10th February 2010

ATL1101 Data Presentation

The Company wishes to inform that Antisense Therapeutics Limited's Research Director Christopher Wraight has given a presentation (attached on the pages to follow) to the Prostate Cancer Foundation of Australia in relation to the Company's second generation antisense anti-cancer drug ATL1101.

The presentation contains background on Antisense Therapeutics Limited, its broader product pipeline and a comprehensive account of the data generated to date on ATL1101.

Prostate cancer is the second most frequently diagnosed cancer in men after skin cancer. It is estimated there will be 218,890 new cases diagnosed in the U.S. this year. Around 1 in 6 men will develop prostate cancer, a third to a half of whom will recur after local treatment and risk progression to metastatic prostate cancer. Metastatic disease invariably progresses to hormone refractory or castrate resistant prostate cancer (CRPC) if given enough time. Prostate tumours are initially androgen (male sex hormone) dependent, and can be treated with androgen ablation therapy (the term "castration" can be used to describe removal of the source of androgen), however once the disease progresses to its most dangerous and aggressive form, CRPC, treatment options are limited and prognosis is poor. Treatment options depend on disease severity and include radiation and chemotherapy, which are designed to induce programmed cell death (apoptosis) of tumour cells. There is a pressing need for the development of new treatment options.

ATL1101 is an antisense inhibitor of IGF-IR, which has shown potent activity in laboratory studies, including in human cancer cells. IGFIR is one of the best known of a family of cell signalling molecules that are referred to as "anti-apoptotic". These molecules prolong cell survival by inhibiting programmed cell death (apoptosis). The connection between IGF-IR activity and prostate cell tumorigenicity has been studied for many years. Drugs targeting IGF-IR are designed to slow down tumour growth and make tumour cells more susceptible to cell death. Inhibition of IGF-IR is also designed to make tumour cells more susceptible to killing by cytotoxic treatments like radiation therapy and chemotherapy. Such therapeutic approaches are under investigation in several large pharmaceutical companies, lending support to our own antisense-based strategy against the same target. Designed to block IGF-IR synthesis, ATL1101 offers potential advantages over other therapies targeting IGF-IR due to its highly differentiated pharmacokinetics and unique antisense mode of action. ATL1101 was a product of a discovery collaboration between ANP and Isis Pharmaceuticals (Nasdaq: ISIS) and utilizes second-generation antisense technology, licensed from Isis. Several antisense drugs to different cancer therapeutic targets, which share the same second generation chemical modifications and design as ATL1101, are advancing in cancer clinical trials, strengthening support for second-generation drugs as targeted cancer therapeutics. For example OGX-011, developed by OncoGenex and Isis, and recently licensed to Teva Pharmaceutical Industries, has demonstrated significant clinical benefit when combined with chemotherapy (increased survival time compared to patients receiving chemotherapy alone) in Phase II clinical studies in CRPC and non-small cell lung cancer (NSCLC).

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. Its mission is to create, develop and commercialise antisense pharmaceuticals for large unmet markets. ANP has two drugs in development and two drugs in pre-clinical research. ATL1102 (injection) is in the advanced stages of a Phase IIa trial as a potential treatment of multiple sclerosis. ATL1103 is a second-generation antisense drug designed to lower blood IGF-I levels and is entering preclinical development as a potential treatment for acromegaly and vision disorders. ATL1102 (inhaled) is at the pre-clinical research stage as a potential treatment for asthma. ATL1101 is a second-generation antisense drug at the pre-clinical research stage being investigated as a potential treatment for prostate cancer. ATL1102 has been licensed to Teva Pharmaceutical Industries Ltd.

Contact Information: Website: www.antisense.com.au
Managing Director: Mark Diamond +61 3 9827 8999
Investor Relations: Simon Watkin +61 (0) 413 153272

ATL1101

A second-generation antisense anti-cancer drug to the IGF-I receptor

Christopher Wraight PhD MBA

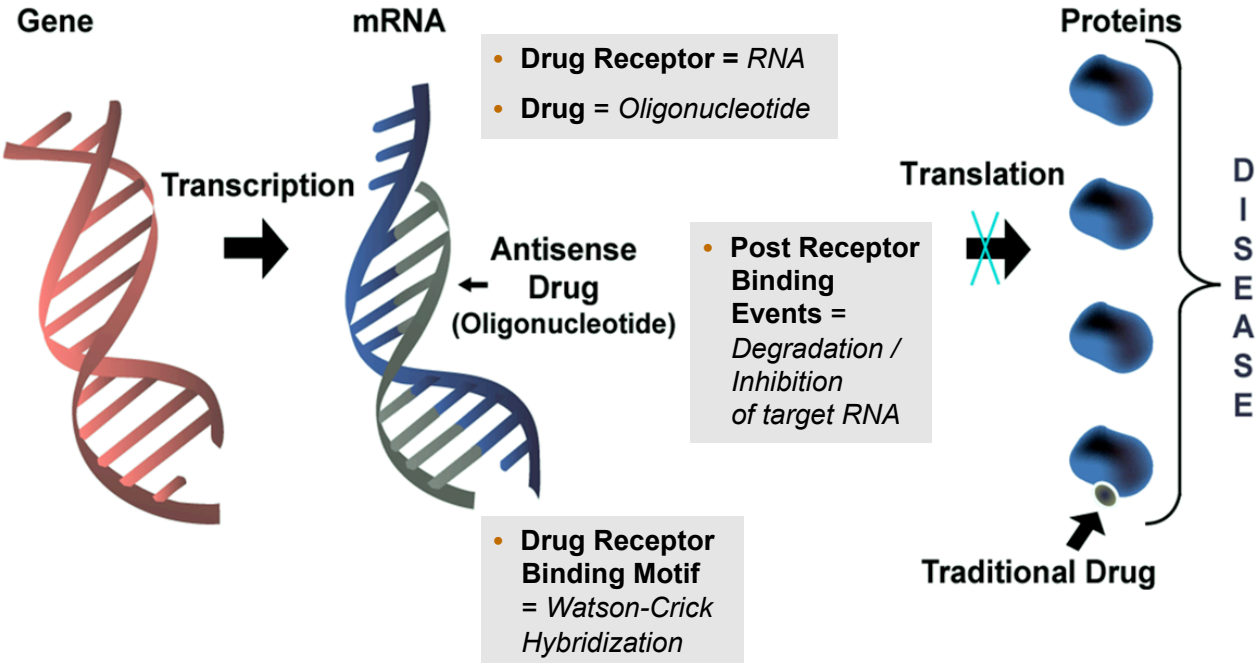
February 2010

Antisense Therapeutics Ltd
Melbourne, Australia
ASX: ANP

Antisense Therapeutics Ltd. Company Introduction

- Biopharmaceutical company developing advanced RNA-targeting antisense drugs through its technology agreement with Isis Pharmaceuticals Inc. (Isis)
- Publicly listed company trading on the Australian Stock Exchange (ASX: ANP) and based in Melbourne
- ATL/TV1102: Most advanced drug in the ATL's drug development pipeline, a second generation antisense drug for relapsing-remitting multiple sclerosis (RRMS), in-licensed from Isis
- ATL/TV1102 was licensed to *Teva Pharmaceutical Industries* in February 2008
- In ATL's Phase II trial, ATL/TV1102 significantly reduced brain lesions in patients with RRMS with only 8 weeks of treatment
  - *Comparable activity to the monoclonal antibody drug Tysabri™ in a similar MS study*

Introduction to Antisense Technology



- **Drug Receptor =** *RNA*
- **Drug** = *Oligonucleotide*

- **Post Receptor Binding Events =** *Degradation / Inhibition of target RNA*

- **Drug Receptor Binding Motif** = *Watson-Crick Hybridization*

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Adapted from diagram courtesy Isis Pharmaceuticals Inc.

