

17 June 2025

ASX Announcement

## **Successful Phase 2 PROTECT trial top-line results: Webinar presentation**

- **Presentation summarises highly encouraging phase 2a/b top-line results that advocate for the continued clinical development of ISLA-101 in dengue virus**
- **ISLA-101 delivered a meaningful reduction in both viremia (viral load) and symptoms in preventative cohort**
- **Evidence of reduced duration of viremia identified in both preventative and treatment cohorts**
- **Improved symptoms and lab abnormalities documented in ISLA-101 dosed participants in both cohorts**

**MELBOURNE Australia, 17 June 2025:** Australian antiviral drug development company, Island Pharmaceuticals Ltd (**ASX: ILA; Island or the Company**) is pleased to provide the following presentation which summarises initial and additional findings from its recently completed, successful Phase 2a/b PROTECT Trial using ISLA-101 in a human challenge model of dengue virus infection.

The presentation provides further insight into the highly encouraging results, which demonstrated anti-dengue activity in ISLA-101 treated subjects. This included ISLA-101 ability to deliver a meaningful reduction in both viremia (viral load) and symptoms in the preventative cohort, as well as signals of drug effect in the treatment arm.

Further to this, additional findings include evidence of reduced viremia duration in both the preventative and treatment cohorts, as well as improved symptoms and some lab abnormalities in patients dosed with ISLA-101.

The presentation will be used in the Company's upcoming webinar, during which CEO and Managing Director, Dr David Foster will provide 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](mailto: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](https://us02web.zoom.us/webinar/register/WN_6kMFre8DSki7Mt60Sc56Eg#/registration)



- Ends -

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**Approved for release to the ASX by:**

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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 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 the Company's share registry, Automatic Registry Services, whose contact info is housed on the Shareholder Services page of the Company's website.*

Visit [www.islandpharmaceuticals.com](http://www.islandpharmaceuticals.com) for more on Island.



**ISLAND**

PHARMACEUTICALS

Antiviral therapeutics

# COMBATTING URGENT VIRAL DISEASE THREATS

**DR DAVID FOSTER, MANAGING DIRECTOR**

June 2025

(ASX: ILA)

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This presentation contains certain "forward-looking statements". The words "expect", "anticipate", "estimate", "intend", "believe", "guidance", "propose", "goals", "targets", "aims", "outlook", "forecasts", "should", "could", "would", "may", "will", "predict", "plan" and other similar expressions are intended to identify forward-looking statements. Any indications of, and guidance on, future operating performance, earnings and financial position and performance are also forward-looking statements. Forward-looking statements in this presentation include statements regarding the Company's future growth options, strategies and new products. Forward-looking statements, opinions and estimates provided in this presentation are based on assumptions and contingencies which are subject to change without notice, as are statements about market and industry trends, which are based on interpretations of current market conditions.

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Nothing in this presentation will under any circumstances create an implication that there has been no change in the affairs of the Group since the date of this presentation.



**Island Pharmaceuticals  
(ASX: ILA) is an antiviral  
therapeutics company  
targeting infectious diseases**



Dengue infects up  
to 400m per year\*



Major market  
potential



Positive results in  
aggressive models



Phase 2a/b PROTECT clinical  
trial in dengue completed



PRV potential  
valued at ~A\$225m



Pipeline expansion  
pending with expedited  
approval route defined



# CORPORATE OVERVIEW



## Snapshot

Share on issue <sup>1</sup> :	236,093,034
Price per share <sup>1</sup> :	\$0.165
Market capitalisation <sup>1</sup> :	\$38.96m
Cash at bank (31 March 2024) <sup>2</sup> :	\$4.82m
May 2025 placement:	\$3.6m
DoD grant funding to directly support the Phase 2a/b PROTECT clinical study	US\$625k

## Price & volume (12 month)



## Substantial shareholders

Dr William James Garner <sup>3</sup>	14.21%
Jason Alan Carroll <sup>4</sup>	13.26%
MWP Partners Limited <sup>5</sup>	8.25%
Dr Daniel Tillett <sup>6</sup>	6.72%

