15 January 2014

Presentation - Biotech Showcase™ 2014

As previously advised on 8th January, Mark Diamond, Antisense Therapeutics' CEO and Managing Director, will be presenting at the Biotech Showcase on 14th January 2.30pm (California, US time). Attached is a copy of the presentation. The presentation will be webcast and can be accessed on the link below and also on the homepage of our website www.antisense.com.au. The replay of the webcast will be available for 90 days.

http://www.media-server.com/m/p/3w8tt8xt

Biotech Showcase is an investor and partnering conference devoted to providing biotechnology and life sciences companies an opportunity to present to and meet with investors and pharmaceutical executives during the course of one of the industry's largest annual healthcare investor conferences. Now in its sixth year, Biotech Showcase is expected to attract upwards of 1,500 attendees.

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise second generation antisense pharmaceuticals for large unmet markets. ANP has 4 products in its development pipeline that it has in-licensed from Isis Pharmaceuticals Inc., world leaders in antisense drug development and commercialisation - ATL1102 (injection) which has successfully completed a Phase II efficacy and safety trial, significantly reducing the number of brain lesions in patients with multiple sclerosis, ATL1103 a second-generation antisense drug designed to block GHr production and thereby lower blood IGF-I levels and is in clinical development as a potential treatment for growth and other GH-IGF-I disorders, ATL1102 (inhaled) which is at the pre-clinical research stage as a potential treatment for asthma and ATL1101 a second-generation antisense drug at the pre-clinical stage being investigated as a potential treatment for cancer.

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Biotech Showcase 2014

14th January 2014

Antisense Therapeutics Ltd

ASX:ANP
OTC:ATHJY

Forward Looking Statements

This presentation contains forward-looking statements regarding the company's business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing the company's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavour of building a business around such products and services. Actual results could differ materially from those discussed in this presentation. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Antisense Therapeutics Limited Annual Report for the year ended 30 June 2013, copies of which are available from the company or at www.antisense.com.au.

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Antisense Therapeutics Limited

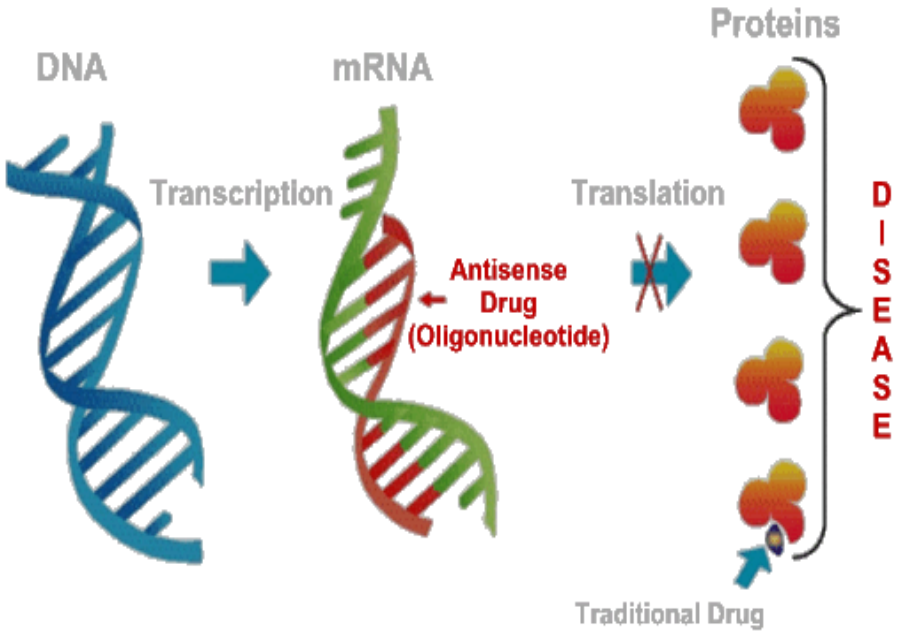
- Antisense Therapeutics is a biopharmaceutical company developing advanced RNA-targeting antisense drugs through its technology agreement with Isis Pharmaceuticals Inc
- Listed on the Australian Stock Exchange in 2001 (ASX: ANP)
- Level 1 ADR program in US (OTC:ATYHJ)
- Based in Melbourne, Australia
- Developing drugs for diseases with large unmet medical need and where the antisense technology has the potential to provide compounds with significant competitive advantages over existing therapies or drugs in development
- Advanced pipeline of 2nd generation antisense drugs for multiple clinical applications

  e.g. Acromegaly, Multiple Sclerosis, Stem Cell Mobilisation, and Cancer

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Antisense Technology

- Rationally designed to block the production of disease causing proteins by binding to the specific messenger RNA sequence
- Highly targeted and potent therapeutics
- Isis 2nd generation antisense technology = modifications to drug chemistry to increase potency and stability
  - *Lower dose and more cost effective;*
  - *Increased stability allows more convenient dosing regimes; and*
  - *Broad disease application*
- 31 drugs in development – 1 on market (KYNAMRO™ for cholesterol reduction in high risk individuals)



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ANP Product Research & Development Pipeline

PRODUCT	INDICATION	RESEARCH	PRECLINICAL	PHASE I	PHASE II	PHASE III
ATL1103 s.c. injection	Acromegaly					
ATL1102 s.c. injection	Multiple Sclerosis					
ATL1102 s.c. injection	Stem cell mobilisation					
ATL1101 s.c. injection	Prostate Cancer					
ATL1102 inhaled	Asthma					

