PITT STREET RESEARCH

Tali Digital

Digital therapeutic pioneer

Share Price: $0.017

ASX: TD1

Sector: Healthcare

2 February 2022

Tali Digital's Tali Train product is an app-based cognitive training programme for children with attention problems while a second product called Tali Detect provides a diagnostic solution. Tali Detect and Tali Train are basically games played on tablet devices by the child being assessed or trained. These products, represent years' worth of research from Monash University to create the Tali Technology, which Tali Digital has been commercialising since 2018. In 2021 Tali Digital underwent a major step change when it started work, in conjunction with a US company called Akili Interactive, on prescription digital therapeutics for ADHD and the Autism Spectrum Disorders.

Tali Train is a ground breaking product

When a child uses the Tali Train app five days a week for five weeks, the result can be a noticeable reduction in attention deficits. Up until Tali Train there was no computerised system that could objectively measure attention in children, could work in the home, and, importantly, could work with children where some measures of attention were satisfactory and others were unsatisfactory. Tali Digital products are now being rolled out globally, with multiple school systems now accessing the Tali system and the products available for use in clinics and by families. Tali Digital earns revenue from license fees and per-use fees.

The Akili Interactive partnership has considerable upside

Akili Interactive, currently going public on Nasdaq, is a pioneer in prescription digital therapeutics best known for EndeavorRx, the first ever prescription video game for children with ADHD. Under a partnership which was announced in August 2021, Tali Digital will now develop prescription digital therapeutics based on the Tali Technology to treat ADHD and the Autism Spectrum Disorders, with the products to be distributed by Akili in the US market. The first product is expected to gain FDA approval in early 2023. Tali Digital can earn US$37.5m in milestone payments from the partnership, and a high single digit royalty on product revenue.

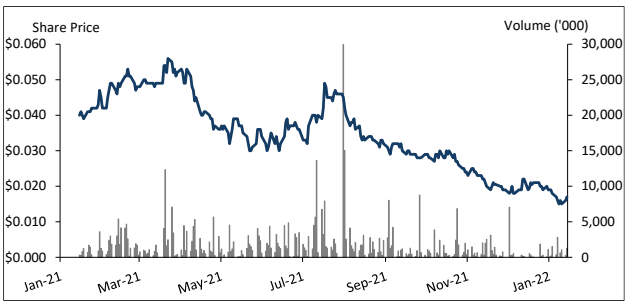
Tali Digital is undervalued on our numbers

We value Tali Digtal using based on a probability weighted DCF approach at A$0.06 per share base case and A$0.11 per share bull case. Key risks we see in Tali Digital include: 1) clinical risk; 2) timing risk; and 3) uptake risk.

Market Cap. (A$ m)	15.8
# shares outstanding (m)	931.9
# share fully diluted	1,057.0
Market Cap Ful. Dil. (A$ m)	18.0
Free Float	100%
12 months high/low (A$)	$0.056 - $0.015
Avg. 12M daily volume ('1000)	1,833
Website	talidigital.com

Source: Company, Pitt Street Research

Share price (A$) and avg. daily volume (k, r.h.s.)



Source: Refinitiv Eikon, Pitt Street Research

Valuation metrics	
DCF fair valuation range (A$)	0.06 – 0.11
Discount rate	14.4%
Assumed terminal growth rate	None

Source: Pitt Street Research

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Introducing Tali Digital, ASX: TD1

Tali Digital is a Melbourne-based digital health company whose Tali Train product provides a treatment solution for childhood attention difficulties. Tail Train is an app-based cognitive training programme for children with attention problems while a second product called Tali Detect provides a diagnostic solution. Tali Detect and Tali Train are basically games played on tablet devices by the child being assessed or trained. These products, represent years' worth of research from Monash University to create the Tali Technology, which has been commercialising since 2018. In 2021 Tali Digital underwent a major step change when it started work, in conjunction with a US company called Akili Interactive, on prescription digital therapeutics for ADHD and the Autism Spectrum Disorders.

Tali Digital's flagship Tali Train product helps treat attention problems. Tali Train consists of four touchscreen activities for children that collectively last about twenty minutes. When a child uses the app five days a week for five weeks, the result can be a noticeable reduction in attention deficits. Up until Tali Train there was no computerised system that could objectively measure attention in children, could work in the home, and, importantly, could work with children where some measures of attention were satisfactory and others were unsatisfactory. Tali Digital products are now being rolled out globally, with multiple school systems now accessing the Tali system and the products available for use in clinics and by families. Tali Digital earns revenue from license fees and per-use fees.

Tali Digital 'gamifies' diagnosis and treatment for attention problems

Tali Digital 'gamifies' diagnosis and treatment for attention problems. A large and growing body of knowledge in the neuroscience space points to the strong utility of games in these settings. Among other things, Tali's products allow measurements to be made thousands of times a day, in real time, through gameplay.

Tali Digital is now going to the next level in prescription digital therapeutics through the Akili Interactive partnership. Akili Interactive is a pioneer in prescription digital therapeutics best known for EndeavorRx, the first ever prescription video game for children with ADHD. Under a partnership which was announced in August 2021 Tali Digital will now develop prescription digital therapeutics based on the Tali Technology to treat ADHD and the Autism Spectrum Disorders, which will be distributed by Akili in the US market. The first product from this collaboration is expected to gain FDA approval in early 2023. Tali Digital can earn US$37.5m in milestone payments from the partnership, and a high single digit royalty on product revenue.

If Tali is this good, why is it currently capitalised at under A$20m? We think investors have held back from embracing Tali Digital until they can be sure the original technology development is complete and the product has been commercialised. With this now more or less achieved by 2021, and the company now going to the next stage with the Akili Interactive partnership, we believe Tali Digital the stock can re-rate. The forthcoming listing of Akili Interactive on Nasdaq can also reasonably help Tali in this regard, by drawing attention to the quality of Akili's Australian partner.

Ten reasons to look at Tali Digital

1. **There is considerable upside in the Akili Interactive partnership**, with the company set to introduce ground-breaking digital therapeutics for the US market for ADHD and the Autism Spectrum Disorders beginning in 2023.
2. **Tali will go after new indications after ADHD and ASD**, with Mild Cognitive Impairment in dementia also a likely candidate for the Akili Interactive partnership. The size of the market opportunity here is in the billions.
3. **With Tali Train, Tali Digital has an approved cognitive training tool for attention problems in children**. The product is easy to use and clinically validated over a number of studies and backed up my multiple peer-review papers. Tali Train has gained FDA approval in the US a well as CE Mark approval in Europe.
4. **Tali now has a second product, with a third coming soon**, with Tali Detect, for the detection of attention problems, having recently been validated. Tali Maintain, a twelve month 'booster' for children who have completed Tali Train, is coming soon.

Tali's products are easy to scale

5. **Tali's products are easy to scal**e, being app-based and being able to process training and detection data in the Cloud in real time.
6. **Tali's existing products are beginning to gain a following**, with users is multiple jurisdictions now accessing both Tali Train and Tali Detect.
7. **The market for ADHD treatments for children is large,** with around 5-10% of children worldwide having ADHD. This has traditionally made for a multi-billion dollar drug market. Another 2% of children have an Autism Spectrum Disorder of some kind, where there are no drug treatments and where cognitive training is expensive.
8. **Many parents do not like drug treatment for the ADHD children,** with more than 40% of parents with ADHD children in the US preferring other therapies. This opens up a large market opportunity for cognitive training tools like Tali Train.
9. **Tali Digital has a first class leadership team**. Managing Director Glenn Smith brings a track record of growing startup ventures into established businesses. Chairperson Dr Sue MacLeman is a skilled bio-entrepreneur who has guided multiple listed and unlisted biotechs to clinical and commercial success over the last two decades.
10. **Tali Digital is undervalued on our numbers**. We value Tali Digital at $0.06 per share base case and $0.11 optimistic case using a DCF valuation approach. We see Tali Digital re-rating towards our target price as Tali Train and Tali Detect grow their user base in multiple jurisdictions.

Tali Digital - the story so far

Tali Digital has its origins in the Tali Technology, which was developed in the laboratory of Professor Kim Cornish at Monash University as a new way of providing attention training for children, where the emphasis was on software that could focus on the measures of attention that were most in deficit. Once the core software had been optimised around 2014, a Monash University spinout company called Tali Health was created to commercialise the Tali Technology. Over the previous two years the Cornish lab had worked with a technology commercialisation house called Grey Innovation[1] and a gaming software developer called Torus Games[2], to create the Tali Train app as well as a Cloud-based data collection and analysis function. The app subsequently generated solid data in 'Study 05', for which data was published in mid-2016[3], and this data encouraged Tali Health to go forward with an ASX listing to go after regulatory approval of Tali Train as a medical device.

