PITT STREET RESEARCH

# Island Pharmaceuticals

## Initial Phase II results look good

**Share Price: A$0.17**

Island Pharmaceuticals (ASX: ILA) investors' patience is (so far) being rewarded. The ASX-listed biotech company has commenced a Phase II study of its flagship drug ISLA-101 for Dengue fever. Results from the first cohort have come through and there are positive signs.

**ASX: ILA**

**Sector: Healthcare**

**5 December 2024**

| | |
|---|---|
| Market cap. (A$ m) | 30.1 |
| # shares outstanding (m)[1] | 176.9 |
| # shares fully diluted (m) [1] | 265.4 |
| Market cap ful. dil. (A$ m) | 45.1 |
| Free float | 100% |
| 52-week high/low (A$) | 0.22 / 0.053 |
| Avg. 12M daily volume ('1000) | 228.7 |
| Website | www.islandpharmaceuticals.com |

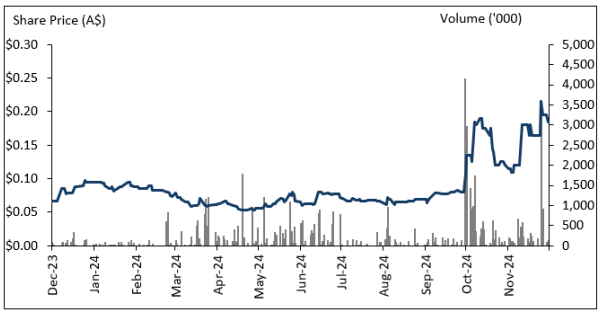
*Source: Company, Pitt Street Research*

### So far so good in the PROTECT clinical trial

Less than 2 months after commencing the trial, Island has received data from the first Phase of the trial (Phase 2a). The cohort in Phase 2a received ISLA-101 and were then exposed to a weakened version of the virus. Evidence of anti-dengue virus activity was observed, and the Safety Review Committee (SRC) found no safety concerns.

The SRC recommended the trial proceed to the next Phase (Phase 2b) and Island plans for this cohort to commence in January 2025. The aim of Phase 2b will be to deduce if ISLA-101 can work as a treatment in patients who have been infected with dengue. Results could occur within Q1 of CY25 and if these are positive, Island could potentially proceed to a Phase 3 trial.

**Share price (A$) and avg. daily volume (k, r.h.s.)**




*Source: Refinitiv Eikon, Pitt Street Research*

### It is an opportune time for ILA

ISLA-101 offers hope for the global fight against Dengue. Dengue is endemic in over 100 countries and infects 400 million people annually. 2023 was one of the worst years ever for infections and 2024 has proven to be even worse. There are no treatments for the fever, only symptomatic relief medicines like paracetamol or mosquito repellents like sprays and nets. Moreover, the spread of flaviviruses is expected to intensify in the future because of climate change and increasing urbanisation. If Island could get ISLA-101 to market, a lucrative opportunity would await.

| Valuation metrics | |
|---|---|
| NPV fair valuation range (A$) | 0.31-0.41 |
| WACC | 15.5% |

