WILSONS
Equity Research

Date
16 December 2020

Theme
Initiating Coverage

Company

Antisense Therapeutics Limited (ANP)

Initiating at O/W: Sensing a Large Opportunity

Recommendation	**OVERWEIGHT**
12-mth target price (AUD)	**$0.57**
Share price @ 15-Dec-20 (AUD)	$0.09
Forecast 12-mth capital return	523.4%
Forecast 12-mth dividend yield	0.0%
12-mth total shareholder return	**523.4%**
Market cap	$53m
Enterprise value	$46m
Shares on issue	574m
Sold short	
ASX 300 weight	n/a
Median turnover/day	$0.1m

We initiate coverage on Antisense Therapeutics with an OVERWEIGHT rating and a risked 12 month price target of $0.57 per share. Antisense is a clinical stage biopharmaceutical company focused on antisense drugs for rare diseases. Their primary asset, ATL1102, is being developed for the treatment of Duchenne muscular dystrophy (DMD), a debilitating, genetic disease affecting boys causing severe muscle wastage leading to premature death. Antisense also have a secondary asset in development, ATL1103, as a novel treatment for acromegaly. Antisense are planning an EU pivotal Phase IIB study in DMD with ATL1102 in 2H21. Success could lead to an early approval and independent product launch in Europe (TAM A$1.7B). Unrisked valuation is $1.34 per share assuming independent commercialisation in major markets.

Key points

Interesting Phase II asset with data to support proof of concept. ATL1102 is an antisense drug that blocks an inflammatory marker, CD49d, shown to be correlated to DMD disease progression. This anti-inflammatory hypothesis is supported by data from their recent Phase II trial in non-ambulatory patients that showed reduced inflammation and stabilisation of muscle fat fractions in boys treated for 6 months with ATL1102; in addition to important subsequent changes in upper body strength. Their impending Phase IIB trial will be seeking to confirm this efficacy to support a potential EMA marketing authorisation.

Independent commercialisation strategy. We are modelling Antisense assuming independent commercialisation of ATL1102 in both major markets (EU5/US) which is supported by market predicates and recent successes in other rare diseases. We believe they are well placed to execute this strategy, which is aided by their receipt of Orphan Drug Designations (ODD) and other benefits (i.e. PRV in the US) from both regulatory agencies.

Valuation. We have used a sum of the parts approach to evaluate Antisense based on their EU and US market prospects in DMD. We initiate at a 12 month price target of $0.57 per share comprised of $0.45 for EU market assumptions and $0.12 for US market expectations. We have made certain assumptions about future financing which are included in our target price. The key sensitivities are: a) clinical risk; b) major market sales forecasts; c) transactional parameters (milestone payments, royalty rates); and d) extensions into indications outside DMD. Our unrisked price target is $1.34 per share.

Risks and catalysts

Risks: a) unfavourable clinical trial results; b) lack of capital to support expenses; c) share dilution; d) competitor development of DMD therapies **Catalysts:** a) EMA approval for trial commencement; b) FDA engagement; c) board renewal; d) partnering opportunities.

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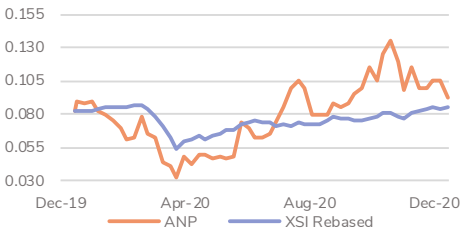
12-mth price performance ($)



	1-mth	6-mth	12-mth
Abs return (%)	-8.0	46.0	12.2
Rel return (%)	-11.3	26.0	8.8

Earnings forecasts

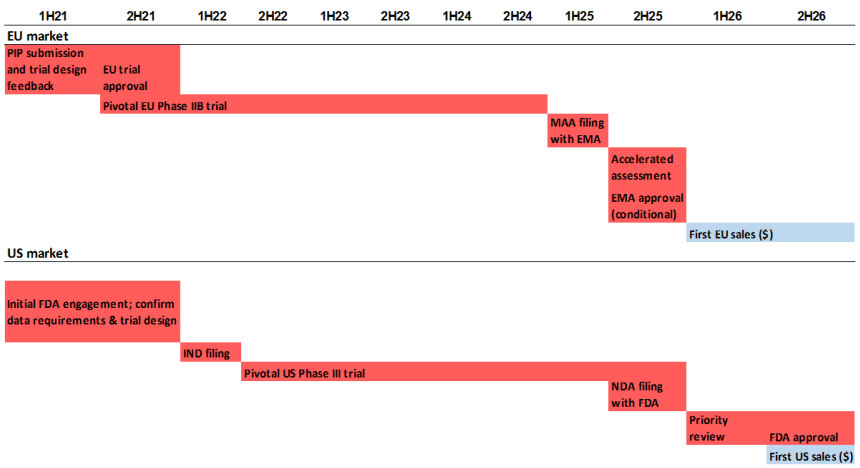
Year-end June (AUD)	FY19A	FY20A	FY21F	FY22F	FY23F
NPAT rep ($m)	-2.9	-5.9	-18.4	-6.5	-4.3
NPAT norm ($m)	-2.9	-5.9	-18.4	-6.5	-4.3
Consensus NPAT ($m)			-4.6	-10.4	
EPS norm (cps)	-0.8	-1.3	-3.4	-1.0	-0.6
EPS growth (%)	36.7	-71.1	-161.9	70.7	42.3
P/E norm (x)	-12.1	-7.1	-2.7	-9.2	-16.0
EV/EBITDA (x)	-15.7	-7.9	-2.5	-6.9	-10.0
FCF yield (%)	-5.5	-7.5	-33.3	-2.9	-2.6
DPS (cps)	0.0	0.0	0.0	0.0	0.0
Dividend yield (%)	0.0	0.0	0.0	0.0	0.0
Franking (%)	0	0	0	0	0

Source: Company data, Wilsons estimates, Refintiv

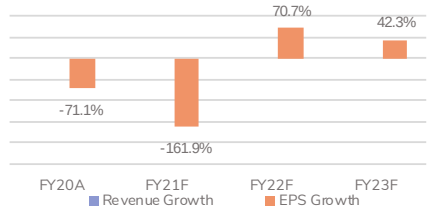
Wilsons Equity Research
Regulatory disclosures

Sum of the parts valuation summary	Valuation	PT
WACC (%)	10.0	
EU Market		
NPV FCF FY26 ($m)	1544.3	
Unrisked ROV ($m)	972.7	
Probability success	46%	
Risk-adj ROV ($m)	431.9	
Unrisked val ($/sh)		1.01
Risk-adj val ($/sh)		**0.45**
US Market		
NPV FCF FY27 ($m)	601.8	
Unrisked ROV ($m)	323.7	
Probability success	40%	
Risk-adj ROV ($m)	120.9	
Unrisked val ($/sh)		0.33
Risk-adj val ($/sh)		**0.12**
SOTP val (unrisked)		$1.34
SOTP val (risked)		**$0.57**

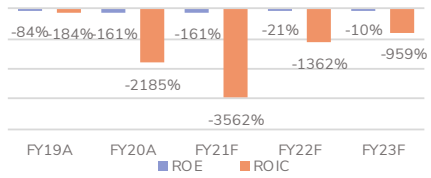
Base case scenario timeline assumptions for ATL1102



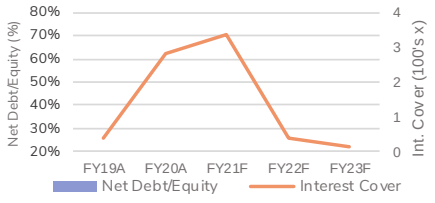
Growth rates



Returns



Solvency



Interims ($m)	1H20A	2H20A	1H21E	2H21E
Sales revenue	0.0	0.0	0.0	0.0
EBITDA	-4.3	-1.5	-5.7	-12.7
EBIT	-4.3	-1.6	-5.7	-12.7
Net profit	**-4.3**	**-1.6**	**-5.7**	**-12.7**
Norm EPS	**-1.0**	**-0.3**	**-1.1**	**-2.2**
EBIT/sales (%)				
Dividend (c)	0.0	0.0	0.0	0.0
Franking (%)	0.0	0.0	0.0	0.0
Payout ratio (%)	0.0	0.0	0.0	0.0
Adj payout (%)	0.0	0.0	0.0	0.0

Financial ratios

	FY17A	FY18A	FY19A	FY20A	FY21F	FY22F	FY23F	FY24F
PE (x)	-5.4	-7.7	-12.1	-7.1	-2.7	-9.2	-16.0	-3.0
EV/EBITDA (x)	-16.8	-19.9	-15.7	-7.9	-2.5	-6.9	-10.0	-2.0
Dividend yield (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
FCF yield (%)	-5.5	-4.4	-5.5	-7.5	-33.3	-2.9	-2.6	-40.4
Payout ratio (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Adj payout (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Profit and loss ($m)

	FY17A	FY18A	FY19A	FY20A	FY21F	FY22F	FY23F	FY24F
Sales revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EBITDA	-2.7	-2.3	-2.9	-5.8	-18.3	-6.6	-4.6	-22.9
Depn & amort	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1
EBIT	**-2.7**	**-2.3**	**-2.9**	**-5.9**	**-18.4**	**-6.7**	**-4.7**	**-23.0**
Net interest expense	-0.1	0.0	-0.1	0.0	-0.1	-0.2	-0.4	-0.4
Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Minorities/pref divs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Equity accounted NPAT	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net profit (pre-sig items)	**-2.8**	**-2.3**	**-2.9**	**-5.9**	**-18.4**	**-6.5**	**-4.3**	**-22.6**
Abns/exts/signif	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Reported net profit	**-2.8**	**-2.3**	**-2.9**	**-5.9**	**-18.4**	**-6.5**	**-4.3**	**-22.6**

Cash flow ($m)

	FY17A	FY18A	FY19A	FY20A	FY21F	FY22F	FY23F	FY24F
EBITDA	-2.7	-2.3	-2.9	-5.8	-18.3	-6.6	-4.6	-22.9
Interest & tax	-0.1	0.0	-0.1	0.0	0.1	0.2	0.4	0.4
Working cap/other	-0.1	0.0	0.1	1.9	0.7	4.9	2.8	1.2
Operating cash flow	**-2.9**	**-2.3**	**-2.9**	**-3.9**	**-17.6**	**-1.6**	**-1.4**	**-21.3**
Maintenance capex	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Free cash flow	**-2.9**	**-2.3**	**-2.9**	**-3.9**	**-17.6**	**-1.6**	**-1.4**	**-21.3**
Dividends paid	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Growth capex	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Invest/disposals	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Oth investing/finance flows	-0.1	-2.7	2.3	-0.4	-2.0	-1.8	0.0	0.0
Cash flow pre-financing	**-3.0**	**-5.0**	**-0.6**	**-4.3**	**-19.6**	**-3.4**	**-1.4**	**-21.3**
Funded by equity	0.1	5.0	1.6	5.5	33.5	30.0	0.0	0.0
Funded by debt	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Funded by cash	2.9	0.0	-1.0	-1.2	-13.9	-26.6	1.4	21.3

Balance sheet summary ($m)

	FY17A	FY18A	FY19A	FY20A	FY21F	FY22F	FY23F	FY24F
Cash	1.9	1.9	2.9	4.1	18.0	44.6	43.3	21.9
Current receivables	0.4	0.3	0.6	0.7	0.5	0.8	0.8	1.1
Current inventories	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net PPE	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Intangibles/capitalised	0.0	0.0	0.0	0.0	0.2	0.2	0.2	0.2
Total assets	**2.5**	**4.8**	**3.7**	**5.4**	**19.2**	**46.1**	**44.8**	**23.8**
Current payables	0.4	0.3	0.6	0.3	0.4	0.5	0.7	0.6
Total debt	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total liabilities	**0.7**	**0.6**	**0.9**	**0.8**	**0.9**	**1.1**	**1.3**	**1.2**
Shareholder equity	**1.9**	**4.2**	**2.8**	**4.5**	**18.2**	**45.1**	**43.5**	**22.6**
Total funds employed	**1.9**	**4.2**	**2.8**	**4.5**	**18.2**	**45.1**	**43.5**	**22.6**

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Glossary

Acromegaly	A rare growth hormone disease that causes enlargement of hands, feet and facial features. Acromegaly is caused by excessive growth hormone production often caused by tumours on the pituitary glands.
Antisense oligonucleotide	These are small, single-stranded nucleic acids that bind to a specific target mRNA sequence and can silence that part of the genetic code to prevent it from being used to drive protein expression. These oligonucleotides can essentially act like biological inhibitors of gene expression.
ATL1102	An antisense oligonucleotide drug by Ionis Pharmaceuticals that blocks CD49d (an inflammatory marker involved in disease processes). ATL1102 is under exclusive license of Antisense Therapeutics for development and commercialisation.
ATL1103	An antisense oligonucleotide drug by Ionis Pharmaceuticals that blocks the growth hormone receptor which is involved in the disease pathology in acromegaly. ATL1103 is under exclusive license of Antisense Therapeutics for development and commercialisation.
CD49d	CD49d is a heterodimer that makes up one half of the integrin receptor, VLA-4. CD49d is upregulated in several disease states including leukaemia, and has been shown to be a biomarker for DMD disease progression and severity; with higher CD49d expression in more advances stages of the disease (i.e. non-ambulatory DMD).
Cell therapy	This involves transplantation of viable cells into the target organ/area where there is an affected disease process occurring. In the case of DMD, cell therapy is being suggested as a way to regenerate muscle fibres and correct the lack of dystrophin (by injecting cells with functioning dystrophin genetic sequences).
DMD	Duchenne Muscular Dystrophy (DMD) is a rare, genetic, degenerative disease affecting mostly boys that causes breakdown of muscles leading to an inability to walk or move, ultimately leading to premature death.
Dystrophin	Dystrophin is a protein involved in muscle connectivity and function. The dystrophin gene is defective in DMD leading to a lack of functional dystrophin production which leads to disease pathology. Correction of this dystrophin deficit is the underlying goal of disease modifying DMD therapies.
Exon skipping	This is a molecular technique that causes cells to skip over faulty sections of genetic code (the mutated exon) so that a truncated, but functional, protein can still be made which can reverse disease pathology caused by the absence of said protein.
Genetic mutation	This is an alteration in genetic code (i.e. RNA) that can sometimes result in deleterious effects rendering the gene inactive or pathogenic. Keeping in mind that not all genetic mutations are harmful and they are responsible for diversity and evolution within the biological world.
Gene therapy	A technique to correct genetic deficits that underlie diseases. Simply, a “corrected” gene can be inserted via a virus-derived transport system to the cells/organs of interest and help to correct the gene defect hopefully mitigating the issue being caused correcting the disease.
Inflammation	On part of a complex process by which the body responses to insult. It is a protective response involving recruitment of different immune cells, mediators and blood vessels that often causes pain, swelling and redness.
Leukocyte	Leukocytes, more commonly known as white blood cells, are the foundation of the body’s immune system – that is, the defence system that protects the body from infection or foreign invasion.
Lymphocyte	Lymphocytes are a type of white blood cell that are involved in innate and adaptive immune responses. There are different subsets of lymphocytes including T cells, B cells and Natural Killer (NK) cells, each with their own functions and purposes within the system.
mRNA	Messenger ribonucleic acid (mRNA) is a double stranded nucleic acid essential for gene expression. mRNA is the messenger code that is used to direct the expression of proteins within the body that can go on to have biological effects.
VLA-4	Very late antigen-4 is an integrin dimer expressed on leukocytes that is involved in immune response and inflammatory processes. VLA-4 is a dimer comprised of two subunits that sit within the cell membrane; CD29 and CD49d, the latter being the target of ATL1102.

Investment view – Antisense Therapeutics

Investment summary

Antisense is a development stage biotech focused on antisense oligonucleotide drugs for rare diseases.

Antisense Therapeutics is an Australian biotechnology company focused on the clinical development of antisense RNA therapies for rare diseases; specifically Duchenne muscular dystrophy (DMD) and acromegaly. Antisense is a clinical development stage company with expected first material revenues forecast in FY26 from anticipated EU approval and sales of ATL1102 for treatment of late stage DMD.

DMD market concentrated with limited existing options and high ASPs.

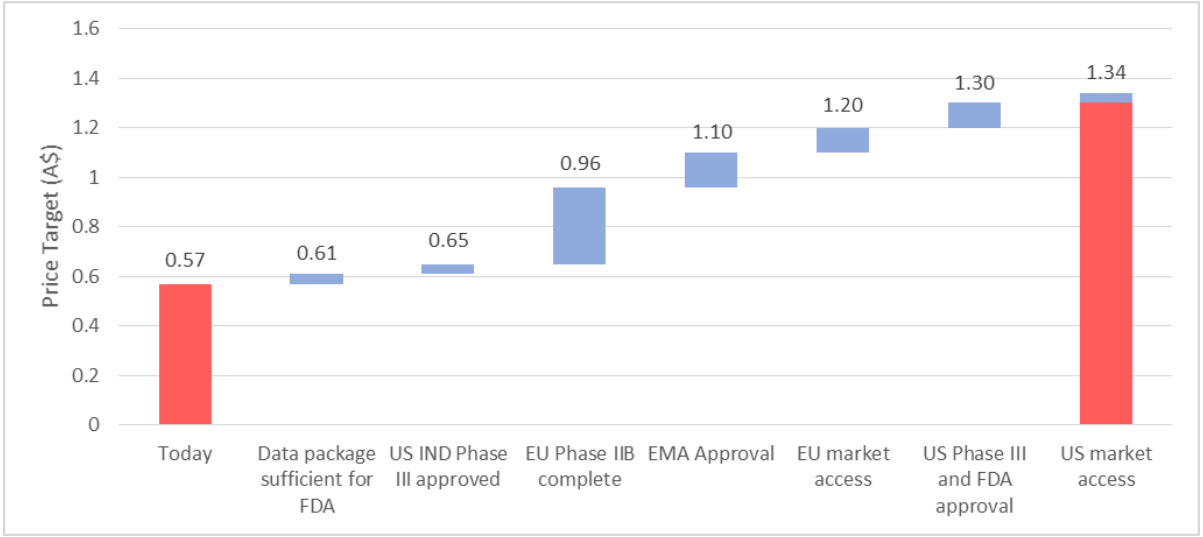
DMD market a priority. We assess Antisense has significant revenue potential given the available unaddressed DMD market with a low level of competition (in non-ambulant patients), the high selling price (ASP) that can be demanded and the prolonged treatment period required to keep this degenerative disease at bay (i.e. continuous lifelong treatment). The incumbent standard of care for these patients is long term corticosteroid use which is associated with incremental benefit in some, yet significant longer term side effects (and not tolerated by many), making it an area of desperate need. Additionally, Antisense are well placed from a regulatory standpoint, having received Orphan Drug Designation (ODD) from both the EMA and FDA for ATL1102 (and ATL1103) and have been granted Rare Paediatric Disease Designation providing a future Priority Review Voucher (PRV) option from the FDA which is a useable asset to expedite NDA review or can be sold on a secondary market (~$100M).