Tali Digital went public on ASX via a reverse takeover in 2016 of a former drug developer called Avexa (ASX: AVX). The acquisition of Tali Health for A$4.5m in Avexa scrip was announced in October 2015 and completed in February 2016. Avexa changed its name to Novita Healthcare (ASX: NHL) in December 2016 and finally to Tali Digital in December 2019.

Tali Train was launched commercially in Australia in 2018. Beta versions of Tali Train were rolled out in 2017 to various clinics, and full versions by the end of 2017. A national rollout commenced in July 2018 after TGA approval was gained in May[4]. Tali Health was named a registered provider by the National Disability Insurance Scheme in April 2018 and expanded disability classes were added in November 2019. This was important because a significant number of 286,000 registered NDIS participants at that time – around 10% of the total – were suitable for treatment with Tali Train.

Tali Train started to go global in 2018

Tali Train started to go global in 2018. The product gained US approval in September 2018, when the FDA cleared it as a Class II medical device. The product was in use in US schools by April 2019. Tali Train gained its CE Mark in August 2019 as a Class I device[5]. A major step forward came in late 2020 when the company started working with the Times Group in India to commercialise the Tali products there.

Tali Detect was introduced in 2019. After the initial Tali Train software was developed Tali's academic collaborators started work on a second product called Tali Detect that could be used a screening device in schools and clinics.

Tali became a global Google for Education partner in January 2020. This was particularly important for Tali because over half of all US school children use a Google product in their education every day and many other jurisdictions are seeing heavy use of Google in their classrooms. In 2019 Google estimated that 80 million educators and students around the world use G Suite for Education while 40 million use Google Classroom[6]. The ability to seamlessly fit with Google for Education products can allow rapid deployment globally, particularly in environments where face-to-face learning has not been feasible in 2020 and 2021 due to Pandemic-related issues.

Tali went to the next stage in digital therapeutics with the Akili Interactive partnership in August 2021. Under that partnership, as we explain below, Tali

[1] greyinnovation.com.
[2] torus.com.au.
[3] See Kirk et. al. (2016), *Computerised attention training for children with intellectual and developmental disabilities: a Randomised Controlled Trial*. J Child Psychol Psychiatry. 2016 Dec;57(12):1380-1389. Epub 2016 Aug 23.
[4] As a Class I medical device.
[5] Credentialed by Malta Competition and Consumer Affairs Authority.
[6] See blog.google/outreach-initiatives/education/around-the-world-and-back.

Digital will develop and license to Akili prescription-only digital therapeutics for ADHD and the Autism Spectrum Disorders for the US market. Tali Digital currently expects that the first products from this partnership will gain FDA approval in early 2023.

The ability to pay attention is a big deal

Attention is an important life skill. Attention, as a psychological phenomenon, is the ability to actively process specific information in the environment while tuning out other details. There are several types of attention that are important to psychologists. 'Sustained attention' or simply 'concentration' is the ability to focus on one thing for a continuous period. 'Alternating attention' is the ability to multitask easily between tasks with different cognitive demands. 'Focused attention' is the ability to focus quickly on something urgent such as a flash of light.

Attention is important to just about everything we do. Attention allows people to focus on and complete specific tasks, and focus on information that is essential to memory creation. Without it the capacity of an individual to work, study and play is limited. The ability to pay attention has grown more important with the rise of the information economy, where there is so much out there demanding our attention. The evidence suggests that so-called attention spans in healthy adults aren't declining as much as adapting to meet the demands of the information age[7]. However, the evidence has suggested that having a low attention span as a young child significantly reduces the chances of completing higher education two decades later[8].

5-10% of the population of children and adolescents globally suffer from ADHD

Large segments of the population can't pay attention. As we note below, something like 5-10% of the population of children and adolescents globally, and 1% of adults, suffer from Attention Deficit Hyperactivity Disorder, which is notable to the inability to pay attention. Around 1% of the population as an Autism Spectrum Disorder of some kind, and autism is often characterised by difficulties in attention. Then there are other conditions which are not attention problems in and of themselves but part of another disorder such as Obsessive-Compulsive Disorder, Post-Traumatic Stress Disorder and various learning disorders such as dyslexia. Without treatment, young children with attention problems do less well in the long-term across a range of measures[9]. A good example was the cohort of American children tracked from kindergarten to grade 5 where attention problems at the beginning led to notable reading problems at the end[10].

The economic costs of attention problems are high. One recent survey that only covered Australia estimated the total social and economic cost of ADHD of US$13-17bn based largely on lost productivity costs, 'deadweight losses' (that is, the extra taxes required to fund services consumed by people with ADHD) and health system costs.

The evidence suggests that early intervention can last to better outcomes. One US study evaluating a cohort of 3-5 year-olds found behavioural training

[7] See *Sorry, Goldfish: People's Attention Spans Aren't Shrinking, They're Evolving* by Nadjya Ghausi, Entrepreneur.com, 19 October 2018. A commonly held view is that the average human in the information age is having his or her attention span eroded by the ease with which information can be accessed on social media and elsewhere. For example, survey work estimated that the average human in 2000 had an attention span of 12 seconds whereas by 2013 this has declined to just 8 seconds, less than that of a goldfish (*Attention Spans*, Consumer Insights, Microsoft Canada, Spring 2015). 2019 research at the Technical University of Denmark has suggested that the length of time a topic 'trends' in the media is growing shorter (*Lorenz-Spreen et. al. (2019), Accelerating dynamics of collective attention.* Nat Commun. 2019 Apr 15;10(1):1759).

[8] See McClelland et. al. (2012), *Relations between Preschool Attention Span-Persistence and Age 25 Educational Outcomes*. Early Child Res Q. 2013 Apr 1; 28(2): 314–324. Published online 2012 Aug 3.

[9] See Shaw et. al. (2012), *A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment*. BMC Med. 2012; 10: 99. Published online 2012 Sep 4.

[10] Rabiner et.al. (2000), *Early Attention Problems and Children's Reading Achievement: A Longitudinal Investigation*. J Am Acad Child Adolesc Psychiatry. 2000 Jul; 39(7): 859–867.

improving higher social skills, and significantly fewer behaviour problems across a variety of teacher-and parent-reported measures[11]. Interventions relevant to young children have strong potential to attract public funding, because of the way in which investments can have a high return on investment over time, as far as the taxpayer dollar is concerned[12].

Digital products for treatment of attention problems represent a game changer.

Digital products for treatment of attention problems represents a game changer. Up until recently the health and education systems only had expensive and labour-intensive behavioural therapies to offer children and adults with attention problems. The introduction of computer-based alternatives that can process data in the Cloud and can scale easily because of delivery via mobile devices changes the game markedly. With its Akili Interactive partnership, Tali Digital is now a leading player globally in this space.

Tali Train: A quality foundation product for Tali Digital, and a harbinger of big things to come

Tali Train is a succession of video games for children played on tablet devices. The games, featuring colourful shapes and cartoon-style objects and characters, have been designed to be fun for children aged three to six and are suitable for children up until age eight. There are four games in all, each running about four or five minutes, and the games are adaptive in terms of speed and complexity depending on the child's ability at the time:

- **Game 1: The 'Selection' game**. This game develops the ability of the child to decide what's important and not be distracted by what's not important. A typical format of the game will see the screen showing fruits of two different colours, and the child has to select fruit from one colour only.
- **Game 2: The 'Control' game**. In this game the child has to use certain controls, such as a button sliding up and down a scale, to make the characters on the screen do things. This game is designed to develop the ability to choose what to ignore and what not to ignore.
- **Game 3: The 'Inhibition' game**. In this game the child is instructed to not do certain things, such as touch a particular character. The idea is to teach the child some impulse control.
- **Game 4: The 'Focus' game**. In this game the child has to perform an activity such as a treasure hunt. Here the aim is to get the child to focus on one thing for a longer period of time.

Collectively the Tali Train games encompass different aspects of attention and behaviour, namely:

- **Selective attention (Game 1)**, the ability to block out certain features of our environment and focus on one particular feature, such as a conversation in a noisy restaurant;
- **Executive attention (Game 2)**, the ability to organise attention to get things done;
- **Activity/hyperactivity (Game 3**), the ability to not act on an impulse
- **Sustained attention (Game 4),** the ability to focus for long periods of time

[11] Feil et. al. (2016), *Early Intervention for Preschoolers at Risk for Attention-Deficit/Hyperactivity Disorder: Preschool First Step to Success*. Behav Disord. 2016 Feb; 41(2): 95–106. Published online 2016 Feb 1.

[12] The work of James Heckman, the American winner of the 2000 Nobel Prize in Economics, has postulated a 13% return on investment per child, per annum, through better education, economic, health, and social outcomes. See heckmanequation.org.

- **Literacy and numeracy**. These skills are evaluated and improved by all the games, through requiring the child to receive instructions via the written word, and to count objects that are being interacted with.

