# **Did**-By TARGETING DIABETES

Investor update September 2007



## Investment highlights

- Large and growing medical need in Type 2 diabetes and its complications
- Lead product in clinical trials with comparative safety advantages
- Three metabolism focused products in development
- Internationally focused product registration strategy for ISF402
- Strong team and partners



## Diabetes – a growing market

- Over 200m people worldwide have diabetes, expected to grow to 380 million by 2025
  - 5% of people have diabetes, another 8% have predisposition
- In the United States, over 20 million of the population has diabetes
- In Australia, over 1.2 million have diabetes
  - >50% remain undiagnosed
  - 275 Australian adults develop diabetes each day (100,000 pa)
- The Australian epidemic is in full flight with estimated treatments costs in excess of \$3b pa

#### DIABETES IS ONE OF THE FEW MAJOR DISEASES IN THE WORLD THAT IS ESCALATING



# Diabetes/ Metabolism focused product portfolio

- ISF402
  - Orally administered insulin sensitiser
  - Novel mode(s) of action
  - Monash University scientific team

#### • IM014

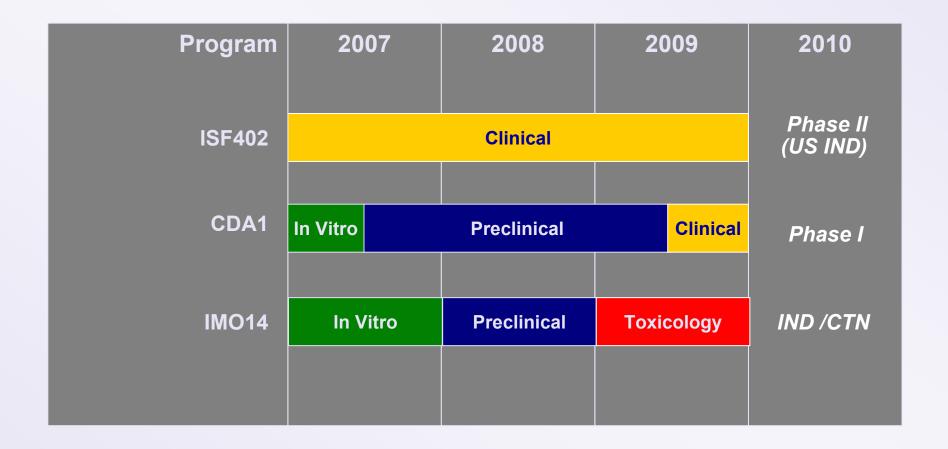
- Joint development with Fusion Biosciences (Victoria)
- Insulin sensitising and inherent insulin-like activity

#### • CDA1

- Novel target involved in fibrosis
- Application in diabetic nephropathy, atherosclerosis
- Baker Medical Research Institute



