



# ANTISENSE THERAPEUTICS

16 March 2004

The Companies Section  
The Australian Stock Exchange Limited  
530 Collins Street  
MELBOURNE VIC 3000

Dear Sir/Madam

**Re: Updated Corporate Presentation**

Please find attached Antisense Therapeutics Limited's updated company presentation.

The attached presentation has been updated to include the company's latest development project, ATL1103 for Growth and Sight Disorders.

Yours sincerely

Mark Diamond  
**Managing Director**



## Antisense Therapeutics Limited

(ASX : ANP)

March 2004

## Antisense Therapeutics Ltd

- ◆ Listed on ASX Dec 2001
- ◆ Total funds raised to date: A\$28.5 M
- ◆ Market Cap: A\$51.5 M
- ◆ Key Shareholders
  - Circadian 20%
  - Syngene 15% (42% Circadian)
  - Isis 11%
  - QIC 5%
- ◆ Cash reserves of A\$15 M, no borrowings



## Board of Directors

- ◆ Bob Moses, Chairman (ex VP of CSL)
- ◆ Mark Diamond, CEO (ex Faulding)
- ◆ Dr Chris Belyea (CEO Metabolic)
- ◆ Dr Stanley Crooke (Founder ISIS Pharmaceuticals, Inc)
- ◆ Prof Graham Mitchell (Foursight/CSL)
- ◆ Prof George Werther (MCRI)



## ANP's Mission

- ◆ Create, develop and commercialize novel antisense pharmaceuticals for large and/or niche unmet markets
- ◆ Select targets where our technology will provide clear competitive advantages



## Business strategy

- ◆ Leverage 14 years of Isis antisense technology development
- ◆ Fast track existing lead projects through pre-clinical and clinical development
- ◆ Create pipeline of new antisense therapeutics
- ◆ Commercialise those that are successful in clinical testing via licensing/partnering



## Strategic Partner ISIS Pharmaceuticals Inc

- ◆ Acknowledged global leader in antisense
- ◆ Over US \$1B invested in antisense chemistries
- ◆ More than 1,000 patents issued
- ◆ 1 FDA drug approved, 8 in late stage clinical development
- ◆ Deals with large market cap companies (eg Lilly and Amgen)



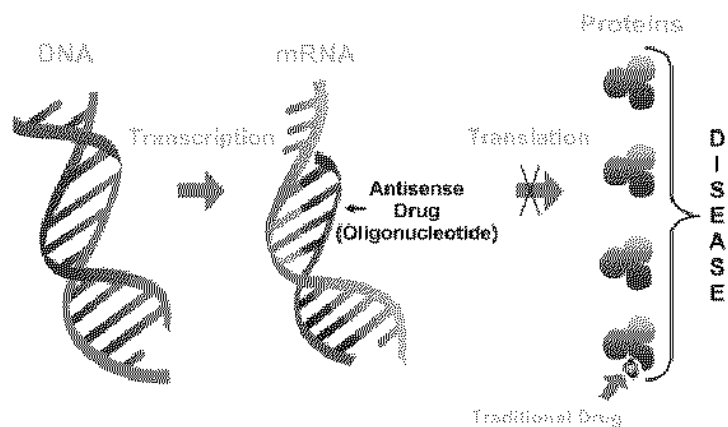
## What is antisense technology?

A fundamentally different approach to making medicine:

- ◆ Unprecedented target specificity and selectivity
- ◆ Most current drugs interfere with the activity of proteins that cause disease
- ◆ Antisense drugs go to work earlier, they block the manufacture of the target protein



## How it works...



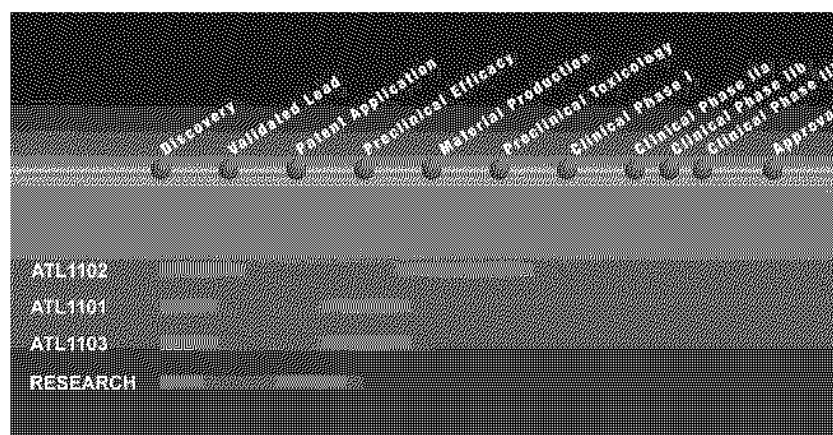
*...Blocks disease-causing proteins from being produced*

