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ASX Release

Outstanding preliminary results from ArTiMist™ Phase III African Malaria Trial in Children

- **Sub-lingual ArTiMist™ superior to quinine in Phase III trial**
- **95.6% of ArTiMist™ patients had reduced parasite counts by >90% in the first 24 hours compared with only 40.6% using intravenous (IV) quinine**
- **Results support that ArTiMist™ is an effective treatment for children with malaria**
- **There are up to 500 million reported cases of malaria a year worldwide**

SUDA LTD (ASX: SUD) is delighted to announce that it has received the preliminary results from the ART004 clinical trial carried out in childhood malaria in Africa. Full results and analysis will be released when the final report is received.

The preliminary results support the proposal that sub-lingual ArTiMist™ is an effective treatment for children with severe or complicated falciparum malaria, or uncomplicated falciparum malaria with gastrointestinal complications. The results also strongly support the potential role that ArTiMist™ may be able to play in the early interventional treatment of malaria in these cases.

The Phase III trial was carried out by ProtoPharma Ltd on behalf of SUDA LTD (SUDA) in malaria endemic areas of Rwanda, Burkina Faso and Ghana over a 22 month period from November 2010 to September 2012.

The study's primary objective was to demonstrate that sub-lingual (under the tongue) ArTiMist™ was superior to IV quinine in reduction of the parasite counts by > 90% within 24 hours in children with severe or complicated falciparum malaria, or uncomplicated falciparum malaria with gastrointestinal complications.

The study convincingly confirmed this objective. The results of the trial demonstrate that 95.6% of patients treated with ArTiMist™ had their parasite counts reduced by > 90% in the first 24 hours. By comparison, only 40.6% of the quinine treated patients had the same reduction.

The secondary efficacy parameters PCT, PRR24, PCT50, PCT90 demonstrated a statistically significant difference overall between the treatments in both efficacy populations ($p < 0.005$), further demonstrating the superiority of ArTiMist™ over IV quinine in clearing parasites. There were 10 early treatment failures for quinine treated subjects. One quinine treated subject required rescue therapy. For ArTiMist™ treated subjects there were no early treatment failures, nor did any subject require rescue therapy. Quinine did not appear to be better than ArTiMist™ for any of the secondary endpoints included in this study. There were no Treatment Related Adverse Events (TEAEs), no deaths or neurological sequelae for either treatment.

These results provide a compelling argument for the potential use of ArTiMist™ as an early interventional treatment for children with severe or complicated falciparum malaria, or uncomplicated falciparum malaria with gastrointestinal complications.

The World Health Organisation through the Rollback Malaria Program has said; "*The majority of deaths from severe malaria in childhood are caused by the delayed administration of effective antimalarial treatment. There is a relentless deterioration in the clinical condition of a young child with malaria who fails to get effective treatment, with death ensuing in a matter of hours or days. Any successful attempt to reduce mortality from malaria will have to explore novel possibilities for minimising such delays.*"

The Management of SUDA believes that ArTiMist™ has the potential to be an effective pre-referral medication, and has the potential to significantly reduce child mortality and potentially the adverse effects suffered by children, particularly within the first 24 hours of infection. We are of the opinion that ArTiMist™ could play a pivotal role in the global Rollback Malaria Program.

It is important to understand that in many rural areas where malaria is a major health problem rural clinics do not have doctors or IV drugs and may only have malaria suppositories/tablets. ArTiMist™ can be used successfully in all situations.

Advantages of ArTiMist™ over other treatments are:

- It does not require medically trained personnel for administration;
- Not affected by GI complications;
- By-passes the Liver and the significant metabolism seen from the first pass effect;
- Does not require fatty diet for maximum effect;
- Rapidly absorbed;
- Can be administered to comatose patients;
- Negates risk of infection from needle use;
- Has a long shelf life; and
- Critically, in hot climates, does not require cold chain storage

Whilst SUDA has received the results of the trial, the draft report is still being finalised by ProtoPharma. This report will provide more insight and more interpretation of the results.

SUDA would like to acknowledge the work carried out by ProtoPharma Ltd and the various clinical sites in Rwanda, Ghana and Burkina Faso, the contractors, clinicians and investigators in the completion of this trial.

SUDA management are working with various groups to finalise the development and regulatory aspects of the project and working to identify a commercially acceptable trade sale opportunity to bring ArTiMist™ to market in the most effective manner.

Further details are attached.

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Summary of ART004 Clinical trial preliminary information

NAME OF TRIAL
A Phase III, randomised, open-labelled, active controlled, multi-centre, superiority trial of ArTiMist™ versus intravenous quinine in children with severe or complicated falciparum malaria, or uncomplicated falciparum malaria with gastrointestinal complications.

TRIAL LOCATIONS
Rwanda, Ghana and Burkina Faso

BLINDING STATUS AND RANDOMISATION PROCESS
This was an open-label, randomised, active comparator, controlled study. Each site was provided with sealed envelopes containing the randomisation schedule prepared by the study statistician for each subject. These envelopes were kept sealed within the pharmacy until opened by the pharmacist immediately prior to preparing the medication for the next eligible subject. In this way, the investigator remained blinded to treatment allocation until such time as the trial medication arrived in the ward area for administration to the subject.