Commercial strategy: independent commercialisation in major markets with opportunities for indication expansion. We believe Antisense have a clear commercial strategy for independent ATL1102 development that is appropriate for the rare disease markets they are entering, which are concentrated and adoption relies upon KOL input, clinician visibility (i.e. in the form of research presentations) and clear interactions with advocacy groups. We believe they are focusing on these parts of their strategy in preparation for their possible EU and US market entries, which, if can be completed successfully, pose significant market growth opportunities. Opportunities to expand the ATL1102 indication from DMD into other areas, including MS, are also still in the pipeline strengthening their portfolio position.

PT of $0.57 per share with upside to $0.96 on a 3-5 year view.

Valuation development over the next 3-5 years. We have forecast Antisense as being EBITDA positive in 1H26, meaning there is a significant period ahead of capital intensive investment with no revenues which investors much appreciate and accept. Keeping this time horizon in mind, the potential revenues from the DMD market are significant and we assess ATL1102 has good supportive evidence to take a meaningful share in the non-ambulant population which supports our OVERWEIGHT rating and risked, 12 month price target of $0.57 per share. Figure 1 shows how our price target shifts with major inflection points in the model being unrisked over the commercialisation cycle for both major markets. Within a 3-5 year period we could hope to reach $0.96 target price following successful completion of EU Phase IIB trial.

Figure 1. Price target build over time with each model stage being unrisked to reach PT of $1.34/share



Source: Wilsons

Investment merits

- **Phase IIB development- the lowest risk, highest upside point to engage with biotechnology assets**. Antisense's ATL1102 is planning to enter Phase IIB trials next year, seeking to replicate results seen this year in Phase II. The Phase II results drew a convincing link between the proposed mechanism of action and pre-specified clinical endpoints. Phase IIB seeks to confirm these observations in a larger number of patients with adequate controls (i.e. placebo). Success in Phase IIB could to lead to approvals and a launch into a lucrative Orphan Drug marketplace. In our experience the risk-reward in biotechnology assets is optimal entering Phase IIB development.

Phase IIB development is key biotech investment entry point.

- **Clear untapped market niche in DMD with large revenue potential.** Antisense has a huge growth opportunity ahead of them in DMD, with their asset ATL1102 having the potential to capture up to 30% of the non-ambulant DMD market given the limited options available (and in the pipeline) for this patient subset. We estimate peak annualised net sales of > $800m, with limited risk of near term competitors in this non-ambulant population which accounts for over half of the current DMD patient cohort.

Antisense has a huge growth opportunity ahead of them in DMD.

- **Drug mechanism provides broad applicability.** ATL1102's mechanism of action, that being, inhibition of inflammation processes in the muscle via blockade of CD49d, has broad applicability to patients with DMD, as opposed to some current approved products which are restricted to genetic patient subsets (i.e. Exondys, Vyondys). For this reason we see the potential market share ATL1102 may achieve as greater than these existing approved products.

- **Phase II ATL1102 data shows clear proof of concept**. The Phase II data, despite being from a small, open-label trial, highlights that the underlying mechanism of action of ATL1102 is leading to functional changes in muscle strength. The lymphocyte data, coupled with the MRI data show that inflammatory cells are suppressed with ATL1102 treatment leading to stabilisation of the fat/muscle fraction (as opposed to deterioration) which in turn appears to have a functional readout in the performance of upper limb (PUL2.0) measure. Interpretation of the clinical validity of this change in upper limb function is challenging to interpret, yet discussions with specialists have highlighted that gains, or even stabilisation, in upper limb strength can make large impacts on disease progression and quality of life in non-ambulant patients. This is an important focus for half of the DMD population that are currently wheelchair bound and progressively losing upper limb function (despite standard of care) which drives further deterioration of lung and cardiac capacity.

Drug mechanism and proof of concept shown in Phase II study. See **Appendix A.2.**

- **Several well developed assets in their portfolio.** Antisense's advanced ATL1103 program in acromegaly provides a second opportunity for market entry, with the most likely outcome being a cash injection following a licensing agreement for this asset's Phase III development. Having a second asset ready for Phase III development reduces the risks associated with a single asset company. Furthermore, ATL1102 has been explored for other indications including Multiple Sclerosis (MS) with some advanced clinical results to support further development in these indications which could be continued should capital become available.

- **Ex-Sarepta expertise on hand.** Antisense have valuable experience from Sarepta Therapeutics, having two team members previously employed there, including being engaged in key activities related to launch of Exondys into the US market. William Goolsbee and Gil Price both bring differing experience and expertise from their Sarepta history. Dr Price having well established connections and networks into the US DMD investor base, key opinion leaders (KOLs) and patient advocacy groups (that wield significantly more power in the regulatory/drug development in DMD than might be expected) is an asset in longer term US market plays with ATL1102.

Sarepta now dominant player in DMD market following two FDA approvals in 2016 and 2019 for exon skipping drugs. Now > US$400M annual revenues from these assets.

- **FSE dual listing provides EU visibility to investor and advocates.** The recent Frankfurt dual listing (FSE:AWY) on November 23rd provides Antisense an opportunity to expand their investor base and exposure into Europe. Parental advocacy groups in DMD are known to be very active in influencing regulatory decisions as well as, in some cases, providing funding support for clinical development programmes and therefore getting in front of these groups (which may occur as a by-product of EU listing) is potentially beneficial.

EU listing may be beneficial for expanding investor base and advocacy base support.

Investment risks

- **Clinical development and regulatory risks.** As with any clinical development stage biotech company there are significant investment risks associated with the future clinical outcomes of drug trials and subsequent regulatory marketing approvals in key jurisdictions. Thus far, Antisense has solid Phase II data to support their DMD and acromegaly development programmes, noting that on average ~40% of drugs fail at the Phase IIB/III trial stage never making it to an NDA filing (however rare disease programmes often have higher success rates overall)[1]. One key factor that elevates clinical risk, is the absence of placebo-controlled data for ATL1102 thus far in DMD which will be gathered first in their EU Phase IIB pivotal study. Comparisons to published comparable control cohorts show efficacy of ATL1102 yet head to head comparison to placebo is currently lacking.

  Valuation premised on ATL1102 approval in DMD in at least one significant market.

- **Reliance on Ionis licensing agreement.** Antisense's licensing agreement with Ionis Pharmaceuticals for the exclusive global rights to ATL1102 and ATL1103 is paramount to their ability to commercialise these assets driving their revenue strategy. We understand that the terms of this agreement allow Antisense exclusive, global rights to both compounds, not restricted to any indication, but require Antisense to pay royalties on any future commercial revenues, notwithstanding any future on-licensing partnerships.

- **Longer term shift in DMD patient cohort phenotype.** Pipeline agents in development for DMD include disease modifying therapies (i.e. gene therapy, exon skipping) which may alter the course of the DMD patient landscape in the years to come (dependent on their efficacy) with the proportion of patients reaching non-ambulatory status being different; be it smaller by proportion, significantly delayed (in terms of years to loss of ambulation) or a less severe disease phenotype that includes less of an inflammatory component (the target for ATL1102). This poses possible risk to future addressable market assumptions.

  Possible longer term reduction in addressable market (non-ambulant) with newer disease modifying therapies in next 10 years.

- **Competitive technology risk.** There are quite a number of active participants in the DMD market with late stage products in Phase III development – several of which we expect to read out within the next 6-18 months. The pipeline is quite unique, in the sense that the diversity of mechanisms being explored is vast, and it appears that a number of niche approaches can be carved out for specific patient subsets with different genetic disease signatures (i.e. specific exon skipping approaches). Gene therapies are also being explored and have the potential to transform the disease market, yet there are questions around the durability of these approaches given a large proportion of the market is paediatric and there is quite a high turnover rate of the target cells. Should any number of the late stage products in development become approved they would present a competitive risk to Antisense and their addressable market share. This risk is somewhat heightened by the number of late stage products in development, in addition to the additional products in earlier phases which has similar promising data. Antisense have some advantage here given the number of products in development for non-ambulant patients is markedly less than the earlier ambulant DMD population.

  Overview of DMD competitive landscape given in ***Appendix A.1.1; Table 11.***

- **Intellectual property risk.** The ATL1102 and ATL1103 candidates are protected by patent rights owned by Ionis, exclusively licensed to Antisense, in addition to patent families owned by Antisense. We have not conducted any explicit analysis of patent validity or freedom to operate. Antisense do have a family of patents around the method of use of ATL1102 for treatment of MS, DMD and AML, in addition to protection of ATL1103 for growth disorders and in combination with somatostatin agonists. Several recent patent applications have yet to be granted to Antisense including their applications to protect ATL1102 for use in MS (PCT/AU/2018/050598) and additional muscular dystrophies (PCT/AU2018/051353, US16/404561). Antisense do have further data and market exclusivity beyond patent protection in the form of their Orphan Drug Designations (ODD) in US/EU for ATL1102 and ATL1103 which afford 7-12 years of market exclusivity (e.g. FDA umbrella exclusivity rule).

- **Management risk.** Antisense has been a public company since 2000 with some advanced clinical success in development of ATL1102 for MS and ATL1103 for acromegaly. We note a somewhat mixed track record of R&D investment and strategy decisions regarding prior programs, and appreciate that a majority of the board and management have been with company for a decade or

  Directions of prior advanced clinical programs have left some questions for investors.

[1] Thomas et al. (2016) Clinical Development Success Rates 2006-2015. BIO Industry Report. 1-28.

more. There are some strategic management risks if the existing administration are unable to deliver a focused development plan in DMD with hopeful commercial outcomes for investors in the next 5-7 years. Recent additions to the Antisense team including Dr Gil Price, for the purposes of supporting a focused DMD development effort, are reassuring.

- **Valuation risk.** Our valuation is premised on a 43% overall probability of commercial success of ATL1102 for DMD in two markets (EU and US). European market success is more important to valuation risk. Should the asset (ATL1102) fail to show efficacy in the Phase IIB trial there is significant downside risk, notwithstanding that potential revenues from other assets/indications have not been factored into the valuation at this time.

Risk valuations are premised on somewhat binary outcomes of success for clinical drug development, all of which are uncertain.

- **Financial risk.** As with any clinical stage company, there are inherent risks associated with cash flow and access to development capital, given that we do not expect sales revenues for at least five years, with significant R&D expenditure required within this period. Access to sufficient capital to fund key development milestones is a financial risk associated with this company. We believe this risk has recently been mitigated somewhat by their dual listing, however of course continues to be a risk and relies upon a dedicated investor base with long term conviction in their investment.

Valuation

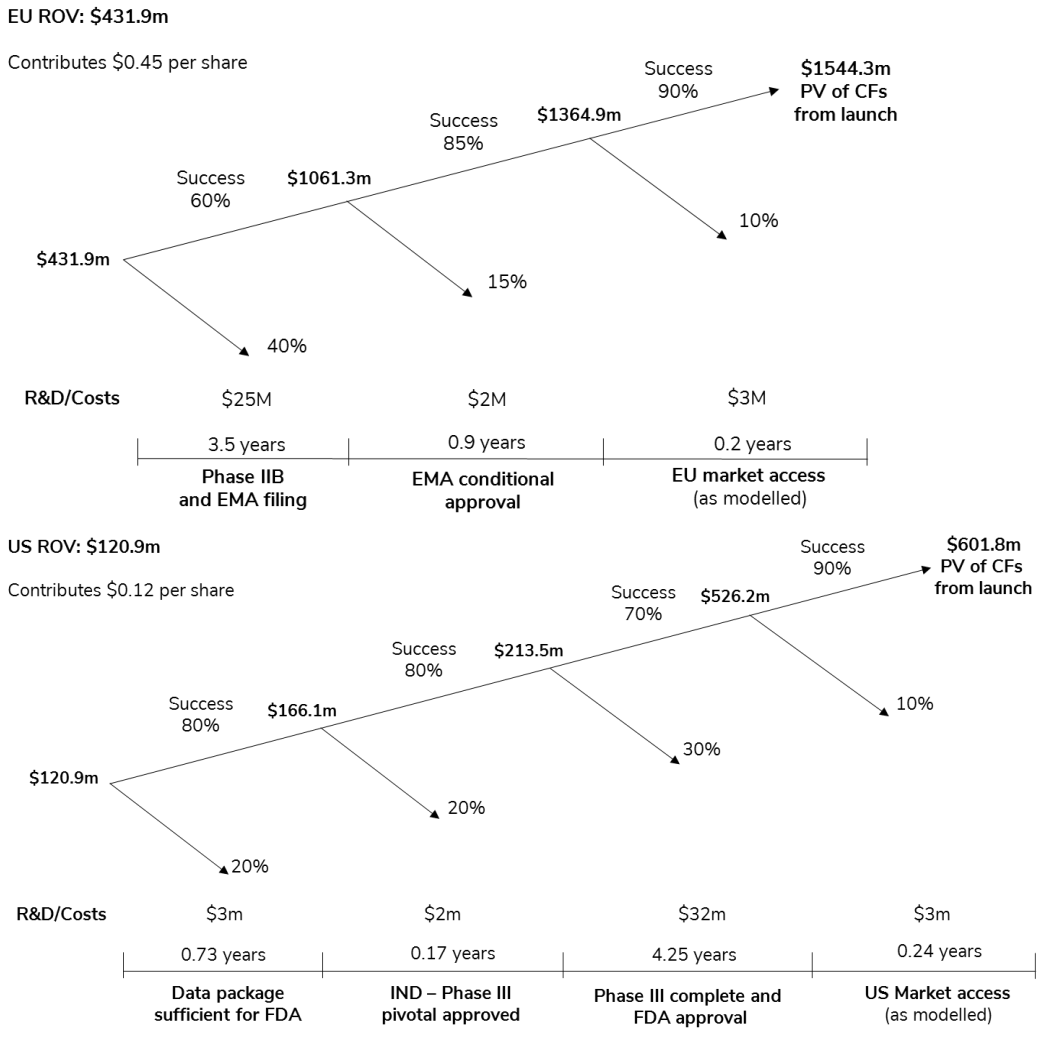
Risk-adjusted real options price target of $0.57/share

We have used a sum of the parts real options valuation approach based on the forecast commercialisation outcomes of ATL1102 in the major European and US markets. This valuation approach leads us to our 12 month price target of $0.57 per share comprised of $0.45 from European market access and $0.12 for US market access. Our unrisked valuation is $1.34 per share.

At this point in time we have not ascribed any value to ATL1103 (in terms of price target attribution) given that it is not the current priority asset in Antisense's commercialisation strategy. Any partnership deal/revenues from ATL1103 would be accretive to valuation. Similarly, we have confined ATL1102's contribution to valuation to DMD exclusively, despite there being other potential indication opportunities (i.e. MS).

Below (Figure 2) we highlight our real-options DCF decision tree for both the EU and US ATL1102 markets. Each forecast cash flow has been discounted by WACC (10%) with real probabilities of success used for each stage-gate in the decision tree. This provides visibility on our valuation approach and investors can track the upside values should each option succeed, which contributes to our sum of the parts (SOTP) price target of $0.57. If all success probabilities are equalled to 100% success we achieve our unrisked valuation of $1.34 (unrisked staged PTs shown in Figure 1).

Figure 2. Real options DCF trees for EU and US markets that comprise our Sum of the Parts Valuation



Source: Wilsons

Valuation sensitivities

Our real options DCF approach factors in probabilities of success for each clinical stage and key milestones associated with market authorisation and access. We have modelled five scenarios to highlight the aspects driving significant variance to valuation and test the robustness of our valuation base case.

Market penetration and ASP are the greatest drivers of valuation variance. Encouragingly, lack of FDA approval (i.e. US market access) does not materially affect valuation, which is positive given the disparity between EMA and FDA decisions regarding past DMD drug approvals.

Table 2. Drivers of valuation sensitivity are market penetration and ASP.

Sensitivity	Assumption	ΔPT	Revised PT range
Market Penetration	50% change of assumed market penetration.	± 56%	$0.26 – 0.90
ASP	20% change to ATL1102 ASP assumption.	± 22%	$0.45 – 0.70
Jurisdiction approvals	No FDA approval following Phase III trial in US.	- 22%	$0.45
R&D timelines and spend	2 year delay in US market approval/access and additional $15M capital expenditure	- 6%	$0.54
US partnering	Pharma partner sought to commercialise US market (as opposed to independent)	-14%	$0.49

Source: Wilsons' estimates

Combining these factors we have created our "bull" and "bear" case valuation sensitivities;

Bear case assumes: PT= $0.38

- 1 year delay in EMA market approval – first revenues FY27.
- 15% reduction in market penetration in EU and US jurisdictions.
- 10% reduction to US ASP and 15% reduction to EU ASP.
- 1 year delay in US market approval to FY28 with additional $5M in associated R&D spend.

Bull case assumes: PT = $0.73

- 20% lift in market penetration in both EU and US jurisdictions.
- 10% increase to ASPs in both US/EU markets.
- Data package accepted by FDA (removes additional study expense/time/risk)
- Possible expansion off-label to ambulant DMD cohort – 5% patient cohort expansion.

Figure 3. Bull and Bear cases for ANP valuation based on sensitivity scenarios.

Source: Wilsons

It is important to note that both scenarios (bull & bear) assume some degree of successful marketing approval of ATL1102 for a DMD indication. Failure of ATL1102 in DMD would likely cause the ANP share price to fall materially and the company to be valued at or below their remaining cash reserves.

Independent vs partnered US commercialisation of ATL1102.

We have also analysed the impact to valuation should Antisense seek a partner to commercialise ATL1102 for DMD in the US market (not our base case scenario). We assess a desirable opportunity for an incoming pharma partner to license ATL1102 for DMD in the US market, likely in FY24, which would potentially allow for top-line data from the Phase IIB DMD trial to inform the agreement terms.

Partnership with a third party for US commercialisation has only a small impact to price target (-14%) based our partnering assumptions, which map a scenario that is reasonable from a pharma partner perspective (~62% of pie).

Detailed partnering scenario analysis in **Appendix A.4.**

Catalysts

Valuation catalysts

We expect Antisense's share price to increase as a function of their clinical development of ATL1102 in DMD, with each incremental piece of clinical evidence (Phase IIB and III trials) and regulatory milestone achieved removing associated risk and closing the gap to our un-risked program valuations.

Clinical development progress with ATL1102. We assess five near term clinical and regulatory catalysts tied to valuation, each associated with regulatory approval of INDs, initiation of pivotal clinical trials and top-line data. These are included in Table 4 below.

Financial reporting by DMD sector peers. Tracking revenues and market growth for DMD market peers will give us insight into the market share and uptake rates of these relatively new DMD agents. Key peers of interest include Sarepta Therapeutics (SRPT) and PTC Therapeutics (PTCT) which have approved DMD agents in both the EU and US markets.

Monitoring of clinical trial results from major peers. There are a number of Phase III and late Phase II trials set to report from competitors within the next 6 – 12 months, including some first-in-class products. These will help to clarify the future DMD landscape which ATL1102 may be entering in the event of an FY25 conditional approval in Europe. The key results in the near term are included in Table 4 below.

Potential partnership opportunities in acromegaly. Any partnering opportunities for assets other than ATL1102 in DMD, would be valuation catalysts with upfront fees, milestones and possible future royalties.

