pharma&'s ATHENA-MONO Clinical Trial Data Suggests That Rubraca® is a Potential Beneficial Therapeutic Option for Patients with HRD-Negative and HRD-Positive Tumors

- *The ATHENA-MONO trial data demonstrates first-line rucaparib maintenance treatment reduced the risk of progression in patients with advanced homologous recombination deficiency (HRD)-negative tumors*[1]
- *The safety profile observed in ATHENA-MONO was consistent with rucaparib labeling*[1]

Intended for the Healthcare Media

Vienna, Austria, June 20, 2025 - pharmaand GmbH (pharma&) announced today data from the randomized, Phase 3 company-sponsored ATHENA trial investigating rucaparib monotherapy versus placebo (ATHENA-MONO) was presented on Friday, June 20, during the 2025 ESMO Gynaelogical Cancers Annual Congress in Vienna, Austria. Professor Vanda Salutari, MD, Department of Health of Woman and Child, Catholic University of Sacred Heart, Rome, Italy, on behalf of lead author Dr. Ana Oaknin, MD, Ph.D., and ATHENA investigators, presented "Efficacy and Safety of Rucaparib Maintenance Treatment in Patients from ATHENA-MONO/GOG-3020/ENGOT-ov45 With Newly Diagnosed Advanced Ovarian Cancer Not Associated with Homologous Recombination Deficiency."

"Rucaparib provides a progression-free survival benefit for patients with advanced high-grade ovarian cancer regardless of whether the tumor is homologous recombination deficiency positive or homologous recombination deficiency negative," said Dr. Salutari. "Based on the data presented at the ESMO-GYN conference, first-line rucaparib maintenance may offer progression-free survival benefit to a broad eligible patient population."

Progression-Free Survival (PFS) in HRD-Negative Subgroup

In ATHENA-MONO (NCT03522246), first-line rucaparib maintenance treatment provided a PFS benefit vs placebo in newly diagnosed, advanced, high-grade ovarian cancer after front-line platinum-based chemotherapy[2]. The largest subgroup of patients in ATHENA-MONO had HRD-negative disease (*BRCA*–wild-type with low loss of heterozygosity (LOH); 44%), which is associated with worse PFS and overall survival (OS) prognosis compared with *BRCA*-mutated or HRD-positive disease.

Previously, in the HRD-negative subgroup, rucaparib imparted a 35% reduction in progression risk versus placebo (HR, 0.65; 95% CI, 0.45–0.95)[2], which was supported by an interim analysis of OS (HR, 0.75; 95% CI, 0.48–1.17).

Based on today's presentation, rucaparib monotherapy reduced the risk of progression for all prognostic factors evaluated in patients with HRD-negative tumors, including by specific baseline characteristics and demographics such as by Eastern Cooperative Oncology Group performance status (ECOG PS), International Federation of Gynecology and Obstetrics (FIGO) stage, timing and outcome of surgery, and response to chemotherapy.

The safety profile observed in ATHENA-MONO was consistent with rucaparib labeling.

"These findings reinforce that regardless of homologous recombination deficiency status, eligible patients with advanced ovarian cancer may benefit from first-line maintenance treatment with rucaparib," said Frank Rotmann, Co-Founder and Managing Director, pharma&. "We are grateful to the patients, caregivers, and physicians who participated in this trial."

About the ATHENA Clinical Trial

ATHENA (GOG 3020/ENGOT-ov45) (NCT03522246) is an international, randomized, double-blind, phase III trial consisting of two separate and fully independently powered study comparisons evaluating rucaparib monotherapy (ATHENA-MONO) and rucaparib in combination with nivolumab (ATHENA-COMBO) as maintenance treatment for patients with newly diagnosed advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer. ATHENA enrolled approximately 1000 patients across 24 countries, all women with newly diagnosed ovarian cancer who responded to their first-line chemotherapy. The trial completed accrual in 2020 and was conducted in association with the GOG Foundation, Inc. (GOG-F) in the U.S. and the European Network of Gynaecological Oncological Trial groups (ENGOT) in Europe. GOG-F and ENGOT are the two largest cooperative groups in the U.S. and Europe dedicated to the treatment of gynecological cancers.