## Technical advantages

- ◆ Mature technology (20 years in development)
- ◆ Drug discovery and research is faster and more predictable
- ◆ Compounds are potentially more selective, effective and less toxic
- ◆ Broad disease application
- ◆ Dosing advantages (route and frequency)



## Development Pipeline

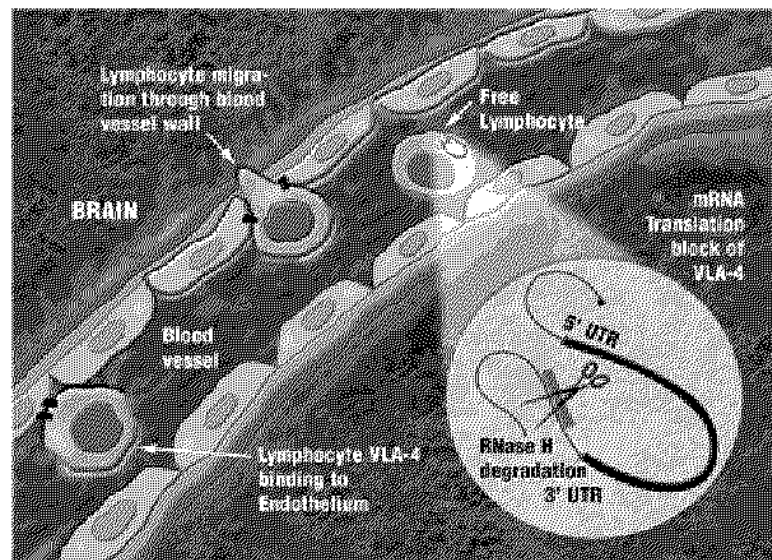


## Multiple Sclerosis - ATL1102

- ◆ MS is a progressive neurological disease
- ◆ Onset of MS is usually at young age (20 -40 years)
- ◆ MS affects 2.5 million people world-wide
- ◆ No cure; drugs aim to delay disease progression
- ◆ Beta-interferon (1a, 1b) leading therapy
  - Biogen, Serono, Schering AG
- ◆ Need for more effective drugs with less side effects
- ◆ Global drug sales for MS >US\$ 2.5 billion in 2003



## Multiple sclerosis - ATL1102



## Multiple Sclerosis - ATL1102

### ◆ Product

- Antisense inhibitor to VLA-4 protein which contributes to onset of disease
- Confirmed activity in pre-clinical mouse model of MS (also other inflammatory disorders asthma & arthritis)



## Multiple Sclerosis - ATL1102

### ◆ Product (cont)

- Biogen Idec's Antegren™ (also targets VLA-4) in Phase III trials
  - Filing marketing application with FDA based on interim 1 year phase III data
  - Provides greater confidence in likelihood of clinical success of ATL1102
  - Anticipate efficacy, dosing and cost advantages with ATL1102



## Multiple Sclerosis - ATL1102

<b>Problems with Current Therapies*</b>	<b>In development Antegren*</b>	<b>ATL1102</b>
◆ Partial or no response to $\beta$ IFNs & Copaxone	◆ Different mechanism of action	◆ Different mechanism/no neutralising antibodies
◆ Flu-like symptoms	◆ No flu-like symptoms	◆ No flu-like symptoms
◆ Dosing too frequent	◆ Only 1x/month	◆ Dosing TBC – potentially 1x/week or 1x/month
◆ Don't want injection responsibility/inconvenience	◆ IV done by doctor	◆ Sub-cutaneous, potential needless injection/oral

\* Source: Biogen website – The JP Morgan 21<sup>st</sup> Annual Healthcare Conference Presentation (14/1/03)



