pharma& Updates on the Phase 3 ATHENA-COMBO Trial Evaluating rucaparib (Rubraca®) in Combination with nivolumab in First-line Maintenance Treatment in Women with Advanced Ovarian Cancer

Intended for the Media

Vienna, Austria, May 31, 2024 – pharmaand GmbH (pharma&) in collaboration with the GOG Foundation, Inc. (GOG-F) and the European Network for Gynaecological Oncological Trial groups (ENGOT) announced today data from the ATHENA-COMBO comparison within the randomized, Phase 3 pharma&-sponsored ATHENA (GOG-3020/ENGOT-ov45) trial investigating the combination of rucaparib (Rubraca®) and nivolumab as maintenance treatment in advanced ovarian cancer. The primary endpoint of investigator-assessed progression-free survival (PFS) comparing the combination of rucaparib and nivolumab with rucaparib monotherapy was not met in the intent-to-treat (ITT) population. The safety profile of rucaparib in combination with nivolumab was consistent with that observed in previously reported studies and the known safety profiles of each medication. The PFS of the rucaparib monotherapy arm in the ATHENA-COMBO analysis was consistent with the PFS previously reported in the ATHENA-MONO (rucaparib vs placebo) analysis.

The ATHENA-COMBO trial results will be submitted to an upcoming medical meeting.

"Though the trial did not meet its primary endpoint, the ATHENA-COMBO trial addresses many of the unanswered questions surrounding the use of PARP inhibitors in combination with immunotherapy in patients with advanced ovarian cancer," said Bradley J. Monk, MD, FACOG, FACS Medical Director, Late-Phase Clinical Research, Florida Cancer Specialists & Research Institute, and global primary investigator of the ATHENA trial. "The progression-free survival from the rucaparib monotherapy arm of the ATHENA-COMBO trial confirms the use of rucaparib monotherapy as a treatment option in eligible patients."

In addition to the ATHENA-COMBO trial findings, the following further support rucaparib monotherapy as maintenance treatment in eligible patients with advanced ovarian cancer who are in complete or partial response to first-line platinum-based chemotherapy:

- Based on the results from the ATHENA-MONO trial evaluating the benefit of rucaparib monotherapy versus placebo in 538 women in this patient population, the European Medicines Agency (EMA) approved in November 2023 and the Medicines and Healthcare products Regulatory Agency (MHRA) approved in January 2024, rucaparib in advanced ovarian cancer as maintenance treatment for patients who are in response (complete or partial) to first-line platinum-based chemotherapy.
- ASCO Clinical Practice Guidelines recommend rucaparib for those with germline or somatic pathogenic or likely pathogenic variants in *BRCA1* or *BRCA2* genes, for those who are HRD positive, determined using FDA-approved companion diagnostic tests, and for non-BRCAmut/HRDneg patients with newly diagnosed stage III-IV high-grade serous (HGS) or endometrioid ovarian cancer who are in complete or partial response to first-line platinum-based chemotherapy.
- The NCCN Guidelines Version 1.2024 Ovarian Cancer/ Fallopian Tube Cancer/Primary Peritoneal Cancer includes category 2A recommendation for rucaparib monotherapy as first-line maintenance post-primary chemotherapy.

Rucaparib is currently approved in the U.S. 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.

"While the primary results of the ATHENA-COMBO trial are disappointing, it illustrates pharma&'s commitment to oncology and reinforces the use of Rubraca monotherapy treatment in approved indications," said Frank Rotmann, Founder and Managing Director of pharma&. "These results are an important reminder of how challenging it may be to treat these patients with advanced ovarian cancer. We sincerely thank the patients, their caregivers, and investigators for their important contributions to this study."

pharma& is dedicated to providing seamless access to rucaparib and all our products. Rubraca tablets are available in all strengths in the U.S. The Company obtained the

Marketing Authorization for rucaparib tablets on June 19, 2023, and rucaparib tablets are available in Europe on a country-by-country basis, dependent on reimbursement.

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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.

The ATHENA-COMBO portion of the trial is evaluating the magnitude of benefit of adding nivolumab to rucaparib monotherapy in the ovarian cancer first-line maintenance treatment setting.

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 the 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.

About Ovarian Cancer

Ovarian cancer is the eighth leading cause of cancer-related death among women worldwide. In 2020, GLOBOCAN estimated 314,000 women received a new diagnosis of ovarian cancer, and approximately 207,200 women died from ovarian cancer. According to the American Cancer Society, an estimated more than 19,000 women will be diagnosed with ovarian cancer in the United States, and there will be an estimated nearly 13,000 deaths from ovarian cancer in 2023. According to GLOBOCAN, an estimated 66,000 women in Europe are diagnosed each year with ovarian cancer, and ovarian cancer is among those cancers with the highest rate of death. According to

the NIH National Cancer Institute, more than 75% of women are diagnosed with ovarian cancer at an advanced stage.

Despite recent advances in the therapeutic landscape of newly diagnosed ovarian cancer, advanced ovarian cancer is still considered incurable for the majority of patients, and the optimal treatment strategy has yet to be determined.[i] Although most respond initially to this treatment, 80% of patients with advanced ovarian cancer will have a recurrence and require subsequent therapies.[ii]

Rubraca Ovarian Cancer U.S. FDA Approved Indication

Rubraca 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 Rubraca, 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 Rubraca 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 Rubraca, MDS/AML occurred in 9 out of 129 (7%) patients treated with Rubraca and 4 out of 66 (6%) patients treated with placebo. The duration of therapy with Rubraca in patients who developed secondary MDS/cancer therapy-related AML varied from 1.2 to 4.7 years.

Do not start Rubraca 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 Rubraca 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 Rubraca.

Based on its mechanism of action and findings from animal studies, Rubraca 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 Rubraca.

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 Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the last dose.

Please Click here for full Prescribing Information for Rubraca.

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.

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

Rubraca 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 platinum-based 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.

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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.

pharma& holds the worldwide rights for Rubraca®.

To the extent that statements contained in this press release are not descriptions of historical facts regarding pharma&, they are forward-looking statements reflecting the current beliefs and expectations of management. Examples of forward-looking statements contained in this press release include, among others, statements of our intentions and expectations for our development programs, including potential indications, tumor types, plans for presentation of data with respect to Rubraca. Such forward-looking statements involve substantial risks and

uncertainties that could cause pharma&'s actual results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in clinical development, including the outcome of clinical trials, whether initial results, findings, or research will support future studies or development, whether future study results will be consistent with previous study findings or other results, results in named-patient or similar programs or clinical trials, whether additional studies not originally contemplated are determined to be necessary, the timing of initiation, enrollment and completion of planned studies and actions by regulatory authorities regarding data required to support drug applications and whether to approve drug applications. pharma& undertakes no obligation to update or revise any forward-looking statements.

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pharma& Media Contact:
media@pharmaand.com

[i] Monk BJ et al. ATHENA (GOG-3020/ENGOT-ov45): a randomized, phase III trial to evaluate rucaparib as monotherapy (ATHENA–MONO) and rucaparib in combination with nivolumab (ATHENA–COMBO) as maintenance treatment following frontline platinum-based chemotherapy in ovarian cancer. Int J Gynecol Cancer. 2021;0:1–6.

[ii] Hanker LC et al. The impact of second to sixth line therapy on survival of relapsed ovarian cancer after primary taxane/platinum-based therapy. Ann Oncol. 2012;23(10):2605-2612. doi:10.1093/annonc/mds203.