Table 4. Catalysts for Antisense over the next two years

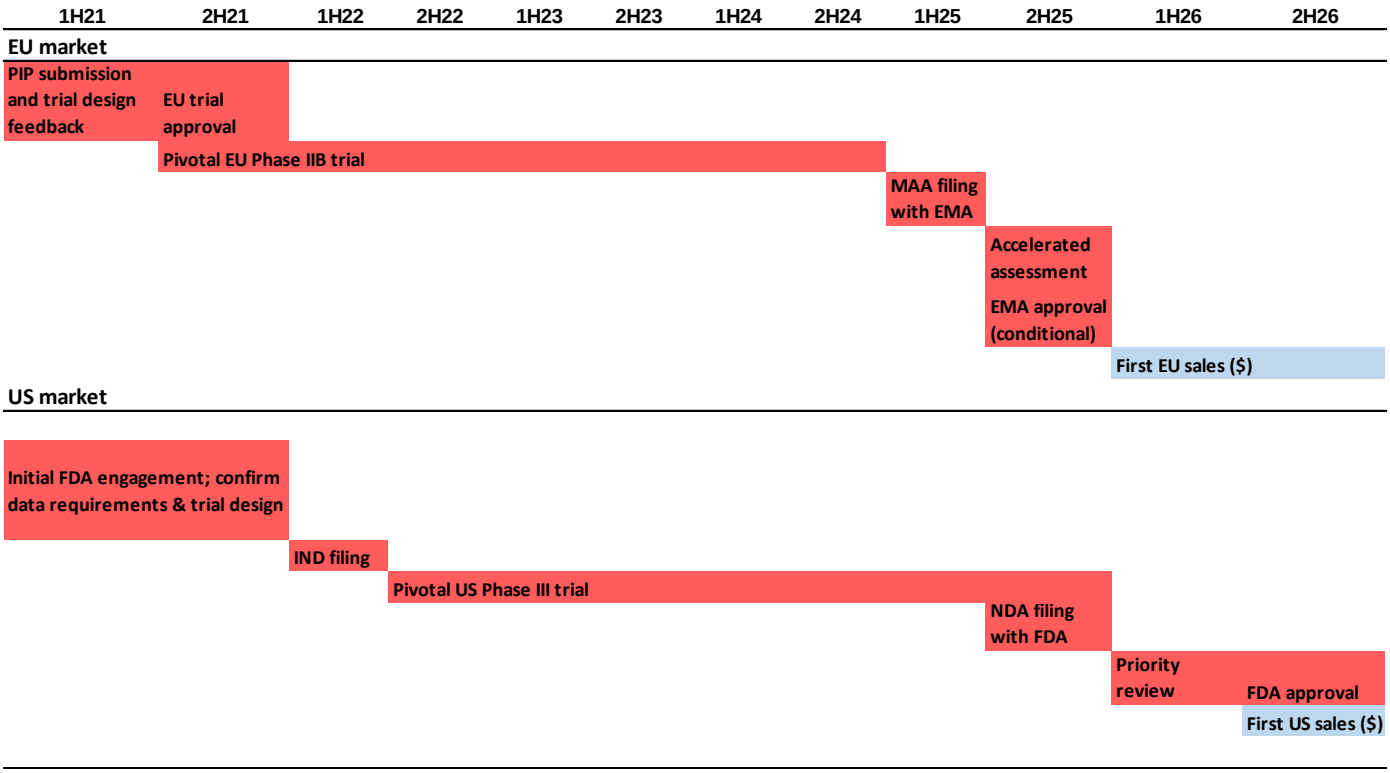
Date (CY)	Company	Event	Significance
1Q21	**ANP**	**PIP submission to EMA**	**Submission of finalised design plan to EMA for Phase IIB pivotal EU trial which has been discussed with EMA scientific advisory committee prior.**
1Q21	**ANP**	**Initial FDA engagement**	**FDA meeting to discuss data package and proposed Phase III pivotal trial plan for ATL1102 in US.**
1Q21	SRPT	Casimersen FDA decision	Sarepta will have a decision regarding their new Exon 45 skipping drug Casimersen on Feb 25th, 2021. Takes share from any amenable patients (<5%)
1Q21	Various	4Q20 earnings for US and EU peers	Update on market growth, competitive positioning
2Q21	**ANP**	**FDA feedback and IND filing.**	**FDA feedback on data package acceptability; notification of subsequent studies if required and/or IND filing for Phase III trial.**
2Q21	SANN	Top-line data Vamorolone trial	Santhera's VISION-DMD study has 6 month readout to support possible 4Q21 NDA submission. Also anti-inflammatory MOA so supports hypothesis.
2Q21	Various	1Q21 earnings for US and EU peers	Update on market growth, competitive positioning
2H21	**ANP**	**Phase IIB approval ATL1102**	**Approval/initiation of (potentially) pivotal ATL1102 EU DMD trial**
3Q21	Various	2Q21 earnings for US and EU peers	Update on market growth, competitive positioning
4Q21	Various	3Q21 earnings for US and EU peers	Update on market growth, competitive positioning
1H22	**ANP**	**Initiation of Phase III US trial**	**Assumes IND acceptance by FDA and sufficient capital to start Phase III DMD pivotal in US.**
1H22	FGEN	Possible first data from LENTOS study	Possible first data from FibroGen's study of pamrevlumab in DMD, with unique MOA focused on muscle connective tissue. Significant as this study is in non-ambulant boys – one of the only direct competitors to Antisense in this regard.
1Q22	Various	4Q20 earnings for US and EU peers	Update on market growth, competitive positioning
1H22	PFE	Top-line data for Pfizer's gene therapy Phase III	Top-line data reported for pivotal gene therapy trial of PF-06939926 in DMD. This is in ambulatory patients with intent of single infusion being curative which could transform existing market if effective in longer term (less non-ambulant).
1H22	Italfarmaco	Phase III results Givinostat	Phase III results for Italfarmaco's therapy aimed at building/slowing muscle degeneration. Unlikely to compete initially in non-ambulant population market.

Forecasts

Revenue model

We have forecast sales revenues for Antisense predicated on approval of ATL1102 for DMD first in Europe and then in the US market. No revenues (or significant costs) from the further development of ATL1103, or ATL1102 for indications other than DMD, have been factored into our model thus far given they are secondary priorities for Antisense at this point in time.

Figure 4. Base case scenario timeline assumptions for ATL1102 development milestones and DMD market entry.



PIP: Paediatric Investigational Plan. IND: Investigational New Drug application. NDA: New Drug application; MAA: Marketing Authorisation Application.
Source: Wilsons

Key assumptions of our base case scenario:

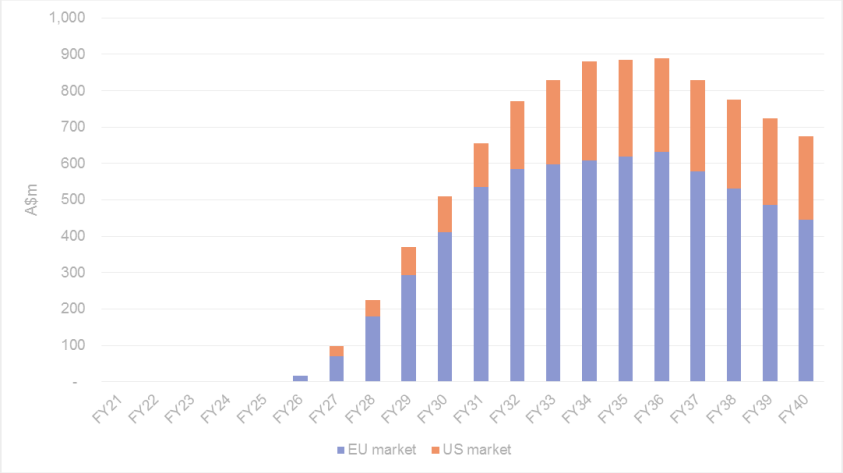
- ATL1102 receives expedited EMA approval based on acceptable Phase IIB data in 2H25.
- Independent launch of ATL1102 in EU markets – within initial revenues in early 1H26.
- IND Filing for US pivotal Phase III trial in 1H22 (assuming positive initial FDA engagement).
- Initiation of Phase III US pivotal trial in 2H22 - with top-line results in 2H25 to support NDA filing.
- Priority/expedited FDA review and approval for US market in 2H26.
- US market entry in late FY26 and first US revenues in 1H27.
- Approved label restricted to non-ambulant DMD population.
- Reach peaks of 12% and 8% total DMD market share in EU and US, respectively.
- Potential sale of PRV in FY25 not included in this revenue model (product sales specific – Figure 5).
- European TAM of ~$1.7B (€1.1B) and US TAM of ~$900M (US$630M)

Base case assumptions are backed by predicates in the DMD market. An expedited EMA approval is predicated by the Translarna (PTC) conditional approval in 2014. This was granted based on data from two trials (Phase II & III) which failed to meet primary endpoints. Orphan and rare disease therapies are routinely approved based on clinical data that is not of the same comprehensive standard as for non-rare diseases (i.e. in terms of randomisation, blinding, placebo-controls, patient numbers etc)[2].

Clinuvel Pharmaceuticals (ASX:CUV) is an Australian biotech peer operating in the rare and orphan disease market that have successfully managed to accomplish effective European distribution of their drug, SCENESSE, given the concentrated number of physicians and treatment centres operating in their respective rare disease market, and are now entering the US market with the same approach.

We view a similar landscape of the DMD market in both EU and US regions; that being, treatment of DMD patients is typically confined to a small number of specialist centres and managed by a relatively few KOLs supported by strong advocacy networks. Given the relatively small number of addressable patients (<5K) we believe Antisense can effectively manage market entry in the absence of a large global commercial partner and distribution network. This approach also allows Antisense to build relationships with clinicians and generate a stronger brand and market awareness within key clinical and advocacy groups which are key to effective market penetration in rare diseases.

Figure 5. ATL1102 DMD revenue model assumptions and forecast summary.



Source: Wilsons' estimates.

Table 5. Key Revenue Assumptions

	EU5	US
Launch year	2025	2026
Exclusivity period^	2037	2032
Peak sales (A$)	632m	271m
Maximum patient penetration	12%	8%
Non-ambulant penetration	30%	25%
TAM (A$)	1740m	895m
Year of PRV sale*	-	2025
Sale price (A$)	-	100m

^ noting that biosimilars are not generics and market shifts are less pronounced following loss of exclusivity. 12 year EU exclusivity vs 7 year minimum US market exclusivity.
*Priority Review Voucher (PRV) sale assumed when received at time of NDA submission to FDA and sold on secondary market. A$100M sale price conservative.

Source: Wilsons

Our revenue forecasts are predicated on our market model estimates for the DMD population (Table 6) which takes into account; a) existing treatments and the successfully treated proportion of the population; b) ambulatory status; c) DMD incidence and population growth in each region; d) pipeline competitor products and their potential market share; e) ATL1102 market penetration.

We assume 2-3% annual growth in the DMD patient population which is in line with estimates of overall population growth and stable DMD incidence rates. Noting that the DMD population could grow in absolute number given that patients are living longer due to improved treatments coming to market.

Our peak sales estimates of ~A$630m and A$270m are also in line with predicates in the market, noting that Sarepta's Exonyds 51 has already ramped to >A$500m within 3 years of US market launch with increasing sales QoQ, and is targeting a much smaller patient population (Exon 51 amendable DMD only).

[2] Logviss et al. (2018) Characteristics of clinical trials in rare vs. common diseases: A register-based Latvian study. *PLoS One*. 13(4): e0194494.

Table 6. Addressable DMD market model for ATL1102 FY26–35e

		FY26	FY27	FY28	FY29	FY30	FY31	FY32	FY33	FY34	FY35
EU MODEL											
EU total DMD population		**30,021**	**30,694**	**31,367**	**32,041**	**32,716**	**33,391**	**34,067**	**34,744**	**35,421**	**36,099**
EU Treated population		1,201	1,535	1,568	1,602	1,636	1,670	1,703	1,737	1,771	1,805
EU Incident population		673	673	674	675	675	676	677	677	678	679
Non-ambulant population		*15,752*	*16,105*	*16,458*	*16,812*	*17,166*	*17,520*	*17,875*	*18,230*	*18,585*	*18,941*
Successfully treated	*Translarna*	*4%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Requiring treatment		***96%***	***95%***	***95%***	***95%***	***95%***	***95%***	***95%***	***95%***	***95%***	***95%***
Potential patient population for ATL1102		**12,411**	**12,526**	**12,801**	**13,076**	**13,351**	**13,627**	**13,903**	**14,179**	**14,455**	**14,732**
Competitor/pipeline products excluding steroids											
Total market penetration	*Givinostat*	*3%*	*4%*	*5%*	*6%*	*7%*	*9%*	*10%*	*12%*	*15%*	*18%*
	PF-06939926	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
	Casimersen (45)	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
Non-ambulant market penetration	***ATL1102***	*1%*	*4%*	*10%*	*16%*	*22%*	*28%*	*30%*	*30%*	*30%*	*30%*
Total EU market share		**0.4%**	**2%**	**4%**	**7%**	**9%**	**11%**	**12%**	**12%**	**12%**	**12%**
# Patients		*124*	*501*	*1280*	*2092*	*2937*	*3816*	*4171*	*4254*	*4337*	*4420*
Peak EU sales		**17**	**70**	**180**	**293**	**412**	**535**	**585**	**597**	**608**	**620**
US MODEL											
US total DMD population		**12,211**	**12,584**	**12,959**	**13,337**	**13,716**	**14,098**	**14,483**	**14,869**	**15,258**	**15,650**
US Treated population		2,442	2,643	2,721	2,801	2,880	2,961	3,041	3,123	3,204	3,286
US Incident population		373	375	377	380	382	384	387	389	391	394
Non-ambulant population		*6,407*	*6,603*	*6,800*	*6,998*	*7,197*	*7,397*	*7,599*	*7,802*	*8,006*	*8,211*
Successfully treated	*Exondys 51*	*12%*	*13%*	*13%*	*13%*	*13%*	*13%*	*13%*	*13%*	*13%*	*13%*
	Vyondys 53	*5%*	*5%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*
	Viltepso (53)	*3%*	*3%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*	*4%*
	TOTAL	***20%***	***21%***	***21%***	***21%***	***21%***	***21%***	***21%***	***21%***	***21%***	***21%***
Requiring treatment		***80%***	***79%***	***79%***	***79%***	***79%***	***79%***	***79%***	***79%***	***79%***	***79%***
Potential patient population for ATL1102		**4,013**	**4,068**	**4,190**	**4,312**	**4,435**	**4,558**	**4,682**	**4,807**	**4,933**	**5,060**
Competitor/pipeline products excluding steroids											
Total market penetration	*Givinostat*	*3%*	*4%*	*5%*	*6%*	*7%*	*9%*	*10%*	*12%*	*15%*	*18%*
	PF-06939926	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
	Casimersen (45)	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
Non-ambulant market penetration	***ATL1102***		*3%*	*5%*	*8%*	*10%*	*12%*	*18%*	*22%*	*25%*	*24%*
Total US market share			**1%**	**2%**	**3%**	**3%**	**4%**	**6%**	**7%**	**8%**	**8%**
# Patients			*122*	*209*	*345*	*443*	*547*	*843*	*1058*	*1233*	*1202*
Peak US sales			**27**	**46**	**76**	**98**	**120**	**186**	**233**	**271**	**264**

Source: Wilsons' estimates

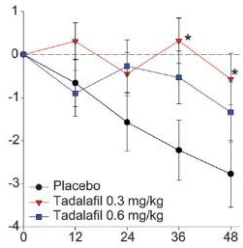
Approved ATL1102 indication restricted to non-ambulatory DMD population. The potential addressable DMD patient population is a highly relevant factor in our Antisense revenue model (Table 8). We have assumed that ATL1102 will be restricted to a non-ambulant DMD population (currently ~53% of all patients) for several reasons including:

- Firstly, the existing clinical trial data and Phase IIB trial design is restricted to a non-ambulant patient cohort and therefore initial approvals will be restricted to this patient subset. There is the potential for a pivotal Phase III study in the US to broaden inclusion criteria to allow for ambulant patient enrolment however this seems speculative at this point in time.
- Secondly, the target of ATL1102, CD49d, has exacerbated expression in the more severe stages of DMD progression and is a progression biomarker[3]. Therefore, there is a risk ATL1102 may lack efficacy in earlier stage ambulatory DMD as these patients possess lower expression of CD49d and therefore modulation of this pathway may not be as functionally relevant or impactful to disease progression at that time (however could potentially have some degree of prophylactic potential but this likelihood is unknown). Noting that CD49d expression is still higher in late ambulatory patients (vs early ambulatory)[3] and therefore subsets within the ambulatory population could still be amenable to ATL1102 treatment.

CD49d expression highest in non-ambulant DMD and may drive efficacy.

[3] Pinto-Mariz et al. (2015) CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne Muscular Dystrophy. *Skeletal Muscle*. 5: 45.

- Finally, there are some questions around how transferrable changes to PUL (upper body total muscle function score) are when looking in ambulatory patient subsets. An example is the unsuccessful large tadalafil Phase III trial (NCT01865084) which failed to show efficacy in terms of slowing ambulatory decline in ambulant boys (7-14yo; n=330), despite showing significant improvement in PUL scores (see inset)[4]. This perhaps indicates that PUL improvement in an ambulatory population is less functionally relevant to disease improvement in ambulatory stage patients, noting that this is one comparative example only. The effect of ATL1102 in ambulatory patients is unknown but cannot be assumed to be equivalent in this sub-population.



Source: Victor et al [4]

Expansion of future ATL1102 approvals to include ambulant DMD patients is only accretive to our forecasts, noting that this accounts for approximately half of the total current DMD population. If ATL1102 were to be effective and approved for treatment of all DMD patients (ambulant + non-ambulant) our addressable patient market would expand considerably, keeping in mind however that there are elevated levels of competition in the ambulant DMD sector of the market so we would not expect double the addressable market to be applicable. We do not assess this being a likelihood in the relevant approval/market access years and therefore exclude this possibility from any of our forecasts and valuation of Antisense at this time. Additionally, we expect the EMA is likely to want a post-authorisation safety registry which is highly prescriptive of which patients may be allowed to access the drug confiscating off-label use.

Table 7. Pricing comparisons and assumptions for ATL1102 vs DMD market peers.

Agent	Company	Approved Market	Annual treatment cost (A$m)
Exondys 51	Sarepta Therapeutics	US	1,448,400
Vyondys 53	Sarepta Therapeutics	US	1,416,213
Viltepso	NS Pharma	US	1,387,813
Emflaza^	PTC Therapeutics	US	79,520
ATL1102		**US**	**220,000 (~US$155,000)**
Deflazacort (Emflaza generic)^	Generic	EU	1,704
Translarna	PTC Therapeutics	EU	726,000
ATL1102		**EU**	**140,250 (~€85,000)**
Prednisone^	Generic	EU/US	800

^Noting that Prednisone, Emflaza/Deflazacort are not niche disease modifying DMD treatments and are standard of care corticosteroids. Comparison pricing normalised to 40kg child dosing (as some drugs are dosed per body weight whereas ATL1102 has a fixed dose form).

Source: Wilsons' estimates, US Federal Supply Schedule, Red Book, Pharma Intelligence.

Our revenue model assumes average selling prices (ASPs) of ATL1102 for DMD of US$155,000 and €85,000 as an annual treatment cost in US and EU markets, respectively. These pricing estimates for ATL1102 are based on placement within the market at a level relative to its broad applicability (i.e. Exon skipping drugs = small market niche (~8% patients total) and demand higher ASPs). The difference in EU and US ASP is in line with the typical premium sought in the US market (~60%) due to differences in payer/payee systems. We believe these ASP assumptions are on the conservative end of the spectrum and therefore any increase to ASP is accretive to valuation forecasts.

