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Arana successfully completes Phase II psoriasis study

- **ART621 meets primary endpoint**
- **Clinical development in rheumatoid arthritis progresses**

Arana Therapeutics Limited (ASX: AAH) today announced positive results from its Phase II trial of ART621 in patients with stable plaque psoriasis. The primary endpoint was met with repeat doses of ART621 being well tolerated and exhibiting a safety profile consistent with anti-TNF activity, the method of administration and the underlying study population. Arana will continue clinical development of ART621 with two ongoing Phase II trials for rheumatoid arthritis (RA) in combination with methotrexate.

Secondary findings from the study provided insight into the efficacy, immunogenicity and pharmacokinetics of ART621. While the study was not designed to demonstrate efficacy, evidence of some anti-TNF activity was seen. A total of four subjects in the ART621 group achieved a 50% reduction in Psoriasis Area and Severity Index (PASI) score at week 12 compared to zero in the placebo group. One of these ART621 subjects also achieved a 90% PASI reduction.

No human anti-ART621 antibody responses were detected for up to four weeks after the last injection, suggesting inherently low immunogenicity of the drug. Consistent with prior Phase I data, ART621 exhibited a half life of approximately 14 days, which compares favourably to market leading anti-TNF products.

“We are pleased with the outcome of our Phase II study which has provided us with the confidence to continue clinical development of ART621. The data indicate that ART621 possesses anti-TNF activity, was well tolerated and has a competitive half life. Importantly we did not see any antibody responses against ART621 and this may be an important differentiator commercially, as other anti-TNF products may have their efficacy reduced by such responses” said Steffen Nock, Acting Chief Executive Officer.

“ART621 is now at an exciting stage with an open IND, encouraging clinical data, scale up of manufacturing progressing well and ongoing clinical trials in RA.”

Further detail on the results and study design are provided in the Appendix (and / or on our website www.arana.com).

ART 621-201 Trial Details

The study known as ART621-201 was designed to evaluate the safety, efficacy and pharmacokinetics of 3 dose levels of ART621 using a randomised, double-blind, placebo-controlled design in subjects with plaque psoriasis. The primary objective was to evaluate the safety and tolerability of subcutaneous injections of ART621 given every 2 weeks for 6 doses as assessed by adverse events and clinical laboratory data. Assessments of efficacy included the Psoriasis Area and Severity Index (PASI), Physician Global Assessment (PGA), photographs and the Dermatology Life Quality Index (DLQI).

Each subject completed a 2-4 week screening period, followed by a 12 week treatment period and then a 4 week follow up. Each subject received their designated dose of study medication on 6 occasions over the 12 week treatment period.

The study was conducted to ICH GCP standard at two Australian study centres – Nucleus Network in Melbourne and CMAX in Adelaide.

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About Arana Therapeutics:

Arana Therapeutics (ASX: AAH) is a biopharmaceutical company focused on developing next generation antibody based drugs that will improve the lives of patients with inflammatory diseases and cancer.

Arana Therapeutics' innovative engineering technologies provide the basis for developing its next generation antibody candidates. Arana Therapeutics has the financial strength and management expertise to develop its product pipeline. Arana has a significant track record of commercialising its technologies and has collaborations with GlaxoSmithKline (GSK), CSL, Kyowa Hakko Kirin (KHK), and licensing arrangements with Centocor (J&J) and Abbott Laboratories.

For further information: www.arana.com

ART 621-201 Trial Results

Appendix

Parameters are reported as mean (standard deviation) unless otherwise stated:

Study Parameter	ART621 Dose Group			Control
	0.5mg/kg	1.0mg/kg	2.0mg/kg	Placebo
Summary of Subject Disposition				
Subjects Randomised (n)	14	15	14	14
Male Sex	79%	67%	79%	71%
Age – years	42 (15)	38 (13)	45 (13)	44 (13)
Duration of psoriasis (years)	18 (8)	19 (7)	22 (12)	20 (13)
Subjects receiving 6 doses (n)	14	13	14	13
Summary of Key Safety Data				
Subjects with at least one AE	11	13	13	12
Subjects with drug related AEs	5	10	12	5
Subjects with SAEs (n)	0	2	0	0
Summary of PASI data– Change from Baseline to Week 12				
Mean percent Change in PASI	-15% (31)	-31% (22)	-27% (16)	-20% (13)
P value (difference compared to placebo)	0.56	0.15	0.25	N.A
PASI 50 at week 12 (Number subjects)	1	2	1	0