## Board of Directors

Phil Lynch, Executive Chairman

Dr David Foster, CEO and Managing Director

Chris Ntoumenopoulos, Non-Executive Director

1. As at 16 June 2025

2. Does not take into consideration cash used since reporting date

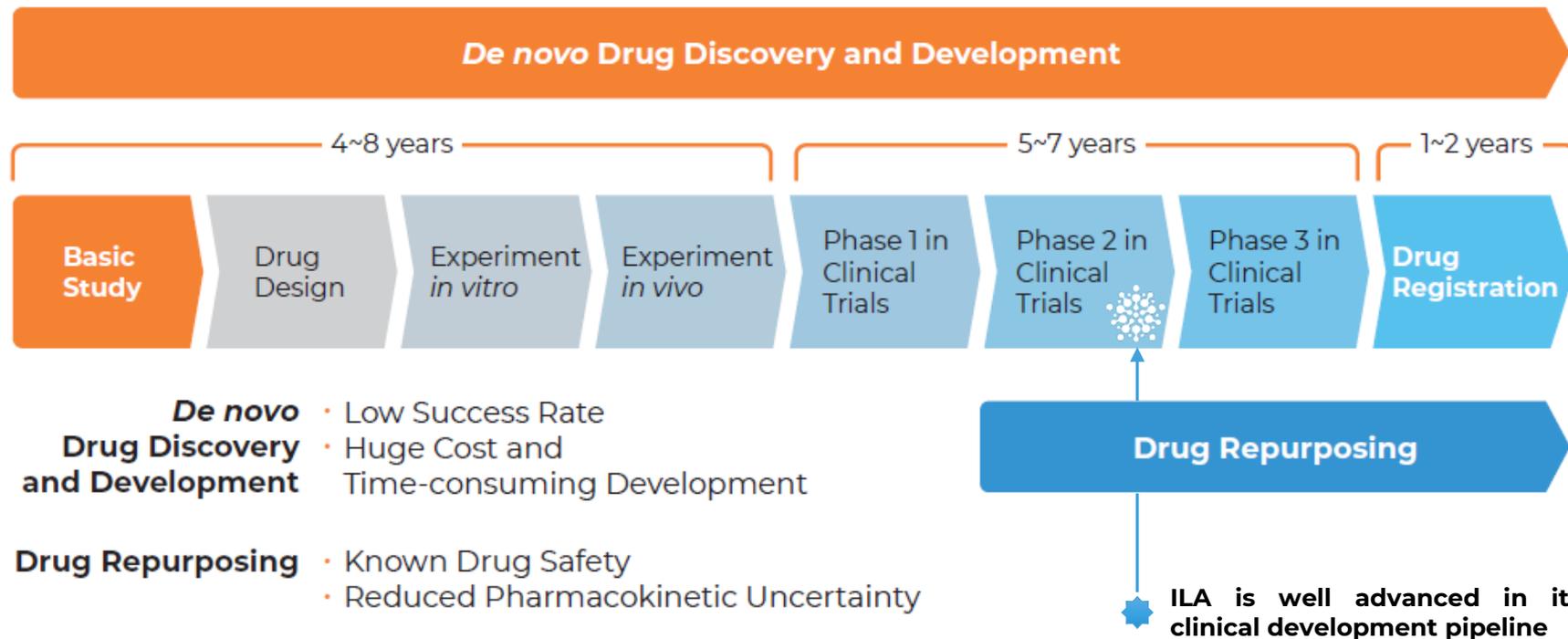
3 Per holding per Substantial interest notices lodged with ASX on 02 June 2025

4. Per holding per Substantial interest notices lodged with ASX on 29 May 2025

5 Per holding per Substantial interest notices lodged with ASX on 03 June 2025

6 Per holding per Substantial interest notices lodged with ASX on 19 March 2025

# BENEFITS OF DRUG REPURPOSING



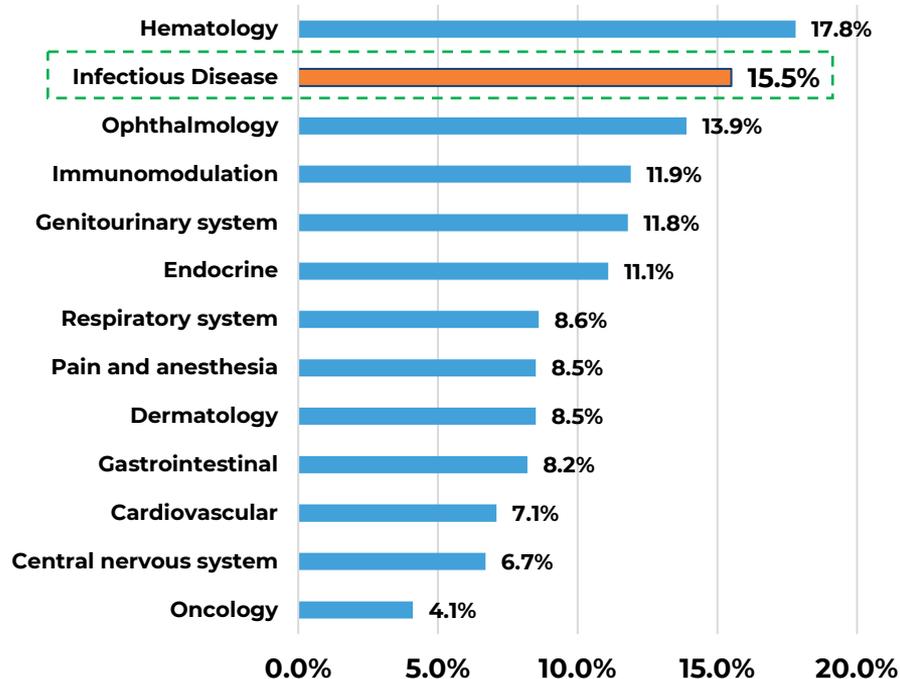
# INCREASED LIKELIHOOD OF SUCCESS



## Probability of successful Phase III transition post phase II) for infectious disease treatments increases to 64%

- Treatments for infectious disease **have a statistically higher likelihood of overall success** in clinical trials
- Anti-infective treatments sit at the low end of the drug development cost curve across all therapeutic areas
- JAMA research shows that **anti-infective drugs were the least expensive to develop**<sup>1</sup>
- Infectious disease treatments have the third-highest probability of phase II success (38.4%), behind hematology (48.1%) and metabolic (45%) treatments<sup>2</sup>
- **Island has considerable potential to advance the next phase of clinical trials and secure a priority review voucher**

## Drug Development - Overall probability of success



<sup>1</sup> JAMA Network: Costs of Drug Development and Research and Development Intensity in the US, 2000-2018

<sup>2</sup> Biotechnology Innovation Organisation: Clinical development success rates and contributing factors 2011-2020