*Source: Pitt Street Research*

### Valuation range of A$0.31-$0.41 per share

We reiterate our valuation of ILA at A$83m in a base case scenario and A$109.1m in an optimistic (or bull) case scenario – equating to $0.31 per share and $0.41 per share respectively under the current number of shares on issue. We expect shares to continue to re-rate subject to continued success in the current clinical trial. A failure of the trial is the key risk facing this stock. Please see page 8 for further risks associated with an investment in ILA.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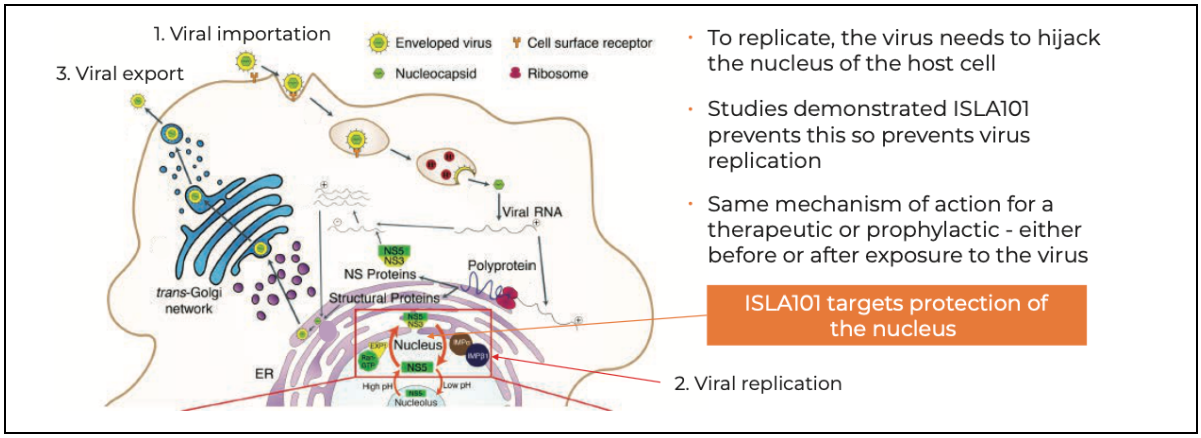
## Re-introduction to Island Pharmaceuticals (ASX: ILA) and ISLA-101

***Island Pharmaceuticals (ASX: ILA) is a biotech company focused on repurposing drugs for viral infections.***

Island Pharmaceuticals (ASX: ILA) is a biotech company with a drug repurposing strategy. Its main objective is repurposing ISLA-101 (fenretinide), against Dengue fever. Fenretinide had been the subject of ~45 Phase I and II human clinical trials as a therapeutic for cancers and various respiratory illnesses, given its chemo-preventative properties. Although the drug was proven safe, it was not efficacious in these indications, and its development was abandoned by Johnson & Johnson.

The program was donated to the US National Cancer Institute (NCI) at which point numerous groups ran clinical trials using the NCI program assets such as drug product and IND. Fenretinide was independently discovered at Monash University which undertook pre-clinical research that showed it has potential as an efficacious anti-viral drug. Island licensed it in from Monash University, retaining a research partnership with Monash. The research found that it prevents the nuclear entry of a particular viral protein into the host cell nucleus, acting as an NS5 nuclear transport inhibitor. In doing so, it prevents a viral infection (Figure 1).

**Figure 1: ISLA-101's Mechanism of Action**




*Source: Company*

## Island's PROTECT trial

When Island Pharmaceuticals listed on the ASX in May 2021, its objective was to take ISLA-101 to a Phase II clinical trial. Although there were unanticipated delays for a variety of reasons, clearance was finally given in early-August 2024 and the trial commenced in early October 2024. The study was renamed PROTECT, short for PROphylactic and TrEatment Challenge Trial, following the redesign of the trial to a prophylactic and therapeutic strategy. It is being conducted at SUNY Upstate Medical University in Syracuse, New York.

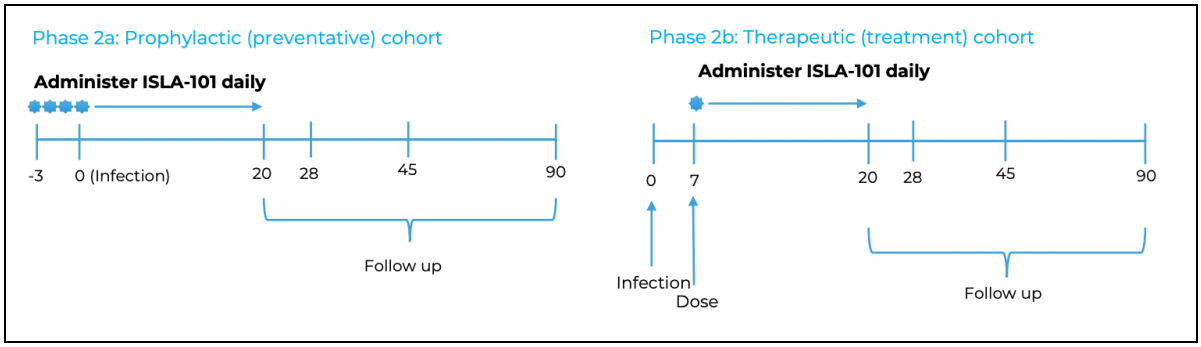
ILA is collaborating with the US Army to use its Dengue Human Infection Model (DHIM), with the Army manufacturing and providing an attenuated strain of the dengue virus that subjects will be exposed to. Given the fast pace of Dengue's spread and ISLA-101's mechanism, the company was anticipating results quickly, and these came within less than 2 months.

