

# Antiviral activity and tolerability of BIT225 plus pegylated interferon alfa-2b and weight-based ribavirin for 28 days in HCV treatment-naïve, genotype 1, mono-infected patients

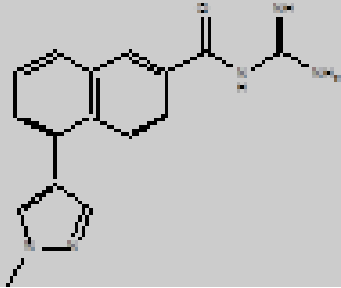
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HepDART - December 6, 2011

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*ASX:BIT*



# BIT225 – p7 Inhibitor

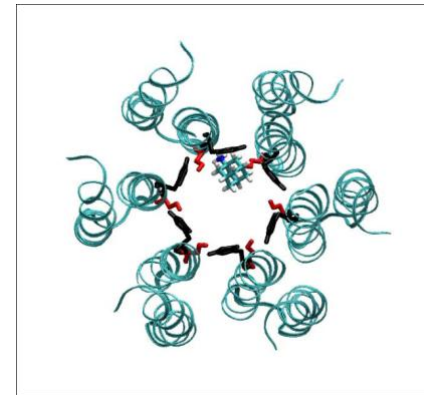
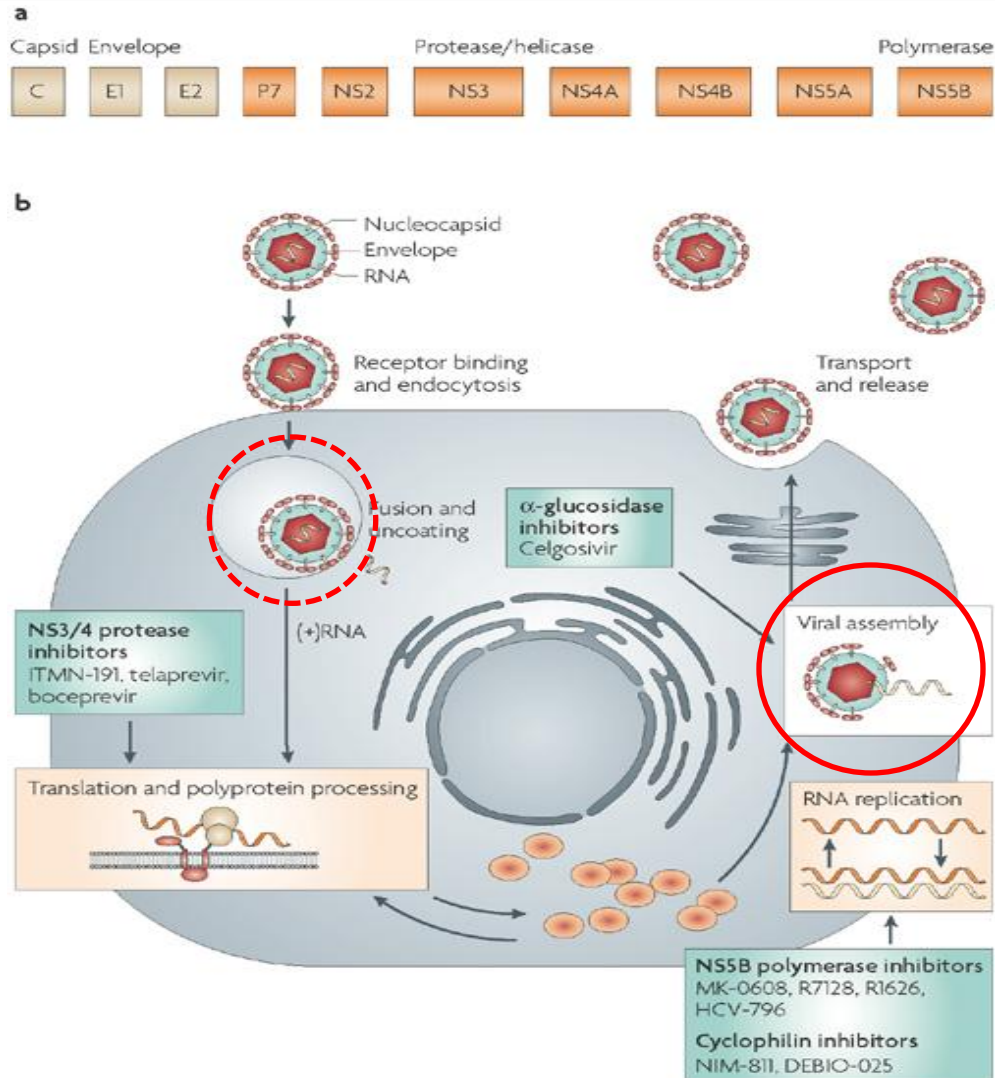
*N*-[5-(1-Methyl-1*H*-pyrazol-4-yl)-naphthalene-2-carbonyl]-guanidine

