ANTISENSE THERAPEUTICS

22 December 2004

SUPPL

Securities and Exchange
Judiciary Plaza
450 Fifth Street
Washington DC 20549
UNITED STATES OF AMERICA

Dear Sir/Madam

Re: Antisense Therapeutics Limited
Announcement to the Australian Stock Exchange

Please find attached copies of announcements lodged with the Australian Stock Exchange (ASX) and also copies of documents lodged with the Australian Securities and Investment Commission (ASIC).

Date of Announcement/Lodgement	To:	Title	No of pages
17 November 2004	ASX	ATL1101 for Psoriasis: Approval for "Proof of Concept" clinical trial	2
23 November 2004	ASX	Presentation – Institutional Science Forum in London	13
26 November 2004	ASX	Market Developments – New Treatment for MS	1
7 December 2004	ASIC	Form 484 – Response to Annual Statement	10
15 December 2004	ASIC	Form 484 – Notify Change of Company Details	7
15 December 2004	ASX	Appendix 3B – Exercise of Options	8
20 December 2004	ASX	Animal Study results point to ATL1102's potential as an Inhaled Drug for Asthma	2
21 December 2004	ASX	Antisense Therapeutics Limited and Isis Pharmaceuticals initiate Phase 2a Trial of Antisense Drug for Multiple Sclerosis	3

Yours sincerely

N. Korchev

Natalie Korchev
Company Secretary

PROCESSED
JAN 07 2005

dlw 1/7

ANTISENSE THERAPEUTICS

17 November 2004

ATL1101 for Psoriasis: Approval for "Proof of Concept" clinical trial

Antisense Therapeutics Limited is pleased to announce that its application to conduct a "proof of concept" study of ATL1101 in patients suffering from psoriasis has been approved by the Institutional Review Board and the Ethics Committee of the Clinical Research Organisation that will conduct the study. Patient recruitment for the study is currently underway.

ATL1101 is a second generation antisense drug designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell overgrowth in psoriasis. ATL1101 is being developed as a cream for the topical treatment of mild to moderate cases of psoriasis.

The trial will take place in Adelaide under the management of CMAX, a Division of the Institute of Drug Technology Australia Limited.

Proof of Concept – Microplaque Assay

In the "proof of concept" clinical trial (also referred to as Small Plaque Assay or Microplaque Assay), a relatively small quantity (100 μL) of ATL1101 cream will be applied to areas of psoriatic skin in patients, once every two days, over a one month period.

A comparison will be made against a placebo cream (cream without the active agent ATL1101), and also against some reference cream products that are currently marketed as prescription medications for treatment of psoriasis.

The patients will be monitored over the duration of the trial, and on completion of dosing, for signs of response and improvement in their skin condition. The final evaluations will include clinical assessments, as well as assessments of laboratory indices of psoriasis in psoriasis skin samples (punch biopsies).

The primary end point will be a clinical assessment of the treated skin areas using a severity index score. The trial will be double-blinded, placebo-controlled, randomised, and two concentrations of ATL1101 cream will be evaluated in 14 psoriasis patients with mild to moderate severity of the disease.

Typically a drug's activity is not established until completion of Phase II clinical trials. However, a "proof of concept" study of ATL1101 can be undertaken relatively inexpensively for a disease such as psoriasis, unlike for many other diseases, which will provide early evidence of activity. While the "proof of concept" study will not replace the requirement to undertake formal (Phase I, II and III) human clinical trials, if early indications of the drug's effectiveness are shown, the company will have increased confidence in the prospects for successful commercial development of ATL1101 and appropriate data to pursue potential early partnering opportunities.

The clinical trial is expected to be completed in the second quarter of 2005 and results reported in the third quarter of 2005.

The Psoriasis project is supported by a Commonwealth Government R&D Start grant of $1.1 million.

Psoriasis *is a chronic, non-contagious skin disorder, which affects 2% of the population. While the precise cause of psoriasis is unknown, it is thought to be triggered by an immune system defect leading to excessive skin cell division. Severity varies, with around 75% of psoriasis cases classified as "mild to moderate", and the remainder classified as "moderate to severe". Topical therapies are first-line treatments for mild to moderate cases of the disease. The worldwide market for psoriasis treatments was more than US$500 million in 2000 and there is an acknowledged unmet medical need for more effective and safer treatments. The market is forecast to grow to beyond US$2 billion with the emergence of new therapies.*

Antisense Therapeutics Limited (ASX: ANP) *is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).*

Contact Information:

Website: www.antisense.com.au
Managing Director – Mark Diamond +61 3 9827 8999
Company Secretary – Natalie Korchev +61 3 9827 8999

ANTISENSE THERAPEUTICS

23 November 2004

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

Dear Sir/Madam

Re: Presentation – Institutional Life Science Forum in London

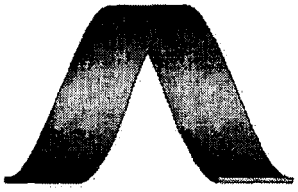
Antisense Therapeutics Limited has been invited to present at the Institutional Life Science Forum in London, which takes place on 26 November 2004 at the London Stock Exchange. The Forum is being run by Intersuisse Bioscience and Elixir Securities.

Mark Diamond, Managing Director, is scheduled to present to an audience of European based investors including small cap and specialist healthcare institutions, where he will provide an overview of the company including progress with respect to its clinical development program and business activities. With respect thereto, please find enclosed a copy of the company's presentation.

Yours sincerely

Natalie Korchev
Company Secretary

LEVEL 1, 10 WALLACE AVENUE TOORAK VICTORIA 3142 AUSTRALIA
TELEPHONE: +61 (3) 9827 8999 FACSIMILE: +61 (3) 9827 1166
ANTISENSE THERAPEUTICS LIMITED ABN 41 095 060 745 www.antisense.com.au



ANTISENSE THERAPEUTICS

ASX:ANP

November 2004

Antisense Therapeutics Ltd

- Listed on ASX Dec 2001
- Total funds raised to date: $28.5 M
- Market Capitalisation: A$44M (undiluted)
- Key Shareholders
  - Circadian 20%
  - Syngene 15% (42% Circadian)
  - Isis 11%
  - QIC 5%
- Cash reserves of $11M, no borrowings

ANP's Mission

Create, develop and commercialize novel antisense pharmaceuticals for large and/or niche unmet markets

- *Multiple Sclerosis (MS), Psoriasis, Acromegaly, Diabetic Retinopathy*

Select targets where our technology will provide clear competitive advantages

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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
  - Early stage partnering strategy for current lead compounds to fund pipeline development

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Key Achievements - FY to 30 June 2004