Product Research & Development Pipeline

PRODUCT	INDICATION	RESEARCH	PRECLINICAL	PHASE I	PHASE II	PHASE III
ATL/TV1102 s.c. injection	multiple sclerosis	*Licensed to Teva*				
ATL1103 s.c. injection	vision, acromegaly	*Toxicology & Clinical Supplies*				
ATL1101 injection	prostate cancer	*Preclinical Efficacy & Rodent Tox*				
ATL/TV1102 inhaled	asthma	*Teva have option*				

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

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Prostate Cancer

- **Second most frequently diagnosed cancer in men after skin cancer**
  - ≈ 1 in 6 men will develop prostate cancer
  - ≈ 1/3 to 1/2 recur after local treatment, risk progression to metastatic prostate cancer
- **Metastatic prostate cancer initially responds to androgen ablation therapy**
  - disease gradually progresses to hormone refractory or metastatic castrate resistant prostate cancer (**mCRPC**)
  - mCRPC is most dangerous and aggressive form
  - treatment options are limited and prognosis is poor
- **mCRPC treatment options**
  - depend on disease severity
  - include radiation and chemotherapy, which are designed to induce programmed cell death (apoptosis) of tumour cells
  - There is a pressing need for the development of new treatment options

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OncoGenex OGX-011 Clinical Outcomes Illustrate Second Generation Antisense Clinical *PK-PD-Pharmacology* Paradigm in Prostate Cancer

Clinical PK-PD

OncoGenex Phase I, Chi *et al.* & Gleave (2005)[1]

OGX-011 (i.v. d1, 3, 5 then weekly d8-29 @ 40 to 640mg) + hormone ablation therapy (start d1) in 25 patients with localised PrCa before prostatectomy (d30-36)

- Dose-dependent increase in ASO detected in prostate tumour
- Dose-dependent inhibition of target mRNA to max 92% in prostate cells & 98% in lymph node
- Apoptotic index in prostate tumour cells increased vs hormone ablation alone

Clinical Outcome

OncoGenex Phase II final results reported at ASCO May 2009[2]:

Standard-of-care prednisone & docetaxel ± OGX-011 i.v. 640mg weekly in patients with advanced metastatic prostate cancer

- Median overall survival: Patients treated with OGX-011 plus docetaxel: **23.8 months**
  Patients treated with docetaxel: **16.9 months**
- Unadjusted hazard ratio (difference in survival between treatment groups): 0.61
  representing a **39%** reduction in the rate of death for patients treated with OGX-011.
- Out-licensed to Teva Pharmaceutical Industries, Phase III studies commencing

antisense THERAPEUTICS

1. Chi, K.N., Eisenhauer, E., Fazli, L., Jones, E.C., Goldenberg, S.L., Powers, J., Tu, D. & Gleave, M.E.: A phase I pharmacokinetic and pharmacodynamic study of OGX-011, a 2'-methoxyethyl antisense oligonucleotide to clusterin, in patients with localized prostate cancer. *J Natl Cancer Inst* **97**, 1287-96 (2005).

2. American Society of Clinical Oncology (ASCO) Annual Meeting, May 2009

IGF-I Receptor (IGF-IR) targeting: Enhancing tumour kill

- New targeted therapy approaches aim to:
  - enhance effect of androgen ablation on induction of tumour cell apoptosis when disease is still androgen dependent
  - delay progression to mCRPC
  - mCRPC: enhance effect of cytotoxic therapies, e.g. Taxotere® (docetaxel)
- IGF-IR is an emerging therapeutic target in oncology
  - IGF-IR signalling up-regulated in androgen resistance
  - IGF-IR inhibition blocks key cell survival and proliferation signalling pathways MAPK & PI3K/AKT
  - IGF-IR inhibition sensitises tumour cells to docetaxel-induced apoptosis

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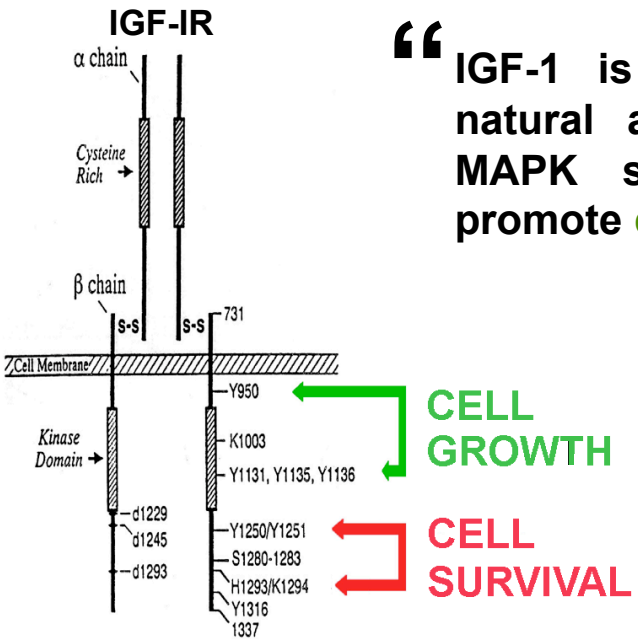
Cancer is a failure of control over cell growth & survival



"IGF-1 is one of the most potent natural activators of the AKT and MAPK signaling pathways, which promote cell growth and cell survival."

Hoffmann-La Roche Inc. (Roche) Company Announcement 23 Oct 2007 (http://www.sarctrials.org/public/press13.aspx): Roche Announces Positive Results in Solid Tumors Using Human Monoclonal Antibody against IGF-1R (R1507)

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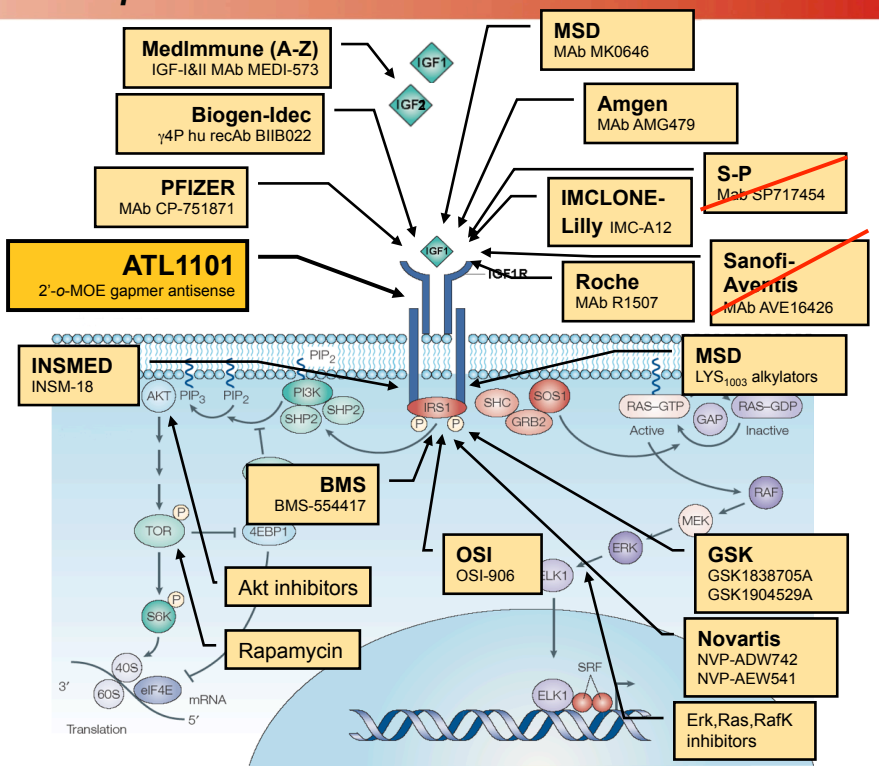
ATL1101 targets IGF-IR: High Interest Area in Oncology