Table 8. Revenue model for ALT1102 in DMD FY26-36e based on market and pricing assumptions.

	FY26	FY27	FY28	FY29	FY30	FY31	FY32	FY33	FY34	FY35	FY36
EU ATL1102 sales	**17**	**70**	**180**	**293**	**412**	**535**	**585**	**597**	**608**	**620**	**632**
EU EBITDA, A$m	7	49	138	228	321	418	457	466	475	485	494
US ATL1102 sales	**-**	**27**	**46**	**76**	**98**	**120**	**186**	**233**	**271**	**264**	**258**
US EBITDA, A$m	(5)	18	31	58	75	93	144	181	211	206	200
TOTAL, A$m	**17**	**97**	**226**	**369**	**510**	**656**	**770**	**829**	**880**	**884**	**889**
- less R&D, other investments	7	5	4	4	4	4	4	4	4	4	4
- less COGS	2	10	23	37	51	66	77	83	88	88	89
- less SG&A	5	9	9	11	14	17	19	21	22	22	22
- less Ionis royalties	2	9	20	33	46	59	69	75	79	80	80
ATL1102 EBITDA, A$m	**2**	**65**	**170**	**284**	**394**	**510**	**601**	**647**	**687**	**690**	**694**
- less notional tax (30%)		15	51	85	118	153	180	194	206	207	208
ATL1102 ATCF, A$m	**2**	**50**	**119**	**199**	**276**	**357**	**421**	**453**	**481**	**483**	**486**

Source: Wilsons' estimates

[4] Victor et al. (2017) A Phase 3 randomized placebo-controlled trial of tadalafil for Duchenne muscular-dystrophy. *Neurology*. 24:89. 1811 – 1820.

Our earnings forecasts are premised on the base case scenario, timelines, regulatory strategy, market assumptions and revenue assumptions outlined above for ATL1102. Noting, that Antisense receive some 'other' revenues in the form of small government grants (<50K), R&D tax refunds and the assumed sale of their Priority Review Voucher in FY25 ($100M). This large lump sum cash inflow is what drives the large blip in revenues in FY25 prior to first product sales in late FY26 which gradually accelerate with increased market access and penetration.

Table 9. Long-range earnings and cash flow forecasts for Antisense assuming base case scenario

	FY21	FY22	FY23	FY24	FY25	FY26	FY27	FY28	FY29	FY30
P&L statement										
Revenues	**0.7**	**5.3**	**2.8**	**1.8**	**101.9**	**17.4**	**97.1**	**225.6**	**369.3**	**509.6**
Sales	-	-	-	-	-	17.4	97.1	225.6	369.3	509.6
Total other income	0.7	5.3	2.8	1.8	101.9	-	-	-	-	-
Operating Expenses	**(19.1)**	**(12.3)**	**(9.9)**	**(27.3)**	**(14.3)**	**(20.9)**	**(41.9)**	**(65.3)**	**(96.9)**	**(129.5)**
COGS	-	-	-	-	-	(1.7)	(9.7)	(22.6)	(36.9)	(51.0)
SG&A	(2.0)	(2.1)	(2.4)	(2.6)	(2.6)	(5.2)	(9.2)	(9.2)	(11.3)	(14.3)
R&D	(15.0)	(8.0)	(5.0)	(22.0)	(9.0)	(7.0)	(5.0)	(4.0)	(4.0)	(4.0)
D&A	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Licensing payments (Ionis)	-	-	-	-	-	(1.6)	(8.7)	(20.3)	(33.2)	(45.9)
EBITDA	**(18.3)**	**(6.6)**	**(4.6)**	**(22.9)**	**90.3**	**(0.1)**	**62.5**	**169.6**	**281.8**	**394.4**
Profit (Loss) before tax	(18.4)	(6.5)	(4.3)	(22.6)	90.4	0.9	63.7	171.8	286.0	401.7
NPAT	(18.4)	(6.5)	(4.3)	(22.6)	90.4	0.9	63.7	171.8	286.0	401.7
EPS (cps)	(3.4)	(1.0)	(0.6)	(3.1)	12.2	0.1	8.6	23.3	38.7	54.4
Shares outstanding (weighted average)	539.5	655.3	738.7	738.7	738.7	738.7	738.7	738.7	738.7	738.7
Cash Flow statement										
Operating cash flow	**(17.6)**	**(1.6)**	**(1.4)**	**(21.3)**	**91.9**	**0.2**	**63.0**	**171.1**	**285.2**	**401.1**
Net proceeds from equity raising	31.5	28.2	-	-	-	-	-	-	-	-
Changes in cash balance	13.9	26.6	(1.4)	(21.3)	91.9	0.2	63.0	171.1	285.2	401.1
Cash at End of period	**18.0**	**44.6**	**43.3**	**22.0**	**113.9**	**114.1**	**177.1**	**348.2**	**633.4**	**1,034.4**

Source: Wilsons' estimates

Investment and expense assumptions

Balance sheet and short term revenues. Antisense reported net cash of $4.1M at the end of the FY20 period, and have since raised an additional $7.3M in equity in a November offer and subsequent $1.2M SPP (both of which were oversubscribed). We also anticipate $100M cash injection from sale of the US PRV on a secondary market in 2H25 at the time of NDA filing with the FDA.

Expense assumptions include the following:

R&D expenses. We have assumed Antisense commence their European Phase IIB trial in mid-2021 which will enrol ~110 patients with associated costs of ~$27M over three-year period from commencement to the point of EMA filing. Within this some allowance for an open-label extension study however could require amendment if much longer/larger than anticipated. Additionally, we assume an overlapping US Phase III trial in DMD commencing in mid-2022, potentially involving ~100 patients with an associated cost of $30-35M over the three-year trial period to point of FDA filing in mid-2025. The elevated cost assumptions are due to higher US trial costs and potential extra expenditure that may be required for trial readiness. We also assume continued annual R&D costs of $4M for the forecast period to support indication expansion, additional analysis or extension studies that may be required to support other jurisdiction approvals/label expansion (i.e. higher dose, ambulant). Antisense expenses all of its R&D investments.

General, administrative and patent expenses. The operating expenses for Antisense, outside of R&D, are relatively small, and cover occupancy, administration, and patent maintenance fees. We estimate these currently as ~$2M per year. We forecast SG&A expense to lift in line with first commercial ATL1102 sales (~FY26) in line with market predicates (CUV ~$9m annual in first years of launch) and forecast this expense as ~25% of COGS moving forward.

Ionis obligations. Under the current licensing terms, Antisense are obligated to single digit royalties to Ionis for any future sales of either ATL1102/ATL1103, assuming these assets are commercialised by Antisense themselves and not a third party (when the Ionis royalty is understood to increase). We have assumed 9% royalty paid to Ionis starting in FY26 as a function of EU and US ATL1102 DMD sales and Antisense commercialising themselves.

Tax. We anticipate R&D tax refunds (currently ~35% of total R&D spend and recognised as 'other income') to cease in FY25. Antisense had $51.5M in accumulated unused tax losses at end FY20 which may be applied to future assessable pre-tax income. We forecast that Antisense will not exhaust these accumulated tax losses until post FY30 and have not included tax payments in our 10 year forecast. We assume a long-term effective tax rate of 30% once tax becomes applicable on future earnings.

Appendix

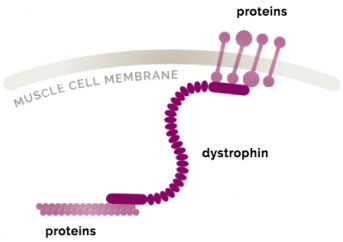
A.1 Relevant clinical settings described in brief

A.1.1 Duchenne muscular dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is a debilitating, inherited, neuromuscular disorder, primarily affecting males, that leads to significant and progressive muscle wasting causing a loss of mobility, ultimately leading to respiratory/cardiac failure and mortality. DMD has significant effects on patient quality of life and impacts on carers. Slowing or halt of disease progression is key to elongate the period for which patients are functionally self-reliant. The birth prevalence of DMD is estimated to be ~16 in every 100,000 live male births in the US[5] and ~21 in every 100,000 live male births in EU[6]. It is estimated there are currently ~10,000 patients in the US and ≥ 25,000 patients in Europe requiring treatment for DMD.

Clinical description and disease progression

Disease affects predominantly males. The dystrophin gene is located on the X chromosome and therefore disproportionately affects males versus females. Dystrophin is a master switch protein that acts a little like a shock absorber, sitting between the outer muscle fibre membrane and the cytoskeleton, connecting the muscle fibres, strengthening them and helping protect them from damage during muscle contraction and relaxation. Dystrophin is one of the key proteins in the body that does not have any compensatory mechanisms – meaning, if you have defects in the function of dystrophin, the body will not find a way to manage this (unlike some other systems) and it will lead to significant functional muscle loss.

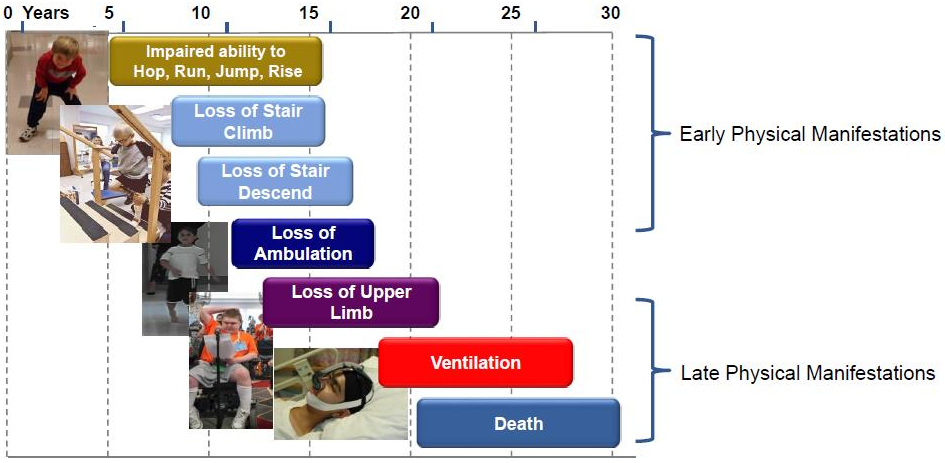


Source: Duchenne.com

DMD is a progressive disease meaning that the level of dystrophin loss increases over time leading to greater physical impairment. This impairment affects many bodily systems requiring a multi-disciplinary approach in terms of patient care teams (i.e. paediatrics, neurology, orthopaedics; psychology).

Functionally there are three key phases in DMD progression for a patient:

- Diagnosis/early ambulatory phase;
- Transition (late ambulatory) phase;
- Non-ambulatory/late phase.



Source: Antisense Therapeutics.

Diagnosis into early ambulatory phase. Diagnosis typically occurs between 2-5 years of age in young boys

[5] Mendell et al. (2012) Evidence-based path to newborn screening for Duchenne muscular dystrophy. *Ann Neurol*; 71(3):304-313.
[6] Crisafulli et al. (2020) Global epidemiology of Duchenne muscular dystrophy: an updated systematic review and meta-analysis. Orphanet Journal of Rare Diseases. 15:141.

when their physical progression is noticed as impaired (i.e. in sitting up, learning to walk, climbing stairs) or they appear potentially weak or clumsy. Blood tests are then used to confirm the diagnosis via measurement of creatinine kinase (CK), an enzyme that leaks out of damaged muscle, which is an indicator of muscle trauma. High CK levels does not identify DMD specifically, rather the presence of a muscle disorder. Genetic testing is used to search for mutations in the dystrophin gene of patients. Positive identification of a mutated DMD gene confirms the diagnosis. Muscle biopsies can sometimes be ordered for further diagnostic evaluation. Typically following a confirmed DMD diagnosis, patients are started on corticosteroids and are monitored with functional testing every 6 months to help define the stage of disease and its progression rate.

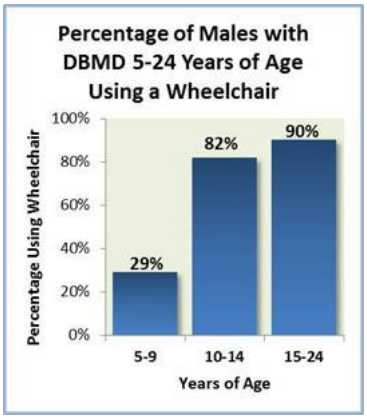
Transition phase. Muscle degradation occurs in the larger muscles of the body first and hence the large leg muscles are first to collapse leading to loss of ambulation. Essentially, in DMD, there is a slow and gradual process whereby the muscles convert from muscle cells into fat cells which causes the muscles to become non-functional. Eventually this muscle loss then progressively moves to the upper limbs to a point where patients may even lose all upper limb function. Within 5-10 years patients typically progress or transition to a non-ambulatory phase where they require a wheelchair and additional support to function as they once did. Greater than 80% of patients require wheelchairs past 10 years of age (see inset figure)[7]. Antisense's ATL1102 has only thus far been assessed in non-ambulant populations.

Necrosis (death) of muscle cells and fibres is driven by several mechanisms, which include an inflammatory component. The body's own inflammatory pathways activate and attack muscle cells promoting a vicious cycle of further necrosis and cell death which perpetuates the disease process.

Non-ambulant phase. Once patients become non-ambulant, they have a reduced capacity to care for themselves independently and become more heavily reliant on outside care. Depending on the severity or aggressiveness of their diagnosis patients may remain in this phase for 5-10 years before significant respiratory problems set in. At which point, mechanical ventilation can be required to support their breathing and cardiac function.

The average life expectancy for a patient with DMD is 25-30 years, which is significantly higher than in the early 1990's when it was < 20 years[8]. Constant advances in cardiac and ventilator care have extended this with some patients living into their 40's and 50's. Development of cardiomyopathy is the key consequence of DMD responsible for mortality and defines late phase disease (typically developed by ~18 years of age). Many patients are treated with steroids and ACE inhibitors for management of their cardiomyopathy in addition to heart-failure medications. Cardiac and respiratory disease progression are of course key targets for new therapies need to combat to prolong life in DMD. Ultimately new therapeutics aim to slow or halt disease progression before the development of cardiomyopathy occurs.

Antisense has focused their clinical development program on the severe end of the disease spectrum, with all clinical studies to date conducted in non-ambulant DMD patients.



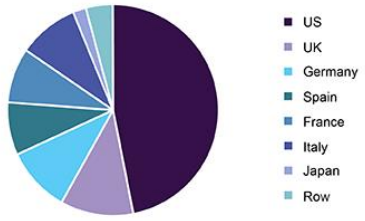
Source:CDC[7].

[7] Centres for Disease Control and Prevention (CDC) (2009). Prevalence of Duchenne/Becker muscular dystrophy among males aged 5-24 years – four states 2007. *MMWR Morb Mortal Wkly Rep*. 58(40): 1119-1122.
[8] Cheeran et al. (2017) Predictors of Death in Adults with Duchenne Muscular Dystrophy-Associated Cardiomyopathy. *JAHA*; 6: e006340.

Market and competitive pipeline

Large growing TAM of >$4B. The TAM for DMD is estimated to reach US$4.1B by 2023 (CAGR 41.3%: 2017-2023)[9]. This high level of market growth is assumed due to increased target population (driven by improved timing of diagnosis and enhanced treatments/longevity – meaning higher prevalence rates over time, despite stable incidence)[10] as well as the increased adoption and approval of new therapies (i.e. Exondys) and increased government/regulatory incentive programmes (i.e. Rare Paediatric Disease Designation). The incidence of DMD is relatively stable and therefore the growth of our incident population (Table 6) is in line with population growth of 2-3% (which is included within our market model). In terms of geographic distribution, the EU5 market accounts for ~49% of total DMD market, with 45% in US and ~6% ROW (see inset figure).

DMD market by share, by country



Source: GrandView Research.

Corticosteroids are current standard of care. Corticosteroids are mainstay therapy for DMD and the first line therapy on treatment guidelines however, they have substantial limitations given detrimental long term side effects and poor tolerability, noting that schizophrenic episodes have been witnessed in patients following long term steroid use, in addition to bone fractures, excessive weight gain and cataracts[11]. It is estimated approximately 65% of the >9 year old (mostly non-ambulant) DMD cohort take regular corticosteroids[12].

Corticosteroids current standard of care with significant drawbacks, leaving market open for new broadly applicable therapies.

At present, the only approved therapies for DMD aside from regular corticosteroid treatment (prednisone, Emflaza) are a number of genetically specific approaches (Exondys, Vyondys, Viltepso, Translarna) that service a small (<20%) segment of the DMD market (Table 10). For these reasons novel MOA approaches and techniques (including antisense agents and gene therapies) are warranted and necessary.

EU and US regulators view DMD approvals very differently. Interestingly the DMD market is quite disparate geographically in terms of regulatory approval (i.e. EMA vs FDA) with several instances of products being approved in one jurisdiction and rejected in the other based on the same clinical data. Examples of this include PTC's Translarna which was given conditional marketing authorisation in European markets in 2016 despite being rejected by the FDA twice (in 2017 and again in 2019). The EU approval was based on surrogate endpoint data which continues to be renewed pending further data from the ongoing 041 study set to complete in 2022. In the case of Translarna the FDA cited inadequate evidence of efficacy to support approval and that further research was needed.

Similarly, the reverse has occurred in the case of Exondys 51 (Sarepta) where the EMA cited a lack of efficacy in 2018, despite the FDA giving the stamp of approval in 2016 based on increases to dystrophin production with future trials required to confirm its functional effect[13]. This has led to two somewhat unique and disparate drug markets for DMD, which are outlined below in Table 10.

Table 10. Current DMD drug approvals in major markets.

Drug	US	EU	ROW	Indication
Translarna (PTC)	Two FDA rejections in 2017 and 2019	Conditional authorisation granted^ 2014 & renewed	Approved in Israel, North Korea	Ambulatory DMD >2yrs with non-sense mutations
Exondys 51 (Sarepta)	Approved 2016	EMA rejection in 2018	Managed access program*	Exon 51 amendable DMD
Vyondys 53 (Sarepta)	Approved 2019	EMA rejection in 2018	NA	Exon 53 amenable DMD
Viltepso (NS Pharma)	Approved 2020	Not applied	Japan	Exon 53 amenable DMD
Emflaza (PTC)	Approved 2017	Generic deflazacort available since 1985	Deflazacort available via special access schemes in most major ROW markets	DMD >2yrs

^ This conditional marketing authorisation required PTC to submit additional results from 041 Study by Sept 2022 to be evaluated for full market approval.
*Sarepta's managed access program grants access within LATAM, EU and UK.

Source: Wilsons, FDA, EMA.

[9] GrandView Research. August 2018. DMD Drugs Market Report.
[10] Giegerich & Stuntz. (2019) DMD prevalence in the U.S.: A novel incidence-based modelling approach using system dynamics. Abstract; ISPOR 2019 Annual Meeting, New Orleans. PMS43.
[11] Gloss et al. (2016) Practice guideline update summary: Corticosteroid treatment of DMD: report of the Guideline Development subcommittee of the American Academy of Neurology. Neurology. 86(5): 465-472.
[12] Vry et al. (2016) European Cross-sectional survey of current care practices for DMD reveals regional and age-dependent differences. *J Neuromuscul Dis*. 3(4): 517-527.
[13] Echevarria et al. (2018) Exon-skipping advances for Duchenne muscular dystrophy. *Human Molecular Genetics*. 27: R2.