Disposition: 57 subjects were enrolled with 54 subjects receiving all 6 doses of study medication. The typical subject was male (74%), 42 years old and having with an average duration of psoriasis of 19 years. Forty three subjects were randomized to ART621 and 14 subjects were randomized to placebo. Three subjects prematurely discontinued study treatment – two subjects in the ART621 1.0mg/kg group and one subject in the placebo group. The reasons for premature

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discontinuation were withdrawal of consent (n=1), serious adverse event (SAE) (n=1) and subject lost to follow-up (n=1).

Safety data: Safety was assessed by reports of adverse events and review of laboratory data. In general repeat doses of ART621 were well tolerated and exhibited a safety profile consistent with anti-TNF activity, the method of administration and the underlying study population. A total of two SAEs were reported, both in the ART621 1.0mg/kg group – one case of pneumonia and one case of intentional anti-depressant overdose (in a subject with a prior history of such behaviour). There were a higher number of suspected drug-related adverse events in the ART621 group compared to placebo. The most commonly reported (>10% subjects) non-serious adverse events were headache and upper respiratory infections although the rates seen with ART621 were not significantly different to the rates seen in the placebo group. Headaches and respiratory tract infections are known side effects of anti-TNF therapy. ART621 therapy was not associated with any clinically significant changes in laboratory parameters (haematology, biochemistry and urinalysis).

Efficacy Data: Assessments of efficacy included the Psoriasis Area and Severity Index (PASI), Physician Global Assessment (PGA) and standardized photography. While the study was not designed to detect statistically significant changes in efficacy, there is evidence of some anti-TNF activity. At an individual level a total of 4 subjects in the ART621 group achieved a 50% reduction in PASI score at week 12 compared to zero in the placebo group. One of these ART621 subjects also achieved a 90% PASI reduction. The reduction in psoriasis severity was also reflected by reductions in PGA ratings in the ART621 groups as well as standardized photography review.

Quality of Life (QOL) secondary endpoint: All ART621 and the placebo groups experienced improvements in QOL as measured by the Dermatology Quality of Life Index (DLQI). These differences were not statistically significant, as expected, due to the small size and short duration of the study.

Immunogenicity: Immunogenicity was assessed using an assay to detect the possible presence of human-anti-ART621-antibodies at baseline and at study weeks 2, 4, 8, 12 and 16. No such antibody response was detected at any time point.

Protocol No.	ART621-201
Trial title:	A randomised, double-blind, placebo-controlled, study to evaluate the safety, efficacy and pharmacokinetics of three doses of ART621 following multiple dose administration in subjects with stable plaque psoriasis
Type of trial:	Phase II dose ranging
Sponsor:	Arana Therapeutics Limited
Investigational Product:	ART621

