

Key Updates:

- New leadership and expanded clinical development team
- Country and site ethics approvals granted
- Chronic monkey toxicology study progressing
- Phase IIB study screening commences

Dear Shareholders,

At the threshold of Antisense Therapeutics (ASX: ANP, the Company) embarking on the late-stage clinical program with its lead asset, ATL1102 for Duchenne Muscular dystrophy (DMD), we find ourselves in a very special position for a relatively small biotechnology company. ATL1102 is a potentially life changing innovative medicine that could benefit a Paediatric, rare disease patient group, namely both the ambulatory and non-ambulatory DMD community with applicability not limited by genetic mutation, as are some other therapies¹. Furthermore, and importantly, the Company has data demonstrating ATL1102 biological concept through aligned mechanism of action and positive changes in muscle in mouse and human (the tissue of interest), and clinical proof of concept through a demonstrated impact on clinical function, while being well tolerated². We believe that for an overall modest investment of time and money, Antisense Therapeutics will harness the value of ATL1102 through its imminent Phase IIB clinical study as the latter is designed to deliver a definitive compelling clinical trial outcome and which would, if that occurred, transform this Company.

It is almost two years since I joined the Antisense Board of Directors and much has changed in that time. Change can be challenging and it's tempting to avoid but as an ancient Chinese proverb says, *if you do not change direction, you may end up where you are heading*. In 2021 the Company's plan was to fund and conduct a large Duchenne Muscular Dystrophy (DMD) study, however as we are aware the financial ask could not be met by the market and a change in strategy was needed. Along with that change has come an opportunity to reset. Today we are a new leadership team with a Board of Directors, CEO and expanded clinical team who combined have a proven track record of developing and bringing commercially successful drugs to global markets. We are a group committed to delivering on our lead asset ATL1102, to patients with DMD and when needed, of making the hard decisions along the journey.

In this update letter to you I hope to lay out why I believe the changes which have occurred, and our path forward, will deliver value to our shareholders and the DMD community. Before doing so, I first want to take this opportunity to thank shareholders for your continued support despite the market challenges this past financial year. While trading of Antisense stock is regularly occurring, this is mostly of small volumes and reassuringly the top 20 and top 40 shareholders have increased their combined holdings in the Company during this financial year. However, shareholders that have reached out to me express their greatest concern remains the decline in the share price. This sentiment is shared by the Board and management. I have taken note of feedback from shareholders that insufficient information on progress may be affecting confidence in the stock, which has prompted this letter.

To this end, I'd like to open a line of communication for issues or questions you might have of the Company as I am always open to constructive input that has the potential to make our Company better. Queries can be submitted via the Company website and in addition to management review, will be shared with myself or the board and our responses communicated back to you. I cannot guarantee

a (detailed) response to every query, however you can be assured that all queries will be reviewed by me or the board.

It is worth acknowledging that nearly every industry has faced financial difficulties in the past year. Biotech has notably experienced struggles despite often being more resilient and protected as part of the healthcare sector. To quote Dr Ogden, fund manager with Platinum Asset Management "Biotech had a very tough year, the macro narrative has dominated, and many investors ran (and still run) a mile from these companies" (*Dr Bianca Ogden: The healthcare insider*, David Thornton, Livewire: 06 March 2023).

Certainly, Antisense Therapeutics has not been immune from such sentiments. It is ironic this is occurring at a very exciting time in the field of DMD research where the first gene therapy to produce micro-dystrophin could potentially be approved by the FDA. If approved, another treatment option would become available for some patients and families and further raise community awareness of the importance of ongoing research in DMD. Additionally, approval would underscore the relevance and acceptance, by FDA, of functional clinical endpoints, such as the North Star Ambulatory Assessment or PUL2.0 (as used in the assessment of non-ambulatory boys), for approval and registration.

The Pharma industry's focus has to date largely been on correcting the underlying defect in DMD, namely replacing dystrophin within the muscle cell with either an exon-skipping or gene therapy approach and depending on the exact mutation present, variable clinical success has been demonstrated¹. The importance of the inflammatory pathogenesis theory advancing clinical deterioration in DMD has, at the same time, gained momentum with 25 peer reviewed academic journal articles on this aspect already published in 2023. It is now widely accepted that inflammation and the subsequent progressive fibrotic tissue scarring, which starts already during the ambulant phase, will still occur even in the presence of micro dystrophin produced by exon skipping drugs or gene therapy. This highlights the ongoing unmet need boys with DMD face and underscoring the importance of abnormally activated blunting cell and tissue pathways with immune/ inflammation dampening treatments such as ATL1102.

Given the reported ameliorative effects of ATL1102 on inflammatory markers³ together with the positive functional impact noted in the non-clinical and the clinical settings, we believe it is imperative that ATL1102 continues clinical development. As the DMD field's understanding of the degenerative changes in cellular and supporting muscle architecture evolves, the Company believes that ATL1102's mechanism of action is likely equally relevant to potentially slowing disease progression in both ambulant and non-ambulant boys. Furthermore, the recent positive functional activity results from Antisense's *mdx* mouse combination study⁴ raises the possibility of benefit from using both ATL1102 and exon skipping drugs in ambulant boys. Further work is ongoing, with results still to be reported, to better understand the cellular pathways involved in the observed functional improvements (i.e., due to dystrophin and/or fibrosis changes).