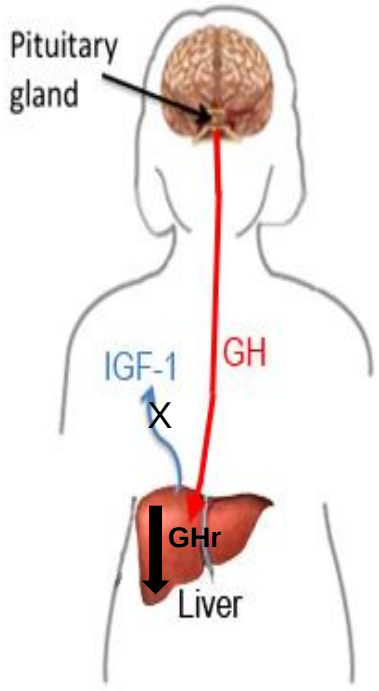
All pipeline drugs are 2nd generation antisense compounds derived via Isis collaboration.

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ATL1103 – Antisense Drug to the Growth Hormone receptor

- ATL1103 is a 2nd generation antisense drug to the Growth Hormone receptor (GHr)
- Acromegaly is caused by a benign tumour of the pituitary gland that over-produces Growth Hormone (GH) leading to elevated blood levels of Insulin-like Growth Factor 1 (sIGF-I)
  - ***Orphan drug indication*** *- regulatory and IP incentives to develop*
  - *Affects ~85 adults per million in the US and Europe (~85,000 adults)*
  - *Elevated sIGF-I causes enlargement of organs and the bones of the face, feet and hands. Can also lead to diabetes, hypertension, and cancer*
  - *Normalising sIGF-I is the treatment goal*
- IGF-I also has a role in the pathogenesis of diabetic retinopathy, nephropathy and certain cancers where ↓ sIGF-I is associated with clinical improvement

ATL1103 reduces liver GHr & blocks GH action on the liver



Reducing IGF-I in blood

Adapted from neurosurgery.ucla.edu/body.cfm?id=101

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ATL1103 – Treatment of Acromegaly

- Approx 60% of patients are treated by surgical removal of the tumour - surgical failures require drug therapy to normalise sIGF-I
- Somatostatin agonists of somatostatin 2 receptor (e.g. octreotide) are first line drug therapy - effective in up to 60-65% of cases
  - *Treatment costs up to $30K/annum*
  - *Existing sales of somatostatin agonists ~$1Billion*
- Pegvisomant (Somavert®) GHr antagonist for first line therapy failures
  - *In clinical trial effective in greater % of patients in normalizing sIGF-I than somatostatins*
  - *Estimated sales of > $200 million/annum: Average treatment cost of $60K/annum*
  - *Use and effectiveness in clinical practice is limited by high cost, inconvenient administration (lyophilized powder that requires reconstitution) and daily dosing regimen that negatively impact its sales potential*
  - *Low market penetration (estimated at approx 25%) means significant percentage of patients untreated*

ATL1103 Target Product Profile

For use in 1st line failures with potential key advantages over Somavert® including lower cost of therapy, improved safety profile, and a more convenient dosing/administration regimen (prefilled syringe; once/twice weekly dosing)

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ATL1103 Development Status

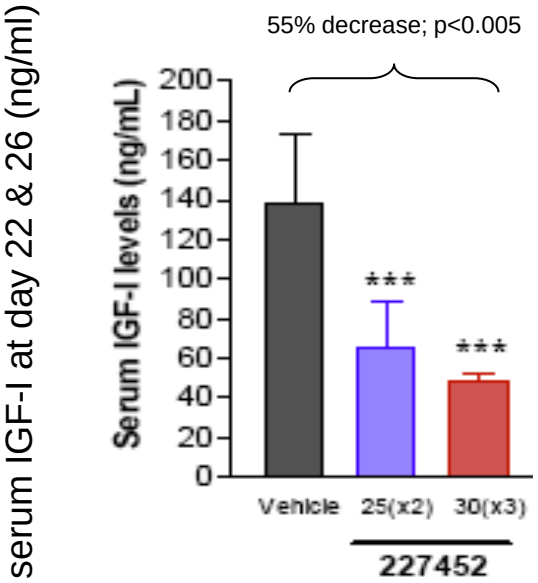
"ATL1103 has suppressed sIGF-I in all animal and human studies undertaken to date"

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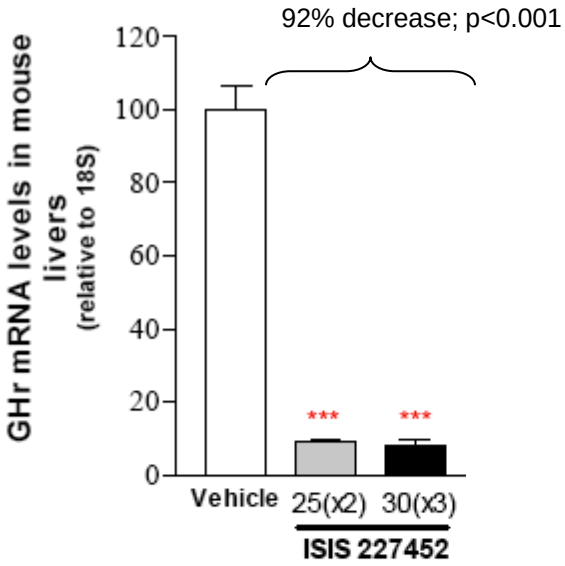
ATL1103 Active in Mice in Reducing sIGF-I