ATL1102 for MS

- successfully completed Phase I human clinical trial

ATL1101 for Psoriasis

- completed animal toxicology study for "Proof of Concept" study
- filed application for "Proof of Concept" study (*approval received Nov '04*)

ATL1103 for Growth and Sight Disorders

- new development project

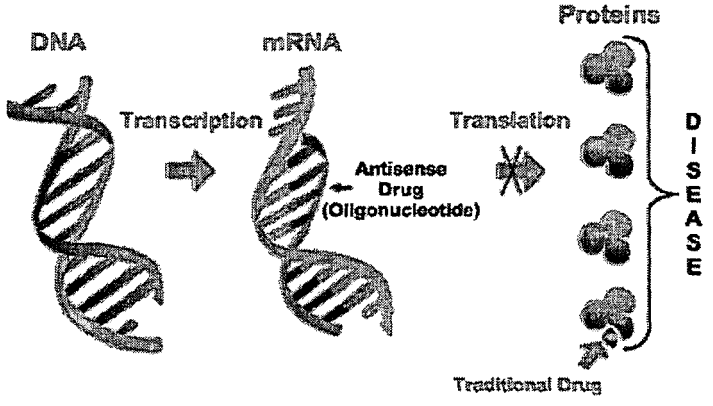
Capital Raising - A$10.4M

Level 1 ADR program

- Accepted proposal from Bank of New York

5

How it works...



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

6

Technical advantages

- Mature technology (20 years in development)
- Drug discovery and research is faster/more predictable
- Compounds potentially more selective, effective and less toxic
- Broad disease application
- Potential dosing (route and frequency) and cost of manufacture advantages

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Multiple Sclerosis - ATL1102

Disease & Market

- Life-long chronic disease of the central nervous system
- Global drug sales of > US$2.5bn in 2002
- Need for more effective drug with less side effects

Product

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

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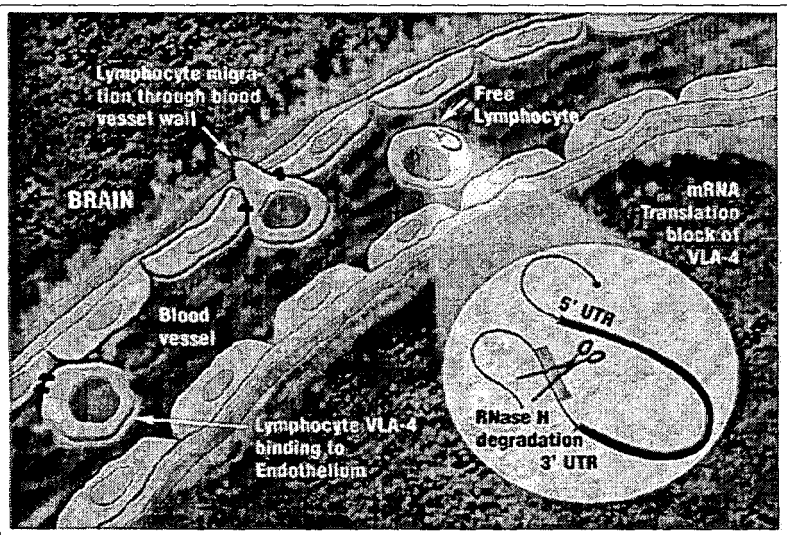
Multiple Sclerosis - ATL1102



Multiple Sclerosis - ATL1102

VLA-4 is a validated target

Biogen Idec's Antegren™ (also targets VLA-4) is in Phase III trials

- Marketing application filed with FDA based on interim 1 year phase III data
- Provides greater confidence in likelihood of clinical success of ATL1102
- Anticipate potential efficacy, dosing and cost advantages with ATL1102

Multiple Sclerosis - ATL1102

Progress

- Completed Phase I human trial

Outlook

- Submitted an application to conduct a Phase IIa clinical trial in MS patients
- Trial to be conducted in Europe
- Regulatory Agency approval and commencement of trial anticipated in 4Q'04

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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-1R (ATL1101); regulates cell growth
- Developing topical formulation

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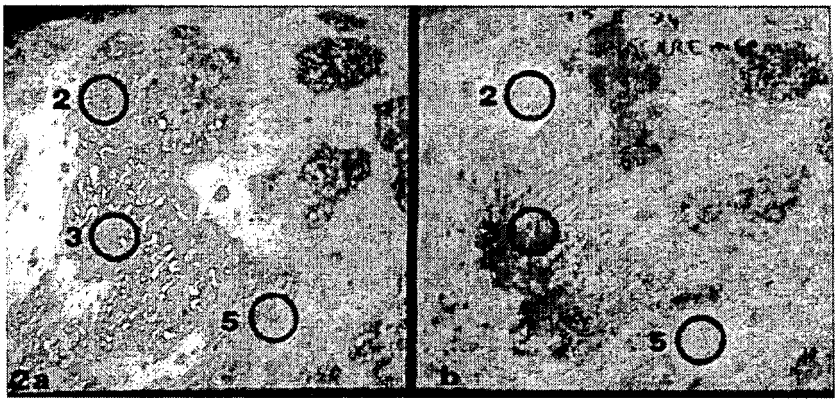
Human proof of concept strategy - Psoriasis microplaque assay



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

13

Psoriasis Treatment – ATL1101

Progress

Approval received to conduct "Proof of Concept" study in psoriasis patients

- Microplaque (small plaque) assay
- Double-blinded, placebo controlled and randomised trial
- Psoriasis patients with mild to moderate disease severity
- Dosing regimen: 2 drug concentrations, applied once every 2 days, over a one month period

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Psoriasis Treatment – ATL1101

Outlook

- Complete "Proof of Concept" study 2 Q '05
- Report results 3 Q'05
- Objective to license out/partner ongoing 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 market leader: effective in ~ 60% of patients

* *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

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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
- Current acromegaly treatment involves normalising IGF-I levels
- Reduction of IGF-I levels is associated with clinical improvement in retinopathy

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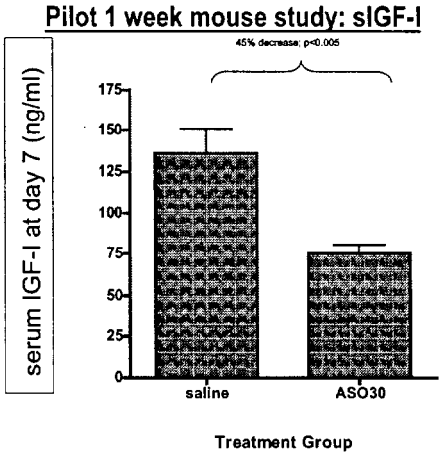
ATL1103 for growth & sight disorders