# DENGUE - COMMON AND SPREADING

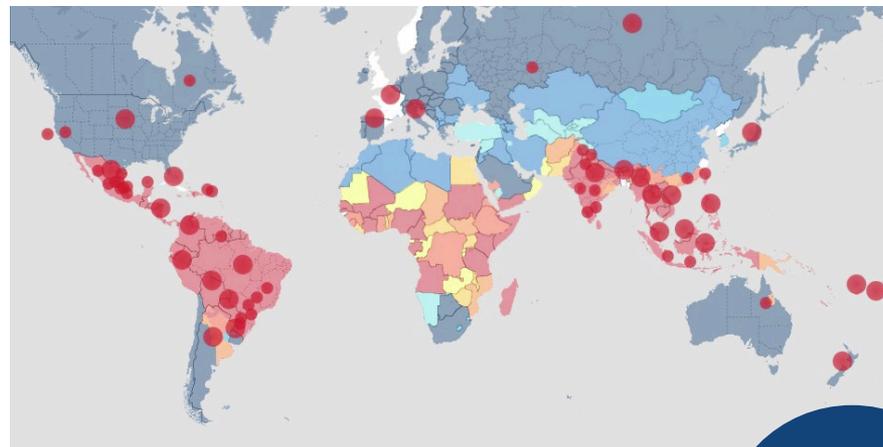


## Global cases of dengue fever rose steeply in 2024

Monthly global cases, millions



Guardian graphic. Source: WHO. Note: case reporting requirements vary by country



Absent Unlikely Uncertain Likely Present

Country Level Local Level

HealthMap: recent reports of local or imported dengue cases (March 2025)

**US\$8.9B**  
Estimated  
impact to the  
economy from  
dengue fever

**“About half of the world's population is now at risk of dengue with an estimated 100 – 400 million infections occurring each year”**

World Health Organisation, 30 May 2024

# A MULTI-BILLION-DOLLAR MARKET OPPORTUNITY



- Currently no specific small molecule targeting dengue – providing ILA with the opportunity to be first to market
- Takeda Pharmaceuticals project global sales (ex-USA) of its Qdenga dengue vaccine at US\$1.6bn to US\$2bn by 2030<sup>1</sup>
- Quick establishment of the anti-malarial drug market highlights potential for dengue drug development trends
- Antimalarial drug market was valued at US\$1.76Bn in 2024 with a potential to grow to US\$2.5Bn by 2030<sup>2</sup>

## Dengue Fever treatment – Growth forecast (USD Bn)



Source: [Market Research Future](#) /Rahul Gotadki, May 2025)

<sup>1</sup>Antimalarial Drugs Market by Drug Class, Drug Type, Route of Administration, Malaria Type, Distribution Channel, End User - Global Forecast 2025-20

<sup>2</sup>Fierce Biotech: [Takeda taps Biological E to ramp up Qdenga manufacturing capacity on quest to make 100M doses a year](#)

# ISLA-101 – BROAD ACTIVITY EVIDENT

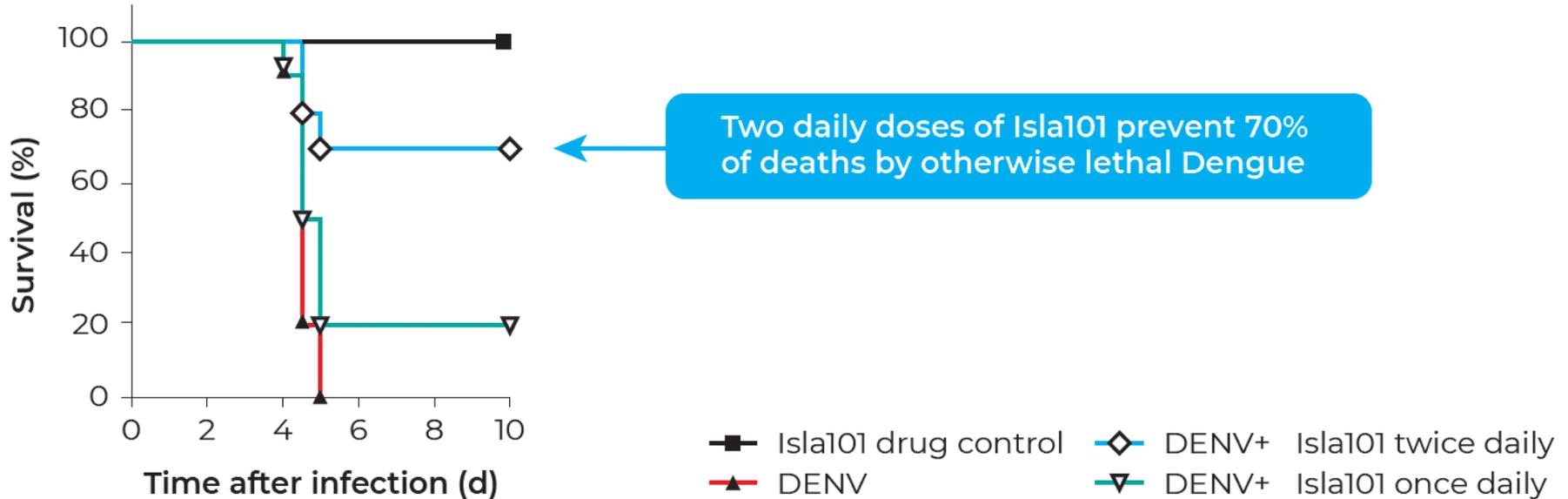


## Demonstrated activity against flaviviruses (subgroup of arboviruses) in models of infection



- ISLA-101 has demonstrated broad anti-viral activity in *in-vitro* models
- Demonstrated potent anti dengue-1 activity in *in-vitro* models using fresh human cells
- Protective in dengue fever and Zika in animal models
- Shown to prevent death in 70% of subjects in extremely lethal animal models
- Increasing concentrations of ISLA-101 prevent death induced by an otherwise lethal dengue fever infection
- 48 human clinical studies completed in other indications
- ILA's Single Ascending Dose study and further modelling reinforced safety / tolerability and identified dosing for Phase 2 trial

# PREVENTING ANIMAL DEATHS FROM LETHAL DENGUE AND PROTECTIVE AGAINST ZIKA



Survival curve showing protection from lethal dengue change by increasing dose of ISLA101 (mouse model).