The main efficacy parameter, parasite counts were read by at least 2 different parasitologists at a central laboratory. They were blind as to treatment allocation.

NO. OF PATIENTS AND INCLUSION AND DROPOUT RATE
180 patients were screened, of which 29 were screening failures.

151 subjects (77 ArTiMist™, 74 Quinine) were randomised at three sites (51 in Rwanda, 50 in Ghana, 50 in Burkina Faso).

10 subjects were excluded from the MITT (Modified Intention to Treat) analysis population, leaving 141 subjects (70 ArTiMist™, 71 Quinine). The MITT population included all randomised subjects who received at least one dose of study medication and had evaluable parasite counts at 24 hours after first dosing.

Reasons for exclusion from the MITT included no evaluable baseline parasite count, baseline parasite count at central laboratory below that required for inclusion, no parasite count sample available at 24 hours.

137 patients (68 ArTiMist™, 69 Quinine) were included in the per protocol population.
The Per Protocol (PP) population included the subjects in the MITT population who had received at least 80% of doses up to the time of discharge from the hospital, had evaluable data up to and including Day 28 and had no major protocol violations.

All data has been analysed for both populations.

RESULTS OF THE PRIMARY AND SECONDARY ENDPOINTS

The secondary efficacy parameters PCT, PRR24, PCT50, PCT90 demonstrated a statistically significant difference overall between the treatments in both efficacy populations ($p < 0.005$), further demonstrating the superiority of ArTiMist™ over IV quinine in clearing parasites.

There were 10 early treatment failures for quinine treated subjects. One quinine treated subject required rescue therapy. For ArTiMist™ treated subjects there were no early treatment failures, nor did any subject require rescue therapy. Quinine did not appear to be better than ArTiMist™ for any of the secondary endpoints included in this study. There were no treatment related SAEs, no deaths or neurological sequelae for either treatment.

Primary Efficacy Variable	**ArTiMist™ (N = 70)**	**Quinine (N = 71)**	**Difference % (95% CI)**	**Difference (p)**
Parasitological Success (MITT)				
Yes (n, %)	66 (94.3)	28 (39.4)	54.85 (42.25-67.45)	P < 0.005
No (n, %)	4 (5.7)	43 (60.6)		
	ArTiMist™ (N = 68)	**Quinine (N = 69)**	**Difference % (95% CI)**	**Difference (p)**
Parasitological Success (PP)				
Yes (n, %)	65 (95.6)	28 (40.6)	55.01 (42.44-67.58)	P < 0.005
No (n, %)	3 (4.4)	41 (59.4)		

Secondary Efficacy Results

	MITT				PP			
Secondary Efficacy Variable	**ArTiMist™ (N = 70)**	**Quinine (N= 71)**	**Difference (95% CI)**	**Difference (p)**	**ArTiMist™ (N = 68)**	**Quinine (N= 69)**	**Difference (95% CI)**	**Difference (p)**
Complete Cure Rate (Crude) (n, %)								
Cure	41 (77.4)	46 (78.0)	1.03 (0.40-2.63)	p = 0.95	41 (77.4)	45 (77.6)	0.99 (0.39-2.53)	p = 0.98
No Cure	12 (22.6)	13 (22.0)			12 (22.6)	13 (22.4)		
PCT (mean(sd)) hours	30.29 (13.21)	68.30 (98.04)	-39.40 (-62.72 – -16.07)	p < 0.005	30.03 (13.23)	61.19 (81.08)	-32.33(-52.22 – -12.45)	p < 0.005
PRR_{12} (mean(sd)) hours	47.6 (70.3)	-132.2 (765.9)	176.76 (-8.14 - 361.66)	p = 0.061	48.5 (70.4)	135.0 (776.85)	176.67 (-13.83 – 367.18)	p = 0.069
PRR_{24}(mean(sd)) hours	98.2 (6.1)	44.5 (114.3)	54.94 (28.13 – 81.74)	p < 0.005	98.6 (5.1)	43.9 (115.9)	54.93 (27.35 – 82.51)	p < 0.005
PCT_{50} (mean(sd)) hours	9.42 (5.72)	18.58 (9.19)	- - 9.16 (-11.71 – - 6.61)	p < 0.005	9.29 (5.73)	18.43 (9.25)	-9.13 (-11.74– -6.53)	p < 0.005
PCT_{90} (mean(sd)) hours	15.02 (5.82)	27.93 (18.03)	-12.91 (-17.38 – - 8.44)	p < 0.005	14.93 (5.87)	26.08 (9.48)	-11.15 (-13.81– -8.49)	p < 0.005
FCT (mean(sd)) hours	42.6 (34.5)	41.6 (22.7)	0.96 (-10.16 -12.08)	p = 0.86	43.4 (34.7)	41.0 (22.57)	2.40 (-8.93=13.72)	p = 0.67
Early treatment failure (n, %)	0 (0.0)	10 (14.1)	N/A	N/A	0 (0.0)	10 (14.5)	N/A	N/A
Late clinical failure (n, %)	3 (4.3)	1 (1.4)	2.63 (0.26 – 26.59)	p = 0.41	3 (4.4)	1 (1.4)	2.56 (0.25 – 25.88)	p = 0.42
Late Parasitological Failure	12 (17.1)	14 (19.7)	1.03 (0.40 – 2.62)	p = 0.95	12 (17.6)	13 (18.8)	1.06 (0.41 – 2.73)	p = 0.91
Time to return to normal *per os* mean(sd)) hours	22.1 (12.9)	25.3 (16.3)	-3.22 (-8.21 – 1.76)	p = 0.20	22.1 (13.1)	25.5 (16.2)	- 3.39 (-8.47 – 1.69)	p = 0.19
Related TEAE n %, SAE n %, respectively	5 (7.1), 0	6 (8.5), 0	N/A	N/A	5 (7.4), 0	5 (7.2), 0	N/A	N/A
Number of deaths/neurological sequelae (n, %)	0	0	N/A	N/A	0	0	N/A	N/A

