



ASX AND MEDIA RELEASE

Exciting results from phase I clinical trial

BRISBANE, Australia, 10 January 2005: Peplin Limited (ASX:PEP) announced today positive safety and efficacy results from its US based phase I clinical trial and confirmed it was on track to start Australian based phase II trials this quarter for its proprietary product PEP005 Topical for the treatment of actinic keratosis or sun spots (AK) and non-melanoma skin cancer (NMSC).

The phase I trial evaluated the safety and tolerability of a single application of PEP005 Topical gel on AK lesions and additionally reported measures of lesion clearance.

Peplin's Managing Director and CEO, Michael Aldridge said the trials proved a single application of PEP005 Topical had a favourable safety profile with local skin responses mild and as expected.

He said no systemic adverse events were reported, any local skin responses resolved rapidly and there were no serious or unexpected adverse events.

"Unexpectedly, the trial also demonstrated exciting indications of PEP005 Topical's ability to clear lesions with 40% of treated lesions either completely cleared or almost cleared. This compares with 15% of lesions treated with placebo.

"These results are hugely exciting. Not only did the trial's results document the drug's favourable safety profile but they also showed that a single, low dose application of PEP005 Topical is able to resolve lesions in less than three weeks.

"Anyone who has used currently available topical products or been subjected to surgical approaches will appreciate the benefit of a short course of therapy and rapid clearance of lesions," he said.

Mr Aldridge said one patient saw all five of his lesions completely cleared by single applications of PEP005 Topical while another saw four of his five lesions completely cleared – all within 21 days after treatment.

"These results fundamentally validate our decision late last year to reacquire PEP005 Topical and secure funding for the important phase II stage of its development.

“To Peplin’s knowledge PEP005 Topical is the only topical therapy either in development or on the market with the potential to treat skin lesions with treatment times of days rather than months and with a side effect profile that is both mild and resolves rapidly” said Mr Aldridge.

Peplin’s Director, Drug Development Dr Peter Welburn said the Australian based phase II clinical trials would explore higher and lower concentrations of PEP005 Topical together with multi day treatments and would monitor patients over longer periods.

“Based on our extensive studies of PEP005 in animal models and the pilot clinical trial we conducted at the Mater Hospital in Brisbane some years ago, we are confident that the phase II development program will confirm the exciting potential of PEP005 Topical as a new and highly competitive topical therapy for actinic keratosis and non-melanoma skin cancer,” said Dr Welburn.

ENDS

ABOUT PEPLIN

Peplin is focused on the discovery, development and commercialisation of prescription human therapeutic products for the treatment of cancer and other diseases with limited treatment options.

Peplin’s lead product is a clinical stage potential topical therapy (PEP005 Topical) for actinic keratosis and non-melanoma skin cancer. Peplin holds global rights for PEP005 Topical and all rights worldwide to other oncology applications of PEP005. Peplin’s lead product is supported by the Australian Federal Government under its R&D Start program.

Peplin’s earlier stage pipeline is targeted at bladder cancer using PEP005 in an intra-cavitary or intravesical formulation (PEP005 IC) and leukaemia (a blood borne cancer) using an intravenous formulation (PEP005 IV). Its 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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APPENDIX

In accordance with ASX and AusBiotech's Draft Code of Best Practice on Reporting for Biotechnology, Medical Device and other Life Sciences Companies Peplin provides the following information.

Background

PEP005 is Peplin's lead compound and chemically is described as an angeloyl substituted ingenane. PEP005 is a well characterised, single molecular entity isolated and purified from a rapidly growing and common non-indigenous plant. It is not a botanical for regulatory purposes and represents the first of a new class of drug in clinical development. PEP005 Topical is a topical formulation of PEP005 which Peplin is developing under investigational new drug applications (INDs) filed with the US Food and Drug Administration (FDA) for the treatment of actinic keratosis (AK) and the most common form of non-melanoma skin cancer (NMSC), basal cell carcinoma (BCC).

Peplin's proprietary rights to PEP005 and other related compounds for the treatment of skin cancer (and other forms of cancer) are by virtue of patents granted in Australia, Singapore and the US and filed and under prosecution in other countries and regions. Following a termination and settlement agreement with Allergan in October 2004 Peplin owns worldwide rights to PEP005's therapeutic applications protected by these patents.

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 in investor presentations on Peplin's web site at www.peplin.com.

In June 2004 Peplin filed INDs with the FDA and in August 2004 initiated a phase I clinical study to evaluate topical treatment of AK using PEP005 Topical. This trial completed in October 2004 and the final results are reported below.

