versus 47% of placebo patients (44% of whom had a subsequent PARP inhibitor) and 45% of LYNPARZA patients versus 21% of placebo patients were alive and had not received a first subsequent treatment.

Additional data showed median time to first subsequent therapy was 64 months with LYNPARZAversus 15.1months with placebo. The safety and tolerability profile of LYNPARZA in this trial was in line with that observed in prior clinical trials, with no new safety signals.

## Summary of results

| PAOLA-1 | | |
|---|---|---|
| | LYNPARZA + bevacizumab (n=537) | Placebo + bevacizumab (n=269) |
| OS1 | | |
| Number of patients with events (%) | 288 (53.6) | 158 (58.7) |
| Median OS (in months) | 56.5 | 51.6 |
| HR (95% CI)<br>p-value | 0.92 (0.76,1.12)<br>0.4118 | |
| OS by HRD status2 | | |

| | | |
|---|---|---|
| HRD positive (including tBRCAm) | | |
| Number of patients randomized | 255 | 132 |
| Number of patients with events (%) | 93 (36.5) | 69 (52.3) |
| Median (in months) | 75.2 | 57.3 |
| HR (95% CI) | 0.62 (0.45, 0.85) | |
| HRD positive (excluding tBRCAm) | | |
| Number of patients randomized | 97 | 55 |
| Number of patients with events (%) | 44 (45.4) | 32 (58.2) |
| Median (in months) | Not reached | 52.0 |
| HR (95% CI) | 0.71 (0.45, 1.13) | |
| BRCAm | | |
| Number of patients randomized | 157 | 80 |
| Number of patients with events (%) | 48 (30.6) | 37 (46.3) |
| Median (in months) | 75.2 | 66.9 |
| HR (95% CI) | 0.60 (0.39, 0.93) | |
| HRD negative | | |
| Number of patients randomized | 192 | 85 |
| Number of patients with events (%) | 140 (72.9) | 58 (68.2) |
| Median (95% CI) (in months) | 36.8 | 40.4 |
| HR (95% CI) | 1.19 (0.88, 1.63) | |
| PFS3 by HRD status2 | | |
| HRD positive (including tBRCAm) | | |
| Number of patients randomized | 255 | 132 |
| Number of patients with events (%) | 136 (53.3) | 104 (78.8) |
| Median (in months) | 46.8 | 17.6 |
| HR (95% CI) | 0.41 (0.32, 0.54) | |

| SOLO-1 | | |
|---|---|---|
| | LYNPARZA (n=260) | Placebo (n=131) |
| OS4 | | |
| Number of patients with events (%) | 84 (32.2) | 65 (49.6) |
| Median OS (in months) | Not reached | 75.2 |
| HR (95% CI)<br>p-value5 | 0.55 (0.40, 0.76)<br>0.0004 | |
| Time to first subsequent therapy | | |
| Number of patients with events (%) | 135 (51.9) | 98 (74.8) |
| Median (95% CI) (in months) | 64.0 | 15.1 |
| HR (95% CI) | 0.37 (0.28–0.48) | |
| Time to second subsequent therapy | | |
| Number of patients with events (%) | 110 (42.3) | 80 (61.1) |
| Median (95% CI) (in months) | 93.2 | 40.7 |
| HR (95% CI) | 0.5 (0.37, 0.67) | |

1. OS analysis was done at 56% maturity (448 events in 797 patients) and boundary for significance 0.0001; statistical significance not reached.
2. Exploratory subgroup analysis by HRD status. The HRD status of patients in PAOLA-1 was determined from post-randomization testing of tumor samples using the Myriad myChoice HRD plus test
3. Investigator-assessed PFS (RECIST 1.1)
4. OS analysis was done at 38.1% maturity (149 events in 391 patients) and boundary for significance 0.01; statistical significance not reached. Survival follow up continues and further analyses were planned.
5. P<0.0001 required to declare statistical significance

LYNPARZA is approved as maintenance treatment of platinum-sensitive relapsed ovarian cancer and as both monotherapy and in combination with bevacizumab for the 1st-line maintenance treatment of BRCA-mutated (BRCAm) and HRD-positive advanced ovarian cancer, respectively.

## IMPORTANT SAFETY INFORMATION

## CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

## WARNINGS AND PRECAUTIONS

**Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML):** Occurred in approximately 1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was 2 years (range: <6 months to >10 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (≤Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood count weekly until recovery.