As the child plays the games, his or her attention and hyperactivity problems tend to reduce as new skills are learned. The usage time that seems to work is five days a week for five weeks. The utility of Tali Train has been established in four notable papers:

- **Study 005.** This double-blind randomised controlled trial showed that Tali Train worked very well in improving selective attention. 76 children aged 4-11 with an IQ under 75 were randomised to Tali Train or a 'nonadaptive control'. After the five weeks of Tali Train the children on that app had seen a strong jump in selective attention that was maintained at three months. The results of this study were published in the *Journal of Child Psychology and Psychiatry* in August 2016[13].
- **Study 006**. This study used the same cohort as Study 005 allowed for three months follow-up. The study found greater improvements in numeracy skills at the 3-month follow-up for children on Tali Train. The results were published in the *American Journal on Intellectual and Developmental Disabilities* in March 2017[14].
- **Study 007**. This randomised controlled trial evaluated Tali Train in the classroom. Here Tali Train was able to reduce inattention and hyperactivity in the classroom and reduced hyperactivity at home. The results of this study were published in the *Journal of Attention Disorders* in November 2019[15].
- **Study 008**. This randomized controlled study evaluated which kind of children would benefit most from Tali Train. Children with lower adaptive functioning but better attention skills benefited the most. The results of Study 008 were published in the *Journal of Intellectual and Developmental Disability* in December 2020.

Tali Train is a breakthrough product, for five main reasons:

- **Interventions at the right time**. Neuroscientists have established that attentional networks develop between ages 2 and 7[16], so a product suitable for use in children around these ages has the potential to deliver long-term favourable outcomes.

Tali Train brings the advantage of strong measurement frequency

- **Measurement frequency**. The app allows measurements thousands of times a day, day after day, with results that can allow easy tracking of the test subject through time.
- **Ease of use by all sorts of children**. Tali Train can be used by children just three years of age, to improve cognitive and academic skills., and it works for both 'neurotypical' children as well as 'neurodiverse' children.
- **Ability to be used in the home or at school**, since the product is delivered on standard tablet devices and is available in both Android and iOS versions.
- **Ease of reporting**. Tali Train allows regular reports to easily be generated for parents and caregivers that flags whether the child is 'vulnerable', 'borderline' or 'on track'.

[13] Kirk et. al. (2016), *Computerised attention training for children with intellectual and developmental disabilities: a Randomised Controlled Trial*. J Child Psychol Psychiatry. 2016 Dec;57(12):1380-1389. Epub 2016 Aug 23

[14] See Kirk et. al. (2017), *Impact of attention training on academic achievement, executive functioning, and behaviour: A Randomized Controlled Trial*. Am J Intellect Dev Disabil. 2017 Mar;122(2):97-117.

[15] Kirk et. al. (2021a), *Gamified attention training in the primary school classroom: A Cluster-Randomized Controlled Trial*. J Atten Disord. 2021 Jun;25(8):1146-1159. Epub 2019 Nov.

[16] Holmboe and Johnson (2005), *Educating executive attention*. Proc Natl Acad Sci U S A. 2005 Oct 11; 102(41): 14479–14480. Published online 2005 Oct 3.

Tali Train allows interventions in the appropriate measures of attention. Attention has various measures. Literacy and numeracy are measures of attention, as is selective attention (the ability to select salient information) and focus. Tali Train can distinguish where a test subject is weak or strong in terms and help train that part of attention. Importantly, Tali Train can distinguish between age-related changes in attention skills.

Does Tali Train have limitations? The 76 children aged four to 11 evaluated in Studies 05 and 06 did well on selective attention and on numeracy at three months, in that the improvements had statistical significance ($p<0.05$). The app did not improve sustained attention, attentional control or inattentive/hyperactive behaviours with statistical significance, but there were still improvements. We think this lack of statistical significance merely represents small sample sizes. The most telling statistic as to the effectiveness of Tali Train is that 93% of all users show improvement in both inattentive behaviour and hyperactive behaviour[17], while Tali Digital's pre- and post-training questionnaires of parents have found 70% of parents seeing an improvement in attention and decrease in hyperactivity[18].

93% of all Tali Train users show improvement in both inattentive behaviour and hyperactive behaviour

Further clinical data on Tali Train is coming. In June 2020 Tali Digital announced a collaboration with Professor Scott Kollins, Adjunct Professor in the Department of Psychiatry and Behavioural Sciences at Duke University in Durham, NC. Tali will be working with the Kollins laboratory to generate more data on the clinical utility of Tail Train. We think that will overcome some of the limitations of Study 05 and 06.

The competition is limited. Tali Digital believes it has strong competitive advantage versus other approaches. Drugs for the management of ADHD are effective but are disliked by many parents. Various software-based training approaches are available, most notably Kneomedia[19], MindMed[20], Play Attention[21], Brainbeat[22] and Attentiv[23]. Unlike Tali Train, these products have not been clinically validated.

Tali Train is a harbinger of big things to come. Tali Train is currently approved for use in multiple jurisdictions around the world. The product, however, is not a prescription therapeutic. The work that Tali Digital is doing with Akili Interactive will help take the science behind the Tali Technology into the word of digital therapeutics, where the big payoff is coming from 2023.

Tali Detect provides an easy-to-deploy screening tool for attention problems.

Tali Detect was developed in 2018. The product, which uses the same game-based approach as Tali Train but for diagnostic purposes, was funded with a government grant worth $1.2m issued under the Australian government's Cooperative Research Centre programme[24].

Tali Detect was initially evaluated in 'Study 001'. This study was the first to evaluate Tali Detect, where randomised 340 'neurotypical' children to evaluation with the standard Test of Everyday Attention for Children (TEA-Ch)

[17] See the Novita Healthcare AGM presentation dated 29 November 2018, slide 23.
[18] See play.google.com/store/apps/details?id=au.com.torus.projectdelta.
[19] kneomedia.com.
[20] mindmed.co.
[21] playattention.com.
[22] brainbeat.com.
[23] attentiv.com.
[24] See the Novita Healthcare market release dated 6 December 2017 and headlined '*Novita Healthcare awarded $1.2m government funding to design, develop and commercialise Tali Detect*'.

and then with Tali Detect[25]. The study, results of which were announced in June 2020[26], established that Tali Detect was as effective in diagnosis as TEA-Ch.

Large samples evaluated with Tali Detect have yielded interesting numbers. In March 2020 Tali reported the results of the first 1,000 school children in the Australian state of Victoria to be tried out with Tali Detect. This study found that perhaps 14% of the children potentially had attention problems. While high, the number was within the range of what other studies could be expected to find. The importance of this study is that it showed the ease with which Tali Detect could deploy in real life school conditions.

Tali Detect was launched in 2020, with an 'early release' programme announced in July 2020 for Australian schools. Launches in other jurisdictions are following. US launch was made easy by the October 2019 finding that the product qualified for reimbursement in American thanks to certain CPT codes.

Tali Train and Tali Detect are now launching globally

Tali Digital will commercialise its foundation products via both B2B and B2C approaches. In many cases parents will be prepared to pay for access to Tali Digital. In other cases the product will be sold to school systems and health departments for use by the children

Tali Train is being marketed as a Freemium SaaS product

The model will be 'Freemium SaaS', where part of the Tali services will be free and others will be via paid subscription to Software as a Service. In mid-2018 the company was talking US$399 for a five week course of Tali Train. By late 2019, after more market research, the company was talking about US$199 for 25 sessions of 20 minutes each, followed by a US$10 per month as an ongoing fee.

Tali Digital and Tali Train are going global. Obviously Australia is the testbed market but coming soon are other markets, most notably the US, UK, India and Japan. Tali's goal is to get to a million children using the product by 2023.

India illustrates the potential of large markets. Both Tali Train and Tali Detect became available in India in October 2020. Shortly after that Tali Digital announced an interesting collaboration with the *Times of India*[27]. That newspaper, the largest in India and one of the largest in the English-speaking world, has been owned since the late 1940s by the Jain family[28]. In December 2020 it was announced that the Jain family office would invest in Tali Digital equity in a placement in order to fund the rollout of the Tali products in India. The investment was relatively small – only A$2.7m via a placement at 3.3 cents per share – but it meant that the Jains are now Tali's largest shareholder.

The market opportunity is probably US$8bn, being 130 million kids accessing the product for around US$5 per month.

[25] Manly et. al. (2001), *The differential assessment of children's attention: the Test of Everyday Attention for Children (TEA-Ch), normative sample and ADHD performance*. Child Psychol Psychiatry. 2001 Nov;42(8):1065-81.
[26] See the Tali Digital market release dated 23 June 2020 and *headlined 'Tali reports positive study results for Detect product'*.
[27] timesofindia.com.
[28] forbes.com/profile/jain. The holding company for the Times of India is Bennett, Coleman & Co. Ltd.

Gamified diagnosis and treatment is a huge opportunity because of neuroplasticity

What is 'gamification'? Gamification is the process of using game elements – such as point scoring, competition, and the following of rules – in daily activities where certain outcomes are desired from those activities. The idea is to turn a necessary task into a game, in order to incentivise people to carry it out, even if that task might otherwise be boring or unpleasant. In recent years gamification has become an important part of healthcare, for both adults and children, with digital games a common element.