Competitive landscape is highly active, but lacks non-ambulant development. There is a highly active development pipeline in DMD, with over six compounds in late stage Phase III trials. However, notably, only three drugs (at different stages of development) are being trialled in non-ambulant patients, FibroGen's pamrevlumab, Capricor's CAP-1002, and repurposed tamoxifen, leaving a large space in the pipeline for therapeutics that are initially targeting the non-ambulant half of the DMD market.

More broadly, the DMD competitive pipeline can be divided based on different mechanistic approaches to treating the disease progression which are being achieved with a number of different techniques. These mechanism of action (MOA) categories include:

- Dystrophin replacement or correction
- Improvement and protection of muscle growth
- Reducing inflammation caused by muscle fibre necrosis
- Combating fibrosis of the connective tissue
- Stabilising calcium balance and muscle membrane
- Restoration of mitochondrial function
- Supporting cardiac function (noting that this approach is likely to be used in conjunction with other mechanisms more specific to muscle restoration)

Each MOA approach has benefits and caveats which we will explore here in brief, in addition to the different technological approaches being taken, such as exon skipping, gene/cell therapy, next generation steroids and repurposing of existing approved drugs. The pipeline overview is shown below in Table 11.

The most promising MOA's include a) dystrophin correction/replacement, b) improving muscle growth and c) reduction of inflammation. This assessment is based several factors including; a) ability to modify underlying disease progression as opposed to symptom control, b) existing clinical development progression and approval of agents utilising these MOA's, and c) the relative importance of each of these MOAs in DMD disease progression.

Disease modifiers. Therapies targeting dystrophin specifically are 'disease modifying' agents, which directly aim to correct the lack of dystrophin either via direct repair of the dystrophin gene through transgene delivery via a viral vector or delivery of mini-dystrophin via similar means, or exon skipping (if appropriate). This is the focus of the Pfizer and Sarepta gene therapy programs in DMD, several of which have progressed to Phase III or are on market. Others attempt to cause disease modification via control of secondary processes such as inflammation and fibrosis that drive further disease pathology and may have meaningful outcomes on disease progression. Corticosteroids are an example of this approach and have been shown to delay disease progression and loss of ambulation by up to 3 years. Alongside ATL1102, other approaches that are well progressed include Pamrevlumab (non-ambulant) and Givinostat (ambulant).

Table 11. Outline of current pipeline therapies for DMD based on mechanistic category and current clinical development status.

Pre-clinical	Phase I	Phase II	Phase III	Approved
AT702 *(Audentes)*	GALGT2 *(Nationwide Children's Hospital)*	SRP-9001 *(Sarepta)*[#]	Translarna *(PTC)*^	Exondys 51 *(Sarepta)*
iPS cell therapy *(Uni Minnesota)*	SGT-001 *(Solid Biosciences)**	SRP-5051 *(Sarepta)*	Casimersen *(Sarepta)*	Vyondys 53 *(Sarepta)*
TVN-102 *(Tivorsan)*	DT-200 *(Akashi)*	DS-5141b *(Daiichi)*[%]	PF-06939926 *(Pfizer)*	Viltepso *(NS Pharma)*
rH Laminin-11 *(Prothelia)*	A0367 *(Astellas)*	CAP-1002 *(Capricor)*	Givinostat *(Italfarmaco)*	Emflaza *(PTC)*
ARM210 *(ARGMO)*	EPM-01 *(Epirium Bio)*	Carmeseal-MD *(Phrixus)*[@]	Vamorolone *(Santhera)*	
AT-300 *(Akashi)*		**ATL1102 *(Antisense)***	Tamoxifen *(University Hospital Basel)*	
		ILARIS *(Children's Research Institute)*	Pamrevlumab *(FibroGen)*	
		Rimeporide *(EspeRare)*		
		Ifetroban *(Cumberland)*		

MOA key
Dystrophin correction
Muscle growth protection
Anti-inflammatory
Anti-fibrotic
Stabilising calcium balance
Mitochondrial enhancement
Cardiac function support

*SGT-001 Phase I/II trial currently paused by FDA waiting on manufacturing information following serious adverse events. Second time FDA has paused the trial.
[#] SRP-9001 Phase II trial completed – awaiting FDA approval of Phase III design. FDA has requested potency testing data for gene therapy penetration. Additionally, Roche recently signed $1B agreement for US commercialisation; Sarepta to keep jurisdictions outside US.
[%] Daiichi recently reported that Phase I/II trial missed its primary endpoint. Forward development pathway uncertain.
[@] Carmeseal-MD is currently available through an EU Access Program for DMD. Phase II underway however suspended due to manufacturing drug supply issue.
^ Translarna has had 2 prior FDA rejections citing more efficacy and manufacturing data required. The pivotal Phase III trial failed to reach significance. PTC now part of registry comparison study (STRIDE) in an effort to show real-world evidence of efficacy in the longer term.

Source: Wilsons, Parent Project Muscular Dystrophy

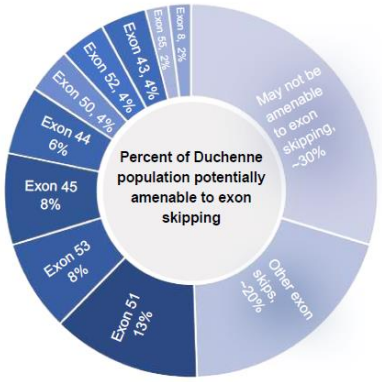
Gene and cell therapy approaches. There are a number of gene and cellular therapy approaches being trialled for DMD currently, the majority of which are aimed at replacing dystrophin, typically through insertion of a micro-dystrophin gene into the muscle cells. The dystrophin gene itself is too large to be effectively inserted into the available viral vectors for delivery of the gene into the target cells (demonstrated by past failures), and therefore identification of a truncated form, micro-dystrophin, has become a popular strategy. In fact, at least eight agents are under development currently based on this premise using various different viral vector formats, largely adeno-associated viral (AAV) vectors.

One key benefit of gene therapy, aside from efficacy, is the convenience aspect, where a single infusion may be beneficial for 3-5+ years before additional treatment is required. For patients that are currently taking upwards of five medications, up to 3-4 times per day, this is a welcome relief – especially given that they are often young children where daily taking of medications or regular injections is already more challenging. Keeping in mind that many patients may still be maintained on regular corticosteroids despite gene therapy which does not completely negate regular medications.

Cell therapy approaches have similar benefits, albeit with a shorter timeframe. For example CAP-1002, currently in Phase II trials, requires a single infusion every 3 months.

There is a caveat regarding the durability of these treatments that is specific to DMD. The rate of muscle fibre necrosis, which is where the gene therapy is targeted, is very high in DMD, meaning that the turnover rate of these cells is high, which affects transfection rates. The rate at which muscle cells die and regenerate, or in the case of DMD, turn into fat cells, is a limiting factor that determines how long a gene therapy could be efficacious and therefore durability data is a key focus for current trials. Additionally, gene therapy carries the common caveat of developing neutralising antibodies to the viral vectors used which can affect efficacy, reduce applicable population and also negate the ability to have a second infusion.

Exon Skipping approaches. There are currently three approved DMD treatments based on an exon skipping approach (Vyondys, Exondys, Viltepso) and more in the development pipeline (SRP-5051, Casimersen, AT702). This approach may appear fruitful however has one large caveat; that being, only a small portion of the DMD market is addressable with each agent. For example, the number of patients amendable to Exon 51 or 53 skipping are approx. 13% and 8% respectively. Therefore between these three existing approved therapies there is a maximum capture of ~20% of the market, leaving the majority of patients still seeking treatment. This is alongside the fact that the levels of dystrophin replacement are suboptimal in some cases. Newer pipeline therapies (i.e. Casimersen, AT702) are aiming for new exon targets, such as Exon 45 or Exon 2, but still experience the same caveat (8%, <5% patients amenable, respectively). There have been estimates made that only 60-80% of the entire DMD cohort may be amenable to exon skipping in some form, therefore other approaches are necessary. Given there is still a large unaddressed market (>60%) which will remain (>30%- see inset figure) despite advances in this therapeutic area, these therapies are not seen as dominant competitors to ATL1102 due to their more niche applicability. Additionally, the overall effectiveness of exon skipping therapies in DMD has been challenged in recent meta-analyses[14].



Source: CureDuchenne™

Next generation steroids. Emflaza/deflazacort is already on the market and used in place of prednisone in some cases, however in the US market carries a much higher price tag given it has a specific label indication for DMD treatment. One next gen steroid in late stage development for DMD is Vamorolone, which differs to prednisone in a key factor; its interaction with mineralocorticoid receptors (MRs) – prednisone being an agonist at MRs whilst Vamorolone is an antagonist. Its actions on MRs are proposed to be why the safety and adverse event profile is superior to prednisone and hence is being assessed a new improved steroid alternative for DMD patients. Six month top-line data from their Phase IIB trial (VISION-DMD study) will readout in 2Q21. Vamorolone is being assessed also on its ability to reduce cardiomyopathy in DMD patients, the current leading cause of death in DMD. We assess that Vamorolone could become a new first line steroid option for DMD, with other adjunct therapies (i.e. ATL1102) still required to manage the disease progression.

[14] Shimizu-Motohashi et al. (2018) Exon skipping for Duchenne muscular dystrophy: a systematic review and meta-analysis. *Orphanet Journal of Rare Diseases*. 13 (93).

Alternative drug repurposing. Drug repurposing is also afoot for DMD with agents such as Tamoxifen and ILARIS in clinical development for DMD. Mechanistically these drugs are both targeting inflammation within the muscle and surrounding tissues that can drive further muscle fibre damage and necrosis (albeit via very different mechanisms to ATL1102). The caveats of using a drug like tamoxifen (typically used for breast cancer treatment) is the adverse event profile (including nausea, hair thinning, bone pain). The tamoxifen phase III study also includes a subset (~20%) of non-ambulant patients which will provide a good comparator for anti-inflammatory mechanisms in this patient cohort once data becomes available.

Cardiac. Focus on the prevention of cardiomyopathy is a key focus in DMD given that it is the major driver of mortality. DMD patients are typically managed closely in terms of their cardiac and respiratory care from diagnosis. Unfortunately the identification of traditional heart failure symptoms becomes challenging in non-ambulatory patients making the need for regular non-invasive imaging (i.e. Echocardiogram, cardio MRI) necessary. Rimeporide is a drug currently in Phase I/II trials in DMD patients, previously developed as a treatment for congestive heart failure, which is showing promise via reduction of inflammation and fibrosis in heart and skeletal muscles. Pamrevlumab is another such anti-fibrotic drug showing promise in heart and lung responses. The use of cardiac drugs to manage this aspect of DMD, including angiotensin blockers and ACE inhibitors, is common and will likely remain a necessary companion therapeutics to other more skeletally focused drugs in development – therefore is not seen as a direct set of competitor assets to ATL1102.

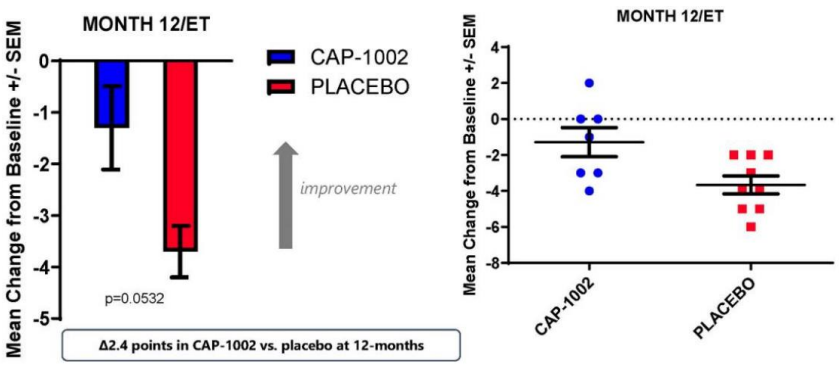
Key contenders for approval in next 12-18 months. Sarepta's Casimersen is set to receive their FDA response on marketing authorisation by Feb 2021, which if approved, would address up to 8% of the population amendable to exon 45 skipping therapies. This has been integrated into our market model. Similarly, Santhera's new steroid, Vamorolone, is expected to have top-line results in 2Q21 (in ambulant children) with an FDA filing soon after. Fast track designation could see this drug approved potentially in early 2022 pending trial outcomes.

Recent notable failures. 2020 has been the year for late stage DMD drug terminations with two of the prominent programmes from Santhera and Catabasis reaching ultimate ends. Santhera's idebonone was discontinued in October after the Phase III interim analysis showed it was unlikely to reach a primary endpoint supporting approval. Since, they have withdrawn their EMA application and are restructuring their pipeline which includes Vamorolone. Similarly the Catabasis' Edasalonexent trial was also discontinued in late October after the Phase III failing its primary endpoint of superiority to corticosteroids, with the open-label extension also being ceased.

Non-ambulant competitors. There are three current trials that include non-ambulant patients, with only one exclusive to non-ambulant patients (pamrevlumab). In both the pamrevlumab and CAP-1002 studies the same PUL2.0 primary endpoint is being used for the non-ambulant patients as with the ATL1102 proposed Phase IIB, which will provide direct comparison data to evaluate ATL1102's magnitude of effect (which has only been compared thus far to corticosteroids or natural history cohorts within the published literature).

The recent HOPE-2 results from Capricor (CAP-1002 cell therapy) showed 12 month treatment lead to a 2.4 point change in PUL2.0 measure compared to placebo. Noting that the mean change from baseline in the CAP-1002 treated cohort was still -1.3 points compared to baseline (vs -3.7 placebo) and that only one patient showed a +2 change, with the remainder either stable or still worsening (Figure 6).

Figure 6. Effect of CAP-1002 in HOPE-2 Phase II trial on PUL2.0 scores following 12 month treatment.

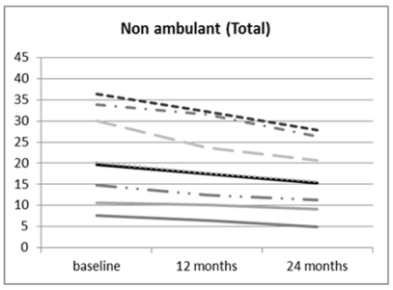


ATL1102 change in PUL2.0 compared to baseline superior to CAP-1002 effect on initial comparison.

Source: Capricor Therapeutics

Importantly, interim 6 month HOPE-2 data showed overall -0.3 score change from baseline with CAP-1002 (n=6) vs placebo (-2.3; n=8) (Figure 10). This 6 month point is the most direct comparison to ATL1102 DMD data. ATL1102 showed an average +0.9 point positive change relative to baseline in the open-label Phase II study at the same time point, noting that the CAP-1002 study included both ambulant and non-ambulant patients and that PUL2.0 scores are known to be higher in ambulant cohorts[15]. This makes it more challenging to compare the mean change from baseline between the two cohorts, in addition to other differences in study design.

As a reminder a large DMD cohort study showed -2.17 point changes on average in 90 non-ambulant patients with DMD over a 12 month period compared to baseline (see inset figure right)[14]. Pamrevlumab Phase II data did not assess via PUL2.0 metric (used PUL1.2) and therefore comparisons are challenging however PUL2.0 is the primary endpoint for their Phase III trial in non-ambulant patients that will have top-line data available in ~ Jan 2023[16]. Finally, the tamoxifen study, "TAMDMD" (NCT033540039), will use D2 domain motor function as the primary endpoint (as it is majority ambulant patients), with PUL measurements being captured as a secondary endpoint[17]. Top-line results from this Phase III are expected mid-2022. Later in Figure 10 we show some compiled PUL2.0 data comparisons.



Source: Pane et al. [14]

A.1.2. Acromegaly

Acromegaly is a hormonal growth disorder caused by an overactive pituitary gland releasing excess growth hormone. Acromegaly affects adults, typically in middle-age. When the same disorder occurs in childhood it is referred to as gigantism. In adults, the main cause of growth hormone overproduction is the presence of noncancerous tumours of the pituitary gland. The disease is defined by abnormal and excessive growth of the skeleton, tissues and organs. Left untreated, acromegaly can lead to major health conditions and complications leading to premature death including cardiomyopathy, spinal cord compression, hypertension, diabetes and osteoarthritis, to name a few.

Clinical description and disease progression

Acromegaly is estimated to affect ~8 per 100,000 people, with a median age of diagnosis of ~45 years of age. It affects men and women equally[18]. It is estimated there are just over 25,500 people in the US with acromegaly based on current prevalence figures[19].

The pathology of acromegaly leads to excessive growth of soft tissues and the skeleton. Typically patients first notice enlargement of their hands and feet early on in the diagnosis followed by more pronounced changes to their facial structure (i.e. jaw, teeth, nose etc). The disease is slow and progressive so early diagnosis can be challenging as it is not immediately obvious to patients that these changes are occurring.

The mechanism underlying acromegaly is driven by overproduction of growth hormone from the pituitary gland which in turn triggers the liver to overproduce insulin-like growth factor I (IGF-I). IGF-I is the hormone then responsible for simulating bone and tissue growth leading to the phenotypic features of acromegaly. Troublingly, this increase in IGF-I can also cause enlargement of organs including the heart, liver and kidneys significantly contributing to mortality of the disease.

Source: Prof. Pietro Mortini.

[15] Pane et al. (2018) Upper limb function in Duchenne muscular dystrophy: 24 month longitudinal data. PLoS One. 13(6): e0199223.
[16] https://clinicaltrials.gov/ct2/show/NCT04632940
[17] Nagy et al. (2019) Tamoxifen in Duchenne Muscular dystrophy (TAMDMD): study protocol for a multicenter, randomized, placebo-controlled, double-blind Phase 3 trial. *Trials*. 20(637).
[18] Lavrentaki et al. (2017) Epidemiology of acromegaly: review of population studies. *Pituitary*; 20(1): 4-9.
[19] Burton et al. (2016) Incidence and prevalence of acromegaly in a large US health plan database. *Pituitary*; 19: 262-267.

Market and competitive pipeline

Current therapies. Current standard of care for acromegaly includes removal of pituitary tumours (if possible) with/or radiation therapy. Typically first line therapy in clinical practice involves use of growth hormone reducing agents in the form of somatostatin analogues (i.e. octreotide. lanreotide) to normalise GH and/or IGF-I levels. Oral dopamine agonists (i.e. bromocripitine, cabergoline) or GH-receptor antagonists (i.e. pegvisomant)[20] can then be used as add-on therapy if SSAs fail. First line failure patients can also be managed via pegvisomant monotherapy to normalise IGF-I.

Each of these treatment options has advantages and disadvantages. ATL1103, similarly to somatostatin analogues and GH-receptor antagonists requires regular injections as opposed to dopamine agonists that are taken orally. There are trade-offs regarding frequency however, with oral forms and some injectables taken daily, as opposed to ATL1103 which is a twice weekly injection only. Recently (2020) new oral forms of older injectable agents have been approved (i.e. oral formulation of octreotide; Mycapssa from Chiasma) which is leading to potentially improved convenience options for patients.