If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. Discontinue LYNPARZA if MDS/AML is confirmed.

**Pneumonitis:** Occurred in 0.8% of patients exposed to LYNPARZA monotherapy, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

**Embryo-Fetal Toxicity:** Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

Males

Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of LYNPARZA and to not donate sperm during this time.

Venous Thromboembolic Events: Including pulmonary embolism, occurred in 7% of patients with metastatic castration-resistant prostate cancer who received LYNPARZA plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving LYNPARZA and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism, and treat as medically appropriate, which may include long-term anticoagulation as clinically indicated.

## ADVERSE REACTIONS—First-Line Maintenance BRCAm Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA in the first-line maintenance setting for SOLO-1 were: nausea (77%), fatigue (67%), abdominal pain (45%), vomiting (40%), anemia (38%), diarrhea (37%), constipation (28%), upper respiratory tract infection/influenza/nasopharyngitis/bronchitis (28%), dysgeusia (26%), decreased appetite (20%), dizziness (20%), neutropenia (17%), dyspepsia (17%), dyspnea (15%), leukopenia (13%), urinary tract infection (13%), thrombocytopenia (11%), and stomatitis (11%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the first-line maintenance setting for SOLO-1 were: decrease in hemoglobin (87%), increase in mean corpuscular volume (87%), decrease in leukocytes (70%), decrease in lymphocytes (67%), decrease in absolute neutrophil count (51%), decrease in platelets (35%), and increase in serum creatinine (34%).

## ADVERSE REACTIONS—First-Line Maintenance Advanced Ovarian Cancer in Combination with Bevacizumab

Most common adverse reactions (Grades 1-4) in ≥10% of patients treated with LYNPARZA/bevacizumab compared to a ≥5% frequency for placebo/bevacizumab in the first-line maintenance setting for PAOLA-1 were: nausea (53%), fatigue (including asthenia) (53%), anemia (41%), lymphopenia (24%), vomiting (22%), and leukopenia (18%). In addition, the most common adverse reactions (≥10%) for patients receiving LYNPARZA/bevacizumab irrespective of the frequency compared with the placebo/bevacizumab arm were: diarrhea (18%), neutropenia (18%), urinary tract infection (15%), and headache (14%).

In addition, venous thromboembolic events occurred more commonly in patients receiving LYNPARZA/bevacizumab (5%) than in those receiving placebo/bevacizumab (1.9%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients for LYNPARZA in combination with bevacizumab in the first-line maintenance setting for PAOLA-1 were: decrease in hemoglobin (79%),

decrease in lymphocytes (63%), increase in serum creatinine (61%), decrease in leukocytes (59%), decrease in absolute neutrophil count (35%), and decrease in platelets (35%).

## ADVERSE REACTIONS—Maintenance Recurrent Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients who received LYNPARZA in the maintenance setting for SOLO-2 were: nausea (76%), fatigue (including asthenia) (66%), anemia (44%), vomiting (37%), nasopharyngitis/upper respiratory tract infection (URI)/influenza (36%), diarrhea (33%), arthralgia/myalgia (30%), dysgeusia (27%), headache (26%), decreased appetite (22%), and stomatitis (20%).

Study 19: nausea (71%), fatigue (including asthenia) (63%), vomiting (35%), diarrhea (28%), anemia (23%), respiratory tract infection (22%), constipation (22%), headache (21%), decreased appetite (21%), and dyspepsia (20%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the maintenance setting (SOLO-2/Study 19) were: increase in mean corpuscular volume (89%/82%), decrease in hemoglobin (83%/82%), decrease in leukocytes (69%/58%), decrease in lymphocytes (67%/52%), decrease in absolute neutrophil count (51%/47%), increase in serum creatinine (44%/45%), and decrease in platelets (42%/36%).

## ADVERSE REACTIONS—Adjuvant Treatment of gBRCAm, HER2-Negative, High-Risk Early Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA in the adjuvant setting for OlympiA were: nausea (57%), fatigue (including asthenia) (42%), anemia (24%), vomiting (23%), headache (20%), diarrhea (18%), leukopenia (17%), neutropenia (16%), decreased appetite (13%), dysgeusia (12%), dizziness (11%), and stomatitis (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the adjuvant setting for OlympiA were: decrease in lymphocytes (77%), increase in mean corpuscular volume (67%), decrease in hemoglobin (65%), decrease in leukocytes (64%), and decrease in absolute neutrophil count (39%).