Gamification is growing in healthcare. Healthcare is all about motivation. If dental work is unpleasant, and there is no one compelling you to go the dentist, you are more likely to not schedule an appointment. A potential gamified solution here would be small payouts from one's insurer for scheduling the appointment at the recommended six month time point. Gamification is showing up most commonly in healthcare as part of encouraging life courses that better manage non-communicable diseases. A good example of the gamification approach here is FitBit, which gamifies exercise with social challenges and badges for milestones. The global healthcare gamification market is anticipated to reach around US$50m by 2026[29].

Gamification is starting to show up in the neurology space.

Gamification is starting to show up in the neurology space. Probably the best example of this is EndeavorRx, the world's first prescription video game for children with ADHD, which we discuss below. Other examples include the use of MindLight as a cognitive behavioural therapy programme for reducing children's anxiety[30], and MindPod Dolphin, a virtual reality game that trains motor control of the upper extremities, by having the patient simulate swimming in the ocean like a dolphin[31].

Neuroplasticity – why gamification works. Time was when neurologists thought the structure of the brain and the central nervous system was more or less hard-wired. Then in the 1960s it was discovered that neurons could reorganize after a traumatic event. Since then neuroscience has learned more and more about the phenomenon of 'neuroplasticity', where, throughout life, the nervous system constantly modifies itself, functionally and structurally, in response to experience and injury[32]. Neuroplasticity is the reason 'brain training' works – because the exercises involve help form new neuronal connections[33] – and there is now a growing body of evidence that gamified therapeutics in neurological conditions work the same way[34].

Tali Digital benefits from the move towards gamification. Now that products such as EndeavorRx are out in the market, providers will be looking to more optimal gamified solutions to attention problems. We look to see Tali to capitalise on this search over the next few years.

[29] See *Healthcare Gamification: An Opportunity to Diversify Your Revenue Stream?* by Bill Loguidice, Physicians Weekly, 25 September 2021.
[30] See Schoneveld et. al. (2017), *Preventing Childhood Anxiety Disorders: Is an Applied Game as Effective as a Cognitive Behavioral Therapy-Based Program*? Prev Sci. 2018; 19(2): 220–232. Published online 2017 Sep 27.
[31] See Krakauer et. al. (2020), *Comparing a Novel Neuroanimation Experience to Conventional Therapy for High-Dose Intensive Upper-Limb Training in Subacute Stroke: The SMARTS2 Randomized Trial*. Neurorehabil Neural Repair. 2021 May;35(5):393-405. Epub 2021 Mar 20.
[32] Fuchs and Flügge (2014), *Adult Neuroplasticity: More Than 40 Years of Research*. Neural Plast. 2014; 2014: 541870. Published online 2014 May 4.
[33] See Nguen et. al. (2019), *Cognitive and neural plasticity in old age: A systematic review of evidence from executive functions cognitive training*. Ageing Res Rev. 2019 Aug;53:100912. Epub 2019 May 30.
[34] See, for a good example, Quialheiro et. al. (2021), *A comprehensive program of cognitive stimulation with digital inclusion, physical activity and social interaction can modify BDNF levels and improve cognition in adults over 50: a randomized controlled pilot study*. Aging Ment Health. 2021 Aug 18;1-9. Online ahead of print.

Going after prescription digital therapeutics with Akili Interactive

Tali Digital is now a player in prescription digital therapeutics. In August 2021 Tali Digital announced a groundbreaking deal with an American company called Akili Interactive, where Tali licensed its technology to Akili with the intention of developing a prescription digital therapeutic for the US ADHD market. Other indications such as the ASDs are expected to follow in this partnership. Tali can earn US$37.5m in milestone payments as well as high single digital royalties on product sales. The Akili Interactive partnership is important because that company is a world leader in prescription digital therapeutics, with its first approved product being EndeavorRx, for the treatment of ADHD.

Prescription digital therapeutics have been a big deal in medicine since 2017

What are prescription digital therapeutics? Until recently digital medicine focused almost exclusively on the use of data to better diagnose and manage disease conditions where the therapy was a drug or physical device of some kind. We are now seeing the emergence of digital therapeutics where the software itself, harnessed in part to the neuroplasticity of the patient, is the therapy and where that therapy is powerful and specific enough to be prescription-only. The first notable prescription digital therapeutics in the neurology spaces were ReSET and Abilify MyCite, both FDA approved in 2017, and NightWare, FDA approved in 2020. ReSET[35], from Pear Therapeutics[36], is indicated for opioid use disorder. Abilify MyCite[37] saw the Japanese drug company Otsuka incorporate an ingestion sensor, developed by a company called Proteus Digital Health, into its Abilify drug, so that patients and caregivers can track if the patients are taking that drug to properly manage their schizophrenia, bipolar disorder or depression. NightWare, developed by a company of that same name[38] is a smartwatch used to interrupt PTSD-related nightmares.

How are prescription digital therapeutics different to regular 'medtech' products such as, say, FitBit? To be a 'prescription' digital therapeutic, the product has to be developed in an environment that complies with Good Manufacturing Practice. It has to show safety and efficacy in randomized controlled trial. It has to gain marketing authorisation from a regulator such as the FDA. And it can only be used under the supervision of a prescribing doctor. The two big advantages of prescription digital therapeutics are the ease with which they can be deployed, and the fact that they allow valuable real-world patient data to be collected.

Who is Akili Interactive and why is it a leader in prescription digital therapeutics? Akili Interactive[39] is famous as the developer of EndeavorRx[40], the first – and so far only – prescription video game for children with ADHD. EndeavorRx is a racing game that uses sensory stimuli and motor challenges to target brain regions involved in attention, and where those stimuli and challenges adapt to the progress of the child playing the game. When EndeavorRx gained FDA approval in June 2020 it was the culmination of years of research that had originated in the laboratory of University of California, San Francisco. The indication is for children ages 8 to 12. In the pivotal study of the device, EndeavorRx improved a measure of ADHD severity called TOVA

[35] See Campbell et. al. (2014), *Internet-delivered Treatment for Substance Abuse: A Multi-site Randomized Controlled Clinical Trial*. Am J Psychiatry. 2014 Jun 1; 171(6): 683–690.
[36] Boston, Ma., Nasdaq: PEAR, peartherapeutics.com.
[37] See abilifymycite.com.
[38] Hopkins, Mn., privately held, nightware.com.
[39] Boston, Ma., privately held, akili.com. Akili is a Swahili word meaning 'mind'.
[40] endeavorrx.com.

API[41] with a high level of statistical significance[42]. EndeavorRx is the lead product of Akili but coming soon is a pipeline of other prescription digital therapeutics for conditions such as Multiple Sclerosis, depression and the 'brain fog' associated with Covid-19 infection.

Why did Akili Interactive partner with Tali Digital? Basically, Akili's August 2021 deal with Tali reflected the fact that Tali had know-how and intellectual property that Akili didn't have. EndeavorRx, for example, is indicated for children with ADHD aged 8 to 12 years while Tali Train's recommended age range is 3 to 8 years.

Akili and Tali are going after more clinical data

Why the Akili Interactive deal is important for Tali Digital. The problem Tali Digital had in mid-2021 was that it had an effective and approved product in Tali Train, but the product was not yet 'prescription grade'. The September 2018 approval from the FDA was 'PTY 510(k) exempt'. 'PTY' is the FDA's classification code for products that are 'Computerized Cognitive Assessment Aids' and, as the term '510(k) exempt' will suggest, these products are considered safe to use without the usual 510(k) process that ordinarily establishes safety and efficacy[43]. Exemption from 510(k) made it easy to get approval, but did not allow for the kind of advanced claims that would allow reimbursement on par with a prescription-only product. The Akili partnership provides the resources to optimise the software, build more machine learning into it so as to better adapt to the user base, and, importantly, run larger studies to better elaborate the clinical utility.

Tali and Akili may be seeking Marketing Authorisation from the FDA for its forthcoming products using the 'De Novo' pathway:

- Traditionally, device developers went for marketing authorisation either via the 510(k) route (where there was a predicate device on the market) or the PMA route (for new devices). The De Novo pathway has been around since the Food and Drug Administration Modernization Act of 1997 but was little used until a 2012 change to the regulations made it an ideal route for low risk devices with no predicate[44].
- The ability to go down the De Novo path is, in our opinion, favourable for Tali because it accords with the fact that the product is already a Class II device.
- The only minor downside for De Novo is that the Agency's Review Cycle for the product is 120 days rather than 90 days for the 510(k) route.

The pipeline for the Akili partnership is powerful. Tali Digital has indicated that after the ADHD product the two companies may also pursue indications in the Autism Spectrum Disorders and in Mild Cognitive Impairment.