Many companies attempting to develop IGF-IR inhibitors

- Monoclonal antibodies, Kinase inhibitors & SMI antagonist strategies have receptor specificity & other challenges
- ATL1101 is designed to specifically block IGF-IR synthesis & inhibit downstream signalling
- ATL1101 also blocks IGF-IR:IR hybrid receptors

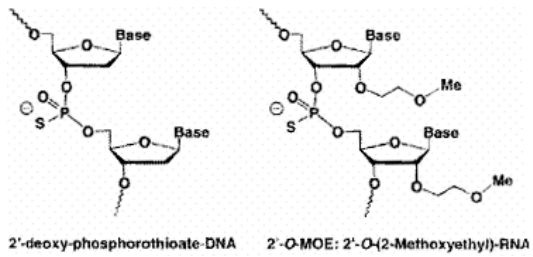
[1] Frasca et al. *Arch Physiol Biochem* 114, 23-37 (2008)
[2] Zhang et al. *Cancer Res* 67, 391-7 (2007)



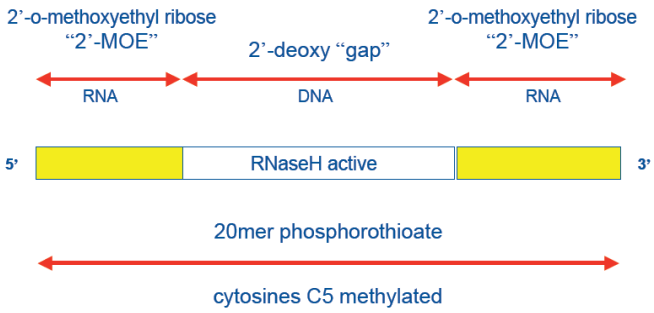
adapted from Pollak et al., 2004 Nature Reviews (Cancer) 4: 505

Properties of ATL1101, human IGF-I receptor antisense

ATL1101 modified backbone and ribose sugar

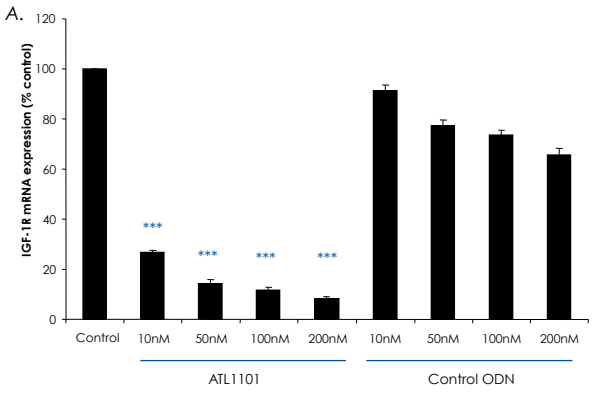


Second generation antisense chemistry

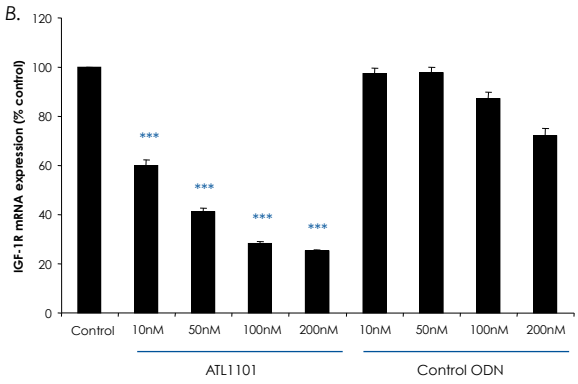


ATL1101 inhibition of IGF-IR mRNA: Potent & sequence-specific

LNCaP cells



PC-3 cells



Sequence-specific and dose-dependent suppression of IGF-1R mRNA expression levels by ATL1101 in LNCaP (*A.*) and PC-3 (*B.*) cells. LNCaP and PC-3 cells were treated with 10 to 200 nM ATL1101 or control ODN for two days. One day after treatment, total RNA was extracted, and IGF-1R mRNA expression was analyzed by quantitative RT-PCR, IGF-1R mRNA levels were normalized to levels of GAPDH mRNA and expressed here as mean ±SE. ***, p≤0.001 differ from control (oligofectamine only) by Student's *t* test. "Control" cells are treated with oligofectamine only.

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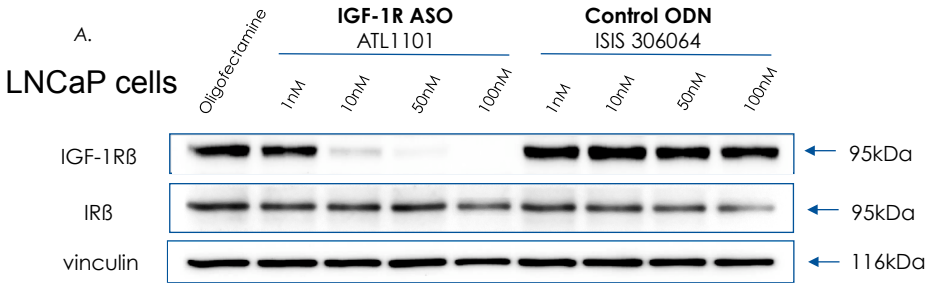
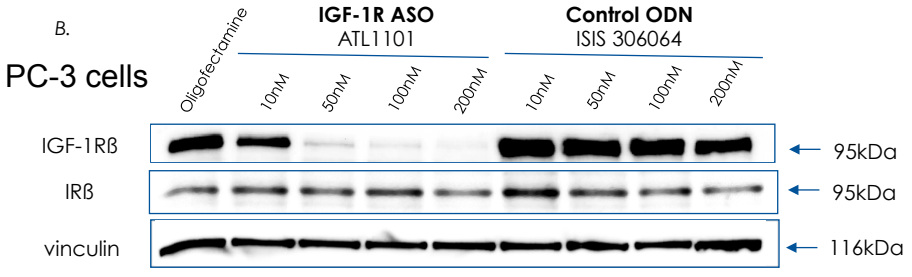
Furukawa, Wraight, Freier, Peralta, Atley, Monia, Gleave & Cox (1st Feb 2010):
Antisense Oligonucleotide Targeting of Insulin-Like Growth Factor-1 Receptor (IGF-1R) in Prostate Cancer. The Prostate , 70(2), 206-18

ATL1101 inhibition of IGF-IR protein: Potent & gene-selective inhibition of IGF-Iβ; IRβ (insulin receptor) unaffected

Sequence-specific and dose-dependent inhibition of IGF-1R protein by IGF-1R ASO in LNCaP (*A.*) and PC-3 (*B.*) cells. LNCaP or PC-3 cells were treated with indicated concentrations of IGF-1R ASO (ATL1101/D3600) and control ODN (ISIS 306064) for two days. Two days after treatment, total proteins were extracted from cultured cells, and IGF-1Rß, IRß and vinculin protein levels were analyzed by Western blotting. Oligofectamine, oligofectamine treated cells only.