# PHASE 2A/B (PROTECT) STUDY OVERVIEW



## Study aim was to determine a path forward for ISLA-101 – Results indicate clear signals of drug effect, highlighting success

### Randomised, double blind, placebo-controlled dengue challenge study – prophylactic and treatment challenge:

- Study included preventative (Phase 2a) and therapeutic (Phase 2b) arm
- Preventative Cohort- 2a: 4 subjects randomized 3:1
- Therapeutic Cohort: 2b: 10 subjects randomized 8:2
- Primary endpoint:
  - Assess effect of ISLA-101 on viremia after challenge with DENV-1-LVHC
- Secondary endpoints:
  - Characterise clinical, immunologic and virologic responses following ISLA-101 after challenge with DENV-1-LVHC
  - Assess effect of ISLA-101 on clinical signs and symptoms after challenge with DENV-1-LVHC
  - Assess safety of ISLA-101 in the challenge with DENV-1-LVHC



Trial conducted at SUNY Upstate Medical University Syracuse, New York.

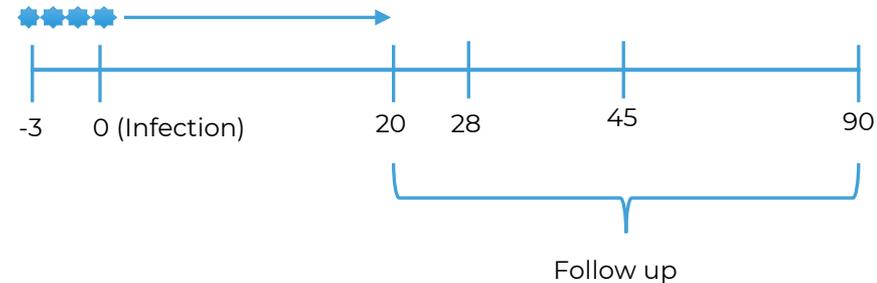
# PHASE 2A/B (PROTECT) DESIGN



- Phase 1 (completed April 2024) achieved all study outcomes relating to safety and dosing, demonstrating benefit of Challenge study approach
- Phase 2a subjects dosed in October 2024
- Safety Review Council review highlighted:
  - Administering ISLA-101 was safe
  - Study achieved appropriate ISLA-101 blood concentrations
  - Dosed subjects exhibited evidence of antiviral activity versus control
  - Unanimous decision to advance 2b cohort
- 2b cohort administered ISLA-101 in February 2025
- Pharmacokinetic analysis of 2b cohort has shown target blood level concentration was achieved in all participants
- Top-line results showed that ISLA-101 achieved anti-dengue activity in humans – highlighting a successful trial**