Data on file

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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 presented at 2nd International Symposium on GH & IGF-I, Cairns, Australia, April 2004
- Patent applications filed

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ATL1103 for growth & sight disorders

- 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

Progress

- Lead compound selected for clinical development

Outlook

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

Outlook

Project	Value Driver / Milestone	Timing
ATL1102 MS	•*Complete Phase I* •Start Phase IIa •Partnering objective	*1st half '04* √ 2nd half '04 Concl Ph IIa
ATL1101 Psoriasis	•*Start "Proof of Concept" study* •*Complete "Proof of Concept" study and report results* •Partnering objective	*2nd half '04* √ 2nd half '05 Concl "PoC"
ATL1103 Acromegaly and Diabetic Retinopathy	•*Commence product manufacture for pre-clinical toxicology (lead selection)* •Order compound for pre-clinical toxicology	1st half'04 √ 2nd half '04

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ANP – Investment Fundamentals

Attractive product pipeline

- Validated targets (lower development risk)
- Products with platform based competitive advantages
- Significant market potential

Track record for hitting development milestones

- Mature, efficient, and predictable platform technology
- High quality and effective collaborations (Isis)
- Experienced management team

Clear commercialisation objectives

Near term key value drivers

- ATL1102 & ATL1101 in patient trials in '04

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ANTISENSE THERAPEUTICS

26 November 2004

Market Developments - New Treatment for MS

On 24 November 2004, Biogen Idec and its partner Elan Corporation plc, announced "that the U.S. Food and Drug Administration (FDA) has approved Tysabri®, formerly referred to as Antegren®, as treatment for relapsing forms of multiple sclerosis (MS) to reduce the frequency of clinical relapses. FDA granted accelerated approval for Tysabri following Priority Review based on one-year data from two Phase III studies."

As reported by Biogen/Elan on 8 November, in the "trial of 942 patients with relapsing-remitting MS, (Tysabri) reduced the rate of relapses by 66 percent compared to placebo." The most prominent result of clinical trials for existing interferon beta treatments (first choice treatment in patients) was a reduction in relapse rate by about one third.

Positive impact on ATL1102 for multiple sclerosis

As previously advised, both Tysabri® and Antisense Therapeutics' MS compound ATL1102 target the same protein (VLA-4), which is considered to be critical to the progression of MS. The FDA approval of Tysabri® is important to Antisense Therapeutics as it medically validates the Company's drug development strategy for ATL1102 and provides the Company with greater confidence in the likely success of its MS compound.

Antisense Therapeutics reported positive results from a Phase I trial of ATL1102 in June 2004 and has submitted an application to conduct a Phase IIa clinical trial in MS patients. Regulatory approval and commencement of the Phase IIa trial are expected to occur before the end of this year.

ATL1102 is a second-generation antisense drug designed to act at an earlier stage of the disease process (than Tysabri®) by preventing excessive amounts of VLA-4 being produced. ATL1102 may also provide important advantages over Tysabri®, in particular dosing convenience, cost of therapy as well as improved effectiveness. ATL1102 is being developed for subcutaneous administration at home by the patient whereas Tysabri is infused requiring medical assistance.

About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

Contact Information:

Website: www.antisense.com.au
Managing Director – Mark Diamond +61 3 9827 8999
Company Secretary – Natalie Korchev +61 3 9827 8999

COPY

ANTISENSE THERAPEUTICS

7 December 2004

Australian Securities & Investments Commission,
PO Box 4000
GIPPSLAND MAIL CENTRE VIC 3841

Dear Sir/Madam

Re: Form 484 – Response to Annual Statement

In response to the Annual Company Statement, we enclose Form 484, Section C, with respect to changes in the top 20 members.

We would be pleased if you would acknowledge receipt in due course.

Yours faithfully

N. Korchev

Natalie Korchev
Company Secretary

Encl

Please Note: The new contact numbers for Antisense Therapeutics are now:
Phone: 9827 8999 Fax: 9827 1166

LEVEL 1, 10 WALLACE AVENUE TOORAK VICTORIA 3142 AUSTRALIA
TELEPHONE: +61 (3) 9826 0949 FACSIMILE: +61 (3) 9826 4399
ANTISENSE THERAPEUTICS LTD ACN 095 060 745 www.antisense.com.au

Australian Securities & Investments Commission

Form 484
Corporations Act 2001

Change to company details

Sections A, B or C may be lodged independently with this signed cover page to notify ASIC of:

A1 Change of address
A2 Change of name - officeholders or members
A3 Change - ultimate holding company

B1 Cease company officeholder
B2 Appoint company officeholder
B3 Special purpose company

C1 Cancellation of shares
C2 Issue of shares
C3 Change to share structure
C4 Changes to the register of members

If there is insufficient space in any section of the form, you may photocopy the relevant page(s) and submit as part of this lodgement

Company details

Refer to guide for information about corporate key

Company name: ANTISENSE THERAPEUTICS LIMITED

ACN/ABN: 41 095 060 745

Corporate key: 78841339

Lodgement details

Who should ASIC contact if there is a query about this form?

Name: NATALIE KORCHEV

ASIC registered agent number (if applicable):

Telephone number: (03) 9827 8999

Postal address: LEVEL 1, 10 WALLACE AVENUE
TOORAK VIC. 3142

Total number of pages including this cover sheet: 9

Please provide an estimate of the time taken to complete this form: ____ hrs ____ mins

Signature

This form must be signed by a current officeholder of the company.

I certify that the information in this cover sheet and the attached sections of this form are true and complete.

Name: NATALIE KORCHEV

Capacity:
- ☐ Director
- ☑ Company secretary

Signature: N. Korchev

Date signed: 07/12/04 [D D] [M M] [Y Y]

Lodgement

Send completed and signed forms to:
Australian Securities and Investments Commission,
PO Box 4000, Gippsland Mail Centre VIC 3841.

Or lodge the form electronically by visiting the ASIC website
www.asic.gov.au

For help or more information
Telephone 03 5177 3988
Email info.enquiries@asic.gov.au
Web www.asic.gov.au

Section C **completion guide**

Standard share codes
Refer to the following table for the share class codes for sections C1, C2, C3 and C4

Share class code	Full title	Share class code	Full title
A	A	PRF	preference
B	B...etc	CUMP	cumulative preference
EMP	employee's	NCP	non-cumulative preference
FOU	founder's	REDP	redeemable preference
LG	life governor's	NRP	non-redeemable preference
MAN	management	CRP	cumulative redeemable preference
ORD	ordinary	NCRP	non-cumulative redeemable preference
RED	redeemable	PARP	participative preference
SPE	special		

If you are using the standard share class codes you do not need to provide the full title for the shares, just the share class code

If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title.