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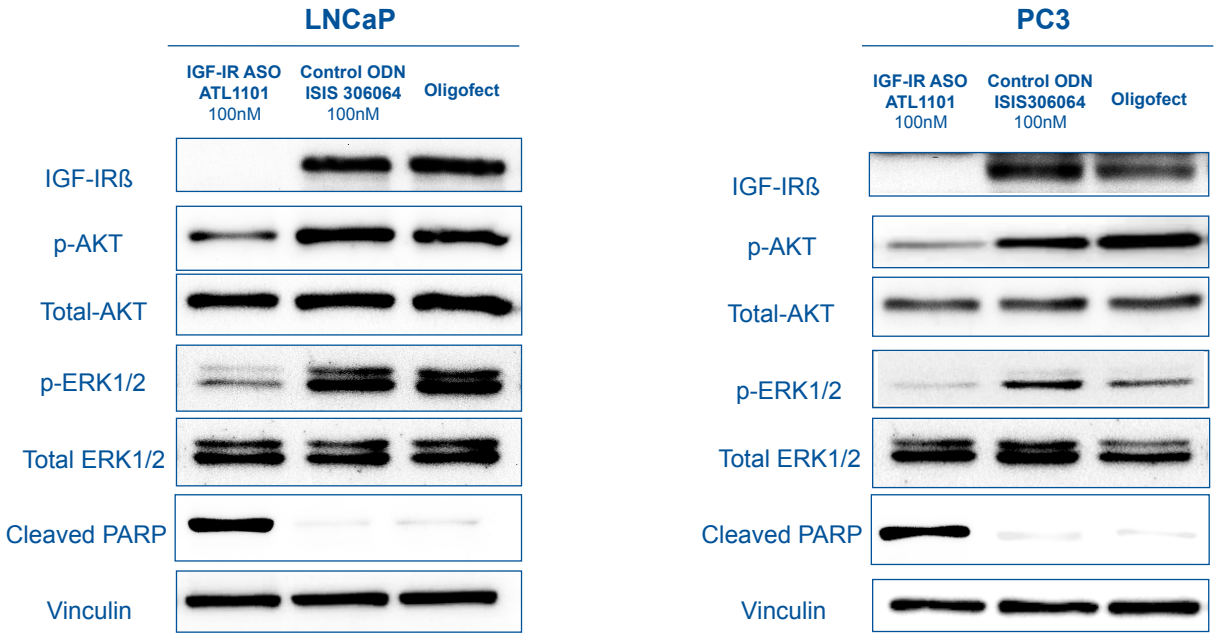
Antisense Oligonucleotide Targeting of Insulin-Like Growth Factor-1 Receptor (IGF-1R) in Prostate Cancer. The Prostate , 70(2), 206-18

ATL1101 suppresses intracellular AKT & MAPK signaling *in vitro*



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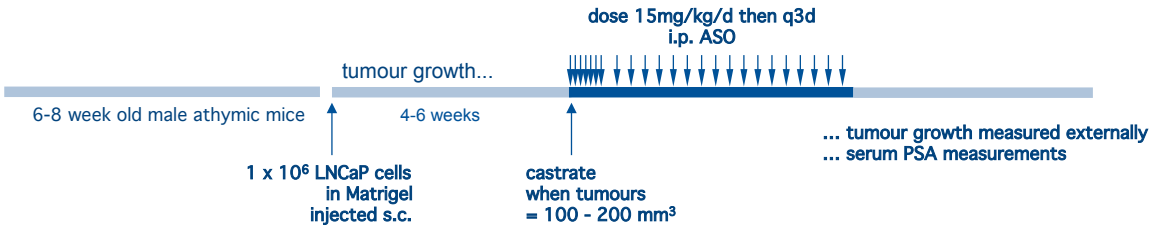
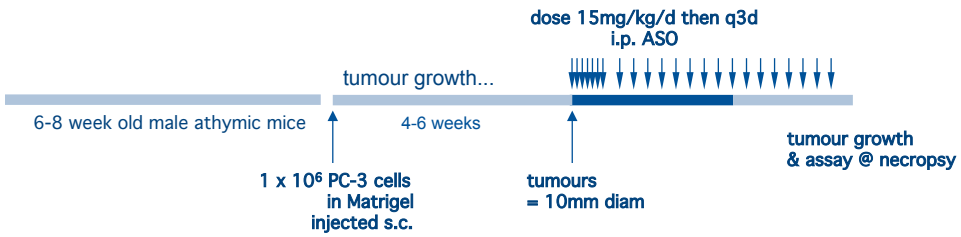
Antisense Oligonucleotide Targeting of Insulin-Like Growth Factor-1 Receptor (IGF-1R) in Prostate Cancer. The Prostate , 70(2), 206-18

ATL1101 Preclinical animal pharmacology: prostate tumour xenograft models:
Systemic delivery with ATL1101 in saline

- Tumour Pharmacology Model I: *Androgen dependence of tumour growth, LNCaP cell line*



- Tumour Pharmacology Model II: *Androgen-independent tumour growth, PC-3 cell line*



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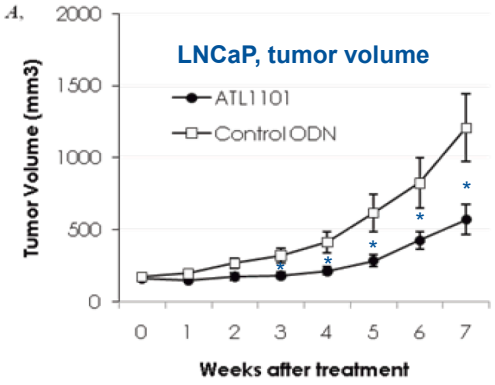
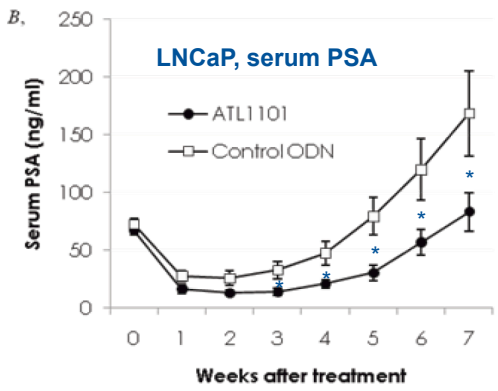
ATL1101 reduces tumour growth and PSA *in vivo*

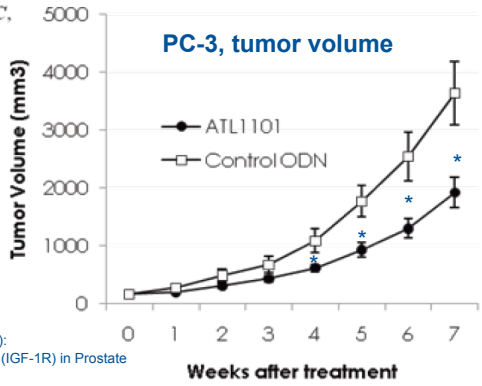




In LNCaP xenografts, ATL1101 significantly delayed the tumor growth and PSA rise rates after castration.