## The PROTECT trial results: So far so good

***Island has announced the first results of the trial.***

On 27 November 2024, Island announced the first data from the trial, with results from the Phase 2a cohort. The Safety Review Committee (SRC) observed that there had been a reduction in viral load in subjects treated with ISLA-101. There were no safety concerns that would necessitate implementing changes to the study. And so, the SRC recommended that the trial proceed to the Phase 2b cohort. Island now has to make a submission to the FDA 30 days before starting, and this would support the commencement of Phase 2b in January 2025 – specifically in the second week of the month. And, barring unanticipated delays there *should* be results within Q1 of CY25.

**Figure 2: The PROTECT trial timeframe**




*Source: Company*

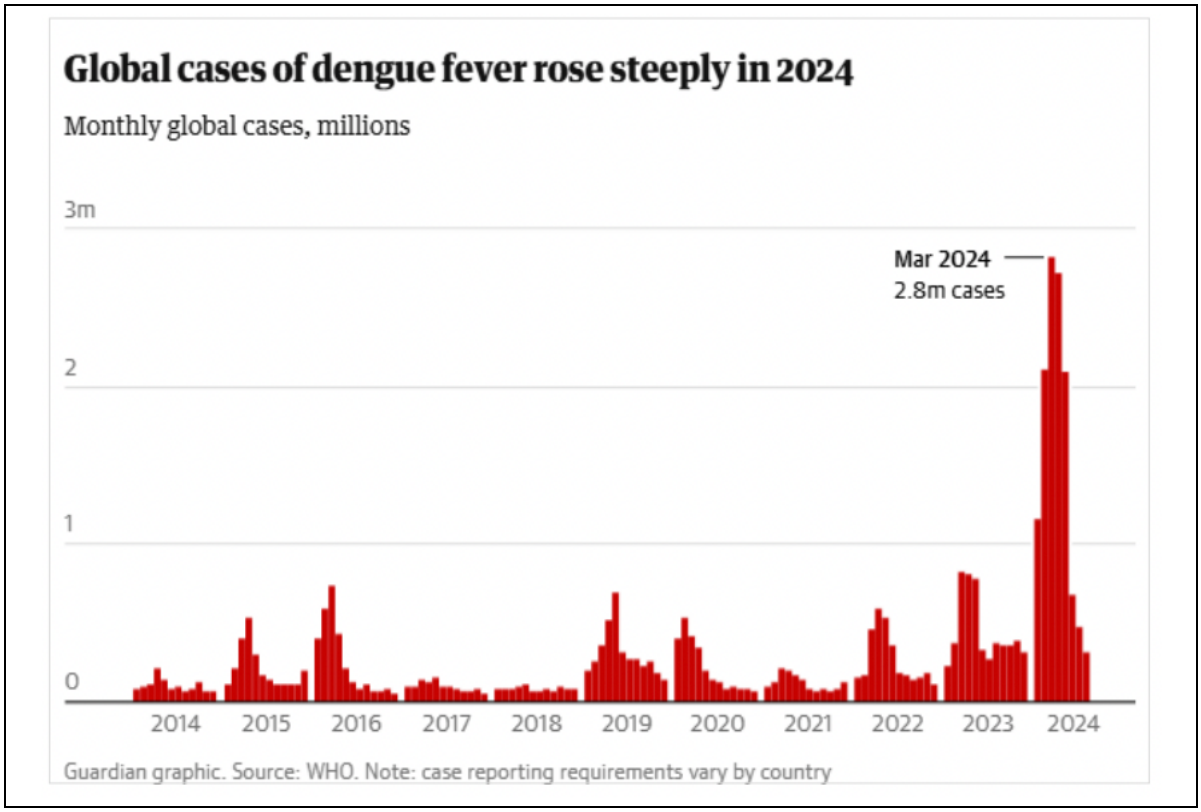
The next cohort will be different to Phase 2a. In Phase 2a, subjects were healthy and pre-treated with ISLA-101 before exposure to a weakened version of the virus. The aim was to see if ISLA-101 could work as a preventative. But in Phase 2b, patients will be already infected with dengue fever and the study will seek to understand if ISLA-101 can act as a treatment, or as a therapeutic (Figure 2).