Sections to complete
Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1 - Cancellation of shares	C2 - Issue of shares	C3 - Change to share structure table	C4 - Change to members register
☐ **Issue of shares**				
☐ Proprietary company	Not required	✓	✓	✓
Public company				
☐ if in response to the Annual company statement	Not required	✓	✓	✓
☐ if not in response to the Annual company statement	Not required	✓	Not required	Not required
☐ **Cancellation of shares**				
☐ Proprietary company	✓	Not required	✓	✓
Public company				
☐ if in response to the Annual company statement	✓	Not required	✓	✓
☐ if not in response to the Annual company statement	✓	Not required	Not required	Not required
☐ **Transfer of shares**				
☐ Proprietary company	Not required	Not required	Not required	✓
Public company				
☑ if in response to the Annual company statement	Not required	Not required	Not required	✓
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required
☐ **Changes to amounts paid**				
☐ Proprietary company	Not required	Not required	✓	✓
Public company				
☐ if in response to the Annual company statement	Not required	Not required	✓	✓
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required
☐ **Changes to beneficial ownership**				
☐ Proprietary company	Not required	Not required	Not required	✓
Public company				
☐ if in response to the Annual company statement	Not required	Not required	Not required	✓
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211 within 28 days of the change occurring.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205B within 28 days of the change occurring.

C1 Cancellation of shares

Reason for cancellation
Please indicate the reason that shares have been cancelled (select one or more boxes)

- Redeemable preference shares — **S.254J**
  - ☐ Redeemed out of profits
  - ☐ Redeemed out of proceeds of a fresh issue of shares
- Capital reduction — **S.256A – S.256E**
  - ☐ Single shareholder company
  - ☐ Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes place
- Share buy-back — **ss.257H(3)**
  - ☐ Minimum holding buy-back by listed company
  - ☐ Other buy-back type. A form 280 or 281 must be lodged at least 14 days, and no more than 1 year before the share buy-back can take place
- ☐ Forfeited shares — **S.258D**
- Shares returned to a public company — **ss.258E(2) & (3)**
  - ☐ Under section 651C, 724(2), 737 or 738
  - ☐ Under section 1325A (court order)
- ☐ Other
  - Description
  - Give section reference

Details of cancelled shares

List the details of shares cancelled in the following table

Share class code	Number of shares cancelled	Amount paid (cash or otherwise)

Earliest date of change
Please indicate the earliest date that any of the above changes occurred.

☐☐/☐☐/☐☐
[D D] [M M] [Y Y]

C2 Issue of shares

List details of new share issues in the following table.

Share class code	Number of shares issued	Amount paid per share	Amount unpaid per share

Earliest date of change

Please indicate the earliest date that any of the above changes occurred.

☐☐/☐☐/☐☐

[D D] [M M] [Y Y]

If shares were issued for other than cash, were some or all of the shares issued under a written contract?

☐ **Yes**

If yes, proprietary companies must also lodge a Form 207Z certifying that all stamp duties have been paid. Public companies must also lodge a Form 207Z and either a Form 208 or a copy of the contract.

☐ **No**

If no, propnetary companies are not required to provide any further documents with this form. Public companies must also lodge a Form 208.

C3 Change to share structure

Where a change to the share structure table has occurred (eg. as a result of the issue or cancellation of shares), please show the updated details for the share classes affected. Details of share classes not affected by the change are not required here.

Share class code	Full title if not standard	Total number of shares (current after changes)	Total amount paid on these shares	Total amount unpaid on these shares

Earliest date of change

Please indicate the earliest date that any of the above changes occurred.

[D D] [M M] [Y Y]

☐☐/☐☐/☐☐

Lodgement details

Is this document being lodged to update the Annual Company Statement that was sent to you?

☐ Yes

☐ No

C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

SEE ATTACHED ANNEXURE A OF 3 PAGES

The changes apply to
Please indicate the name and address of the member whose shareholding has changed

☐ Family name | Given names

OR

☐ Company name

ACN/ARBN/ABN

Office, unit, level, or PO Box number

Street number and Street name

Suburb/City | State/Territory

Postcode | Country (if not Australia)

Earliest date of change
Please indicate the earliest date that any of the following changes occurred.

Date of change ☐☐/☐☐/☐☐ [D D] [M M] [Y Y]

The changes are

Share class code	Shares increased by (number)	Shares decreased by (number)	Total number now held	*Total $ paid on these shares	*Total $ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member (y/n)

*Public companies are not required to provide these details

Date of entry of member's name in register
(New members only)

Date of entry ☐☐/☐☐/☐☐ [D D] [M M] [Y Y]

C4 Continued... **Further changes to the register of members**

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to
Please indicate the name and address of the member whose shareholding has changed

☐ Family name

Given names

OR

☐ Company name

ACN/ARBN/ABN

Office, unit, level, or PO Box number

Street number and Street name

Suburb/City

State/Territory

Postcode

Country (if not Australia)

Earliest date of change
Please indicate the earliest date that any of the following changes occurred.

Date of change
☐☐/☐☐/☐☐
[D D] [M M] [Y Y]

The changes are

Share class code	Shares increased by (number)	Shares decreased by (number)	Total number now held	*Total $ paid on these shares	*Total $ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member (y/n)

*Public companies are not required to provide these details

Date of entry of member's name in register
(New members only)

Date of entry
☐☐/☐☐/☐☐
[D D] [M M] [Y Y]

This is annexure A of 3 pages referred to in form 484 Part C "Change to Company Details"

ANTISENSE THERAPEUTICS LIMITED
TOP 20 SHAREHOLDERS AS AT 3 DECEMBER 2004

	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares decreased by	Number now held	Fully Paid (y/n)	Beneficially held (y/n)
1	Polychip Pharmaceuticals Pty Ltd ACN 006 455 456 Level 1 10 Wallace Avenue TOORAK VIC 3142	ORD	-	-	72,436,800	Y	Y
2	Syngene Limited ACN 006 161 753 Level 1 10 Wallace Avenue TOORAK VIC 3142	ORD	-	-	54,413,467	Y	Y
3	Isis Pharmaceuticals Inc ACN - N/A 2292 Faraday Avenue, Carlsbad, CA, 92008 USA (US Listed Company)	ORD	-	-	40,333,333	Y	Y
4	Queensland Investment Corporation ACN: N/A C/- National Nominees Limited, GPO Box 2242, Brisbane, QLD, 4001	ORD	-	-	15,845,000	Y	Y
5	National Nominees Limited ACN 004 278 899 GPO Box 1406M, Melbourne, VIC. 3001	ORD	-	146,057	12,263,943	Y	N
6	Murdoch Childrens Research Institute ACN 006 566 972 10th Floor, Royal Children's Hospital, Flemington Road, Parkville, VIC, 3052	ORD	-	3,375,000	6,925,000	Y	Y
7	Health Super Pty Ltd ACN 084 162 489 C/- National Nominees Limited GPO Box 1406M, Melbourne, VIC. 3001	ORD	4,120,000	-	4,120,000	Y	Y

