Stockholm, Sweden **Press release October 26, 2022**

Oncopeptides phase 3 LIGHTHOUSE study further confirms clinical benefit of melflufen

STOCKHOLM — October 26, 2022 — Oncopeptides AB (publ) (Nasdaq Stockholm: ONCO), a biotech company focused on research and development of therapies for difficult-to-treat hematological diseases, today announces data from the phase 3 LIGHTHOUSE study that further confirms the clinical benefit of melflufen in patients with relapsed refractory multiple myeloma (RRMM). The LIGHTHOUSE study investigated the efficacy and safety of the combination of melflufen plus daratumumab subcutaneous (sc) plus dexamethasone in comparison with daratumumab sc. (with supportive dexamethasone) in patients who were refractory to at least an immunomodulatory agent and a proteasome inhibitor or have received at least three prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent.

LIGHTHOUSE is a randomized, open label phase 3 trial, designed as a confirmatory study in addition to the phase 3 OCEAN study. The primary endpoint was progression free survival (PFS). The study started in December 2020 and was planned to include 240 patients. In July 2021, the US Food and Drug Administration (FDA) requested a partial clinical hold of all studies with melflufen. Consequently, patient recruitment in LIGHTHOUSE was halted after 54 patients had been randomized. The clinical study was prematurely terminated in February 2022. Twenty-seven patients were randomized to each treatment arm. Patient characteristics were balanced between the two study arms. The observed efficacy and safety profile for the daratumumab sc. control arm in LIGHTHOUSE was in line with the approval labels in EU and USA with numerically higher PFS and Overall Response Rate (ORR).

Despite the small number of patients enrolled in LIGHTHOUSE at the time of study termination (n=54), the PFS in the ITT population was superior for the melflufen treatment arm in comparison with the control arm with a hazard-ratio (HR) of 0.18 and a nominal p-value of 0.0032. The ITT ORR was superior with a nominal p-value of 0.030, and the ITT Overall Survival (OS) HR was 0.47 with a nominal p-value of 0.37.

“Data from the phase 3 LIGHTHOUSE study are very encouraging and clearly indicate that the combination of melflufen and daratumumab has a clinical benefit in patients with RRMM,” says María-Victoria Mateos, MD, PhD, from Salamanca’s University Hospital Haematology Department, and Lead Investigator of the LIGHTHOUSE study. “Multiple myeloma is still an incurable disease for most patients, and we welcome additional evidence on how to combine treatment options with different mode of actions in clinical practice.”

In the patient population where the European Medicines Agency (EMA) confirmed melflufen clinical benefit based on the OCEAN trial, the LIGHTHOUSE study (n=29) demonstrated superior PFS with a HR of 0.062 with a nominal p-value of 0.0005, superior ORR with a nominal p-value of 0.0051, and superior OS with a HR of 0.00 with a nominal p-value of 0.037. This patient population excludes patients with post-ASCT time-to-progression <36 months.

“LIGHTHOUSE is the second phase 3 study to confirm the clinical benefit of melflufen in multiple myeloma patients with a treatment history with no stem-cell transplant or a successful prior stem-cell transplant in line with the recent full European approval,” said Jakob Lindberg, CEO, Oncopeptides. “In addition, the LIGHTHOUSE data support the EMA conclusion that there is no indication of absolute overall survival harm from treatment with melflufen.”

The safety profile of the melflufen and daratumumab sc combination was in line with what was observed in the phase 1/2 ANCHOR study, with predominantly clinically manageable cytopenias. The ANCHOR study was evaluating safety and efficacy of melflufen plus dexamethasone in combination with either daratumumab sc or bortezomib in patients with RRMM.

For more information, please contact

Global Head of Corporate Communications, Oncopeptides AB (publ)
E-mail: rolf.gulliksen@oncopeptides.com
Mobile: + 46 70 262 96 28

The information in the press release is information that Oncopeptides is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact person above, on October 26, 2022, at 08:00 (CET).