Phase I study results

The PEP005 Topical phase I study was a randomized, double-blind, placebo-controlled, multicentre clinical trial evaluating the safety of a single application of up to 200 micro litres of 0.01% PEP005 Topical to five actinic keratosis lesions (an average of up to 40 micro litres per lesion) on the shoulders, chest, back and arms followed by a post treatment follow-up period lasting at least two weeks compared to a vehicle gel control (placebo). The study was conducted at four U.S. trial centres. All patients provided written informed consent and the study was conducted in accordance with ICH-GCP guidelines. Patients were required to have at least five AK lesions on the shoulders, chest, back and / or arms to participate in the study.

A total of 16 patients were randomized (four per study site). Eleven patients received a single, topical application of 0.01% PEP005 Topical to each of the five AK lesions and five patients received placebo (vehicle gel) treatment to each of five AK lesions. During the study all patients and study personnel were blinded to the treatment received. The median age of the patients was 72 years (minimum 42 years; maximum 82 years), 88% were male and 56% of patients were classified as having a skin type that burns easily and tans minimally or rarely. A total of 55 AK lesions (median diameter of longest lesion: 6 mm; minimum 3 mm; maximum 14 mm) were treated with 0.01% PEP005 Topical and 25 AK lesions (median diameter of longest lesion: 7 mm; minimum 3mm; maximum 13 mm) were treated with vehicle gel. The majority of the 0.01% PEP005 Topical and vehicle-treated lesions were located on the arm (90%); no facial lesions and only one shoulder lesion were treated.

Patients completed follow-up visits at day 1, day 7 and day 14 post-treatment. Four patients that received 0.01% PEP005 Topical were also seen at an additional follow-up visit at day 21 post-treatment. Study evaluations included physical exam, vital signs and laboratory parameters. Patients were assessed at each visit for both local and systemic toxicity using the National

Cancer Institute-Common Toxicity Criteria grading scale (Version 2.0) and all concomitant medications were recorded at each study visit. All treated lesions were also subjected to safety and efficacy evaluations including lesion photography and grading of the AK lesion clearance using an eight-point rating scale.

There were no drop-outs from the trial but one patient, who was treated with placebo, did not complete his final day 14 follow-up visit for personal reasons.

Safety

The study evaluated the safety of a single topical application of 0.01% PEP005 Topical for the treatment of AK. The results of this study showed that PEP005 Topical treatment had a favourable safety profile, with absence of systemic toxicity.

Erythema, scaling and scabbing (73%, 27% and 27%, respectively) were the most common adverse events occurring in patients treated with 0.01% PEP005 Topical. Nine of the 11 patients (82%) treated with 0.01% PEP005 Topical experienced at least one adverse event (local skin reactions including erythema, scaling, scabbing, oedema or tenderness). Seven (64%) of these patients reported more than one type of dermatological adverse event. Mild erythema was reported in eight (73%) of the 11 patients and in 31 (56%) of the 55 lesions. Additionally, scaling and scabbing were each reported in three patients (27%) treated with 0.01% PEP005 Topical in 24% and 16% of lesions, respectively. Desquamation, oedema and skin tenderness were each reported in one (9%) PEP005 Topical-treated patient.

Local dermatologic adverse events in patients treated with 0.01% PEP005 Topical.

Adverse Event	Patients (N = 11 total)		Lesions (N = 55 total)		Median time to onset in days (min - max)	Median duration of AE in days (min - max)
Erythema	8	73%	31	56%	1 (1-14)	7 (6-21)
Scaly rash	3	27%	13	24%	1 (1-14)	13 (7-20)
Scabbing	3	27%	9	16%	7 (7-11)	7 (2-7)
Skin desquamation	1	9%	2	4%	6 (-)	11 (8-15)
Oedema	1	9%	4	7%	1 (-)	6 (-)
Tenderness	1	9%	5	9%	2 (-)	2 (-)

The only adverse event seen in any of the five patients treated with vehicle (placebo) was mild erythema. Two patients experienced this adverse event in 28% of AK lesions.

Local dermatologic adverse events with patients treated with vehicle gel.

Adverse Event	Patients (N = 5 total)		Lesions (N = 25 total)		Median time to onset in days (min - max)	Median duration of AE in days (min - max)
Erythema	2	40%	7 ^a	28%	1 (-)	8 (6-1)
Scaly rash	0	-	0	-	-	-
Scabbing	0	-	0	-	-	-
Skin desquamation	0	-	0	-	-	-
Oedema	0	-	0	-	-	-
Tenderness	0	-	0	-	-	-

^a Events were considered not related in two lesions: patient #1001 had crusting because the lesion was accidentally scratched and patient #1020 had flaking.