This is annexure A of 3 pages referred to in form 484 Part C "Change to Company Details"

ANTISENSE THERAPEUTICS LIMITED
TOP 20 SHAREHOLDERS AS AT 3 DECEMBER 2004

	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares decreased by	Number now held	Fully Paid (y/n)	Beneficially held (y/n)
8	J P Morgan Nominees Australia Limited ACN 002 899 961 Locked Bag 7, Royal Exchange NSW 1224	ORD	3,243,332	-	3,243,332	Y	N
9	Spotlight Superannuation Pty Ltd <Spotlight Provident Fund A/c> ACN 070 073 853 100 Market Street, South Melbourne, VIC. 3205	ORD	-	-	2,071,795	Y	N
10	Link Traders (Aust) Pty Ltd ACN 002 065 849 Unit 405, 25 Lime Street, Sydney, NSW. 2000	ORD	-	-	2,000,000	Y	Y
11	ANZ Nominees Limited ACN 005 357 568 GPO Box 2842AA, Melbourne, Vic. 3001	ORD	687,959	-	1,732,200	Y	N
12	Professor George A Werther 65 Bellett Street, Camberwell, VIC 3124	ORD	1,687,500	-	1,712,500	Y	Y
13	Dr Christopher Wraight 6 Maple Street, Blackburn, VIC. 3130	ORD	1,687,500	-	1,687,500	Y	Y
14	Miss Tu Cam Thi Dinh & Mr Hung Xuan Nguyen 21 Spinnaker Street, Jamboree Heights, QLD. 4074	ORD	1,487,499	-	1,487,499	Y	Y
15	Mr Joshua Andrew Eagle 108 Park Road, Wooloowin, QLD 4030	ORD	-	642,862	1,331,424	Y	Y
16	Danewell Pty Ltd <Danewell Business A/C> ACN 078 417 651 100 Market Street, South Melbourne, VIC, 3205	ORD	-	-	1,276,924	Y	N
17	Monit Nominees Pty Ltd <Fraid Family A/C> ACN 005 373 615 100 Market Street, South Melbourne, VIC, 3205	ORD	-	-	1,205,128	Y	N

This is annexure A of 3 pages referred to in form 484 Part C "Change to Company Details"

ANTISENSE THERAPEUTICS LIMITED
TOP 20 SHAREHOLDERS AS AT 3 DECEMBER 2004

	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares decreased by	Number now held	Fully Paid (y/n)	Beneficially held (y/n)
18	Mrs Tung Yueh-Ying Tsai 50 Monomeath Avenue, Canterbury, VIC 3126	ORD	150,000	-	1,050,000	Y	Y
19	Mr Nicholas Szabo 2 Winston Way, Murrumbeena, VIC 3165	ORD	1,000,000	-	1,000,000	Y	Y
20	Invia Custodian Pty Limited <Catumnal Noms. No. 2 A/C> ACN 006 127 984 C/- M3788015M IPNM GPO Box 4595 SS, Melbourne, VIC 3001	ORD	-	-	950,000	Y	N

Signed: N. Korchev Date: 7/12/2004

Natalie Korchev
Company Secretary

ANTISENSE THERAPEUTICS

15 December 2004

COPY

Australian Securities & Investments Commission,
PO Box 4000
GIPPSLAND MAIL CENTRE VIC 3841

Dear Sir/Madam

Re: Notification of New Shares Issue

Please find enclosed Form 484, Section C with respect to the exercise of 1,700 Antisense Therapeutics Limited options for the purchase of 1,700 ordinary shares in Antisense Therapeutics Limited.

Please note that this is not in response to an Annual Company Statement.

We would be pleased if you would acknowledge receipt of this letter in due course.

Yours faithfully

N. Korchev

Natalie Korchev
Company Secretary

Encl

Please Note: The new contact numbers for Antisense Therapeutics are now:
Phone: 9827 8999 Fax: 9827 1166

LEVEL 1, 10 WALLACE AVENUE TOORAK VICTORIA 3142 AUSTRALIA
TELEPHONE: +61 (3) 9826 0949 FACSIMILE: +61 (3) 9826 4399
ANTISENSE THERAPEUTICS LTD ACN 095 060 745 www.antisense.com.au

Australian Securities &
Investments Commission

Form 484
Corporations Act 2001

Change to company details

Sections A, B or C may be lodged independently with this signed cover page to notify ASIC of:

A1 Change of address
A2 Change of name - officeholders or members
A3 Change - ultimate holding company

B1 Cease company officeholder
B2 Appoint company officeholder
B3 Special purpose company

C1 Cancellation of shares
C2 Issue of shares
C3 Change to share structure
C4 Changes to the register of members

If there is insufficient space in any section of the form, you may photocopy the relevant page(s) and submit as part of this lodgement

Company details

Refer to guide for information about corporate key

Company name
Antisense Therapeutics Limited

ACN/ABN
41 095 060 745

Corporate key
78841339

Lodgement details

Who should ASIC contact if there is a query about this form?

Name
Natalie Korchev

ASIC registered agent number (if applicable)

Telephone number
(03) 9827 8999

Postal address
Level 1, 10 Wallace Avenue

TOORAK VIC 3142

Total number of pages including this cover sheet

Please provide an estimate of the time taken to complete this form.
hrs mins

Signature

This form must be signed by a current officeholder of the company.

I certify that the information in this cover sheet and the attached sections of this form are true and complete.

Name
Natalie Korchev

Capacity
☐ Director
☒ Company secretary

Signature
N. Korchev

Date signed
1 4 / 1 2 / 0 4
[D D] / [M M] / [Y Y]

Lodgement

Send completed and signed forms to:
Australian Securities and Investments Commission,
PO Box 4000, Gippsland Mail Centre VIC 3841.