In PC3 xenografts, ATL1101 monotherapy significantly reduced tumor volume compared to the mice treated with control ODN (ISIS306064).

A, LNCaP cells were inoculated s.c. and when PSA values exceeded 50 ng/ml, mice were castrated and randomly selected for treatment with ATL1101 or control ODN (15 mg/kg) injected i.p. once daily for 7 days and 3 times per week thereafter.
B, blood samples were obtained from the tail vein of the mice once weekly to measure serum PSA by ELISA.
C, PC-3 cells were inoculated s.c. and when tumors reached 100 mm^3, mice were randomly selected for treatment with the same protocol as LNCaP. Each point represents the mean tumor volume in each group containing 10 mice;
bars, SE. * differs from control ODN treatment group ($p < 0.05$) by Student's t test.



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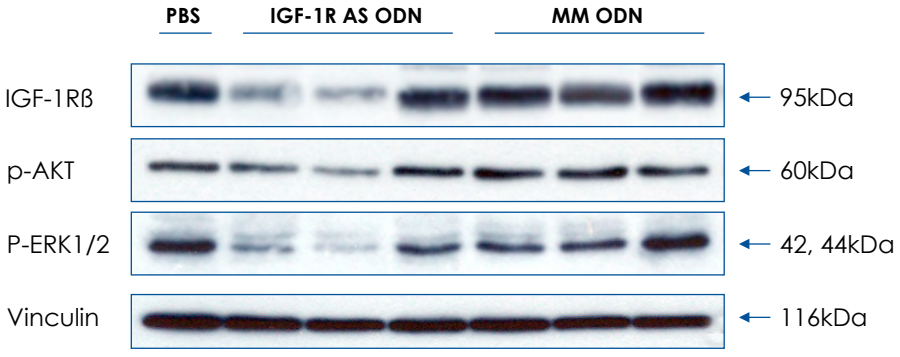
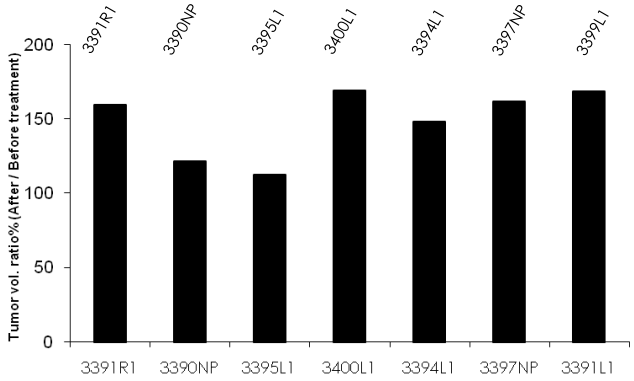
Furukawa, Wraight, Freier, Peralta, Atley, Monia, Gleave & Cox (1st Feb 2010): Antisense Oligonucleotide Targeting of Insulin-Like Growth Factor-1 Receptor (IGF-1R) in Prostate Cancer. The Prostate , 70(2), 206-18

Tumour growth inhibition correlates with target effects

in preliminary study on six PC-3 mice; apparent correlation after only 7 days treatment





Total PC-3 xenograft proteins were extracted in RIPA buffer after control or IGF1-R ASO treatment for 7 days and Western blots done with p-AKT, pERK1/2, and IGF-1R antibodies; vinculin was used as a loading control.

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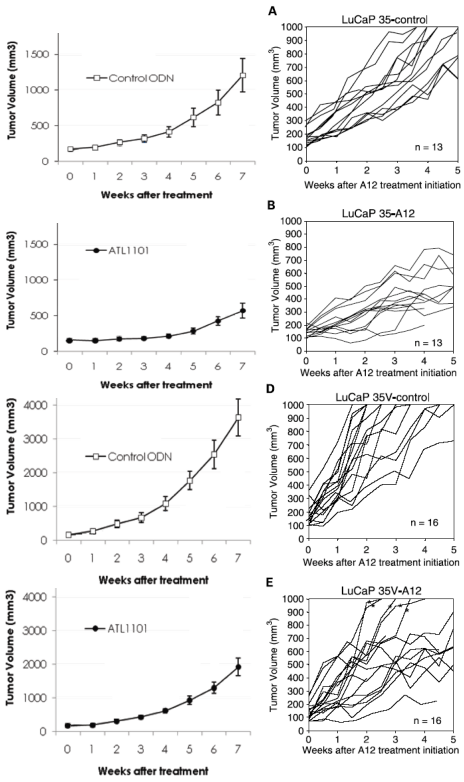
Antisense Therepeutics Ltd. proprietary data on file

ATL1101 & ImClone mAb A12 compared *in vivo* (NB: different cell lines)

LNCaP androgen-dependent tumour cell

Furukawa, Wraight, Freier, Peralta, Atley, Monia, Gleave & Cox (1st Feb 2010): Antisense Oligonucleotide Targeting of Insulin-Like Growth Factor-1 Receptor (IGF-1R) in Prostate Cancer. The Prostate , 70(2), 206-18

PC3 androgen-dependent tumour cell



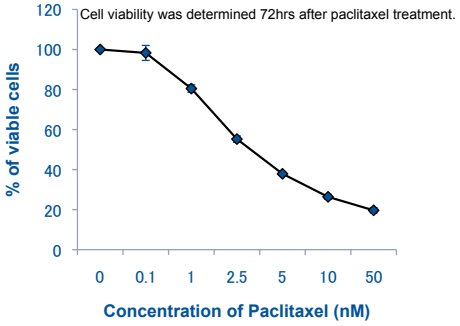
LuCaP 35 androgen-dependent tumour cell

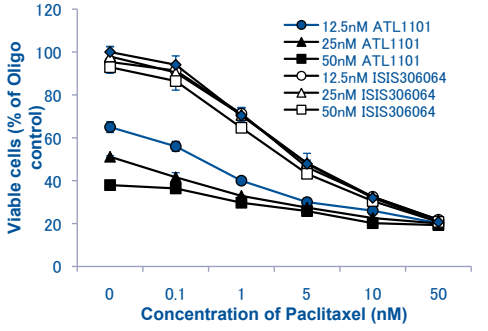
Wu, J.D., Odman, A., Higgins, L.M., Haugk, K., Vessella, R., Ludwig, D.L. & Plymate, S.R. *Clin Cancer Res* **11**, 3065-74 (2005).

