



NEWS RELEASE

# LYNPARZA® (olaparib) Reduced the Risk of Disease Progression or Death as First-Line Maintenance Treatment in Germline BRCA-Mutated Metastatic Pancreatic Cancer

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Phase 3 POLO Trial Met Its Primary Endpoint of Progression-Free Survival

AstraZeneca and Merck's LYNPARZA Is the First PARP Inhibitor to Demonstrate Benefit in gBRCAm Metastatic Pancreatic Cancer in a Phase 3 Trial

KENILWORTH, N.J.--(**BUSINESS WIRE**)--AstraZeneca and Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced positive results from the Phase 3 POLO trial.

Results from the trial showed a statistically-significant and clinically-meaningful improvement in progression-free survival (PFS) with LYNPARZA versus placebo. The safety and tolerability profile of LYNPARZA was consistent with previous trials.

POLO is a randomized, double-blinded, placebo-controlled trial exploring the efficacy of LYNPARZA tablets as first-line maintenance monotherapy in patients with germline BRCA-mutated (gBRCAm) metastatic adenocarcinoma of the pancreas (pancreatic cancer) whose disease has not progressed on platinum-based chemotherapy.

José Baselga, executive vice president, research and development, oncology, AstraZeneca, said, "This is the first positive Phase 3 trial of any PARP inhibitor in germline BRCA-mutated metastatic pancreatic cancer, a devastating disease with critical unmet need. Most patients are diagnosed late, leaving them with a poor prognosis and very



limited treatment options. Based on POLO, LYNPARZA becomes the first PARP inhibitor to demonstrate positive Phase 3 results beyond ovarian cancer and breast cancer.”

Dr. Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories, said, “Trials like POLO demonstrate the shared commitment of Merck and AstraZeneca to assess treatments for difficult-to-treat cancers. The clinically-meaningful results of this trial potentially support the value of testing for germline BRCA mutations in patients with metastatic pancreatic cancer. We will discuss these results with global health authorities as soon as possible.”

AstraZeneca and Merck plan to present the full data from the trial at a forthcoming medical meeting.

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

### WARNINGS AND PRECAUTIONS

**Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML):** Occurred in <1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The duration of therapy in patients who developed secondary MDS/AML varied from <6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy, and some also had a history of more than one primary malignancy or of bone marrow dysplasia.

Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy ( $\leq$ 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 <1% of patients exposed to LYNPARZA, 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.

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

Most common adverse reactions (Grades 1-4) in  $\geq 10\%$  of patients in clinical trials of 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%), UTI (13%), thrombocytopenia (11%), and stomatitis (11%).

Most common laboratory abnormalities (Grades 1-4) in  $\geq 25\%$  of patients in clinical trials of 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—Maintenance Recurrent Ovarian Cancer

Most common adverse reactions (Grades 1-4) in  $\geq 20\%$  of patients in clinical trials of 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  $\geq 25\%$  of patients in clinical trials of 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—Advanced gBRCAm ovarian cancer**

Most common adverse reactions (Grades 1-4) in  $\geq 20\%$  of patients in clinical trials of

LYNPARZA for **advanced gBRCAm ovarian cancer after 3 or more lines of chemotherapy** (pooled from 6 studies) were: fatigue/asthenia (66%), nausea (64%), vomiting (43%), anemia (34%), diarrhea (31%), nasopharyngitis/upper respiratory tract infection (URI) (26%), dyspepsia (25%), myalgia (22%), decreased appetite (22%), and arthralgia/musculoskeletal pain (21%).

Most common laboratory abnormalities (Grades 1-4) in  $\geq 25\%$  of patients in clinical trials of LYNPARZA for **advanced gBRCAm ovarian cancer** (pooled from 6 studies) were: decrease in hemoglobin (90%), mean corpuscular volume elevation (57%), decrease in lymphocytes (56%), increase in serum creatinine (30%), decrease in platelets (30%), and decrease in absolute neutrophil count (25%).

### **ADVERSE REACTIONS—gBRCAm, HER2-negative metastatic breast cancer**

Most common adverse reactions (Grades 1-4) in  $\geq 20\%$  of patients in **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  $\geq 25\%$  of patients in **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%).