Or lodge the form electronically by visiting the ASIC website
www.asic.gov.au

For help or more information
Telephone 03 5177 3988
Email info.enquiries@asic.gov.au
Web www.asic.gov.au

Section C **completion guide**

Standard share codes
Refer to the following table for the share class codes for sections C1, C2, C3 and C4

Share class code	Full title	Share class code	Full title
A	A	PRF	preference
B	B...etc	CUMP	cumulative preference
EMP	employee's	NCP	non-cumulative preference
FOU	founder's	REDP	redeemable preference
LG	life governor's	NRP	non-redeemable preference
MAN	management	CRP	cumulative redeemable preference
ORD	ordinary	NCRP	non-cumulative redeemable preference
RED	redeemable	PARP	participative preference
SPE	special		

If you are using the standard share class codes you do not need to provide the full title for the shares, just the share class code.

If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title

Sections to complete
Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1- Cancellation of shares	C2 – Issue of shares	C3 – Change to share structure table	C4 – Change to members register
Issue of shares				
☐ Proprietary company	Not required	√	√	√
Public company				
☐ if in response to the Annual company statement	Not required	√	√	√
☒ if not in response to the Annual company statement	Not required	√	Not required	Not required
Cancellation of shares				
☐ Proprietary company	√	Not required	√	√
Public company				
☐ if in response to the Annual company statement	√	Not required	√	√
☐ if not in response to the Annual company statement	√	Not required	Not required	Not required
Transfer of shares				
☐ Proprietary company	Not required	Not required	Not required	√
Public company				
☐ if in response to the Annual company statement	Not required	Not required	Not required	√
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to amounts paid				
☐ Proprietary company	Not required	Not required	√	√
Public company				
☐ if in response to the Annual company statement	Not required	Not required	√	√
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to beneficial ownership				
☐ Proprietary company	Not required	Not required	Not required	√
Public company				
☐ if in response to the Annual company statement	Not required	Not required	Not required	√
☐ if not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211 within 28 days of the change occurring.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205B within 28 days of the change occurring.

C1 Cancellation of shares

Reason for cancellation
Please indicate the reason that shares have been cancelled (select one or more boxes)

Redeemable preference shares – **S.254J**

- ☐ Redeemed out of profits
- ☐ Redeemed out of proceeds of a fresh issue of shares

Capital reduction – **S.256A – S.256E**

- ☐ Single shareholder company
- ☐ Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes place

Share buy-back. – **ss.257H(3)**

- ☐ Minimum holding buy-back by listed company
- ☐ Other buy-back type. A form 280 or 281 must be lodged at least 14 days, and no more than 1 year before the share buy-back can take place

☐ Forfeited shares – **S.258D**

Shares returned to a public company – **ss.258E(2) & (3)**

- ☐ Under section 651C, 724(2), 737 or 738
- ☐ Under section 1325A (court order)

☐ Other

Description

Give section reference

Details of cancelled shares

List the details of shares cancelled in the following table

Share class code	Number of shares cancelled	Amount paid (cash or otherwise)

Earliest date of change

Please indicate the earliest date that any of the above changes occurred.

[D D] / [M M] / [Y Y]

C2 Issue of shares

List details of new share issues in the following table.

Share class code	Number of shares issued	Amount paid per share	Amount unpaid per share
ORD	1,700	$0.20 cents	Nil

Earliest date of change

Please indicate the earliest date that any of the above changes occurred

[D	D]	[M	M]	[Y	Y]
0	8	1	2	0	4

If shares were issued for other than cash, were some or all of the shares issued under a written contract?

☐ **Yes**
if yes, proprietary companies must also lodge a Form 207Z certifying that all stamp duties have been paid. Public companies must also lodge a Form 207Z and either a Form 208 or a copy of the contract.

☐ **No**
if no, proprietary companies are not required to provide any further documents with this form. Public companies must also lodge a Form 208.

C3 Change to share structure

Where a change to the share structure table has occurred (eg. as a result of the issue or cancellation of shares), please show the updated details for the share classes affected. Details of share classes not affected by the change are not required here.

Share class code	Full title if not standard	Total number of shares (current after changes)	Total amount paid on these shares	Total amount unpaid on these shares
ORD	ORDINARY FULLY PAID SHARES	355,260,090	35,107,219.53	Nil
OPTIONS	OPTIONS OVER ORDINARY SHARES	125,161,025	789,759.95	Nil

Earliest date of change

Please indicate the earliest date that any of the above changes occurred

[D	D]	[M	M]	[Y	Y]
0	8	1	2	0	4

Lodgement details

Is this document being lodged to update the Annual Company Statement that was sent to you?

☐ Yes
☒ No

C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to
Please indicate the name and address of the member whose shareholding has changed

☐ Family name

Given names

OR

☐ Company name

ACN/ARBN/ABN

Office, unit, level or PO Box number

Street number and Street name

Suburb/City

State/Territory

Postcode

Country (if not Australia)

Earliest date of change
Please indicate the earliest date that any of the following changes occurred

Date of change

☐☐ / ☐☐ / ☐☐☐☐
[D D] [M M] [Y Y]

The changes are

Share class code	Shares increased by ...(number)	Shares decreased by ...(number)	Total number now held	*Total $ paid on these shares	*Total $ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member(y/n)

* Public companies are not required to provide these details

Date of entry of member's name in register
(New members only)

Date of entry

☐☐ / ☐☐ / ☐☐☐☐
[D D] [M M] [Y Y]

C4 Continued... **Further changes to the register of members**

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to
Please indicate the name and address of the member whose shareholding has changed

☐ Family name

Given names

OR

☐ Company name

ACN/ARBN/ABN

Office, unit, level or PO Box number

Street number and Street name

Suburb/City

State/Territory

Postcode

Country (if not Australia)

Earliest date of change
Please indicate the earliest date that any of the following changes occurred

Date of change

☐☐ / ☐☐ / ☐☐☐☐
[D D] [M M] [Y Y Y Y]

The changes are

Share class code	Shares increased by ...(number)	Shares decreased by ...(number)	Total number now held	*Total $ paid on these shares	*Total $ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member(y/n)

* Public companies are not required to provide these details

Date of entry of member's name in register
(New members only)

Date of entry

☐☐ / ☐☐ / ☐☐☐☐
[D D] [M M] [Y Y Y Y]

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

Appendix 3B

New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Name of entity

ANTISENSE THERAPEUTICS LIMITED

ABN

41 095 060 745

We (the entity) give ASX the following information.

Part 1 - All issues

You must complete the relevant sections (attach sheets if there is not enough space).

1	+Class of +securities issued or to be issued	Ordinary Shares
2	Number of +securities issued or to be issued (if known) or maximum number which may be issued	1,700
3	Principal terms of the +securities (eg, if options, exercise price and expiry date; if partly paid +securities, the amount outstanding and due dates for payment; if +convertible securities, the conversion price and dates for conversion)	Exercise of 1,700 ANPO options at 20 cents each to purchase 1,700 ordinary shares in ANP.