## **Product Portfolio**



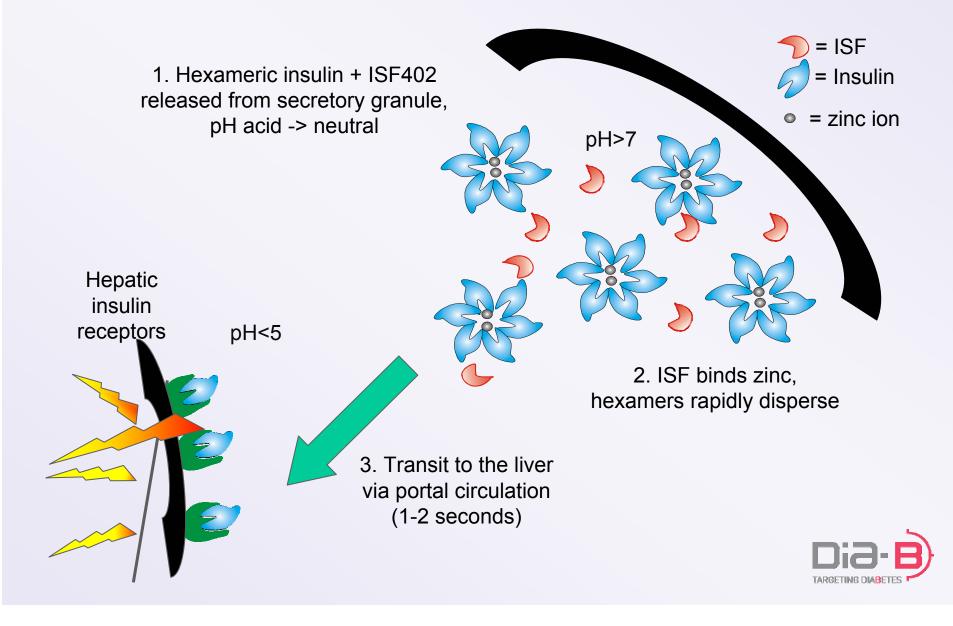


## ISF402 – a new generation insulin sensitiser

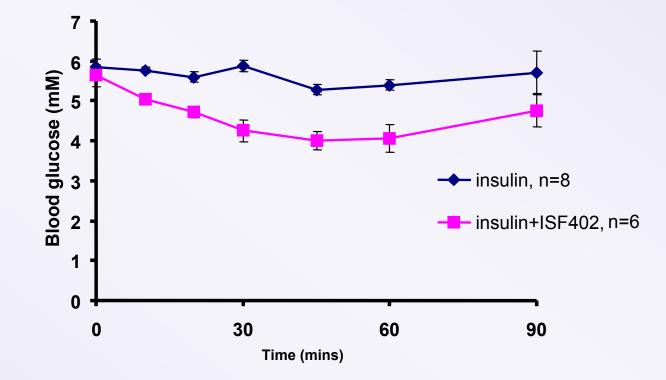
- Mechanism of action
  - ISF402 is a pro-drug for the active species HTD-amide
  - Accelerates dispersal of insulin from secreted hexamers into active monomers
  - Increases insulin levels without increasing insulin secretion, by possibly decreasing insulin clearance
  - Increases whole body glucose disposal



### **ISF402:** Mechanism of action



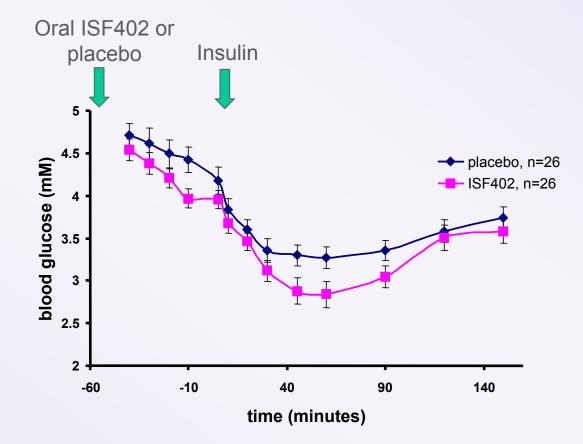
## ISF402 shows activity in diabetes animal models



 Zucker fatty rats were injected with either insulin or insulin with ISF402. Insulin reduced blood glucose by 0.6 mM. Insulin with ISF402 reduced blood glucose by 1.6 mM.



## ISF402 is active when given orally



 Rats (Wistar) were given oral ISF402 or placebo and one hour later an insulin tolerance test was performed. ISF402 reduced blood glucose and increased the response to insulin



# Phase Ia: clinical evaluation of ISF402

• Completed in August 2007

#### Protocol & End Points:

- 32 healthy male volunteers randomised to receive an initial starting dose of 100 mg ISF402 or placebo with a dose escalation to1600 mg
- The safety and tolerability was reviewed prior to dose escalation to the next treatment
  - Blood and urine samples collected for the first 24 hours
- At the end of treatment subjects returned for an outpatient visit on Day 7±1

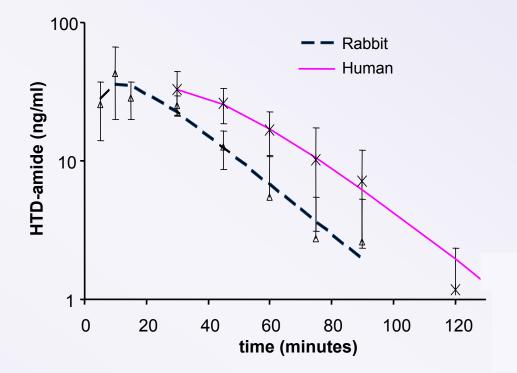
#### Results:

• No material adverse events



#### Pharmacokinetic data supports ISF402 bioavailability

- A robust procedure has been developed for measuring ISF402 in plasma
- Identifies the major clinically active metabolite (HTD-amide)
- The assay measures ISF402 and HTD-amide in plasma from humans and animals
- Plasma concentrations of HTDamide in dosed subjects from the Phase la trial are similar to the concentrations that improve insulin activity in rabbits.