3 weeks of ATL1103 treatment reduces serum IGF-I >55% (to below detection)

IGF-I suppression



GHr mRNA target inhibition

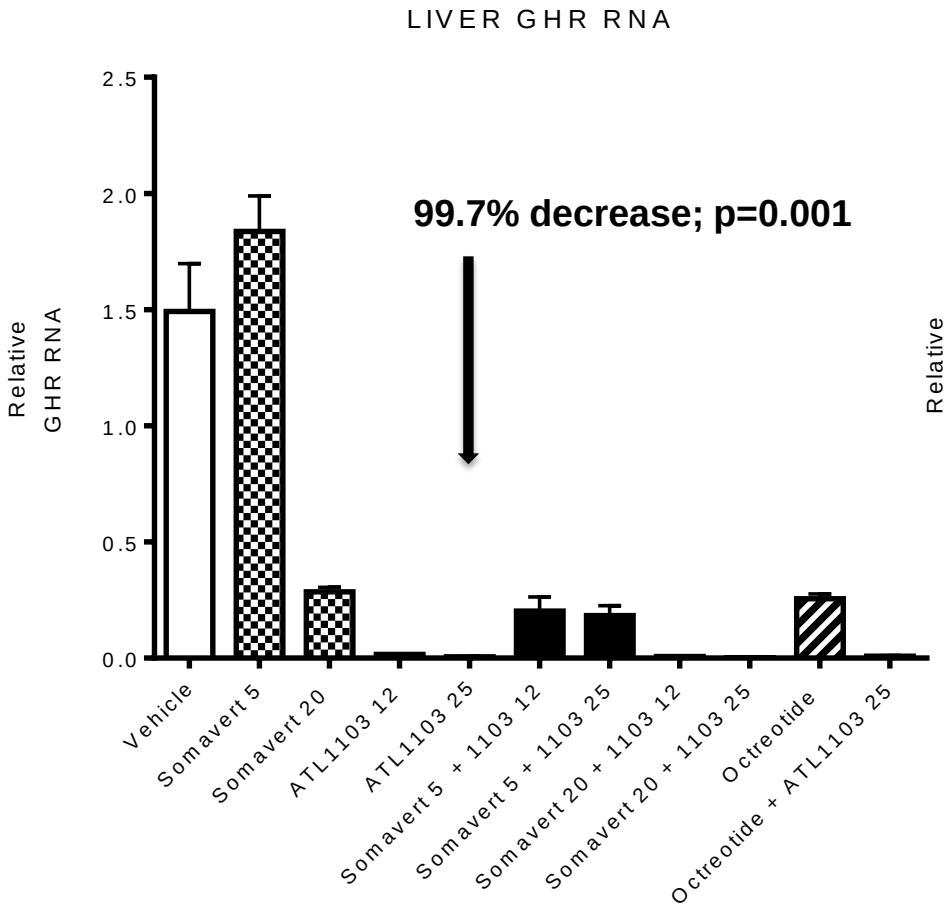


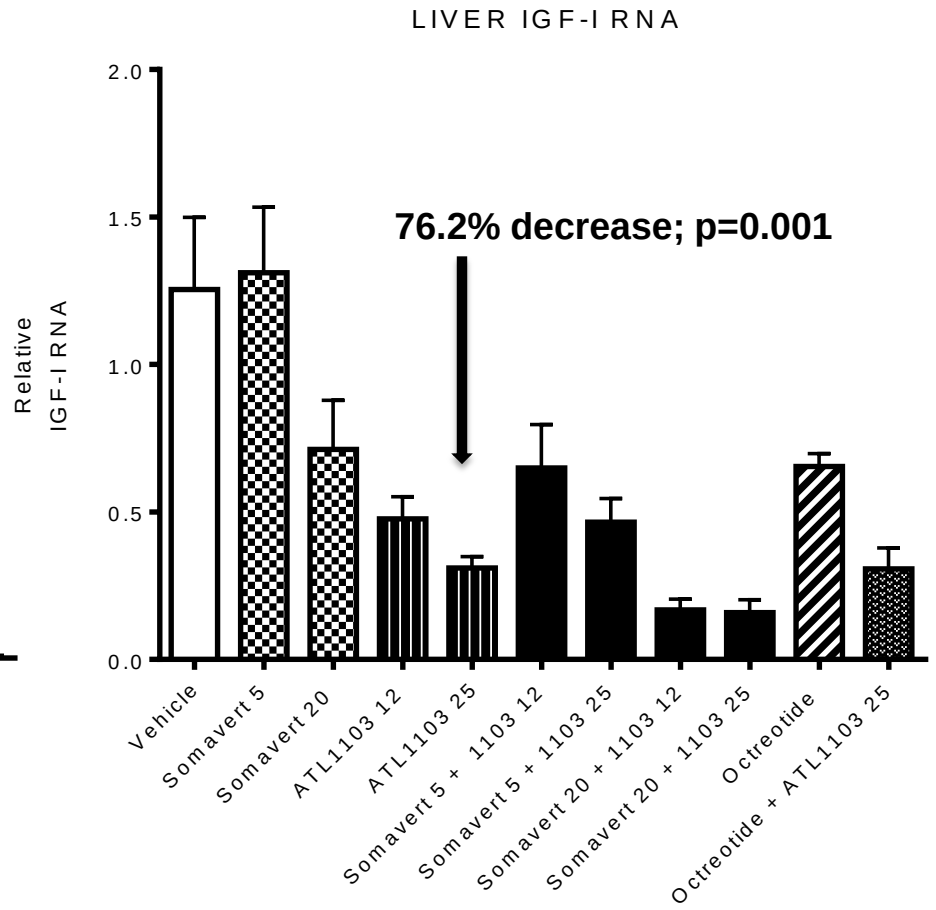
Data on File:

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Relative Liver GHR and IGF-I RNA levels in mice treated with saline, ATL1103, Somavert and Octreotide as monotherapies or in combination

3 weeks of ATL1103 treatment reduces liver GHr RNA by >99%





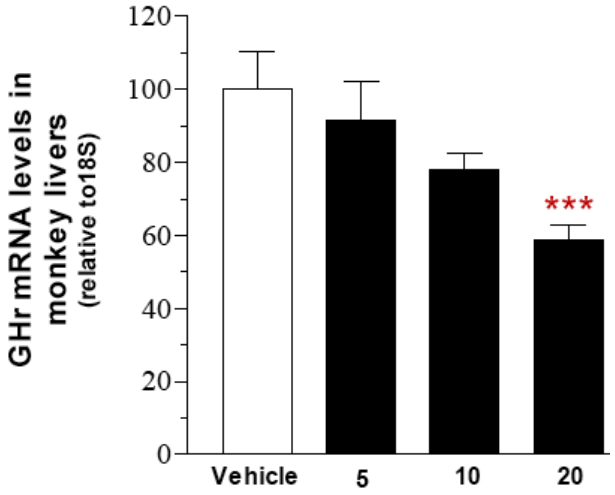
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Antisense Therapeutics Ltd; data on file

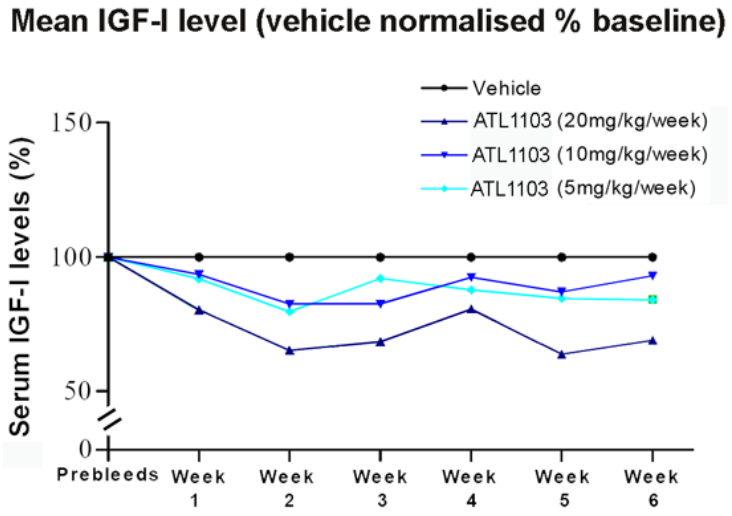
ATL1103 Active in Primates

- Pharmacologically relevant suppression of circulating sIGF-I
- Significant suppression of hepatic target mRNA
- Pharmacological paradigm demonstrated in normal primates

GHr mRNA target inhibition



sIGF-I suppression



Antisense Therapeutics Ltd data on file

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ATL1103 Phase 1 clinical trial

Study

Randomised, placebo-controlled, double-blind study of ATL1103 in healthy male subjects

- Single Ascending Dose (SAD): 25, 75, 250, and 400mg
- Multiple Dosing: 250mg
  - *12 subjects (8 active, 4 placebo)*
  - *Six doses over 3 weeks (on Day 1, 3, 5, 7, 14 & 21). Last visit Day 35 monitoring*
  - *Serum IGF-I, GH, IGF-II, IGF-BP3, ALS and GHBP levels monitored*

Results

Safety - study met primary endpoint. ATL1103 was safe and generally well tolerated at the doses tested. No serious adverse events (AE) reported

- ***SAD****: all AEs reported as mild or moderate. Most common AE's reported were pain at injection site, headache, influenza-like illness (at 400mg dose only).*
- ***Multiple Dosing****: all AE's reported as mild. Most commonly reported AE was injection site reactions. Increased ALT levels was reported for one subject at Day 11. ALT levels returned to the normal range by pre-dose day 21 and remained within normal range for the rest of the study*

Activity - preliminary indication of drug activity with reduction of sIGF-I and other markers of GH activity

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ATL1103 Phase I trial
Reduction in sIGF-I and other markers of GH activity