## A sign of hope right when it is needed

***2023 was a horror year for Dengue cases, and 2024 is proving even worse.***

Island's efforts are coming at an opportune time with a substantial rise in Dengue fever cases in 2024 (Figure 3). 2023 saw the largest number of cases ever with 4.5m cases just in the Americas. In 2024, there were 2.8m cases just in the month of March.

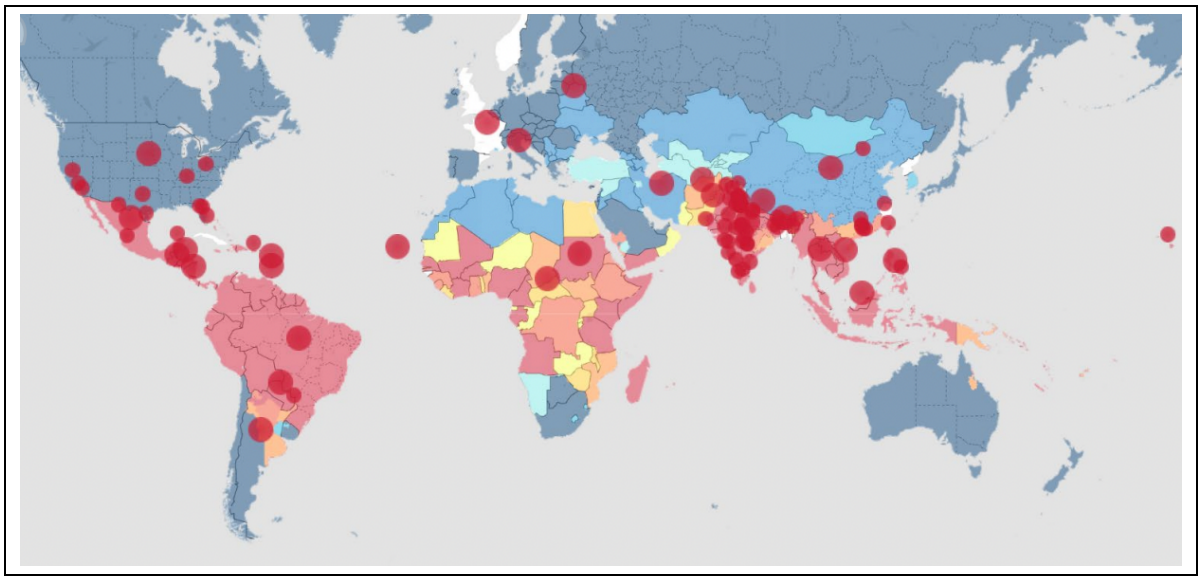
**Figure 3: Dengue cases**




*Source: Company*

As we outlined in our initiation report, flaviviruses such as Dengue are a major burden on the world's health. Dengue is one of the most rampant with 400 million people impacted annually and the virus being endemic in over 100 countries. This is reasons, including that there are multiple strains and ways of transmission beyond mosquito bites such as blood transfusions or tissue transplants. Although Dengue has historically been perceived to only be a problem in Tropical countries, particularly in Southeast Asia and South and Central America, there have been cases emerging in other parts of the world including the United States, Australia and in Europe (Figure 4).