Trial design:	Randomised, double-blind, placebo-controlled, dose ranging study
Trial duration	18-20 weeks: 2-4 weeks screening, 12 week treatment period (6 doses ART621) and 4 week follow-up period
Doses to be studied:	Placebo (0mg/kg) or ART621: 0.5 mg/kg, 1 mg/kg or 2 mg/kg (1:1:1:1 ratio)
Dosage forms:	49 mg/mL solution for parenteral administration (2 mL per vial)
Route:	Subcutaneous injection to lower abdomen
Patient selection	Adult subjects between 18-75 yrs, with active, clinically stable, plaque psoriasis of at least 12 months duration and of at least moderate severity and involving > 5% body surface area.
Trial centres:	Nucleus Network, Melbourne and CMAX, Adelaide
Primary objective:	Evaluate the safety and tolerability of subcutaneous injections of ART621 given every 2 weeks in subjects with stable plaque psoriasis
Secondary objective:	<ul style="list-style-type: none"> - Change in Psoriasis Area Severity Index (PASI) and Physician Global Assessment (PGA) scores between baseline and Week 12 - Change in Dermatology Life Quality Index (DLQI) between baseline and week 12) - Assess ART621 pharmacokinetic parameters following multiple dosing
Quality	Conducted to ICH Good Clinical Practice
Recruitment	40-60 planned - 57 subjects randomised.
Dosing regimen:	Subcutaneous injections of ART621 every 2 weeks for 12 weeks (6 doses)
Safety parameters:	Adverse event (AE) reports and clinical laboratory parameters (haematology, liver function, electrolytes, renal function) and electrocardiogram (ECG) recording
Efficacy parameters:	Psoriasis Area Severity Index (PASI) Score, Physician's Global Assessment (PGA) and Dermatology Life Quality Index (DLQI)
Statistical	Descriptive statistics will be used to assess selected demographic, safety, pharmacokinetic and efficacy endpoints.

Glossary of Terms:

ART621 – A human domain-based antibody consisting of a domain antibody directed against TNF combined with an antibody Fc region. The Fc region is the part of an antibody that provides immune effector function and other characteristics such as half-life.

Dermatology Quality of Life Index (DLQI) used with permission. © A Y Finlay, G K Khan April 1992 www.dermatology.org.uk

Domain antibody – Molecules which exhibit the binding properties to a biological target characteristic of a full-sized antibody, but are considerably smaller in size. As such domain antibodies are expected to possess characteristics of both small molecules and conventional antibodies. Like small molecules, domain antibodies are small in size and highly stable, resulting in a choice of therapeutic formats, delivery formulations and manufacture options. And, like conventional antibodies, domain antibodies can be designed to have specificity and high affinity for the biological target of interest.

Domain-based antibody - A therapeutic molecule which incorporates a domain antibody within a larger antibody-derived framework.

Double blind trial – A clinical trial in which the method for analysing data has been specified in the protocol before the study has begun (prospective), the patients have been randomly assigned to receive either the study drug or alternative treatment, and in which neither the patient nor the physician conducting the study know which treatment is being given to the patient during the study.

Endpoint – The specified disease, symptom, sign or assessment(s) that constitutes one of the target outcomes of a clinical trial.

ICH GCP - An internationally agreed standard for the conduct of clinical trials using medicinal products to ensure a) the protection of subjects participating in the trial b) clarity on responsibilities for all parties involved in conducting the trial and c) the integrity of the data generated by the trial is maintained.

Immunogenicity: the development of human antibodies directed against protein biologics such as ART621. A positive immunogenicity response may reduce the clinical effectiveness of such therapies.

Pharmacokinetics - The study of the process by which a drug is absorbed, distributed, metabolised, and eliminated by the body.

PASI - The PASI score stands for Psoriasis Area and Severity Index which allows researchers to objectively rate psoriasis using a score from 0 (no psoriasis) to 72 (severe & complete body coverage). The score rates the redness, scaling and thickness of a subject's psoriasis as well as the extent of coverage of the body.

PGA – Physician's Global Assessment of psoriasis condition classified in seven categories: severe, moderate to severe, moderate, mild to moderate, mild, almost clear and clear.

Psoriasis - an inflammatory disease of the skin associated with increased levels of TNF. Anti-TNF therapy has shown major benefit in the treatment of this disease.

Randomised Trial - A trial to see if a drug may be effective and safe at treating a condition. Groups of patients are divided and randomly (by chance) allocated to either receive the drug being tested or its matching inactive form (placebo).

Subcutaneous injection – A method of introducing medicinal products into the body by means of a needle injected into the layer of tissue just under the skin.

Tumour necrosis factor (TNF) – A protein which is up regulated in many inflammatory diseases. Inhibition of TNF has been shown to have therapeutic advantages in the treatment of several major human inflammatory diseases such as rheumatoid arthritis and psoriasis.

URTI – upper respiratory tract infection (a common side effect of anti-TNF therapies)