ATHENA-MONO is evaluating the benefit of rucaparib monotherapy versus placebo in 538 women in this patient population. The primary efficacy analysis evaluated two prospectively defined molecular sub-groups in a step-down manner: 1) HRD-positive (inclusive of *BRCA* mutant) tumors, and 2) the intent-to-treat population, or all patients treated in ATHENA-MONO.

About the GOG Foundation, Inc. (www.gog.org)

The GOG Foundation, Inc. is a not-for-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and translational scientific research in the field of gynecologic malignancies. The GOG Foundation is committed to maintaining the highest standards in clinical trials development, execution, analysis, and distribution of results. The GOG Foundation is the only clinical trialist group in the United States that focuses its research on patients with pelvic malignancies, such as cancer of the ovary (including surface peritoneal malignancies), uterus (including endometrium, soft tissue sarcoma, and gestational trophoblastic neoplasia), cervix, and vulva. The GOG Foundation is multi-disciplinary in its approach to clinical trials, and includes gynecologic oncologists, medical oncologists, pathologists, radiation oncologists, oncology nurses, biostatisticians (including those with expertise in bioinformatics), basic scientists, quality of life experts, data managers, and administrative personnel.

About the GOG Partners Program

Supported by industry, GOG Partners program is structured to work directly with pharmaceutical organizations and operate clinical trials outside the National Cancer Institute (NCI) framework. The GOG Partners program promotes the mission of the GOG Foundation dedicated to transforming care in Gynecologic Oncology. By providing an alternative venue for patient accrual and site infrastructure support, GOG Partners has helped provide additional trials and opportunities for patients outside the national gynecologic clinical trials network.

About ENGOT (www.engot.esgo.org)

The European Network for Gynaecological Oncological Trial (ENGOT) groups is a research network of the European Society of Gynaecological Oncology (ESGO) and was founded in Berlin in October 2007. Currently, ENGOT consists of 21 trial groups from 33 European countries that perform cooperative clinical trials. ENGOT's ultimate goal is to bring the best treatment to gynaecological cancer patients through the best science and enabling every patient in every European country to access a clinical trial.

Rucaparib European Union (EU), including Northern Ireland, authorized use and Important Safety Information

Rucaparib is indicated as monotherapy for the maintenance treatment of adult patients with advanced (FIGO Stages III and IV) high-grade epithelial ovarian, fallopian

tube, or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy.

Rucaparib is indicated as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinumbased chemotherapy.

Efficacy of rucaparib as treatment for relapsed or progressive epithelial ovarian cancer (EOC), fallopian tube cancer (FTC), or primary peritoneal cancer (PPC) has not been investigated in patients who have received prior treatment with a PARP inhibitor. Therefore, use in this patient population is not recommended.

Summary warnings and precautions:

Hematological toxicity

During treatment with rucaparib, events of myelosuppression (anemia, neutropenia, thrombocytopenia) may be observed and are typically first observed after 8–10 weeks of treatment with rucaparib. These reactions are manageable with routine medical treatment and/or dose adjustment for more severe cases. Complete blood count testing prior to starting treatment with rucaparib and monthly thereafter is advised. Patients should not start rucaparib treatment until they have recovered from hematological toxicities caused by previous chemotherapy (< CTCAE grade 1).

Supportive care and institutional guidelines should be implemented for the management of low blood counts for the treatment of anemia and neutropenia. Rucaparib should be interrupted, or dose reduced according to Table 1 (see Posology and Method of Administration [4.2] of the Summary of Product Characteristics [SmPC]), and blood counts monitored weekly until recovery. If the levels have not recovered to CTCAE grade 1 or better after four weeks, the patient should be referred to a hematologist for further investigations.
MDS/AML

MDS/AML, including cases with fatal outcomes, have been reported in patients who received rucaparib. The duration of therapy with rucaparib in patients who developed MDS/AML varied from less than 2 months to approximately 6 years.