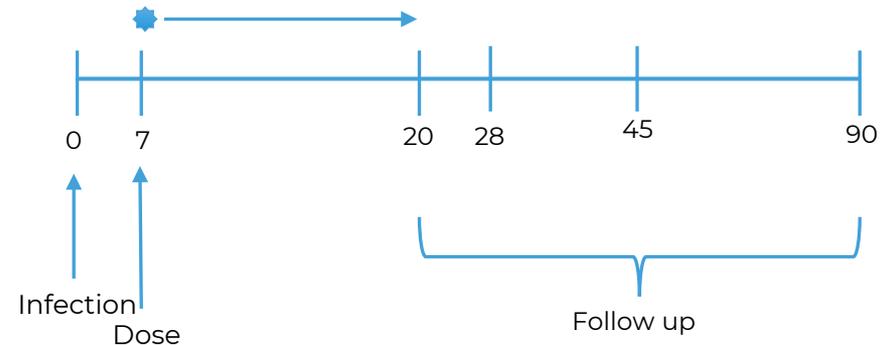
## Phase 2A: Preventative cohort

### Administer ISLA-101 daily



## Phase 2B: Treatment cohort

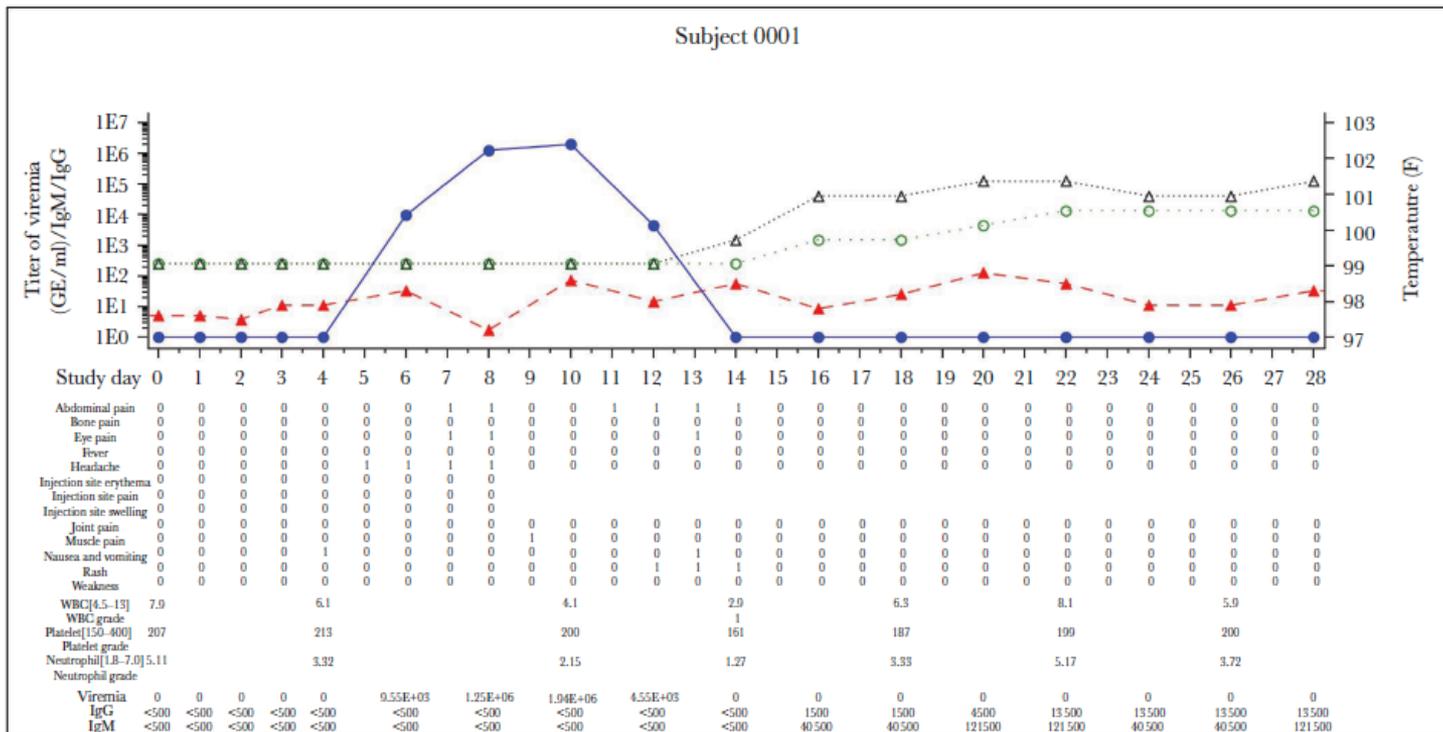
### Administer ISLA-101 daily



# PROTOTYPICAL DENGUE CHALLENGE INFECTION

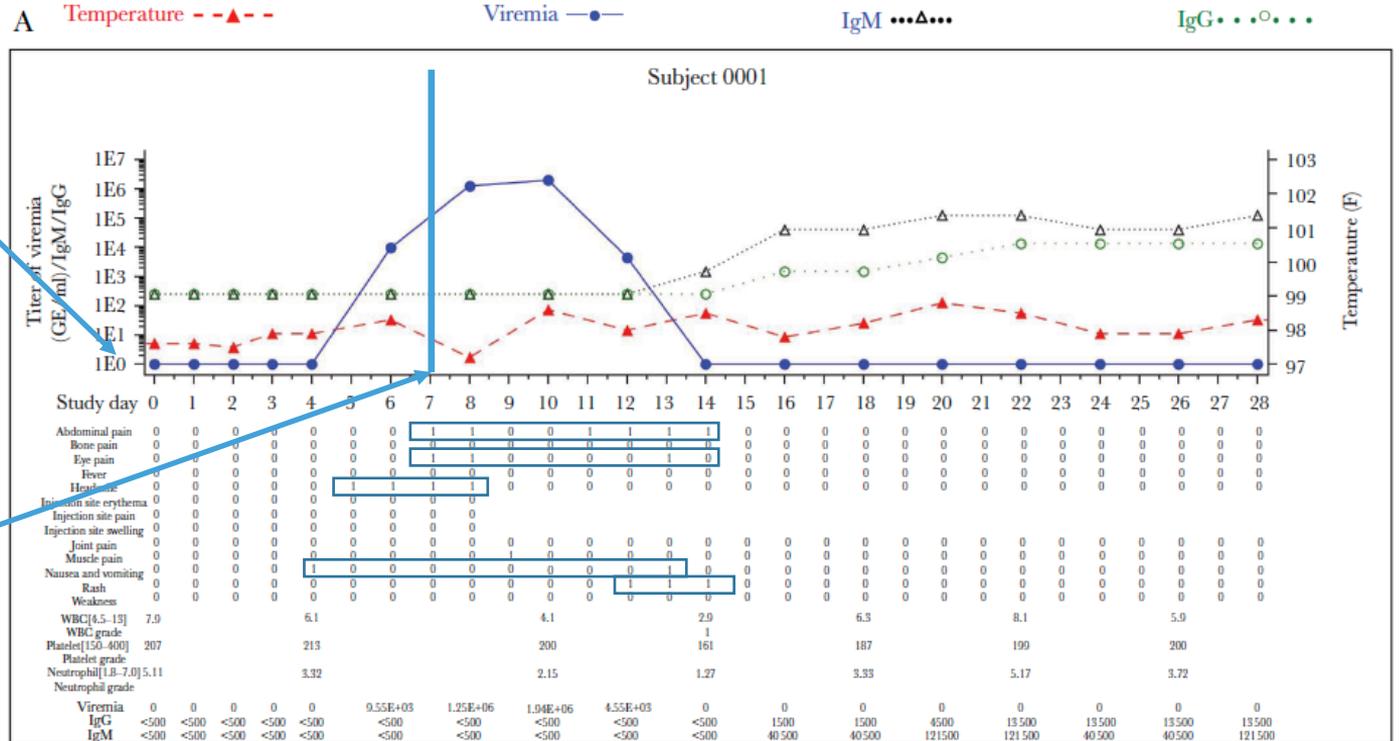


A Temperature ---▲--- Viremia —●— IgM ...▲... IgG ...○...



