27 November 2024

ASX Announcement

ISLA-101 shows anti-dengue activity in Phase 2a study readout

- **Reduction of viral load seen in subjects treated with ISLA-101, showing evidence of ISLA 101's anti-dengue virus activity in Phase 2a cohort**
- **No safety concerns seen by Safety Review Committee (SRC) that necessitate implementing any defined individual or study changes**
- **SRC recommends that Island proceed with the Phase 2b cohort (the therapeutic cohort) of the Phase 2a/b PROTECT clinical trial**

MELBOURNE Australia, 27 November 2024: Australian antiviral drug development company, Island Pharmaceuticals Ltd (**ASX: ILA**; **Island** or **the Company**) is pleased to announce that ISLA-101 has shown safety and anti-dengue activity in the Phase 2a cohort of the PROTECT Phase 2a/b trial.

The SRC further noted that blood levels of ISLA -101 were seen as expected, and given positive safety and efficacy signals, recommended that Island proceed with the therapeutic Phase 2b cohort. That recommendation will now be filed with the FDA 30 days before starting the Phase 2b cohort. The planned submission to the FDA would support a January 2025 study start.

Island's CEO and Managing Director, Dr David Foster said: *"Through the past 12 months, we have recorded several important achievements, but this one stands out as the most exciting — and the very reason we started this company. While we are blinded to the full dataset, the unblinded Safety Review Committee has clearly and unanimously stated there were no safety issues with ISLA-101 and also that the drug showed evidence of anti-dengue virus activity."*

"With the support of the recent $3.5m placement, the Phase 2b trial remains fully funded and Island is well positioned to pursue its additional pipeline targets."

Phase 2a trial and data readout

In Island's Phase 2a trial, subjects received ISLA-101 before being infected with a weakened dengue virus developed by the US Army. The trial aims to assess whether ISLA-101 can prevent or reduce viremia and symptoms, compared to placebo control.

On 18 November 2024, Island announced it had collected all data samples

following dosing of all subjects in the Phase 2a (prophylactic) trial as part of its Phase 2a/b PROTECT clinical trial in dengue fever. This data was consolidated for review by the Safety Review Committee (SRC).

The SRC has completed its process of evaluating the safety of ISLA-101 in dengue infected individuals and has now confirmed:

- No safety concerns seen that necessitate implementing any defined individual or study stopping rules, confirming the study was safe
- Blood levels of ISLA-101 were seen as expected in subjects that received the drug, confirming that it hit its target concentration. This excellent outcome demonstrates that the dose-finding work and in silico modelling conducted during and after the ISLA-101 Single Ascending Dose study (ASX: 3 June 2024) has led to an appropriate therapeutic dose
- Reduction of viral load was seen in subjects treated with ISLA-101, showing there was evidence of ISLA-101 anti-dengue virus activity in the Phase 2a cohort. As a result, the SRC recommended proceeding with the Phase 2b component.

Stephen Thomas, MD, the Frank E Young, MD '56 and Leanne Young Endowed Chair of Microbiology and Immunology at SUNY Upstate and member of Island Scientific Advisory Board commented that *"Completing the SRC review process of interim data was a crucial step for the trial and the program, and it is promising that the SRC recommended moving to the therapeutic phase of the trial. Finishing the trial will be a big step towards better understanding ISLA-101's potential to impact dengue disease."*

Island is now in the process of preparing to submit the SRC report to US FDA, with the report expected to be submitted in the coming days. Presuming the FDA agrees, Island remains on target to start the Phase 2b cohort in January 2025.

A video is available to investors where CEO / Managing Director, Dr David Foster talks to the Phase 2a outcomes in more detail. Follow the link below to watch the video: https://youtu.be/cWlj64xB_3o.

Q&A

Q: Will you share the full dataset from the Phase 2a cohort?

A: Today's results reflect the SRC's study conclusions with respect to safety, efficacy and a decision to recommend progressing with the Phase 2b cohort. The additional datasets remain with them as they are more completely analysed. We look forward to sharing more detailed information as it becomes available.

Q: Will you share unblinded data?