LuCaP 35V androgen-dependent tumour cell

antisense THERAPEUTICS

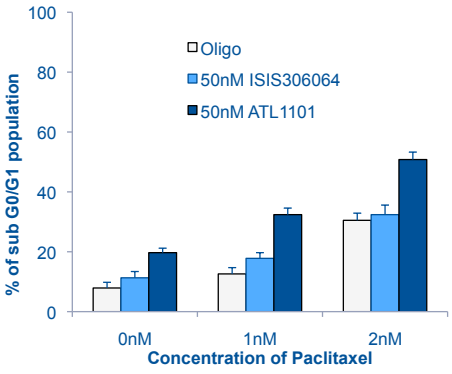
ATL1101 enhances Taxol® tumour cell cytotoxicity *in vitro*



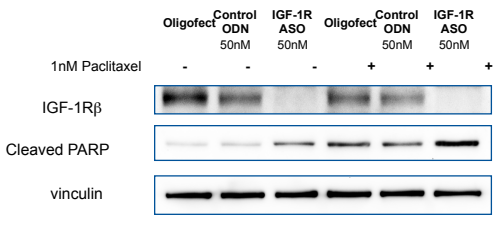


After 2nd transfection with ASO, PC3 cells were treated with indicated concentrations of paclitaxel. Cell viability was determined 72hrs after paclitaxel treatment.

Furukawa, Wraight, Monia, Gleave & Cox (2009), presented at 10th National Prostate Cancer Symposium, Melbourne, Australia



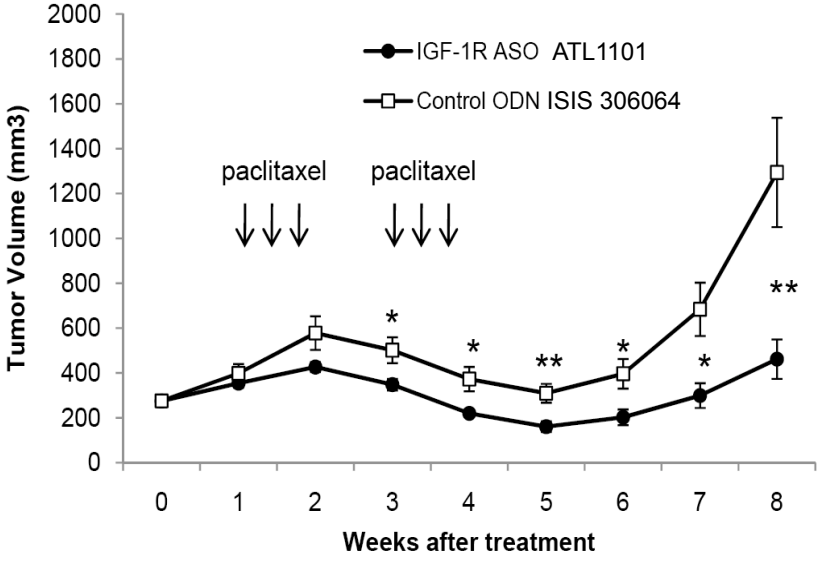
Percentage of apoptotic cells was determined 48hrs after paclitaxel treatment by FACS.

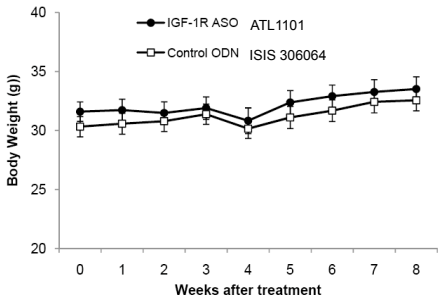


After 2nd transfection with ASO, PC3 cells were treated with indicated concentrations of paclitaxel.Total protein was lysated 48hrs after paclitaxel treatment.

antisense THERAPEUTICS

ATL1101 enhances Taxol® tumour cell cytotoxicity *in vivo*





Combination therapy ATL1101 and Paclitaxel
For *in vivo* study, 2 X 10^6 PC-3 cells were inoculated s.c. in the flank region of 6-8 week-old male athymic nude mice via a 27-gauge needle under methoxyfluorane anesthesia. When mice bearing PC-3 tumors reached a palpable tumor volume of 200 mm^3 they were randomly assigned for treatment with 15 mg/kg IGF-1R ASO (ATL1101) or mismatched ODN(ISIS306064) once daily for 5 days and three times per week thereafter by i.p. injection. At days 7, 9, 11 and 21, 23, 25, 0.5 mg of micellar paclitaxel was administrated i.v. once daily. Each experimental group consisted of 10 mice.

antisense THERAPEUTICS

Furukawa, Wraight, Monia, Gleave & Cox (2009), presented at 10th National Prostate Cancer Symposium, Melbourne, Australia

ATL1101 activity in taxane-resistant prostate cancer cells:
A Taxol® (Ptx)-resistant PC3 cell line with multiple drug resistance

A PC3 cell line that is additionally resistant to the cytotoxic effects of the taxane drug paclitaxel (Taxol®) was selected under *in vitro* culture conditions, named PtxR-PC3 & examined for the effects of ATL1101 treatment on (i) IGF-IR inhibition, (ii) cell viability, and (iii) paclitaxel sensitivity.

- **PtxR-PC3 cell retained their sensitivity to sequence-specific inhibition of IGF-IR mRNA and protein**
- **Treatment of PtxR-PC3 cells with up to the highest tested level of 200nM had no effect on the closely related insulin receptor, either mRNA (IR-A and IR-B) or protein (IRβ).**
- **PtxR-PC3 cells retained sensitivity to the cytotoxic effects of ATL1101 under standard culture conditions and exhibited a similar loss of cell viability in an ATL1101 concentration-dependent manner**
- **Treatment of PtxR-PC3 cells with ATL1101 increased their sensitivity to the cytotoxic effects of paclitaxel**

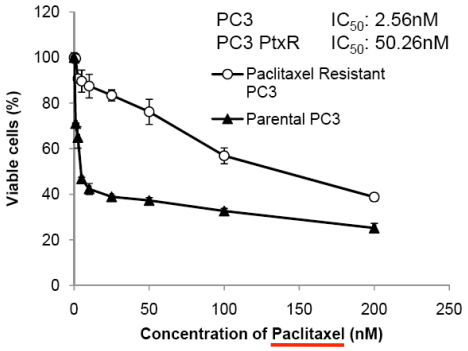
antisense THERAPEUTICS

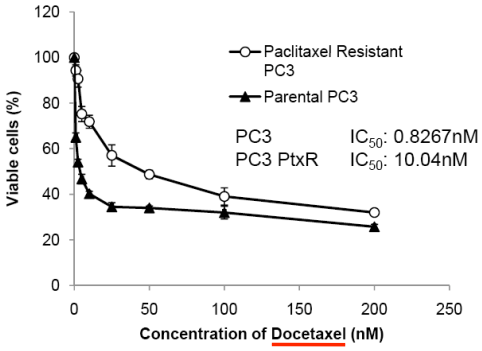
ATL1101 activity in taxane-resistant prostate cancer cells:
A Taxol® (Ptx)-resistant PC3 cell line with multiple drug resistance

PtxR PC3 cell line is less sensitive to growth inhibition by:

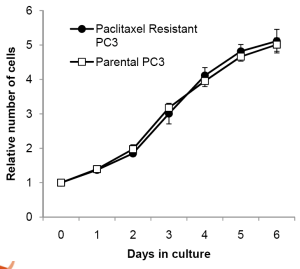
paclitaxel	~ 20 x
docetaxel	~ 10 x
mitoxantrone	~ 40 x
cisplatin	~ 2.5 x