I mention these different clinical applications to highlight the potential of ATL1102. Despite our initial focus in non-ambulant boys using ATL1102 as monotherapy, the Phase IIb study has the potential to deliver an important contribution to the understanding and treatment of DMD. The study is designed to demonstrate (i) a difference in PUL2.0 against placebo at 6 months; (ii) stabilisation or improvement of clinical effect after 12 months of treatment; and (iii) the clinical impact of delayed treatment between the placebo and active treatment groups. Clinically significant results, from a Phase IIb study, would represent a major advancement in the treatment of DMD. It is our intent to share the study results with the FDA as precedent exists in the space of rare neuromuscular disease for positive results from a well-designed and executed study serving as the basis for an accelerated approval. With the FDA IND 9-month monkey toxicology study underway (12 out of 40 doses successfully administered to

date), we are likely permitted to submit either a DMD clinical study protocol or the Phase IIb study results to initiate lifting of the partial hold on the IND. This latter activity, which opens the USA market, is planned for 2H-2024.

Completing the Phase IIb clinical trial and moving toward an approval for DMD in both the EU and US regulatory jurisdictions are key strategic imperatives and we are laser focused on achieving these goals. I appreciate that since announcing our amended strategy in late 2022 it may not be obvious what has been achieved. Much headway has been made since an agreement was signed with Parexel in October 2022 for them to be the clinical research organisation running the trial on our behalf. Parexel advised that study set-up activities would take at least six months if no unforeseen delays eventuated.

The tasks that had to be undertaken included qualification assessments and agreements with all fourteen vendors associated with the study, updated feasibility of using specific countries and sites and confirmation of investigator interest and availability. All study documentation was completed, databases built and validated, and study drug and placebo commenced quality testing, packaging, and labelling with study drug and placebo released in April 2023. Country specific submissions were drafted with the first submission made in November 2022 to the United Kingdom, with Bulgaria and Turkey thereafter and the Australian submission in early 2023. These activities reflect many complex moving parts and unfortunately the reality of clinical study set-up is that many aspects are sequential and cannot be accelerated.

Parexel timelines had estimated all twelve selected clinical investigation sites could be open and recruiting by June 2023. At the time of writing this letter, both Turkey and Bulgaria have regulatory approval with the Turkish sites open and the Bulgarian site due by end of first week in June. In Australia, ethics approval has been granted and the Clinical Trial Notification submitted to the Therapeutic Goods Administration and only final institutional (hospital) approval is awaited. The UK, due to their internal procedural delays are still to provide their approvals on the study submission, and we hope this will shortly be received to facilitate site initiation before end of June.

Screening, which can be up to a 4-week process, has commenced in Turkey and when participant dosing occurs, we will communicate this important milestone to the market. Recruitment is competitive and can come from any country and based on initial feasibility assessments has been estimated to complete in December 2023. However, it is only as the study progresses and we confirm potential patients' eligibility for enrolment that we can determine recruitment rate and timelines. This is something we keep a very close eye on, implementing remediation action if required, such as additional sites or countries. We will not report regularly on participant numbers as recruitment rates are not linear but will share relevant milestones such as key target thresholds or if timelines require adjusting. The last enrolled patient will complete the blinded phase of the study after six-months of treatment, at which stage the database will be frozen with the data then being programmed and analysed to assess the six-month efficacy and safety of ATL1102.

Delivering on a quality clinical trial necessitates a strong, experienced clinical team. To this end we have boosted the internal team with individuals adept at delivering on global studies, and particularly familiar with Paediatric and rare disease programs. Lynne Atley is overseeing the toxicology study and all activities around drug manufacture. Louise Tremper and Louise McCrossin are providing support to Annabell Leske, Clinical Operations Manager, with clinical program management. Dr. Andrew McKenzie has been appointed as Clinical Development Director, replacing Nuket Desem who has left the Company. This team will manage timelines and integrate inter-dependent milestones across vendors, proactively addressing challenges and ensuring appropriate escalation for the CEO and Board. Additionally, the internal team will interact with our investigators, key opinion leaders, ethics

committees and patient advocacy groups as well as oversee all analysis, data interpretation and presentation. This will afford us greater control over aspects critical for success.

We are often asked by shareholders if and when a licensing deal with Pharma or Biotech will occur. Dialog in this regard repeatedly resulted in advice that placebo-controlled data in a relevant number of study participants would improve business development outcomes. The Phase IIb study design addresses this opinion. In addition, we engaged Dr Anthony Filippis to develop new, and strengthen existing, relationships with potential partners and to facilitate their improved understanding of the clinical and financial value of ATL1102. I appreciate that shareholders are keen to know where we are at as Anthony's interactions are confidential and not within the public domain. I assure you he is very active in the space and is making headway in terms of inbound interest. However, this work and achieving positive results takes time and extensive diligence, and once we are in a position to do so, we will communicate with the market. The Company also continuously reviews its funding position and future capital requirements. Similarly with business development progress mentioned earlier, any updates will be communicated to the market at the relevant time.

Soon we will reach our 2023 financial year end and reflect on achievements and set focused goals for the following year. There is much to do, and I invite you to continue on the journey with us. I plan to share further relevant background in future communications of this nature. We, the Board, and management, take your investment in Antisense and belief in the science seriously and on behalf of the whole team, I thank you for your continued interest and support.

With Regards

A handwritten signature in blue ink, appearing to read "Charmaine Gittleson", with a stylized flourish extending to the right.

Charmaine Gittleson MD
Board Chair, Antisense Therapeutics

References:

1. Aartsma-Ru, A. Human Gene Therapy 17 May 2023, Vol 34, N 9-10
2. Ryan, MM. <https://www.medrxiv.org/content/10.1101/2022.01.16.22269029v1>
3. ASX announcement Poster Presentation at 2022 MDA Clinical & Scientific Conference 01 March 2022
4. ASX announcement Positive outcomes in DMD combination therapy animal study 01 February 2023