Endy et al, J Inf Dis 2021

# ISLAND'S 'PROTECT' STRATEGY



Prophylactic-dose before infection

Treatment-dose 7 days post infection - some subjects are symptomatic and viremic

# PROTECT INITIATIVE – GO OR NO-GO



**Study goal was to investigate if ISLA-101 shows activity against dengue in humans. If yes, ILA can proceed with the program. If not, the program would not proceed.**

Preventative	Therapeutic	Decision
Positive	Negative	GO
Negative	Positive	GO
Positive	Positive	GO
Negative	Negative	NO GO

## POSITIVE PHASE 2A/B TOP-LINE RESULTS:

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- Highly encouraging top-line results advocate for the ongoing clinical development of ISLA-101 in dengue
- ISLA-101 associated with meaningful reduction in viremia (viral load) and symptoms in preventative cohort
- Treatment cohort demonstrated signals of drug effect – additional work being undertaken to investigate further
- ISLA-101 is the first molecule to demonstrate potential benefit in the SUNY Dengue Human Infection Model
- Encouraging results increase success probability in future clinical trials

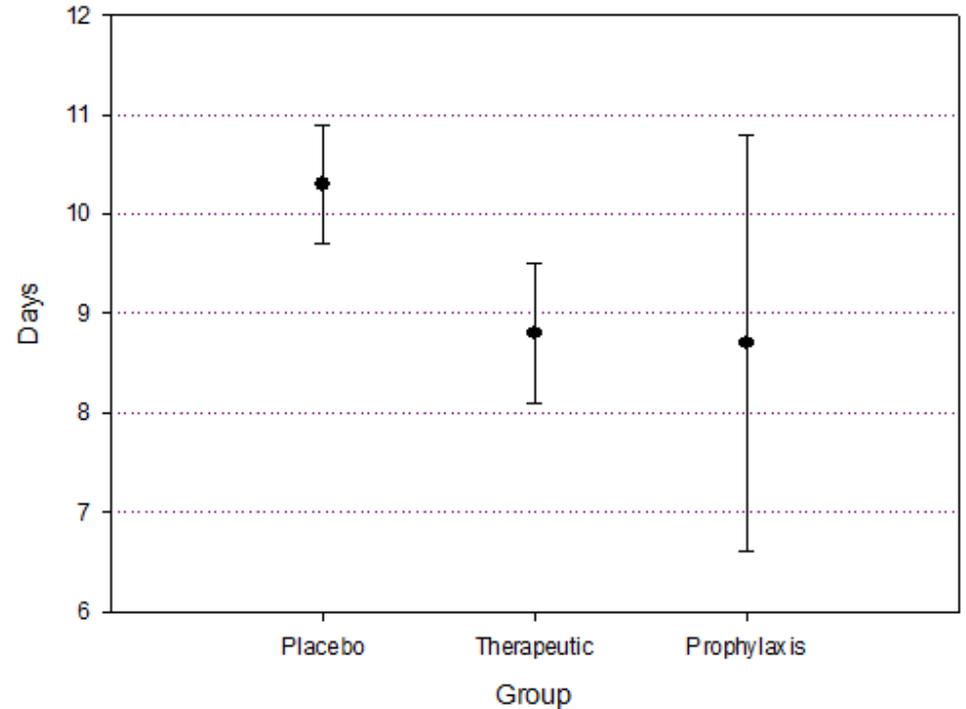
# DURATION OF VIRAL LOAD- RNAEMIA



## ISLA-101 treated subjects exhibited shorter exposure to virus

- Control subjects had detectable viral RNA for ~10.5 days
- Both treatment and preventative cohorts exhibited detectable viral RNA for ~8.5 days – two days shorter than control