Pegvisomant (Pfizer) has shown superior efficacy (long-term) to all other treatment options[21] (barring complete surgical resection) and therefore is the most significant competitor to ATL1103.

One issue with pegvisomant is in regards to patients with concurrent diabetes mellitus taking insulin or other hypoglycaemic agents. Although not formally contraindicated, caution is needed for this patient subset using pegvisomant as it can decrease insulin sensitivity requiring monitoring and dose titration of insulin/other diabetic agents. ATL1103 has not shown to have this same effect on insulin sensitivity potentially expanding its use profile over that of the incumbent, pegvisomant.

Side effect profile comparison? Somatostatin receptor agonists (SSAs) have been shown to cause transient gastrointestinal adverse events (AEs) and injection site reactions but are otherwise quite well tolerated. In some cases SSAs can cause pernicious anaemia requiring a B12 injection and in rare cases has been linked with reversible alopecia or acute kidney failure, making them not without drawbacks.

Long term treatment with dopamine agonists is also known to have potentially serious AEs including development of excessive daytime sleepiness or sleep attacks, compulsive behaviour including addiction (i.e. gambling/shopping/eating) and augmentation (a pronounced reliance on dopamine agonists as the body starts to stop its own production of dopamine).

Interestingly, several of the prominent market drugs have recently come off patent (i.e. pegvisomant, sandostatin) however there has been little impact to the market overall due to the absence of generics in this space. We assess a possibility of ATL1103 being used as an adjunct to existing treatments, noting there is a strong R&D pipeline of new SSAs and GH antagonists under development. Antisense propose to develop ATL1103 as a monotherapy in first-line failure patients, where they will seek to match pegvisomant in clinical practise.

Total market size. The global acromegaly market is estimated to be ~US$1.4B currently with a CAGR of 7.5% (based on 2019-2025 forecast period)[22] and expected to reach US$2.1B by 2025.

Currently, somatostatin analogues account for the majority of the market (~60% accounted for by octreotide/pasireotide/lanreotide), with a lesser proportion (~20%) from GH antagonists (pegvisomant).

There is a rising prevalence rate of acromegaly supporting a growing market size, despite stable incidence, that is driven by advanced detection techniques and elevated diagnosis rates. This supports TAM expansion and opportunities for ATL1103.

[20] Gariani et al. (2013) Implications of Somatostatin Analogues in the Treatment of Acromegaly. *Eur Endocrinol.* 9(2): 132-135.
[21] Buchfelder et al. (2018) Long-term treatment with pegvisomant: observations from 2090 acromegaly patients in ACROSTUDY. *European Journal of Endocrinology*. 179(6): 419-427.
[22] GrandView research report: Acromegaly treatment market report; Published Feb 2019.

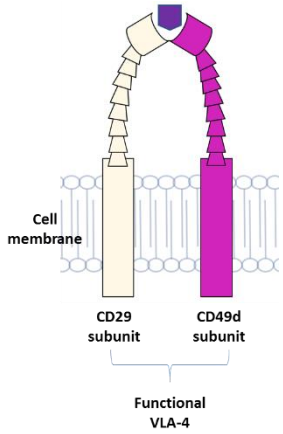
A.2 Antisense's ATL1102 development program

The CD49d hypothesis for DMD

Unlike other drugs in development, Antisense have focused their efforts in DMD on a novel mechanism of action, inhibition of CD49d; one half of the VLA-4 protein which is a pro-inflammatory, disease progression and severity marker in DMD, expressed on activated lymphocytes (a type of white blood cell). Inhibition of CD49d expression on lymphocytes reduces their survival, activation and migratory ability to enter sites of inflammation (in this case driven by degrading/necrotic muscle fibres). This anti-inflammatory action is hypothesized to have meaningful benefit in the treatment of DMD.

What is the link between CD49d and VLA-4?

VLA-4, known as very late antigen 4, is a receptor expressed on lymphocytes and other cells which is involved in immune response and cell signalling related to inflammation. VLA-4 is a dimer protein (meaning it has two parts – see inset) composed of CD49d and CD29. The actions of ATL1102 reducing expression of CD49d in turn prevents formation of the complete and functional VLA-4 dimer therefore reducing its presence on immune cells and its ability to drive inflammatory processes in the body.



Graphical representation only for descriptive purposes.

CD49d upregulated in DMD and correlates with disease severity. Research studies in DMD patients have shown that CD49d expression is upregulated on certain T cells (lymphocyte) subtypes; those responsible for adaptive immune response to pathogens and the body's subsequent response ($CD8^+$ "cytotoxic" T cells & $CD4^+$ "helper" T cells)[23]. Analysis of 75 DMD patients at various disease stages showed correlation of their CD49d-positive lymphocyte levels with disease severity (i.e. ambulatory capacity, rapidness of disease progression), making CD49d a good biomarker for DMD progression and potentially a treatment target. In a prospective study it was shown that higher levels of CD49d expression on these cells was present in patients that lost ambulation early (<10yo) compared to those that lost it later. Additionally, significantly increased CD49d expression was observed on $CD8^+$ (+32%) and $CD4^+$ (+28%) cells compared to healthy controls (p=0.009 and p=0.007 respectively) supporting the inflammatory nature of the DMD disease phenotype.

Inhibition of CD49d blocked unwanted actions and suggests therapeutic target. Finally, it has been shown with *ex vivo* studies that blocking CD49d could abrogate migration of lymphocytes (which is beneficial to inflammatory site development) and also reduced adhesion ability of these cells thus reducing their ability to drive pro-inflammatory processes at necrotic muscle sites. This research was the foundation to support targeting of CD49d for DMD treatment, particularly in late disease stage patients known to have elevated expression of CD49d driving inflammation and fibrosis.

Complete VLA-4 inhibition has adverse outcomes. Natalizumab (Biogen), a monoclonal antibody to VLA-4, has been trialled previously as a treatment for MS and inflammatory bowel disease, with clinical benefit, albeit with a severe adverse effect profile. In <0.1% of patients, following chronic dosing (>2 years), development of progressive multifocal leukoencephalopathy occurred – a rare viral brain infection causing blindness and rapid mental decline. The cause for development of this adverse effect is not yet well understood, however likely stems from its long presence within the blood, causing the immune system to weaken significantly. Immune function is paramount to the body's natural defences and therefore drugs that completely block pathways can adversely affect its functioning when there is an infection or pathogen. This also drives release of JC virus positive cells which reside in health individuals. In this case latent JC virus activation occurred. Natalizumab is contraindicated for use with immunosuppressive agents (i.e. corticosteroids).

[23] Pinto-Mariz et al. (2015) CD49d is a disease progression biomarker and a potential target for immunotherapy in Duchenne muscular dystrophy. *Skeletal muscle*. 5:45.

CD49d inhibition with ATL1102. Unlike natalizumab, ATL1102 does not completely inhibit VLA-4 but rather selectively reduces expression of CD49d RNA (the messenger molecule that makes half of the VLA-4 dimer), and subsequently functional VLA-4 expression also. Importantly ATL1102 still allows for some degree of CD49d expression to occur helping to maintain normal immune function (helping to prevent adverse outcomes due to a weakened immune system). ATL1102 also has a relatively short half-life in the blood of 4.8 hours and is cleared from the blood into the tissues. As ATL1102 exerts its effects via blockade of RNA which in turn reduces subsequent protein expression as opposed to via direct binding to proteins (VLA-4), there is no signalling to activate latent JC virus. This is because you are inhibiting the expression of the target detrimental protein, as opposed to blocking its actions directly after it is expressed on the cell, as you might with a conventional antagonist drug or antibody. Additionally, ATL1102 does not block VLA-4 actions once it is present/expressed on lymphocytes and therefore VLA-4 is able to act in an immune defence capacity as required. This is a highly important feature of antisense drugs, as opposed to monoclonal antibodies, which can bind and block all VLA-4 positive cells for a long period of time, impairing the entire immune system negatively (as in the case of natalizumab).

Phase I results summary in healthy volunteers

A Phase I trial in n=10 18-50yo healthy male volunteers was completed in 2014 which evaluated ATL1102 and Neupogen, a granulocyte colony stimulating factor (G-CSF) that is commonly used for patients undergoing chemotherapy to stabilise their white blood cell count, as well as a combination of the two drugs together. This trial was designed and executed to support clinical studies outside of DMD but was likely used to support the initial Phase II DMD trial approval.

Primary outcomes. Safety and tolerability of subcutaneous injection of ATL1102 alone or in combination with G-CSF over a 14 day study period, including full body assessments and full haematological evaluation. A second primary objective was to assess the plasma pharmacodynamics and distribution of ATL1102 and in combination with G-CSF throughout the body.

Drug distribution and binding. Drug levels were evaluated following a single, and multiple (x3) doses of 400mg ATL1102 (8 fold higher than the current DMD study). The study confirmed the safety and tolerability of ATL1102 at relatively high doses (400mg) with rapidly distribution to the bone marrow, spleen and lymph nodes (all key immune signalling sites) at high concentrations[24]. ATL1102 had a plasma half-life of 4.8 hours. This distribution pattern was deemed similar to other antisense drugs[25] and is important for effective modulation of CD49d within the immune response.

Phase II results summary for DMD

Antisense recently completed (May 2020) an open label, Phase II trial of ATL1102 in nine non-ambulant boys (10-18yo) with DMD (ACTRN12618000970246). The trial evaluated a 25mg weekly injected dose of ATL1102 for a 24 week treatment period and compared outcomes with baseline evaluations for each study subject. The study was conducted at a single Australian site; Royal Children's Hospital (Melbourne, VIC). The study was not powered for an efficacy endpoint.

ATL1102 is safe, tolerated and effective when adjunct to existing corticosteroid therapy.

Primary outcomes. The safety and tolerability of ATL1102 in non-ambulant boys with DMD was the primary focus of the study as measured by adverse event (AE) occurrences, injection site reactions and laboratory assessments (i.e. blood tests). Safety assessments were conducted every 2 weeks throughout the treatment period until 8 weeks (Week 32) post treatment cessation to monitor for any withdrawal consequences.

ATL1102 was safe and well tolerated. The study showed ATL1102 to be generally well tolerated with no serious AEs reported or patient withdrawals. The confirmed safety data will be used to support a longer dosing timeframe (to 52 weeks) and higher drug doses (>25mg/week) in the follow on Phase IIB study. Importantly, 8 of 9 patients (89%) were taking concomitant corticosteroids (prednisone or deflazacort) during the trial highlighting that ATL1102 is safe when taken in combination with steroids and has additive effects. This is key given that >65% of non-ambulant patients currently take corticosteroids for DMD management and we assess ATL1102 as an adjunctive therapy, rather than as a sole therapeutic.

[24] Tachas G. Antisense Therapeutics Ltd assignee. Method of mobilizing stem cells. PCT application PCT/AU2011/001205 (WO2012/034194). September 19, 2011.
[25] Geary et al. (2001) Pharmacokinetic Properties in Animals: Antisense Drug Technology Principles, Strategies and Applications. *Crook ST*. Ed. 119-154.

Secondary outcomes. There were a number of key secondary outcome measures related to drug proof of concept and drug efficacy including; a) lymphocyte modulation, given this is the proposed mechanism of action of ATL1102 in DMD, and b) several upper limb function tests to evaluate functional changes to upper body muscle strength as a result of ATL1102 treatment (including pinch strength, grip strength and hand function specific assessments). These assessments were conducted five times throughout the trial at Week 1, 5, 8, 12 and 24. MRI was also used at baseline and to evaluate the changes in muscle:fat proportions in muscles which is related to disease pathogenesis. Respiratory function was assessed using spirometry.

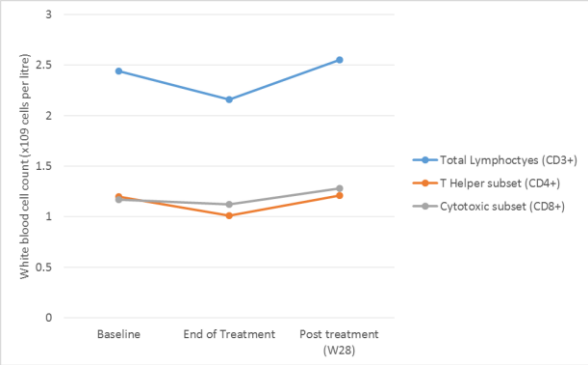
Data supports proposed mechanism of action in DMD. Results of the trial showed significant evidence of to support the proposed mechanism of action of ATL1102 in DMD, that being lymphocyte modulation via CD49d, fat fraction stabilisation, potential muscle preservation and functional changes in strength. This cohesive story is beneficial as it supports ATL1102's future approval likelihood in DMD, as drugs without a proven mechanism of action face potentially more challenges to gain approval (~10-20% current FDA drugs approved with no known mechanism)[26].

Stabilisation of fat fraction key finding. One important result speaking to the potential for ATL1102 to preserve and somewhat modify disease progression is the stabilisation of percentage fat fraction in the muscles as measured by MRI. When these data were compared to published data, again, significant improvements were seen. Put simply, ATL1102 was able to preserve or in some cases increase the muscle area whilst reducing the percentage of fat in the muscle which is a key driver of muscle function loss in DMD (as the remaining muscle fibres turn to fat rendering them non-functional). Noting, it is difficult to interrogate this data in terms of variability of response based on the available information (and the very small sample size), however is incrementally positive to the underlying hypothesis and supports the functional muscle changes in upper body strength observed.

Strength of lymphocyte modulation from Phase II data. Changes to T cell populations following treatment with a 25mg weekly dose of ATL1102 were measured at 5 time points over a 28 week period (24 weeks of treatment). A median 9.78% reduction in CD49d positive total lymphocytes (CD3) was reported[27] (specifically -16.7% reduction in $CD4^+$ and -5.8% reduction in $CD8^+$). This reverted back to above baseline levels (+9.93%) after 4 weeks of ceasing ATL1102.

This fast rebound (with minor elevation) in inflammatory response following end of treatment is something to monitor and evaluate in the longer term dosing Phase IIB trial, and at a later post-treatment time point (>4 weeks). Noting that in the prior MS trial, similar rebound response was observed and returned to baseline levels by 4 and 8 weeks post the last dose[28] (Figure 7). The rebound does support a clear drug-mediated effect however which is positive.

Figure 7. Changes to CD49d+ lymphocytes as a result of ATL1102 treatment for 24 weeks.



Source: Antisense Therapeutics, Wilsons

[26] Moffat et al. (2017) Opportunities and challenges in phenotypic drug discovery: an industry perspective. *Nature Reviews Drug Discovery*. 16: 531-543.
[27] Desem at al. (2020) ATL1102 Phase II non-ambulant DMD study (1102-DMD-CT02)Poster presentation at Muscular Dystrophy Association Annual Conference, March 2020. p
[28]Limmroth et al. (2014) CD49d antisense drug ATL1102 reduces disease activity in patients with relapsing-remitting MS. *Neurology*. 83: 1780-1788.

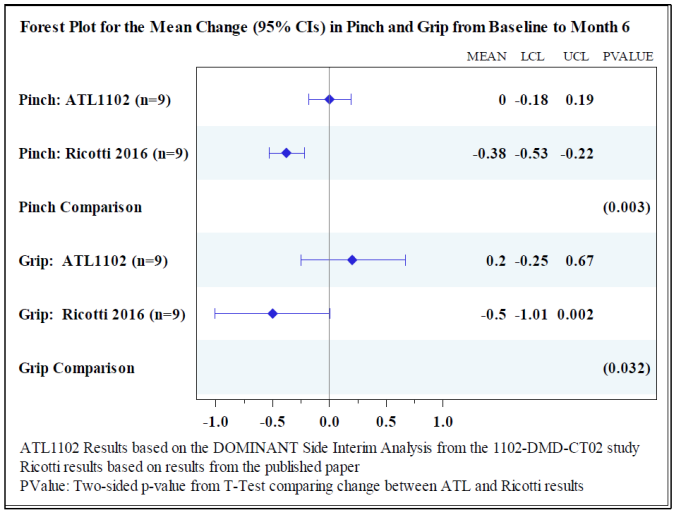
Effect size potentially dose-dependent based on prior data. The magnitude of effect (~10% average reduction) is likely dose-related given that a 2.5 fold greater effect was seen in the MS trial which administered a much higher 400mg/week ATL1102 dose for 8 weeks. Peak reductions in CD49d positive lymphocytes were ~25% in this study highlighting that a larger magnitude of effect at the lymphocyte level is possible with ATL1102 at higher dose ranges (which could be observed in the Phase IIB study – noting that detailed flow cytometry will not be available to make direct comparisons to this MS data.) It is important to note however that the changes to CD49d expressing lymphocytes (across all subsets) were not significantly different at the end of treatment compared to baseline in the current Phase II trial (Figure 7).

Cell populations intact, with response CD49d selective. Importantly the absolute number of natural killer (NK) cells, another key immune lymphocyte subgroup similar to T cells (however act in a faster, more immediate manner as needed for rapid immune response to an insult), were not affected by ATL1102 treatment in the MS study, however the number of NK cells expressing CD49d was significantly lower at the end of treatment compared to baseline (p=0.018) in the DMD study, in line with other lymphocyte subset findings in the DMD trial.

High variability somewhat inevitable. The level of variability in response was also high between patients. There are several reasons for this which may relate to individual immune response, drug distribution or possibly differences in relative dosing when equated for body weight. The small sample size also promotes variability. Unfortunately further data to clarify this is unlikely in Phase IIB trial.

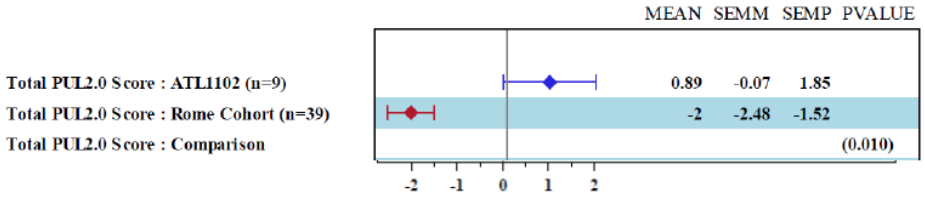
Subsequent comparisons to natural history cohort controls positive. Comparison of changes in pinch and grip strength in the Phase II cohort were compared to published natural history cohorts[29] and showed a significant (p>0.05) improvement of ATL1102 in both measures (Figure 8). Further subsequent natural history cohort comparisons (to a different cohort) focused on PUL2.0, as a measure of total muscle function, also showed significant differences favouring ATL1102 (Figure 9).

Figure 8. Comparison between Phase II ATL1102 functional results and published natural cohort data (Ricotti et al). 2016



Source: Antisense Therapeutics

Figure 9. Comparison between Phase II ATL1102 PUL2.0 data and Rome cohort control.



Source: Antisense Therapeutics.

[29] Ricotti et al. (2016) Upper Limb Evaluation in Duchenne Muscular Dystrophy. PLoS One, 11(9)e0162542.