## Multiple Sclerosis - ATL1102

- ◆ Progress
  - Manufactured drug product for Phase I and IIa studies
  - Phase I human trial underway – dosing completed
  - Preliminary results presented at Australian Neurosciences Conference in January '04



## Multiple Sclerosis - ATL1102

### ◆ Outlook

- Phase I trial final reports due mid '04
- Following successful completion of Phase I trial company will make an application for the Phase IIa patient trial
- Phase IIa trials scheduled to commence in 2<sup>nd</sup> half 2004



## Psoriasis Treatment - ATL1101

### ◆ Disease & Market

- Chronic non-contagious skin disorder
- Affects 1-2% of population
- Global drug sales forecast to exceed US\$2 billion by 2007 (Frost & Sullivan)
- Need for more effective therapies

### ◆ Product

- Antisense inhibitor to IGF-IR regulates cell growth
- Developing topical formulation



## Psoriasis Treatment - ATL1101

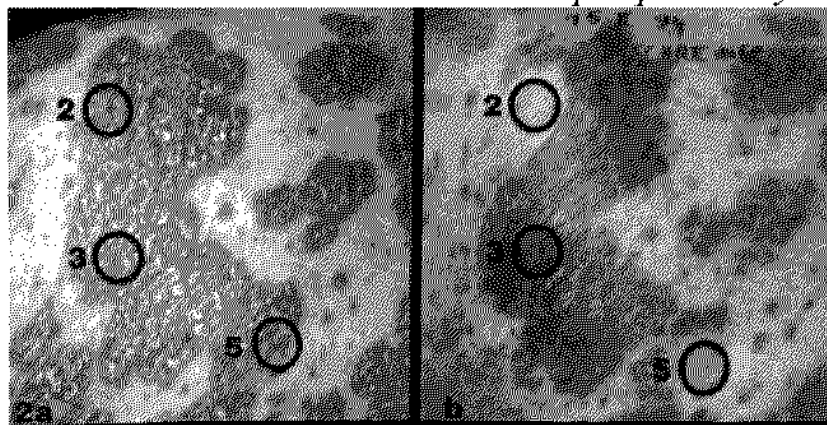
### ◆ Progress

- Completed pre-clinical efficacy program
- Awarded A\$1.1 million government grant
- “Proof of Concept” (PoC) study in psoriasis patients
  - Manufacture of compound for study underway
  - Contracted commercial laboratory to conduct animal toxicology program



### Human proof of concept strategy:

#### *Psoriasis small plaque assay*



Rappersberger et al., Clearing of psoriasis by a novel immunosuppressive macrolide. *J Invest Dermatol* **106**, 701-10 (1996).



## Psoriasis Treatment - ATL1101

### ◆ Outlook

- Commence PoC trial in 2<sup>nd</sup> half 2004 after toxicology studies successfully completed and relevant approvals received



## Research Pipeline

- ◆ Projects that target diseases of growth, vision and major inflammatory diseases
- ◆ Animal studies are at various stages of completion
- ◆ Most advanced research pipeline project:  
*ATL1103 for growth & sight disorders*
  - Project to move into development



## ATL1103 for growth & sight disorders

### Growth - Acromegaly

- ◆ The Disease
  - A disorder of excess growth hormone in adults associated with excess serum IGF-1
  - Affects 40,000\* people
- ◆ The Market
  - High treatment costs (from A\$14K-\$33K/annum)
  - Somatostatin analogue effective in ~ 60% of patients
  - Trovert™ sales projected to reach US\$500 million



\* US, Europe and Japan

## ATL1103 for growth & sight disorders

### Sight - Diabetic Retinopathy

- ◆ The Disease
  - Neovascularisation of the retina leading to blindness
  - High prevalence: over 5 million Americans affected by diabetic retinopathy
  - 12,000-24,000 new cases of blindness per year in US
- ◆ The Market
  - No approved drug treatments for diabetic retinopathy
  - \$Billion market potential



## ATL1103 for growth & sight disorders

### ◆ Product

- Antisense inhibitor to the GH receptor
- GH action is mediated through IGF-1 hormone
- Acromegalics have elevated levels of both GH and IGF-1
- Acromegaly treatment involves normalising IGF-I levels
- Reduction of IGF-I levels is associated with clinical improvement in retinopathy