PCT = Parasite Clearance Time
PRR = Parasite Reduction Ratio
SAE = Serious adverse events
TEAE = Treatment Emergent Adverse Event
FCT = Fever Clearance Time
OS = Normal clinical status

(12) = at 12 hour time point
(24) = at 24 hour time point
(50) = 50%
(90) = 90%
(sd) = Standard deviation
(n) = Number of patients

SAFETY AND TOLERABILITY

There were no serious adverse events related to ArTiMist™. Local tolerability was good and there were no adverse events related to local tolerability. In total, there were 4 SAE's in ArTiMist™ patients and 11 in quinine patients. Serious adverse events are to be expected in a trial with such sick patients. Overall there were no other safety concerns relating to either treatment.

LATE PARASITOLOGICAL FALIURE

Whilst this data is still being fully evaluated we know that these patients had late parasitological failure for a number of reasons which include new/re-infection (14 of which 9 Art / 5 quin) and recrudescence (4 of which 2 Art / 2 quin). The investigators are confirming the reasons for the others and any relationships that may be relevant. This data will be released in the final report.

OVERALL STATUS OF THE TRIAL

The trial is complete and the data base has been locked. There is still some final statistical analysis that needs to be confirmed. The first draft of the report is expected to be available for review by 30 April 13.

Note: after the draft report is issued it undergoes a further review process prior to issuing the final results, therefore it should be noted that there is a possibility that there may be some changes to the preliminary data.

Malaria the Facts

Malaria is a serious, infectious disease. About half the world's population (3.3bn) live in areas that have some risk of malaria transmission, 36.4% (1.2bn) of which are living in regions considered at high risk (≥1 reported case(s) per 1,000 population p.a. in 2006) and the balance (63.6% or 2.1bn) at low risk (<1 reported case(s) per 1,000 population p.a.).
The populations most affected live in the poorest countries in tropical and sub-tropical regions of the world, with an estimated 300-500m clinical cases p.a. (WHO) and death-rates have doubled over the last 30 years and estimated to be between 1.1 and 2.7m (WHO). The great spread in the deaths is attributed primarily to the difficulties in establishing 'the cause of death' as some of the affected individuals who die at home without reaching a health facility and national government systems of civil registration in Sub-Saharan Africa are incomplete.

The African region has a notoriously weak system of reporting infectious diseases, epidemiological evidence from carefully conducted prospective 'active' case-detection studies of malaria morbidity, disability, mortality in populations living under different transmission intensity risks. Nevertheless, Sub-Saharan Africa (SSA) is the hardest hit with between 152 and 287m malaria clinical cases (WHO) occurring each year with 80% of the cases concentrated in 13 countries. In the African region 90% of the malaria deaths are concentrated in 18 countries. The above-mentioned figures have been around for a few years and by looking, for example at the estimated size of <5 years old malaria patient population at high-risk, one of the most vulnerable together with pregnant women, according to our calculations it is estimated to be >100m is SSA and with each child potentially suffering multiple malaria episodes per year, it is easy to see that the overall number of clinical episodes has been underestimated and also how the market size ought to be much bigger.

35-45% of deaths are from the severe forms of malaria, with children <5 years and pregnant women carrying the greatest burden. The majority of deaths from severe malaria in childhood are caused by the delayed administration of effective anti-malarial treatment. There is a relentless deterioration in the clinical condition of a young child with malaria who fails to get effective treatment, with death ensuing in a matter of hours or days. The mortality of untreated severe malaria is thought to approach 100% and, if treated, the death rate falls to 10-15% but increases in the presence of renal failure and respiratory distress. Any successful attempt to reduce mortality from malaria will have to explore novel possibilities for minimising such delays.