+ See chapter 19 for defined terms.

4	Do the +securities rank equally in all respects from the date of allotment with an existing +class of quoted +securities? If the additional securities do not rank equally, please state: • the date from which they do • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	Yes N/A
5	Issue price or consideration	20 cents per share.
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 1,700 ANPO options to purchase 1,700 ordinary shares in ANP.
7	Dates of entering +securities into uncertificated holdings or despatch of certificates	8 December 2004

8	Number and +class of all +securities quoted on ASX (*including* the securities in clause 2 if applicable)	Number	+Class
		355,260,090 91,461,025	Ordinary shares (ANP) Options (ANPO)

+ See chapter 19 for defined terms.

9	Number and +class of all +securities not quoted on ASX (*including* the securities in clause 2 if applicable)	Number	+Class
		11,500,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAM)
		20,000,000	Options expiring 30 November 2006 exercisable at 20 cents each (ANPAO).
		2,200,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAQ)
10	Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests)	N/A	

Part 2 - Bonus issue or pro rata issue

11	Is security holder approval required?	N/A
12	Is the issue renounceable or non-renounceable?	N/A
13	Ratio in which the +securities will be offered	N/A
14	+Class of +securities to which the offer relates	N/A
15	+Record date to determine entitlements	N/A
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	N/A
17	Policy for deciding entitlements in relation to fractions	N/A
18	Names of countries in which the entity has +security holders who will not be sent new issue documents Note: Security holders must be told how their entitlements are to be dealt with. Cross reference: rule 7.7.	N/A
19	Closing date for receipt of acceptances or renunciations	N/A

+ See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of +security holders	N/A
25	If the issue is contingent on +security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do +security holders sell their entitlements *in full* through a broker?	N/A
31	How do +security holders sell *part* of their entitlements through a broker and accept for the balance?	N/A

+ See chapter 19 for defined terms.

32	How do +security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	+Despatch date	N/A

Part 3 - Quotation of securities

You need only complete this section if you are applying for quotation of securities

34 Type of securities
(tick one)

(a) [√] Securities described in Part 1

(b) [ ] All other securities

Example: restricted securities at the end of the escrowed period, partly paid securities that become fully paid, employee incentive share securities when restriction ends, securities issued on expiry or conversion of convertible securities

Entities that have ticked box 34(a)

Additional securities forming a new class of securities

Tick to indicate you are providing the information or documents

35 [ ] If the +securities are +equity securities, the names of the 20 largest holders of the additional +securities, and the number and percentage of additional +securities held by those holders

36 [ ] If the +securities are +equity securities, a distribution schedule of the additional +securities setting out the number of holders in the categories
1 - 1,000
1,001 - 5,000
5,001 - 10,000
10,001 - 100,000
100,001 and over

37 [ ] A copy of any trust deed for the additional +securities

+ See chapter 19 for defined terms.

Entities that have ticked box 34(b)

38	Number of securities for which +quotation is sought	N/A
39	Class of +securities for which quotation is sought	N/A
40	Do the +securities rank equally in all respects from the date of allotment with an existing +class of quoted +securities? If the additional securities do not rank equally, please state: • the date from which they do • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A
41	Reason for request for quotation now Example: In the case of restricted securities, end of restriction period (if issued upon conversion of another security, clearly identify that other security)	N/A

42	Number and +class of all +securities quoted on ASX (*including* the securities in clause 38)	Number	+Class
		N/A	N/A

+ See chapter 19 for defined terms.

Quotation agreement

1 +Quotation of our additional +securities is in ASX's absolute discretion. ASX may quote the +securities on any conditions it decides.

2 We warrant the following to ASX.

- The issue of the +securities to be quoted complies with the law and is not for an illegal purpose.
- There is no reason why those +securities should not be granted +quotation.
- An offer of the +securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

  Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any +securities to be quoted and that no-one has any right to return any +securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the +securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the +securities to be quoted, it has been provided at the time that we request that the +securities be quoted.
- If we are a trust, we warrant that no person has the right to return the +securities to be quoted under section 1019B of the Corporations Act at the time that we request that the +securities be quoted.

+ See chapter 19 for defined terms.

3 We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.

4 We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before +quotation of the +securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here: Natalie Korchev Date: 15 December 2004
Company secretary

Print name: Natalie Korchev

ANTISENSE THERAPEUTICS

20 December 2004

Animal study results point to ATL1102's potential as an Inhaled Drug for Asthma

Antisense Therapeutics Limited (ASX: ANP) has been investigating the therapeutic potential of inhaled antisense compounds targeting the VLA-4 protein in asthma and is pleased to announce that encouraging results have been obtained in an animal model of the disease. The Company's lead drug ATL1102 is an antisense inhibitor that suppresses the production of the inflammatory disease target VLA-4, and as previously reported, is scheduled to enter Phase II clinical trials in multiple sclerosis patients before the end of this year.

The studies which were performed in an experimental mouse model of asthma showed that delivery of an antisense drug against VLA-4 via inhalation to the lung significantly suppressed the key asthma indicators in allergen-sensitised mice. Importantly, the drug was active at low inhaled doses. The results are to be presented at the Annual Scientific Meeting of the Thoracic Society of Australia and New Zealand in March 2005.

Associate Professor John Wilson, of the Monash Medical School's Department of Allergy, Immunology and Respiratory Medicine, and Director of the National Asthma Council, is an advisor to Antisense Therapeutics in respiratory medicine, and is encouraged by the new data. "There is a great need for safe and effective asthma medicines. Antisense to VLA-4 appears to be effective in an accepted animal model, and there has been significant scientific interest in the drug's therapeutic target VLA-4 for asthma and other inflammatory indications," said Prof Wilson.

Antisense Therapeutics' Managing Director Mark Diamond said, "the Company is very pleased with the data emerging from this pre-clinical asthma programme. As we previously announced, ATL1102 has been shown to be safe in animal and Phase I human studies. Our ATL1102 clinical development programme is advancing well, and it is an ideal time for us to exploit our advances with ATL1102 in other inflammatory disease areas. Our animal asthma studies are teaching us a great deal about the anti-inflammatory mechanism of antisense to VLA-4 in the lung and the potential of ATL1102 as an asthma treatment."

The data package that has been developed to date on ATL1102 together with these animal asthma studies would potentially provide the Company, or a licensing partner, the opportunity to move quickly into testing ATL1102 as an inhaled drug in patients with asthma.

Background Information

Asthma is a chronic lung condition characterised by periodic episodes of airway inflammation and constriction resulting in wheezing, coughing, chest tightness and shortness of breath. The episodes typically occur in response to stimuli such as allergens, chemical irritants or low temperatures. Up to 1 in 4 children, and 1 in 10 adults will experience asthma symptoms at some time in their lives.