Multiple-dose arm

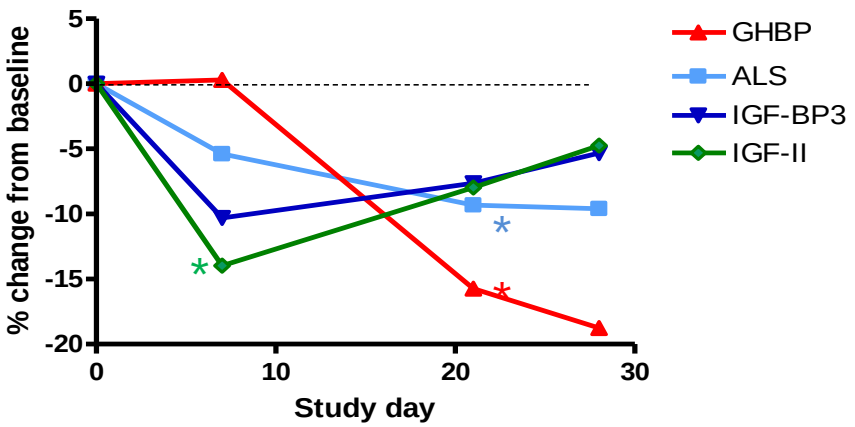
- Clear trend for mean sIGF-I levels to be lower than baseline on Days 14, 21, 28 and 35 with a statistically significant effect on Day 21
- Reduction in sGHBP levels suggests reduced expression of target GHr
- Reductions in insulin-like growth factor binding protein 3 (IGF-BP3) and the acid-labile subunit (ALS) are consistent with the effect of ATL1103 on sIGF-I

sIGF- I change from predose

Pre-dose IGF-I: 36.57 ± 13.16 nmol/L:mean ± SD		
Study day	**Change from pre-dose** Mean ± SD (% change from pre-dose)	**Probability < (-t)[a]**
Day 3	+ 2.65 ± 9.47 (12%)	> 0.500
Day 5	+ 0.32 ± 7.42 (6%)	> 0.500
Day 7	+ 0.77 ± 7.51 (6%)	> 0.500
Day 14	-1.43 ± 7.19 (-2%)	0.323
Day 21	**-3.40 ± 3.59 (-7%)**	**0.034**
Day 28	-3.43 ± 7.53 (-7%)	0.157
Day 35	-1.9 ± 5.08 (1%)	0.201

[a] 1-sided t-test on change from pre-dose at each time point; alternate hypothesis is suppression
Per protocol population; (n=6 at each time point)

Exploratory Pharmacodynamic Markers in Stage B
(per protocol population, n=6)



** P-value < 0.05*

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ATL1103 Phase II Clinical Trial

- Trial being conducted in Europe (UK, France, Australia, Hungary and Spain) by international CRO - Orion Clinical Services Ltd
- 13 week dosing study in 24 acromegaly patients
- Open label, baseline comparison study of 2 subcutaneous doses of ATL1103 – 200mg once weekly and twice per week
- Endpoints: safety, pK, tolerability and drug activity including the level of sIGF-I reduction and normalisation
- Chief Investigator for the study - Dr Peter Trainer**,** Professor of Endocrinology, The Christie NHS Foundation Trust, UK; acknowledged global opinion leader in the field of acromegaly
- Completed interim analysis of ATL1103's effect on sIGF-I levels – **positive results reported with reduction in sIGF-I**
- Final efficacy results on sIGF-I effects anticipated mid-2014
- **Next stage of development post Phase II: Phase III registration studies**

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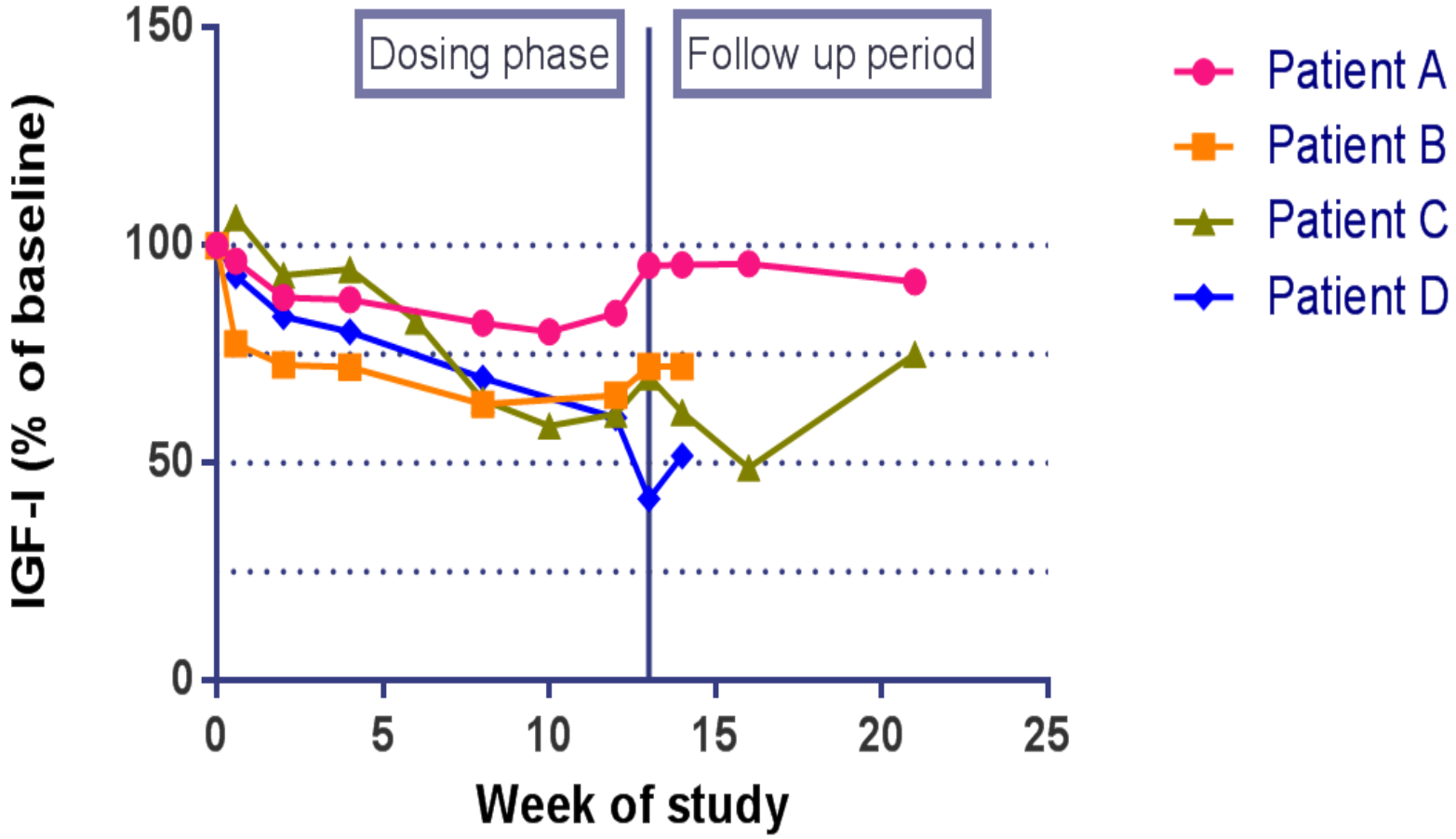
ATL1103 Acromegaly Phase II Interim Analysis