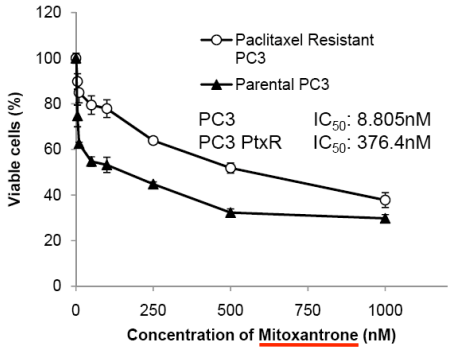
Cell viability was determined 72hrs after indicated treatment by crystal violet method

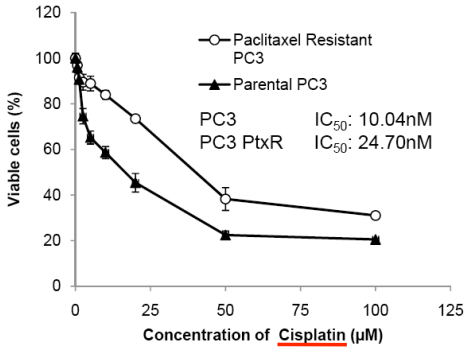




Basal growth rate in normal medium is the same as parental PC3 cells



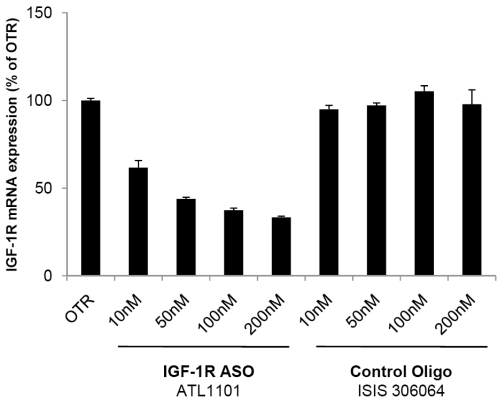


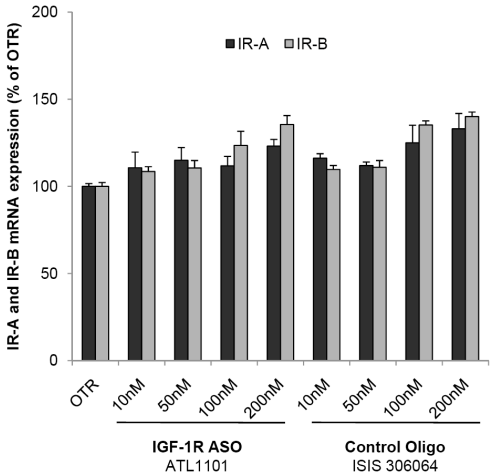


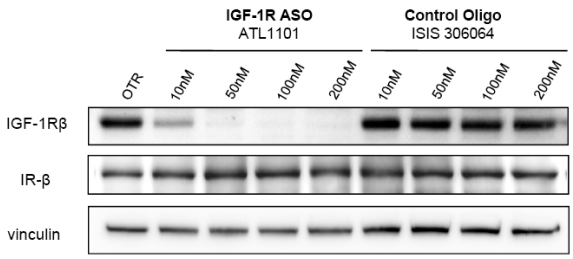
antisense THERAPEUTICS

ATL1101 activity in taxane-resistant prostate cancer cells:
Taxol® (Ptx)-resistant PC3 cells retain sensitivity to IGF-1R mRNA & protein inhibition by ATL1101

…Insulin Receptor (IR) expression unaffected



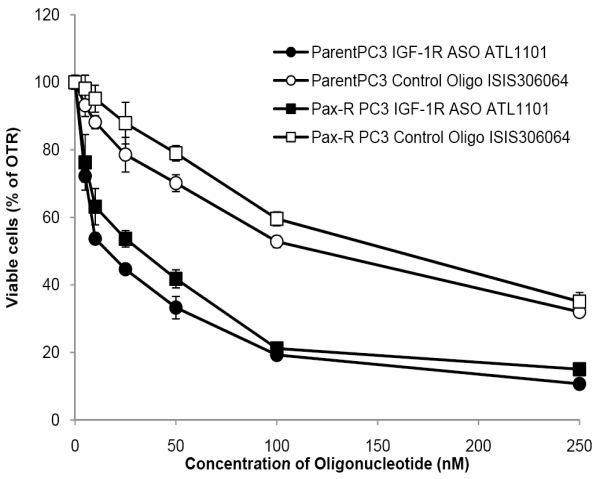




antisense THERAPEUTICS

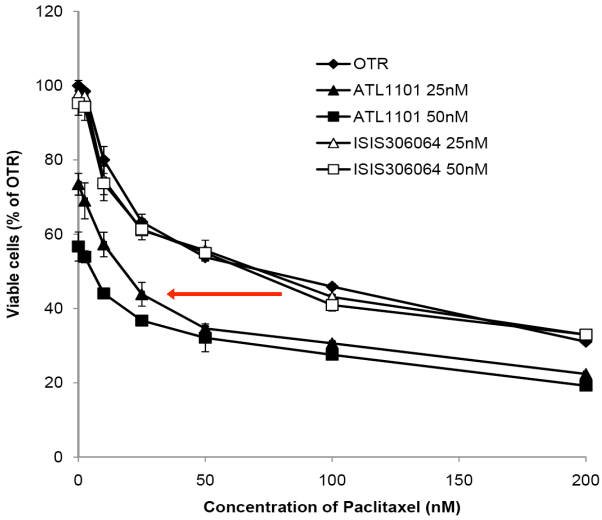
ATL1101 activity in taxane-resistant prostate cancer cells:
ATL1101 retains cytotoxicity & re-sensitises to Taxol® effects *in vitro*

Taxol® (Ptx)-resistant PC3 retain ATL1101 sensitivity under standard culture conditions



Taxol® (Ptx)-resistant PC3 recover sensitivity to Ptx after ATL1101 treatment

"Left shift" in Ptx sensitivity: Ptx sensitivity restored



Cell viability was determined 72hrs after indicated treatment by crystal violet method after 2nd transfection with ASO

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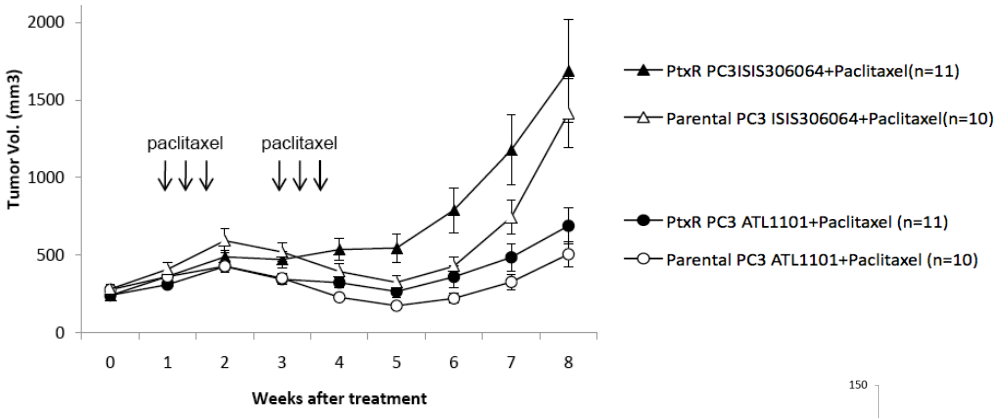
ATL1101 activity in taxane-resistant prostate cancer cells:
ATL1101 retains cytotoxicity & re-sensitises to Taxol® effects *in vivo*



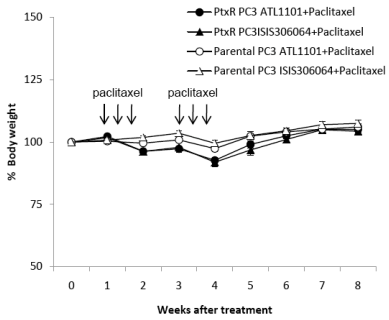
For *in vivo* xenograft studies, 2 x 10^6 either parental PC3 or PtxR PC3 cells were inoculated s.c. in the flank of 6-8 week-old male athymic nude mice.