If MDS/AML is suspected, the patient should be referred to a hematologist for further investigations, including bone marrow analysis and blood sampling for cytogenetics. If,

following investigation for prolonged hematological toxicity, MDS/AML is confirmed, rucaparib should be discontinued.

Photosensitivity

Photosensitivity has been observed in patients treated with rucaparib. Patients should avoid spending time in direct sunlight because they may burn more easily during rucaparib treatment; when outdoors, patients should wear a hat and protective clothing and use sunscreen and lip balm with sun protection factor of 50 or greater.

Gastrointestinal toxicities

Gastrointestinal toxicities (nausea and vomiting) are frequently reported with rucaparib and are generally low grade (CTCAE grade 1 or 2) and may be managed with dose reduction (refer to Posology and Method of Administration [4.2], Table 1 of the SmPC) or interruption. Antiemetics, such as 5-HT3 antagonists, dexamethasone, aprepitant, and fosaprepitant, can be used as treatment for nausea/vomiting and may also be considered for prophylactic (i.e., preventative) use prior to starting rucaparib. It is important to proactively manage these events to avoid prolonged or more severe events of nausea/vomiting, which have the potential to lead to complications such as dehydration or hospitalization.

Intestinal obstruction

Cases of intestinal obstruction have been observed in ovarian cancer patients treated with rucaparib in clinical trials; 3.5% of patients treated with rucaparib experienced a serious event of intestinal obstruction, with a fatal outcome in 1 rucaparib treated patient (less than 0.1%). The underlying disease may play a role in the development of intestinal obstruction in patients with ovarian cancer. In the event of suspected intestinal obstruction, a prompt diagnostic evaluation should be conducted, and the patient should be treated appropriately.

Embryofetal toxicity

Rucaparib can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings from animal studies. In an animal reproduction study, administration of rucaparib to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 600 mg twice daily (see Preclinical Safety Data [5.3] of the SmPC).

Pregnancy/contraception

Pregnant women should be informed of the potential risk to a fetus. Women of reproductive potential should be advised to use effective contraception during treatment and for six months following the last dose of rucaparib (see section 4.6 of the SmPC). A pregnancy test before initiating treatment is recommended in women of reproductive potential.

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say, essentially 'sodium-free.'

Click here to access the current EU SmPC (including for Northern Ireland).

Healthcare professionals should report any suspected adverse reactions via their national reporting systems.

For medical information inquiries outside of the U.S., contact pharma& at medinfo@pharmaand.com.

Rucaparib Medicines and Healthcare products Regulatory Agency (MHRA) authorized use and Important Safety Information

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Myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML)

MDS/AML, including cases with fatal outcomes, have been reported in patients who received rucaparib. The duration of therapy with rucaparib in patients who developed MDS/AML varied from less than 2 months to approximately 6 years.

If MDS/AML is suspected, the patient should be referred to a hematologist for further investigations, including bone marrow analysis and blood sampling for cytogenetics. If, following investigation for prolonged hematological toxicity, MDS/AML is confirmed, rucaparib should be discontinued.

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Rucaparib Ovarian Cancer U.S. FDA Approved Indication

Rucaparib is indicated for the maintenance treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy.

Select Important Safety Information

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) occur in patients treated with rucaparib and are potentially fatal adverse reactions. In 1594 treated patients with ovarian cancer [see Adverse Reactions (6.1)], MDS/AML occurred in 32 patients (2%), including those in long term follow-up. Of these, 14 occurred during treatment or during the 28-day safety follow-up (0.9%). The duration of rucaparib treatment prior to the diagnosis of MDS/AML ranged from < 2 months to approximately 72 months. The cases were typical of secondary MDS/cancer therapy-related AML; in all cases, patients had received previous platinum-containing chemotherapy regimens and/or other DNA damaging agents.