### **DRUG INTERACTIONS**

**Anticancer Agents:** Clinical studies of LYNPARZA in combination with other

myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

**CYP3A Inhibitors:** Avoid concomitant use of strong or moderate CYP3A inhibitors. If a strong or moderate CYP3A inhibitor must be co-administered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

**CYP3A Inducers:** Avoid concomitant use of strong or moderate CYP3A inducers when using LYNPARZA. If a moderate inducer cannot be avoided, there is a potential for decreased efficacy of 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 adjustment to the starting dose is necessary in patients with mild renal impairment (CL<sub>cr</sub>=51-80 mL/min) but patients should be monitored closely for toxicity. In patients with moderate renal impairment (CL<sub>cr</sub>=31-50 mL/min), reduce the dose to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CL<sub>cr</sub> ≤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 with gBRCAm advanced epithelial ovarian, fallopian tube or primary peritoneal cancer 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.

## Advanced gBRCAm ovarian cancer

For the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with 3 or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

## gBRCAm, HER2-negative metastatic breast cancer

In 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.

Please see complete **Prescribing Information**, including Patient Information (Medication Guide).

## About POLO

POLO is a Phase 3 randomized, double-blinded, placebo controlled, multi-center trial of LYNPARZA tablets (300 mg twice daily) as maintenance monotherapy versus placebo. The trial randomized 154 patients with gBRCAm metastatic pancreatic cancer whose disease has not progressed on first-line platinum-based chemotherapy. Patients were randomized (3:2) to receive LYNPARZA or placebo until disease progression. The primary endpoint was PFS, and key secondary endpoints include overall survival, time to second disease progression, overall response rate, disease control rate and health-related quality of life.

## About LYNPARZA® (olaparib)

LYNPARZA is a first-in-class PARP inhibitor and the first targeted treatment to potentially exploit DNA damage response (DDR) pathway deficiencies, such as BRCA mutations, to preferentially kill cancer cells. 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 tumor types with defects and dependencies in the DDR.

LYNPARZA, which is being jointly developed and commercialized by AstraZeneca and Merck, has a broad and advanced clinical trial development program, and AstraZeneca and Merck are working together to understand how it may affect multiple PARP-dependent tumors as a monotherapy and in combination across multiple cancer types. LYNPARZA is being tested in a range of DDR-deficient tumor types.

## About Pancreatic Cancer

Pancreatic cancer is the 12th most common cancer worldwide. Germline BRCA-mutated pancreatic cancer accounts for five to seven percent of all cases globally. With the worst survival rate of the most common cancers, pancreatic cancer is the fourth leading cause of cancer death, and less than seven percent of patients survive more than five years after diagnosis. Early diagnosis of pancreatic cancer is difficult, as often there are no symptoms until the disease has advanced. Around 80 percent of patients are diagnosed at the metastatic stage.

In the U.S. this year, approximately 56,700 people will be diagnosed and more than 45,000 will die from pancreatic cancer, which accounts for about seven percent of all U.S. cancer deaths. The five-year survival rate in the U.S. for all stages is just nine percent and for the 52 percent of people who are diagnosed after the cancer has spread to a distant part of the body, the five-year survival rate is just three percent.

## About BRCA Mutations

BRCA1 and BRCA2 are human genes that produce proteins responsible for repairing damaged DNA and play an important role in 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 the AstraZeneca and Merck Strategic Oncology Collaboration

In July 2017, AstraZeneca and Merck, known as MSD outside the United States and Canada, announced a global

strategic oncology collaboration to co-develop and co-commercialize 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.

## Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, the potential to bring new hope to people with cancer drives our purpose and supporting accessibility to our cancer medicines is our commitment. As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types. We also continue to strengthen our portfolio through strategic acquisitions and are prioritizing the development of several promising oncology candidates with the potential to improve the treatment of advanced cancers. For more information about our oncology clinical trials, visit [www.merck.com/clinicaltrials](http://www.merck.com/clinicaltrials).

## About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

## Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

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