When tumors reached 200 mm^3, mice were randomly selected for treatment with 15 mg/kg ATL1101 or control oligonucleotide (ISIS 306064) injected i.p. once daily for 7 days and 3 times per week thereafter.

For combination setting with paclitaxel, at days 7, 9, 11 and 21, 23, 25: 0.5 mg of paclitaxel was administered i.v. once daily.

Each experimental group consisted of 10 or 11 mice.

Tumor volume measurements were performed once weekly.



antisense THERAPEUTICS

ATL1101 Intellectual Property

- ATL believes it has all appropriate licenses to work ATL1101, the most advanced RNA-targeting drug to IGF-IR, via its collaboration with the world leader in the field of antisense technology, Isis Pharmaceuticals

- Protection of ATL1101 Intellectual Property:
  - ATL1101 product patents granted in the US to December 2024 and Australia and NZ to February 2024, with potential for up to 5 year extensions to 2029 in the US and Australia.
  - ATL1101 product patent applications pending in Canada, Japan and Europe claiming ATL1101 to Feb 2024 with potential for up to 5 year extensions to 2029 in Europe and Japan.
  - ATL1101 prostate cancer patent application seeks protection to 2029 in US*

    * There is scope to extend patent coverage for ATL1101 to other cancer indications
  - Relevant ISIS Manufacture and ISIS Platform patents that provide additional protection

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ATL1101 Intellectual Property

Country	Patent application or Patent No.	Current Status	Expiry
International	PCT/AU2004/00160	National Phase applications	
Australia	2004210882	Patent Granted	2024 *
Canada	2515484	Awaiting Examination	2024
Europe***	04709958.5	Under Examination	2024*
Japan	2006-501357	Under Examination	2024*
New Zealand	541637	Patent Granted	2024
USA	US7468356	Patent Granted	2024**
USA	US12/342,025 Continuation of 10/545354 2006/0234239	Awaiting examination	2024
US	US12/578,471	Awaiting examination	2029

* ATL1101 is protected by the above patent applications to 2024 with potential for up to 5 year extensions to the patent term to 2029.

** The expiry date on the US patent is 17 December 2024, extended 309 days from 11 February 2024 under US law 35U.S.C. 154(b). There is potential for up to 5 year extensions to the patent term from the December 2004 date.

*** Designates all member states of European patent countries including all extension states.

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ATL1101 Manufacture and Toxicology

- **ATL1101 API manufacture process is established**
  - **GLP & cGMP**

- **ATL1101 Toxicology**
  - **A mouse toxicology study has been completed**
  - **Multiple second-generation 2'MOE antisense drugs have completed IND enabling tox studies**

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ATL1101 Summary I

ATL1101 is proposed as a monotherapy or an adjuvant therapy to enhance the tumour-killing efficacy of current chemo- & radiotherapy approaches

IGF-I receptor is a high profile & broadly applicable drug target in oncology

- IGF-IR: target of interest to major pharmaceutical companies; several programmes in the clinic for range of cancers
- Pfizer (Phase III NSCLC & Phase II prostate cancer), ImClone & Insmed (Phase II prostate cancer)
- Amgen, Hoffman-LaRoche (Phase I), Merck & Co, others (preclinical)

ATL1101 is the most advanced RNA-targeting drug to the IGF-I receptor

- ISIS second-generation antisense drug that has shown potent activity in prostate cancer animal studies
- The ISIS second-generation antisense drug platform is accepted by the major pharmaceutical companies, with drugs recently in-licensed by Genzyme (Phase II/III), TEVA (Phase II), BMS and J&J
- ATL1101 cGMP manufacturing method is established & mouse toxicology studies have been completed

ATL1101 presents as an attractive development programme in prostate cancer

- A differentiated drug to a high-profile oncology target
- Rapid and relatively inexpensive path to the clinic
- Providing support for the ATL1101 approach for cancer is the 2nd generation antisense OGX-011 in prostate cancer & NSCLC, and other 2nd generation ASO drugs being developed by Lilly
- IP protection to 2024 and potentially to 2029

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ATL1101 Summary II

The ATL1101 program has a range of potential advantages over the monoclonal antibody (mAb) based products, including a potentially better safety profile

General advantages of antisense drugs compared to mAbs	
1 *Lower cost of manufacture*	• The lower cost of production allows antisense to be potentially more profitable and less expensive to take into development than mAbs
2 *Lower immune response*	• Antisense does not elicit a neutralising immune response as mAbs do. While 'humanised' and 'fully-human' mAb technology has reduced this issue, a loss of efficacy still occurs in some patients
3 *Convenient sub-cutaneous delivery*	• Antisense drugs lend themselves to be more easily delivered in a quick, convenient sub-cutaneous formulation than mAbs

Specific advantages of ATL1101 over IGF-IR targeting mAbs – potential for increased safety	
1 *Doesn't trigger ADCC*	• Most mAbs in development have IgG1 or IgG3 Fc regions which can trigger antibody dependent cell cytotoxicity (ADCC). This has the danger of recruiting the immune system to damage any tissue that expresses IGF-IR, increasing the side-effect profile. Antisense does not trigger ADCC
2 *Impact on Circulating immune cells*	• ATL1101 is rapidly cleared from the blood, lowering potential undesirable impact on the immune system cells
3 *Highly gene specific*	• ATL1101 is highly selective for the IGF-IR gene, while IGF-IR mAbs may also have slight specificity for the insulin receptor, causing hyperglycemia.

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ATL1101 Summary III

There are also theoretical rationales for differentiation with regard to increased efficacy.

Specific advantages of ATL1101 over IGF-IR targeting mAbs – potential for increased efficacy	
1 *Preferential tissue distribution*	• Pre-clinical work has shown that antisense drugs based on the same platform as ATL1101 distribute well to the prostate and other tissues where IGF-IR knock down is desirable for tumour treatment
2 *Early target knock down ablates signalling*	• ATL1101 acts to block the assembly of the IGF-IR heterodimer in the membrane. In contrast, an IGF-IR mAb would allow for the assembly of IGF-IR, allowing the chance for intracellular signalling to occur. • In addition mAbs can briefly activate some receptors before clearing them from the cell surface. ATL1101's mechanism does not have this risk
3 *Blocks all hybrid IGF-IR receptors*	• ATL1101's mechanism allows it to also knock-down IGF-IR hybrid receptors, which mAbs may not recognise

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