European Commission Approves pharmaand GmbH's Rubraca® (rucaparib) as a First-Line Maintenance Treatment in Advanced Ovarian Cancer

- European Commission approval is based on the results from Phase 3 ATHENA-MONO trial and follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) in October 2023
- The trial demonstrated that rucaparib significantly improved investigator-assessed progression-free survival compared with placebo in women, regardless of their BRCA mutation status

Vienna, Austria, November 20, 2023 – pharmaand GmbH (pharma&) announced today that the European Commission (EC) has granted marketing authorization for a Type II variation for Rubraca® (rucaparib) as a first-line maintenance treatment for all women with advanced ovarian cancer regardless of their *BRCA* mutation status, who have responded to first-line platinum-based chemotherapy.

Rucaparib was previously approved as a monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who have a complete or partial response to platinum-based chemotherapy.

"We are pleased to announce that the European Commission has granted approval, affirming rucaparib as a first-line maintenance treatment therapy for eligible patients with advanced ovarian cancer," said Frank Rotmann, Founder and Managing Director, pharma&. "Today's approval by the European Commission will help to ensure that healthcare providers and eligible patients, regardless of their BRCA mutation status, have access to and may benefit from rucaparib earlier in their treatment journey."

"Over the last five years, pharma& has firmly established itself as a globally integrated and agile company, with a focus on growing our portfolio of medicines and maintaining and developing the value of essential medicines for all who depend on them," said Elmar Zagler, Founder and Managing Director, pharma&. "This approval by

the European Commission marks another step towards delivering on that commitment, and we look forward to broadening access to the potential benefits of rucaparib to a wider group of eligible patients living with advanced ovarian cancer in Europe."

The EC based its approval on the randomized, double-blind, placebo-controlled, Phase 3 ATHENA-MONO trial results. As a first-line maintenance treatment in advanced ovarian cancer, rucaparib significantly improved investigator-assessed progression-free survival (PFS) compared with placebo in women, regardless of their BRCA mutation status in each of the populations studied. The safety profile observed in the ATHENA-MONO trial was consistent with both the current U.S. and European labels for rucaparib.

The ATHENA-MONO trial results were presented during the 2022 American Society of Clinical Oncology Annual Meeting and published in tandem in the Journal of Clinical Oncology.

"In the ATHENA-MONO trial, rucaparib prolonged progression-free survival, irrespective of molecular characteristics, and its approval by the European Commission as a first-line maintenance treatment is an important step forward in this difficult-to-treat population," said Dr. Rebecca Kristeleit, Consultant Medical Oncologist and Adjunct Reader, Guy's and St. Thomas' NHS Foundation Trust and King's College London, London, UK, and European Network of Gynaecological Oncological Trial (ENGOT) lead of the ATHENA trial. "Women with advanced ovarian cancer need and deserve new treatment options to improve outcomes, and today's approval is hopeful news for eligible patients in Europe."

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 [SPC]), 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 SPC).

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 SPC). 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 a period of 3 years from 1 January 2021, when determining an application for a Great Britain Marketing Authorisations (MA), the MHRA may rely on a decision taken by the European Commission (EC) on the approval of a new MA in the centralised procedure. The MHRA aims to determine the Great Britain MA as soon as possible after EC approval. A delay in submission may affect the delivery of a decision within the 67-day timeline. (Source: European Commission (EC) Decision Reliance Procedure - GOV.UK (www.gov.uk), Accessed Nov 2023.)

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 1,000 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 Gynecologic Oncology Group (GOG) in the US and the European Network of Gynaecological Oncological Trial groups (ENGOT) in Europe. GOG and ENGOT are the two largest cooperative groups in the US 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 Opdivo (nivolumab) to rucaparib monotherapy in the ovarian cancer first-line maintenance treatment setting.

About Ovarian Cancer

Ovarian cancer is the seventh leading cause of cancer-related death among women worldwide. In 2020, the Global Cancer Observatory (GLOBOCAN) estimated that 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 deaths. 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]

About pharma&

pharmaand GmbH (pharma&), a privately owned global company, aspires to breathe new life into proven medicines through an agile and fully integrated business model, guaranteeing 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 manufacturing, distribution, healthcare providers, administration/access, and patient support.

pharma& holds worldwide rights for Rubraca®. Rubraca® is an unlicensed medical product outside the U.S., Europe, and Israel.

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 may include, among others, statements regarding our expectations for submission of regulatory filings, reimbursement, our plans for the presentation of data from ongoing trials, our expectations regarding ongoing or planned trials, and the timing and pace of commencement of and enrollment in our clinical trials, including those being considered, planned, or conducted in collaboration with partners. Such forward-looking statements involve substantial risks and uncertainties that could cause our future 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 regulatory filings, reimbursement, our clinical development programs for our drug candidates and those of our partners, whether future study results will be consistent with study findings to date, and whether future study results will support continued development or regulatory approval, the timing of availability of data from our clinical trials and the results, the initiation, enrollment, timing, and results of our planned clinical trials. pharma& does not undertake to update or revise any forward-looking statements.

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[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.