- New investigational oral DAA drug for treating HCV infection
- First in class; targets HCV p7 protein
  - p7 critical role in production of infectious HCV
  - Small hydrophobic protein (63 aa);
  - Viroporin (Ion channel activity)
  - A number of possible roles in viral replication:
    - Viral uncoating like influenza M2 (amantadine)
    - Viral assembly and release like HIV-1 Vpu and alphavirus

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# Potential sites of action for p7 inhibitors in the HCV life cycle



Mann *et al.*, 2007



# Phase 2a (BIT225-005): 28-day Combination Study with SOC

## *Trial design*

0                      2                      4    Weeks    48

8 pts	400 mg BIT225 + IFN/RBV	IFN/RBV
8 pts	200 mg BIT225 + IFN/RBV	IFN/RBV
8 pts	Placebo + IFN/RBV	IFN/RBV

- Trial commenced Sept 2010 in Bangkok, Thailand
- 24 patients, genotype 1, treatment-naïve
- Randomized 1:1:1 to BIT225 - 400 or 200 mg or placebo BID X 28 d plus SOC
- BIT225 powder mixed with 25 ml of OraSweet<sup>SF</sup>, or lactose placebo
- Peg-IFN alfa-2b dosed at 1.5 ug/kg weekly + wt based RBV
- After 28 days, IFN/RBV SOC continued X 44 weeks



# Phase 2a (BIT225-005): 28-day Combination Study with SOC

## **Primary objective :**

- to evaluate the safety and tolerability of 200 and 400 mg of BIT225 twice daily compared with placebo in combination with PEG-IFN and RBV in patients with chronic HCV infection that are treatment-naïve

## **Secondary objectives :**

- to evaluate the pharmacokinetics of 200 and 400 mg of BIT225 administered daily on Day 0 and Day 28 and twice daily on Days 1 - 27 for 28 consecutive days in combination with PEG-IFN and RBV in patients with chronic HCV infection
- to evaluate the antiviral activity of BIT225 administered for 28 consecutive days in combination with PEG-IFN and RBV in patients with chronic HCV infection that are treatment-naïve



