PRESS RELEASE
PledPharma AB

PledPharma to close POLAR phase 3 program in the third quarter

Stockholm, April 6, 2020. PledPharma AB (STO: PLED) today announced that the company has decided to close its pivotal phase III program POLAR with lead candidate PledOx®, with a data cut-off targeted for the third quarter. A robust evaluation of the safety and efficacy will follow to determine the future of PledOx. The decision was taken after a recommendation from the independent Drug Safety Monitoring Board (DSMB) to stop the studies due to a number of severe allergic reactions, which have been observed after repeated dosing. The company's clinical program with its other drug candidate, Aladote®, administered as a single dose, is not affected.

Early in March, PledPharma decided to place recruitment and dosing of patients in the POLAR program on hold. The decision followed interactions with the French regulatory authority, ANSM, and the clinical hold issued by the US Food and Drug Administration (FDA) earlier in the year and was due to a few numbers of observed CNS related adverse events. PledPharma maintain its position that these events are not related to PledOx, a position which is also supported by the DSMB and an additional independent external evaluation of these cases. However, in a meeting in March, the independent Drug Safety Monitoring Board (DSMB) for the POLAR program recommended that the program should be stopped due to a number of severe allergic reactions observed after repeated dosing.

"Allergic hypersensitivity reactions are not uncommon in relation to platinum-based chemotherapy. However, the DSMB recommendation implies that there is an increased risk in subjects treated with PledOx. We are currently working to better understand why these allergic hypersensitivity reactions occur with coadministration of oxaliplatin and why they occur after repeated dosing.", said Chief Medical Officer Stefan Carlsson, M.D., Ph.D.

Patients currently enrolled in the POLAR program will continue with their scheduled study procedures, while not receiving the study drug, until the data cut-off targeted in the third quarter. The POLAR program with PledOx, developed to reduce nerve damage associated with chemotherapy, consists of two studies, POLAR-A and POLAR-M, with the aim of randomizing 700 patients. POLAR-A is conducted in patients undergoing adjuvant chemotherapy treatment for colorectal cancer and was fully recruited in December 2019. POLAR-M is conducted in patients undergoing chemotherapy treatment for metastatic colorectal cancer and is not fully recruited. A total of 590 patients have been randomized in the POLAR program, of which 420 have completed more than six cycles of treatment and about 250 subjects have completed more than nine cycles. Taken together, this data will enable a robust efficacy and safety evaluation and an assessment of the benefit/risk of PledOx to evaluate if further activities to find a path forward for PledOx to treat nerve damage associated with chemotherapy are motivated.

The continuation of the development program with Aladote, developed to reduce liver damage caused by paracetamol poisoning, is not affected by the DSMB recommendation and the early closure of the POLAR program. Aladote is administered as a single dose after which severe allergic-hypersensitivity reactions have not been observed in the POLAR program. A Phase I/IIa Proof-of-Principle study has been successfully completed. A pivotal phase II/III study is under planning.

"The safety of patients in our clinical studies is our most important responsibility. Of course, the early closure of the POLAR program is a major setback for us. We will now concentrate on collecting the remaining data in the challenging COVID-19 environment and how we can best use the robust data from the POLAR studies to potentially support future clinical trials, as we believe nerve damage associated with chemotherapy remains an unmet medical need. The focus on Aladote and the forthcoming regulatory interactions and clinical study remains. For Aladote, it is reassuring that no severe allergic-hypersensitivity reactions have been observed after single dose administration", said Nicklas Westerholm, Chief Executive Officer and President, PledPharma.

In order to continue the development of its clinical portfolio, PledPharma is well financed with approximately 255 million SEK in cash and cash equivalents reported at year end 2019.

PledPharma will host a telephone conference on April 6, 2020, at 14.00 CET.
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About PledPharma

PledPharma is an innovative, unique and integrated pharmaceutical drug development company, focusing on improving treatments for diseases with substantial unmet medical need. The company's most advanced project **PledOx®** is being developed to reduce nerve damage associated with chemotherapy. A global phase III program is ongoing. The drug candidate **Aladote®** is being developed to reduce the risk of acute liver injury associated with paracetamol/acetaminophen poisoning. A proof of principle study has been successfully completed and the design of the next study is being finalised. Aladote® has been granted Orphan Drug Designation in the US. PledPharma (STO: PLED) is listed on the Nasdaq Stockholm main market. For more information, see http://www.pledpharma.com/

About PledOx®

PledOx® is a "first in class" drug candidate developed to provide patients, that are treated adjuvantly or for metastatic colorectal cancer, prevention against the nerve damage that can occur in conjunction with chemotherapy treatment. The results from a completed Phase IIb trial (PLIANT), where patients with metastatic colorectal cancer were treated with the chemotherapy combination FOLFOX and PledOx®, indicates that the patients who received PledOx® had a lower risk than the placebo group to suffer from nerve damage during the chemotherapy. PledOx® showed 38% effect (odds ratio=0.62; p=0.16) on investigator reported sensory nerve damage, the primary endpoint, compared with the placebo group. This was not statistically significant, but a difference of this magnitude is considered clinically relevant. After completion of chemotherapy, PledOx® showed 77% effect (odds ratio=0.23; exploratory analysis: p=0.014) on patient-reported moderate and severe neuropathy compared to the placebo group. This is considered valuable for the success of the forthcoming POLAR studies, where patient-reported symptoms after completion of treatment will be the primary efficacy parameter. No apparent negative effect on the efficacy of the cancer treatment was observed. The phase III program for PledOx® consists of two double blinded randomized placebo-controlled trials, POLAR-M and POLAR-A. POLAR-M includes 420 patients undergoing chemotherapy treatment for metastatic colorectal cancer and is being conducted in Asia, Europe and the US. The study compares PledOx® at doses of 2 µmol/kg and 5 µmol/kg with placebo. POLAR-A includes 280 patients undergoing adjuvant chemotherapy treatment for colorectal cancer and is being conducted in Asia and Europe. The study compares PledOx® at a dose of 5 µmol/kg with placebo. POLAR-A was fully recruited in December 2019 and POLAR-M is not fully recruited.

This information is information that PledPharma is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact persons set out above, at 2020-04-06, 08:30 CEST.