- As we note below, a company called Cognoa, which has an approved digital diagnostics for Autism Spectrum Disorders, is currently doing feasibility work on a prescription digital therapeutic. If Tali and Akili can move quickly, they will be potentially develop the first approved prescription digital therapeutic for an Autism Spectrum Disorder.
- Mild Cognitive Impairment can be a huge market opportunity in adults. There are now ~5.5 million Americans with Alzheimer's and by 2030 there are expected to be 8.4 million. Worldwide around 40-50 million people have dementia of some kind, of which around 20 million live in high

[41] Test of Variables of Attention (TOVA) Attention Performance Index (API).
[42] See Kollins et. al. (2020), *A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD): a randomised controlled trial*. Lancet Digit Health. 2020 Apr;2(4):e168-e178. Epub 2020 Feb 24.
[43] accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?id=3936.
[44] Before 2012 sponsors had to first submit a 510(k) and be told that their device was 'NSE', that is, Not Substantially Equivalent with the predicate the sponsor would suggest, and then go down the De Novo route.

income countries[45], including >400,000 in Australia[46]. The vast majority of Alzheimer's cases are where the condition is still mild. Any prescription digital therapeutic that can slow the cognitive decline of Alzheimer's has the potential to enjoy the kind of multi-billion dollar sales enjoyed by new Alzheimer's drugs.

Akili is expected to list on Nasdaq in mid-2022 with a market cap of around US$1bn

- **Akili Interactive is currently going public on Nasdaq at a very high valuation.** Akili Interactive secured US$160m Series D financing in May 2021, led by the respected Neuberger Berman Funds. In January 2022 Akili announced that it was going public on Nasdaq via a reverse takeover of a SPAC[47]. The transaction, which is expected to complete in mid-2022, will value Akili at around US$1bn and the new ticker symbol will be AKLI. Akili's listing is expected to provide the company with up to US$412m in gross cash proceeds, US$162m of which will come from a PIPE (what we call in Australia a 'placement'). The quality of the investors in this deal, which includes Temasek, JAZZ Venture Partners and Omidyar Technology Ventures, as well as the size of the valuation, suggests a very high interest in prescription digital therapeutics on Wall Street.

Akili isn't the only prescription digital therapeutic developer currently attracting some serious investment dollars.

- **Better Therapeutics**[48], developer of a prescription digital therapeutics platform for treating cardiometabolic diseases, went public via a SPAC in October 2021 in a deal that raised US$110m.
- **Click Therapeutics**[49] announced a US$52m Series B funding round in October 2021. That company's initial product is for smoking cessation but the pipeline includes other mental health conditions including major depressive disorder, insomnia and schizophrenia. In September 2020 Click Therapeutics announced a US$500m partnership with Boehringer Ingelheim, related to prescription digital therapeutic for patients with schizophrenia.
- **Closed Loop Medicine**[50], whose platform allows the creation of single prescription drug plus digital therapy combination products, raised £13m from various UK and European venture capital investors in November 2021. Closed Loop has two products in clinical development to treat insomnia and hypertension.

Prescription digital therapeutics are currently attracting some serious investment dollars.

- **Limbix**[51], developer of a prescription digital for treating depression in teenagers, secured US$15m 'Series A2' funding in December 2021.
- **MedRhythms**[52], which is developing a prescription digital therapeutics to improve walking for patients with a neurologic injury or disease, raised US$25m in a series B round in July 2021.
- **Mahana Therapeutics**[53], whose lead product is Parallel, an app-based, digital prescription digital therapeutic for irritable bowel syndrome (IBS), completed a US$61m Series B round in August 2021. Parallel gained FDA approval in December 2020.

[45] Source: World Alzheimer Report 2015.
[46] Source: Dementia Australia, www.dementia.org.au.
[47] SPAC stands for Special Purpose Acquisition Company, a publicly traded company created for the purpose of acquiring or merging with an existing privately-held company. The SPAC for Akili's deal is Social Capital Suvretta Holdings Corp. I (Nasdaq: DNAA)
[48] San Francisco, Ca., Nasdaq: BTTX, bettertx.com.
[49] New York, NY, privately held, clicktherapeutics.com.
[50] Cambridge, UK, privately held, closedloopmedicine.com.
[51] San Francisco, Ca., privately held, limbix.com.
[52] Portland, Me, privately held, medrhythms.com.
[53] San Francisco, Ca., privately held, mahanatx.com.

- **MindMaze**[54] raised US$125m for its neuro-rehabilitation video game platform in October 2021.
- **Pear Therapeutics** is currently capitalised at over US$500m on Nasdaq.

We believe Tali Digital can attract the kind of dollars suggested by the above transactions, given the recently established relationship with Akili, the fact that there is peer-reviewed clinical data with Tali Train, and the years that the Tali platform has been development.

ADHD is a huge issue globally

There's a lot of kids out there with ADHD. Attention Deficit Hyperactivity Disorder, or ADHD, is a neurological condition where a person has difficulty maintaining attention, is hyperactive or impulsive, and may have trouble with organisation and planning. ADHD occurs in both children and adults, but it is much better known in children because of the noticeably higher prevalence. In 2016 the National Survey of Children's Health in the US[55] suggested that a massive 9% of children between the ages of 2 and 17 had previously received an ADHD diagnosis. By comparison, another survey for which results became available in 2019 estimated adult US prevalence of ADHD at only about 1%[56]. ADHD is more than twice as prevalent in boys as girls[57].

ADHD has only been a defined 'condition' in recent decades. While medicine has been aware of attention and hyperactivity problems since very early in the 20th Century[58], it took until the late 1980s before Attention Deficit Hyperactivity Disorder was formally classified as such. Specifically, 1987 saw the first inclusion of ADHD in the 'DSM', the Diagnostic and Statistical Manual of the American Psychiatric Association. The DSM is used by clinicians and psychiatrists not just in the United States around the world to diagnose mental disorders and psychiatric illnesses[59] and is therefore regarded as authoritative.

Perhaps 10% of US children and adolescents have ADHD

Until recently ADHD diagnoses in America had been rising rapidly. The National Survey of Children's Health (NSCH) estimated that 4.4 million children in the US aged 4 to 17, or 7.8% of the total, had at some point had an ADHD diagnosis in 2003[60], but that figure had risen to 6.4 million by 2011, or 11%[61]. Interestingly, by the next NSCH in 2016 the figures were only 6.1 million for a prevalence rate of 9.4%[62]. However the data is not conclusive because in 2016 the NSCH had changed, with the survey conducted via mail and online rather than by telephone, and the age range extended to include two and three year-olds. Estimates using consistent data from another American survey, the National Health Interview Survey, pointed to a doubling

[54] Lausanne, Switzerland, privately held, mindmaze.com.

[55] The National Survey of Children's Health (cdc.gov/nchs/slaits/nsch.htm) is an ongoing health survey sponsored by the Maternal and Child Health Bureau of the Health Resources and Services Administration, which in turn is an agency of the U.S. Department of Health and Human Services. Surveys have been conducted in 2003, 2007, 2011/12, and annually since 2016.

[56] See Chung et. al. (2019), *Trends in the Prevalence and Incidence of Attention-Deficit/Hyperactivity Disorder Among Adults and Children of Different Racial and Ethnic Groups*, JAMA Netw Open. 2019 Nov 1;2(11):e1914344.

[57] See Ramtekkar et. al. (2010), *Sex and age differences in Attention-Deficit/Hyperactivity Disorder symptoms and diagnoses: Implications for DSM-V and ICD-11*. J Am Acad Child Adolesc Psychiatry. 2010 Mar; 49(3): 217–28.e1-3.

[58] Sir Frederic Still (1868–1941), the father of British paediatrics, first lectured on the subject in 1902 – see Klaus et. al. (2010), *The history of attention deficit hyperactivity disorder*. Atten Defic Hyperact Disord. 2010; 2(4): 241–255. Published online 2010 Nov 30.

[59] DSM-II, the Second Edition of the DSM published in 1968 had included 'hyperkinetic reaction of childhood' for the first time. When DSM-III was released in 1980 it changed the name of the disorder to attention deficit disorder (ADD), while a 1987 revision to DSM-III saw the switch to Attention Deficit Hyperactivity Disorder.

[60] See CDC, *Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder--United States, 2003*. MMWR Morb Mortal Wkly Rep . 2005 Sep 2;54(34):842-7.

[61] Visser et. al. (2014), *Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011*. J Am Acad Child Adolesc Psychiatry. 2014 Jan;53(1):34-46.e2. Epub 2013 Nov 21.

[62] Danielson et. al. (2018), *Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016*. J Clin Child Adolesc Psychol. 2018 Mar-Apr; 47(2): 199–212. Published online 2018 Jan 24.

in diagnosed ADHD in US children and adolescents from 6.1% in 1997-1998 to 10.2% in 2015-2016[63].