## ADVERSE REACTIONS—gBRCAm, HER2-Negative Metastatic Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients who received LYNPARZA in the metastatic setting for OlympiAD were: nausea (58%), anemia (40%), fatigue (including asthenia) (37%), vomiting (30%), neutropenia (27%), respiratory tract infection (27%), leukopenia (25%), diarrhea (21%), and headache (20%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the metastatic setting for OlympiAD were: decrease in hemoglobin (82%), decrease in lymphocytes (73%), decrease in leukocytes (71%), increase in mean corpuscular volume (71%), decrease in absolute neutrophil count (46%), and decrease in platelets (33%).

## ADVERSE REACTIONS—First-Line Maintenance gBRCAm Metastatic Pancreatic Adenocarcinoma

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA in the first-line maintenance setting for POLO were: fatigue (60%), nausea (45%), abdominal pain (34%), diarrhea (29%), anemia (27%), decreased appetite (25%), constipation (23%), vomiting (20%), back pain (19%), arthralgia (15%), rash (15%), thrombocytopenia (14%), dyspnea (13%), neutropenia (12%), nasopharyngitis (12%), dysgeusia (11%), and stomatitis (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the first-line maintenance setting for POLO were: increase in serum creatinine (99%), decrease in hemoglobin (86%), increase in mean corpuscular volume (71%), decrease in lymphocytes (61%), decrease in platelets (56%), decrease in leukocytes (50%), and decrease in absolute neutrophil count (25%).

## ADVERSE REACTIONS—HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA for PROfound were: anemia (46%), fatigue (including asthenia) (41%), nausea (41%), decreased appetite (30%), diarrhea (21%), vomiting (18%), thrombocytopenia (12%), cough (11%), and dyspnea (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA for PROfound were: decrease in hemoglobin (98%), decrease in lymphocytes (62%), decrease in leukocytes (53%), and decrease in absolute neutrophil count (34%).

## DRUG INTERACTIONS

**Anticancer Agents:** Clinical studies of LYNPARZA with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

**CYP3A Inhibitors:** Avoid coadministration of strong or moderate CYP3A inhibitors when using LYNPARZA. If a strong or moderate CYP3A inhibitor must be coadministered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

CYP3A Inducers: Avoid coadministration of strong or moderate CYP3A inducers when using LYNPARZA.

## USE IN SPECIFIC POPULATIONS

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of LYNPARZA have not been established in pediatric patients.

Hepatic Impairment: No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). There are no data in patients with severe hepatic impairment (Child-Pugh classification C).

Renal Impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51-80 mL/min estimated by Cockcroft-Gault). In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the dose of LYNPARZA to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

## INDICATIONS

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

### First-Line Maintenance BRCAm Advanced Ovarian Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

### First-Line Maintenance HRD-Positive Advanced Ovarian Cancer in Combination with Bevacizumab

In combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either:

- a deleterious or suspected deleterious BRCA mutation, and/or
- genomic instability

Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

## Maintenance Recurrent Ovarian Cancer

For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

## Adjuvant Treatment of gBRCAm, HER2-Negative, High-Risk Early Breast Cancer

For the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

## gBRCAm, HER2-Negative Metastatic Breast Cancer

For the treatment of adult patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

## First-Line Maintenance gBRCAm Metastatic Pancreatic Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

## HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

For the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an

FDA-approved companion diagnostic for LYNPARZA.

Please see complete **Prescribing Information** , including **Medication Guide** .

## Notes

## Ovarian cancer

Ovarian cancer is the eighth most common cancer in women worldwide.9 There were more than 313,000 new cases of ovarian cancer in 2020, and over 207,000 deaths. The 5-year survival rate of newly diagnosed advanced ovarian cancer patients has typically been 30-50%.4,5 Roughly half of women with advanced ovarian cancer have homologous recombination deficiency (HRD)-positive tumors including those with a BRCA mutation and up to one in five women have a BRCA mutation.6-8 The primary aim of 1st-line treatment is to delay disease progression for as long as possible with the intent to achieve long-term remission.10-12

## PAOLA-1

PAOLA-1 is a double-blinded Phase III trial testing the efficacy and safety of LYNPARZAadded to standard-of-care bevacizumab versus bevacizumab alone, as a 1st-line maintenance treatment for newly diagnosed advanced FIGO Stage III-IV high-grade serous or endometroid ovarian, fallopian tube, or peritoneal cancer patients who had a complete or partial response to 1st-line treatment with platinum-based chemotherapy and bevacizumab. AstraZeneca and Merck **announced in August 2019** that the trial met its primary endpoint of PFS in the overall trial population.