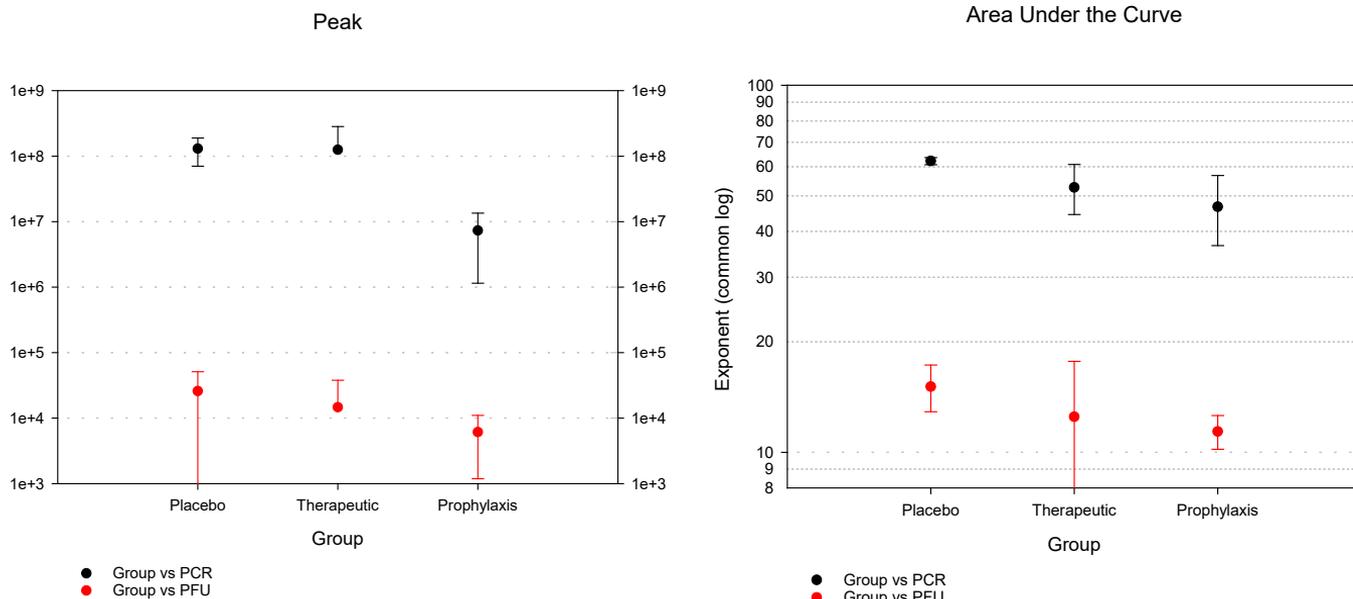
Duration of RNAemia



# EVIDENCE OF ANTI-DENGUE ACTIVITY



- Using two measures of viral load, a clear reduction in viral load was witnessed in the preventative arm and trend towards viral load reduction in the treatment arm
- Mean peak virus level (RNA) detected – 13,000,000 units in control and ~73,000 units in preventative arm – a reduction of 10-15 times



## Two measures of virus:

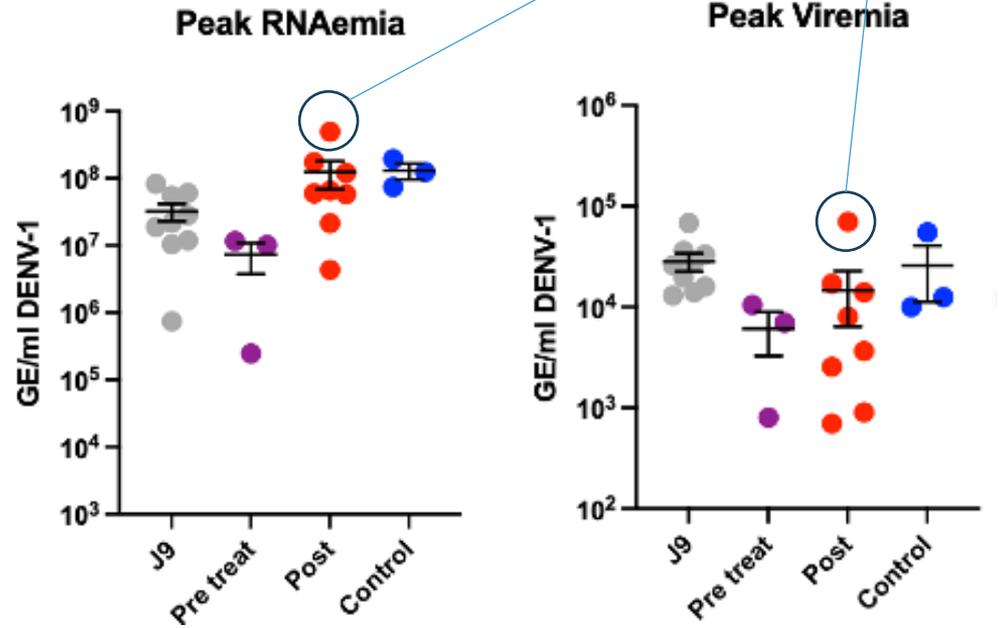
RNA (black) as detected by PCR and active virus (red) as detected by plaque forming units.

# EVIDENCE OF REDUCED VIRAL LOAD



## Peak viral load reduced in ISLA-101 treated subjects

- Viral RNA substantially reduced in preventative arm compared to internal control (blue) and historical controls (J9 in grey)
- Mean virus level decreased from ~13,000,000 units to ~73,000 units in the presence of ISLA-101, when examining RNA
- Active virus reduced in preventative arm compared to internal control (blue) and historical control (J9 in grey).
- Treatment arm (red) shows trend to reduced virus barring one outlier. It was determined that this subject had the lowest ISLA-101 blood concentration.\*



# SUMMARY OF SIGNS/SYMPTOMS

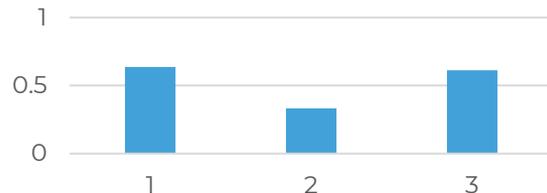


## TREF 16

### Summary of Signs and Symptoms Associated with Dengue Virus Infection over 29 days from Inoculation - by Group (Full Analysis Set)

Subjects experiencing at least one:	Control (N=3) n(%)	Prophylaxis & Treatment (N=3) n(%)	Delayed treatment (N=8) n(%)	All subjects (N=14) n(%)
Signs and symptoms associated with dengue virus infection	3/3(100)	3/3(100)	8/8(100)	14/14(100)
Abdominal Pain	2/3(66.7)	0/3(0.0)	5/8(62.5)	7/14(50.0)
Bone Pain	0/3(0.0)	0/3(0.0)	1/8(12.5)	1/14(7.1)
Eye Pain	2/3(66.7)	1/3(33.3)	7/8(87.5)	10/14(71.4)
Fatigue	3/3(100)	2/3(66.7)	7/8(87.5)	12/14(85.7)
Fever $\geq 38^{\circ}$ C (100.4 $^{\circ}$ F)	2/3(66.7)	0/3(0.0)	2/8(25.0)	4/14(28.6)
Headache	3/3(100)	2/3(66.7)	8/8(100)	13/14(92.9)
Joint Pain	2/3(66.7)	1/3(33.3)	5/8(62.5)	8/14(57.1)
Muscle Pain (Myalgia)	2/3(66.7)	2/3(66.7)	7/8(87.5)	11/14(78.6)
Nausea	2/3(66.7)	1/3(33.3)	5/8(62.5)	8/14(57.1)
Rash	2/3(66.7)	2/3(66.7)	7/8(87.5)	11/14(78.6)
Vomiting	1/3(33.3)	0/3(0.0)	1/8(12.5)	2/14(14.3)