The reasons for increasing ADHD are not 100% clear. This massive increase in diagnoses is often attributed to parents having become more aware of ADHD and therefore reporting symptoms to healthcare professionals with increased frequency[64]. There may, however, be other issues at work, such as various prenatal factors[65], attachment-related factors in early infancy[66] or even environmental contamination[67]. One recent study has suggested high 'screen time' in adolescents as a risk factor[68].

The search term 'ADHD' has been trending on Google since late 2016

ADHD isn't just an American problem, with awareness and diagnoses increasing globally. While the US seems to have a higher ADHD prevalence that many other countries, to the point where there was a time when people tended to dismiss ADHD as an 'American condition'[69], the global prevalence in children seems to be at least 5%[70] and potentially 8%[71], which would represent in excess of 130 million children[72]. That ADHD awareness is clearly increasing over time, and not just in the United States, is suggested by a Google Trends search which showed the term 'ADHD'[73] trending strongly from late 2016.

Part of the awareness may relate to newer ADHD medications. Many people who know about ADHD also generally know about the Novartis psychostimulant Ritalin, one of the drugs approved for treatment. Ritalin, generic name methylphenidate, first gained FDA approval way back in 1955, albeit but not for ADHD at that time. It was initially marketed by the Novartis precursor company Ciba for conditions such as chronic fatigue and depression but in 1961 the FDA approved it for hyperactivity[74]. It was only about 2001 that Ritalin's mechanism was properly understood[75]. For a long time Ritalin was the only viable drug treatment option. That changed in the 15 years to 2009, and it's reasonable to suggest that news coverage surrounding increased ADHD awareness and led to the increases in diagnoses we noted above.

- In 1996 the British specialty pharma company Shire[76] gained FDA approval for Adderall, a mix of two stimulants, amphetamine and dextroamphetamine;
- In 2000 J&J gained a march on Ritalin with Concerta[77], which is a long-acting methylphenidate, as opposed to Ritalin's short-acting mechanism;
- In 2001 Novartis expanded its methylphenidate franchise with Focalin, which is dexmethylphenidate, the active isomer of methylphenidate;
- In 2006 Shire gained FDA approval for Daytrana, a methylphenidate patch, and therefore the first non-oral medication for ADHD;

[63] Xu et. al. (2018), *Twenty-Year Trends in Diagnosed Attention-Deficit/Hyperactivity Disorder Among US Children and Adolescents, 1997-2016.* JAMA Netw Open. 2018 Aug 3;1(4):e181471.
[64] See *ADHD Rising in the U.S., but Why?* by Jennifer Clopton, WebMD, 26 November 2018
[65] See Sciberras et. al. (2017), *Prenatal Risk Factors and the Etiology of ADHD-Review of Existing Evidence*. Review Curr Psychiatry Rep. 2017 Jan;19(1):1.
[66] See Fearon and Belsky (2004), *Attachment and attention: protection in relation to gender and cumulative social-contextual adversity*. Child Dev. Nov-Dec 2004;75(6):1677-93.
[67] Thapar et. al. (2013), *What have we learnt about the causes of ADHD?* J Child Psychol Psychiatry. 2013;54(1):3-16.
[68] See Ra et. al. (2018), *Association of Digital Media Use With Subsequent Symptoms of Attention-Deficit/Hyperactivity Disorder Among Adolescents*. JAMA. 2018 Jul 17;320(3):255-263.
[69] Faraone et. al. (2003), *The worldwide prevalence of ADHD: is it an American condition?* World Psychiatry. 2003 Jun;2(2):104-13.
[70] See, for example, Polanczyk et. al. (2007), *The worldwide prevalence of ADHD: a systematic review and metaregression analysis*. Am J Psychiatry. 2007 Jun;164(6):942-8.
[71] See Fayyad et. al. (2017), *The descriptive epidemiology of DSM-IV Adult ADHD in the World Health Organization World Mental Health Surveys*. Atten Defic Hyperact Disord . 2017 Mar;9(1):47-65. Epub 2016 Nov 19.
[72] We estimate that in 2021 there are around 1.8 billion children and adolescents in the world (see CIA World Factbook.
[73] https://trends.google.com/trends/explore?date=all&q=ADHD.
[74] See *Ritalin at 75: what does the future hold?* By Matthew Smith, The Conversation, 18 September 2019..
[75] It increases dopamine levels in the brain - see Volkow et. al. (2001), *Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in the human brain.* J Neurosci
. 2001 Jan 15;21(2):RC121.
[76] Acquired by the Japanese pharmaceutical major Takeda in 2018.
[77] concerta.net.

- 2007 saw FDA approval for Shire of Vyvanse, a pro-drug of dextroamphetamine[78].
- 2008 saw the treatment scene changed markedly when Eli Lilly gained FDA approval for Strattera[79], the first non-stimulant ADHD drug[80]. Shire followed in 2009 with another non-stimulant called Intuniv[81]

The recently approved Qelbree may prompt another increase in awareness. After Intuniv the pace of innovation in ADHD slowed, with last big branded drug, Strattera, going generic in 2017 after having enjoyed peak sales of US$855m in 2016. In April 2021 the American specialty pharma company Supernus Pharmaceuticals[82] gained FDA approval for Qelbree[83], another non-stimulant. This drug, generic name voloxazine, had actually been marketed in Europe between the 1970s and 2002 for depression, thanks to its mechanism of action as a serotonin reuptake inhibitor[84]. The drug's new approved use in ADHD represents another step forward for ADHD because of the rapid onset of action compared to Strattera[85].

Critics have suggested that ADHD is 'over-diagnosed', for two main reasons. Firstly, ADHD does not have unequivocal biological markers, so that a diagnosis has to be made on the basis of behaviour that may or may not represent ADHD. Secondly, with drug treatments available, doctors can offer solutions with their diagnosis, making it easier for those doctors to make such a diagnosis[86].

Over 40% of parents of American kids with ADHD do not like drug treatment

There is widespread parental concern over drug treatment of ADHD in children. Surveys have suggested that a significant minority of parents tend not to like drug treatment. One 2010 survey in the US from the respected Consumer Reports organisation found that '*only 52 percent of the parents agreed strongly that if they had to do it over again, they would have their kids take medication, and 44 percent wished there was another way to help their child*'[87]. 29% of parents surveyed were 'dissatisfied' with drug treatment. This dissatisfaction opens up a large opportunity for non-drug alternatives such as Tali Train.

Tali Train is particular important for parents of ADHD concerned about drug therapy. It's important to remember that ADHD therapy is more than just drugs. Doctors have been experimenting since the mid-1970s on 'neurofeedback', that is, brain training, with some success[88]. We argue that Tali Digital with its Tali Train app can takes the non-drug approach to a new level.

[78] Generic name lisdexamfetamine dimesylate, see www.vyvanse.com. This drug, because it has to be metabolised by the body before it can work, results in longer therapeutic action.
[79] Generic name atomexetine, see www.strattera.com.
[80] A selective norepinephrine reuptake inhibitor.
[81] A selective alpha-2A-receptor agonist.
[82] Rockville, Md, Nasdaq: SUPN, supernus.com.
[83] See qelbree.com.
[84] Pinder et. al. (1977), *Viloxazine: a review of its pharmacological properties and therapeutic efficacy in depressive illness*. Drugs. 1977 Jun;13(6):401-21.
[85] Nasser et. al. (2021), *A Phase 3, Placebo-Controlled Trial of Once-Daily Viloxazine Extended-Release Capsules in Adolescents With Attention-Deficit/Hyperactivity Disorder*. J Clin Psychopharmacol. 2021 Jul-Aug; 41(4): 370–380. Published online 2021 May 8.
[86] An interesting book on the subject is *The ADHD Explosion and Today's Push for Performance: Myths, Medication, and Money* by Richard Scheffler and Stephen P. Hinshaw (Oxford University Press, 2014). See also Kazda et. al. (2021*), Overdiagnosis of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents: A Systematic Scoping Review*. JAMA Netw Open. 2021 Apr 1;4(4):e215335; and Paris et. al. (2015), *Is Adult Attention-Deficit Hyperactivity Disorder Being Overdiagnosed?* Can J Psychiatry. 2015 Jul; 60(7): 324–328.
[87] See *Pros and cons of ADHD medication*, consumerreports.com, published July 2010.
[88] See, for example, Eur Child Adolesc Psychiatry. 2011 Sep;20(9):481-91. Epub 2011 Aug 13.

The Autism Spectrum Disorders represent huge area of unmet medical need

What is autism and what is the Autism Spectrum? The term 'autism' covers a range of neurodevelopmental disorders characterised by difficulties with social interaction and communication, and by restricted and repetitive behaviour. The reason autism has a 'Spectrum' is that some types of autism have behaviors that are not really problematic, while other autisms represent a disability necessitating full-time care in a special facility. Asperger's Syndrome[89] is an example of the former while Rett Syndrome is an example of the latter[90].