ATL1102 is a second-generation antisense inhibitor of CD49d, a sub-unit of VLA-4 (Very Late Antigen-4). In inflammation, white blood cells (leukocytes) are believed to move out of the bloodstream into the inflamed tissue, for example, the CNS in MS, and the lung airways in asthma. The inhibition of VLA-4 may prevent white blood cells from entering sites of inflammation, thereby halting progression of the disease. Inhibition of VLA-4 in animals has demonstrated positive effects

on a number of inflammatory diseases such as MS. Several other VLA-4 inhibitors are in clinical development for inflammatory conditions.

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

Contact Information:

Website: www.antisense.com.au
Managing Director – Mark Diamond +61 3 9827 8999
Company Secretary – Natalie Korchev +61 3 9827 8999

ANTISENSE THERAPEUTICS

21 December 2004

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

ANTISENSE THERAPEUTICS LIMITED AND ISIS PHARMACEUTICALS INITIATE PHASE 2A TRIAL OF ANTISENSE DRUG FOR MULTIPLE SCLEROSIS

Please find attached a joint announcement by Antisense Therapeutics Limited and Isis Pharmaceuticals Inc for release to the market regarding the initiation of the company's Phase 2a clinical trial of ATL1102 in patients with multiple sclerosis. This announcement is being conjointly released in the US.

Yours faithfully

Natalie Korchev
Company Secretary

Contact Information:
Website: www.antisense.com.au
Managing Director – Mark Diamond +61 3 9827 8999
Company Secretary – Natalie Korchev +61 3 9827 8999

Contact: Natalie Korchev
AntisenseTherapeutics Limited
+61 3 9827 8999

Kristina Peterson
Isis Pharmaceuticals
760-603-2331

ANTISENSE THERAPEUTICS LIMITED AND ISIS PHARMACEUTICALS INITIATE PHASE 2A TRIAL OF ANTISENSE DRUG FOR MULTIPLE SCLEROSIS

Melbourne, Australia and Carlsbad, CA, USA, December 21, 2004 – Antisense Therapeutics Limited (ASX: ANP) and Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the initiation of a Phase 2a clinical trial of ATL1102 in patients with multiple sclerosis (MS). ATL1102 is a second-generation antisense inhibitor of an immune system protein called VLA-4 (alpha-4 integrin chain; CD49d). ATL1102 is designed to block the synthesis of VLA-4 which is known to play a part in both the onset and progression of MS.

"We are pleased to move ATL1102, our lead drug candidate, into patient trials," said Mark Diamond, Managing Director of Antisense Therapeutics. "VLA-4 is a clinically validated target in MS and antisense inhibition of VLA-4 has demonstrated positive effects in multiple animal models of inflammatory diseases, including MS. This Phase 2a trial will provide important efficacy data on ATL1102 and thereby, an indication of our compound's potential as an effective treatment for MS."

"ATL1102 represents a novel therapeutic approach to the treatment of MS and I am delighted to be associated with clinical trials using a technology that aims to stop the production of the disease causing protein, rather than deal with it after it is produced in the body," said Professor Volker Limmroth of the University of Essen Germany, an eminent Professor of Neurology, internationally recognized clinical expert on MS, and Principal Investigator for this Phase 2a study. "ATL1102 may have clinical advantages over currently available MS treatments and my co-clinical investigators and I will be attempting to elucidate these in the next several months as the trial progresses."

In this multi-center, randomized, double-blinded, placebo-controlled clinical trial, approximately 60 patients with relapsing-remitting MS will receive ATL1102 or placebo over eight weeks. ATL1102 will be delivered by subcutaneous injection on a twice-a-week dosing schedule at a dose of 400 mg per week. The goal of the Phase 2a trial is to obtain preliminary evidence of the drug's effectiveness which will be evaluated using MRI (magnetic resonance imaging) indices. MRI's will be conducted at monthly intervals over the 8 week dosing period and at monthly intervals during the 8 week period following completion of dosing.

MRI is a non-invasive technique which allows physicians to monitor the effects of drug therapy on the brain lesions of MS patients, and has now become the accepted clinical end-point for evaluating drug effectiveness in early-phase MS clinical trials. These indices permit an evaluation of the degree of disease-related injury in the central nervous system (CNS), and any treatment-related modification brought about following administration of a drug.

The Phase 2a trial has been initiated on schedule at the University of Essen in Germany following the approval of the Clinical Trial Application by the Institutional Review Board and Ethics Committee of the University. The trial has also been authorised by the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM) in Germany.

Antisense Therapeutics Limited has provided guidance that the treatment and patient monitoring stages of the trial are expected to be complete by early 2006, assuming patient recruitment proceeds at the anticipated rate. Antisense Therapeutics Limited anticipates reporting results by mid-2006.

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About MS and ATL1102

MS is a life-long chronic, incurable autoimmune disease that progressively destroys the CNS. It is commonly diagnosed between the ages of 20 and 40 years. According to the U.S. National Multiple Sclerosis Society, approximately 400,000 Americans acknowledge having MS, and every week about 200 individuals are diagnosed. Worldwide, MS may affect more than two million people.

ATL1102 is an inhibitor of CD49d, a sub-unit of VLA-4 (Very Late Antigen-4). In MS, white blood cells (leukocytes) are directed into the CNS from the blood. The inhibition of VLA-4 may prevent white blood cells from entering the CNS to stop the progression of MS. Inhibition of VLA-4 in animals has demonstrated positive effects on a number of inflammatory diseases such as MS. One VLA-4 inhibitor has recently been approved for marketing in the U.S. for the treatment of MS, and several other VLA-4 inhibitors are in clinical development for inflammatory conditions. Isis discovered this compound and licensed it to Antisense Therapeutics Limited in 2001.

About Antisense Therapeutics Limited

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company (ASX: ANP). ANP's mission is to create, develop and commercialize novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101). ANP plans to commercialize its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. The company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals, Inc., and Queensland Investment Corporation. Further company details are available on the Antisense Therapeutics website at www.antisense.com.au.

About Isis Pharmaceuticals, Inc.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 10 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases, and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and is discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,400 issued patents worldwide. Additional information about Isis is available at http://www.isispharm.com.

This press release includes forward-looking statements regarding Isis Pharmaceuticals and Antisense Therapeutics Limited's drug development collaboration and the development, therapeutic potential and safety of ATL1102 in treating multiple sclerosis. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology, in discovering and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products. Actual results could differ materially from those discussed in this press release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended September 30, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

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