The median time to onset of erythema for patients treated with 0.01% PEP005 Topical or vehicle gel was one day after treatment application. The median duration of erythema was seven and eight days respectively for the 0.01% PEP005 Topical and vehicle treatment groups. The median time to onset and the median duration of scaling was one day and 13 days respectively for the 0.01% PEP005 Topical treatment group. The median time to onset of scabbing and

desquamation in PEP005 Topical-treated patients was seven and six days respectively with a median duration of seven and 11 days.

All adverse events had resolved by the last available follow-up visit. None of the patients reported pain and / or burning at the treatment site and no scarring or abnormal proliferation was observed in any patient. No deaths or serious adverse events were reported and no patients discontinued the study due to adverse events.

These results indicate that topical application of 0.01% PEP005 Topical is well-tolerated, with the predominant toxicity being mild but manageable erythema when the gel was applied to AK lesions located on the arms and back.

Efficacy

Efficacy was also evaluated in the PEP005 Topical phase I study. This study showed that topical application of 0.01% PEP005 Topical was associated with AK lesion clearance activity. Follow-up data at day 14 post-treatment were available for 15 of the 16 patients randomized and treated. At day 14 of follow-up none of the 15 patients evaluated had complete clearance of all five (100%) treated lesions and two patients had two out of five (40%) treated lesions completely cleared; both patients were in the 0.01% PEP005 Topical treatment group. However, of the four 0.01% PEP005 Topical-treated patients with day 21 follow up, complete clearance of all five (100%) AK lesions was observed in one patient and complete clearance of four out of five (80%) lesions was reported in a second patient.

Assessment of patients with complete lesion clearance at day 14 or last follow-up in patients treated with 0.01% PEP005 Topical or vehicle gel.

Lesions with complete clearance	Day 14				Last overall follow-up ^b			
	0.01% PEP005		Vehicle		0.01% PEP005		Vehicle	
N patients	11	100%	4 ^a	100%	11	100%	4 ^a	100%
N patients with								
100%	0	-	0	-	1	9%	0	-
80%	0	-	0	-	1	9%	0	-
40%	2	18%	0	-	2	18%	0	-
20%	4	36%	2	40%	3	27%	2	40%
0%	5	45%	2	40%	4	36%	2	40%

^a Missing data for one patient

^b Data taken from day 21 follow-up visits where available (4 patients) or from day 14 for other patients.

The extent of lesion clearance on a per lesion basis was analysed using an eight-point rating scale. These data are presented below for all patients at day 14 and / or the last available follow-up visit available (either day 14 or day 21 post-treatment). At day 14 of follow-up, 8 of the 55 (15%) AK lesions treated with 0.01% PEP005 Topical had complete clearance. By the last follow-up (i.e. including day 21 follow-up data), 16 of the 55 (29%) of the 0.01% PEP005 Topical-treated AK lesions were completely cleared. Thus an additional eight lesions had complete clearance between day 14 and day 21. In the vehicle treatment group, two of the 20 assessed vehicle-treated lesions (10%) had complete clearance at day 14 (no data were available for one patient at day 14). None of the five patients who received vehicle had day 21 follow-up data.

Extent of AK lesion clearance in patients treated with 0.01% PEP005 Topical or vehicle at either day 14 or last follow-up visit.

	Day 14				Last overall follow-up ^a			
	0.01% PEP005		Vehicle ^b		0.01% PEP005		Vehicle ^b	
N lesions	55	100%	20	100%	55	100%	20	100%
Complete clearance	8	15%	2	10%	16	29%	2	10%
Almost cleared	5	9%	1	5%	6	11%	1	5%
Marked clearance	11	20%	6	30%	8	15%	6	30%
Moderate clearance	5	9%	3	15%	3	5%	3	15%
Slight clearance	10	18%	2	10%	9	16%	2	10%
Unchanged	13	24%	6	30%	12	22%	6	30%
Worsened	2	4%	0	-	1	2%	0	-
Unable to determine	1	2%	0	-	0	-	0	-

^a Data taken from Day 21 follow-up visits where available (4 patients, 0.1% PEP005 treatment group only) or from Day 14 for all other patients.