In ARIEL3, of patients with a germline and/or somatic *BRCA* mutation treated with rucaparib, MDS/AML occurred in 9 out of 129 (7%) patients treated with rucaparib and 4 out of 66 (6%) patients treated with placebo. The duration of therapy with rucaparib in patients who developed secondary MDS/cancer therapy-related AML varied from 1.2 to 4.7 years.

Do not start rucaparib until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1). Monitor complete blood counts for cytopenia at baseline and monthly thereafter for clinically significant changes during

treatment. For prolonged hematological toxicities (> 4 weeks), interrupt rucaparib or reduce dose and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks or if MDS/AML is suspected, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue rucaparib.

Based on its mechanism of action and findings from animal studies, rucaparib can cause fetal harm when administered to a pregnant woman. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of rucaparib.

Most common adverse reactions in patients with *BRCA*-mutated ovarian cancer in ARIEL3 (≥ 20%; Grade 1-4) were nausea (79%), fatigue/asthenia (74%), abdominal pain/distention (48%), rash (45%), anemia (41%), constipation (39%), vomiting (37%), thrombocytopenia (35%), diarrhea (34%), dysgeusia (33%), AST/ALT elevation (33%), nasopharyngitis/upper respiratory tract infection (29%), stomatitis (28%), decreased appetite (23%), and neutropenia (20%).

Co-administration of rucaparib can increase the systemic exposure of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, which may increase the risk of toxicities of these drugs. Adjust dosage of CYP1A2, CYP3A, CYP2C9, or CYP2C19 substrates, if clinically indicated. If co-administration with warfarin (a CYP2C9 substrate) cannot be avoided, consider increasing frequency of international normalized ratio (INR) monitoring.

Because of the potential for serious adverse reactions in breast-fed children from rucaparib, advise lactating women not to breastfeed during treatment with rucaparib and for 2 weeks after the last dose.

Please click here for full Prescribing Information for rucaparib.

You may report adverse events to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Alternatively, to report an adverse event or reaction, contact pharma& at pv@pharmaand.com.

To report a product complaint, contact pharma& at complaints@pharmaand.com.

For medical information inquiries within the U.S., contact pharma& at medinfo.us@pharmaand.com.

About pharma& (pharmaand.com)

pharmaand GmbH (pharma&), a privately owned global company, aspires to breathe new life into proven medicines through an agile and fully integrated business model, and aims to guarantee the enduring availability, dependability, and quality of essential drugs worldwide that patients and healthcare providers rely on. Over the past five years, pharma& has acquired and integrated 10+ medicines, expanding its portfolio across a wide range of therapy areas, with an increasing focus on hematology and oncology treatments. The Company's unique synthesis of subsidiaries, joint ventures, and partners enables pharma& to provide its portfolio of medicines to eligible patients worldwide by spanning the continuum of development, product and API manufacturing, partner distribution, healthcare provider engagement, distribution and services to patients.

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pharma& cautions that any forward-looking statements or projections made, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. pharma& does not undertake to update or revise any forward-looking statements.

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pharma& Media Contact:
media@pharmaand.com

References

1. Oaknin A, Prendergast E, Salutari V, et al. Efficacy and Safety of Rucaparib Maintenance Treatment in Patients from ATHENA-MONO/GOG-3020/ENGOT-ov45 with Newly Diagnosed Advanced Ovarian Cancer not Associated with Homologous Recombination Deficiency. Presented at ESMO Gynaecological Cancers Annual Congress 2025, 20 June, Vienna, Austria.

2. Monk BJ, Parkinson C, Lim MC, et al. A Randomized, Phase III Trial to Evaluate Rucaparib Monotherapy as Maintenance Treatment in Patients with Newly Diagnosed Ovarian Cancer (ATHENA-MONO/GOG-3020/ENGOT-ov45). J Clin Oncol. 2022;40:3952-3964