12 June 2025

ASX Announcement

Successful Phase 2 clinical trial of ISLA-101 achieves anti-dengue activity in humans

- **Highly encouraging phase 2a/b top-line results advocate for the continued clinical development of ISLA-101 in dengue virus**
- **ISLA-101 associated with meaningful reduction in both viremia (viral load) and symptoms in preventative cohort**
- **Treatment cohort demonstrated signals of drug effect**
- **Investor webinar scheduled for Tuesday, 17 June at 11:00am AEST**

MELBOURNE Australia, 12 June 2025: Australian antiviral drug development company, Island Pharmaceuticals Ltd (**ASX: ILA**; **Island** or **the Company**) is pleased to provide top-line results from its successful Phase 2a/b PROTECT Trial using ISLA-101 in a human challenge model of dengue virus infection.

Initial review shows that ISLA-101 was associated with both a reduction in viremia (viral load) and a clinically meaningful reduction in symptoms in the preventative cohort. ISLA-101 was also associated with tangible drug effects in the treatment cohort.

Island's Phase 2a/b PROTECT trial included two patient cohorts. The Phase 2a arm examined ISLA-101's ability to prevent dengue fever in four subjects randomised 3:1 (active: placebo). The Phase 2b cohort included 10 subjects, randomised 8:2 (active: placebo) and assessed if ISLA-101 can reduce virus level and symptoms in subjects already infected with the dengue challenge virus. The subjects that received the active treatment in both cohorts received 600 mg/m2/day.

The challenge virus was provided by the US Army under a Cooperative Research and Development Agreement (CRADA), alongside support from the Walter Reed Army Institute of Research (WRAIR). This strain is weaker than wild type dengue, yet subjects are infected with replicating virus and have mild to moderate dengue symptoms.

The trial was conducted at the State University of New York (SUNY) Upstate, in Syracuse, NY, in accordance with the SUNY Dengue Human Infection Model (DHIM), which is a robust protocol that elicits detectable dengue viremia (viral load) and symptoms.

While other small molecules have been explored in this model, ISLA-101 is the first to demonstrate a potential benefit.

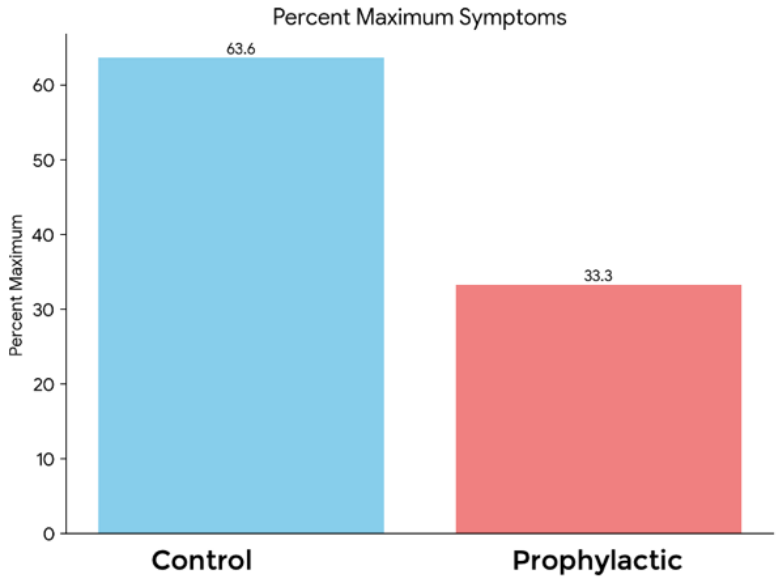
Phase 2a (preventative) results:

In the Phase 2a arm, subjects received ISLA-101 or placebo three days before being inoculated with dengue to investigate whether ISLA-101 can reduce or prevent viremia and dengue symptoms, compared to placebo control.

Results show that ISLA-101 demonstrated clinically meaningful anti-dengue activity, which included a material reduction in viral load and symptoms.

The three subjects treated with ISLA-101, exhibited a clear reduction in virus level. Further, dosed subjects exhibited a clinically meaningful reduction in symptoms compared to control.

When evaluating the maximum possible number of recorded symptoms, the control reported ~63% of all potential symptoms while the ISLA-101 pre-treated subjects reported circa 33% of all possible symptoms. This left patients that were dosed with ISLA-101 less sick than those that received the placebo and highlights ISLA-101's potential as a preventative measure in dengue.



Phase 2b (treatment) results:

During Phase 2b, subjects were inoculated with dengue, then administered either ISLA-101 or placebo, seven days post virus exposure. The primary endpoint of Phase 2b was to assess viremia load in subjects.

Based on preliminary review, ISLA-101 impacted viral replication. Because some subjects were viremic and symptomatic at the time of first dosing, alterations in symptoms were less pronounced and are being investigated further.

Next steps:

Following receipt of initial unblinded results, the Company has undertaken an in-person meeting with its Clinical Advisory Board to review the data and obtain guidance on recommended subsequent actions for the clinical development of ISLA-101. The Company will continue to work with its Advisory Board to gain a better understanding of the data, which will determine the potential course of action. Additional findings will be provided, as developments materialise.