**Figure 4: Reports of Dengue cases in 2024**



*Source: Company*

Dengue can cause several symptoms including headaches, gastrointestinal bleeding, a reduction in blood platelets, seizures, itching, rashes and vomiting. The typical host of hospitalisation is US$7,000, yet there are no pharmaceutical treatments that attack the virus, only symptomatic relief medicines or general mosquito repellents. Climate change and urbanisation is expected to increase the populations of mosquitos that carry viruses such as Dengue.

The good news is that ISLA-101 provides hope, not just to Dengue but other flaviviruses too including Zika, Yellow Fever, West Nile virus and Chikungunya virus. For the time being, Island Pharmaceuticals is focusing on Dengue, but it could target those other viruses down the track.

## What will happen after the PROTECT trial?

***Phase 2b will occur across the March quarter of 2025. If successful, a Phase 3 trial is the likely next step.***

Phase 2b is expected to be the final cohort of the trial. After this, the company proposes to meet with the FDA and consult with them about the next steps. We think that is likely that a Phase 3 trial will be needed, but this could potentially be shorter than the usual Phase 3 trial just like Phase 2 will be, given the nature of Dengue fever. Nonetheless, such a trial would be more lengthy than Phase 2 on account of the larger number of patients that could be required. We will not discern exactly how long it could take.

ILA is fortunate that the ISLA-101 program currently is eligible to receive a Priority Review Voucher (PRV) upon approval. This will mean that in the event ISLA-101 is approved by the FDA, the company will be permitted to expedite the approval process for another drug or sell that voucher to another company. PRVs can sell for over US$100m – as judged by the ten most recent PRVs. In fact, the last two sold for US$150m[1]. It goes without saying that such a non-dilutive cash injection would be spectacular for the company.

[1] Both were in November 2024. One exchanged between PTC Therapeutics and Kebilidi for US$150m the other one, jointly held by Acadia and Neuren, to an anonymous buyer.

## Our Valuation of Island Pharmaceuticals

***We derived a value of A$83.0m in our base case and A$109.1m in our bull case, or $0.31 per share and $0.45 per share.***

We reiterate our valuation Island Pharmaceuticals at A$83.0m in our base case and A$109.1m in our bull case, which is $0.31 per share and $0.42 per share respectively (Figure 5). Investors interested in a full outline of our model inputs should see our initiation report, but they are briefly recapped in Figure 6. These are based on the assumption that Island passes Phase 2 (the PROTECT trial) then commences Phase 3 within 12 months from now, using a licensing model, then obtains FDA approval in mid-FY28 and has a 7-year period of market exclusivity.

**Figure 5: Our modelling assumptions for Island Pharmaceuticals**

| Model Assumptions | Base | Bull |
|---|---|---|
| *Launch* | FY28 | FY28 |
| *Estimate market size (patient numbers)* | 10,000,000 | 12,000,000 |
| *Growth* | 3.0% | 3.0% |
| *Potential market penetration* | 8.0% | 8.5% |
| *Realised price (US$)* | 1,000 | 1,000 |
| *Peak sales (US$m)* | 1,533 | 1,954 |
| *Peak royalty revenue (US$m)* | 307 | 391 |
| *Gross milestone revenue (US$m)* | 80 | 80 |
| *Commercial exclusivity period (years)* | 7 | 7 |
| *Drug development cost (US$m)* | 40 | 40 |
| *Partner's share of costs* | 50.0% | 50.0% |
| *Discount rate* | 14.7% | 14.7% |
| *Royalty rate* | 20.0% | 20.0% |
| *Tax rate* | 30.0% | 30.0% |
| *Probability of success* | 50.00% | 50.00% |
| *Risk-adjusted NPV (A$m) - base case* | 83.01 | 109.10 |
| *rNPV per share (A$) - base case* | 0.313 | 0.411 |

