



ASX AND MEDIA RELEASE

PEP005 shows highly selective activity against leukaemia

BRISBANE, Australia, 28 July, 2004: Peplin Biotech Ltd (ASX: PEP) today announced that its lead molecule (PEP005) had shown highly selective activity against acute myelogenous leukaemia (AML) in pre-clinical studies. Based on this and other pre-clinical data which it is generating, Peplin intends to prepare and lodge an IND application with the U.S. FDA, to initiate clinical trials of an intravenous formulation of PEP005 (PEP005 IV) to treat leukaemia.

Peplin's Managing Director & CEO, Michael Aldridge said "The potential of any chemotherapeutic drug as an intravenous treatment for cancer is based not only on the sensitivity of cancer cells to the drug but also on the relative insensitivity of normal healthy cells."

"The two studies that we have recently completed indicate that AML cells are dramatically more sensitive to PEP005 than normal healthy cells" Mr Aldridge said.

In the first study, Peplin evaluated PEP005's activity against a form of leukaemia called acute myelogenous leukaemia (AML). This evaluation was performed in what Peplin believes is a highly relevant pre-clinical model of this disease. This model evaluates the activity of PEP005 against primary AML blast cells which have been extracted directly from humans with AML.

In this study, the AML blast cells were extracted from eight patients and then each patient's cells were treated *ex vivo* with PEP005. PEP005 induced programmed cell death (apoptosis) in seven of the eight patients' samples at very low concentrations.

In a second study to evaluate selectivity, healthy human cord blood myeloid cells from three individuals were extracted and then treated *ex vivo* with PEP005. In all three cases, Peplin demonstrated that the myeloid cells were dramatically less sensitive to PEP005 than the AML blast cells. This selective activity confirms the significant potential of PEP005 as a therapeutic agent against leukaemia.

The investigator in this study Dr. Chris Bunce said the pre-clinical model used provided a valid indication of a drug's potential activity against AML.

"The highly selective activity that we have been able to demonstrate with PEP005 is as impressive as we have seen for any other agent in this model," said Dr Bunce.

These results build on previously announced research which showed that PEP005 demonstrated anti-cancer effects including apoptosis in a number of established leukaemia cell lines at very low concentrations.

"Leukaemia is a very serious form of cancer with few therapeutic alternatives. Peplin is squarely focused on the goal of bringing its intravenous product, PEP005 IV, to market to provide clinicians and their patients a new weapon in the fight against this life threatening disease," Mr Aldridge said.

ABOUT PEPLIN

Peplin is focused on the discovery, development and commercialisation of prescription human therapeutic products for the treatment of cancer and other diseases which have limited therapeutic options. Peplin's strategy is to leverage its pipeline of novel proprietary products through collaborative development and commercialisation arrangements with international pharmaceutical companies. Peplin's lead product is a potential topical therapy for actinic keratosis and non-melanoma skin cancer. It is the subject of a joint development agreement with Allergan, Inc. of Irvine, California for commercialisation in North and South America. Peplin retains rest of world rights for PEP005 Topical and all rights world wide to other oncology applications of PEP005.

Peplin's earlier stage pipeline is targeted at bladder cancer using PEP005 in an intracavity or intravesical formulation (PEP005 IC) and leukaemia using an intravenous formulation (PEP005 IV). Its new portfolio of EPUFA compounds opens additional potential opportunities in cancer and adds candidates for cardiovascular disease, pain, inflammation and diabetic complications.

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NOTES FOR EDITORS

The development process:- From IND to market

An IND filing is the culmination of an extensive pre-clinical (or pre-human) development program. Its filing typically follows a pre-IND meeting with the FDA at which the proposed content of the IND is discussed and broad parameters agreed. There are three main sections to the IND, comprising:

- The chemistry, manufacturing and controls (CMC) section in which the chemistry of the therapeutic agent and a validated manufacturing process and quality control system are documented
- The pharmacology and toxicology section which documents the pre-clinical efficacy and safety profile of the drug using a number of well validated models and studies
- A clinical section which contains the clinical investigators' brochure (CIB) and the clinical trial protocol for the proposed trial which is to be conducted under the IND.

Following acceptance of the IND by the FDA (actually tacit and defined by a 30 day period post filing) the sponsor is then free to initiate clinical (or human) development of the drug.

The clinical stage of a drug's development program is typically conducted in three phases. These comprise phase I (safety), phase II (safety, efficacy and dose ranging) and phase III or pivotal (efficacy and safety). This clinical phase of the development program typically takes a number of years. The completion of this phase is then followed by the filing of a New Drug Application (NDA) with the FDA. The FDA may take a year or more to review and potentially approve the NDA, based on its assessment of the drug's demonstrated safety and efficacy. Following approval of the NDA filing by the FDA the sponsor of the NDA can market the drug for the uses or indications approved by the FDA.

There are specific fast track programs available with the FDA and other regulators. The fast track programs of the FDA are intended to facilitate the development and expedite the review of new drug products that are intended to treat serious or life threatening conditions and that demonstrate the potential to address unmet medical needs. Drug development programs with an FDA approved fast track designation benefit from:

- Priority review of NDA filings
- Submission of portions of an NDA (so called rolling submission) and
- Accelerated approval regulations

About PEP005

PEP005 is Peplin's lead compound (or lead molecule). PEP005 is a well characterised, single molecular entity isolated and purified from a rapidly growing and common non-indigenous plant and represents the first of a new class of drug in clinical development. Peplin's proprietary rights to PEP005 and other related compounds for the treatment of cancer are by virtue of patents granted in Australia and Singapore and under prosecution in the US (notice of allowance received) and in other countries and regions.

Peplin's lead product, PEP005 Topical, is a potential topical therapy for actinic keratosis (AK) and non-melanoma skin cancer (NMSC). It is the subject of a joint development agreement with Allergan, Inc. of Irvine, California for commercialisation in North and South America. Peplin retains rest of world rights for PEP005 Topical and all rights world wide to other oncology applications of PEP005.

Peplin's earlier stage pipeline is targeted at bladder cancer using PEP005 in an intracavity or intravesical formulation (PEP005 IC) and leukaemia using an intravenous formulation (PEP005 IV). Peplin initiated a proof of concept pilot clinical study using a topical application of PEP001 (the raw sap from which PEP005 is purified) on patients suffering from NMSC and AK at the Mater Misericordiae Hospital in Brisbane, Australia in May 1999. This trial has completed, further details are available at Peplin's web site at www.peplin.com.

Leukaemia and acute myelogenous leukaemia (AML)

Leukaemia is a cancer that starts in blood-forming tissue such as bone marrow, causing large numbers of cancer cells to be produced and enter the blood stream. Each year, leukaemia is diagnosed in about 29,000 adults and 2,000 children in the United States. There are a number of forms of leukaemia with terminology typically based on the cell type that is cancerous and whether the progression of the disease is rapid (acute) or progressive (chronic). Examples include acute myelogenous leukaemia and chronic lymphocytic leukaemia.

In AML, the most common form of leukaemia, the stem cells usually develop into a type of immature white blood cell called myeloblasts (or myeloid blasts or just blasts). The myeloblasts in AML are abnormal and do not mature into healthy white blood cells. Leukaemia cells are unable to do their usual work and can build up in the bone marrow and blood so there is less room for healthy white blood cells, red blood cells, and platelets. When this happens, infection, anaemia, or easy bleeding may occur. The leukaemia cells can spread outside the blood to other parts of the body, including the central nervous system (brain and spinal cord), skin, and gums.