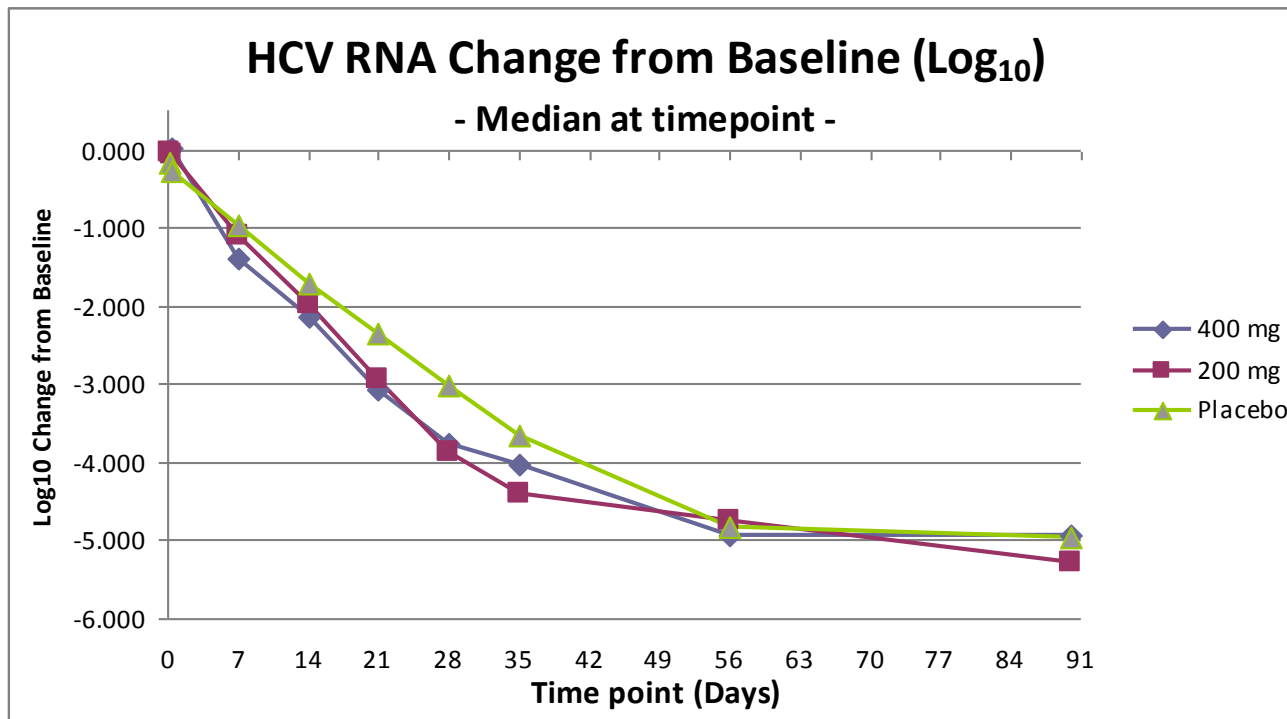
# Baseline Patient Characteristics

	400 mg	200 mg	Placebo
N	8	8	8
Age, yrs	38 (36,44)	44 (37,47)	35 (33,39)
Male sex, %	50	62.5	75
Asian race, %	100	100	100
Weight, kg	64 (56,78)	70 (55,79)	63 (54,72)
BMI	23 (22,29)	26 (21,30)	22 (20,26)
HCV Genotype 1a, %	75	50	25
HCV RNA, log <sub>10</sub>	6.69 (5.98;6.88)	6.61 (6.26;6.75)	6.47 (6.32;6.80)

*Median (IQR) unless otherwise noted*

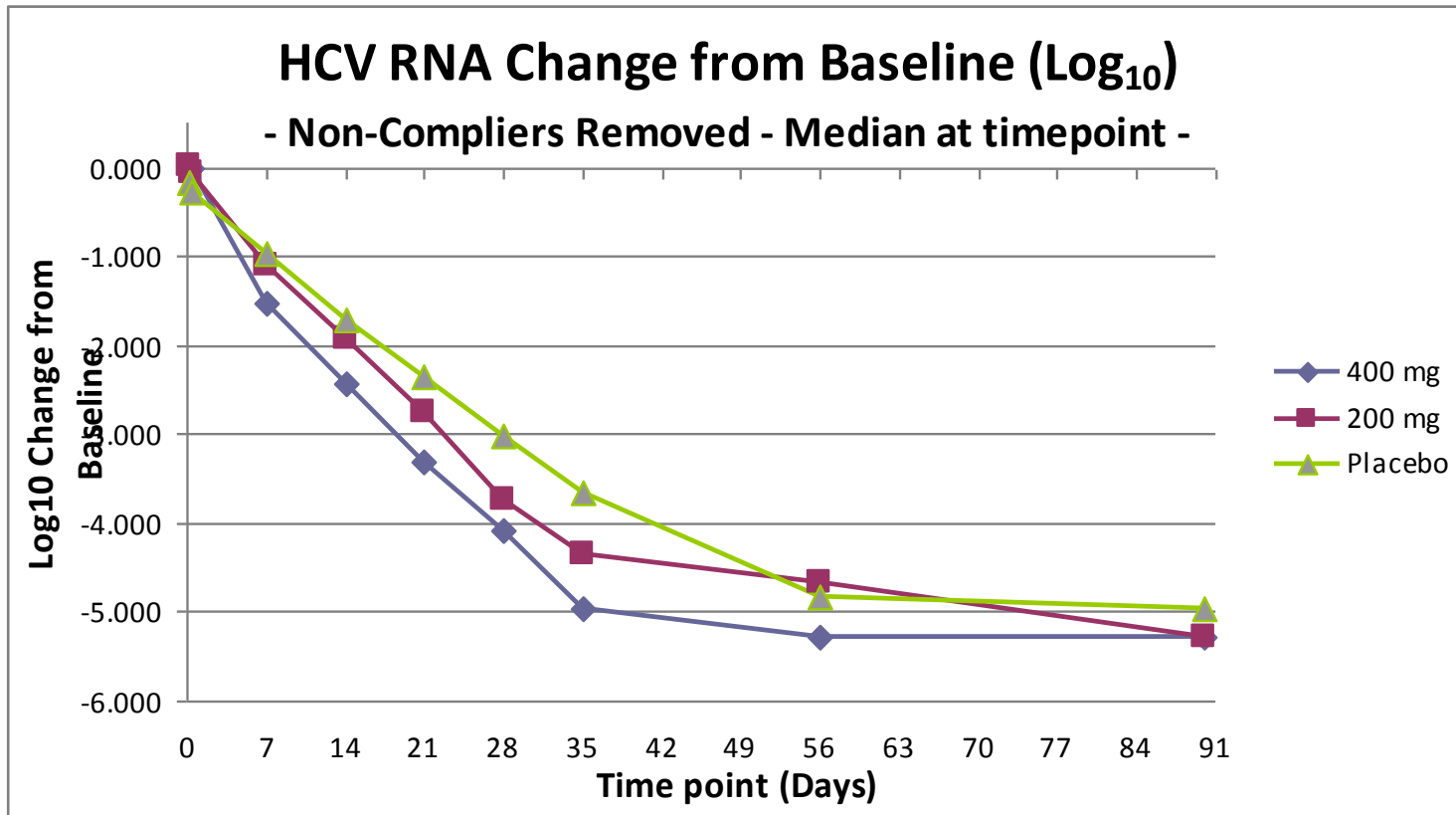
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# ITT: HCV RNA change in first 3 months