PAOLA-1 is an ENGOT (European Network of Gynaecological Oncological Trial groups) trial, sponsored by ARCAGY Research (Association de Recherche sur les CAncers dont GYnécologiques) on behalf of GINECO (Groupe d'Investigateurs National des Etudes des Cancers Ovariens et du sein). ARCAGY-GINECO is an academic group specializing in clinical and translational research in patients' cancers and a member of the GCIG (Gynecologic Cancer InterGroup).

## SOLO-1

SOLO-1 is a Phase III randomized, double-blinded, placebo-controlled, multicenter trial to evaluate the efficacy and safety of LYNPARZA tablets (300 mg twice daily) as maintenance monotherapy compared with placebo, in newly-diagnosed patients with advanced BRCAm ovarian cancer following platinum-based chemotherapy. The trial randomized 391 patients with a deleterious or suspected deleterious BRCA1 or BRCA2 mutation who were in clinical complete or partial response following platinum-based chemotherapy. Patients were randomized (2:1) to

receive LYNPARZA or placebo for up to two years or until disease progression (at the investigator's discretion). The primary endpoint was PFS and key secondary endpoints included time to second disease progression or death, time to first subsequent treatment and overall survival. AstraZeneca and MSD **announced in June 2018** that the trial met its primary endpoint of PFS in the overall trial population.

## BRCA

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.13 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 alterations that can lead to cancer. Cancers with BRCA mutations are more likely to be sensitive to PARP inhibitors including LYNPARZA.13-16

## Homologous recombination deficiency

HRD, which defines a subgroup of ovarian cancer, encompasses a wide range of genetic abnormalities, including BRCA mutations and beyond. As with BRCA gene mutations, HRD interferes with normal cell DNA repair mechanisms and confers sensitivity to PARP inhibitors including LYNPARZA.2

## LYNPARZA

LYNPARZA® (olaparib) is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response (DDR) in cells/tumors harboring a deficiency in homologous recombination repair (HRR), such as those with mutations in BRCA1 and/or BRCA2, or those where deficiency is induced by other agents (such as new hormonal agents – NHAs).

Inhibition of PARP proteins 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 currently approved in a number of countries across multiple tumor types including maintenance treatment of platinum-sensitive relapsed ovarian cancer and as both monotherapy and in combination with bevacizumab for the 1st-line maintenance treatment of BRCA-mutated (BRCAm) and homologous recombination repair deficient (HRD)-positive advanced ovarian cancer, respectively; for gBRCAm, HER2-negative metastatic breast cancer (in the EU and Japan this includes locally advanced breast cancer); for gBRCAm, HER2-negative high-risk early breast cancer (in Japan this includes all BRCAm HER2-negative high-risk early breast cancer); for gBRCAm metastatic pancreatic cancer; and HRR gene-mutated metastatic castration-resistant prostate cancer (BRCAm only in the EU

and Japan).

LYNPARZA, which is being jointly developed and commercialized by AstraZeneca and Merck, is the foundation of AstraZeneca's industry-leading portfolio of potential new medicines targeting DDR mechanisms in cancer cells.

## The AstraZeneca and Merck strategic oncology collaboration

In July 2017, AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the US and Canada, announced a global strategic oncology collaboration to co-develop and co-commercialize LYNPARZA, the world's first PARP inhibitor, and selumetinib, a mitogen-activated protein kinase (MEK) inhibitor, for multiple cancer types.

Working together, the companies will develop LYNPARZA and selumetinibin combination with other potential new medicines and as monotherapies. The companies will develop LYNPARZA and selumetinibin combination with their respective PD-L1 and PD-1 medicines independently.

## AstraZeneca in oncology

AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyze changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care 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 commercialization of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit **www.astrazeneca-us.com** and follow the Company on Twitter **@AstraZenecaUS**.

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