About Oncopeptides

Oncopeptides is a global biotech company focused on research and development of therapies for difficult-to-treat hematological diseases. The company uses its proprietary Peptide Drug Candidate platform, PDC, to develop compounds that rapidly and selectively deliver cytotoxic agents into cancer cells. On August 18, 2022, the European Commission granted Pepaxti® (melphalan flufenamide, also called melflufen) Marketing Authorization in the European Union and countries in the European Economic Area, in combination with dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least three prior lines of therapies, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapy. For patients with a prior autologous stem cell transplantation, the time to progression should be at least 3 years from transplantation. Pepaxto® (melphalan flufenamide) was granted accelerated approval in the US in February 2021 but is currently not marketed due to regulatory hurdles.

Oncopeptides is developing several new compounds based on its technology platforms. The company is built on a Swedish innovation and is listed in the Mid Cap segment on Nasdaq Stockholm with the ticker ONCO. More information is available on www.oncopeptides.com.

About Multiple Myeloma

Multiple myeloma is a cancer that originates in plasma cells, a type of white blood cells which produce antibodies to help fight infection, and cause cancer cells to accumulate in the bone marrow. Multiple Myeloma is the second most common hematologic malignancy, and accounts for approximately 1-2% of all new cancer cases, with a global incidence rate of 1.7 per 100,000 and an age-standardized incidence rate of 2.1-3.4 per 100,000 in France, Germany, Italy, Spain, and the UK. An estimated 35,842 patients were diagnosed in the EU27 during 2020, with an estimated 23,275 deaths due to the disease (ECIS 2020).

Patients with multiple myeloma may have symptom-free periods, however the disease always relapses, and patients will become refractory to all available treatment options due to mutations and/or clonal evolution of the tumor cells. A growing subset of patients are triple-class refractory, and develop disease refractory to immunomodulatory drugs, proteasome inhibitors, and CD38- targeting monoclonal antibodies. These patients have a very short expected overall survival.

About phase 3 LIGHTHOUSE study

The LIGHTHOUSE study investigated the efficacy and safety of a combination of melflufen, dexamethasone plus daratumumab sc. in comparison with daratumumab sc in patients with multiple myeloma exposed to both a proteasome inhibitor and an immunomodulatory agent with at least 3 prior lines of therapy or who were refractory to at least one immunomodulatory agent and a proteasome inhibitor. The randomized, open label trial was designed as a confirmatory study in addition to the phase 3 OCEAN study, with a primary endpoint of progression free survival (PFS).

About Pepaxti

Pepaxti® (melphalan flufenamide, also called melflufen) is a lipophilic peptide conjugated alkylating drug that rapidly and selectively is delivering cytotoxic agents into tumor cells. The drug is composed of a di-peptide and an alkylating moiety. The lipophilicity allows a faster cellular uptake whereas the peptide hydrolysis mediated by aminopeptidases, results in accumulation of alkylating moieties in cancer cells. This results in an improved efficacy without an increased toxicity compared to melphalan. Pepaxti inhibits proliferation and induces apoptosis of hematopoietic and solid tumor cells. It shows synergistic cytotoxicity in combination with dexamethasone in melphalan resistant and non-resistant multiple myeloma cell lines.

Pepaxti has been granted marketing authorization in EU and EEA-countries and is indicated in combination with dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least three prior lines of therapy, whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one anti-CD38 monoclonal antibody, and who have demonstrated disease progression on or after the last therapies. For patients with a prior autologous stem cell transplantation, the time to progression should be at least 3 years from transplantation. Pepaxti® is the trademark for melphalan flufenamide in Europe, the trademark in the US is Pepaxto®.

About anti-CD38 mAbs

Anti-CD38 monoclonal antibodies (mAbs) are targeting the CD38 antigen on plasma cells in multiple myeloma. The treatments have a distinct mode of action and have an immunomodulatory effect provided by the depletion of CD 38 immunosuppressive immune cell populations. The products can be used as monotherapy or in combination therapy, in the relapsed setting as well as in earlier lines of therapy. The monotherapy of anti-CD38 monoclonal antibodies with steroid support as studied in the LIGHTHOUSE study currently represents 30-40 % of anti-CD38 prescription in the US in RRMM (1+prior line of therapy). European use of anti-CD38 monoclonal antibody therapy is similar (Source IntrinsiQ IMATS, 2021).