- Analysis undertaken on 8 patients who had completed the 13 weeks of dosing
- 4 patients received 200 mg once per week and 4 received 200 mg twice per week
- Analysis assessed % reduction in patient's sIGF-I levels from baseline to their levels one week post dosing
- At the twice weekly 200mg/week dose, ATL1103 reduced sIGF-I levels by a mean of 30% (range 4% to 48%)
  - *Mean 38% (28 - 48%) reduction in sIGF-I in 3 of the 4 patients with body weight less than 85kg*
- No drug related SAEs or withdrawals to date
- Drug appears well tolerated at the doses employed in the study
- Based on positive safety experience to date, expect to be able to dose escalate with ATL1103
- Anticipate higher and longer dosing in Phase III to lead to further reductions in sIGF-I

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ATL1103 Acromegaly Phase II Interim Analysis

ATL1103 twice weekly 200mg sIGF-I reduction



ATL1102 in MS

Product

- 2nd generation antisense inhibitor of VLA-4 protein
- VLA-4 is a clinically validated target in MS
- Successful Phase II trial of ATL1102 confirming its activity and safety in RRMS patients
  - *ATL1102 demonstrated comparable/potentially superior activity to the VLA-4 monoclonal antibody drug Tysabri® at the same stage of development*
  - *Tysabri® is the current efficacy benchmark for RRMS treatment – sales of $1.6 Billion/annum*
  - *In 2013 Biogen Idec gained all rights to Tysabri from Elan for an upfront of US$3.25Billion plus payments on future sales*

ATL1102 profiles as a highly potent, self administrable drug for the treatment of RRMS (Tysabri® is an iv infusion) and potentially safer and cheaper to manufacture than Tysabri®