- 23/24 patients completed initial 28 days of study therapy
  - 1 discontinued in the first week for intolerance – blurred vision (400 mg group)
- 4 patients (3 @ 400 mg and 1 @ 200 mg groups) held study treatment for 1 to 7 days due to nausea; resumed drug by day 7 with no further nausea reported

# HCV RNA change in first 3 months



- Linear regression comparison of the 400 mg and placebo groups to day 35 were different favoring the 400 mg group ( $p=0.05$ )
- After day 7, viral load decreases were greater in the 400 mg group compared to placebo

# HCV RNA at 4 and 12 weeks

<b>Treatment</b>	<b>Median log10 reduction at 28 days</b>	<b>Median log10 reduction at 35 days</b>
400 mg BIT225 + SOC	-4.077	-4.957
200 mg BIT225 + SOC	-3.871	-4.351
Placebo + SOC	-3.013	-4.649

<b>Treatment</b>	<b>No. Complete EVR (&lt;50IU/ml at 12 weeks)</b>	<b>% Complete EVR (&lt;50IU/ml at 12 weeks)</b>
400 mg BIT225 + SOC	6/7	86%
200 mg BIT225 + SOC	7/8	88%
Placebo + SOC	5/8	63%



# Safety and Tolerability

- Drug was generally well tolerated – only one drop out from study
- Drug-related AEs may be formulation related (gastrointestinal/nausea)
  - Nausea in first week; 3 pts - 400 mg; 1 pt - 200 mg stopped drug for 1 – 7 days
  - Resumed drug and continued on drug till day 28 with no further nausea reported
- Others include headache, fever, etc in line with expected SOC AEs



# Summary

- BIT225 demonstrates clear antiviral activity
  - ~ 4 logs with BIT225 + SOC vs ~3 logs with SOC at d28
  - Enhanced rate of reduction in VL during treatment phase with BIT225
  - 3 month complete EVR for BIT225 + SOC was 87% vs 63% for SOC
- Pharmacokinetic and genome sequencing currently in progress
- Formulation studies in progress
- Potential for use with HCV and HIV co-infected patients
  - Also targets Vpu of HIV
  - Phase 1b trial in HIV+, treatment naïve patients commenced Sept '11

# Acknowledgements

## **Bangkok, Thailand**

Dr Tawesak Tanwandee (Principal Investigator) and colleagues  
Clinical Trial Site Staff, Siriraj Hospital, Bangkok, Thailand  
ACLIRES International, Bangkok, Thailand  
Trial participants

## **Medical Monitor**

Dr Rob Murphy, Northwestern University, Chicago USA

## **DSMB**

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Baiba Berzins, MPH, Northwestern University, Chicago, USA

## **Biotron Limited**

Dr Michelle Miller, Dr Carolyn Luscombe, Dr Gary Ewart, Dr John Wilkinson

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