*Source: Pitt Street Research*

**Figure 6: Our modelling assumptions for Island Pharmaceuticals**

| ISLA-101 Valuation | Base | Bull |
|---|---|---|
| NPV (US$) | $ 104,596,288 | $ 137,468,583 |
| Risk Factor | 50% | 50% |
| rNPV (US$) | $ 52,298,144 | $ 68,734,291 |
| AUD/USD | 0.63 | 0.63 |
| **rNPV (A$)** | **$ 83,012,927** | **$ 109,102,050** |
| Shares on issue (diluted) | 265,357,245 | 265,357,245 |
| **Implied price** | **$ 0.313** | **$ 0.411** |
| Current share price | $ 0.170 | $ 0.170 |
| *Premium* | *84%* | *142%* |

*Source: Pitt Street Research*

## Key Risks facing Island Pharmaceuticals

We see the risk of failure of the PROTECT trial as the key risk facing the company. A failure of the clinical trial would essentially send the Company back to 'Square One', spelling the likely death knell for ISLA-101's commercialisation against flaviviruses.

Other risks include:

- **Regulatory risk**. There is a risk that ISLA-101 may not be approved by regulators. Even if data suggests efficacy, the FDA may not find the data acceptable, or decline to approve ISLA-101 on other grounds such as the potential for negative interaction with other drugs. Even when approved, there is the risk that approval may be withdrawn, or that further regulations may be imposed on the company to be able to continue to market, manufacture and/or produce the drug.
- **Market acceptance risk**: There is the risk that even if the drug passes clinical trials, it will fail to be approved and/or attract a strong following in its applicable markets.
- **Key personnel risk**. There is the risk that the company may lose key personnel and be unable to replace them and/or their contribution to the business.
- **Capital risk**. Notwithstanding this risk has been significantly diminished with the recent placement and the prospect that Island could obtain a PRV, the prospect of Island needing debt or equity sources of funding cannot be entirely ruled out. In such an event, there is no guarantee that the company will be able to raise such capital, let alone on favourable terms. Even if successful, this would be dilutive to existing shareholders.

**Risks related to pre-revenue Life Science companies in general.**

The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.

Since most biotechnology and medical device companies listed on the Australian Securities Exchange fit this description, the term 'speculative' can reasonably be applied to the entire sector.

The fact that the intellectual property base of most biotechnology and medical device lies in science not generally regarded as accessible to the layman adds further to the riskiness with which the sector ought to be regarded.

***Caveat emptor***. Investors are advised to be cognisant of the abovementioned specific and general risks before buying any the stock of any biotechnology or medical device stock mentioned on this report, including ILA.

## Appendix I – Analysts' Qualifications

Stuart Roberts, lead analyst on this report, has been an equities analyst since 2002.

- Stuart obtained a Master of Applied Finance and Investment from the Securities Institute of Australia in 2002. Previously, from the Securities Institute of Australia, he obtained a Certificate of Financial Markets (1994) and a Graduate Diploma in Finance and Investment (1999).
- Stuart joined Southern Cross Equities as an equities analyst in April 2001. From February 2002 to July 2013, his research speciality at Southern Cross Equities and its acquirer, Bell Potter Securities, was Healthcare and Biotechnology. During this time, he covered a variety of established healthcare companies, such as CSL, Cochlear and Resmed, as well as numerous emerging companies. Stuart was a Healthcare and Biotechnology analyst at Baillieu Holst from October 2013 to January 2015.
- After 15 months over 2015–2016 doing Investor Relations for two ASX-listed cancer drug developers, Stuart founded NDF Research in May 2016 to provide issuer-sponsored equity research on ASX-listed Life Sciences companies.
- In July 2016, with Marc Kennis, Stuart co-founded Pitt Street Research Pty Ltd, which provides issuer-sponsored research on ASX-listed companies across the entire market, including Life Sciences companies.
- Since 2018, Stuart has led Pitt Street Research's Resources Sector franchise, spearheading research on both mining and energy companies.

Nick Sundich is an equities research analyst at Pitt Street Research.

- Nick obtained a Bachelor of Commerce/Bachelor of Arts from the University of Sydney in 2018. He has also completed the CFA Investment Foundations program.
- He joined Pitt Street Research in January 2022. Previously he worked for over three years as a financial journalist at Stockhead.
- While at university, he worked for a handful of corporate advisory firms

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