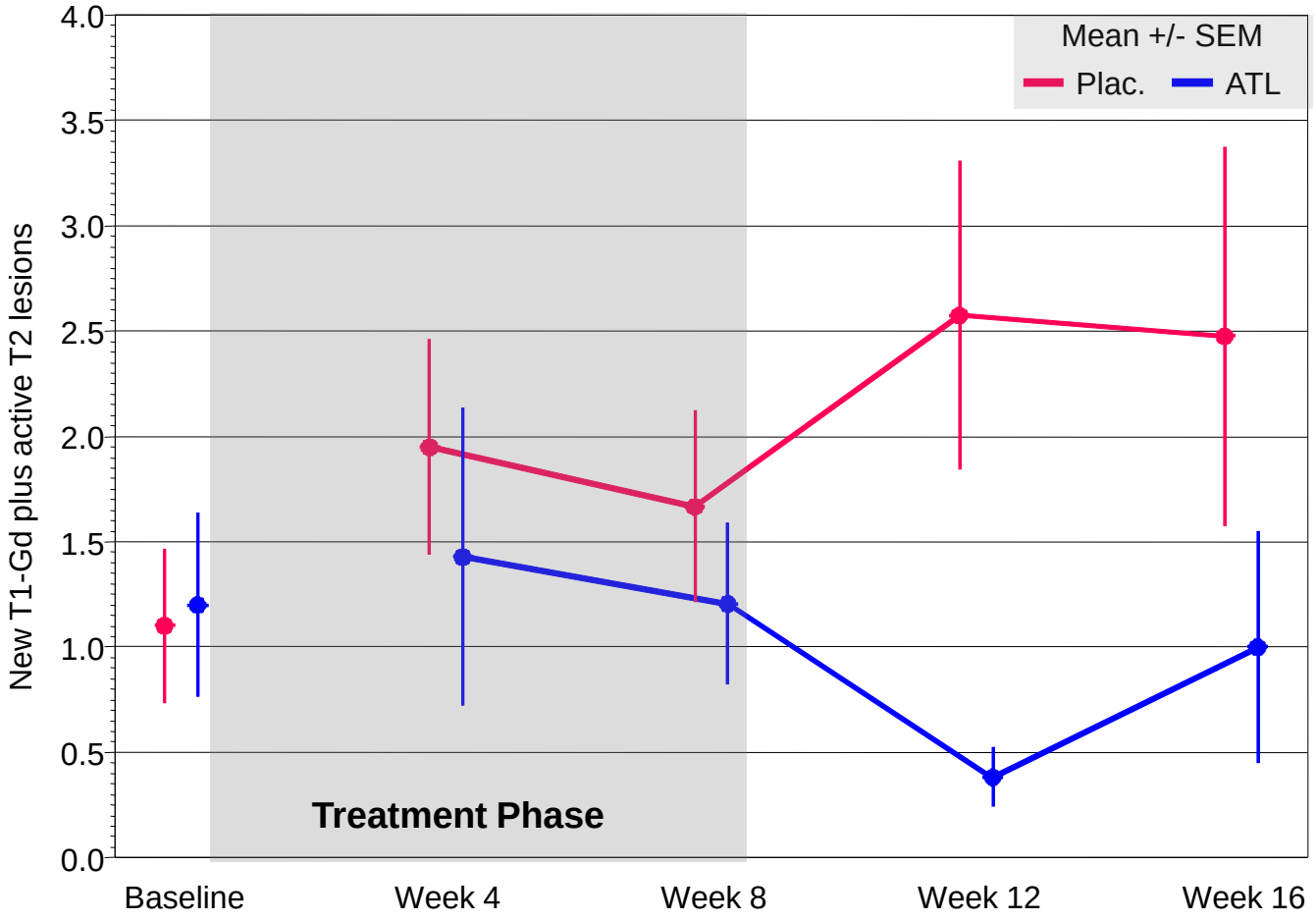
Project Status

- Chronic monkey toxicology study underway with results due Q1'2014 to support a potential Phase IIb study of ATL1102 in MS patients in 2014
- New US patent granted to 2029 and potentially extendable to 2034

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ATL1102 Phase II study met primary end-point: reduction cumulative no of new active lesions at week 12 (CNNAL)

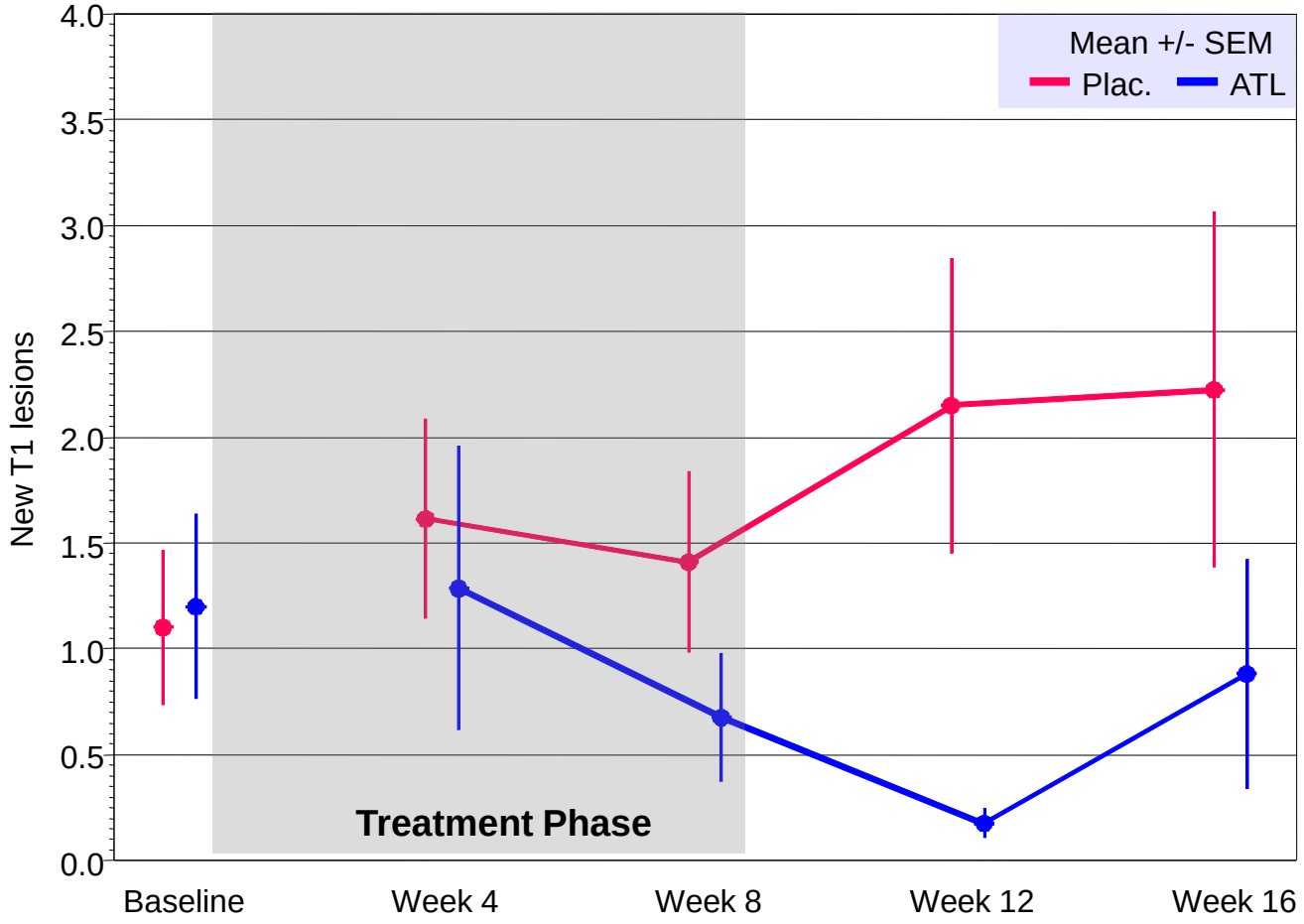
ATL1102 reduced CNNAL by 54.4%, p = 0.01