^b Missing data for one patient at Day 14; no day 21 follow-up data available

In addition, 5 of the 55 (9%) lesions treated with 0.01% PEP005 Topical were considered as having almost cleared (i.e. $\geq 90\%$ clearance according to the investigator) at day 14 of follow-up, with 6 of 55 (11%) lesions almost cleared by day 21. In comparison, only one of the 20 vehicle-treated lesions (5%) was assessed as almost cleared at day 14 of follow-up. Thus the combined clearance rate of completely cleared and almost cleared AK lesions treated with 0.01% PEP005 Topical was 40% (22/55 lesions). The combined rate of clearance of the vehicle-treated lesions was 15% (3/20 lesions). The phase I trial was not powered for statistical significance in terms of efficacy.

Inflammatory responses were observed in 12 lesions treated with 0.01% PEP005 Topical at day 7 of follow-up. Of these 12 lesions, 7 (58%) had complete clearance at the last available follow-up, suggesting that the inflammatory response may be related to lesion clearance. Importantly, these inflammatory responses were mild and no additional medical intervention was required.

Implications

Peplin believes these trial results have several important implications which it will continue to develop as it moves into larger and more comprehensive clinical trials.

Safety:

The study has provided important information relating to the safety profile of PEP005 Topical. The local skin responses reported in the clinical trial were entirely consistent with Peplin's expectations and are consistent with findings in its animal model studies and the pilot clinical trial. There were no unexpected adverse events and no serious adverse events and no medical intervention was required.

PEP005 Topical works by two primary mechanisms: direct cytotoxicity and local immune response. Peplin believes the local skin responses are a direct result of and are important to the way that PEP005 Topical works. Direct cytotoxicity is responsible for the initial killing of the tumour cells. The local immune response elicited by the drug includes the recruitment of neutrophils into the lesion site. In combination direct cytotoxicity and local immune response result in erythema (redness and inflammation) and in some cases skin shedding and scab formation. Peplin believes this combination is important for the complete resolution of lesions and the study demonstrated a potential correlation of inflammatory response to lesion clearance.

Efficacy:

The phase I trial reported today was structured to rapidly evaluate the safety profile of PEP005 Topical and Peplin chose to focus on the more common AK disease to ensure the fastest recruitment rate. Accordingly the trial was a single application of PEP005 Topical and at

significantly lower concentrations and quantities than Peplin's PEP001 pilot trial conducted at the Mater Hospital. Additionally patients were only followed for up to 21 days.

In the context of this trial being only a single application of drug (the pilot study had used three applications on three consecutive days), at an average quantity of up to 40 micro litres per lesion (the pilot study had used between 100 and 300 micro litres per lesion on each treatment day) and in which patients were only followed for up to 21 days (the pilot study had followed patients for up to 31 months), Peplin believes that the results of this trial in which 40% of lesions were either completely cleared or almost cleared are impressive. Further, there is evidence to suggest that the clearance of lesions improved over time.

In pending phase II studies Peplin will be exploring treatments with PEP005 Topical with a higher (and for completeness lower) load of PEP005, dosing on multiple days and will follow patients for longer periods. Peplin plans to treat both AKs and BCCs. Peplin expects to see a consequential higher level of direct cytotoxicity and inflammatory response and an improved lesion clearance rate.

These phase II studies will be conducted in Australia which is an attractive location for skin cancer trials and would form an integral component of Peplin's global skin cancer program.

Competitive situation:

In the market for therapies to treat AK and NMSC, Peplin expects to compete with various surgical techniques (primarily cryosurgery (liquid nitrogen), curettage and electro-desiccation and surgical excision) and various topical treatments comprising primarily Aldara a product marketed by 3M Pharmaceuticals, topical formulations of 5-fluoruracil (e.g. Effudex and Carac) and Solaraze. In addition photodynamic therapies such as Levulan Kerastick and PhotoCure have recently been approved.

The key short comings of cryosurgery are the acute pain and redness and irritation that often occur on treatment and longer term occasional scarring or hypopigmentation. The major short comings of surgical techniques generally comprise cost, time, painful side effects and disfiguration and scarring.

Topical approaches to the treatment of AK and NMSC generally seek to deliver a more cosmetically appealing treatment outcome. The major short comings of presently available topical approaches are the long treatment times that many of them require and the unsightly and sometimes intolerable side effects that accompany the treatment period.

To Peplin's knowledge PEP005 Topical is the only topical therapy either in development or on the market with the potential to treat skin lesions with treatment times of days rather than months and with a side effect profile that is both mild and resolves rapidly. Peplin believes these product attributes would represent important competitive advantages in the market for topical treatments for AK and NMSC.