NEWS RELEASE

LYNPARZA® (olaparib) Receives Positive Opinion from EU CHMP for First-Line Maintenance Treatment of Patients with Germline BRCA-Mutated Metastatic Pancreatic Cancer

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Only PARP Inhibitor to Demonstrate Patient Benefit in a Phase 3 Trial in This Setting

KENILWORTH, N.J.--(BUSINESS WIRE)--

AstraZeneca and Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion, recommending LYNPARZA for approval as monotherapy for the maintenance treatment of adult patients with germline BRCA1/2 mutations (gBRCAm) who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen.

The CHMP based its positive opinion on results from the Phase 3 POLO trial, which were previously published in TheNew England Journal of Medicine.

The trial demonstrated LYNPARZA nearly doubled the time patients with gBRCAm metastatic pancreatic cancer lived without disease progression or death to a median of 7.4 months vs. 3.8 months on placebo (HR 0.53 [95% CI 0.35-0.82] p=0.004).

The safety and tolerability profile of LYNPARZA in the POLO trial was consistent with previous trials. The most

common adverse reactions (ARs) ≥10% were fatigue/asthenia (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%). The most common ≥ Grade 3 ARs were anemia (11%), fatigue/asthenia (5%), decreased appetite (3%), abdominal pain (2%), vomiting (1%) and arthralgia (1%). Among patients taking LYNPARZA, dose interruptions due to an AR of any grade occurred in 35% and dose reductions due to an AR occurred in 17%. Discontinuation due to ARs occurred in 6% of patients receiving LYNPARZA.

Dr. José Baselga, executive vice president, oncology R&D, AstraZeneca, said, “Patients with advanced pancreatic cancer have seen limited treatment advances over the last few decades. We are now one step closer to potentially bringing the first targeted medicine to certain biomarker-selected patients with advanced pancreatic cancer in the EU.”

Dr. Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories, said, “A pancreatic cancer diagnosis is devastating, and we are committed to research that aims to change the prognosis for patients. The POLO trial demonstrated that treatment with LYNPARZA extended time without disease progression in certain patients with advanced pancreatic cancer – we are hopeful that we will be able to bring this treatment to patients in the EU soon.”

LYNPARZA is approved in the U.S. as a first line maintenance treatment for patients with gBRCAm metastatic pancreatic cancer whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

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 (≤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.

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 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 ≥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—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 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 ≥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 ≥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 ≥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 ≥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 ≥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%).

ADVERSE REACTIONS—First-Line Maintenance gBRCAm Metastatic Pancreatic Adenocarcinoma

Most common adverse reactions (Grades 1-4) in ≥10% of patients in clinical trials of 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 in clinical trials of 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 in clinical trials of 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 in clinical trials of 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.

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

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 **click here for 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 vs. placebo. The trial randomized 154 patients with gBRCAm metastatic pancreatic cancer whose disease had 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 progression-free survival and key secondary endpoints included overall survival, time to second disease progression, overall response rate and health-related quality of life. Phase 3 POLO results were published in The New England Journal of Medicine and presented at the 2019 American Society of Clinical Oncology Annual Meeting.

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.

About Pancreatic Cancer

Pancreatic cancer is the 12th most commonly occurring cancer worldwide and the 7th leading cause of cancer death globally. The disease has the lowest survival rate of the most common cancers,and is the only major cancer with a single-digit five-year survival rate (2-9%) in nearly every country. There were approximately 460,000 new cases worldwide in 2018.As there are often no symptoms, or symptoms may be non-specific in the early stages, it is most commonly diagnosed at an incurable stage. Around 80% of pancreatic cancer patients are diagnosed when the disease has metastasized and for these, the average survival is less than a year.Despite advances in treatment, few improvements have been made in diagnosis and treatment over the decades. Current treatment is surgery (for which approximately only 10-20% of patients are eligible), chemotherapy and radiotherapy, highlighting a critical unmet medical need for more effective treatment options.12

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 certain oncology products including LYNPARZA, the world's first PARP inhibitor, for multiple cancer types. Working together, the companies will develop these products in combination with other potential new medicines and as monotherapies. Independently, the companies will develop these oncology products 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**.

About Merck

For more than 125 years, Merck, 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 in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit **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 the recent global outbreak of novel coronavirus disease (COVID-19); 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 2019 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**).

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