## ATL1103 for growth & sight disorders

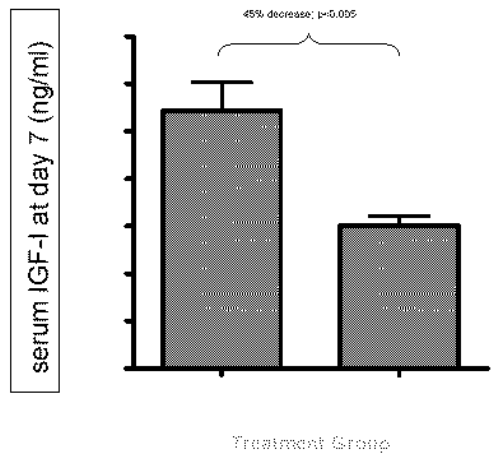
### ◆ Results of Animal Studies

- IGF-1 suppression by ATL1103 comparable to Trovert™ (existing treatment for acromegaly) in an equivalent mouse model
- Data to be presented at 2nd International Symposium on GH & IGF-I, Cairns, Australia, April 2004
- Patent applications filed



## ATL1103 for growth & sight disorders

### Pilot 1 week mouse study: sIGF-I



Data on file



## ATL1103 for growth & sight disorders

### Why ATL1103?

- ◆ Consistent with and validates ATL business plan
  - Grow business and diversify risk through product pipeline development
- ◆ Attractive Project
  - Significant market potential
  - GHr target is clinically validated
  - Ability to test for clinical endpoint (serum IGF-I) in early human studies
  - Limited competition
  - Potential dosing, administration and cost advantages



## ATL1103 for growth & sight disorders Competitor drugs in acromegaly

Drug	Efficacy	Route	Dosing Frequency	Cost (A\$)
<b>GHR antagonist</b> Trovert™	90-95%	sc	1 x per day	\$20-25,000/yr estimated
<b>Somatostatin analogues (octreotide)</b> Sandostatin™ Sandostatin LAR™	65% 65%	sc im depot	3 x per day 1 x per month	\$14 -33,000/yr*
<b>Dopamine agonists</b> Parlodel™ Dostinex™	10% >10%	oral oral	4 x per day 2 x per week	



\*Annual treatment costs vary depending on dosage and frequency from A\$14-33000 per patient/year

## ATL1103 for growth & sight disorders

### Outlook

- ◆ Place order for bulk drug product to commence preclinical safety studies



Outlook		
Project	Value Driver	Timing
ATL1102 MS	<ul style="list-style-type: none"> <li>◆ Complete Phase I</li> <li>◆ Start Phase IIa</li> <li>◆ Partnering objective</li> </ul>	1 <sup>st</sup> half '04 2 <sup>nd</sup> half '04 Concl Ph IIa
ATL1101 Psoriasis	<ul style="list-style-type: none"> <li>◆ Complete product manufacture and toxicology program</li> <li>◆ Start "Proof of Concept" study</li> <li>◆ Partnering objective</li> </ul>	1 <sup>st</sup> half '04 2 <sup>nd</sup> half '04 Concl "PoC"
ATL1103 Acromegaly	<ul style="list-style-type: none"> <li>◆ Commence product manufacture for pre-clinical toxicology</li> </ul>	1 <sup>st</sup> half '04

ANP – Investment Fundamentals	
<ul style="list-style-type: none"> <li>◆ Attractive product pipeline               <ul style="list-style-type: none"> <li>– Validated targets (lower development risk)</li> <li>– Products with platform based competitive advantages</li> <li>– Significant market potential</li> </ul> </li> <li>◆ Track record for hitting development milestones               <ul style="list-style-type: none"> <li>– Mature, efficient, and predictable platform technology</li> <li>– High quality and effective collaborations (Isis/MCRI)</li> <li>– Experienced management team</li> </ul> </li> <li>◆ Clear commercialisation objectives</li> <li>◆ Near term key value drivers               <ul style="list-style-type: none"> <li>– ATL1102 &amp; ATL1101 in patient trials in '04</li> </ul> </li> </ul>	