Management commentary:

Island's CEO and Managing Director, Dr David Foster said: *"We are very excited to share top-line results from our successful Phase 2a/b PROTECT study, which show clear anti-dengue activity in humans."*

"Despite being in a small number of subjects, initial findings are highly encouraging and advocate for continued development of ISLA-101. We are pleased to advance the pre-clinical work from both Monash and Harvard to further highlight the potential for ISLA-101 as a measure to impact a widespread condition with no treatment."

"Additional work into the dataset alongside our Scientific and Clinical Advisory Boards is ongoing and will be the primary focus for the Company in the near term. We are confident that additional data will provide a clear determination for the next steps in our clinical trial pipeline and look forward to sharing this as it materialises."

Island's Chairman, Mr Phil Lynch said: *"The ISLA-101 results build positively on the drugs historical assessment and support us consulting with our clinical advisory group to determine the most optimal and economical means of progressing clinical plans. Dengue remains a large and growing unmet healthcare need - our ability to address that meaningfully would be well received by patients and the medical community, and remains a significant commercial opportunity."*

Scientific Advisory Board member, Prof. Stephen Thomas MD added: *"Dengue human challenge studies are complex to execute but can provide a wealth of information about candidate countermeasures early in their development. Our collaboration was fortunate to be able to consolidate resources from Island, Upstate Medical University, WRAIR, and the US CDMRP to support this study and we are pleased the challenge was successful and performed as expected."*

"The dengue problem is worsening and the number of candidate countermeasures in clinical testing does not align with the global scope of the problem. For this reason, we are very excited Island's candidate compound demonstrated evidence of antiviral activity against a rigorous dengue human infection model. These results set the stage for continued clinical development."

Investor webinar:

CEO and Managing Director, Dr David Foster will provide investors with an overview of the top-line results, as well as an update on the Company's anticipated next steps and broader portfolio expansion initiatives. The briefing will be followed by a Q&A session. Questions can be submitted now to henry.jordan@sdir.com.au or in written form during the webinar. Anyone wishing to attend the webinar must register via the following link:

Date and time:

11:00am AEST (9:00am AWST) on Tuesday, 17 June

Registration:

https://us02web.zoom.us/webinar/register/WN_6kMFre8DSki7Mt60Sc56Eg#/registration

Q&A:

Will you share the full dataset from the trial?

The company intends to share more detailed information as analysis is completed and it is likely that the data will form the basis of a publication.

What is the difference between the Phase 2a and 2b cohorts?

In the Phase 2a cohort, subjects were pre-treated with ISLA-101 before exposure to the dengue challenge virus to assess if ISLA-101 can prevent or reduce infection.

In Phase 2b, subjects were exposed to the dengue challenge virus and then treated ISLA-101 to determine if there is therapeutic benefit against infection.

Did ISLA-101 prevent or reduce infection in Phase 2a?

Initial results show that ISLA-101 was effective in reducing dengue infection.

Did ISLA-101 have therapeutic benefit in Phase 2b?

Preliminary results suggest that ISLA-101 impacted viral replication, symptoms and lab abnormalities. However, because many subjects were viremic and symptomatic when they started taking ISLA-101 and late-stage symptoms are generally mild, additional work needs to be undertaken to identify whether or not there is a clear reduction in symptoms. To this end, the Company will actively advance lab analyses and provide updates, based on relevant findings.

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)?

In contrast to dengue caused by the bite of an infected mosquito, which can be 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.

We expect the duration of viremia between the wild-type virus and challenge virus to be roughly the same. Symptoms caused by the wild-type virus are generally more intense than those caused by the challenge virus.

Do these results mean success for all dengue infections?

A challenge study is a mechanism to determine if a molecule has activity against dengue in a study that is fast, well-controlled, includes a smaller number of subjects and is comparatively inexpensive, relative to a larger study in a country with endemic disease. It is currently unknown whether ISLA-101 can reduce the risk of developing the severe life-threatening form of the disease.

Given ISLA-101 has exhibited anti-dengue activity, the Company has confidence that it has potential in a broader clinical study in a country with a more widespread dengue issue.

Is Island funded to commercialise ISLA-101 in as either a preventative or treatment measure?

The Company had $4.82m at bank based on its last quarterly activities report (refer ASX announcement: 30 April 2025) and $3.6m placement (refer ASX announcement: 21 May 2025), with some of the funds from this placement earmarked for larger clinical trial opportunities using ISLA-101.

Details around future clinical trials and associated budgets will be made available following consultation with FDA and the Company's Scientific and Clinical Advisory Boards, but management remain confident in the Company's current financial flexibility.

Where can I get more information on these results?

Island will host an investor webinar on Tuesday, 17 June at 11:00am AEST (9:00am AWST), during which CEO and Managing Director, Dr David Foster will provide further insight. To register, please visit the following link:

https://us02web.zoom.us/webinar/register/WN_6kMFre8DSki7Mt60Sc56Eg#/registration

An email confirmation with access details will be sent to you, following registration. The webinar will also be recorded in case you cannot attend.

- Ends -

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:

David Foster (CEO and Managing Director)
Island Pharmaceuticals Limited
info@islandpharmaceuticals.com

Investors and media, for further information, please contact:

Henry Jordan
Six Degrees Investor Relations
+61 (0) 431 271 538
henry.jordan@sdir.com.au

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 dengue2 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.