### Reported symptoms



- 1: Control- 21/33 reported symptoms (63.6%)
- 2: Prophylaxis- 11/33 reported symptoms (33.3%)
- 3: Delayed treatment- 54/88 reported symptoms (61.4%)

# SELECT SYMPTOMS AND LAB ABNORMALITIES



	Placebo	All Treated	Prophylaxis
Abdominal pain	2/3=.67	5/11=.45	0/3=0.00
Fever	2/3=.67	2/11=.18	0/3=0.00
Joint pain	2/3=.67	6/11=.54	1/3=0.33
Nausea	2/3=.67	6/11=.54	1/3=0.33
<i>Mann-Whitney</i>	<i>p=0.0202</i>		

	Placebo	All Treated	Prophylaxis
Leukopenia	2/3=0.67	3/11=0.27	1/3=0.33
Thrombocytopenia	1/3=0.33	0/11=0.00	0/3=0.00
ALT	3/3=1.00	6/11=0.55	2/3=0.67
AST	2/3=0.67	3/11=0.27	1/3=0.33
Hypernatremia	1/3=0.33	0/11=0.00	0/3=0.00
<i>Mann-Whitney</i>	<i>p=0.0344</i>		

# KEY FINDINGS AND NEXT STEPS



**Top-line results demonstrate clear positive signal and provide evidence of activity in humans, answering the first study inquiry with a resounding signal to proceed with program. Results from both arms are encouraging and advocate for additional clinical trials using ISLA-101.**

Preventative	Treatment	Decision
Positive	Negative	GO
Negative	Potentially positive	GO
Positive	Potentially positive	GO
<del>Negative</del>	<del>Negative</del>	<del>NO GO</del>

## Next steps:

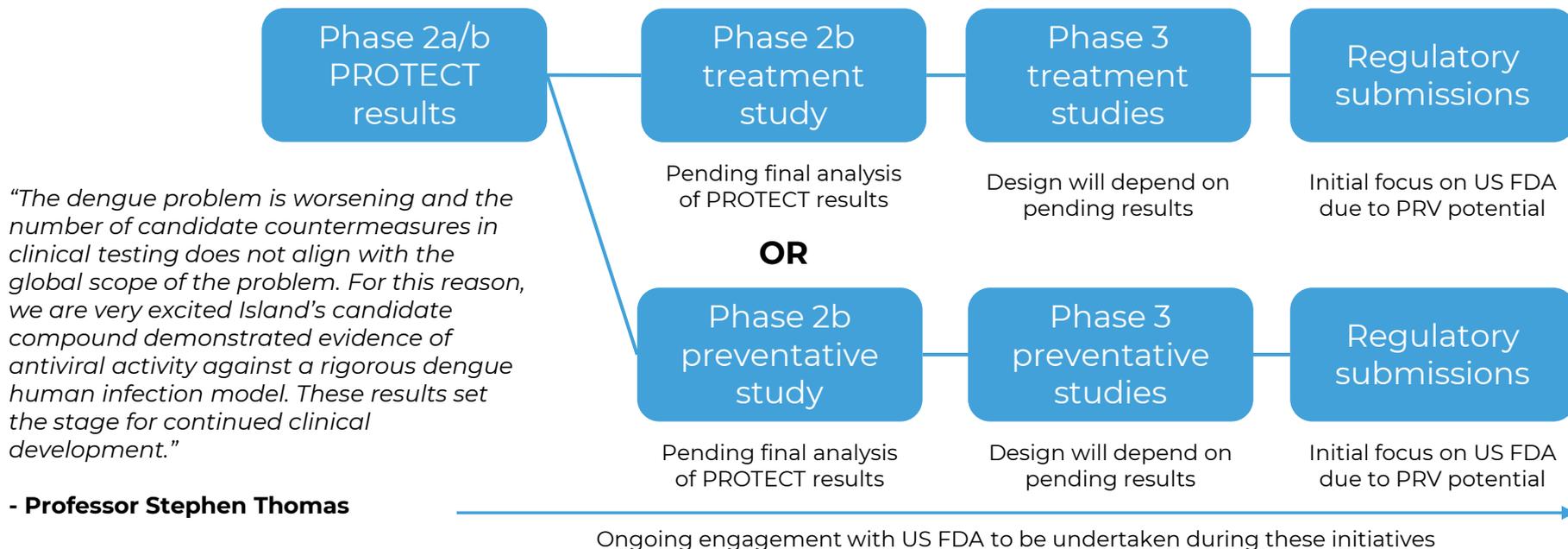
- Continue investigation in preventative and treatment data to determine clinical trial pathway
- Advance engagement with US FDA regarding potential trial pathway
- Progress engagement with potential partners and industry participants to fast track clinical trials

# POTENTIAL TRIAL AND REGULATORY PATHWAYS



## Defined clinical and regulatory route based on Phase 2a/b study results

- Two potential pathways based on further investigation of Phase 2a/b results
- Discussions advancing with multiple potential strategic partners for additional phase 2 and 3 clinical trials



# Island Pharmaceuticals (ASX: ILA)



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