The prevalence of Autism Spectrum Disorder is surprisingly high. One 2020 estimate has suggested that 2.2% of adults in the United States have an ASD of some kind[91], about the same as for children[92]. Global prevalence estimates vary widely but could be at least 0.6% of adults and children[93]. Males are at least two or three times more impacted than females[94].

The Autism Spectrum Disorders often come with attention difficulties. One American study found that there were sufficient symptoms to diagnose ADHD is reported in around 60-80% of children with an ASD[95]. Having both ADHD and an ASD together is associated with a lower quality of life and poorer adaptive functioning than having just one[96].

The Autism Spectrum Disorders may cost the US economy US$350-400bn p.a.

Autism Spectrum Disorders are costly to treat, making for a large market opportunity. There is currently no medication to treat any of the ASDs, meaning that approaches such as Applied Behaviour Analysis (ABA) are most commonly used. This kind of treatment in turn needs trained therapists, of which there have been notable shortages in recent years[97]. One study has suggested that the current cost of managing ASDs in the US along could currently be US$350-400bn p.a.[98]

Autism can now be diagnosed using an app, and is increasingly treated with apps. In June 2021 the FDA granted marketing authorisation for a machine learning tool called the Cognoa ASD Diagnosis Aid[99]. This product combines parent-report questions with videos from parental smartphones to calculate ASD risk[100]. Cognoa is a privately held company[101] with the ASD Diagnosis Aid is its maiden product. Cognoa is currently doing feasibility work on a prescription digital therapeutic for autism. App-based therapy, albeit not FDA-approved, is commonly used in ASDs, with many apps currently available.

[89] See Khouzam et. al. (2004), *Asperger's disorder: a review of its diagnosis and treatment*. Compr Psychiatry. May-Jun 2004;45(3):184-91. Sir Isaac Newton and Albert Einstein are believed to have had Asperger's – see J R Soc Med. 2003 Jan; 96(1): 36–39.
[90] See Neul et. al. (2010), *Rett syndrome: revised diagnostic criteria and nomenclature*. Ann Neurol. 2010 Dec;68(6):944-50.
[91] See Dietz et. al. (2020), *National and State Estimates of Adults with Autism Spectrum Disorder*. J Autism Dev Disord. 2020 Dec;50(12):4258-4266.
[92] Maenner et. al. (2021), *Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network*, 11 Sites, United States, 2018. MMWR Surveill Summ. 2021 Dec 3;70(11):1-16.
[93] Elsabbagh et. al. (2012), *Global prevalence of autism and other pervasive developmental disorders*. Autism Res. 2012 Jun;5(3):160-79. Epub 2012 Apr 11.
[94] Loomes et. al. (2017), W*hat Is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis*. J Am Acad Child Adolesc Psychiatry. 2017 Jun;56(6):466-474. Epub 2017 Apr 5.
[95] Goldstein and Schwebach (2004). *The comorbidity of Pervasive Developmental Disorder and Attention Deficit Hyperactivity Disorder: results of a retrospective chart review*. J Autism Dev Disord. 2004 Jun;34(3):329-39.
[96] Sikora et. al. (2012), *Attention-deficit/hyperactivity disorder symptoms, adaptive functioning, and quality of life in children with autism spectrum disorder*. Pediatrics. 2012 Nov;130 Suppl 2:S91-7.
[97] See the American Psychiatric Association press release dated 11 December 2019 and headlined '*New Study Finds a Shortage of Therapists to Treat Children with Autism; Significant Variation by Region'*.
[98] Adjusted data from Leigh and Du (2015), *Brief Report: Forecasting the Economic Burden of Autism in 2015 and 2025 in the United States*. J Autism Dev Disord. 2015 Dec;45(12):4135-9. The authors of this study have actual costs for 2015 and estimated costs for 2025. A steady increase in costs would suggest US$380bn by 2021.
[99] The product was approved via the FDA's 'De Novo' regulatory pathway for medical devices. Basically De Novo is for novel devices where there is no 510(k)-relevant predicate but where the device is deemed a low or moderate risk. The De Novo process leads to a Class I or Class II classification and has a 120-day review cycle, compared to a 90-day review period for a 510(k). Cognoa was approved as a Class II device, that is, one with only moderate risk, as opposed to a low-risk Class I.
[100] Kanne et. al. (2018), *Screening in toddlers and preschoolers at risk for autism spectrum disorder: Evaluating a novel mobile-health screening tool.* Autism Res. 2018 Jul;11(7):1038-1049. Epub 2018 May 7.
[101] Palo Alto, Ca., cognoa.com.

One recent 2020 review found that app-based therapy in autism worked well in terms of early academic development[102].

Valuing Tali Digital

Based on a risk-adjusted DCF analysis of the Tali technology, we value Tali at A$0.06 per share base case and A$0.11 per share bull case. Our key modelling assumptions are detailed as follows:

- **Market share approach**. We model only the US market for treatment of ADHD. According to Tali Digital, the estimated market value for US in 2020 was US$10bn. We then apply a market penetration rate to derive our expected sales for TALi's product. As discussed earlier in this report, we see a large likelihood for TALi's product to be considered as useful tool for detecting and training cognitive attention skills for early childhood. For the sake of conservatism, we assume a market penetration of 10-15% of its total addressable market.
- **Royalty on future sales**. We acknowledge Tali has entered into a commercial partnership with Akili for the potential commercial rollout of its technology product. We conservatively assume Tali will earn a royalty rate of 7% base case and 8% bull case on future gross sales.
- **Opex**. We model R&D and SG&A expenses as our key opex. We assume another A$11.1M in total opex for Tali before its US commercialisation. After commercial launch, we model SG&A expenses to represent around 25% of royalty-based sales, reflecting the industry average for healthcare IT companies.[103] On the R&D front, we model it to be 15% of royalty-based sales to reflect both the ongoing development costs associated with further improving the technology.
- **Probability factor**. Given that the product is yet to obtain full De Novo US regulatory approval, there is a chance that it will not make commercialisation. Accordingly, we adjust our future cashflows with a 50-60% probability to account for its probability of success.
- **Discount rate.** We apply a discount rate of 14.4%, appropriate in our view for a 'Speculative' risk rating[104]. Tali is in pre-revenue phase which we see as more risky than other more commercialised Life Sciences ventures.
- **Commercialisation period**. We model 10 years of commercial exclusivity, with first sales to commence in FY24.
- **Capital**. As at the end of 1Q FY22, Tali had c.A$2.2M in cash. We assume a further A$9M to be raised sometime between FY22-23 to take Tali through to its US commercialisation.

[102] See Griffith et. al. (2020), *Apps As Learning Tools: A Systematic Review*. Pediatrics. 2020 Jan;145(1):e20191579.
[103] Data from the website of Aswath Damodaran at the Stern School of Business at New York University.
[104] For a relevant discount rate, we use varying WACCs depending on the risk for Life Science companies. We start with an RFR of the Australian ten-year bond rate (1.7%) and an ungeared beta of 1.1 but use a variable MRP of 7.5%-11.5% (7.5% for 'medium risk' companies, 9.5% for 'high risk' companies and 11.5% for 'speculative' companies). Ordinarily we regard Life Science companies with existing businesses, or who have enough capital to reach the market with their products, as 'Medium' risk. Companies that have small revenue streams from marketed products but that are still potentially in need of capital are 'High' risk. Everything else is 'Speculative'. We have used a Speculative risk rating for Tali Digital considering it is at a pre-revenue stage.

Valuation (A$)	Base Case	Bull Case
PV of FCF de-risked	57.3	109.7
PV of terminal FCF	-	-
Enterprise Value (A$M)	**57.3**	**109.7**
Net debt (cash)	(2.7)	(2.7)
Equity value (A$M)	**60.1**	**112.4**
Diluted shares (M)	994.4	994.4
Implied price (A$)	**0.06**	**0.11**
Current price (A$)	0.017	0.017
Upside (%)	*255.3%*	*564.9%*

Solid management

Tali Digital has, in our opinion, a first-class management team that can take the company forward in terms of creating shareholder value.

CEO **Glenn Smith** brings a strong background in the development of Life Science startups which has included time at Resonance Health (ASX: RHT, General Manager, 2004-2006) and Hollista Colltech (AWX: HCT, Director of Marketing and Sales, 2006-2008). In his time at Tali Digital from late 2017 Smith has brought the company from mere concept through to a mature software developer nearing its first FDA approved product with a reputable partner.

Chairperson **Dr Sue Macleman** has a long track record of helping to build early stage and mid-stage Life Science companies such as Benitec and Mesoblast (ASX: MSB) as well as working on government initiatives to grow the Australian Life Science sector through her leadership of the MTPConnect initiative.

Non-Executive Director **Jefferson Harcourt** knows the medical device sector well through his leadership of Grey Innovation, which developed the original Tali Technology with the Cornish lab at Monash and Torus Games.