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ATL1102 Phase II study: reduction in New T1-Gd lesions

ATL1102 reduced Cumulative No of New T1-Gd Lesions at week 12 by 66.7%, p = 0.002



ATL1102 vs Tysabri: Comparison of PoC Trial Outcomes

ATL1102 summary of clinical endpoints

- 54.4% reduction (p=0.01) in cumulative new active lesions at week12 vs placebo
- 66.7% reduction (p=0.002) in cumulative new T1-Gd lesions at week 12 vs placebo
- 84% reduction (p=0.017) of T1 enhancing lesion volume at week 12 vs placebo
- Relapse rates and EDSS: no significant changes though study considered too short for definitive conclusions

Tysabri®: PoC study: Turbridy *et al*. (1999) Neurology 53(3), 466-72

- 72 patients, RR-MS + 2° progressive; 8 weeks treatment, 16 weeks follow up
- 50% reduction (p = 0.042) in cumulative new active lesions at week 12 vs placebo
- 52% reduction (p = 0.017) in new T1-Gd lesions at week 12 vs placebo
- Lesion volume not reported
- Relapse rates and EDSS: study considered too short for definitive conclusions

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ATL1102 potential product advantages

Potent efficacy = potentially more effective than existing therapies

- Phase II data comparable/superior to Tysabri ® at same stage of development

Self administration = more convenient

- Subcutaneous injection allows potential self administration unlike Tysabri®
- Potential for infrequent dosing (e.g. once weekly or less frequent)

Chemically synthesized = cheaper to make

- Anticipate lower manufacturing costs than protein drugs (mAbs, beta interferon)

Unique mechanism = potentially less immunosuppressive = potentially safer

- Drug employs unique (antisense) mechanism
- Differentiated distribution and tissue accumulation profiles and cellular PD
- More selective VLA-4 immunomodulator

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ATL1102 Stem Cell Mobilization in Cancer

Product

- ATL1102 as an acute treatment (1 week dosing) for use with standard GCSF treatment to enhance stem cell mobilisation (SCM)
- SCM = bone marrow hematopoeitic stem cells (CD34+) are mobilized to the blood for collection before high dose chemotherapy and then re-infused to re-establish immune system post chemotherapy
- Neupogen® (Filgrastim) a GCSF agonist is the market leader in SCM: Sales of US$1.3 Billion/annum
- Mozobil® (Plerixafor) - used with GCSF to increase SCM. Expensive ($7,500 per vial) and ~30% of patients still fail to achieve threshold mobilisation level: Sales of ~US$130 million/annum
- In 2008 estimated that 55,000 patients could benefit from more SCM than with GCSF alone and in 2011 it was reported that globally around 10,000 patients/annum still failing mobilization

Project Status

- ATL1102 increased CD34+ RNA in blood of MS patients at 8 weeks by 1.5 fold v baseline (P< 0.027)
- Animal safety studies completed to support human trials. Clinical safety data established in Phase I volunteer and Phase II MS patient studies
- Orphan drug indication (regulatory and IP incentives). Patent application seeking protection to 2031
- **PoC trial planned in volunteers** to test the drug's potential to release CD34+ SCs; Trial application submitted; **results potentially available by mid 2014**

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ATL1101 for Prostate Cancer

Product

- ATL1101 is a 2nd generation inhibitor of IGF-IR (emerging target in oncology)
- IGF-IR inhibition blocks key cell survival/proliferation pathways
- Major Pharma Co's have mAb programs targeting IGF-IR confirming the attractiveness of the target in cancer drug development
- ATL1101 only antisense or 'gene silencing' approach to the target in development

Project Status

- Significant suppression of key tumour signalling pathways and prostate cancer tumour growth demonstrated in animal studies
- Select toxicology studies completed
- Drug potentially positioned to move into clinical development in prostate cancer patients
- ANP currently assessing development and partnering options for the drug

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ANP Investment Highlights

- Commercializing a platform technology via technology collaboration with the leader in RNA therapeutics development, Isis Pharmaceuticals
- Technology validation provided by the first of the class approved for systemic administration (Kynamro™) and Isis's antisense technology licensing deals with Big Pharma
- 4 advanced development programs with multiple disease applications and significant commercial potential
  - ***ATL1103 in Acromegaly*** *- Phase II trial underway with positive interim results reported; Final efficacy results anticipated mid 2014*
  - ***ATL1102 in MS*** *- Chronic toxicology study results due Q1'2014 to support a potential Phase IIb study in MS patients*
  - ***ATL1102 in SCM*** *– PoC Trial application submitted; Trials results potentially available mid -2014*
  - ***ATL1101 in Prostate Cancer*** *- Positioned to move into clinical trials*

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