# Phase Ib: clinical evaluation of ISF402

#### Trial protocol:

- Patients are randomized to receive ISF402 or placebo on two separate occasions followed by a standard meal
- Dosing was separated by a minimum of 14 days
- Patients are to be dosed with 900mg of ISF402 based on the pharmacokinetic data from the Phase Ia trial

#### Trial end-point:

 To evaluate the safety, tolerability and pharmacokinetics of a single oral dose of ISF402

#### Results:

• Data available in Q4 2007



## **ISF402 differentiators**

AGENT	ACTION	SIDE EFFECTS	DOSES/DAY
ISF402	Potentiation of insulin activity	None observed	1-2
Thiazolidinediones (Actos, Avandia)	Increase insulin sensitivity	Weight gain, liver damage, heart failure	1-2
DPP-IV inhibitors (Januvia)	Increase pancreatic insulin secretion	Nasopharyngitis, resp. tract infection	1
GLP-1 agonist (Exenatide)	Increase pancreatic insulin secretion	Nausea, vomiting, diarrhea	2 (sub-cut)
Meglitinides (Prandin)	Increase pancreatic insulin secretion	Hypoglycemia	2-4 with food
Sulfonylureas (Glyburide)	Increase pancreatic insulin secretion	Hypoglycemia, rash weight gain	1-2
Biquanides (Metformin)	Decrease hepatic glucose output	GI effects, diarrhea	1-3 with food
α-Glucosidase inhibitors (Acarbose)	Delay carbohydrate absorption	Gas, cramping	1-3 with food



## IMO14: insulin sensitiser

- A specific alkaloid that improves insulin sensitivity in Type 2 diabetes patients
  - Acts in an "insulin-like" manner
  - Mechanism of action studies being completed
- Active Pharmaceutical Ingredient (API) identified and provisional patent application lodged in 2006
- Animal studies have commenced
  - Efficacy, pharmacokinetic and dose range studies being completed
  - Tested invitro and invivo with
- API formulation and manufacture being assessed



## CDA1: diabetic nephropathy and atherosclerosis

- Developing a drug/product to prevent complications caused by CDA1
- CDA1 is a protein that causes scarring/complications downstream in kidney and vascular systems after the onset of diabetes
- A potential receptor for CDA1 has been identified that mediates the action of the protein



## Intellectual property

- 2 patent lodged in 2005 for ISF402
  - Further updated 2006, based on new discoveries of mechanism of action for ISF402
  - Patents issued in United States and New Zealand
  - Patents pending in Australia and Europe
- Provisional patent lodged for the treatment of diabetes using post-modified active formulations for ISF402 in August 2007
- All patents protect alternative formulations and potential new drug applications involving ISF402



## Strong Board & Management

#### **Board**

- Dr Michael Wooldridge
- Neil Hewitt OAM
- Sir George Alberti

#### **Management**

- Ken Smith
- Dr Mark Myers

#### **Scientific Advisory Board**

Prof Paul Zimmet AO

#### Chairman

- Former Australian Minister for Health and Family Services

#### **Non-Executive Director**

- Former Managing Partner of KPMG

#### **Non-Executive Director**

- Past President of the International Diabetes Foundation

#### CEO

#### **Chief Scientist (Monash University)**

#### **Chairman of SAB**

- Head of International Diabetes Institute



# Key financials

Current share price<sup>(1)</sup>: L12M High: L12M Low:

Issued shares: Issued options: \$0.08 per share\$0.165 per share\$0.043 per share

143,920,019 87,381,699

Market Capitalisation<sup>(1)</sup>:

Cash as at 30 June 2007:

\$11.5 million

\$1.84 million



Notes: (1) As at September 25, 2007

## Future milestones & next steps

- Phase Ib data to be released in Q4 2007 for biological effect
- Prepare ISF402 for US FDA registration strategy
  - API manufacture and formulation
  - Animal toxicology dependent on indicative dosing strategy
  - Pre-IND meeting
- Phase IIa trial under IND
- Further development of IMO14 and CDA1 through to proof of concept in pre-clinical animal models



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## **Contact Details**

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