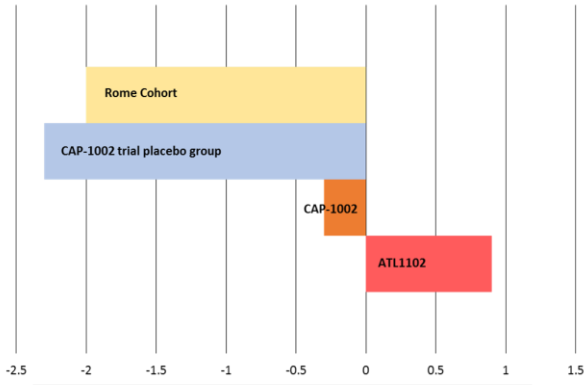
Does not discount lack of controlled trial result. These cohort comparisons are certainly promising to put the ATL1102 results into context, however they are not a supplement for a blinded, controlled trial. Given that PUL2.0 is a key efficacy endpoint for seeking approval in non-ambulatory DMD patients, the Rome cohort data comparison further strengthens the conviction in the PUL2.0 results thus far and supports progression to a Phase IIB efficacy study. Keeping in mind the key step change in the Phase IIB study will be the number of patients and the double-blinded, placebo-controlled nature of the study (which introduces a placebo effect to overcome as well as potential clinician bias).

PUL2.0 as a primary outcome measure for approval in non-ambulant patients. PUL2.0 is an FDA defined outcome measure appropriate for non-ambulant DMD approval and will be the primary endpoint for Antisense's Phase IIB study. As previously mentioned, there are several other promising competitors also using PUL2.0 as the primary endpoint for their studies (Pamrevlumab & CAP-1002).

Comparisons of PUL2.0 data in non-ambulant patients show ATL1102 as superior, even when we accommodate for the shorter trial duration.

At present the only available 6 month data for PUL2.0 measures in a DMD population including non-ambulant patients is the Phase II CAP-1002 randomised controlled HOPE-2 trial. The Phase II pamrevlumab trial captured PUL1.2 measures and is therefore not comparable to ATL1102, however the follow on Phase III will be, as it is using the updated PUL2.0 measure endpoint. A comparison of the available 6 month PUL2.0 data (Figure 10) shows ATL1102 is superior to CAP-1002 and controls.

Figure 10. Comparison of 6 month PUL2.0 data in non-ambulant DMD patients.



	Mean change in PUL2.0 from baseline	n
Rome cohort	-2.0	39
CAP-1002 placebo group	-2.3	8
CAP-1002	-0.3	6
ATL1102	+0.9	9

Fig 10 note: a positive change in PUL2.0 denotes improvement in upper limb function/strength, whereas a negative change from baseline denotes worsening muscle function.

Source: Wilsons, Capricor, Antisense Therapeutics

Dose limited by prior FDA hold. The 25 mg per week dose was the lowest dose of ATL1102 used thus far in a Phase II trial and is the dose limit stipulated by the FDA following the prior Phase IIA trial of ATL1102 in MS patients (up to 200mg twice weekly) where there was concern with regards to non-human primate adverse event data at these higher doses This mandated a 10 fold margin requirement on the monkey no-observed-adverse-effect-level (down to 25mg). The data from this Phase IIA study provides Antisense with possible scope to increase the dose in subsequent trials in the hopes of more pronounced outcomes. Observation of dose-dependent effects in a parallel arm trial would be highly supportive of the drug's mechanism and would hope provides increases to observed effect sizes (in PUL2.0 and other measures).

25mg dose limit stipulated by FDA from prior Phase IIA MS trial. Scope to increase in Phase IIB.

Dose by weight equates to 10 fold lower than existing approved therapies. As a reminder, most DMD drugs are dosed by weight as opposed to a fixed dose, potentially providing further scope for Antisense to explore a broader dose range that is weight derived. Noting, there are benefits to remaining with a fixed dose format (albeit a higher fixed dose) including during manufacture and end user convenience. Based on the current Phase II cohort, the dose range by weight may have ranged anywhere between 0.35mg/kg to 0.75mg/kg which likely affected the distribution, uptake and possible efficacy of ATL1102 between patients. For context, both of Sarepta's DMD drugs, Vyondys and Exondys are currently dosed at 30mg/kg weekly via intravenous infusion and therefore the relative does of ATL1102 being received in >10 fold lower than currently approved therapies. If adequate efficacy is shown by ALT1102 at this lower dose range there may be potential advantages for Antisense relative to competitors (i.e. lower COGS).

Respiratory data underwhelming. The changes in respiratory measures (FVC and PEF) with 6 months of ATL1102 treatment were clinically non-significant and highly variable between patients making any conclusions challenging to draw. Antisense have noted this issue and suggest 12 month treatment and observation periods should allow for more clarity of response in these respiratory measures, in addition to having greater patient numbers. Comparatively competitors such as pamrevlumab have shown significant improvements to FVC, albeit when measured over a 12 month treatment timeframe.

Regulatory strategy overview

EMA engagement. Antisense have been engaged in discussions with the EMA, including their scientific advisory committee following the completion of their Australian Phase II study. Antisense are finalising the Phase IIB trial design following feedback from the committee and expect to file their Paediatric Investigational Plan (PIP) in late 2020/early 2021. This plan will outline the final design and pivotal status of the Phase IIB study in Europe which we expect to extend upon the existing Phase II data in both dose and treatment duration length.

Potential pivotal Phase IIB trial to support EMA approval and assess higher, longer (12 month) dosing regimen.

We view this EU trial as having both Phase IIB and III attributes. Firstly, the 25mg dose has already been assessed for initial efficacy in the Phase II study and therefore this expanded sample size dose extension study is verifying efficacy (e.g. Phase III), keeping in mind however this will be the first efficacy assessment of ATL1102 compared to a placebo control and not a baseline/natural history control. Secondly, the third higher dose arm (likely between 50-100mg) will act like a Phase II for that dose, meaning any data generated for that dose is unlikely to support a label approval initially however may help with additional safety data support and supports future trial designs and extension studies supporting label extension.

FDA engagement. We understand Antisense are yet to engage with the FDA regarding ATL1102 clinical development but that this is planned for first half of CY21. The focus of this engagement will be around the development path including the Phase III trial design and strategy and is likely to include detailed discussions around the data package required to support ATL1102 dosing requirements (i.e. dose range and dosing period). We understand that there are differences between the EMA and FDA with regards to data package requirements to support chronic (>6 month) paediatric dosing in clinical trials. We appreciate there could be some additional data required by the FDA prior to trial design approval, which could include some degree of US Phase II trial (however we do not assess this as the base case). We assess an 80% probability of the current Antisense data package being sufficient to gain a Phase III trial approval in the US, however in the event the FDA does not deem their existing data sufficient to proceed, Antisense may need to complete additional studies which we assess may add ~$3M (or more) and ~10months to the US pre-IND phase. If this is the case, initiation of a US Phase III pivotal trial may be delayed to 1H23 assuming a sufficient data is collected and accepted by the FDA.

Parallel pivotal Phase III US trial to support FDA approval assuming data package sufficient.

Phase IIB pivotal trial in Europe

Antisense are poised to submit their Paediatric Investigational Plan (PIP) to the EMA for their Phase IIB trial design in early 2021. Trial submission is pending the outcomes of EMA scientific committee feedback regarding their initial PIP. Following this feedback final trial design can be confirmed. We expect initiation of the trial in 2H21 (assuming trial approval proceeds as planned) and may possibly include sites from Germany, France, the United Kingdom, and potentially Australia.

First scrutiny of ATL1102's efficacy compared to placebo in DMD.

To date, all ATL1102 efficacy data in DMD has been collected in an open-label fashion which must attract a healthy level of scepticism around how the results will hold up in a blinded, placebo-controlled study.

Trial design. Antisense have proposed a randomised, three arm, parallel, double-blinded, placebo-controlled trial to evaluate ATL1102 at two dose ranges (25mg, and higher ~50-100mg) compared to placebo. This will be the first placebo controlled study to evaluate efficacy of ATL1102 in DMD patients. Thirty-six patients per arm are anticipated (n=108 total). This trial design includes Phase IIB and Phase III components as it will confirm efficacy with 25mg ATL1102 dose observed in the Phase II study in a larger cohort, whilst evaluating a new dose range not previously evaluated for DMD (~50-100mg). The study will deliver weekly doses of treatment for a 12 month period with a further open-label extension study to follow.

Study cohort. The inclusion criteria is expected to be similar to the Phase II study inclusion/exclusion criteria for consistency. That being, non-ambulant boys with DMD +/- corticosteroid treatments between ~10 and 18 years of age.

Primary outcome measure. The primary outcome measure for this study is the change in the PUL2.0 measure over the 12 month treatment window with ATL1102 compared to placebo.

More limited secondary outcome measures expected. We expect these to be consistent with the Phase II study secondary outcome measures (including crucial MyoSet measures) with a few key exceptions being lymphocyte evaluation and fat fraction via MRI.

MRI and full lymphocyte panel unlikely to be included in Phase IIB design.

Specifically, detailed evaluation of lymphocyte CD49d response via flow cytometry, like in the Phase II trial, is not expected to be included with only high level blood cell counts to be conducted. We understand this could be omitted due to difficulties in logistics and costs across trial sites however note it is disappointing this same CD49d expression data will not be collected to confirm and inform the underlying drug mechanism hypothesis in the larger patient subset (and with a higher dose).

Perhaps there is an opportunity to include lymphocyte analysis in subset of patients only, however this will be only be confirmed once Antisense submit their PIP/final trial design that has been discussed with the EMA.

It is also understood that MRI to evaluate fat/muscle mass will not be included in the Phase IIB design due to the challenges with calibrating MRI between different sites, in addition to costs. This will remove one measure which helps to support the functional outcomes seen, however is not unexpected given the additional cost and logistical challenges associated with this.

We perhaps expect some additional measures or increased focus on respiratory capacity and cardiac function given how important these metrics are and the inaccuracies around spirometry (which was used in the Phase II trial).

Phase III pivotal trial in US

The likelihood of a Phase III pivotal trial in the US will likely be independent of the outcomes of the European Phase IIB study as it is likely to overlap and run in parallel (prior to top-line data being available for the EU study). Additionally, Antisense have inferred they are soldiering on with their US development plan in parallel to the European pivotal bringing these two market opportunities more in line with one another.

Overlapping EU and US trials seem likely.

US patient involvement likely required for FDA approval. We assess a US pivotal trial is necessary to service the anticipated requirements of the FDA, as it is highly unlikely the FDA would consider ATL1102 for market approval in the absence of any US patient data. We assess that Antisense are currently working to align the future trial design with that of the imminent European Phase IIB to harmonise outputs. Estimated timelines for this Phase III are initiation in 1H23, with completion by 1H25. It is possible this US pivotal trial could provide an opportunity to further assess a higher dose (>25 mg) which is also planned to be included in the EU Phase IIB.

Data package to support FDA trial approval. The available data package to support a US pivotal trial in DMD will be critically reviewed and evaluated by the FDA. This data package will include all prior clinical studies of ATL1102, namely Phase II in DMD, as well as standard preclinical studies (in vivo pharmacology & toxicology etc.). There are questions as to whether Antisense's existing data package can support the dosing and treatment period being put forth in the EU Phase IIB design proposal (25mg and higher for 12 months), which we assume will be similar for the US Phase III. The FDA has additional requirements when chronic dosing (> 6months) is proposed in paediatric populations which Antisense must consider. We have factored in some risk probability (20%) and additional expenses to our base case scenario to account for the event in which the FDA requires additional supporting data be generated prior to giving trial approval. We understand Antisense have engaged regulatory experts who are guiding them around this initial FDA engagement and ways to optimise these first discussions.

Uncertainty regarding acceptability of existing data package for FDA chronic dosing approval.

Orphan Drug Designations and Priority Review Voucher

Antisense are in the fortunate position to have been awarded Orphan Drug Designation (ODD) in both US and EU jurisdictions, and have received Rare Paediatric Disease Designation (RPDD) from the FDA in relation to development of ATL1102 for DMD.

Rare Paediatric Disease Designation and Priority Review Voucher (PRV). RPDD's are granted to companies working within rare disease areas that have a desperate need for new treatments, including in rare paediatric disorders, of which DMD falls. This designation was granted earlier in the year (29 Sept) by the FDA and puts them in good stead when they reach a position of NDA filing. This designation gives the bearer a future option on a Priority Review Voucher (PRV) at the time of NDA filing (~2025), which if granted, can be used to expedite NDA review and remove associated costs (US$2M), or can be sold on a secondary market which has become commonplace in recent years. Sales of PRVs have reached historic highs of up to US$350M (AbbVie purchase from United Therapeutics in 2015), with some of the more recent sales closer to US$100M (e.g. Lumos Pharma sale to Merck in July 2020) becoming more the norm. We assume a conservative A$100M sale price of the potential Antisense PRV in 2025 in our forecast model. Keeping in mind, the current PRV scheme legislation is under review by the US senate – we do not expect changes to this scheme or a lack of extension that would be detrimental to Antisense.

Orphan Drug Designation (ODD). Antisense have ODD status from both the FDA and EMA for ATL1102 as a DMD treatment which grants them an expedited review timeline should they file in either jurisdiction for marketing authorisation, as well as market exclusivity of 7 years minimum in the US and 12 years in Europe (10 year + 2 year paediatric use extension) should ATL1102 be approved with a DMD indication.

Indication extensions into MS and beyond

Successful Phase II trial in MS. Antisense have completed a Phase IIA randomised, controlled trial of ATL1102 in patients with relapsing remitting multiple sclerosis with positive results[30]. Briefly, 77 patients were treated with 200mg twice weekly injections of ATL1102 for 8 weeks (plus 1 additional loading dose in Week 1) or placebo and were followed up for another 8 weeks. The key focus of the study, aside from safety and tolerability, was the number of new active brain lesions as assessed by MRI every 4 weeks.

Positive results on new lesion formation. The trial (ACTRN12608000226303) showed a significant reduction in the number of new active lesions compared to placebo (p=0.01), as highlighted below (Figure 11), which provided the first evidence that modulation of CD49d has effects on MS progression.

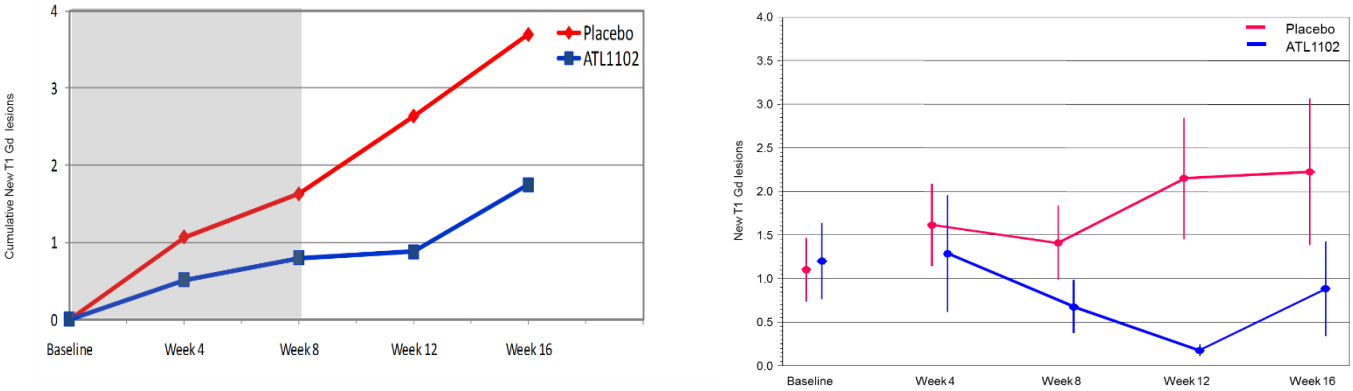
Reductions in platelet count observed. This reduction in ~11% of patients of platelet levels below the lower limit of normal was reversed following treatment cessation, and has been commented on in the literature as a consequence of high dose (400mg) antisense drugs more generally[31].

Safety concern in monkeys led to FDA clinical hold. Subsequent to the results of this trial Antisense proceeded with a Phase IIB IND filing with the FDA only to have a clinical hold placed on the study due to safety concerns regarding monkey immune responses to high dose ATL1102. It is understood that the monkey immune response is species specific and bears little relevance in this case to human response to ATL1102, however this led the FDA to stipulate a much lower dose limit of 25mg in order to proceed into Phase IIB studies in MS. The Phase IIB trial in MS did not proceed at this lower dose and no further development has continued to date. The reasons behind this ATL1102 pivot from MS into DMD are potentially opportunistic where DMD was viewed as a way to enter the orphan disease market which provides a shorter potential path to drug approval, in comparison to MS where trials are much longer and more expensive involving thousands of patients. Ultimately this shift into DMD we assess as a positive strategic move for Antisense but note that this shift could be a lingering query for many investors.

[30] Limmroth et al. (2014) CD49d antisense drug ATL1102 reduces disease activity in patients with relapsing-remitting MS. *Neurology*. 83: 1780-1788.

[31] Crooke et al. (2017) The effects of 2'-O-methoxyethyl containing antisense oligonucleotides on platelets in human clinical trials. *Nucleic Acid Therapeutics*. 27(3):121-129.

Figure 11. Results from Phase IIA trial of high dose ATL1102 in relapsing-remitting multiple sclerosis.



Source: Antisense Therapeutics.

Teva licensing agreement terminated. As a result of this development the licensing agreement that was in place with Teva Pharmaceuticals (since 2008) for the development of ATL1102 in MS was terminated.

MS most advanced opportunity for indication expansion of ATL1102. If Antisense were to pursue indication expansion of ATL1102 outside of DMD, MS is their most advanced asset and opportunity given the advanced clinical development they have already completed. A key obstacle for Antisense in pursuing this indication again would be providing clarification as to why they ceased this development opportunity back in 2017, following the full clinical hold being lifted by the FDA. It is understood that having 25mg dosing data from DMD patients (with some efficacy) provides support for continued MS development at this lower dose (~25mg/week), keeping in mind that the relative body weight exposure in DMD is higher than MS, which potentially further assists in supporting higher resumed MS dosing trials. Notwithstanding this, the choice to pivot to DMD from MS, as noted above, is still an area of speculation for the market which requires clarity should any further work in MS proceed in the future.

A.3 Antisense's ATL1103 development program

ATL1103 as an inhibitor of growth hormone receptor

ATL1103 is an antisense oligonucleotide to the growth hormone receptor (GHr) which binds to its mRNA sequence reducing its subsequent expression on cells. ATL1103 is targeted toward inhibition of the growth hormone receptor to prevent downstream upregulation of insulin-like growth factor I (IGF-I), which is responsible for the pathogenesis of acromegaly (being, uncontrolled growth of bodily features and organs).

Antisense have sponsored and completed three clinical trials to evaluate ATL1103 for treatment of acromegaly; the results of which are summarised below.

Phase I trial for ATL1103

The Phase I study of ATL1103 (ACTRN12611000854932) was conducted in 24 healthy male volunteers (18-45yo) using a standard SAD/MAD (single ascending dose/multiple ascending dose) trial design to evaluate safety, tolerability and drug actions (pharmacokinetics and pharmacodynamics) of ATL1103.

The trial assessed four dose ranges (25, 75, 250 and 400mg) of ATL1103 first as a single dose and then given as a subcutaneous injection on a fixed dose regimen over a 3 week period (dosing on days 1, 3, 5, 7, 14, 21) compared to a placebo group. There were five parallel patient cohorts in total.

Safety outcomes. Generally ATL1103 was safe and well tolerated with more prevalent adverse events experienced in the two higher dose groups (250-400mg) compared to the lower doses (25, 75mg) evaluated. All reported adverse events were mild or moderate in nature, with no serious adverse events reported.

