Innate Immunotherapeutics

ABN 16 165 160 841

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Innate Immunotherapeutics announces top-line results for trial of MIS416 in patients with secondary progressive multiple sclerosis

Summary:

- *Initial analysis of Phase 2B trial data on a total enrolled patient population basis show no clinically meaningful or statistically significant differences in measures of neuromuscular function or patient-reported outcomes*
- *Further analysis to be undertaken on patients who adhered to the trial protocol (the per protocol population) and at the level of individual patient responses; expected to be reported within the next month. It is unlikely the result will significantly change*
- *Compassionate Use Program is continuing, pending the results of further analysis*
- *Investor conference call scheduled for 10.30 am AEST, Tuesday, June 27th, 2017*

Innate Immunotherapeutics Limited (ASX Code: IIL) today announced that its Phase 2B randomised, double-blind, placebo-controlled trial of the efficacy and safety of MIS416 in the treatment of subjects with secondary progressive multiple sclerosis (SPMS) did not show clinically meaningful or statistically significant differences in measures of neuromuscular function or patient reported outcomes.

The study was designed to evaluate the efficacy, safety, tolerability, and immune pharmacodynamics of MIS416, compared to placebo, when administered intravenously once a week for a year. Subjects enrolled in the study were randomised on a 2:1 ratio to receive either MIS416 or a saline placebo. The subjects, the study site staff treating, and evaluating subjects and MRI evaluators at the MRI reading centre were blinded to the treatments being administered.

The trial was conducted at five sites in Australia and two sites in New Zealand. A total of 93 subjects were enrolled in the study with 62 randomised to receive MIS416 and 31 to receive placebo. The demographics of the two groups were well balanced relative to age, sex, duration of multiple sclerosis and expanded disability status scale score. There were 17 (27%) subjects who prematurely discontinued treatment in the MIS416 group and four (13%) in the placebo group. The main reasons for early discontinuation were subjects not wanting to continue (MIS416=8%, Placebo=6%), subjects being noncompliant with the protocol (MIS416=3%, Placebo=0%), and an adverse event leading to a subject being withdrawn (MIS416=11%, Placebo=6.5%).

To determine the efficacy of MIS416 relative to placebo on measures of neuromuscular function, assessments were carried out at baseline, at three monthly intervals during the trial, and at end of dosing. The assessments comprised multiple measures of upper extremity function and strength, walking speed and distance, visual acuity, and two measures of cognitive processing speed.

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The top-line results from these assessments comprise an analysis of the means relative to changes between baseline scores and end of dosing scores.

The population used for this analysis was the 'intent to treat' population (ITT) which comprises all 93 patients randomised on to the study irrespective of whether they completed the trial. This ITT population analysis showed no overall clinically meaningful or statistically significant differences across the multiple measures of neuromuscular function assessed during the trial.

The efficacy of MIS416 relative to placebo based on patient-reported outcome questionnaires comprising the Multiple Sclerosis Impact Scale, the Neurological Fatigue Index for patients with multiple sclerosis, and the Brief Pain Inventory, was also assessed for the ITT population at the same time points. Again, this analysis showed no overall clinically meaningful or statistically significant differences in these patient-reported outcomes.

The analysis of the expanded disability status scale (EDSS) score showed no change between the two groups at the ITT population level.

The analysis of percentage brain volume change, as assessed by magnetic resonance imaging, showed no significant difference between the two groups.

A separate analysis of possible treatment effect is underway on the 'per protocol' population (PPP). The PPP comprises patients who followed the trial protocol and completed at least 75% of the required study visits. There is nothing to suggest at this time that this analysis will result in a favourable conclusion.

The safety and tolerability of MIS416 relative to placebo was assessed continuously throughout the trial. There was at least one treatment related adverse event in 60 of the 63 subject (97%) MIS416 group and 23 of the 31 (74%) subject placebo group. There was at least one treatment related serious adverse event in 16 subjects (26%) in the MIS416 group and five subjects (16%) in the Placebo group. Based on the timepoint at which the adverse event(s) took place, it is expected to show that the higher incidence in the MIS416 group could be associated with the previously observed fever, chills, muscle weakness response to initial MIS416 dosing. Further analysis of these findings is ongoing.

In the MIS416 group, six subjects (9.7%) withdrew from the study due to at least one adverse event (which may or may not have been treatment related) and 2 subjects (6.5%) withdrew from the Placebo group.

The results for cranial magnetic resonance imaging of the number of gadolinium-enhances lesions and the number and volume of new or enlarged T2-weighted lesions, showed no significant difference between the two groups.

"These results are a shock and definitely not what we were expecting based on our previous clinical experience with MIS416 and the reporting of treatment benefits we have received from many compassionate use patients over an extensive 8-year period. These data will be as distressing to them as they will be for all the stakeholders who were relying on the outcome of this study," said Simon Wilkinson, Innate Immunotherapeutics' Chief Executive Officer.

Professor Pam McCombe, a principal investigator on the trial commented: "I am extremely disappointed by this outcome. Looking for measurable changes in patients with progressive MS using the assessment tools currently at our disposal is frustrating and complicated. We were hopeful that MIS416 would be an option to treat this group of patients who currently do not have effective treatment options"

Innate Immunotherapeutics' Chief Scientific Officer, Gill Webster, advised that the Company will be sponsoring an analysis of the trial results at the patient level to see if there is a group of clinical responders which might not be evident from the top line population-based analysis. If there is such a group, the extensive immune pharmacodynamics monitoring of the patients that took place during the study may identify a biomarker that could be used to pre-identify responders in any future clinical development of MIS416.

If further analysis bears out the apparent clinical failure of lead drug candidate MIS416 in patients with SPMS, the Company will be reviewing whether there are grounds for further clinical development of MIS416 in SPMS or another indication and whether a business case can be made for any such development.

Innate Immunotherapeutics will also need to review the future of its MIS416 Compassionate Use Program. As there were no dose limiting safety concerns reported, the Company has received clinical advice that there is no immediate need to halt this program. The Company expects to be able to update program participants and their health practitioners of our decision pertaining to the MIS416 compassionate use program in about a month.

Investor conference call

An investor conference call will be held at 10.30am AEST.

Conference code: 832946

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