Non-Executive Director **Dr David Brookes** has been involved in the Life Sciences sector since the 1990s and is best known for his Chairmanship of RHS Ltd, the genomics company acquired by PerkinElmer in 2018.

Non-Executive Director **David Williams**, who joined the board in December 2021, brings commercial and financial skills gained from 25 years with Cochlear (ASX: COH). That included a stint as Senior Vice President of Finance & Operations for Cochlear Americas, where Williams led the introduction of new digital products and cloud-based platforms.

The Tali Digital Scientific Advisory Board has the kind of knowledge base highly relevant to the right positioning of Tali's technology. The board is Chaired by **Dr Scott Kollins** of Duke University, who, as we noted above, has been working with Tali to generate more data on clinical utility of Tail Train. **Sarah Gerwig** of Houston is a tech entrepreneur with strong connections to Baylor and Rice. **Professor Con Stough** of Swinburne University of Technology is an authority on human cognition. And **Dr Phil Lambert** of the University of Sydney brings an educationist's perspective.

Appendix I - A Tali Digital glossary

ADHD – Short for Attention Deficit Hyperactivity Disorder, a mental health condition in which a patient finds it hard to pay attention, be organised, think slowly and sit still.

Autism Spectrum Disorder (ASD) – One of a number of conditions considered to be autism.

Autism – A developmental disability characterised impaired communication, difficulty in social interaction, and restricted and repetitive interests and behaviours.

CE Mark – European approval for a medical device. CE stands for Conformité Européenne.

Class – In medical device regulation, a device goes in one of three classes – Class I (low risk), Class II (moderate risk) and Class III (high risk).

CPT – Short for Current Procedural Terminology, a code set developed by the American Medical Association used to bill outpatient and office procedures in the US healthcare system.

Dementia – An umbrella term for a group of similar conditions characterised by gradual impairment of brain function. People with dementia experience loss of memory, language, problem-solving and other thinking abilities.

De Novo – An FDA regulatory pathway for medical devices. Basically De Novo is for novel devices where there is no 510(k)-relevant predicate but where the device is deemed a low or moderate risk. The De Novo process leads to a Class I or Class II classification and has a 120-day review cycle, compared to a 90-day review period for a 510(k).

Executive Function – A general term to describe the brain's ability to organise itself to get things done.

Mild Cognitive Impairment – A slight but noticeable decline in memory and thinking skills compared with others of the same age.

Neurotypical – Characteristic of typical neurological development or functioning. Basically, 'normal', where behaviours associated with ADHD or ASD are considered 'non-normal'.

Tali – Short for Training Attention and Learning Initiative.

Tali Detect – A Tali Digital product to detect attention skills in early childhood.

Tali Train – A Tali Digital product to train attention skills in early childhood.

Working memory – Short-term memory used to execute specific tasks.

Appendix II - Tali Digital Intellectual Property

As well as the software behind the Tali Technology, Tali Digital's intellectual property includes one patent family, called *System and Process for Cognitive Assessment and Training* (WO/2016/154658, priority date 31 March 2015). The inventors of this patent application are Andrew Somers, Grace Lethlean, Hannah Kirk and Kim Cornish. US Patent No. 10,621,882 was granted from this patent family in April 2020. Monash University assigned this patent family and related Intellectual Property to Tali Digital in June 2020.

Appendix III – Papers related to Tali Digital

Kirk et. al. (2015), *Cognitive training as a resolution for early executive function difficulties in children with intellectual disabilities.* Res Dev Disabil. 2015 Mar;38:145-60. Epub 2015 Jan 2.

- This paper reviews the various cognitive training programs focused on improving Executive Function that were available prior to Tali Train, and found them somewhat lacking.

Kirk et. al. (2016), *Computerised attention training for children with intellectual and developmental disabilities: a Randomised Controlled Trial*. J Child Psychol Psychiatry. 2016 Dec;57(12):1380-1389. Epub 2016 Aug 23.

- This paper describes 'Study 05', a randomised, controlled trial that compared Tali Train to a control programme, with Tali Train bringing about greater improvement in selective attention performance.

Kirk et. al. (2017a), *Visual attention and academic performance in children with developmental disabilities and behavioural attention deficits*. Dev Sci. 2017 Nov;20(6). Epub 2016 Sep 21.

- This paper describes 'Study 03', which used Tali Train to establish the important of visual attention in building literacy and numeracy skills.

Kirk et. al. (2017b), *Impact of attention training on academic achievement, executive functioning, and behaviour: A Randomized Controlled Trial*. Am J Intellect Dev Disabil. 2017 Mar;122(2):97-117.

- This paper describes 'Study 06', which used the test subjects from Study 05 but evaluated three-month follow-up data. The study found greater improvements in numeracy skills for children on Tali Train.

McKay et. al. (2019), *Training attention in children with acquired brain injury: a study protocol of a randomised controlled trial of the Tali attention training programme*. BMJ Open. 2019 Dec 4;9(12):e032619.

- This paper describes a clinical trial to evaluate the use of Tali Train in children with brain injuries.

Kirk et. al. (2021a), *Gamified attention training in the primary school classroom: A Cluster-Randomized Controlled Trial*. J Atten Disord. 2021 Jun;25(8):1146-1159. Epub 2019 Nov 13.

- This paper describes 'Study 07', a randomised controlled trial which evaluated Tali Train in the classroom. Tali Train was able to reduce inattention and hyperactivity in the classroom and reduced hyperactivity at home.

Kirk et. al. (2021b), *Examining potential predictors of attention training outcomes in children with intellectual and developmental disorders*, Journal of Intellectual & Developmental Disability, 46:3, 197-203.

- This paper 'Study 8', which was evaluating which kind of children would benefit most from Tali Train. Children with lower adaptive functioning but better attention skills benefited most in this study.

Appendix IV – Tali Digital capital structure

		% of fully diluted	Note
Ordinary shares, ASX Code TD1 (million)	931.9	88.2%	
Unlisted options (million)	125.0	11.8%	Estimated average exercise price 3.7 cents, average expiry date 17-Feb-2024
Fully diluted shares	1,057.0		

Current market cap:	A$15.8 million (US$11.2 million)
Current share price	$0.017
Twelve month range	$0.056 - $0.015
Average turnover per day ('000 last three months)	847

Appendix IV – Risks related to Tali Digital

Risks specific to Tali Digital. We see four major risks for Tali Digital as a company and as a listed stock:

- **Timing risk.** There is the risk that the progression of Tali Digital's products in the clinic may take longer than expected.
- **Regulatory risk**. There is the risk that the FDA and other regulators may decline to approve Tali Digital's products, even if Tali Digital considers the data submitted to be adequate.
- **Commercial risk**. There is the risk that Tali Digital may lose Akili Interactive as a partner.
- **Uptake risk**. Tali Digital's future products may not find significant usage in ADHD and the Autism Spectrum Disorderss as other therapies come onto the market.

Risks related to pre-revenue Life Science companies in general.

The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.

Since most biotechnology and medical device companies listed on the Australian Securities Exchange fit this description, the 'term' speculative can reasonably be applied to the entire sector.

The fact that the intellectual property base of most biotechnology and medical device lies in science not generally regarded as accessible to the layman adds further to the riskiness with which the sector ought to be regarded.

Caveat emptor. Investors are advised to be cognisant of the abovementioned specific and general risks before buying any the stock of any biotechnology and medical device stock mentioned on this report, including Tali Digital.

Appendix VI – Analyst Qualifications

Stuart Roberts, lead analyst on this report, has been covering the Life Sciences sector as an analyst since 2002.

- Stuart obtained a Master of Applied Finance and Investment from the Securities Institute of Australia in 2002. Previously, from the Securities Institute of Australia, he obtained a Certificate of Financial Markets (1994) and a Graduate Diploma in Finance and Investment (1999).
- Stuart joined Southern Cross Equities as an equities analyst in April 2001. From February 2002 to July 2013, his research specialty at Southern Cross Equities and its acquirer, Bell Potter Securities, was Healthcare and Biotechnology. During this time, he covered a variety of established healthcare companies such as CSL, Cochlear and Resmed, as well as numerous emerging companies. Stuart was a Healthcare and Biotechnology analyst at Baillieu Holst from October 2013 to January 2015.
- After 15 months in 2015 and 2016 doing Investor Relations for two ASX listed cancer drug developers, Stuart founded NDF Research in May 2016 to provide issuer-sponsored equity research on ASX-listed Life Science companies.
- In July 2016, with Marc Kennis, Stuart co-founded Pitt Street Research Pty Ltd, which provides issuer-sponsored research on ASX-listed companies across the entire market, including Life Science companies.

Cheng Ge is an equities research analyst at Pitt Street Research.

- Cheng obtained a B.Com in Finance and LL.B from University of New South Wales in 2013, and has passed all three levels of the CFA Program.
- Before joining Pitt Street Research, he has worked for several financial services firms in Sydney, where his focus was on financial advice.
- He joined Pitt Street Research in January 2020.

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