Proof of concept regarding mechanism. The reduction in IGF-I levels in patient serum following treatment with ATL1103 (-7% reduction, p=0.034) confirms that the drug was mechanistically working in patients as expected and supported advancement into the acromegaly indication (given that healthy volunteers have a lower IGF-I baseline level to lower from). Additional reductions in growth hormone binding protein were also seen (-16%, p=0.007) to further support proof of concept.

Pharmacokinetic parameters. ATL1103 was shown to reach blood concentrations of > 14µg/ml at the highest 400mg dose level and peak in the blood at ~3.3 hours after injection.

Phase II trials for ATL1103 in acromegaly

Antisense have conducted two Phase II trials of ATL1103 in acromegaly patients: one multicentre in Europe/Australia (ACTRN12612000989842 and one single site in Australia (ACTRN12615000289516).

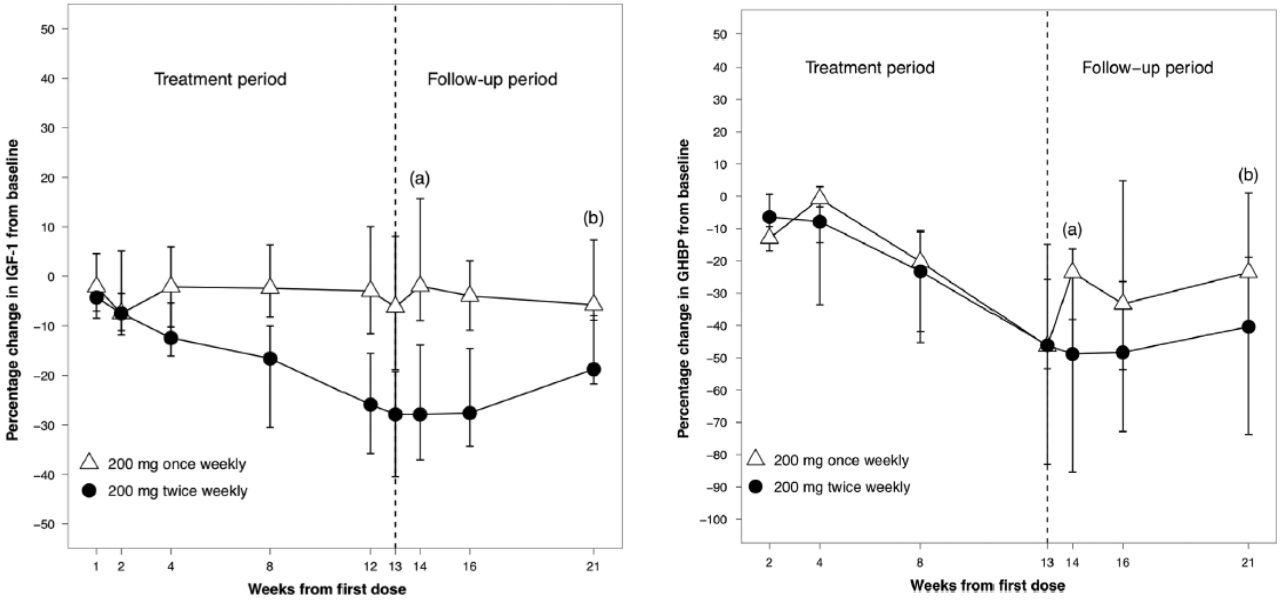
The first trial, completed in 2014, focused on dose frequency, the second, completed in 2016, tested a higher dose in a small number of patients (n=3).

The first study (ACTRN12612000989842) assessed 200mg ATL1103 dose given either weekly or twice weekly for a 12 week period in 26 patients (18-80yo) with acromegaly that was specifically due to diagnosed pituitary adenoma. Patients were either treatment naïve or ceased other indication-specific medications prior to study enrolment. This was a randomised, open-label parallel design study that was conducted across multiple sites in Europe (FR, UK, ESP) and Australia.

The second study (ACTRN12615000289516) was also open label, however only evaluated a single, higher dose regimen (300mg twice weekly) in a small number of patients (n=3).

Primary outcomes. Importantly the trial achieved its primary endpoint and showed ATL1103 could cause a significant reduction in serum levels of IGF-I in acromegaly patients compared to baseline when treated with ATL1103 twice weekly (-27.8%, p=0.0002). Additionally significant reductions in GH binding protein (GHBP) were also observed in both dose cohorts supporting the mechanism in this disease cohort (Figure 12).

Figure 12. Significant reductions in target IGF-I and GHBP with twice weekly ATL1103 in acromegaly patients.



Source: Antisense Therapeutics, Trainer et al.[31]

Physical changes accompanied serum changes. Physical changes as a result of excess growth hormone inhibition were observed including a significant reduction in hand ring size circumference (cm) (-37.5%).

Safety profile confirmed. Safety and tolerability of ATL1103 in acromegaly patients was shown with once or twice weekly 200mg dosing with the majority of patients experiencing mild-moderate injection site reactions (84.6%)[32]. Four serious adverse events were reported however none were deemed to be study drug related and both patients completed the full course of therapy.

Orphan Drug Designation received. As with ATL1102, Antisense have received ODD status from both the FDA and EMA for ATL1103 in acromegaly which will afford them the same benefits should they pursue a marketing authorisation in either major jurisdiction.

Next steps

The next clinical development step for ATL1103 in acromegaly is completion of a pivotal Phase III trial. Ideally this would be multi-centre incorporating both US and EU sites at a minimum to allow for cross-jurisdictional applications to be made, however an EU/APAC study is most likely given the prior Phase II data excludes US patients to this point.

Antisense have previously mentioned that seeking a licensing partnership for ATL1103 in this indication is the most likely next step to further its development. Given the uncertainty surrounding timelines associated with ATL1103 development we have not included it in our current model or forecasts. Should a licensing deal appear, it would be additional icing on the cake that is accretive to valuation.

[32] Trainer et al. (2018) A randomised, open-label, parallel group phase 2 study of antisense oligonucleotide therapy in acromegaly. European Journal of Endocrinology. 179(2): 10.1530/EJE-18-0138

A.4 Partnering opportunities and assumptions

Existing Ionis Pharmaceuticals Licensing Agreement. In 2001 Antisense entered into a licensing partnership with Ionis Pharmaceuticals (NASDAQ:IONS), a well-established, US biopharma, that provides exclusive global rights to commercialise ATL1102 and ATL1103. The terms of this agreement stipulate that Antisense have global, exclusive rights to commercialise both assets for any indication. There are no milestone payments associated we know of however there is a royalty fee based on future revenues for either asset being commercialised. We understand that this royalty is "single-digit" in nature, which we have assumed to be 9% in our models, but may change depending on further on-licensing/third-party agreements.

Ionis royalty amenable to possible change.

Partnering in DMD

'Going it alone' is base case assumption. We propose Antisense are unlikely to seek a Pharma partner to complete clinical development and subsequent commercialisation of ATL1102 for DMD. There are several reasons to support this line of reasoning including:

Base case assumption is that Antisense do not partner for US commercialisation.

- DMD is a concentrated market which will only require a small specialised marketing effort, as opposed to large scale distribution networks, therefore it is manageable for Antisense to develop the required marketing infrastructure alone;
- KOL relationships built by Antisense now and in subsequent clinical trials will help drive the commercialisation effort which may not be as specific/personalised in a third-party model;

Antisense possess management expertise in commercial drug market launches (i.e. Dr Gil Price's experience is particularly notable, having been involved in Sarepta's Exondys US launch).

Keeping this in mind we have modelled two scenarios: our base case Scenario 1 where they "go it alone" vs Scenario 2 where Antisense partner for US commercialisation. This exercise is to evaluate the potential upside to a US Phase III development partner or a sole commercialisation strategy.

Scenario 1:

Our base case scenario assumes Antisense develop and commercialise ATL1102 for DMD in both EU and US markets alone. This assumes:

- All R&D and regulatory costs associated with Phase IIB (EU) and Phase III (US) trials are funded by Antisense (totalling A$70M)
- 9% of royalties for sales revenues generated (EU+US) paid to Ionis

Scenario 2:

In the event of a US Pharma commercialisation partnership, the most likely timing of such a partnership would be following the successful top-line data readout from the EU Phase IIB trial. We forecast this to be 1H24. Our proposed partnership for US development assumes:

- Partner covers majority of costs of US Phase III trial and regulatory approval (A$20M of $35M total)
- Partnership in FY24 (mid-way through US Phase III – recruitment completed).
- Upfront and milestone payments to Antisense totalling A$190M over FY24-FY33 period.
- Royalties for sales revenue begin in FY27 at 9% (first 5 years) and then step up to 15% in FY32.

Likely US Pharma partners include Sarepta Therapeutics or PTC Therapeutics given their existing interest and success in the US DMD market. Both companies could utilise their existing US distribution networks and familiarity with DMD drug regulatory approvals to their advantage in a partnership such as this. Sarepta is potentially a more likely partner given the shared history of board members and management between Antisense and Sarepta (e.g. Dr Gil Price & William Goolsbee).

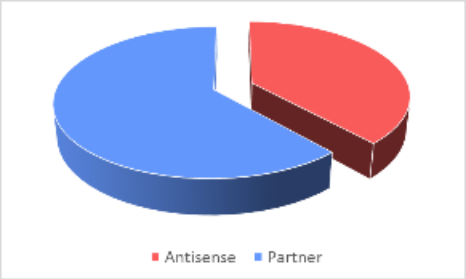
Overleaf (Table 12) we compare FY24 NPV for Antisense and their US partner given that this is the likely timing of such a transaction. We assess a desirable opportunity for an incoming pharma partner to license ATL1102 for DMD in the US market should this be of interest to Antisense.

Table 12. Scenario analysis for future revenue share based on partnership for US commercialisation.

	FY24e NPV^ (A$m)	US benefit split
Antisense US share	194	38%
Pharma partner US share	312	62%
Scenario 1 (Antisense alone)	**1708**	**100%**
Scenario 2 (Antisense partners)	1595	38%

^NPV calculated on an after tax EBITDA.

Source: Wilsons' estimates



There is a small financial downside (-7% FY24 NPV) to Antisense partnering for US development and commercialisation based on these partnering assumptions, which map a scenario that is reasonable from a pharma partner perspective (~62% of pie). The potential benefits to Antisense in a partnership agreement would be distribution of the risk associated with clinical approval in the US market, and reduced R&D expenditure which may be challenging for them to source. This analysis further supports our base case scenario where Antisense will likely commercialise ATL1102 for DMD in both EU and US markets in the absence of a pharma partner, however should they choose to at a later date, our valuation is not significantly impacted.

US partnership has no financial upside but distributes risk and near term R&D investment.

Partnering in Acromegaly

Future partnering opportunity for ATL1103 in acromegaly.

Antisense have spoken recently about opportunities and interest in partnering for the further development of ATL1103 in acromegaly. The next step in development is execution of a pivotal Phase III trial which would require significant investment (>$15M) which Antisense are not in a position to fund for > 5 years given their DMD programme status. We have not ascribed any value to this asset at present, however based of similar stage partnering agreements for rare indications there is the possibility for Antisense to seek terms potentially involving >$25M in combined upfront and milestone payments with a single-digit royalty fee on future revenues (~acromegaly TAM of US$2.1B by 2025)[33].

[33] GrandView Research. (2019) Acromegaly Treatment Market Size and forecasts 2019-2025. https://www.grandviewresearch.com/press-release/global-acromegaly-treatment-market

A.5 Board and management

Board of Directors

Robert Moses. Independent Non-Executive Chairman of the Board.

Robert Moses was appointed chairman of the board for Antisense in 2001. Mr Moses has >40 years of experience in the pharmaceuticals/biotechnology industry. He has previously held influential positions with a number of large corporations including CSL (Corporate vice president), Freehills law firm (Management Director), IntegraMed (CEO and Chairman), TGR Biosciences Pty Ltd (Non-executive chairman) and Eli Lilly (17yrs in various management roles). Robert holds a BA and an MBA from the University of Chicago.

Mark Diamond. Managing Director and Chief Executive Officer.

Mark Diamond has served as MD and CEO for Antisense Therapeutics since 2001. Mr Diamond has >30 years' experience in the pharmaceutical and biotechnology sector. Mark held several senior leadership roles at Faulding Pharmaceuticals prior to joining Antisense in the UK, US and Australian offices. Mark holds a BSc, MBA and MAICD.

William Goolsbee. Non-Executive Director.

William Goolsbee has served on the Antisense board since 2015. Mr Goolsbee has extensive experience within the biotechnology sector. He has served on the boards of BMG Pharma, Metrodora Therapeutics and until recently, Sarepta Therapeutics. He was founder, CEO and Chairman of Horizon Medical until its acquisition by UBS Private Equity and was a founding director of ImmunoTherapy Corporation until its successful acquisition by (now) Sarepta Therapeutics. William holds a BA from University of California, Santa Barbara.

Dr Graham Mitchell. Independent Non-Executive Director.

Graham Mitchell has served on the board since 2001. Dr Mitchell is a research scientist and currently joint Chief Scientist for Victorian Dept. of Environment and Primary Industries. Graham has previously held positions including Director of Research at CSL and academic fellowship positions at the Walter and Eliza Hall Institute in Melbourne. Dr Mitchell also currently serves as a director on the board of several public (ASX:CMP) and private companies (Avipep; Adelaide Research and Innovation). Graham holds a BVSc from the University of Sydney and PhD from the Walter and Eliza Hall Institute in Melbourne. He has also received an Order of Australia (AO) for his contributions to science.

Dr Gary Pace. Non-Executive Director.

Gary Pace has been a board member since 2015. Dr Pace has >40 years' experience within the pharmaceutical, biotechnology and medical device industries. He was awarded the Centenary Medal by the Australian government for "service to Australian society in Research and Development" in 2003 and is a fellow of the Australian Academy of Technological Sciences and Engineering. Dr Pace currently holds a number of director positions for both public (NASDAQ: PCRX, ASX:SVA, ASX:IVQ) and private companies. Gary holds a BSc (Hons I) from University of NSW and a PhD from MIT, where he was a Fulbright Fellow and General Foods Scholar.

Management team

Mark Diamond. Managing Director and Chief Executive Officer.

See above.

Dr George Tachas. Director- Drug Discovery and Patents.

Dr Tachas was a founding member of Antisense and has been a director since the ASX listing in 2000. Dr Tachas has a strong and extensive research background in antisense oligonucleotides, which were the focus of his postdoctoral research. Dr Tachas has held various research scientist positions at the University of Melbourne as well as working at both Griffith Hack and Callinan Lawrie in the capacity of a biotechnology-patent law consultant. George holds a PhD and a Diploma of Intellectual Property Law both from the University of Melbourne.

Phillip Hains. Chief Financial Officer and Company Secretary.

Phillip Hains has severed as CFO and secretary since 2006. Mr Hains brings >30 years' experience in corporate secretarial, accounting and general financial management to his position at Antisense. Mr Hains also founded and operates a specialist public practice, The CFO solution, in addition to acting as Secretary and CFO to several other public and private companies including Immuron Ltd, Alterity Therapeutics Ltd, Total Brain Ltd, SelfWealth, Imugene, Bkm Mgmt Ltd, Sensera Ltd and Savcor Group Ltd. Phillip holds an MBA from RMIT and is a Chartered Accountant.

Nuket Desem. Director of Clinical and Regulatory Affairs.

Nuket has served as Director of Clinical and Regulatory Affairs since 2018 and was previously Development Director from 2004-2010. She has 25 years' experience in global regulatory affairs, clinical development and project management. Nuket has previously held senior/director regulatory affairs roles at Prana Biotechnology, Spinifex Pharmaceuticals (now acquired by Novartis), CSL and Paranta Biosciences. She has extensive experience with clinical trial program management and was project lead for the ATL1102 Phase II trial in MS. Nuket holds a BSc (Hons) from La Trobe University and an MBA from Monash University.

Dr Gil Price. Consultant Medical Director (US-based).

Gil Price is a recent addition (Feb 2020) to the Antisense management team. Dr Price is physician with training in internal medicine that also had extensive experience with biotechnology commercialisation. Dr Price served as a Director on the board of Sarepta Therapeutics for 9 years (2007-2016) during a key development phase of the company. He has extensive experience within the DMD therapeutic development field and brings this to the role. Dr Price is currently on the board of Rexahn Pharmaceuticals (NYSE:RNN). Gil holds a BSc from University of Rio Grande and an M.D. from Santiago University. He also completed postgraduate studies in Political Science and Economics from Cambridge University.

Antisense Therapeutics Limited (ANP)

Business description

Antisense Therapeutics is a clinical stage biopharmaceutical company focused on development of antisense oligonucleotides targeting rare diseases. Their primary asset, ATL1102, is currently in Phase II trials for the treatment of Duchenne Muscular Dystrophy (DMD) with positive results thus far in the more advanced, non-ambulant disease population. Antisense have also conducted some advanced clinical work on ATL1102 as a treatment for multiple sclerosis (MS) and with another asset ATL1103, for the growth disorder, Acromegaly.

Investment thesis

We initiate coverage on Antisense Therapeutics with an OVERWEIGHT rating and a risked 12 month price target of $0.57 per share. Antisense is a clinical stage biopharmaceutical company focused on antisense drugs for rare diseases. Their primary asset, ATL1102, is being developed for the treatment of Duchenne muscular dystrophy (DMD), a debilitating, inherited disease affecting boys causing severe muscle wastage leading to premature death. Antisense also have a secondary asset in development, ATL1103, as a novel treatment for acromegaly. Antisense are planning an EU pivotal Phase IIB study in DMD with ATL1102 in 2H21. Success could lead to an early approval and independent product launch in Europe (TAM A$1.7B). Unrisked valuation is $1.34 per share assuming independent commercialisation in major markets.

Revenue drivers

Underlying growth in DMD market driven by greater diagnosis rates

Partnering transactions related to ATL1103 or ATL1102 assets with upfront payments/milestones and royalties

Balance sheet

- Net cash of ~$7.1M as at Dec 2020.

Margin drivers

- Not applicable.

Board

- Robert Moses (Chairman)
- Mark Diamond (Managing Director)
- William Goolsbee (Non-executive Director)
- Dr Graham Mitchell (Independent Non-executive Director)
- Dr Gary Pace (Non-executive Director)

Key issues/catalysts

Clinical trial results

Regulatory interactions with EMA and FDA

Competitor development progress in DMD market

Partnering opportunities

Management

Mark Diamond (Chief Executive Officer)

Dr George Tachas (Director – Drug Discovery & Patents)

Phillip Hains (Chief Financial Officer & Secretary)

Nuket Desem (Director of Clinical & Regulatory Affairs)

Dr Gil Price (Consultant Medical Director)

Risk to view

Failure of ATL1102 to show adequate efficacy in DMD to achieve regulatory approvals

Development of superior disease modifying/curative drugs by competitors

Availability of capital to fund intensive period of R&D in near term with limited catalysts

Ability of management to deliver on commercialisation outcomes given past experiences with Antisense's MS program.

Contact details

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Toorak, VIC 3142 Australia
antisense.com.au

Disclaimers and disclosures

Recommendation structure and other definitions

Definitions at wilsonsadvisory.com.au/Disclosures.

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