A: We are unable to share unblinded data because we ourselves are not unblinded. Only the SRC has seen the unblinded data and based on their review of the data they recommended moving to the next cohort, a conclusion that is incredibly positive and indicates that the results from the Phase 2a cohort were positive.

Q: You mention that the FDA has requested a review of the SRC recommendation. Do they have to review the results of the Phase 2a prophylactic arm.

A: Yes. The FDA has requested to see the SRC recommendation 30 days before we dose the Phase 2b cohort. The phase 2b cohort is scheduled to enrol during the second week of January.

Q: What is the difference between the Phase 2a and Phase 2b cohorts.

A: The difference is significant in respect of study aim. In the Phase 2a cohort, the subjects were pre-treated with ISLA-101 before exposure to the challenge virus. The question we were exploring in Phase 2a was: can ISLA-101 prevent or reduce infection when administered prior to exposure to the virus?

In contrast, in the Phase 2b cohort we are asking: can ISLA-101 reduce symptoms in an individual who is already infected with the dengue virus? Between the two studies we aim to understand whether or not ISLA-101 can be an effective prophylactic (preventative) and/or therapeutic (treatment) against a dengue infection.

Q: How does a challenge study compare to a wild-type infection (ie. the type of infection you would get if bitten by a mosquito in natural conditions)?

A: In contrast to dengue caused by the bite of an infected mosquito, which can be quite variable and unpredictable, the goal of a challenge study is to use a model virus that provides a *reproducible* infection. The infection mimics a mild form of the disease in question (i.e. dengue) in a way that can be studied in a well-controlled, hospital setting. This reduces the risk to trial subjects and provides well-controlled data.

Q: Does success in a challenge trial mean success for all dengue infections?

A: A challenge study is a mechanism to determine if your molecule has activity against dengue in a study that is fast, well-controlled, includes a small number of subjects and is comparatively inexpensive, relative to a larger study in a country with endemic disease. Should a molecule not be successful in a challenge study it would not likely support continuing to a study with a wild type virus in an endemic setting.

The fact that ISLA-101 has exhibited anti-dengue activity in a challenge trial in a prophylactic setting gives us confidence to move forward with a therapeutic challenge trial.

Q: These results seem to have come out quicker than expected. Why is that?

A: It is correct that the SRC decision came quickly. The faster than expected response is due to the hard work of the team at SUNY, our clinical team, the SRC and the compelling data.

Q: Now with the Phase 2a component complete, are you funded to complete the Phase 2b section of the PROTECT clinical study?

A: Yes. Phase 2b trial remains fully funded and that the recent $3.5 million placement allows ILA to pursue its additional pipeline targets.

Q: Where can I get more information on the study outcomes?

A: Island is hosting a webinar today, Wednesday 27 November 2024 at 11:00am AEDT, where CEO and Managing Director, Dr David Foster will discuss this announcement, together with a Q+A session. To register for the webinar, please click on the link below:

https://us02web.zoom.us/webinar/register/WN_i9QuJWg-QM-BSytHAtE4QA

Once you have registered for the briefing, you will receive an email confirming access details.

To subscribe to Island's monthly newsletter, IslandWatch, and other forms of email communications, please visit this page of our website.

Approved for release to the ASX by the Board of Directors.

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About Island Pharmaceuticals

Island (ASX: ILA) is a drug repurposing company, focused on areas of unmet need for antiviral therapeutics to address infectious diseases. Our lead asset is ISLA-101, a drug with a well- established safety profile, being repurposed for the prevention and treatment of dengue fever and other mosquito (or vector) borne diseases.

If ISLA-101 achieves FDA approval, and certain other criteria are met, Island may be eligible to obtain a "Priority Review Voucher" at the time of FDA approval. This means that as well as getting approval to manufacture and sell ISLA-101, the Priority Review Voucher (PRV) could permit Island to expedite the FDA approval process for a new drug or sell the PRV in a secondary market.

Island encourages all current investors to go paperless by registering their details with theCompany's share registry, Automic Registry Services, whose contact info is housed on theShareholder Services page of the Company's website.

Visit www.islandpharmaceuticals.com for more on Island.